COMPACTION CHARACTERISTICS OF POWDER MIXTURES

BY

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ABSTRACT

Compaction Characteristics of Powder Mixtures

Ivan Michael Jackson

The compression characteristics of single components and binary mixtures of plastic, brittle and elastic materials have been studied.

Under conditions of static compression, using a modified Instron Testing Machine, the addition of relatively small quantities of polyethylene has been shown to significantly modify plastic deformation of sodium chloride, reducing both short and long term interparticle bonding. In contrast, the compression characteristics of lactose, a material exhibiting brittle fracture, remained unaffected by the addition of similar quantities of polyethylene. By defining compaction behaviour in terms of energy distributions, both post compaction and on sequential compression, the instrinsic elastic component of each of the three powders has been defined. By evaluating energy distributions during the first compression, for mixtures containing sodium chloride and polyethylene, it has been shown that work done during compression was almost totally utilised in promoting plastic flow. Elastic recovery was minimal and the work done during sequential compression was negligible. In contrast, energy distributions during the compression of lactose-polyethylene mixtures were more evenly divided between brittle fracture and elastic recovery, sequential compression continued to promote structural modifications.

Under conditions of dynamic compression, modifications to the behaviour of plastically deforming materials, on the addition of identical quantities of polyethylene, were much greater than those observed under static conditions. Irrespective of applied pressure time dependent interparticle bonding, expressed as a function of diametral breaking strength, was shown to be significantly reduced. Intact compacts could only be attained at relatively high pressures. Electron microscopy indicated that, without the introduction of an elastic component, sodium and potassium chlorides deformed plastically to produce compacts with integrated internal structures. In the presence of polyethylene, both halides tended to retain their original identity. A reduction in the particle size of sodium chloride partially overcame the elastic recovery affect incurred by the inclusion of polyethylene. By comparison lactose, irrespective of particle size, was able to accommodate similar amounts of polyethylene to those which produced such detrimental effects on the alkali halides. Such behaviour would be expected with any material which compressed by a brittle fracture mechanism.

Stress relaxation studies have highlighted the relationship between post compaction pressure decay and displacement for plastic, brittle and elastic materials. By measuring both decay and displacement simultaneously, the stress relaxation relationships of compacts prepared from binary mixtures of materials having different intrinsic compaction properties have been shown to be extremely complex in the presence of a highly elastic component. Such was the case with sodium chloride and polyethylene mixtures. Post compaction stress relaxation measurements indicated that, even in the presence of large quantities of polyethylene, significant plastic flow occurred. However, the extent of flow was

considerably reduced when compared to that observed with sodium chloride alone. In addition, stress relaxation determinations have highlighted immediate decay effects with plastic, brittle and elastic materials, such effects were produced to varying degrees depending upon material type. The data would suggest that all the materials continued to flow after maximum applied pressure had been attained.

The stress relaxation study has been expanded to cover other pharmaceutical powders. Pressure decay data for paracetamol, dicalcium phosphate dihydrate and Avicel, both as single components and as binary mixtures with polyethylene, emphasised the elasticity of paracetamol, the brittle nature of dicalcium phosphate and the complex brittle-plastic behaviour of Avicel.

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1. INTRODUCTION

1.1 Compression and Compaction Processes

The study of the interrelationships between materials during compaction can be defined as tablet technology and some aspects of this technology have been described in recent reviews by Hiestand (1978) and Jones (1981). Advances in tableting theory and practice have benefited from improvements in instrumentation technology and progress in this important field has been reviewed by Sixsmith (1977).

The following sections consider some aspects of compaction research relevant to the work reported in this thesis.

The purpose of the present research was to add further to the fundamental knowledge of tableting and thus enhance the skill of the formulation scientist.

1.1.1. Introduction to Compaction Mechanisms

Seelig and Wulff (1946) divided the process of pressing metal powders in a die into three phases and their definition has remained the basis for extrapolation to pharmaceutical powders. A recent definition, by Carstensen, Marty, Puisieux and Fessi (1981), outlined the following mechanisms:-

1. Rearrangement of particles to give closest packing.
2. Elastic deformation of particles.
3. At stresses or pressures above the elastic limit, plastic or fracture deformation leading to bonding between particles and hence tablet formation.
4. Pressure release with sequential stress relaxation.
5. Tablet ejection.

The first three stages form the basis of the Seelig and Wulff definition.

Train (1956) went further in successfully applying mechanisms of powder compaction to magnesium carbonate. By defining the relationship between applied pressure and relative volume he suggested four stages of compaction equivalent to 1 - 3 above plus a load supporting stage.

During rearrangement of particles in Stage I, the manner in which materials achieve contact prior to elastic deformation would be important. This was studied by Gregory (1962) when he derived the role played by microsquashing and particle interlocking during the formation of coal briquettes. He also drew attention to the consequences of air entrappment, the ease with which particles fill void spaces being particularly relevant to such consequences.

Stage II, involved with elastic deformation, would be affected by ease of particle rearrangement and would modify sequential plastic and/or brittle deformation. Determination of elastic contributions have generally not been extensively explored, although Carless and Leigh (1974) derived a relationship between mean stress and elastic behaviour by comparing the development and transmission of radial pressure during loading and unloading of a powder bed. However, Rippie and Danielson (1981) have focussed attention on both the unloading portion of the compression cycle and the post compression relaxation period. By the use of a three-dimensional viscoelastic model, they found that the strain necessary to maintain motion, once begun in a perfectly plastic material, was independent of the strain rate. In the absence of fracture or flow, particles can elastically distort into voids while shearing stresses can produce distortion only through elastic deformations.

Stage III, which defined the role played by plastic or brittle deformation on tablet compaction, has been extensively studied and will be outlined in greater detail in a later section. Hardman and Lilley (1970, 1974) carried out a series of studies which showed that sodium chloride deformed plastically and sucrose by brittle fragmentation. Hersey and Rees (1971) substantiated Hardman and Lilley's findings using lactose rather than sucrose to investigate brittle fragmentation. Hersey, Cole and Rees (1974) went on to classify sodium and potassium chloride as plastically deforming materials while potassium citrate and lactose compacted principally by fragmentation. Cole, Rees and Hersey (1975) verified these findings.

Although the vast majority of compaction mechanism studies have been based on the postulates of Seelig and Wulff, mechanisms of compaction have also been explained in terms of energy utilisation, Nurnberg and Hopp (1981) measured the distribution of heat during tableting. They attributed Total Energy as being composed of work lost as friction plus energy in forming tablets plus energy released on ejection.

During the compaction process the various mechanisms involved would each play a contributory role although any mechanism acting in isolation would be impossible to identify. The extent to which each mechanism affected both consequent stages of the compaction process and final properties of the compact would depend upon the physical properties of the material under investigation (i.e. hardness, crystallinity, shape, porosity), how it deformed (plastic, brittle, elastic) and the nature of the compaction cycle (speed, dwell time, punch shape and size, lubrication).

The effects that such factors can have on compaction technology are dealt with in the following sections.

1.1.2. Interparticulate Bond Formation and Porosity

In order for powder adhesion and tablet cohesion to occur, particle-particle contact is essential, at that instance the potential would then be influenced by secondary factors such as pressure and length of compaction cycle. With increase in pressure a parallel increase in density, dependent on initial pore fraction, would occur resulting in enhanced particle contact. By studying, at "pressure" and "zero pressure", density relationships for different mesh sizes of powders of electrolytic iron, precipitated copper, nickel and tungsten, Heckel (1961) was able to show that the rate of change of density with pressure at any pressure was proportional to the pore fraction in the compact at that pressure. He derived the relationship:

$$\ln \frac{1}{1-D} = KP + \ln \frac{1}{1-D_o}$$

where D = relative density

D_o = relative density of loose powder at zero pressure

P = pressure

K = a proportionality constant

In an earlier study, Stewart (1950) had suggested that increasing particle contact, resulting from increasing pressure, was essential before elastic deformation, followed by plastic and/or brittle deformation, could play any significant role in powder compaction. A similar relationship has been shown by Stanley-Wood (1978) and Stanley-Wood and Johansson (1980) who compared changes in porosity and surface contact of magnesium oxide, bentonite and magnesium trisilicate during compaction, and applied the resultant data in explaining possible bonding mechanisms. The area of contact formed the basis of Hardman and Lilley's (1973) studies where they found that the strength of sodium chloride compacts was greater than of either coal or sucrose, such strength being determined mainly by the area of contact. They deduced that plastically deforming sodium chloride, being prone to greater dependent contact, would produce a strong compact. Such a deduction has since been shown to be oversimplified.

Some of the most significant explanations of the influence of porosity and interparticulate bond formation on the compaction properties of materials have evolved from the study of granulations. Hence, granule structure greatly enhanced inter and intraparticulate pores and granule shape lent itself to enhanced packing densities. Such densities related, under increasing compaction pressures, to increased granule binding and resultant strength. By comparing dibasic calcium phosphate - lactose granulations with a standardised sugar granulation, Seitz and Flessland (1965) observed that, at lower compressional pressure, only small differences in crushing strength values occurred. As compressional pressure increased, tablet porosity decreased resulting in greater intergranulate surface contact leading to enhanced granule binding and strength. Many other workers have studied the influence of granule surface properties and porosity on compaction characteristics. Since the subject of this thesis relates to nongranulated powders then no further detail will be given.

When interparticulate interactions are reduced then bonding mechanisms will be modified. Thus the region of contact must be clean and free from adsorbed materials or contaminants. Shotton and Rees (1966) found that an increase in moisture content decreased the crushing strength of sodium chloride tablets, whilst Bolhuis, Lerk, Zijlstra and de Boer (1975) attributed a similar decrease, in the presence of magnesium stearate, to the formation of hydroplastic friction between particles. Recently, Irono and Pilpel (1982) have coated dried lactose with various amounts of different paraffins and determined how tensile strength varied at various temperatures. They found that tensile strength initially increased with increase in amount of paraffin, decreased to a minimum, then increased again as paraffin content was further increased. Initially, a combination of paraffin - lactose and lactose - lactose bonds dominated, giving high tensile strength. As more liquid paraffin was added, lactose - lactose bonds were reduced, the further addition of liquid paraffin leading to paraffin - paraffin dominance. One aspect of the work described in this thesis will attempt to explain how modifications to surface contact in admixtures can significantly affect the compaction properties of materials.

1.1.3. Particle Size and Surface Area

Any packing conditions which exist within a powder bed, either before, during or after compaction, will be extensively controlled by the particle size and surface area of the materials during the compaction cycle. The role played by particle size in the nature and extent of tablet compaction forms the basis of most fundamental studies reported on organic and inorganic materials. Again, the historical background to present day knowledge is rooted in non-pharmaceutical sciences. Gregory (1962) claimed that anthracite could not be briquetted because of its highly elastic behaviour on compression. By grinding the material in a ball mill for various time periods, he found that by increasing the number of fine particles he produced a corresponding increase in strength after compaction. In addition, density and ratio of permanent deformation to elastic recovery also increased. Gregory assumed that the most important factor involved was the formation of multiple contact areas produced as a result of particle breakdown. However, the study did not consider the particle breakdown during compaction, as explored by Vlajic and Stammenkovic (1971). They measured the change in surface area and particle size of several uranium dioxide powders after compression and calculated the unit force per particle contact area responsible for crushing particles. It was found to be proportional to contact area and particle diameter and they concluded that evaluating contact areas and contact area pressures could help to explain surface area changes during compaction.

In the pharmaceutical field, much work has been concentrated on the changes in particle size and surface area produced during the compaction of lactose and lactose mixtures, with contradictory evidence being submitted. Thus, Hersey and Rees (1970) found that, when crystalline lactose and spray-dried lactose were compacted at pressures greater than $490 MNm^{-2}$, volume changes were independent of particle size. Fell and Newton (1971) drew a number of different conclusions from a similar study. From a comparison of the effects of particle size and speed of compaction on density changes in tablets they related particle size to changes in relative volume at all applied values, the smaller the size the greater the change in relative volume. On tablet ejection, the difference in relative volume between the larger fractions of lactose and spray-dried lactose was considerably reduced. Applying the Heckel equation, which related densification to applied pressure, they concluded that the smallest size fraction gave the greatest rearrangement. At both high and low compaction speeds particle rearrangement was generally greater for spray-dried lactose. The same workers (1971), comparing tensile strength with work of compaction showed that, for a given work input, there was a greater displacement of spray-dried lactose than crystalline lactose, a similar treatment could also distinguish the difference between various size fractions. In a further extension to the study of lactose, although essentially related to the flow properties of crystalline and spray-dried lactose, Fell (1976) indicated that the superior strength of tablets produced from the latter, at a given compaction pressure, may well be influenced by the percentage of fines present.

Although the effects of particle size and surface area, as described above, are directly related to studies of the compaction cycle, the researcher should be aware that pre-compaction mixing can have a significant influence on variability of post-compaction findings. For instance, preferential adsorption of small particles onto the surface of larger particles will mean that initial contact will be influenced by the compaction properties of the smaller particles. Verraes and Kinget (1980) have shown how a small particle size drug substance could be non-homogenously adsorbed onto the surface of a large size fraction of spherical lactose granules or sucrose crystals, with varying influence on compaction properties. Lai and Hersey (1981) have carried out similar experiments using magnesium stearate and illustrated how the latter "stripped" salicylic acid from a sugar carrier.

The role of particle size in tableting mechanisms is extensive and has recently been reviewed by Hüttenrauch (1977). Because of its influence on the behaviour of plastic, elastic and brittle materials during compaction, to be reviewed in a later section, particle size has been rigorously studied in the work reported in this thesis.

1.1.4. Crystallinity

Shape, crystallinity and crystal hardness can all contribute to the behaviour of materials under compaction. Shape will clearly affect packing properties while hardness will relate to deformation potential and will be discussed in Section 1.1.5.

The importance of crystallinity, however, has gained considerable favour as a fundamental property of compaction capability, especially in those compounds where plastic deformation is the dominating mechanism. Jaffe and Foss (1959) were among the first to suggest that a relationship appeared to exist between crystal structure e.g. alkali halides and tablet formation properties. They suggested that only substances of the cubic system showed a general pattern of tablet formation upon direct compression. At this time, however, the effect of crystal anisotropism was unknown, an aspect whose importance was underlined by Ridgway, Shotton and Glasby (1969) during their studies with sodium chloride. They suggested that sodium chloride, having a face-centred cubic lattice would readily deform while body centred crystals would tend to work harden. Researchers have continued extensive studies on the compaction properties of sodium chloride as a model compound. Shotton and Obiorah (1973), comparing the tableting properties of cubic and dendritic crystals of sodium chloride, concluded that the crushing strengths of tablets prepared from the latter were always greater than those prepared from the former although they offered no explanation. Compression cycle plots for both forms of crystals were identical and seemed to indicate the materials behaved as Mohr's bodies, such behaviour would be consistent with substances undergoing brittle fracture.

The degree to which a material recovers during decompression (elastic recovery) will depend on the extent of lattice distortion produced during the compression stage. Thus, if a material is prone to low energy dislocations, then at higher pressures elastic recovery would be minimised by energy dissipation in the form of plastic deformation. On this basis, alkali halides would be expected to show little elastic recovery. York and Bailey (1977), in observations on two methyl cellulose powders, attributed a large initial degree of elastic recovery during decompression to a significant storage of energy, indicating large numbers of dislocations in the non-regular crystal structure of the polymer molecules.

Any procedure which can give rise to changes in structure and activation energy of crystal forms would lead to compaction mechanism modification. Many such procedures were highlighted in a review on technological changes by Hersey and Krycer (1980) who drew attention to changes of crystalline structure which might occur only at the surface and may go unnoticed. Such highly activated zones would be responsible for particle agglomeration being produced during a milling operation. Similar conclusions have been drawn by Hüttenrauch (1978), in that surface energy also varied with particle shape and crystal structure both of which were important in predicting tableting behaviour. Many examples of the effect of milling on compaction properties are cited by Hersey and Krycer who also indicated that further mechanical activation occured during the actual compaction cycle. Unfortunately, milling may affect the properties of the material under test, as pointed out by Aldeborn and Nystrom (1982) in their studies on milled sodium chloride. They showed how changes in particle shape, brought about as a result of milling the compound in a mortar, increased the axial strength of tablets prepared from it. Sodium citrate and sacharose tablets, prepared from materials treated in a similar way, showed no such changes. However, the authors admitted that they were unable to account for the part played by crystallinity and surface contamination in their findings.

Thus, it would appear that any deviation from the ideal, in terms of lattice order, would almost certainly influence the compaction properties of materials, such an opinion has been expressed by

Jones (1981) who considered that co-crystallisation of drug and low concentrations of degradation products could well lead to potentially deleterious effects on particle morphology particularly with regard to crystal dislocation, surface microrugosity and wettability. Such factors would then lend themselves to modification of particle strength, cohesiveness and compression and lubrication properties. There would appear little doubt that any study related to compaction properties of materials should include an awareness of the above factors.

1.1.5. Material Hardness

The term "hardness" can be used in two different contexts with respect to compaction properties. In the first instance there is the difference between "hard" inorganic materials and "soft" organic materials. Secondly there is the relationship between hardness and the ability of a material to deform under pressure. Cooper and Eaton (1962) interrelated both these concepts in their classical studies on alumina, silica, magnesium and calcite. They suggested that fractional compaction was greater, at any given pressure, the harder the particles tested, with the highest ultimate porosity being attained by the hardest and most brittle powders, only the softest materials achieving their highest theoretical density. A difference in compaction mechanisms, with voids filled by brittle fracture or plastic flow, accounted for porosity differences. From their studies, they derived the Cooper-Eaton equation which related volume compaction to applied pressure for plastic materials and was expressed by

$$V^* = a_1e - \left(\frac{K_1}{P}\right) + a_2e - \frac{(K_2)}{P}$$

where V^* = fractional volume compaction

P = Pressure

a_1, a_2, K_1 and K_2 are constants.

This relationship is discussed further in the section devoted to mechanisms of tablet formation. By studying a range of organic and inorganic materials of different particle size and hardness, Otsuka, Danjo and Sunada (1973) derived a relationship between changes in powder volume and compression pressure, the softer materials giving rise to the greatest decrease in powder volume as the pressure increased. They based their conclusions on the proviso that the two softest materials they used, sulfathiazole and chloramphenicol, might be expected to undergo considerable plastic deformation at particle-particle contact points. In an earlier study Shell (1962) had suggested that, with respect to tableting behaviour, the anisotropy of cohesion and hardness possessed by low symmetry organic crystals and, therefore, of most pharmaceutically important compounds, would sometimes be the dominating influence.

However, researchers no longer speak of hardness as a physical property of a material but rather its ability to deform under pressure, such comparisons are best illustrated in either studies involving granulated and non-granulated materials or where material deformation was hindered by the introduction of a second "soft" material to a mixture. As an example of the former, Khan and Musikabhumma (1981) showed how the slugging of potassium phenethicillin, in conjunction with a range of tablet adjuvants, affected properties such as density, crushing strength, friability and disintegration. Porosity measurements on tablets indicated that the overall reduction in surface area caused by an increase in tableting pressure was greater for tablets made from softer granules than harder granules. Examples of material hardness being modified by the addition of a soft component are given in the work of Sakr and Pilpel (1982) who showed how the tensile strength of lactose tablets decreased when they were coated with increasing amounts of non-ionic surfactant. The latter being softer and more readily compressible than the uncoated powder. They later (1982) calculated values for the range and magnitude of the physical forces that acted between the surfaces of lactose powder coated with a series of Spans.

This extremely important aspect of material hardness as applied to deformation potential is more extensively discussed in a later section on tableting mechanisms.

1.1.6. Additional Factors Affecting Compaction

The classification of material characteristics, before study, into the areas outlined in previous sections should be carefully considered before specific conclusions are drawn which define compaction properties. In addition, other factors also warrant prior consideration. For instance, it would be inadvisable to compare the behaviour of two materials which were quite different in shape without being aware of such differences.

The most important influence of particle shape will be felt during the precompaction stage as illustrated by Kurihara and Ichikawa (1973) in studies on rod-like and irregular or spherical particles. The effect of rod-like particles on the initial fractional voidage was much greater, on powder mixing, than for spherical particles. They attributed this to mechanical resistance of interlocking rods. Such packing would then give quite a different tableting performance, irrespective of brittle or plastic material, during the compaction cycle. That elongated shapes can be retained under pressure has been shown by Rubinstein (1974) for dibasic calcium phosphate granules which remained cylindrical throughout processing.

One of the most important variables in material composition, whether concerned with direct compression formulation or granulation, is that of water content. Unless strict control over moisture is observed, its presence either intra or extra particular can affect, for instance, the plasticity of a material as shown by Price (1972) using a spray-dried earthenware body with and without the addition of water. During compression, Sekiguchi, Kiyama and Tohata (1972) monitored the relationship between apparent specific volume and stress-strain ratio for damp powders. They were able to derive a mathematical relationship for the stages involved and denote the relative effects of moisture on the process. Stage I was under the control of agglomeration energy between adjacent particles while Stage III encountered a resistant region, governed by interparticulate friction. Between existed a transient Stage II. Moisture contamination is especially detrimental to tablet crushing strength, either during or post compaction and conclusions about strength being related to stress relaxation should not be drawn until moisture dependent effects have been eliminated. Tablets prepared from granules having different initial moisture contents were shown, by Bolhuis,Lerk and Soer (1973), to undergo changes in crushing strength when stored at different humidities. Tablets containing residual moisture were observed to lose moisture at low humidity leading to the formation of solid crush-resistant bridges. A similar effect has been shown by Nyquist, Nicklasson and Lungren (1981) who initiated strength and disintegration decreases on storage at high humidities resulting from aqueous dissolution of water soluble components.

During compaction, tablet properties can also be affected by moisture content. Chowhan and Palagyi (1978) considered induced moisture loss, during compression, as a function of consequent tablet hardness. Under normal conditions, as the load increased, tablet porosity decreased, the resultant voids becoming filled with solution of the water-soluble excipient(s). The extent of this solution would depend on both the water content and the applied pressure. As both the water content and the applied pressure increased, liquids driven out of the void spaces would form a continuous film at the die wall, such a film acting as a lubricant and resulting in reduced contact between the die and the tablet granulation. The manner in which water was lost would determine both the immediate and longer-term hardness.

The above factors (Sections 1.1.1 - 6) all contribute, either singly or in multiples, to the compaction properties of powders and granules, both organic and inorganic. An awareness of such contributions is invaluable to any researcher who is, or plans to be, involved in understanding the mechanisms of compaction. Since the objective of the present research was to study the effect of some of the above factors on the elastic, plastic and brittle characteristics of powders and their effect on tablet compaction; an extensive overview of compaction mechanisms was considered appropriate.

1.2. Mechanisms of Compaction

1.2.1. Sequence of Effects

If a force of sufficient magnitude is applied to a powder held within the confines of a restricting die the particles will normally adhere to each other and a coherent mass, having some degree of porosity, will be produced. The cohesiveness of the powder, on removal of the compacting force, would have to be maintained for the successful production of tablets. Many papers have been published on powder compaction but, prior to 1947, they contained little reference to the complexities of the compaction process until Seelig and Wulff presented their theory of rearrangement and close-packing of particles followed by elastic/plastic deformation. However, there were alternative explanations of compaction behaviour. For instance, Turba and Rumpf (1964) offered an approach which involved (1) solid bridges (2) interfacial forces and capillary pressure at freely movable liquid surfaces (3) adhesion and cohesion forces at non-freely movable binder bridges (4) attractive forces between solid particles, principally by Van der Waals forces (5) mechanical interlocking. Since 1964, findings have emerged that indicate that Turba and Rumpf's definition was too empirical, but, nevertheless, scientists today continue to study the influence of the five suggested stages of the compaction event. Turba and Rumpf's approach was supported to some extent by Milosovitch (1963) who had earlier highlighted the fusion of separate crystals, under compression, giving rise to the formation of solid bridges. This process was referred to as cold welding or bonding. However, all consequent studies have presupposed that the suggested stages of compaction, as outlined by Seelig and Wulff, were basically correct and efforts have been concentrated on establishing the importance of each stage on the character of the final product. Such studies have varied in degree of complexity, that of Jungerson and Jansen (1972) being perhaps the most involved. They divided tablet compaction into three stages of pressure induction, pressure equilization and ejection. Further sub-division into a total of 11 contributing mechanisms required considerable theoretical treatment.

1.2.2. Elastic, Plastic and Brittle Contributions in Single Component Systems

By passing a polarised light beam through a Perspex die holding a material which had been subjected to varying pressure differentials, Ridgway (1966) used the fringe patterns produced to indicate that radial pressure on the die wall increased as punch pressure increased. By means of such an approach, one of the very first attempts to correlate radial pressure with compaction mechanisms, Ridgway was able to relate plastic deformation dominance to the production of good sodium chloride tablets and a significant elastic component to weak paracetamol and phenacetin tablets.

Much research in areas of plastic and/or brittle fragmentation has been concentrated on sodium chloride as an example of the former and lactose the latter, the studies of Hardman and Lilley (1970-74) forming the basis for assigning such properties. By differentiating between the behaviour of sodium chloride, sucrose and coal under pressure they were able to assign plastic deformation of sodium chloride as being the method of coherent bonding, with little or no tendency to fragment. Sucrose, on the other hand, underwent brittle fragmentation giving a tablet of reduced volume as particles moved into closer proximity. Coal was the subject of considerable particle fracture, fragments remained wedged between large particles to form chain bridges which constituted a more open structure than that of sucrose. By measuring changes in surface area before and after compaction they postulated that, in the case of coal, some plastic deformation had taken place at high pressures. These findings were substantiated by Hersey and Rees (1971) using sodium chloride and lactose, the latter mimiced the behaviour of sucrose. Okada and Fukimori (1974) also verified the plastic properties of sodium and potassium chloride and the brittle fragmentation of lactose, later (1975) comparing and classifying three types of powder, namely potassium chloride, lactose and those belonging to neither of those types. Changes in pressure transmission ratio patterns with increase in upper punch pressure were used to derive such classifications. Okada and co-workers (1979) went on to compact potassium chloride powders in a die with a single punch, they were able to derive a significant relationship between pressure and ratio of actual contact area to total surface area.

Data which showed that potassium and sodium halides were the subject of plastic deformation whereas other potassium salts, such as citrate, deformed by brittle fragmentation, formed the basis of Hersey, Cole and Rees's findings in 1974, findings which they later substantiated in 1975. No explanation for such behavioural differences was offered. More comprehensive evidence for the fragmentation behaviour of lactose was generated by Fell and Newton (1971). By comparing the behaviour of crystalline and spray-dried lactose in relation to the effect of speed of compaction and particle size on density changes in tablets, they calculated, by means of the mathematical concepts of both Heckel and Cooper and Eaton, that densification of crystalline lactose due to particle rearrangement was greatest for the smallest size fraction irrespective of dwell-time. Amongst their other conclusions they stipulated that pressures required to cause particle fracture and plastic flow are always greater than those required to effect rearrangement.

The use of Heckel plots as a means of defining material character led to additional compounds being classified as having plastic or brittle character. Rue and Rees (1978) and Rees and Rue (1978) treated raw data generated from a reciprocating tablet machine to assign plastic deformation properties to microfine cellulose and brittle behaviour to calcium phosphate. The plastic nature of microcrystalline cellulose has also been shown by David and Augsburger (1977) with particular reference to effect on tablet strength. By prolonging the duration of compression time at maximum pressure and measuring the resultant tablet strength, they showed that, of the materials studied, microcrystalline cellulose and compressible starch, as opposed to compressible lactose and sugar, were most markedly affected. Such evidence suggested that plastic flow might play a more important role in particle/particle bonding in these two materials. They went on to suggest that, by determining the viscoelastic slopes of materials, based on compression force decay curves, the possibility existed of classifying direct compression fillers according to their degree of plastic flow. These findings supported previous suggestions of Sulpekar and Augsburger (1974) that crystal fracture, leading to new surfaces under compaction, may be the predominant factor in the bonding of tablets from lactose and sugar fillers. Neither of these two research groups referred to the role played by elastic recovery in the compaction of cellulose although Sixsmith (1977) showed how, on compaction, a series of microcrystalline celluloses (Avicels PH101-105) gave a slight initial decrease in surface area following an increase, influenced by elastic recovery of particles. He later extended his investigation (1982), stressing the same series of Avicels. Initially, the powders underwent elastic deformation throughout the range of pressures studied. By plotting porosity against log compaction force he showed that a linear relationship existed. By means of Heckel plots, relating force to relative density, differences associated with particle shape and size also emerged.

1.2.3. Elastic, Plastic and Brittle Contributions in Two or More Component Systems

The mechanism by which a given material compacts under pressure will undergo different degrees of modification when it is admixed with one or more diluents. The nature of such modifications will be dependent not only on the inherent properties of the materials involved but also on secondary factors which might influence the compaction cycle. Such factors might include ease of compaction, lubrication effects during compaction and on ejection and precompaction mixing ability where nonhomogeneity might lead to matrix artifacts. By similar reasoning the process may become even more complex if the constituents were in a granulated form, when the external characteristics of the materials are extensively changed and the minor component is randomly incorporated. Nevertheless, such systems have been extensively studied, especially in the area of binders and lubricants. Armstrong and Morton (1977) investigated the role of binding agent in modifying the elastic and plastic properties of a tablet filler (calcium phosphate dihydrate) and derived a measure of granule plasticity by calculating both the work of compression and that necessary to overcome the elasticity of the granule. The nature in which a second component may, by means of conferring elasticity to a system, make significant contributions to tableting properties, is probably the most important aspect of compaction behaviour. By studying the effects of binders such as polyvinylpyrollidine, maize starch and methyl cellulose on the compaction properties of dicalcium phosphate and paracetamol, Doelker and Shotton (1977) found that the modulus of elasticity increased as the crushing force increased. They monitored both applied and radial pressure at peak maxima and defined radial pressure as being the most important parameter since it gave a clearer indication of maximised plastic flow. A similar situation was shown to exist with paracetamol granules. On decompression, they suggested that the strength of tablets may have the reverse order of correlation resulting from an increase in area of contact producing plastic flow or fragmentation. They also stipulated that good tablets must have bonding properties which can absorb elastic recovery.

In studies on binders, Rue, Seager, Ryder and Burt (1980) determined, from data generated using stress-relaxation methods, that the greatest tensile strength was achieved with tablets where the binder was held at the granule surface whereas granules with the least surface binder deformed more easily. On the other hand, Nystrom, Mazur and Sjögren (1972) used direct compression methods to elucidate the interaction between methylcellulose binder and lactose, paracetamol, ascorbic acid or sodium chloride. Tablet strengths were seen to increase with increasing amounts of binder for the first three materials. With respect to sodium chloride a decrease occurred followed by an increase, as more binder was added. They suggested that, at lower binder concentrations, elastic recovery of tablets occurred on addition of binder. This elastic recovery became less important as the concentration of binder increased.

Although they made no attempt to elaborate the above it seemed likely that at low concentrations binder - sodium chloride bonding is both small in number and weak in cohesion such that the elastic recovery of the binder plays an important role. At higher binder concentrations, the sodium chloride particles can be visualised as being held within a continuous binder layer having significant internal cohesion such that the elastic recovery of the system is less critical.

The incorporation of a lubricant into a powder bed, prior to compaction, significantly affects the compaction mechanisms of the material. In an extensive study, David and Augsburger (1977) found that the presence of a lubricant significantly reduced the compressibility of either microcrystalline cellulose or starch whereas spray-dried lactose or sugar remained relatively unaffected. They postulated that, in the latter case, more new surfaces, uncontaminated with lubricant, would be formed which could participate in essentially unhindered bonding. Where plastic flow was involved, as in the case of cellulose and starch, although the area of contact available for bonding would increase some fraction of that area would be coated with particles of lubricant which would hinder bonding.

As an extension of the lubricant effect, modern researchers are now examining the effects of adding more viscous materials to tablet excipients. For instance Sakr and Pilpel (1982) have coated lactose with varying amounts of Spans and measured the tensile strength and consolidation achieved during compaction. By increasing the thickness of coating, enhanced particle cohesion was achieved, preventing slipping and rearrangement. Based on Cheng's theory of tensile strength, values were calculated for the range and magnitude of physical forces that act between the surfaces of coated and uncoated particles. The same researchers later (1982) showed that the tensile strength of lactose tablets decreased when the powder was coated with increasing amounts of non-ionic surfactants prior to compaction. Based on calculations involving application of the Heckel equation, they suggested that lactose coated with non-ionic surfactants was softer and more readily compressible than the uncoated powder. Extending the above prognosis, Irono and Pilpel (1982) coated samples of dried lactose with varying amounts of paraffins and tested the resultant tensile strength, after compaction, as a function of temperature (T). A relationship emerged which was shown to fit the equation

$$\mathrm{Log}\ T = A''Pf + B'$$

where Pf was the packing fraction, A" and B' constants depending on the nature, amount and viscosity of paraffin used at the temperature employed. Tensile strength was observed to increase initially as paraffin content increased, followed by a strength decrease to a minimum followed by a further increase. They suggested such changes were controlled by the matrix passing from a predominantly lactose - lactose bonded system to paraffin - paraffin dominance.

1.2.4. Effects at the Molecular Level

During powder compaction, after the initial consolidation stage, where particles undergo rearrangement to become a closely packed mass, a further decrease in porosity will occur if the elastic limit of the material is exceeded and it suffers plastic deformation or brittle fracture. The stage at which a material yields elastically has been defined by Rippie and Danielson (1981) as the point at which the system undergoes an instantaneous and totally reversible response to an applied load. Between this stage and plastic deformation Newtonian flow occurs where the rate of strain is directly proportional to the applied stress. Once the irreversible stage is attained the total energy applied can be expressed by the equation

$$E_T = E_1 + E_2 + E_3$$

where E_1 is work lost in the form of friction

E_2 is energy spent in the formation of the tablet and is equivalent to the area transcribed by the force-displacement curves

E_3 is the elastic deformation energy

In order to assess the influence of E_2 and E_3 on any compaction mechanism it is essential to understand the physico-chemical nature of materials at the molecular level.

1.2.4.1. The Elastic Effect

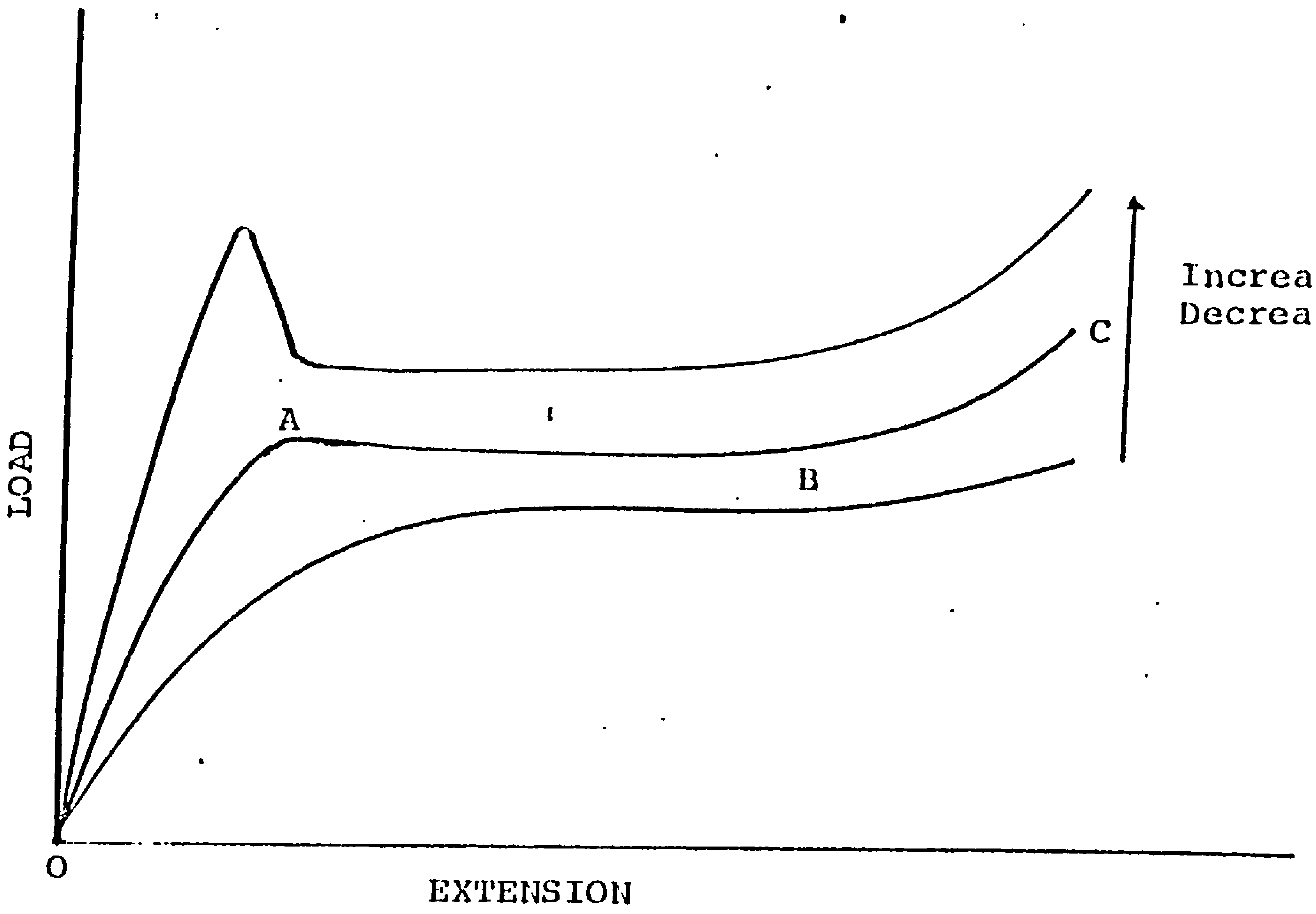
Since elastic deformation occurs at the initial stage in compaction the amount of energy absorbed and the degree to which such energy absorption exceeds the elastic limit can significantly effect the behaviour of materials. The amount of energy which a material can absorb before the elastic limit is exceeded is governed by its modulus of elasticity. Hooke's Law states that

$$\text{Stress} = E \times \text{Strain}\ (\text{Nm}^{-2})$$

where E = Young's Modulus and, if changes in dimensions are involved, is called the Modulus of Elasticity.

A material with a low modulus would be polyethylene which has a relatively low molecular density. In the case of polyethylene, an experiment involving short-time or high-frequency loading would give values of elastic modulus substantially higher than those obtained from a similar study carried out under longer periods of test. Load-extension curves are normally used to express tensile properties of polyethylene, an example of which is shown in FIG.1.1. where the region between the origin and A covers the total useful range of stress and strain for most applications, since fabricated forms are rarely serviceable if stressed beyond this point. Between point A and B cold-drawing commences where strain occurs at a nearly constant stress, beyond this point the material tends to rupture. Because of the highly structured nature of polyethylene, tensile properties under compression can be expected to be almost completely governed by the ability of the material to exhibit viscoelastic properties, where significant input of energy will result in little cohesion but high elastic recovery. The admixture of such a compound with sodium chloride and/or lactose would be expected to extensively modify the compaction properties of these materials. Preferential absorption of energy or physical deformation of polymer particles inhibiting surface interactions and lattice distortion of both sodium chloride and lactose would operate, the latter being less affected because of the brittle nature of the material on compaction.

FIG. 1.1. Schematic Load-Extension Curves for Polyethylene



Increasing Density or Testing Rate
Decreasing Temperature

1.2.1.2. The Plastic Effect

A schematic of bond formation is shown in FIG.1.2.

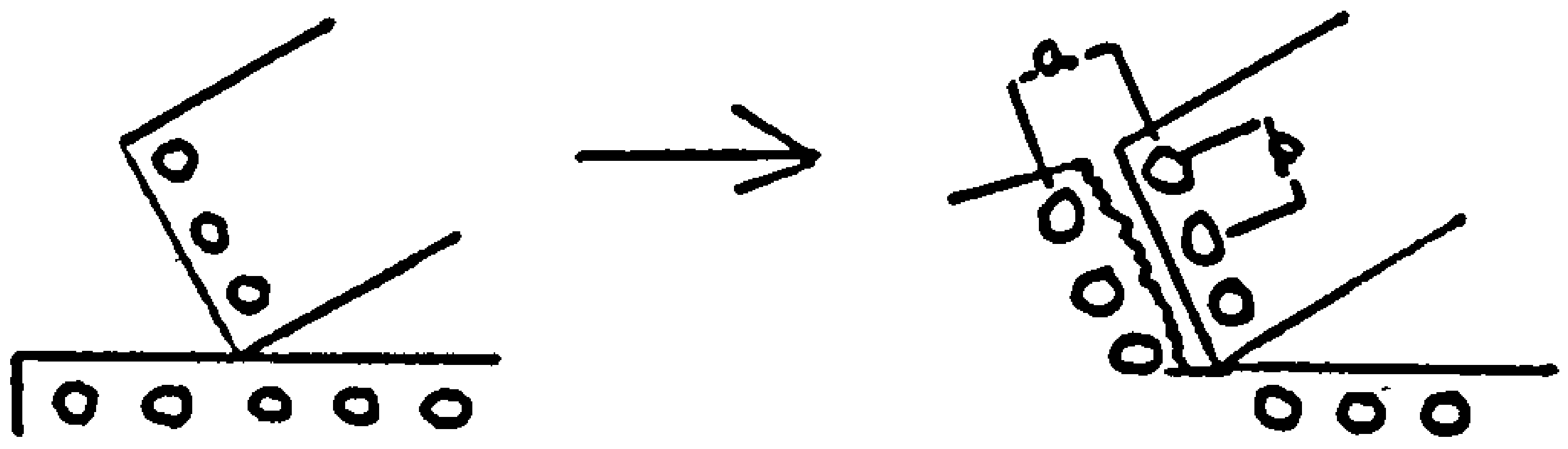


FIG.1.2.

(Schematic of bond formation in plastic deformation after Carstensen 1980)

Plastic deformation and increase in dislocation density will coincide leading to growth in internal energy. The result will be the production of particles both activated and unstable.

The energy thus available can be dissipated in several ways but part of it is almost certainly absorbed by the crystals and stored in the form of lattice defects, with particles at the surface acquiring a higher reactivity as a result of mechanical activation. Activated surfaces release this excess energy via specific reactions to regain a stable state, as during tablet formation, such reactions are similar to crystallisations. Thus, in the process of tablet forming there is a structure loosening and deactivation stage followed by sintering-like reactions between the active particles. A material susceptible to such behaviour would be an alkali halide such as sodium chloride with a face-centred cubic structure and ionic radii of 0.97Å (Na^+) and 1.81Å (Cl^-). Such a configuration might be expected to deform, under the influence of pressure, along well defined glide planes. The introduction of a high energy of activation would result in a final stability represented by a high degree of pseudocrystallinity.

1.2.4.3. The Brittle Effect

A schematic of bond formation is shown in FIG.1.3.

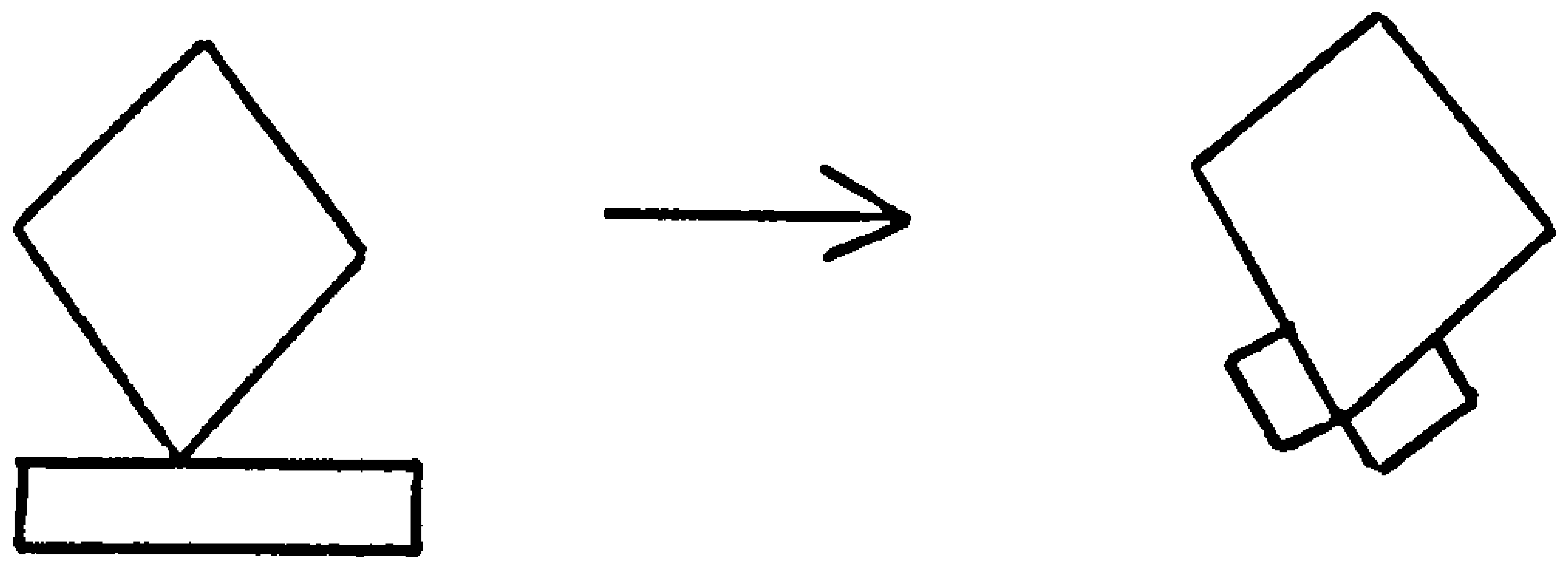


FIG.1.3.

(A schematic of bond formation by brittle fracture after Carstensen 1980)

Although materials traditionally classified as either plastic or brittle may be subject to varying intrinsic degrees of either mechanism, one type tends to dominate. Brittle materials break under pressure allowing realignment of broken particles. Under the influence of applied pressure the strength of the compact produced from a brittle material will depend upon both the extent of particle breakage during compaction and the limits placed on particle interaction. Lactose monohydrate is an example of a material which undergoes brittle fracture, the lattice consists of a loosely interlocked arrangement of lactose and water molecules with considerable potential for dislocation.

Molecular distances are great with low-energy bonding and little tendency for linear flow under load. Consequently, stress relief takes the form of brittle fracture rather than plastic deformation although it might be anticipated that elastic deformation might be more pronounced in a brittle material than a plastic compound such as sodium chloride.

Relatively little work has been done on studying the relationship between mixtures of plastic, brittle and elastic materials when submitted to varying degrees of compaction, although Sakr and Pilpel (1982(2)) have shown how the tensile strength of powdered lactose and its resistance to consolidation changed after being coated with a series of Spans and non-ionic surfactants. Cohesion was observed to increase with increase in coating thickness the former being dependent on the degree and manner of particle slippage and adherence. However, the coating materials used in the study could be anticipated as being elastic in nature, an aspect underplayed by the investigators.

1.3. Derivation of Compaction Data

Apart from both the Heckel and Cooper and Eaton equations already referred to in the text and derived as a result of studies involving metals or inorganic powders, several workers have adopted a more theoretical approach to the subject of compaction. Sagawa, Sakamoto and Maekawa (1976) measured the duration of stress against strain for different time periods and from the relationship they derived an equation which they considered to be a valuable contribution in explaining the viscoelastic behaviour of powders. By application of the concept they were able to forecast "good" tableting conditions. In one of several theoretical treatments of powder compaction, Carstensen and Toure (1980) dealt with the stages involved from consolidation through to ejection as a function of die wall force or lower punch pressure. Assuming the solid to be a non-porous body, two types of cycle were involved and a hysteresis loop was obtained, the area of which was either a linear or quadratic function of the maximally applied pressure. Within the elastic limit, the strain for a non-porous solid was proportional to stress (Hooke's Law).

$F = \gamma P$, where P = applied pressure

F = die wall pressure

γ = Poisson ratio $= \dfrac{\text{Lateral Strain}}{\text{Longitudinal Strain}}$

The same investigators, in conjunction with Duchene and Puisieux (1981) extended their studies to examine the hysteresis loop areas of granules compressed at various maximum pressures and moisture contents. Compression cycles of Px vs P and Py vs P, where Px = die wall pressure, Py = lower punch pressure, P = upper punch pressure were plotted. Based on this study plus that of Carstensen, Marty, Puisieux and Fess (1981) they were able to suggest that some assumptions, generally made in treating compression cycles, may be invalid. By compressing a series of polymers and plotting areas of hysteresis loops against maximal pressure they showed that a quadratic relationship occurred which, surprisingly, predicted brittle fracture as opposed to the anticipated plastic behaviour.

Finally, Leuenberger (1982) has defined an equation

$$P = P_{max} \; (1 - \exp(-\gamma \sigma_c \rho_r)$$

where P_{max} = theoretical maximal possible deformation hardness at $\sigma_c \rho_r \rightarrow \infty$. The compactability of a system was defined by the value of P_{max} while the compressibility was defined in the parameter γ. He claimed validity for binary as well as single systems and, on application of the equation to tablets prepared from mixtures of lactose and sucrose, he was able to attribute the strength of such tablets to individual particle binding at three different levels.

1.4. Interpretation of Powder Compaction Data

1.4.1. Introduction

Many methods are available for interpreting compaction data. These include the use of Heckel plots, compaction energy vs hardness profiles, stress relaxation and elastic recovery determinations and radial vs axial pressure relationships. An excellent review by Krycer, Pope and Hersey (1982) covers all the above possibilities and, in addition, critically reviews their various applications.

To provide data for interpretation, instrumentation has progressed accordingly. Axial, radial and ejection forces can all be measured by the use of either piezoelectric transducers or strain gauges with Linear Variable Differential Transformers (LVDT's) monitoring punch displacement. The outputs from such devices can be determined using UV oscillographs or microprocessors.

Monitoring equipment has been used with both static (one punch stationary) and dynamic (single stroke machines, rotary presses) instruments. Sixsmith (1977) has reviewed many aspects of instrument technology which have emerged since the early 1950's.

Although the above innovations have considerably aided the investigator in his attempts to more clearly define conditions of tableting, the sensitivity of such measuring techniques and the modifications which must be made to the tablet press to achieve instrument installation can give rise to the generation of misleading data. Lammens, Polderman, de Blaey and Armstrong (1980) have drawn attention to eight possible problematic areas. They ranged from punch-punch block movements, through elastic deformation of punch stems and tablet press frame, to selection of reference positions when measuring distance of punch movement.

The work outlined in this thesis deals with both static and dynamic aspects of tablet compaction.

1.4.2. Static or Quasistatic Compaction

Early investigations on compaction properties of materials invariably involved the study of non-pharmaceutical powders where the powder was placed into a die of known dimensions. The material was then subjected to varying loads, the extent of the load being measured by some form of pressure gauge. Cooper and Eaton (1962) examined the compaction behaviour of four ceramic powders using a Carver laboratory press and, from their results, developed a compaction theory involving both the filling of large holes and filling of small pores. They expressed the fractional volume compaction V in terms of applied pressure P.

$$V = a_1 \exp - \left(\frac{k_1}{P}\right) + a_2 \exp - \left(\frac{k_2}{P}\right)$$

where a and k described the behaviour of all powders.

As the area under investigation expanded, hydraulic presses were adapted and used extensively to investigate pore structures after compaction (Selkirk and Ganderton 1970), changes in surface area (Armstrong and Griffiths 1970), the effect of particle size on the consolidation powder under compaction (Hersey and Rees 1970) and the packing efficiency of fragile powders during pressing (Vlajic and Stamenkovic 1971).

The advent of the Instron Testing Machine, with its capability for applying loads at varying rates, saw more definitive data emerging under static conditions. Price (1972) applied the technique in determining the optimum moisture content to achieve maximum densification of an earthenware body. By use of a loading and unloading rate of 0.01cm min^{-1} he was able to carefully control his conditions. Hersey, Cole and Rees (1974) increased the cross head speed by a factor of 10 to compare the force recorded by a strain gauge with punch displacement measurements. They were able to compare the compaction properties of sodium and potassium chloride with potassium citrate and lactose. More recently Sheikh Salem and Fell (1981) have used the Instron to relate compact relative density to compression pressure for sodium chloride and lactose. To study the influence of initial packing on powder compression they used a cross head speed of 0.1cm min^{-1} but employed a large die (1.905cm diameter and 2.5cm long) to obtain more accurate measurements of powder bed movement. Applying faster cross head movement (0.5 to 50cm min^{-1}) Welikowa and Dinev (1981) compared the deformation behaviour of noramidopyrine methanesulphonate sodium (Analgin) in both direct compression and granulated forms. They studied the stress relaxation at constant deformation by recording the relaxation pressure as a function of time at three force values of 4, 8 and 16KN. Under static conditions, where material is filled into a die by hand, only the upper punch moves. Speed of compaction and consequent dwell time are, respectively, slow and prolonged such that the mechanism of compaction will be influenced by factors which will have varying degrees of importance when the same materials are compacted on single punch or rotary machines. Nevertheless, with model systems, the evolution of compaction data from static instrumentation continues to make an important contribution to understanding mechanisms and provides an important link in understanding dynamic behaviour.

1.4.3. Dynamic Compaction

1.4.3.1. Single Punch Instruments

With the advent of piezo electric transducers, strain gauges and LVDT's as "in situ" measuring devices, the single punch tableting machine, with its direct application in tablet manufacture, became the most important tool in elucidating tableting mechanisms. In addition to axial forces acting at upper and lower punches, radial forces could also be measured by suitably modifying the die wall to admit the introduction of measuring devices into close proximity with the punch-die interface. Leigh, Carless and Burt (1967) used such techniques in their studies on the compression cycles of a number of pharmaceutical materials. They compared the relationship between radial force and axial force, stipulating three types of compression patterns as defined in FIGS. 1.4, 1.5 and 1.6 for models of solid, isotropic bodies under uniaxial compression and assuming that die-wall friction was absent. They were able to draw certain analogies between the graphical data generated from their study and ideal situations. De Blaey and Polderman (1970) modified a single punch eccentric tablet machine in an attempt to quantitatively interpret force-displacement curves. They located the strain gauges for measuring compressional forces inside the guide blocks and linked an inductive displacement transducer directly between top and bottom punches to eliminate play

FIG. 1.4.

Compressional cycle of an ideal elastic body.

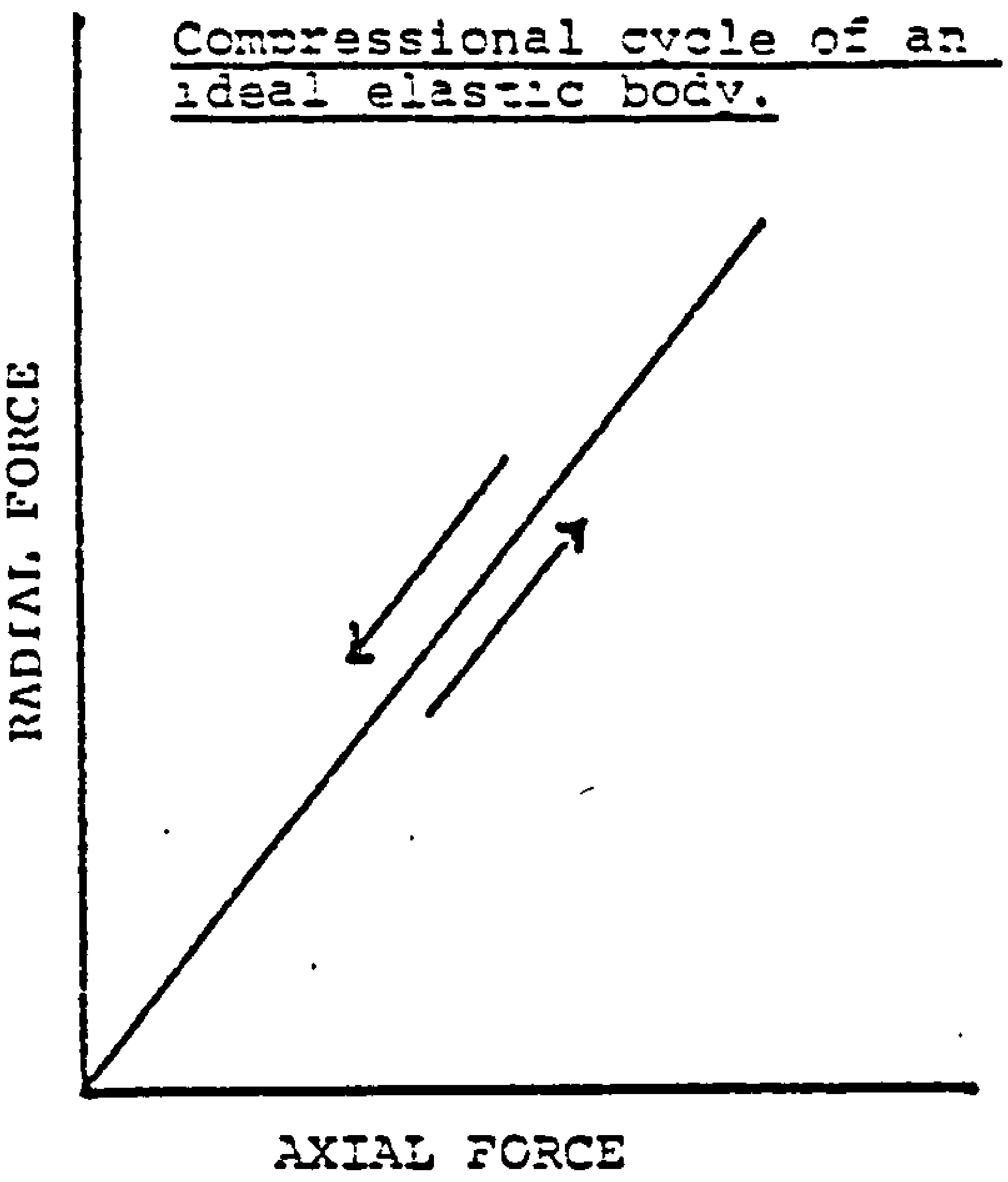
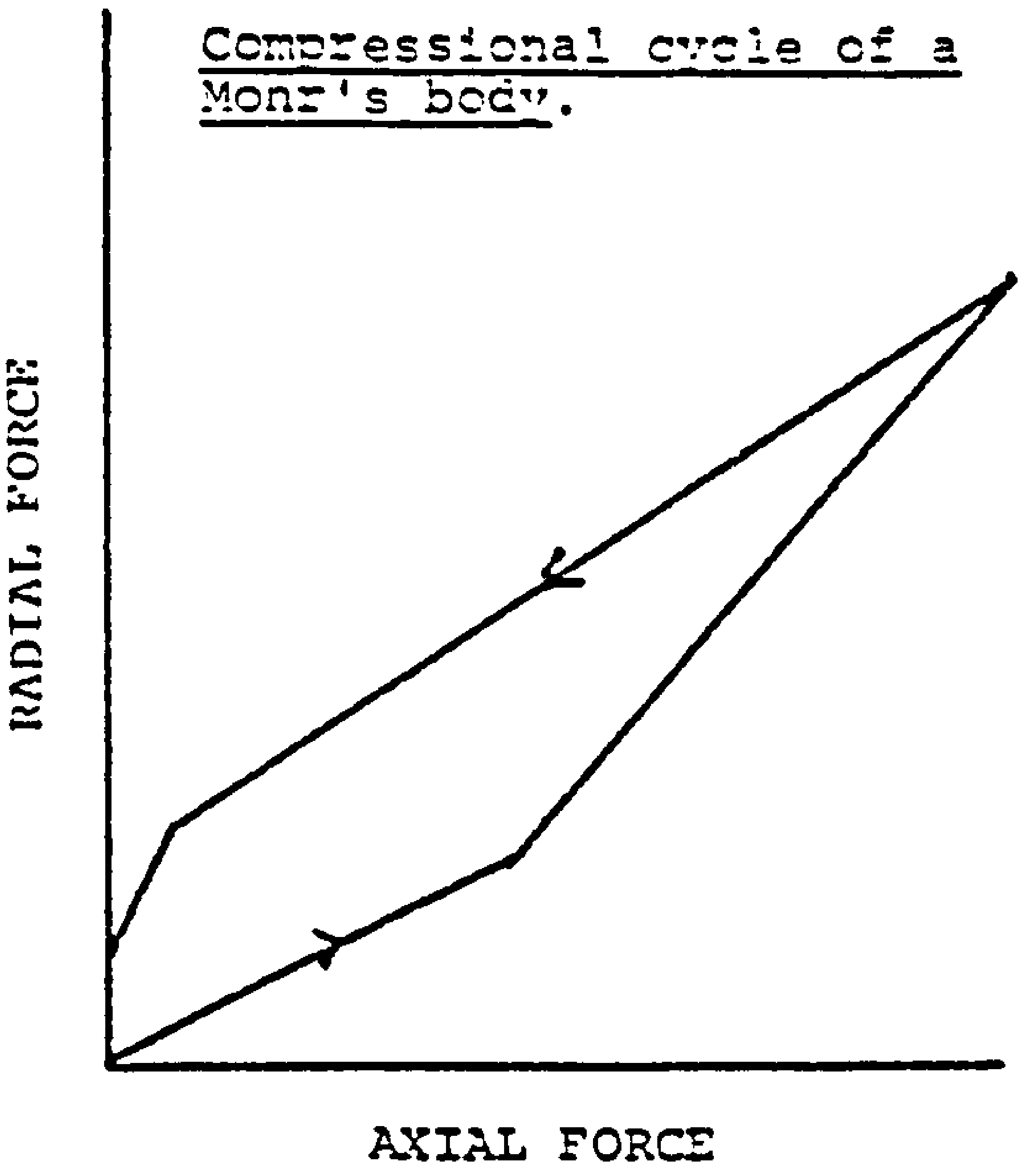


FIG. 1.5.

Compressional cycle of a Mohr's body.



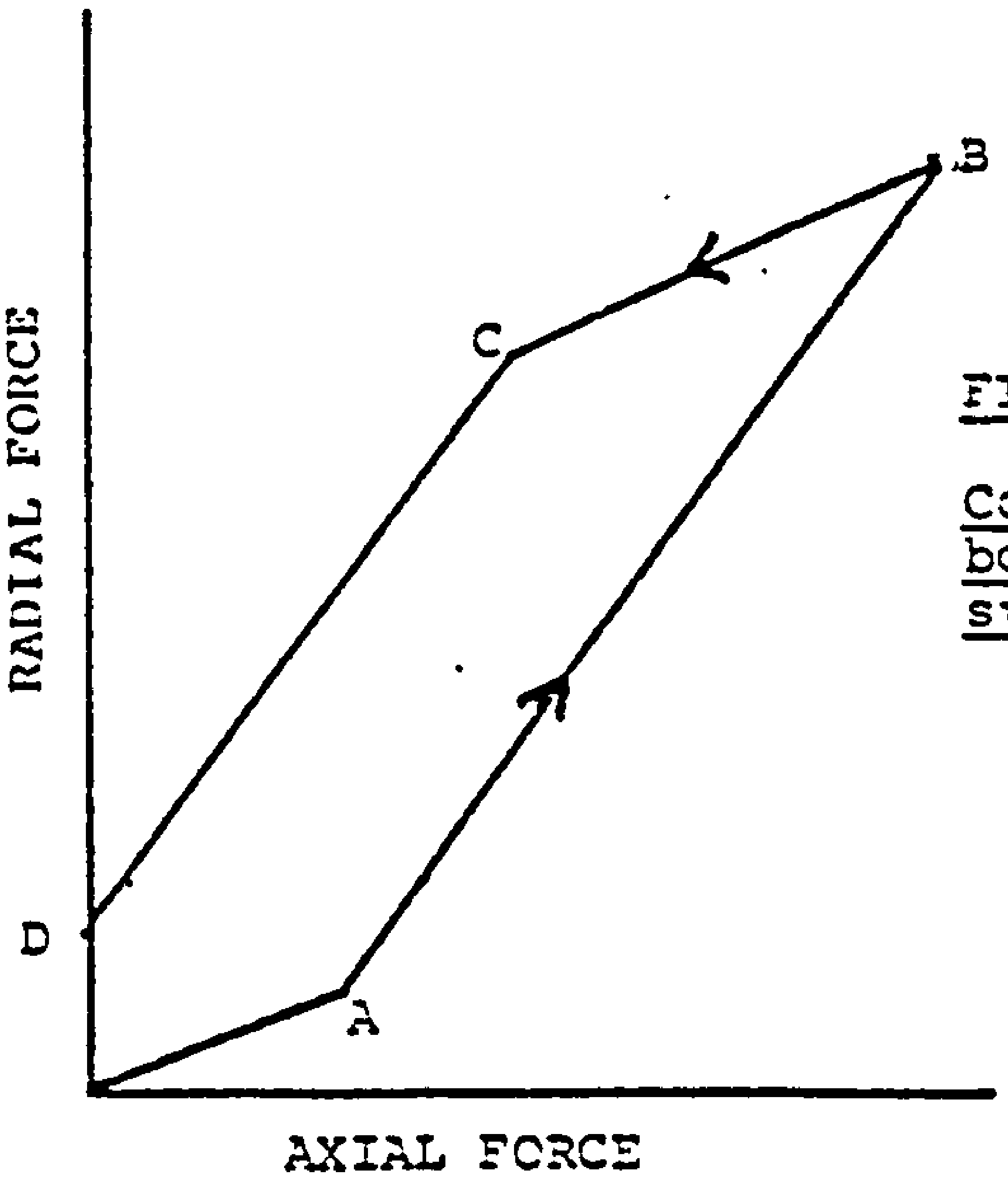


FIG. 1.6.

Compressional cycle of a body with constant yield stress, in shear.

(Compression patterns after Leigh, Carless and Burt, 1967).

in the bottom punch, during compression, from the FD curve. In a later publication (1971) they updated the monitoring technique by replacing the visual readout with a small digital computer.

A similar system was employed by Bolhuis and Lerk (1973) when attempting to correlate compression conditions with tablet crushing strength, weight variation and disintegration. Among the variables they measured were coefficient of variation of upper punch force, the ratio of lower to upper punch force, ejection force and percentage of total energy recovered immediately, on decompression, as elastic energy. More recently Chilamkurti, Rhodes and Schwartz (1982) have investigated tableting materials using an instrumented single punch tablet press interfaced with a digital computer. Differences between tablet matrices were detected in both computer parameters and finished tablets and they found that several properties of the force-time curves were apparently linearly related to the force applied. The work reported was proposed as a basis for bridging the gap between basic research and the manufacturing facility and to generate "fingerprints" for formulation processing.

Unfortunately, instrumentation and tableting machines can vary extensively in their mechanical properties and the role played by artefact production, both within a machine and between machines, can often tend to misleading conclusions. A critique of the art of instrumental applications is given in an excellent review by Krycer, Pope and Hersey (1982).

1.4.3.2. Instrumentation of Rotary Presses

Since the findings in this thesis relate to compaction carried out using static (Instron) and single-punch dynamic (Manesty F) systems, it is considered inexpedient to expand further on rotary machine instrumentation. However, it is considered essential that, when working in the area of compaction mechanisms, any scientist should be aware of the continuity which exists in instrumentation technology. Recently, data has begun to emerge based on rotary press instrumentation and Møller-Sonnergaard and Gjelstrup Kristensen (1978) adopted a system which had the ability to differentiate punch force variations due to irregularities in punch dimensions. They introduced their system after deciding that the empirical assessment of signal output as a measure of distinguishing tablets not agreeing with weight specification was inadequate. However, some of the most interesting findings from the use of instrumented rotary presses have come from the study of tablet adhesion, such a property can be related to lubrication and its optimisation. By attaching an instrumented cantilever beam in front of the sweep-off blade, Mitrejev and Augsburger (1982) have assessed the effects of blending time, running time and lubricant concentration of microcrystalline cellulose and hydrous lactose admixed with magnesium stearate. They were able to confirm that, at a given compression force, an increase in blending time or intensity of blending of magnesium stearate with microcrystalline cellulose coincided with an increase in tablet adhesion to the bottom punch. When mixtures of cellulose or lactose and magnesium stearate were run on a rotary press for a fixed time period, adhesion was shown to increase to peak values and then decline. Data generated on rotary presses are limited in quantity and applicability but there seems little doubt that the elucidation of compaction mechanisms, which function at high speed, will become increasingly important.

1.5. Post-Compaction Assessment - Methods

1.5.1. Choice of Methods

The majority of investigators confine their post compaction assessment of matrix properties to a few well-defined and measurable parameters. Among these are included hardness (several definitions), friability, disintegration, dissolution, wettability, porosity and surface area.

Because of the nature of the present studies, which are concerned with the interrelationship between elastic, plastic and brittle materials, compact strength was considered to be the most suitable property to evaluate.

1.5.2. Tablet Strength

1.5.2.1. Diametral Crushing Strength

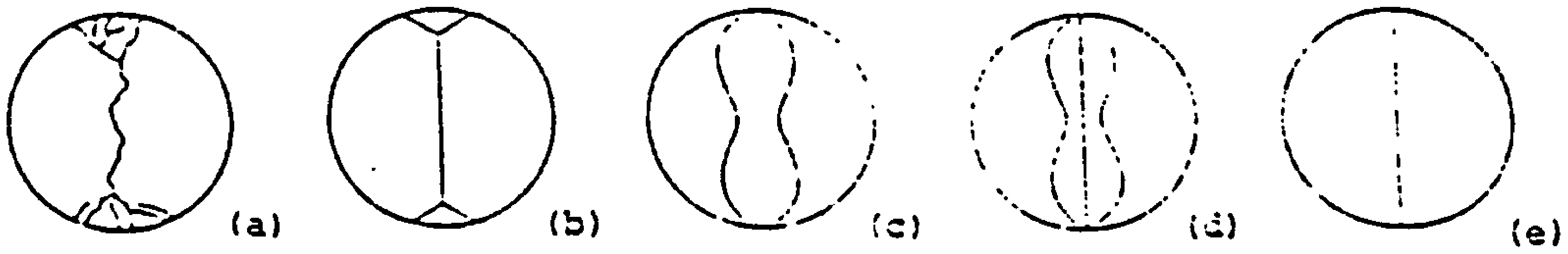
Following compaction, the structure of tablets so produced will depend on several factors, among them being (a) bulk density of materials and the resulting tablet density (b) pore size and (c) the cohesive strength and hardness. Higuchi and co-workers (1952) commented on the above factors and went on to stress the part played by tensile strength in the breakage and abrasion of tablets. At that time, tensile strength testers were available but the modulus of tablets remained unquantified. Investigators have attempted, with considerable success, to predict a more theoretical description of hardness (see following sections) but diametral crushing force retains its popularity. Many workers still include its measurement in studies related to compaction. For example, Bolhuis and Lerk (1973) monitored crushing strength as a function of applied force to illustrate how the strength of tablets decreased on the addition of a lubricant such as magnesium stearate. A very similar study was reported by Chilamkurti, Rhodes and Schwartz(1982) while Chowhan and Chow (1981) utilised hardness testing in defining the role of granulation moisture on the compression properties of granules.

As will be explained in the following section, tensile strength is now considered to have superseded hardness as descriptive of the fundamental packing properties of a material, since it is related to tablet dimensions. However, Krycer, Pope and Hersey (1982), in an investigation of techniques employed to characterise powder compaction behaviour, considered both tensile strength and crushing strength as compaction parameters. Strength was determined using a tablet hardness tester with constant loading rate. The plattens were padded with filter paper and only tablets that failed in diametral crushing, where the tensile stress was the major stress, were accepted. Their study involved the comparison of tablets of varying thickness and they concluded that, as a reliable method of assessing relative tensile strength, the use of crushing force versus lower punch work was preferred to tensile strength versus axial pressure.

1.5.2.2. Tensile Strength

Newton and co-workers (1971) adopted a different approach to tablet hardness, postulating that tablets prepared from the same formulation but having varying dimensions would be better described by defining tensile strength as a measure of tablet hardness. Such a definition would differentiate between tablets which, while subjected to different compaction pressures during manufacture, attained the same crushing strength.

A series of five varying failure patterns for tablets failing in diametral compression is outlined below, ranging from failure at local point of loading (a) through to ideal failure (e)



With careful control of the force applied to break the tablet, purely tensile fracture, as illustrated by example (e), occurred. The ultimate tensile strength of the tablet could be calculated from the equation

$$\sigma_x = \frac{2P}{\Pi Dt}$$

where P = load (Kg) required to cause fracture

D = Tablet diameter

t = Tablet thickness

Newton and co-workers applied the above to the study of diametral compression properties of a series of lactose monohydrate tablets, which varied in weight and thickness. All tablets were considered to fracture ideally as in example (e). Their findings showed that tablets of lowest weight possessed lower strength values than expected on comparison with thicker ones. They hypothesised that the thinner tablets (lowest weight) were intrinsically more variable and thus concluded that compaction of materials to the same tensile strength would produce tablets of near identical properties. Fell and Newton (1971) employed tensile strength measurements to highlight differences in compaction behaviour of crystalline and spray-dried lactose. keeping total work of compaction constant, tablet strength increased as particle size decreased in the case of spray-dried lactose. In comparing three size fractions of crystalline lactose, they found that tablets prepared from an intermediate (75-104 micron) fraction were found to be the strongest.

The above studies have been expanded further by Jarosz and Parrot (1982) who derived values for axial and radial tensile strength and also incorporated work of failure into their consideration of the tableting properties of microcrystalline cellulose. A suitably modified tensiometer enabled the measurement of maximum tensile failure force F. From the equation

$$\sigma_x = \frac{2F\sigma}{\Pi Dt} \text{ Kg cm}^{-2}$$

they were able to calculate radial tensile strength X_1 where D and t are tablet diameter and thickness respectively. To determine axial tensile strength they attached a tablet, by means of a cyanoacrylate resin, between the machined heads of two bolts held in a tensiometer. The axial tensile strength was calculated from the equation

$$\sigma_z = \frac{4F\sigma}{D^2} \text{ Kg cm}^{-2}$$

In addition to the above they also included in their results a value for work of failure which they calculated by integration of

$$W_f = \int Fdx$$

where W_f = work of failure

F = applied force

The concept of work of failure will be more fully explored in a later section.

The restrictions placed on tensile strength i.e. should only be employed in ideal cases, makes its use somewhat arbitrary. As tablet fracture deviated from idealism complicated fracture patterns would emerge. Consequently, Leuenberger (1982) proposed that the Brinell hardness number, as defined by the equation

$$P = \frac{2K}{\Pi D(D - \sqrt{D^2 - d^2})}$$

where d = diameter of indentation

D = diameter of test sphere

K = force applied to the material by the test sphere,

be preferred in compactibility characterisation. He went on to derive a series of equations based on single and binary component systems and checked the validity of his equations from compaction data generated on aspirin, ibuprofen, lactose, methenamin, sodium chloride, phenacetin and sucrose as single components alongside a binary mixture of anhydrous lactose and sucrose. Within the limits of experimental error, he concluded that radial tensile strength could be evaluated by an equation which included terms in applied pressure and relative density plus a qualitative interaction function.

1.5.2.3. Indentation Hardness

Indentation testing measures stress relief at specific points at or near a compact's surface and is determined using a spherical indenter which is lowered onto the surface under a pre-selected load.

The depth of the indentation and recovery when the load is removed can both be measured. Ridgway, Aulton and Rosser (1970) described an apparatus for measuring such parameters and produced a loading curve which included an indication of the depth of penetration. It also showed the elastic recovery of the specimen from the indentation and thus the permanent indentation could be measured. In applying the test to aspirin tablets, they were able to calculate both the Brinell hardness number and the Modulus of Elasticity showed that there was an increase in surface hardness of the tablet as the compaction pressure was increased, this behaviour typified a work-hardening substance.

Under the influence of thrust (i.e. one punch only moving) surface hardness was found to be greater at the tablet face adjacent to the moving punch. Hardness was also more pronounced at the tablet centre compared to the edges.

The main drawback to the use of indentation hardness profiles is that, since it is a point determined measurement, precision suffers. Nevertheless, Aulton (1981) has continued to use the test principally to monitor tablet hardness as a function of punch dynamics and curvature.

1.5.2.4. Work of Failure

Rees and Rue (1977) were the first investigators to relate work failure to the mechanical properties of tablets, such properties, Rue (1978) suggested, were not adequately characterised by tensile strength. By attaching a displacement transducer to the moving lower platten of a diametral compression testing machine the authors could record the resistance of tablets to mechanical change. Tablets were subjected to multiple diametral impaction by means of a modified jolting voltmeter. FIG.1.7 shows the force-displacement curve produced, integration of the area under the curve gives an indication of the work of failure. A linear relationship existed between work of failure and the number of impacts required to cause failure. Rees and Rue calculated non-recoverable deformation (NRD) using the equation

$$NRD = X_1 - X_o$$

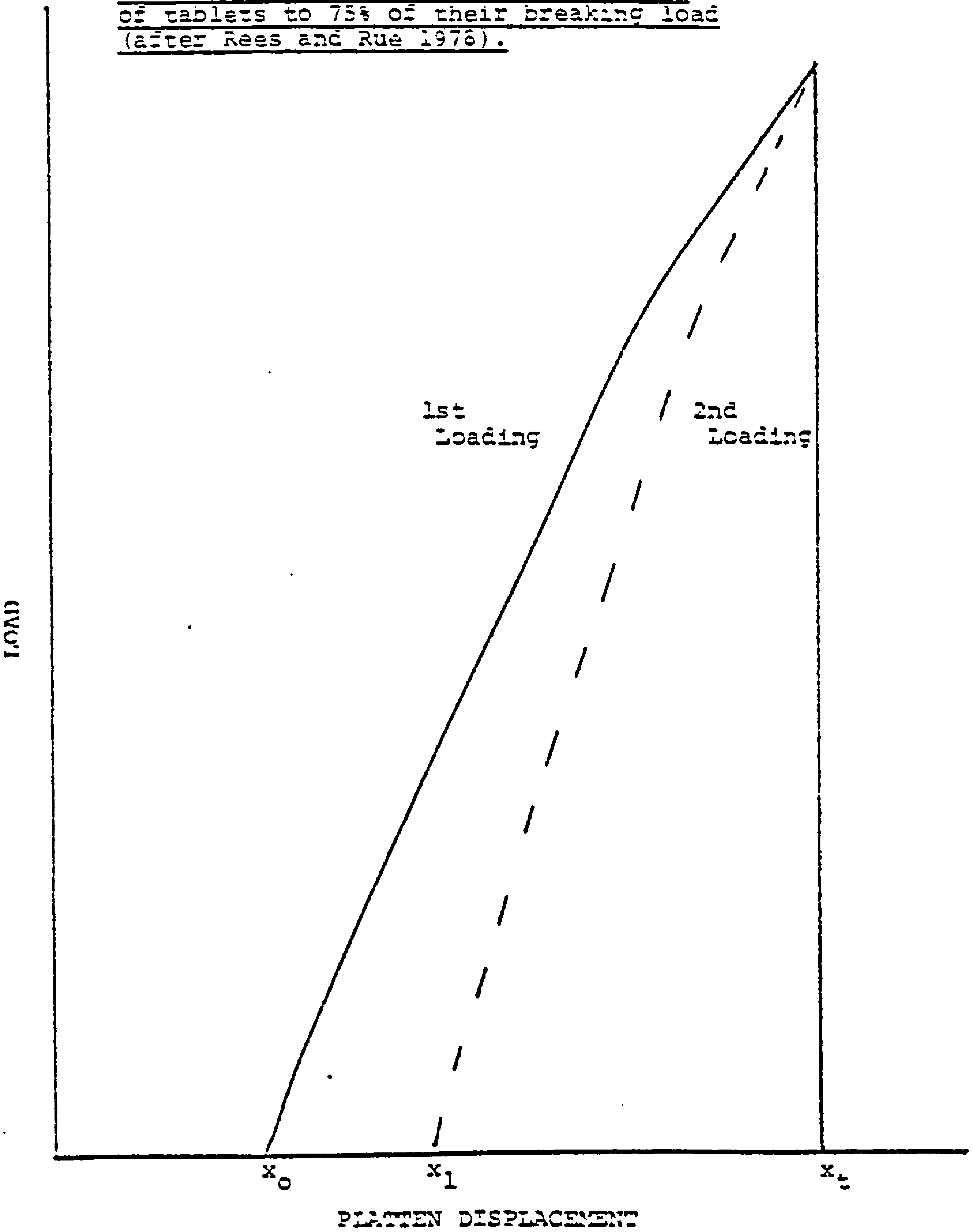
where X_o is the platten displacement during the first loading

X_1 is the displacement during the second loading.

By applying the technique in studying the breaking patterns of sodium chloride, they were able to show that, following extensive plastic deformation in compaction, the resulting tablets underwent brittle fracture during the diametral compression test.

FIG. 1.7.

X-Y Recording of the diametral loading of tablets to 75% of their breaking load (after Rees and Rue 1978).



Krycer, Pope and Hersey (1982) have expressed reservations regarding the use of work of failure as a measure of tablet strength since it is difficult to measure precisely and thus its applications are minimal. In the light of the evidence presented for alternative techniques such an objection seems superfluous since the imprecision of such alternatives must also be great.

1.6 Conclusions

That the compression characteristics of powders have been extensively studied cannot be disputed in the light of the preceding discussions. One of the most significant outcomes of such studies has been that of the role played by the different contributions of plastic, brittle and elastic components to the compaction process. In defining such contributions, the majority of investigations have been concerned with the behaviour of single systems and have concentrated mainly on materials which deformed either plastically or by brittle fracture. The evaluation of elastically deforming materials, either as single components or in the form of multiple mixtures with dissimilar materials remains relatively ill-defined. In an attempt to expand this particular area of research, studies involving binary mixtures of plastic, brittle and elastic materials were considered to be an essential addition to the present-day knowledge exemplified in Section 1.

Thus, a well-defined plastically deforming material (an alkali halide, but particularly sodium chloride), a brittle powder (lactose) and an elastic component (polyethylene) were chosen for study.

In order to clearly define the compression properties of the above, both singly and as binary mixtures, it was deemed necessary to evaluate in both the static mode (under the influence of thrust only) and the dynamic mode (low dwell time, high pressure). Several investigators have allocated their research to one or the other modes but very few to both.

In the static mode, the most important aspects to be included in any investigation on compression characteristics were considered to be force-displacement and force-time profiles in addition to stress relaxation studies. In the dynamic mode, where low dwell-times and post compaction ejection were controlling factors, tablet strength was chosen as a measure of energy distribution during compression.

Such studies as described above will lend considerable knowledge to that already generated by previous investigators.

2. MATERIALS and METHODS

2.1. Materials

Three classes of materials i.e. elastic, plastic and brittle, were chosen for study. A reasonably well-defined polyethylene product was chosen for its low Modulus of Elasticity, a selection of alkali halides as examples of materials which deform plastically and lactose monohydrate as a brittle material.

The materials chosen were:

Sodium chloride - Analytical reagent grade (BDH Chemicals Ltd.,
Potassium chloride Poole, Dorset).
Caesium chloride

α-Lactose monohydrate - Laboratory grade (BDH Chemicals Ltd.,
Poole, Dorset).

Polyethylene - "SCLAIR" 8705
"SCLAIR" 8405
(All obtained from Rotec Chemicals Ltd.,
Rotec House, 7, Grove Place, Bedford).

Polyethylene TYPE 8705 was a high density (0.950gm cm^{-3}) material provided as milled material with a particle size specification of $\ngtr$ 400 microns. TYPE 8405 (medium density) was also milled to the same size specification but contained a small amount of red dye. The red material was initially chosen as an aid to homogeneity since admixtures containing very low levels of polyethylene were submitted to compaction testing. Selective testing indicated that both types of polymer behaved similarly under compression, but the red material was favoured because of its propensity to favour visual homogeneity testing.

2.1.1. Characterisation of Materials

2.1.1.1. Bulk Density Measurements

The flow of material into a restricted volume such as a tableting die may well affect the bulk density properties of the material within the die giving rise to inconsistent particle packing and consequent imprecise compaction conditions. Consequently, bulk density determinations were carried out in a 10cm^3 measuring cylinder having an internal diameter of 12mm.

The measuring cylinder was tared and a mass of powder equivalent to about 10cm^3 was carefully poured, from a glass weighing boat, into the cylinder, held at an angle of approximately 70^{o} to the vertical. Without levelling the surface of the powder the exact volume of powder was estimated to the nearest 0.1cm^3 and then weighed to the nearest 0.01gm. The bulk density was determined by dividing the mass of the powder by its bulk volume. Three determinations were made for each material and examples of densities of both "as is" materials and relevant size fractions are given in TABLE 2.1.

2.1.1.2. True Density Measurements

True densities of materials were measured using a helium air comparative pycnometer (Model 930, Beckmann Instruments). The instrument is shown diagramatically in FIG. 2.1.

There are two chambers and two pistons. For purposes of illustration the chambers are assumed to be equal in volume and there is no sample in either cylinder. With the connecting valve closed, any change in the position of one cylinder must be duplicated by an identical stroke in the

FIG. 2.1

Beckmann Pycnometer Model 930

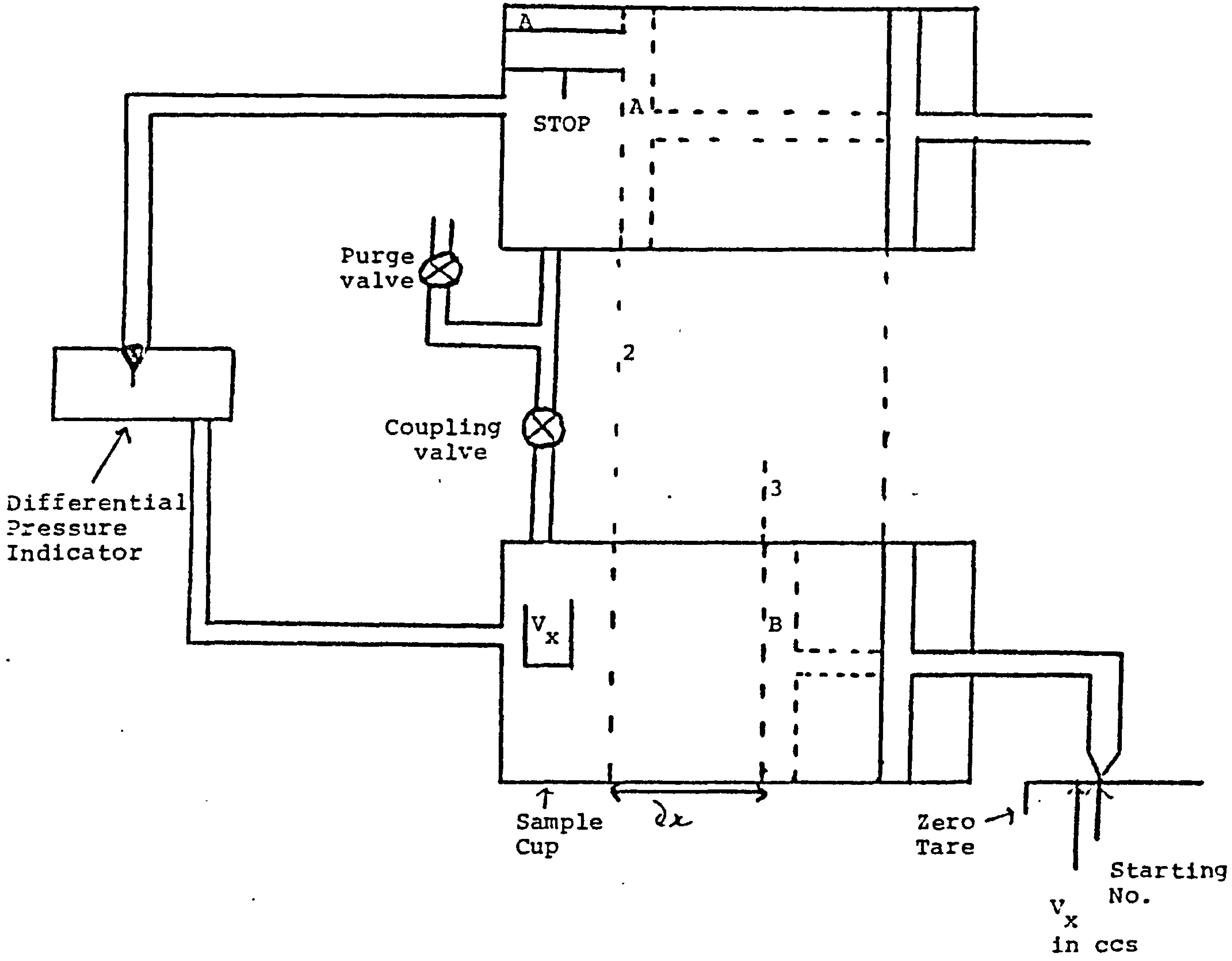


Table 2.1.

Bulk Densities of Powders (gm cm^{-3})

Powders were pre-dried, in the case of sodium and potassium chloride and polyethylene at 105°C for 6 hours, lactose monohydrate at 60°C for 6 hours. All dried powders were stored in sealed bottles prior to testing.

Materials	Sample 1	Sample 2	Sample 3	Mean
Sodium Chloride				
180-250 microns	1.12	1.11	1.13	1.12
355-500 microns	1.11	1.10	1.10	1.10
"as is"	1.13	1.12	1.12	1.12
63-90 microns (Milled)	0.98	0.99	0.99	0.99
Potassium Chloride				
355-500 microns	0.92	0.91	0.92	0.92
"as is"	0.95	0.96	0.95	0.95
Lactose				
"as is"	0.57	0.60	0.60	0.59
Polyethylene				
"as is"	0.33	0.32	0.32	0.32
90-125 microns	0.29	0.28	0.30	0.29
180-250 microns	0.31	0.33	0.31	0.32
355-500 microns	0.32	0.31	0.32	0.32

The data reflect the broad range of powder densities employed in the studies described in this thesis and defines the various physical forms of the materials under test (see Electron Microscopy Section).

other in order to maintain the same pressure on each side of the differential pressure indicator. If the connecting valve is closed and both pistons are advanced by the same amount to position 2 with a sample V_x inserted in chamber B, the pressures will not remain the same. However, the pressures in the two chambers can be made equal by withdrawing piston B from position 2 to position 3, an amount equivalent in volume to V_x. If piston A always is advanced exactly the same distance each time a measurement is made, the distance that piston B differs from piston A, when the pressures in both cylinders are equal, will always be proportional to the volume V_x.

The distance between positions 2 and 3(dx) can be calibrated and read directly in cubic centimetres. A digital counter is employed to indicate the distance dx so that the instrument can be read directly in cubic centimetres.

The true volume of a sample (the volume enclosed by its outer surface and excluding its open pores) is measurable by this instrument. From this volume the true density is calculated.

The simplest operational mode uses air as the gas. Measurements are made by starting at initial pressures of one atmosphere and compressing the gas to two atmospheres. This method is suitable for the analysis of nonsurface active, non-compressible materials.

The pycnometer is calibrated using steel ball-bearings of known volume after first determining the zero volume (i.e. with pycnometer empty). Typical values obtained with the Beckman 930 were:

Empty (ccs)	Small Bearing (Theory = 8.58ccs)	Large Bearing (Theory = 28.96ccs)
0.45	8.57	28.92
0.44	8.56	28.92

Samples to be analysed were dried as per Section 2.1.1.1. The sample volume was determined using the pycnometer and the mass of sample was determined accurately to ±1mg. True densities, calculated by this method, are shown in TABLE 2.2, two measurements were made for each specimen.

2.1.1.3. Particle Size Analysis

The method of choice depended on the approximate size and physical nature of each material. Alkali metal halides lend themselves readily to mechanical sieve sizing whereas lactose, with a mean particle size of 45 - 63 microns and a tendency to fracture under conditions of mechanical handling, would normally be sized by Alpine Air Jet. A comparison of the two methods, w.r.t. lactose, showed them to be compatible. Hence mechanical sieving under carefully controlled conditions was also chosen for the sizing of lactose. Particle sizing of polyethylene was much more difficult (see section on electron microscopy for indication of particulate appearance). Apart from complications due to irregularities in particle shape the material displayed a tendency for smaller particles to adhere to larger ones in the form of surface aggregates. In addition, the mass as a whole tended to associate, presumably due to surface static. For sizing purposes, extremely well controlled sequential mechanical sieving alongside scanning electron microscopy of sieve fractions was the method of choice.

Table 2.2.

True Density of Powders (gm cm^{-3})

Materials	Sample 1	Sample 2	Mean
Sodium Chloride			
-500 microns*	2.105	2.129	2.117
-355 microns	2.115	2.100	2.108
1250 microns	2.123	2.097	2.105
Potassium Chloride**			
-355 microns	1.923	1.932	1.928
-250 microns	1.953	1.948	1.951
Caesium Chloride**			
-355 microns	3.852	3.850	3.851
-250 microns	3.896	3.888	3.892
Lactose			
-45 microns	1.481	1.488	1.485
-90 microns	1.467	1.452	1.460
"as is"	1.522	1.520	1.521
Polyethylene			
"as is"	0.927	0.929	0.928
-180 microns	0.910	0.918	0.914
-125 microns	0.892	0.905	0.899

* Material passed through 710 micron sieve and retained on 500 micron sieve. See Sieve Analysis section for description of sieving analysis.

** Additional alkali metal halide density determination necessary for comparative study on compression properties of metal halides.

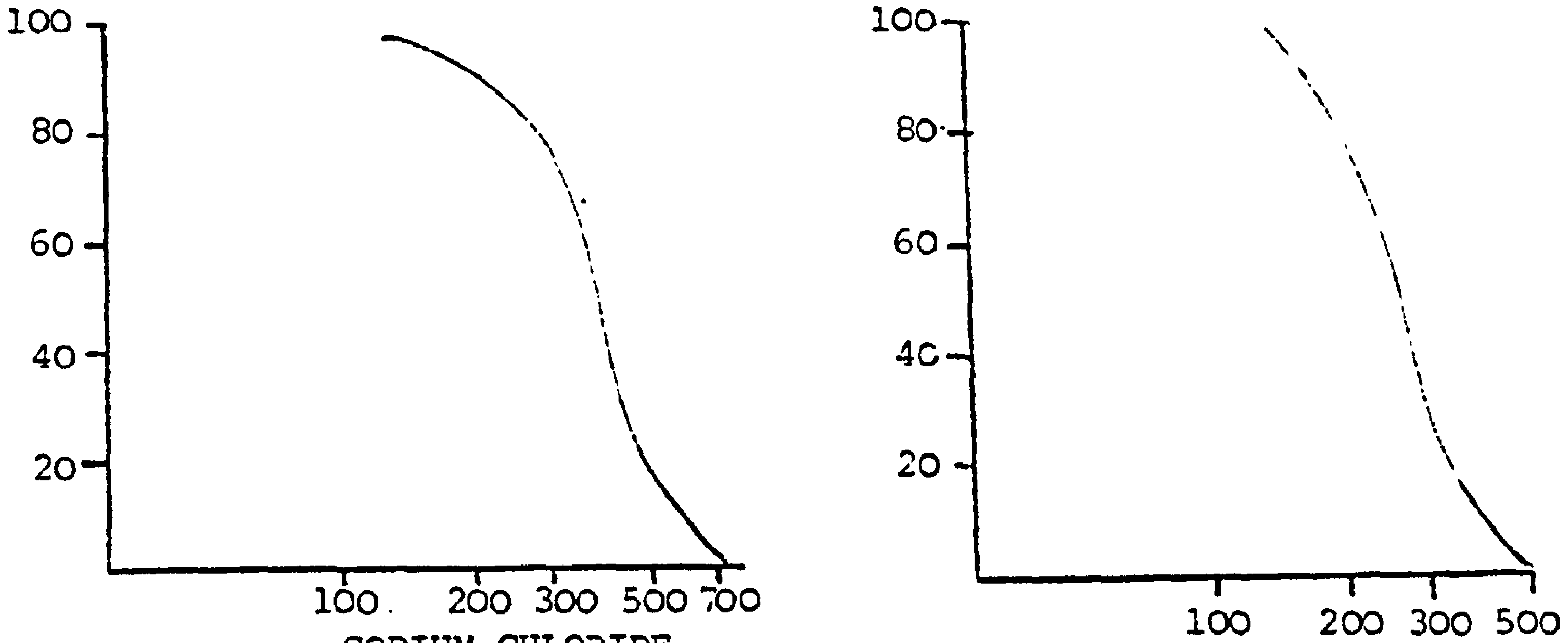
Method

Samples were sieved using a Fritsch Analysette shaker at an amplitude setting of 8 and an interval of 3. Initially, Endecott Sieves (large) of approximately 185mm available mesh diameter were employed, these were considered to be imprecise and Endecott microsieves were substituted thereby reducing the mesh diameter to 85mm. In the case of alkali metal halides and lactose, 20gm of dried material was placed on the top screen of a nest of wire sieves and sieved for a period of fifteen minutes. For polyethylene, a much lighter sample was necessary to achieve efficient separation, 10gms being the weight of choice. The material on each sieve was then weighed and returned to the sieve and, after a further two minutes shaking, the material retained was reweighed. If the amount of material passing through the screen during the second sieving was less than 0.2% w/w of the initial sample then sieving was considered to be complete. Excessive sieving can always cause problems, since breakdown of primary particles to give secondary finer particles or enhanced aggregation of finer particles to larger particles, as occurs with polyethylene, can lead to spurious results. Two sievings were considered acceptable for alkali halides and lactose but inadequate for polyethylene. However, by taking scanning electron microscopy pictures of samples taken from various fractions throughout the sieving process, satisfactory separations could be achieved provided the initial bulk sample was small (in this case 10gms). When size separation was complete on all sieves, the amount of material retained by each sieve was determined and the cumulative percent by weight undersize was calculated. Particle size distributions are shown in FIG 2.2.

2.1.1.4. Scanning Electron Microscopy

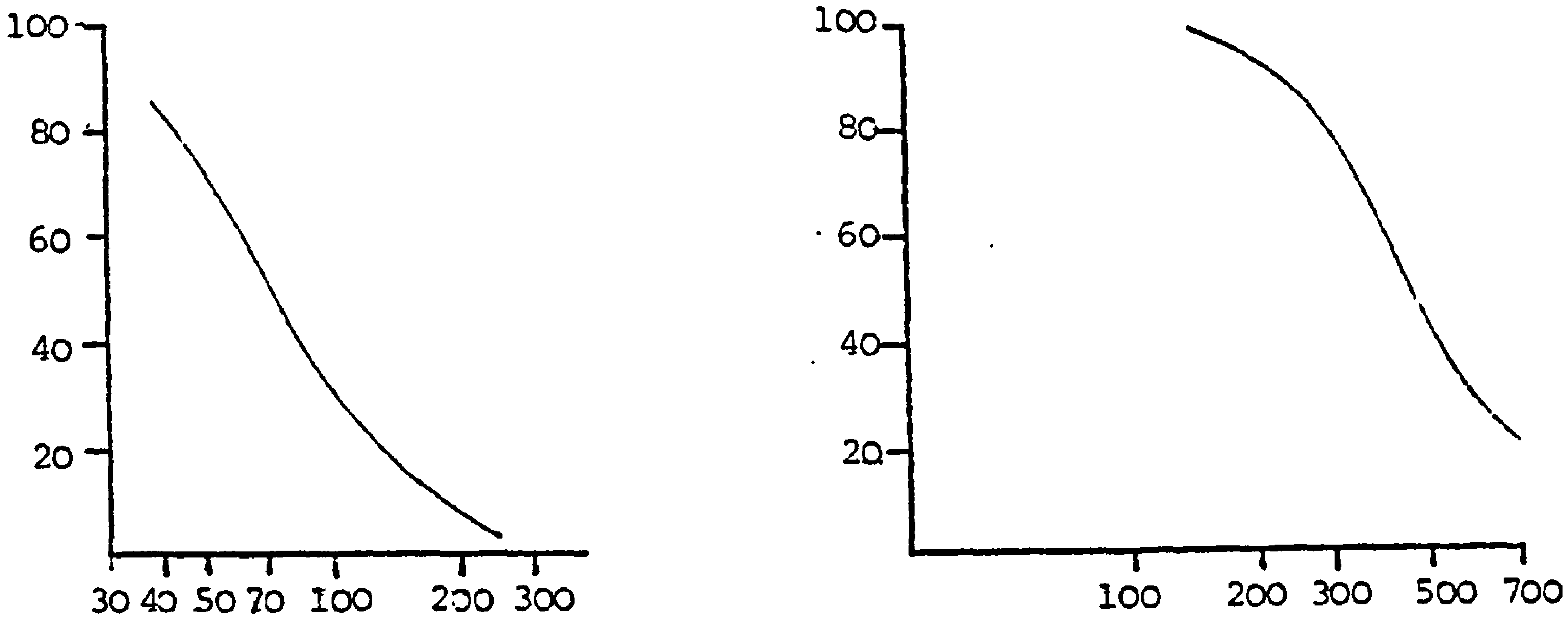
Selected samples of sodium chloride, α -lactose monohydrate and polyethylene were submitted to Scanning Electron Microscopy (SEM) using an International Scientific Instruments (I.S.I.) Mini-SEM, a desk top microscope. Its fundamental performance is similar to that of larger S.E.M.s, but the instrument is compact in design, is easy to operate and simple to instal, functioning on the following principles: An electron beam emitted from the electron gun is accelerated by a voltage of 15 KV (fixed), focussed by a three-stage electro-magnetic lens system and scanned over the specimen surface, where secondary electrons, emitted from the specimen surface, are collected by the secondary electron detector (scintillator-photomultiplier) to obtain video signals. The enlarged image of the surface of the specimen is displayed on a cathode-ray oscilloscope (CRT) in synchronization with the scanning system of the electron beam column, where either 35mm film or 5' & 4' Polaroid Land Film is used to obtain photomicrographs.

Prior to placing in the specimen chamber, the sample is coated with a thin layer of gold, approximately 400A in depth, using a Polaron E5000 Sputter Coater. The diode sputtering method of coating gives a uniform surface coating. Once the ideal film thickness has been established, for a particular specimen, then it can be accurately and easily reproduced, made possible by the linear relationship between input and deposition rate,



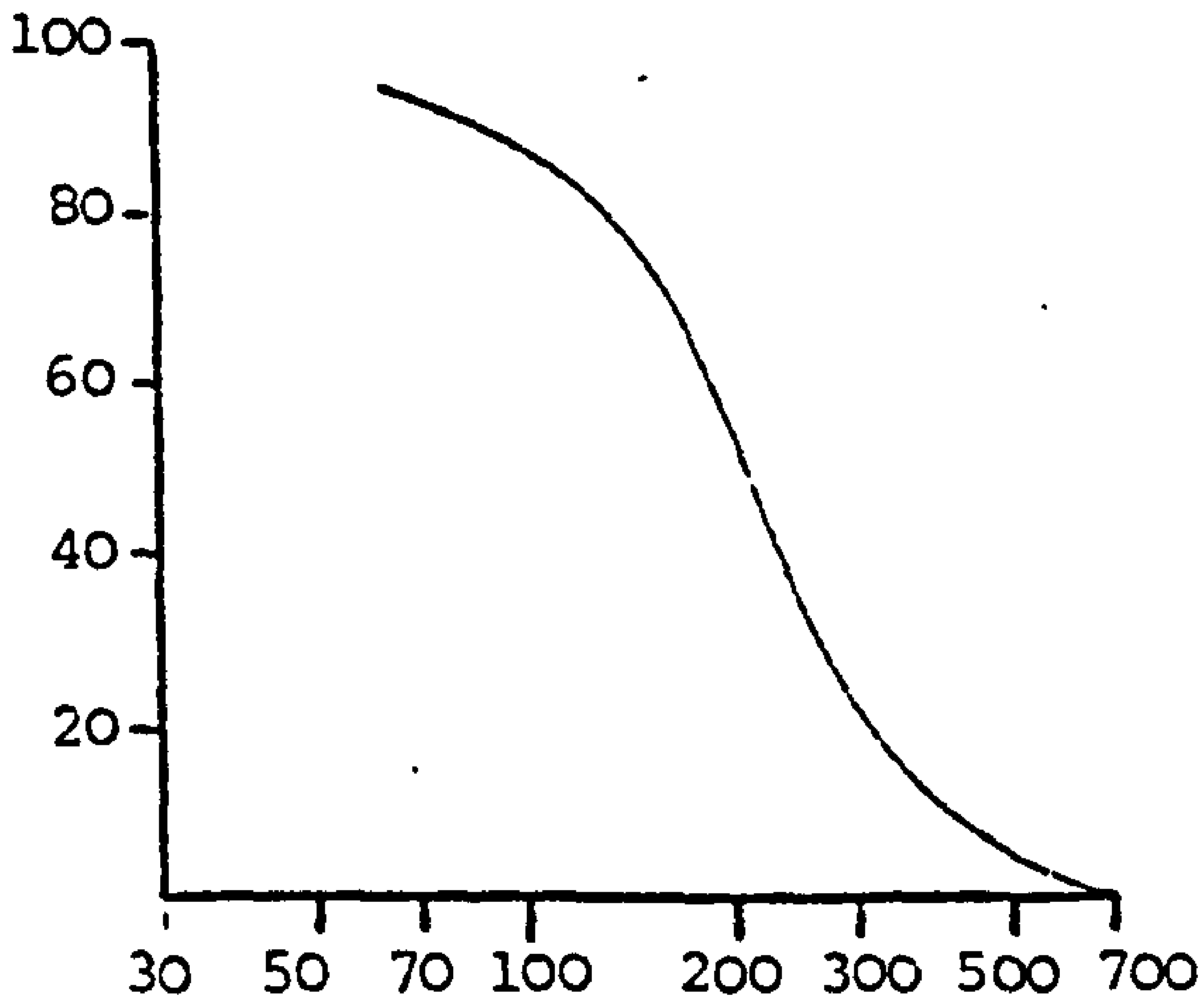
SODIUM CHLORIDE

POTASSIUM CHLORIDE



LACTOSE

CAESIUM CHLORIDE



POLYETHYLENE

FIG. 2.2 Particle Size Distributions, (ordinate = percentage cumulative, abscissa = log size in microns) controlled by an accurate preset timer. Specimens are simply placed on the specimen table, the chamber is threefold evacuated and then refilled with argon, and the gold atoms are emitted at 1.2KV. By coating for not greater than 30 seconds at any one time, both the optimum coating thickness can be achieved and, more importantly, the temperature within the holder box retained at ambient. Photomicrographs of sodium chloride, lactose monohydrate and polyethylene are shown in FIG 2.3. (a,b,c.)

2.1. Preparation of Compacts

2.2.1. Dynamic Compaction Machine Instrumentation

Powders were compressed in an instrumented single punch machine (Manesty). Forces exerted on top and bottom punches were measured by means of piezoelectric transducers (KISTLER 9301) having a measuring range of 60KN and a sensitivity of -4.38C/N. Signals from both punches were amplified (KIAG SWISS TYPE 5001 Charge Amplifier) and recorded on a Bryans Southern U.V. recorder fitted with moving coil galvanometers.

The ejection force could be determined by adjustment of the range (Mechanical Units per Volt) control on the amplifier during the upward movement of the bottom punch. Various stages of the compression cycles were classified as functions of maximum peak heights generated throughout the cycle. An update on measurement execution involved feeding amplified signals into a Rockwell microcomputer fitted with an AIM65 8-channel 12 Bit A/D interface and appropriate software.

Upper punch displacement was determined, when required, using a Linear Voltage Differential Transformer (LVDT), the output from which was fed through a KIAG SWISS TYPE 5211A galvanometer amplifier

FIG. 2.3(a)

Sodium Chloride (355 micron)

Magnification 100x

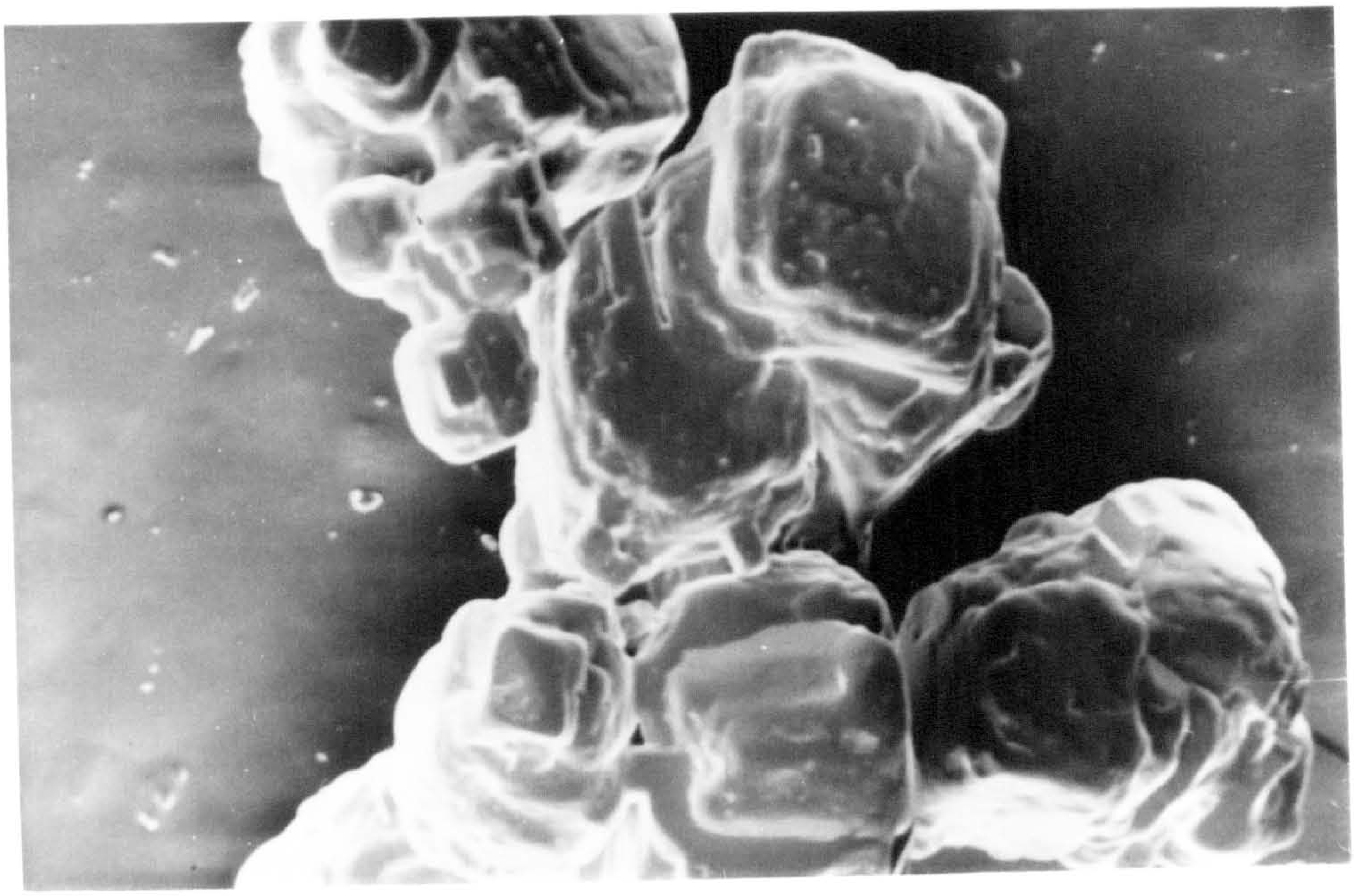


FIG. 2.3(b)

Lactose (45 micron)

Magnification 700x

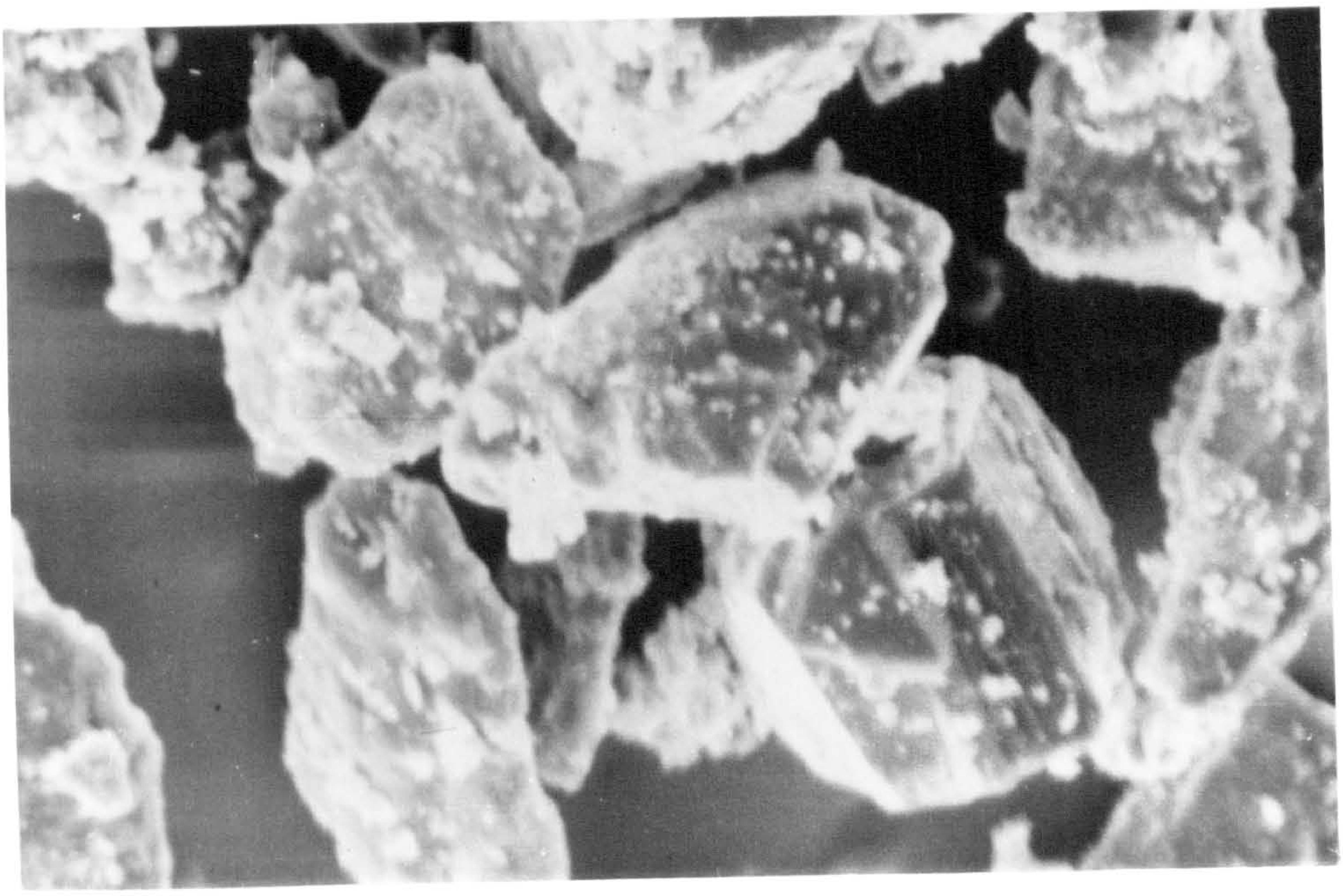
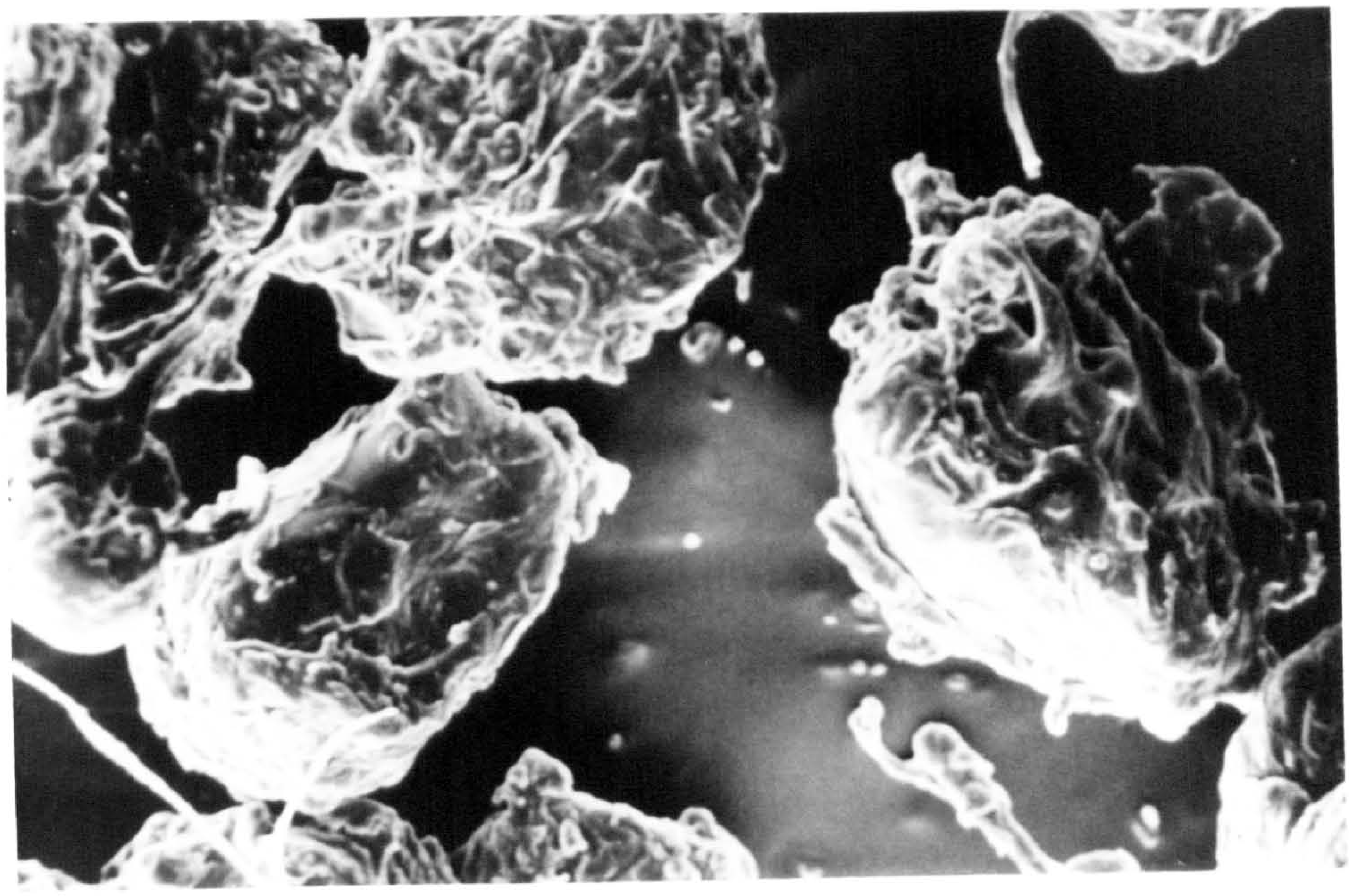


FIG. 2.3 (c)

Polyethylene (250 micron)

Magnification 200x



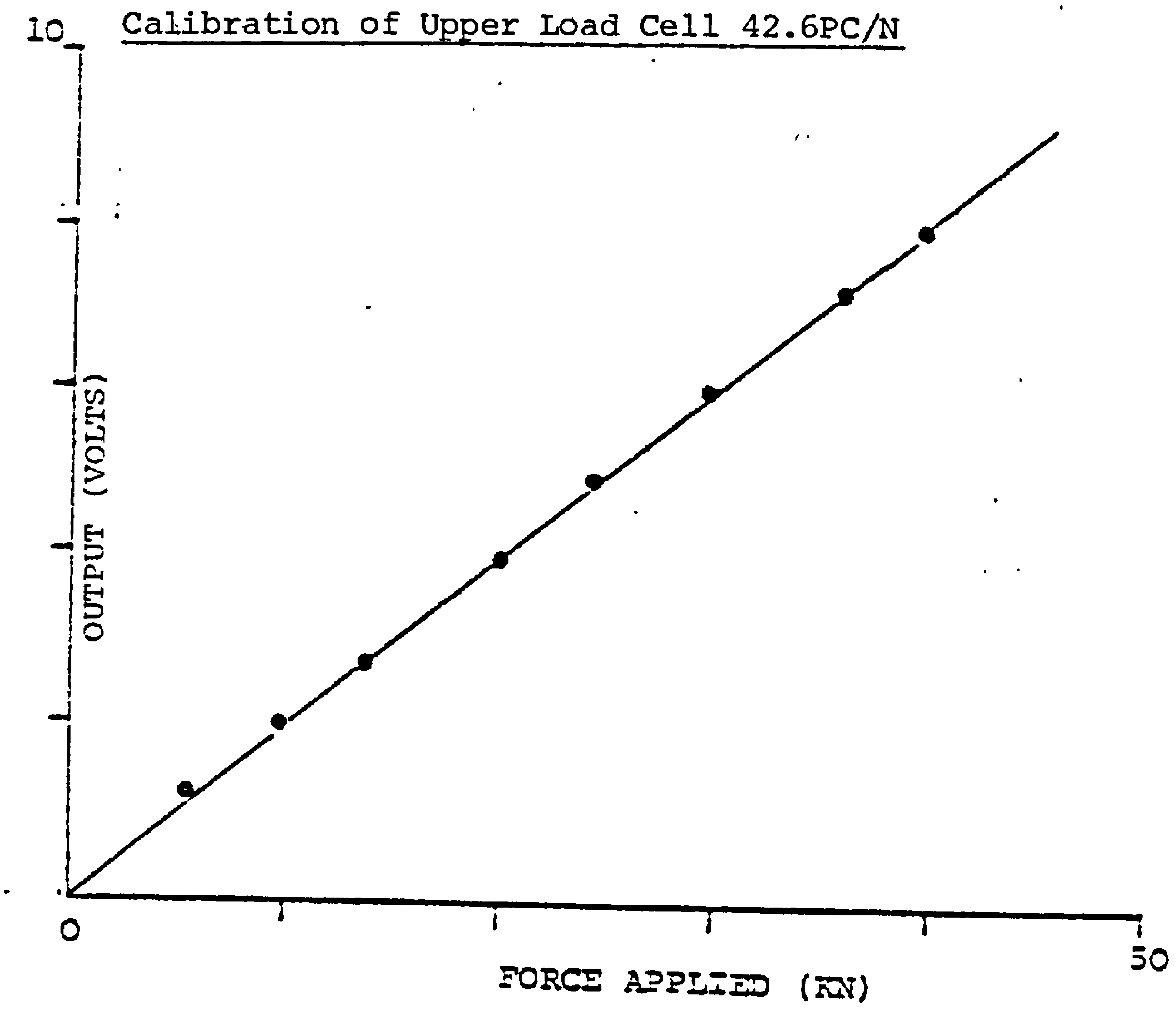
to the U.V. recorder via a moving coil galvanometer. The output from the above instrument was in Kilopons (1Kp = 1Kgm) and the instrumented punches and recording systems were calibrated so that by adjustment of the amplifier sensitivity control 200Kp corresponded to 10mm of movement on the U.V. recorder at a Range setting of 200. The instrumented punch and recording system were calibrated using a universal testing instrument (Instron testing machine) prior to fixing the above conditions. FIG. 2.4. illustrates linearity of response for the system.

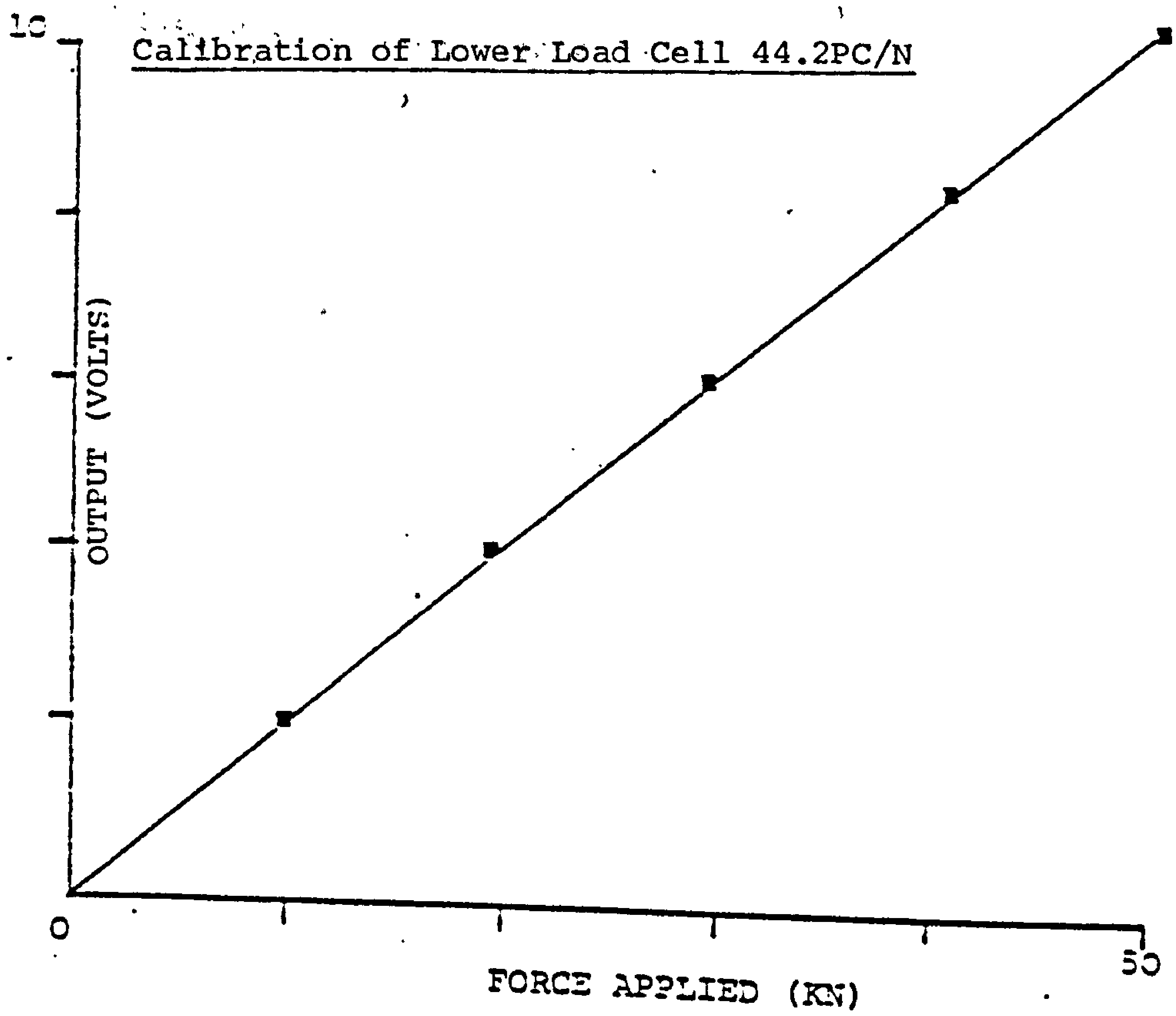
2.2.2. Static Compaction - Machine Instrumentation

Static compaction mechanisms were determined using an Instron Testing Machine Model 1132 fitted with a 10KN load cell. The basic instrument comprises two assemblies, the loading frame and an electronic control console. The loading frame can be used in either tensile or compression mode, in the former the sample under test is fastened between two grips and a known load applied at a fixed speed, generally to test the specimen to destruction. In the compression mode the crosshead descends at a fixed speed and is automatically withdrawn when the applied load attains a preset value. Compression mode testing requires the production of a specially engineered sample holder. Consequently, careful calibration of the instrument is essential to correct for sample holder deformation during operation.

The electronically controlled console offers a variety of options in the study of material behaviour. Among these are variable crosshead speeds (0.5mm min^{-1} to 1,000mm min^{-1}), a range of loads (0 to 10KN), cycling, hold or reverse control of the crosshead and the ability to run the instrument for preselected time intervals. By means of applying a fixed load at a fixed rate,

FIG. 2.4 Calibration of Load Cell


Calibration of Upper Load Cell 42.6PC/N


Calibration of Lower Load Cell 44.2PC/N

compression energy C_e can be expressed as

$$C_e = \int_o^e \frac{dl}{dt} \qquad \text{where } l = \text{load in KN}$$

t = time in minutes

such energy being expressed as a function of the load/time curve drawn automatically on a pen recorder system or directly as an electronic readout. At the start of the test the electronic integrator counts from zero until the cessation of increased load, the "frozen" value being directly proportional to the amount of work done during the test. By pressing the LOOP switch, the integrator displays a value proportional to irrecoverable work. FIG.2.5. shows the instrument used and in addition the special jig designed for compression studies described in this thesis.

The latter is shown more clearly in FIG.2.6. and serves both as a static punch and die holder (i.e. bottom punch stationary) and as a means of projecting force-displacement (FD) profiles.

Several investigators offer an alternative means of comparing the compression properties of starting materials and several investigators have adopted them to calculate an index of the work involved in compaction. By adapting a single punch eccentric tablet machine so that the filling and ejection mechanism worked only once during two compression cycles, de Blaey and Polderman (1970) were able to calculate both die wall friction and net work of compression by subtracting the area under the second FD curve from that of the first. Toure and coworkers (1980) have suggested that the elastic limit of the material being compressed and the total energy input during compression can be derived from data obtained from FD curves up to the point of maximum compaction force, assuming the FD curves are considered hyperbolic. Force-displacement evaluation has

FIG. 2.5

Instron Testing Machine with Jig

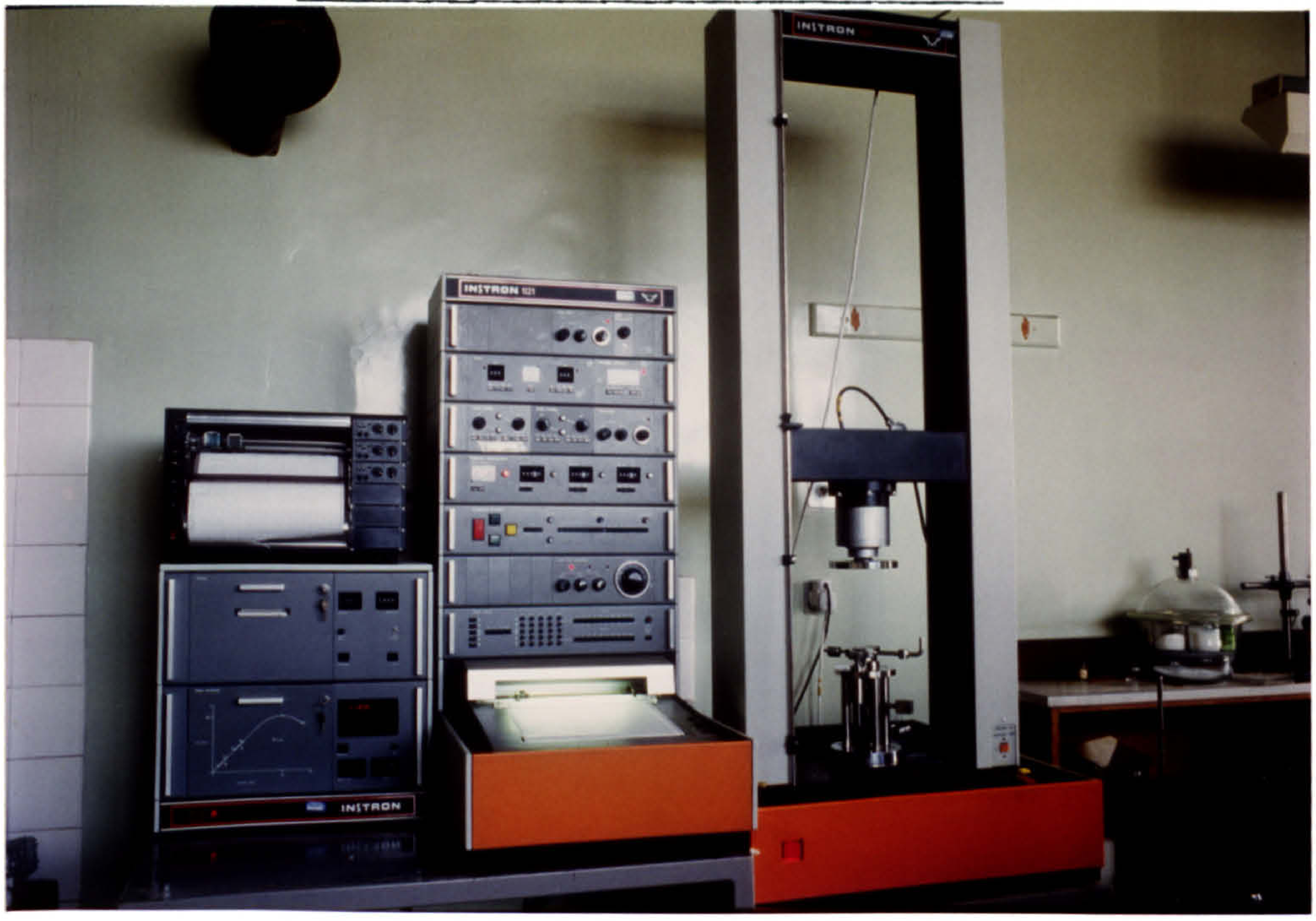
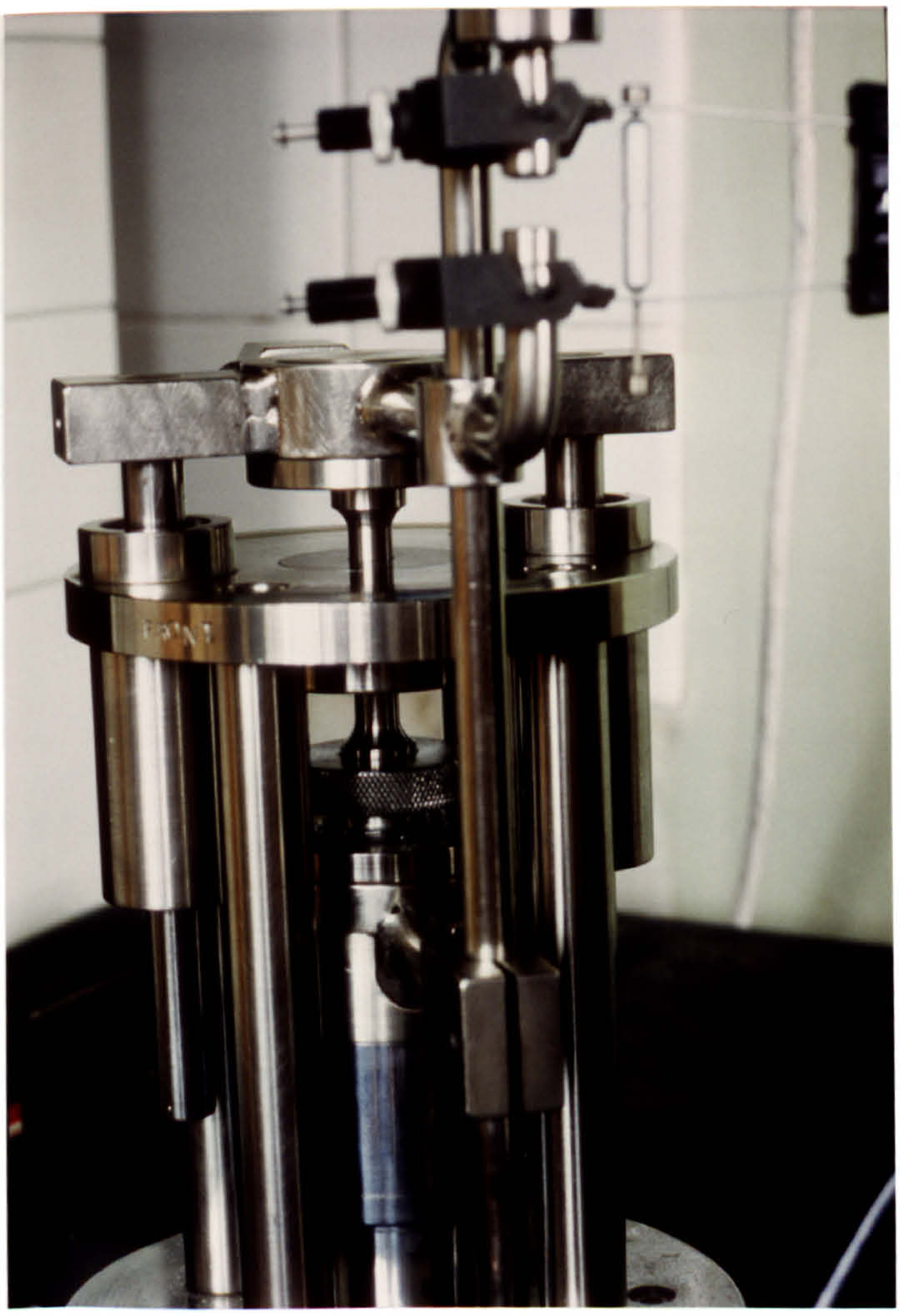


FIG. 2.6

Jig Showing Top Punch Assembly and Extensiometer



suffered both from lack of precision and the inability to detect very small changes in displacement during the compression cycle. In addition, great care must be taken to eliminate errors which might occur during the measuring process. Lammens and coworkers (1980) have drawn attention to many such potential errors.

To heighten the degree of detection and precision and minimise instrumental error a special jig, mentioned earlier, was designed. The principal function of such a jig was to simultaneously monitor both force-time and force-displacement relationships during a single compression. The base of the jig was made from stainless-steel of compact design and bolted to the base plate of the Instron cross-head unit. Into the base was threaded the bottom punch held in a screw-thread holder. The die was contained in a cylindrical stainless-steel disc which was then bolted to the base by means of four legs extending upwards from the base. The bottom punch entered the die to the same extent each time. Also attached to the base were two "friction - reduced" extending legs through which two complementary legs from the upper punch holder fitted smoothly such that when powder was placed into the die, the top punch rested lightly on the powder. Top punch displacement, during both compression and decompression stages, was determined by attaching an Instron extensiometer (Model G51-12MA: 25mm-50%) between the top punch and the jig base. Adjustment was such that the extensiometer could be removed after each compression cycle, the compact ejected manually, and the extensiometer replaced in exactly the same position for the next measurement.

Since accuracy and precision of displacement are prerequisites to studying compaction mechanisms, an Instron Calibration unit, in conjunction with the strain unit on the Instron electronic control console, was used to align extensiometer movement to chart pen movement.

By feeding displacement (X-axis) and Load (Y-axis) to an independent X-Y recorder FD curves and force-time curves could be produced simultaneously. Accurate calibration of the extensiometer allowed displacements of 1-2 microns to be resolved.

As mentioned previously, because of the movement (deformation and recovery) within both the loading frame and the jig during the compression and decompression stages, calibration of the machine was necessary whenever the load and/or crosshead speed were changed. Without material being introduced into the die any deflections on either the integrator dial (energy related) or displacement axis during the compaction cycle will be solely related to instrument deformation. TABLE 2.3. and FIG.2.7. indicate electron counts and force-displacement deflections when the two punches are compressed with the die empty. All measurements must be adjusted to allow for such artifacts, this is especially important during second and subsequent compression of the same compact.

2.2.3. Prelubrication of Die

Prior to tablet compaction, a method for die lubrication was evaluated, the same method to be used in both static and dynamic modes. Since the objective of this study was to establish compaction properties for a single component system followed by the addition of a further component to give a binary system, any lubricant could not be added to the material(s) prior to compaction but had to be coated onto the punch and/or die prior to hand-filling the die.

One approach to prelubrication is that of Rees and Rue (1978) who compressed a mixture of equal parts of the test mixture and

FIG. 2.7

Force-Displacement Profiles with Die Empty
Profiles Generated at 4 and 8KN Loads
Sensitivity of Displacement Measurement Increased
After 1st Compaction

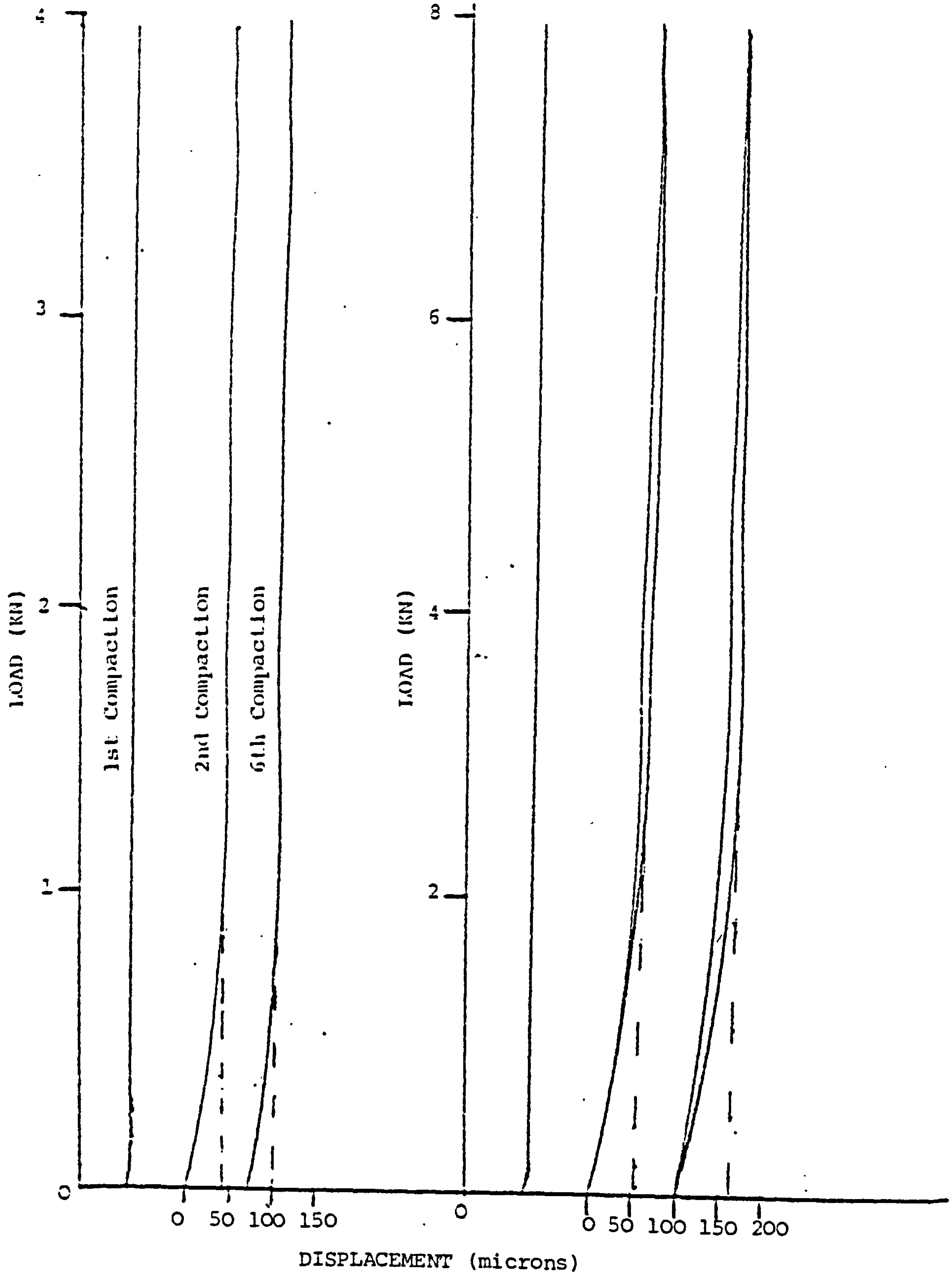


Table 2.3.

Integrator Readings with Die Empty

Load	Speed	1st Cycle		2nd Cycle		6th Cycle	
		Total	Loop	Total	Loop	Total	Loop
4KN	2mm min^{-1}	393	10	393	10	393	10
"	10mm min^{-1}	81	0	81	0	81	0
"	20mm min^{-1}	47	0	47	0	47	0
8KN	2mm min^{-1}	790	53	785	51	781	51
"	10mm min^{-1}	151	0	151	0	151	0
"	20mm min^{-1}	77	0	77	0	77	0

magnesium stearate prior to compacting the pure test material. An alternative method, and that chosen for these studies, involves applying the lubricant either in the form of a solution or suspension in a volatile solvent. Shotton and Obiorah (1975) applied a 2% solution of stearic acid in acetone:carbon tetrachloride (50:50) while Carli, Colombo and Simioni (1981) chose an identical system except that they replaced carbon tetrachloride with chloroform.

For this reported work, a fine layer of lubricant was applied, to the die only, by lightly brushing on a 2% solution of stearic acid in chloroform and removing the solvent with a hair dryer.

2.2.4. Characterisation of Tablets

2.2.4.1. Strength of Tablets

2.2.4.2. Alkali Halides

Because of the non-ideal breaking behaviour of alkali halide compacts formed at relatively high pressures, diametral crushing strength was selected as being the most realistic method for monitoring compact cohesion. The need to compress at relatively high pressures was essential since the introduction of small amounts of elastic material into an alkali halide bulk drastically reduced cohesive properties at lower pressures. Crushing strength of compacts were determined using a Heberlein strength tester with plattens covered (filter papers). On ejection from the die, tablets dimensions were determined by micrometer (accurate to 1×10^{-3} mm) as well as tablet weight. Tablets were then either crushed immediately or retained in sealed containers for an extended storage period. After a fixed time interval, stored tablets were then remeasured and the crushing strengths determined, selected samples being retained for scanning electron microscopy. At least five tablets were evaluated at each tableting pressure.

2.2.4.3. Lactose Monohydrate

By comparison, lactose monohydrate compacts, with and without the addition of an elastic component, were seen to behave in a manner closer to ideal. In this event, both crushing strength and tensile strength were determined. No increase in strength was observed with time therefore strength testing was judged almost immediately after ejection. At least five tablets were tested at each pressure and selected samples were retained for microscopy.

3. COMPACTION of POWDERS - The Static System

3.1. Lactose and Polyethylene as Single Components and Binary Mixtures

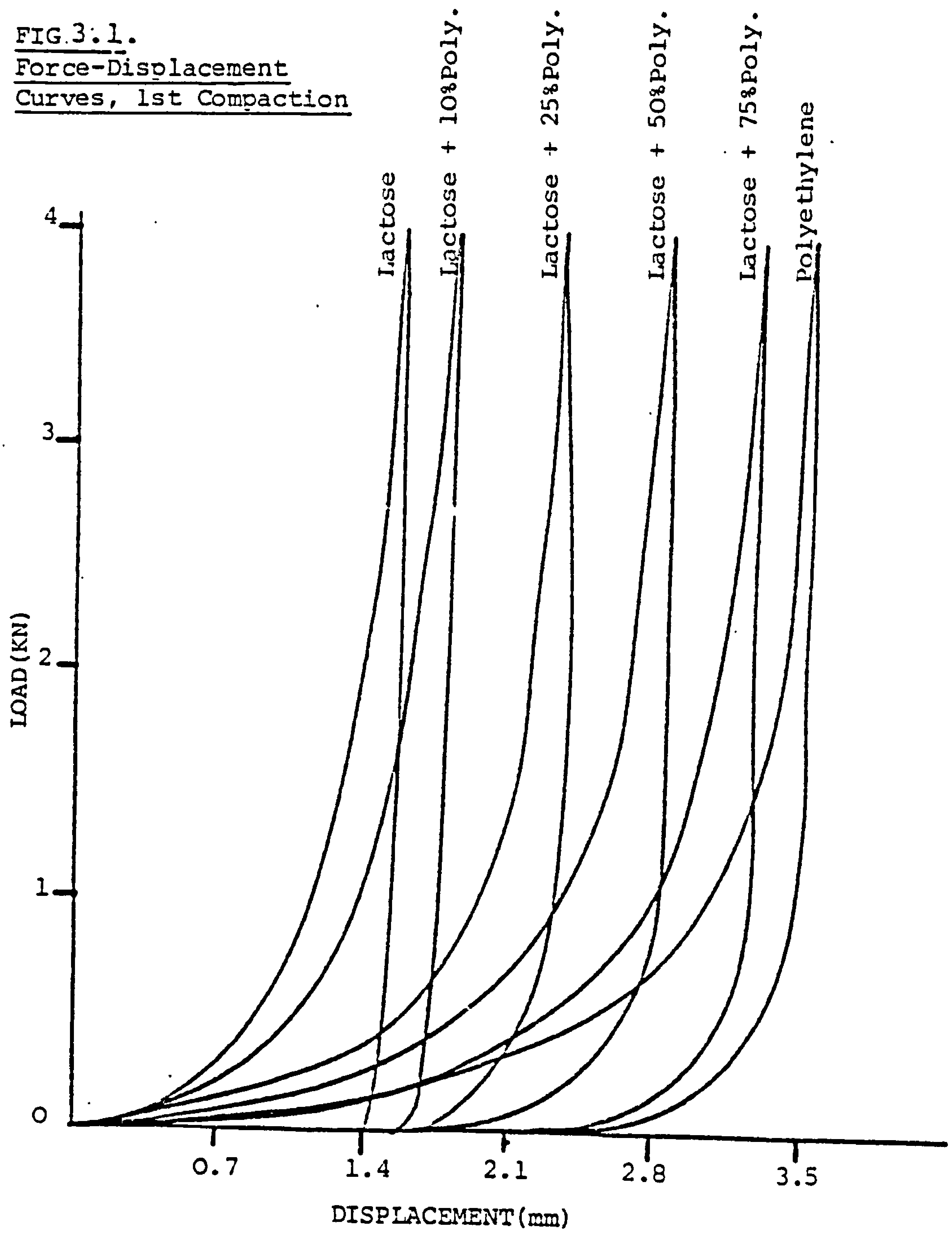
3.1.1. Interpretation of Behaviour

3.1.1.1. The Force-Displacement Relationship

When a force is applied to a powder constrained within a die varying degrees of powder displacement will occur as different mechanisms of compactions come into operation. FIG.3.1. shows the first compaction force displacement curves for lactose (45 micron) with and without the addition of 250 micron polyethylene, the material being compressed at a cross-head speed of 2mm min^{-1}. The shapes of the curves are similar but indicate how the compaction profile changes as the materials vary from brittle through various dilution stages to totally viscoelastic. Seelig and Wulff (1964) suggested that the first stage of compaction involved rearrangement and close packing as work was done to overcome interparticle spacing. Further increases in compaction force would result in elastic and plastic deformation or brittle fragmentation, depending on the nature of material. At this stage of the compaction process extensive interparticle bond formation occurred. These stages cannot normally be separated but, depending on the magnitude of the compression force, one mechanism will predominate.

Because of the small size and relatively ~~low~~ high density of lactose, consolidation would occur at relatively low loading, the FD curve indicated this to be the case. On increased loading elastic deformation and brittle fragmentation operated with only slight displacement as the

FIG.3.1.
Force-Displacement
Curves, 1st Compaction



load approached its maximum. Energy would be utilised in bond formation with consequent energy release determined by the degree of elastic recovery. The FD curve suggested that lactose behaved, to a slight degree, as an elastic body. At such low pressures and relatively long dwell-times and with friction minimised by use of a prelubricated die, the area under the curve can be assigned to work done in forming bonds.

Dilution with polyethylene resulted in an extended consolidation stage and a greatly enhanced elastic deformation effect, presumably due to both a reduction in bulk density and the introduction of a viscoelastic component. The latter behaviour tends to dominate the mechanical properties of polymers. Viscoelasticity in polymers is not unexpected in the light of the complicated molecular adjustments which underlie any microscopic mechanical deformation. In deformation of, say, sodium chloride, atoms are displaced from fields of force which are quite local in character. In a liquid, viscous flow reflects the change with time, under stress, of the distribution of molecules surrounding a given molecule. In a polymer, on the other hand, each flexible threadlike molecule overlaps an average volume much greater than atomic dimensions thus enabling if to adopt a configuration which will be influenced by both gross long-range contours and more local relationships. As stress is applied the response to local aspects is fast as opposed to the stimulus of long range factors.

From a knowledge of such properties, the relationship between energy endowed to the system and the proportion regained due to elastic recovery could be progressively followed as the polymer content increased. Elastic recovery was seen to increase with polyethylene content although polymer alone did not undergo complete recovery since the compacted material could be recovered from the die as a cohesive plug. In binary mixtures with high polyethylene contents a considerable portion of energy donated to the system was used in promoting elastic deformation of polyethylene. Prior to that, as illustrated by low FD ratios, considerable particle consolidation occurred, unlike lactose alone which consolidated rapidly with little further powder displacement as stress increased. With respect to lactose, a similar pattern of behaviour has been shown by Hersey, Cole and Rees (1974) who alluded to the high yield strength of lactose in differentiating between the compaction behaviour of lactose (brittle) and sodium and potassium chloride (plastic). However, thay made no reference to the elastic nature of their materials nor did they elaborate on the causation of the high yield strength.

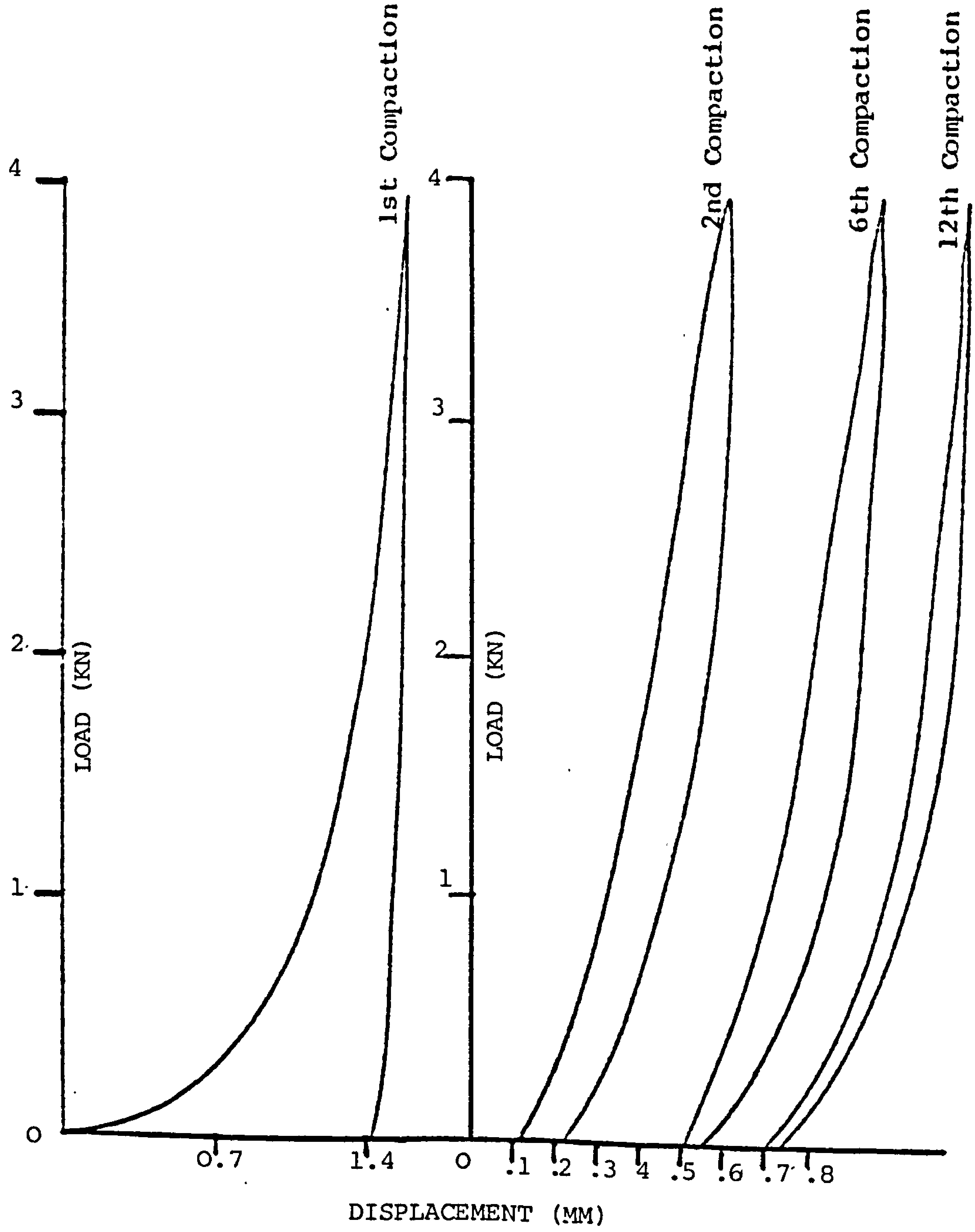
The extent to which lactose recovers elastically, in a uniaxial direction, is illustrated in FIG.3.2. which shows FD curves for selected subsequent compression cycles. The data indicated that at each compression, with the compact retained within the die, the material underwent some further displacement and consequent recovery.

The first compaction of a low particle size material (45 - 63 micron in the case of lactose) would significantly reduce

FIG. 3.2

Force-Displacement Profiles for Sequential Lactose Compaction

Sensitivity of Displacement Measurement Increased After 1st Compaction.



void space and give rise to concentrated interlocking of particles with inter particle bond formation. The static nature of the compaction process would compel forces to act in fairly well-defined planes to produce a more ordered system than that visualized in dynamic compression. Similar results for lactose have been obtained by Armstrong, Abourida and Krijgsman (1982) who modified a Manesty tablet press to retain tablets after compression. They defined the relationship:

$$F_{REL} = \frac{\text{force exerted at the nth compression}}{\text{force exerted at the first compression}}$$

where F = Relative force

They correlated a volume decrease with compression number and demonstrated that such a decrease was a function of the initial applied force. They suggested that at higher forces, where F_{REL} plateaued after 10 compressions, the compact attained its ultimate porosity relatively quickly due to extensive fragmentation. At lower forces, a smaller degree of fragmentation occurred and a greater number of compressions were required to achieve minimal porosity. However, their study did not take into account the elastic recovery of the lactose compact which, at the lower forces, would be expected to contribute significantly to second and subsequent compressions.

Upon dilution with polyethylene (FIGS.3.3. and 3.4. exemplify low and high dilution effects) the first compression cycle was shown to define the compaction properties of the admixtures. The abscissa scale was adjusted on completion of the first cycle, subsequent FD curves were shown to be almost superimpossible irrespective of sequence.

FIG. 3.3

Force Displacement Profiles for Lactose - 10% Polyethylene Compaction

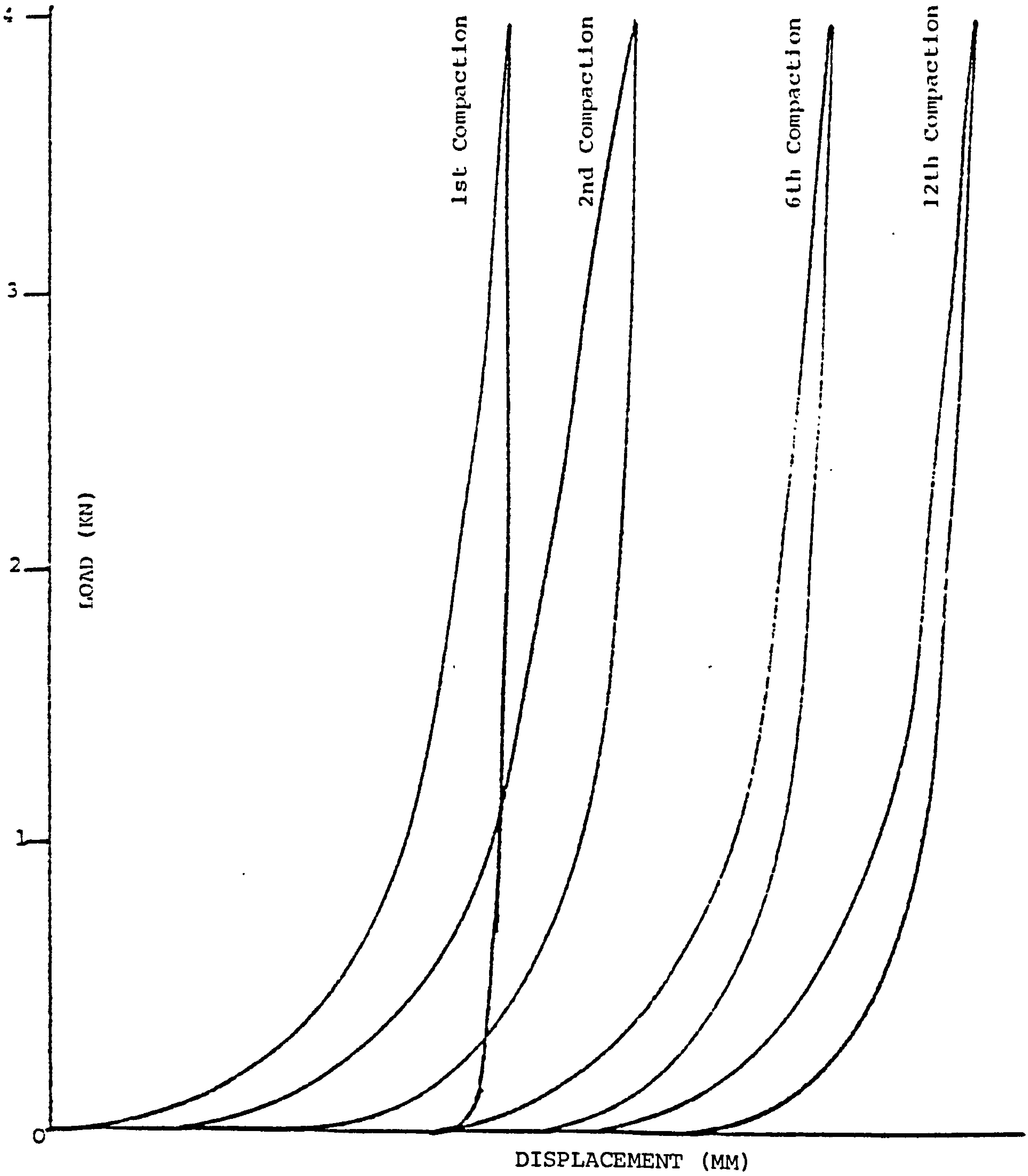
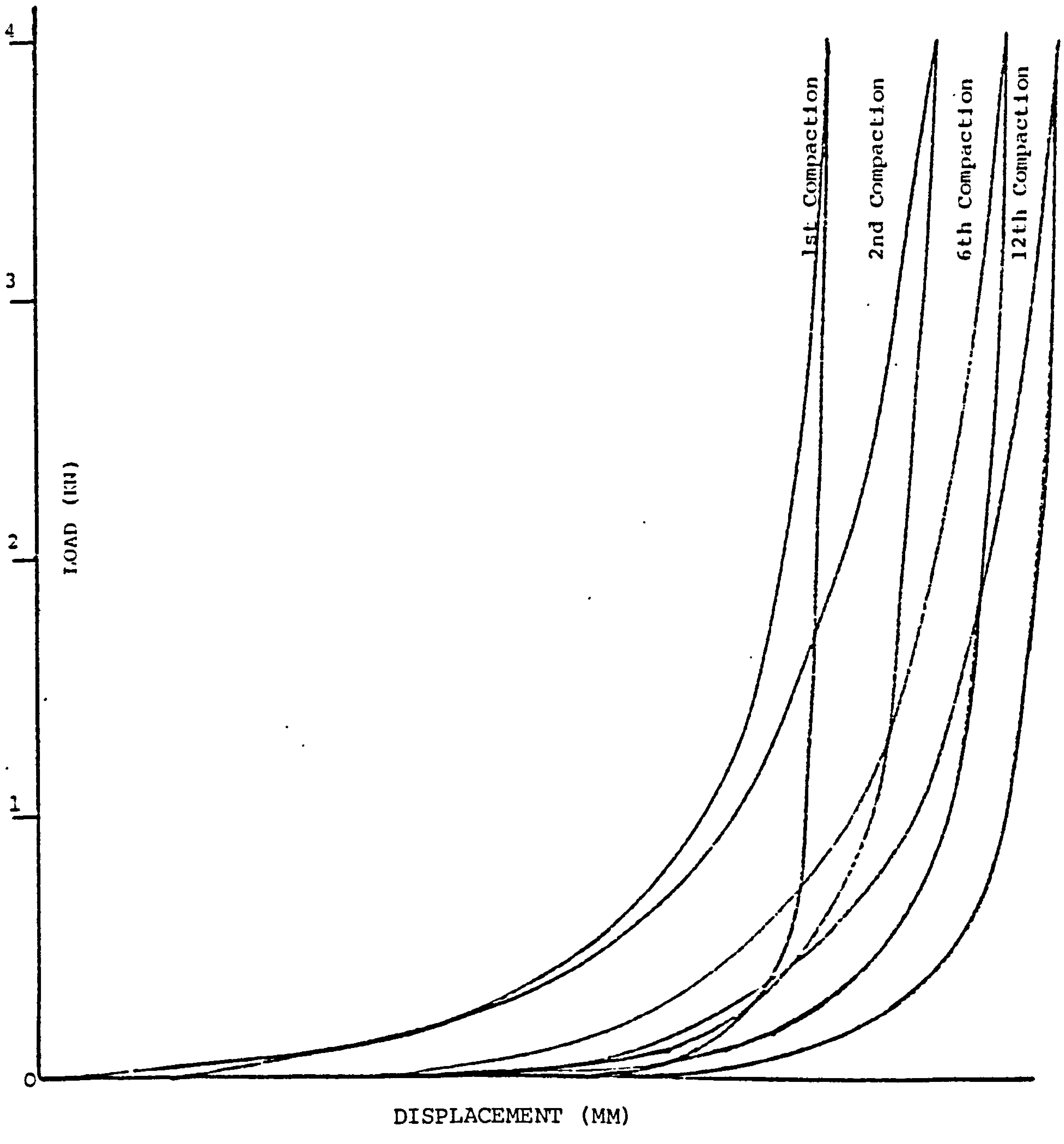


FIG. 3.4

Force Displacement Profiles for Lactose - 75% Polyethylene



The compact was observed to deform and relax to the same degree. Recovery time had little effect on energy balance, the graphs in FIGS. 3.3. and 3.4. were each generated following a 5 minute recovery period.

3.1.1.2. The Force-Time Relationship

By analysing force-time data, generated concurrently with FD curves, compression energies could be calculated and elastic, plastic and brittle energy components allocated to each compression stage. Tables 3.1. and 3.2. illustrate energy distributions involved during 1st and 2nd compactions of various single and binary systems.

On the first compression an increase in load from 4KN to 8KN, keeping dwell time constant, resulted in a corresponding increase in elastic recovery with the plastic brittle component almost exactly doubled. Irrespective of compaction force an addition of 10% polyethylene produced a similar response to lactose alone suggesting that the close packing of lactose and subsequent interparticle bonding accentuated by induced surface activity arising through brittle fragmentation, were sufficient to minimise elastic recovery of polyethylene.

At the lower load, a significant increase in the elastic energy component only became apparent at polyethylene dilutions of 50% and more, the plastic/brittle component remained unchanged when compared to the 25% dilution. At such high concentrations of polyethylene work of compaction becomes dependent upon an increasingly complex overlap of viscoelastic and brittle properties with the compact almost certainly containing areas concentrated in polyethylene or

Table 3.1.

Energy Distributions during 1st and 2nd Compaction Cycles of Lactose (45-63 microns) - Polyethylene (180-250 microns) Mixtures, Compacted at 4KN and 2mm min^{-1}, Energy in Joules x 10^{-2}

Sample	1st Compaction	2nd Compaction
100% Polyethylene		
Total:	1.86	1.14
Plastic/Brittle:	1.34	0.63
Elastic:	0.52 (28.0)*	0.51 (44.7)
75% Polyethylene		
Total:	1.45	0.90
Plastic/Brittle:	1.00	0.44
Elastic:	0.45 (31.7)	0.46 (51.1)
50% Polyethylene		
Total:	1.24	0.73
Plastic/Brittle:	0.83	0.32
Elastic:	0.41 (33.0)	0.41 (56.2)
25% Polyethylene		
Total:	1.19	0.56
Plastic/Brittle:	0.85	0.22
Elastic:	0.34 (28.6)	0.34 (60.7)
10% Polyethylene		
Total:	1.22	0.48
Plastic/Brittle:	0.89	0.14
Elastic:	0.33 (27.0)	0.34 (70.0)
100% Lactose		
Total:	1.25	0.42
Plastic/Brittle	0.91	0.09
Elastic:	0.34 (27.2)	0.33 (78.6)

* Figures in parenthesis are elastic energy expressed as a percentage of total energy.

Table 3.2.

Energy Distributions during 1st and 2nd Compaction Cycles of Lactose (45-63 microns) - Polyethylene (180-250 microns) Mixtures, Compacted at 8KN and 2mm min^{-1}, energy in Joules x 10^{-2}

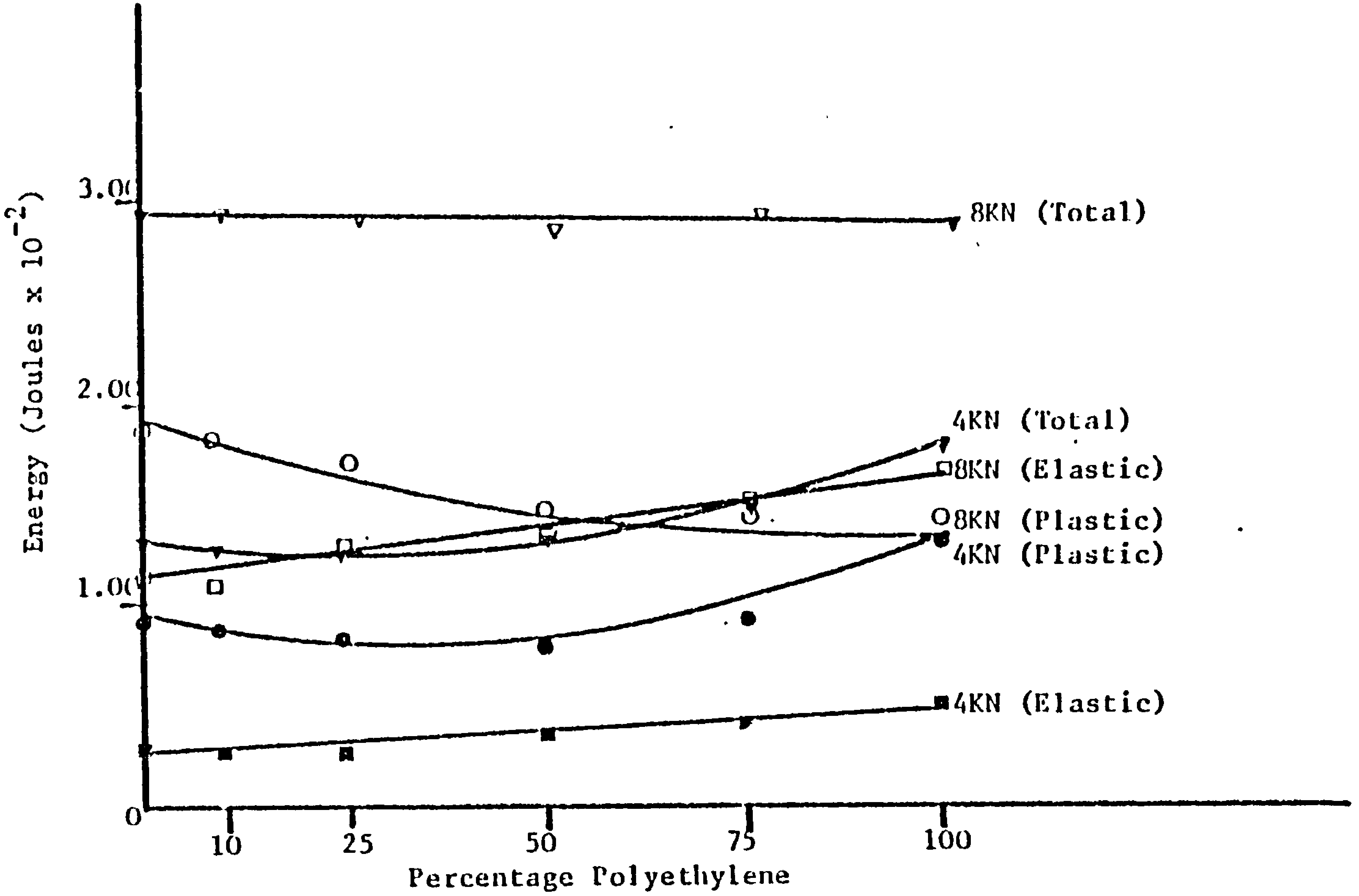
Sample	1st Compaction	2nd Compaction
100% Polyethylene		
Total:	2.74	2.17
Plastic/Brittle:	1.26	0.68
Elastic:	1.48 (54.0)	1.490 (68.7)
75% Polyethylene		
Total:	2.82	2.08
Plastic/Brittle:	1.40	0.67
Elastic:	1.42 (50.4)	1.41 (67.8)
50% Polyethylene		
Total:	2.71	1.81
Plastic/Brittle:	1.44	0.53
Elastic:	1.27 (46.9)	1.28 (70.7)
25% Polyethylene		
Total:	2.87	1.69
Plastic/Brittle:	1.60	0.41
Elastic:	1.27 (44.2)	1.28 (75.7)
10% Polyethylene		
Total:	2.92	1.48
Plastic/Brittle:	1.83	0.30
Elastic:	1.10 (37.7)	1.18 (79.7)
100% Lactose		
Total:	2.98	1.35
Plastic/Brittle:	1.86	0.23
Elastic:	1.12 (37.6)	1.12 (83.0)

lactose. Such areas would control the cohesive nature of the compact. At the higher force void space would be further reduced with an analogous increase in lactose-lactose bonding. In fact, although both plastic and brittle energy increased at the higher load the trend in energy retention reversed w.r.t. the brittle/plastic component, indicating the immediate effect of polyethylene on the bonding mechanism of lactose. The fact that polyethylene itself retains almost 50% of the total energy imparted to the system during compaction testifies to the viscoelastic nature of the material. It seems reasonable to deduce that were the force increased further while maintaining the same dwell time, the trend would be similar with the brittle fracture of lactose and viscoelastic deformation of polyethylene utilising the major portion of energy input. A comparison of high and low load energy profiles is given in FIG.3.5.

3.1.1.3. The Particle Size Effect

The importance of the role played by particle size in tablet cohesion has been described (see Section 1.1.3.), of particular relevance to the present work are the findings of Fell (1971) and Carless and Leigh (1974). The former, in his comparison of spray dried and crystalline lactose, suggested that the superior strength of compacts produced from the former originated as a result of the percentage of fines present in the material. Such an environment would favour increased interstitial void filling and multiple particle-particle contact. The author also stressed the importance of both fracture under compaction and particle morphology on compact strength, the irregular shape of spray

FIG. 3.5.
1st Compactions(4KN and 8KN/2mm min^{-1})
using 45 micron Lactose



dried lactose being more conducive to interparticle locking. Carless and Leigh drew attention to the effect of particle size on initial packing conditions in the die and how, in the case of sucrose, such differences would influence stress-density relationships.

The compaction of a larger particle size fraction of lactose might, therefore, be expected to modify the energy profile in, at least, two major areas. Firstly, a decrease in energy retention would be anticipated as a result of reduced particle-particle contact. However, it might also be forecast that particles of (say) 90-125 micron size would fracture more favourably, on compression, than those of 45-63 microns. Consequently, a continuous source of energy would be present which would, in part, negate any decrease arising from reduction in primary particle contact.

TABLES 3.3. and 3.4. outline the energy distributions observed when 90-125 micron lactose was subjected to loads of 4 and 8KN. At the lower load a small increase in plastic/brittle component was observed as opposed to 45-63 micron material which would suggest that any reduction in interparticle contact due to original size had been eliminated.

On the addition of polyethylene, the elastic component was seen to play a more significant role than at the smaller size level. Since die-wall friction was independent of area of contact and only a slight increase in elastic energy occurred, increased plastic/brittle energy can be attributed to energy absorption by the viscoelastic component.

Compaction mechanisms were influenced at concentrations of polyethylene below 50%

Table 3.3.

Energy Distributions during 1st and 2nd Compaction Cycles of Lactose (90-125 microns) - Polyethylene (180-250 microns) Mixtures, Compacted at 4KN and 2mm min^{-1}, Energy in Joules x 10^{-2}.

Sample	1st Compaction		2nd Compaction	
100% Polyethylene				
Total:	1.86		1.14	
Plastic/Brittle:	1.34		0.63	
Elastic:	0.52	(28.0)	0.51	(44.7)
75% Polyethylene				
Total:	1.76		1.06	
Plastic/Brittle:	1.26		0.57	
Eastic:	0.50	(28.4)	0.49	(46.2)
50% Polyethylene				
Total:	1.68		0.95	
Plastic/Brittle:	1.18		0.45	
Elastic:	0.50	(29.8)	0.50	(52.6)
25% Polyethylene				
Total:	1.47		0.65	
Plastic/Brittle:	1.08		0.28	
Elastic:	0.39	(26.5)	0.37	(57.0)
10% Polyethylene				
Total:	1.34		0.52	
Plastic/Brittle:	0.99		0.17	
Elastic:	0.35	(26.1)	0.35	(67.3)
100% Lactose				
Total:	1.30		0.44	
Plastic/Brittle:	0.96		0.10	
Elastic:	0.34	(26.2)	0.34	(77.3)

Table 3.4.

Energy Distribution during 1st and 2nd Compaction Cycles of Lactose (90-125 microns) - Polyethylene (180-250 microns) Mixtures, Compacted at 8KN and 2mm min^{-1}, Energy in Joules x 10^{-2}.

Sample	1st Compaction	2nd Compaction
100% Polyethylene		
Total:	2.74	2.17
Plastic/Brittle:	1.26	0.68
Elastic:	1.48 (54.0)	1.49 (68.7)
75% Polyethylene		
Total:	2.93	2.20
Plastic/Brittle:	1.40	0.70
Elastic:	1.53 (52.2)	1.50 (68.2)
50% Polyethylene		
Total:	2.87	2.08
Plastic/Brittle	1.46	0.67
Elastic:	1.41 (49.1)	1.41 (67.8)
25% Polyethylene		
Total:	3.01	1.78
Plastic/Brittle:	1.71	0.49
Elastic:	1.30 (41.9)	1.29 (72.5)
10% Polyethylene		
Total:	2.95	1.49
Plastic/Brittle	1.79	0.32
Elastic:	1.16 (39.3)	1.17 (78.5)
100% Lactose		
Total:	2.96	1.35
Plastic/Brittle:	1.81	0.20
Elastic:	1.15 (38.9)	1.15 (85.2)

By favouring energy absorption the viscoelastic component constrained that available for particle fracture and bonding. At the higher load particle size differences did not significantly influence energies of compaction, sufficient pressure being exerted to effect similar bonding mechanisms as observed with smaller size fractions. FIGS.3.6. and 3.7. illustrate graphically the relationship between particle size and energy.

The studies defined above serve to illustrate the effect of adding varying amounts of an elastic component to a material which fragments, under pressure, in a static environment. Attempts have been made previously to explain mechanistic changes occurring during the compression cycle but with only a limited success. For instance, Kurup and Pilpel (1978) studied powder mixtures under dynamic conditions, analysis of the data in terms of the compression equations of both Heckel and Cooper and Eaton failed to resolve the separate contributions of different mechanisms operating during the compaction cycle. Unfortunately, the issue became more clouded when, in a later study, Malamataris and Pilpel (1982) suggested that the addition of a plastic coating such as polyethylene glycol heightened the development of cohesive bonding, they made no mention of any elastic behaviour of polyethylene glycol.

The involvement of an elastic component during material compaction cannot be lightly ignored, a point made by Krycer, Pope and Hersey (1982) when defining the important parameters for achieving defined tablet strength and eliminating capping tendency. By measuring the heights of paracetamol tablets

FIG.3.6:
1st Compaction(4KN/2mm min^{-1})
of 2 Particle Size Fractions
of Lactose

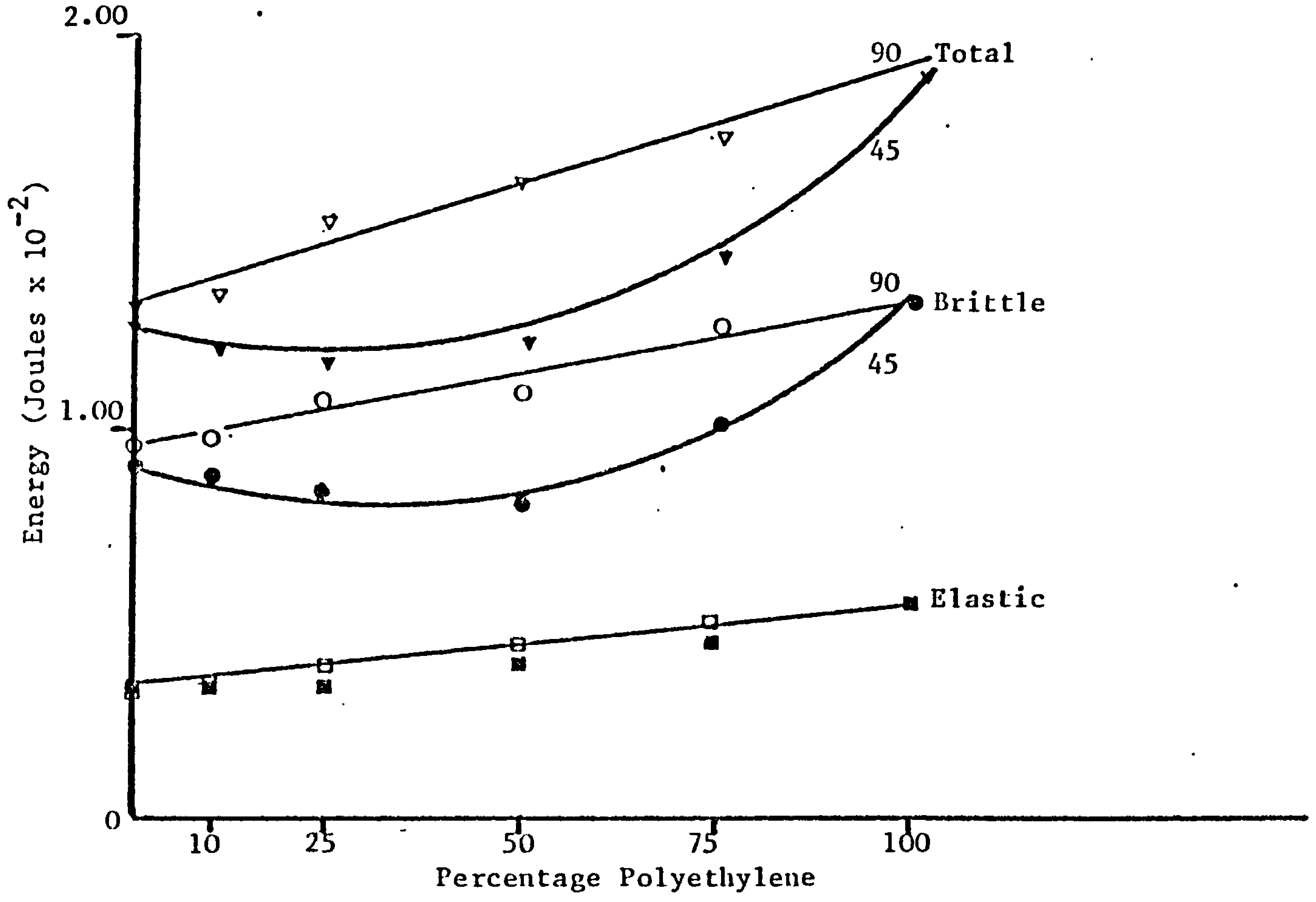
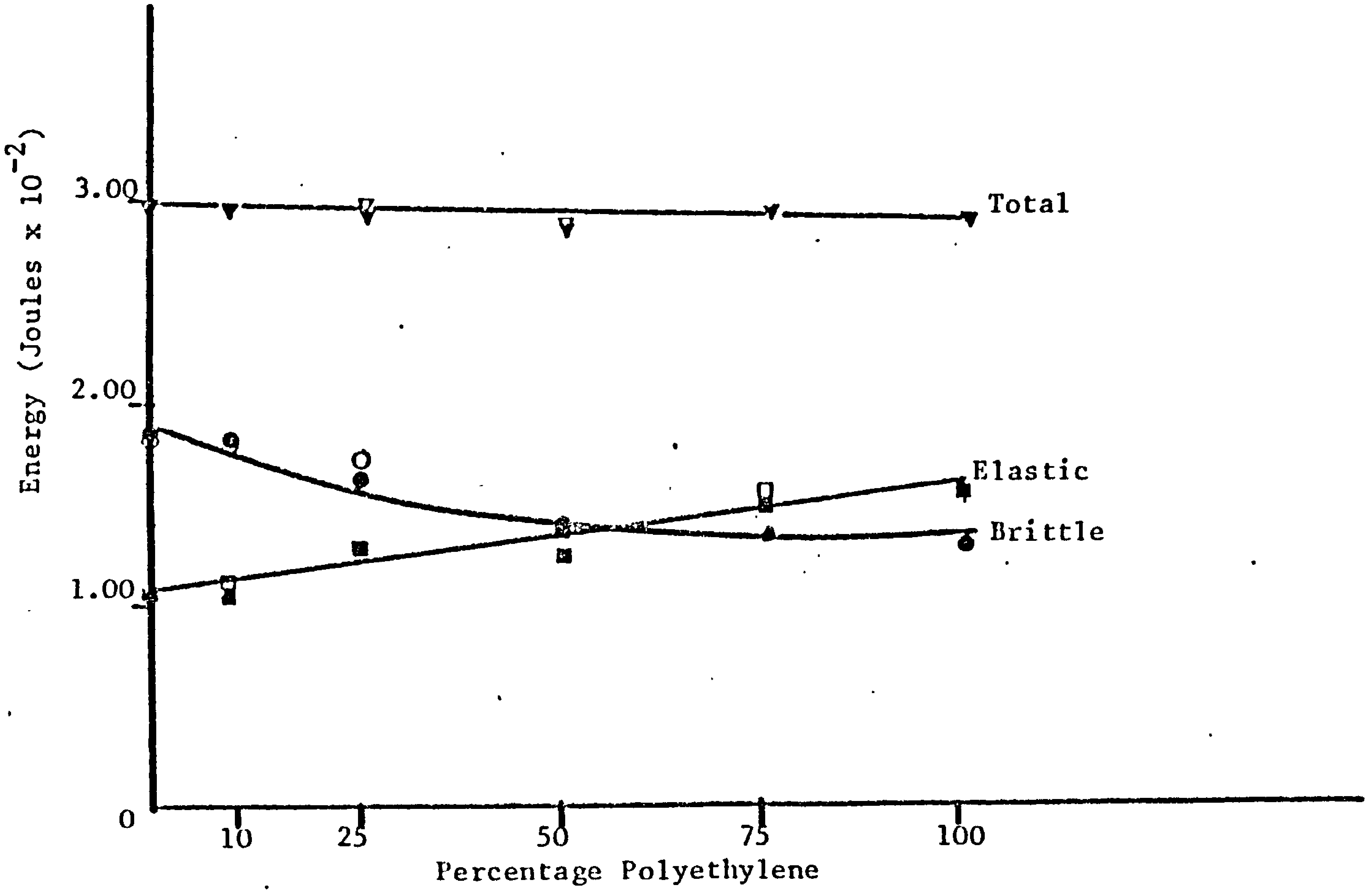


FIG. 3.7.
1st Compaction(8KN/2mm min^{-1})
of 2 Particle Size Fractions
of Lactose



both under pressure (H_c) and 24 hours after ejection (H) an expression to calculate elastic recovery (E) was derived, such that

$$E = 100 \times \frac{H - H_c}{H_c}$$

They demonstrated attained tablet strength and incidence of capping to be a function of the relative magnitudes of elastic deformation and plastic flow. This postulate seemed reasonable when dealing with a single-component system where stress-strain relationships within a compact can be well defined and an homogenous bonding mechanism assumed. However, the nature of stress relief distribution would place a constraint on such a postulate.

Investigations carried out under static conditions must be reviewed in the light of limitations placed on the system by such conditions. The most important differences, when compared to single punch or rotary press operations, are those of low compaction pressure, extended dwell times and inhibition of radial pressure release on ejection. The latter plays a particularly important role in tablet mechanics and will be dealt with more comprehensively in the section on dynamic systems. However, under the static conditions employed in this study where it was assumed that energy release occurred only in a uniaxial direction, polyethylene alone achieved some degree of cohesion even at very low pressures as evidenced by the production of a cohesive compact. Under dynamic conditions, even at relatively high pressures, cohesion could not be achieved. The significance of radial pressure release has been demonstrated by Amidon, Smith and Hiestand (1981) when, by the application of a three-dimensional punch and die system, they were able to release both radial and axial pressure simultaneously. Materials which capped under normal tableting conditions retained their integrity under biaxial release.

In terms of dwell-time, the static process was concerned with relatively long periods and such periods would need to be significantly reduced for differences in energy relationships to be observed. This was illustrated in TABLE 3.5. where an approximate five-fold increase in dwell time produced similar energy profiles.

3.1.1.4. Sequential Compaction

The manner in which a compact deploys energy during the decompression stage will clearly affect post compaction properties such as tablet strength, friability and disintegration. One method of evaluating the extent to which a compact relaxes once the load has been removed is to submit it to a further one or more sequential compactions while retaining the compact within the constraints of the die. A comparison of the energies involved during 1st and 2nd compactions is given in Tables 3.1. and 3.2. To ensure that an optimised recovery time elapsed before recompression, secondary and subsequent force displacement curves were generated at 1, 5, 10 and 20 minute recovery times after the first compression. From such profiles it was obvious that, where applicable, complete elastic recovery was attained after as little as one minute for all compression cycles except the primary cycle. Consequently, a five-minute recovery time was selected.

Table 3.5.

Energy Distributions during 1st Compaction Cycle of Lactose (90-125 microns) - Polyethylene (180-250 microns) Mixtures, Compacted at 4KN and 2, 5 and 10mm min^{-1}, Energy in Joules x 10^{-2}

Sample		2mm min^{-1}	5mm min^{-1}	10mm min^{-1}
100% Polyethylene				
	Total:	1.86	1.75	1.77
	Plastic/Brittle:	1.34	1.22	1.21
	Elastic:	0.54 (29.0)	0.53 (30.3)	0.56 (31.6)
75% Polyethylene				
	Total:	1.76	1.74	1.81
	Plastic/Brittle:	1.26	1.24	1.28
	Elastic:	0.50 (28.4)	0.50 (28.7)	0.53 (29.3)
50% Polyethylene				
	Total:	1.63	1.61	1.64
	Plastic/Brittle	1.18	1.14	1.15
	Elastic:	0.50 (29.8)	0.47 (29.2)	0.49 (29.9)
25% Polyethylene				
	Total:	1.47	1.47	1.49
	Plastic/Brittle:	1.08	1.08	1.11
	Elastic:	0.39 (26.5)	0.39 (26.5)	0.38 (25.5)
10% Polyethylene				
	Total:	1.34	1.36	1.38
	Plastic/Brittle	0.99	1.00	1.00
	Elastic:	0.35 (26.1)	0.36 (26.5)	0.38 (27.5)
100% Lactose				
	Total:	1.30	1.34	1.34
	Plastic/Brittle:	0.96	0.98	0.97
	Elastic:	0.34 (26.2)	0.36 (26.9)	0.37 (27.6)

The resultant energy relationship indicated that, on the second compaction, a further slight decrease in void volume had occurred even though the total energy involved in the second compaction exceeded that recovered from the first. It would be likely that the greater percentage of the former would be involved with elastically deforming the compact to the same extent as that regained during the first decompression stage. The appearance of hysteresis in the FD curve of the second compression cycle supported the conclusion that some further slight compaction had occurred. Such a prediction was supported by data generated at both 4 and 8KN loadings.

On adding increasing amounts of polyethylene to lactose, a similar energy distribution was observed at concentrations of polyethylene at 50% and below.

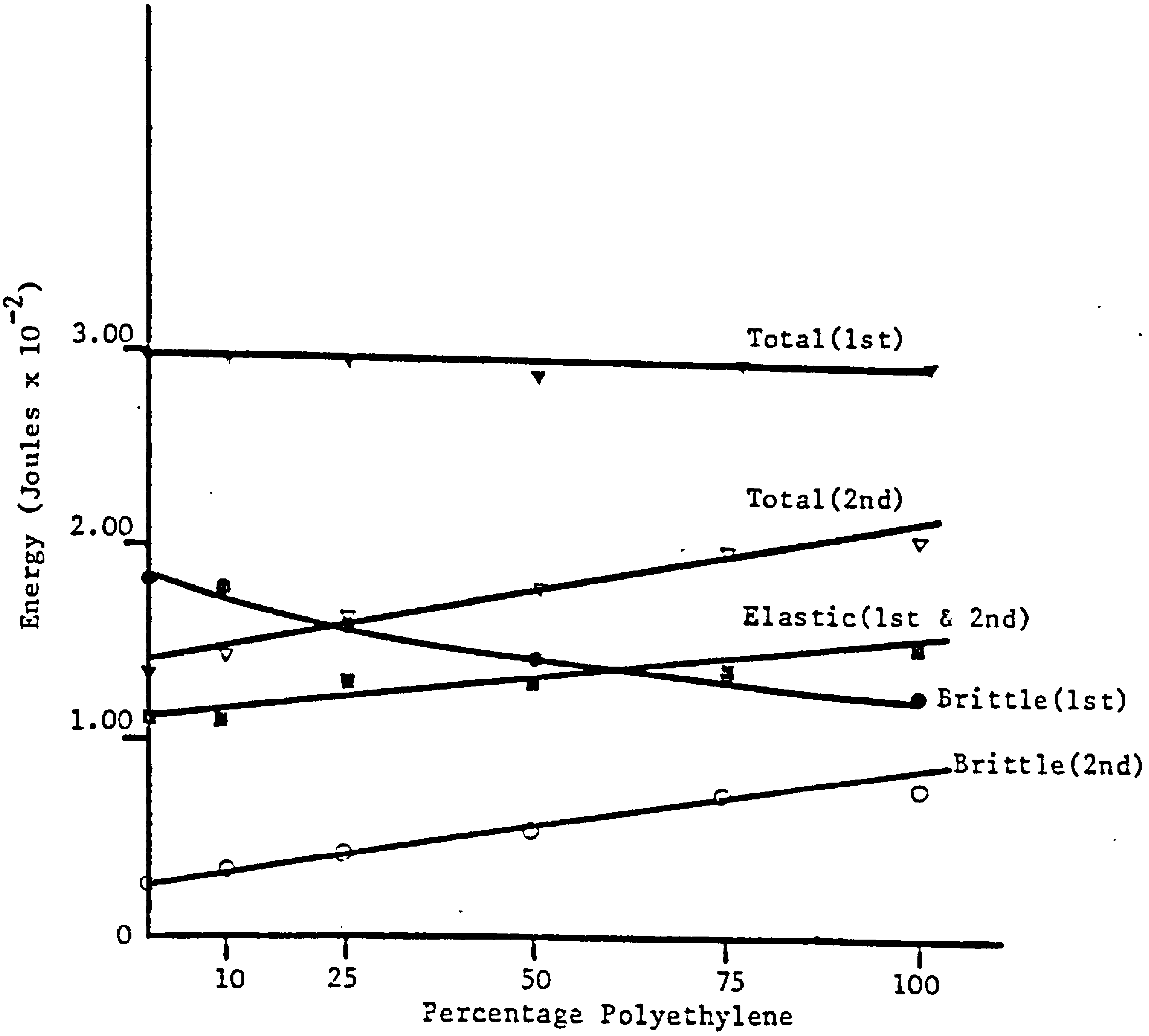
On applying a 4KN load to mixtures of 75% or more of polyethylene, the elastic and plastic/brittle component began to merge. Such evidence, plus the almost superimposable nature of the accompanying FD curves, indicated that compression energy was now all but completely concerned with elastic deformation and recovery.

During subjections of the same dilution to loads of 8KN greater contributions from the viscoelastic component were observed, even at the lowest polyethylene content studied. In all instances energies recovered after 1st and 2nd compactions were essentially identical. FIG.3.8. represents graphically the relationships between the various energy components as the polyethylene content changes.

The effect of further sequential compaction, to a total of

FIG.3.8.

1st and 2nd Compactions(8KN/2mm min^{-1})
Using 45 micron Lactose



12 cycles, is illustrated in FIG.3.9. where it was seen that little further permanent work was done on the material(s) after the first compaction.

This latter condition was reinforced by submitting compacts to an initial compression of 4KN followed by a second of 8KN. Assuming that, at the lower load, bonding would be complete after the first compaction, then the effect of a further compaction of 8KN would be additive, the whole being equivalent to a single compression of 8KN. Comparison of the data in Tables 3.1. and 3.2. with that of Table 3.6. showed this to be the case, bearing in mind that elastic recovery at 4KN must be subtracted from the total at 8KN. Such an additive effect tended to exist at polyethylene concentrations up to and including 75%, above that the viscoelastic nature of the polymer dominated the compaction process.

Overall, the employment of static compaction has led to an understanding of the effects of particle size, compression force and compression speed on the behaviour of single system and binary mixtures of brittle and elastic components. Such findings have been reported by Jackson, Ridgway and Rubinstein (1982).

3.2. Sodium Chloride and Polyethylene as Single Components and Binary Mixtures

3.2.1. Interpretation of Behaviour

3.2.1.1. Modification of Energy Distributions - Effects

In the case of a material such as sodium chloride (chosen to represent the alkali halide series) plastic deformation on compaction would result in a continuous bonding process dependent upon electrostatic interactions. The density of

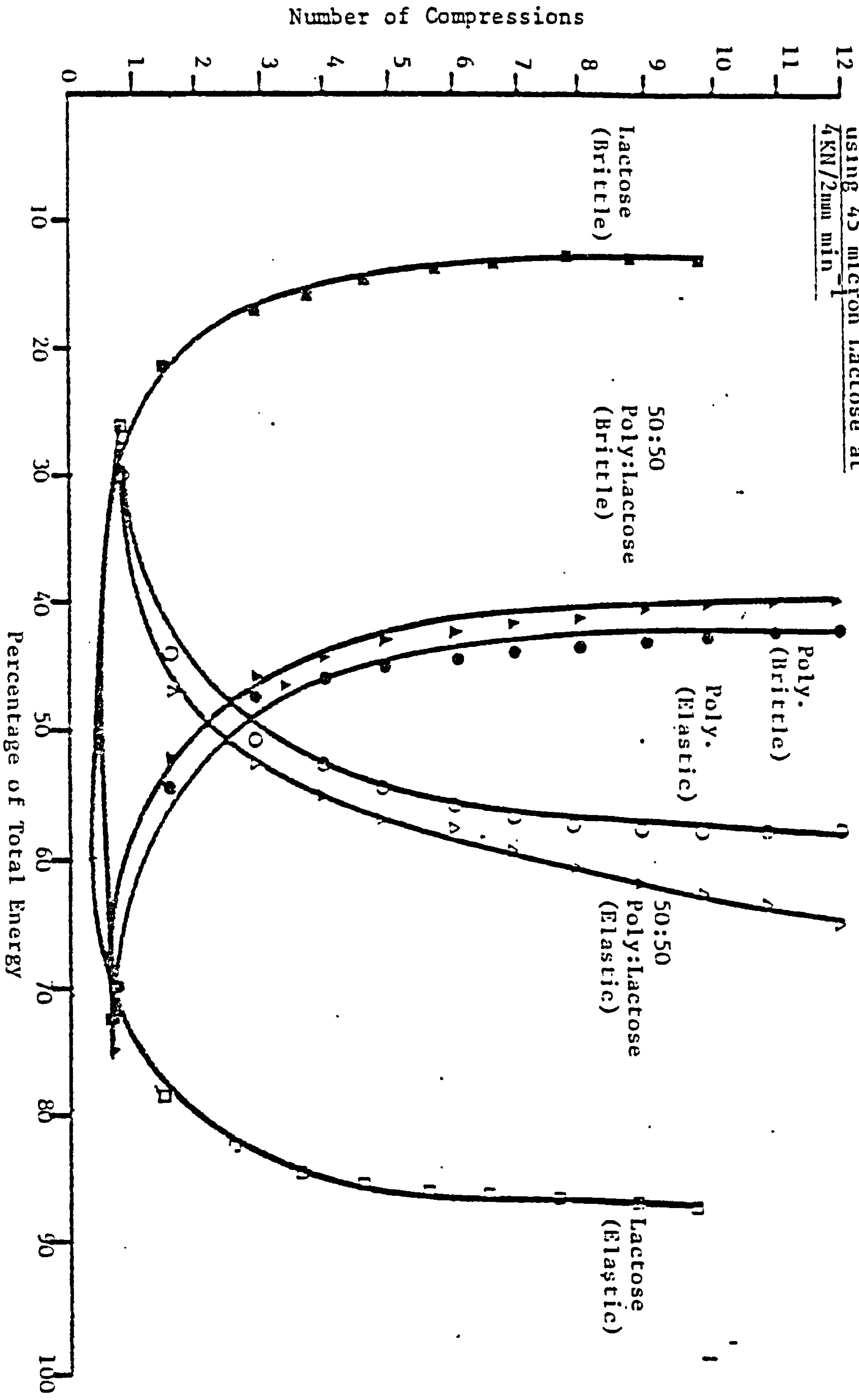


FIG. 3.9. Sequential Compaction: using 45 micron Lactose at 4KN/2mm min^{-1}

Table 3.6.

Energy Distributions during 1st Compaction Cycle of Lactose (45-63 microns) - Polyethylene (180-250 microns) Mixtures, compacted at 4KN and 2mm min^{-1} then at 8KN and 2mm min^{-1}, after the compound had recovered. Energy = Joules x 10^{-2}

Sample	4KN	8KN
100% Polyethylene		
Total:	1.86	2.08
Plastic/Brittle:	1.34	0.58
Elastic:	0.52 (30.0)	1.50 (72.1)
75% Polyethylene		
Total:	1.45	2.01
Plastic/Brittle:	1.00	0.59
Elastic:	0.45 (31.0)	1.42 (70.6)
50% Polyethylene		
Total:	1.25	1.86
Plastic/Brittle:	0.83	0.60
Elastic:	0.42 (33.6)	1.26 (67.8)
25% Polyethylene		
Total:	1.19	1.92
Plastic/Brittle:	0.85	0.65
Elastic:	0.34 (28.6)	1.27 (66.1)
10% Polyethylene		
Total:	1.22	1.91
Plastic/Brittle:	0.89	0.73
Elastic:	0.33 (27.0)	1.18 (61.8)
100% Lactose		
Total:	1.25	1.96
Plastic/Brittle:	0.91	0.84
Eastic:	0.34 (27.2)	1.12 (57.1)

such interactions would be controlled by the net effects of attraction and repulsion of ions. Any constraint placed on either (a) the amount of energy available for promotion of plastic flow or (b) the net energy which controlled the degree of bonding arising during the stress relaxation period, would give rise to significant changes in compaction properties. Three major modifying contributions are visualised when a plastic material (sodium chloride) is diluted with a component which has a low modulus of elasticity (polyethylene). Firstly, the elastic component preferentially absorbs energy leading to reduced bonding energy. Secondly, polyethylene physically deforms during compression to increase interstitial contact and thus reduces sodium chloride interparticulate contact. Finally, significant post compaction elastic recovery by polyethylene would result in bond fracturing of sodium chloride. In a sodium chloride-polyethylene system, where both particle shape (see scanning electron photomicrographs) and size are similar and where furtherance of compaction relies upon particle-particle contact, then all three of the postulates mentioned above would contribute. How such effects would contribute would depend not only on the spatial arrangement and rearrangement of the minor component (polyethylene) during the compaction process but also the distribution of polyethylene particles prior to entry of powder into the die. Unless highly efficient mixing of materials was attained areas of high and low density polyethylene would give rise to nonhomogenous stress-strain profiles during compression.

The availability of coloured (red) polyethylene facilitated ease of mixing and allowed an optimum mixing time (20 minutes in a tumble mixer) to be defined. Visual observation was supported by electron microscopy of random samples, above a particle size ceiling (355-500 microns) mixing of sodium chloride and polyethylene could not be achieved due to the exclusion of the latter from the void spaces of large particles of sodium chloride.

3.2.1.2. The Force Displacement Relationship

Cole, Rees and Hersey (1975) used a technique of static compaction similar to that described in this study in their evaluation of the powder consolidation properties of sodium chloride. With an Instron Universal Testing machine, operating at a cross head speed of 1mm min^{-1} and pressure up to 60MNm^{-2} they failed to distinguish between the consolidation behaviour of sodium and potassium chloride and that of lactose. However, they were able to postulate on the plastic flow behaviour of materials and referred to stress relaxation during compaction leading to void filling.

In the studies reported herein, materials were compacted in a punch and die set at cross head speeds between 2 and 20mm min^{-1} and at pressures of 56 and 112MNm^{-2}. Lower pressures and smaller tablet dimensions were employed than those reported in a similar investigation by Hersey, Cole and Rees (1974). FIGS. 3.10a, b and c illustrate the force-displacement relationship for sodium chloride with and without the addition of polyethylene (Force = 4KN, Cross-head speed = 2mm min^{-1}).

Powder consolidation for sodium chloride alone was

FIG. 3.10(a)

Force-Displacement Curves for Successive Compactions of Sodium Chloride (355 microns) Sensitivity of Displacement Measurement Increased After 1st Compaction

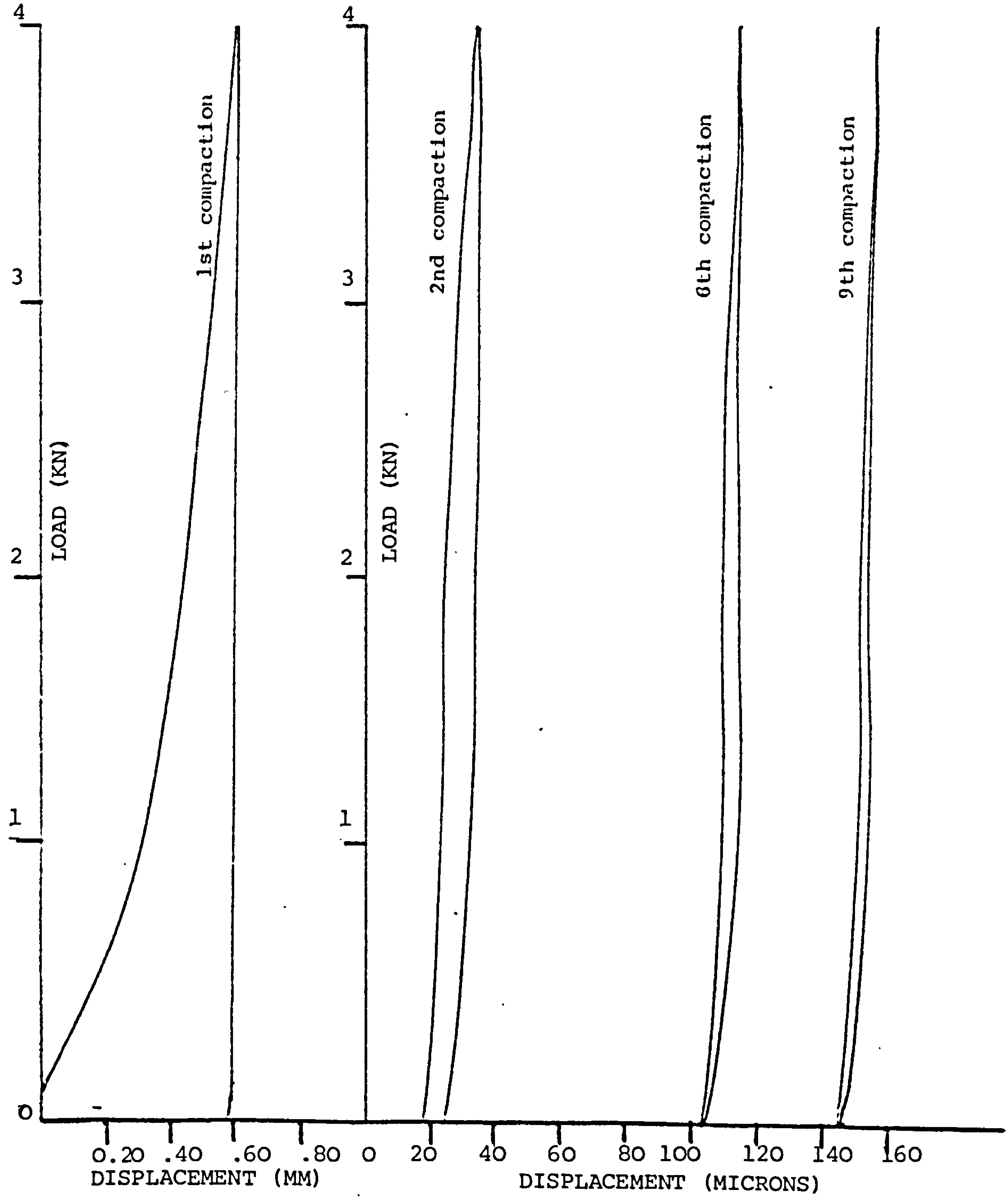


FIG. 3.10(b)

Force-Displacement Curves for Successive Compactions of Sodium Chloride plus 0.5% w/w Polyethylene. Sensitivity of Displacement Measurement Increased After 1st Compaction

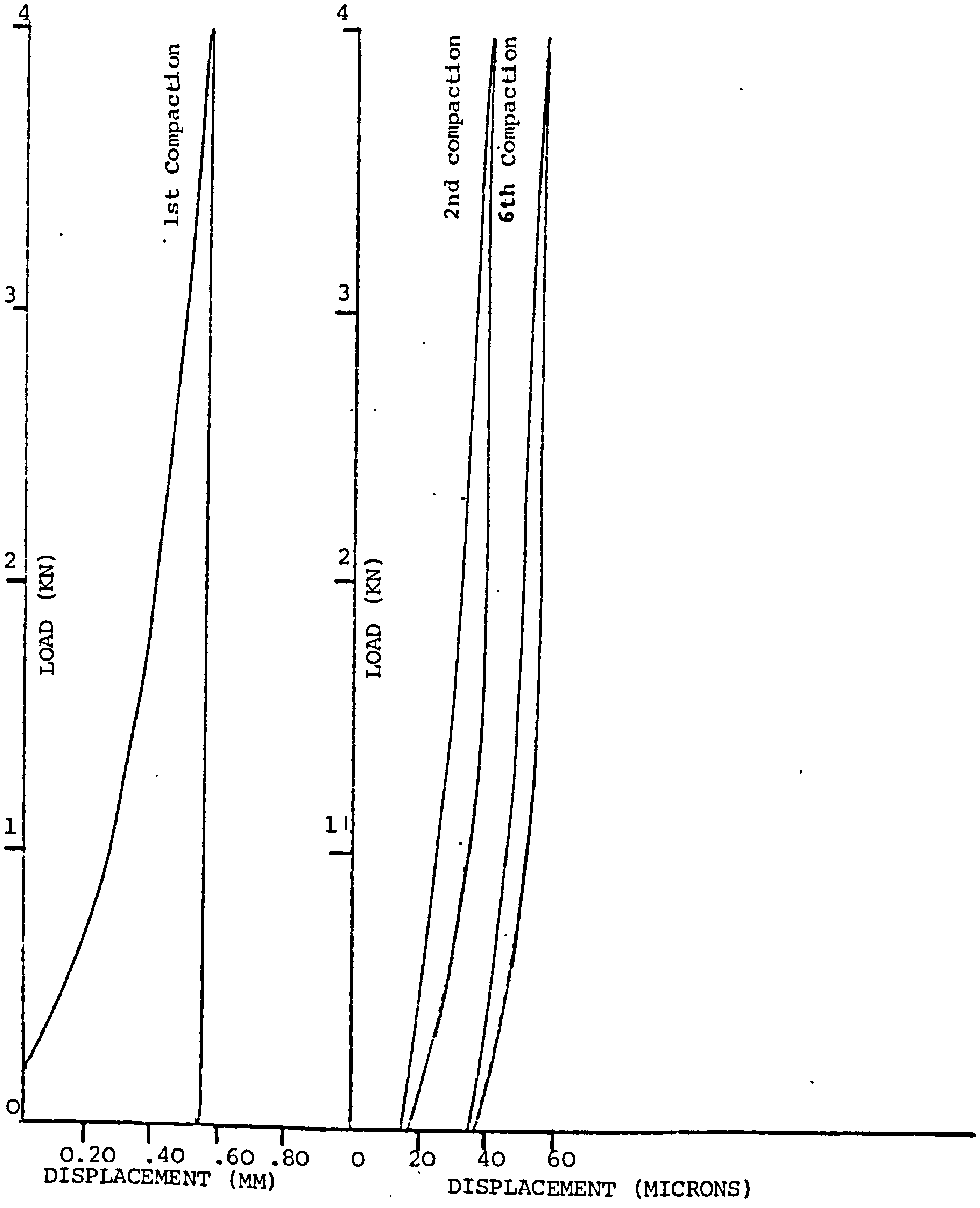
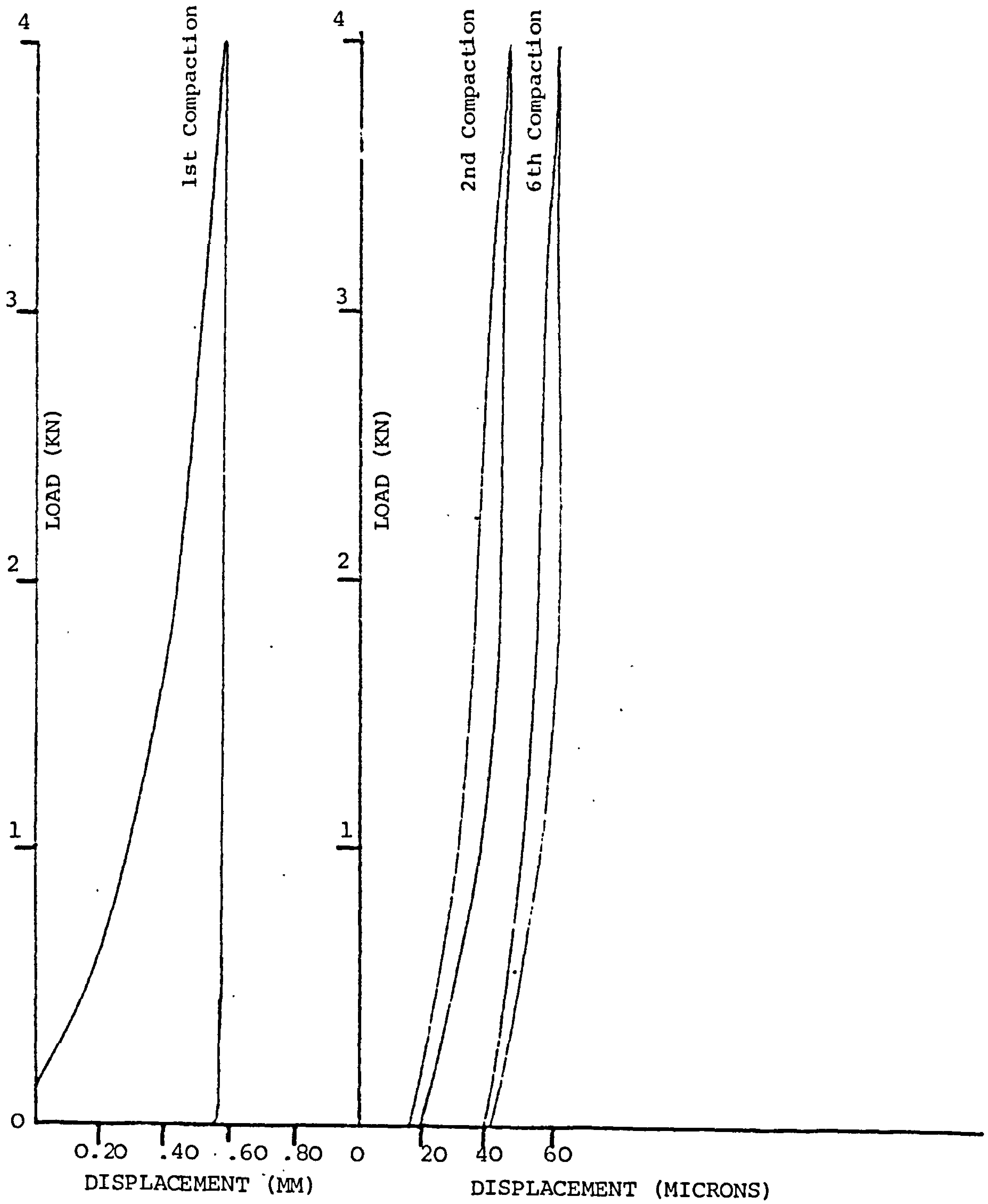


FIG. 3.10(c)

Force-Displacement Curves for Successive Compactions of Sodium Chloride plus 1% w/w Polyethylene. Sensitivity of Displacement Measurement Increased After 1st Compaction



significantly less than that for lactose with the bed supporting the load, without displacement, at the onset of compression. Once this initial stage was completed powder deformation occurred rapidly and, on decompression, only slight elastic recovery was observed.

Addition of 0.5 and 1% polyethylene to sodium chloride produced similar FD curves to those seen with sodium chloride alone. (The justification for the addition of such small quantities of polyethylene as compared to the much greater amounts added to lactose is explained in the section on dynamic compaction). Unlike studies on polyethylene-lactose systems, sequential compaction was discontinued after the sixth event since almost all work of compaction was completed during the first cycle.

When sodium chloride and sodium chloride plus 1% polyethylene are subjected to higher loads, the powder consolidation commenced with the onset of pressure, as shown in FIGS.3.11a and b.

In addition, although identical weights of material were compressed at both 4 and 8KN loads, compact thickness was reduced at the higher load resulting in a larger displacement of the top punch.

3.2.1.3. The Force-Time Relationship

Conclusions derived from the FD curves were substantiated by data on energy distribution, as outlined in Table 3.7. At 4KN load and cross head speed of 2mm min^{-1} the absence of elastic recovery during decompression was confirmed from the energy profile data with zero energy recovered post compaction. Similar behaviour was observed with and without the addition of polyethylene. Thus, it was inferred that

FIG. 3.11(a)

Force-Displacement Curve for Successive Compactions of Sodium Chloride (355 microns) Sensitivity of Displacement Measurement Increased After 1st Compaction

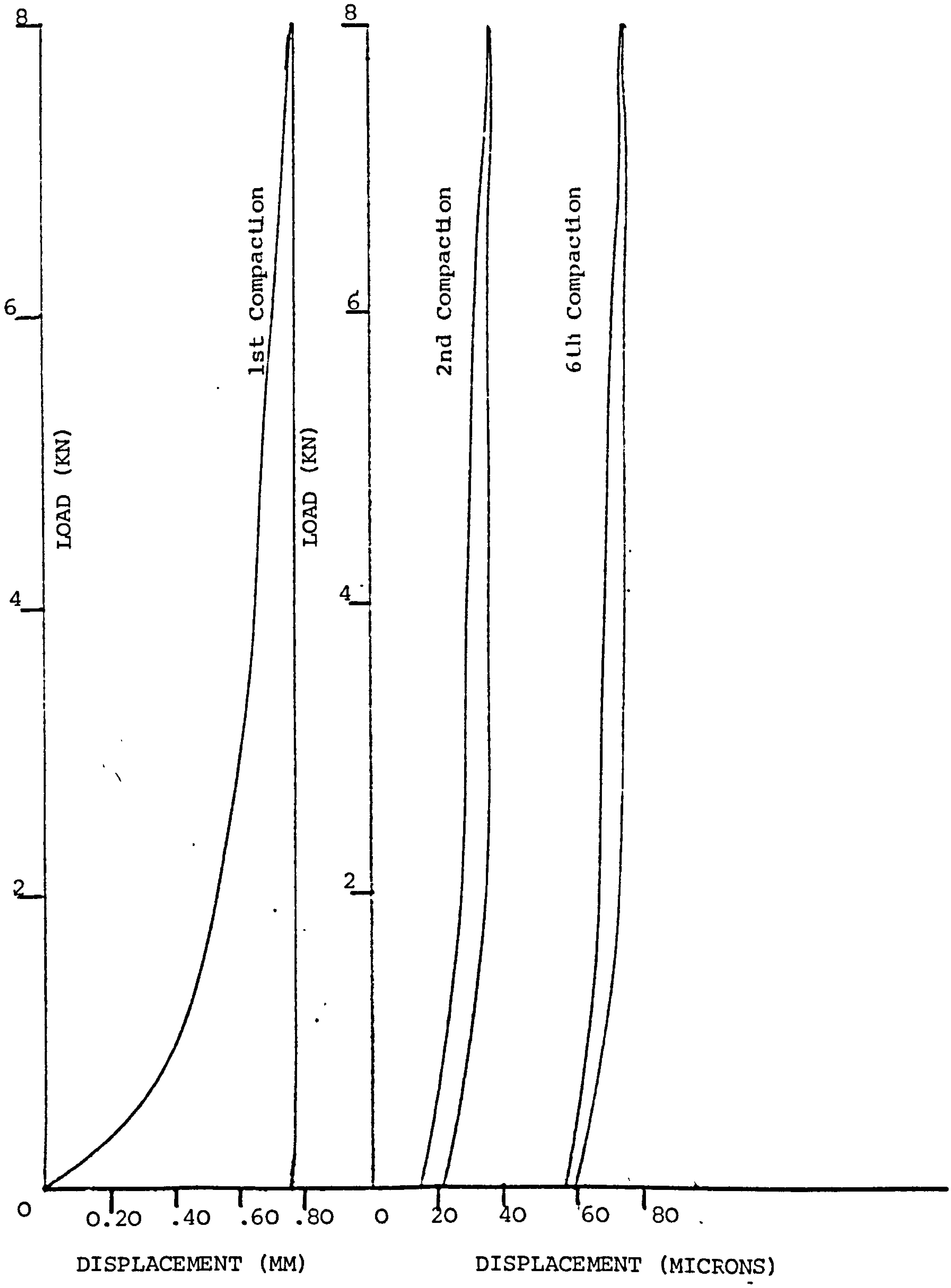


FIG. 3.11(b)

Force-Displacement Curves for Successive Compactions of Sodium Chloride plus 1% w/w Polyethylene. Sensitivity of Displacement Measurement Increased After 1st Compaction

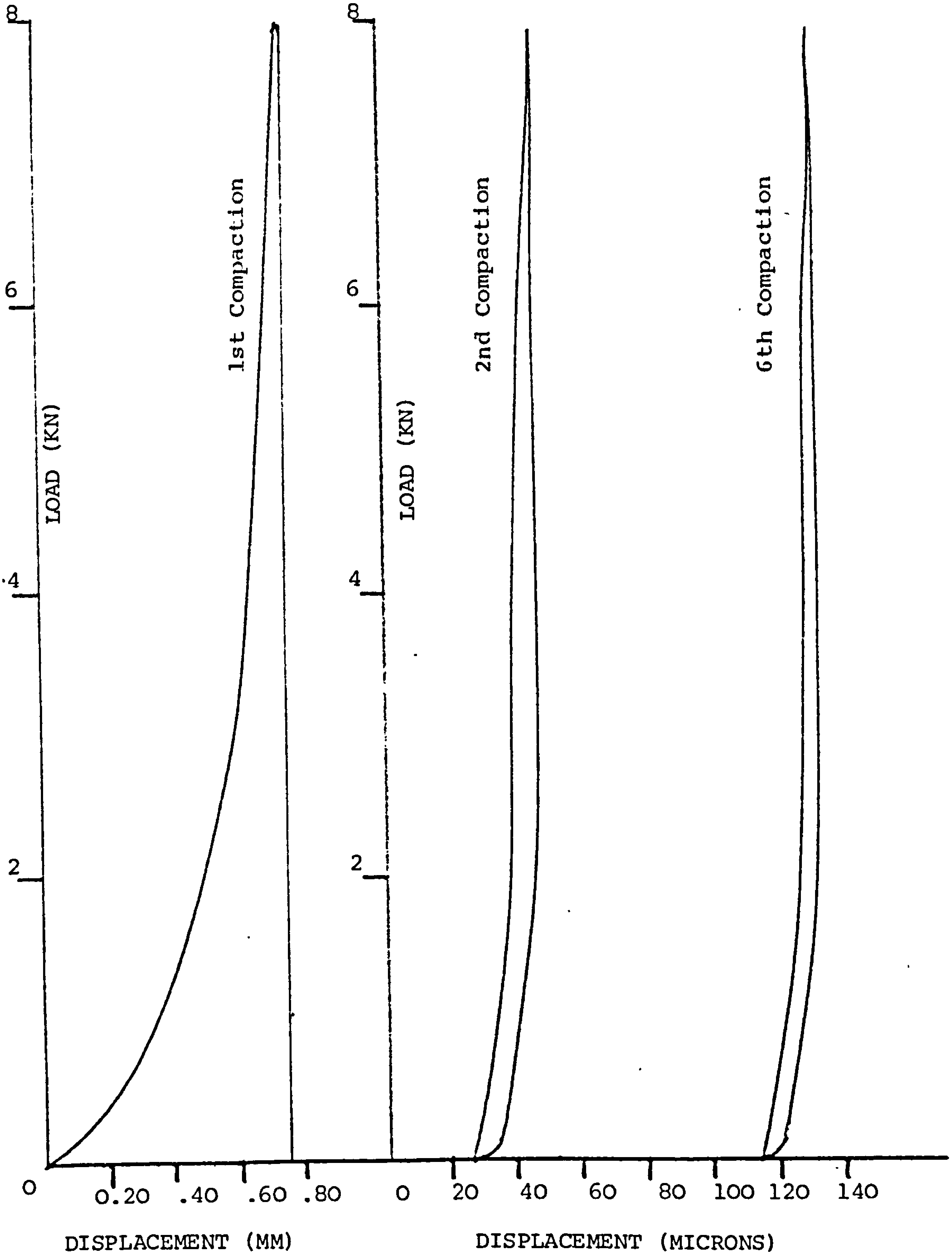


Table 3.7.

Energy Distribution during 1st and 2nd Compactions of Sodium Chloride (355-500 microns) - Polyethylene (355-500 microns) Mixtures compacted at 4KN and 2, 10 and 20mm min^{-1}, Energies in Joules x 10^{-2}.

Sample	4KN/2mm min^{-1}		4KN/10mm min^{-1}		4KN/20mm min^{-1}	
	1st Comp.	2nd Comp.	1st Comp.	2nd Comp.	1st Comp.	2nd Comp.
Sodium Chloride						
Total:	1.31	0.06	1.24	0.05	1.18	0.05
Plastic/Brittle:	1.31	0.06	1.24	0.04	1.13	-
Elastic:	-	-	-	0.01	0.05	0.05
Sodium Chloride + 0.5% Polyethylene						
Total:	1.27	0.06	1.23	0.06	1.22	0.06
Plastic/Brittle:	1.28	0.06	1.22	0.04	1.17	-
Elastic:	-	-	-	0.02	0.05	0.06
Sodium Chloride + 1.0% Polyethylene						
Total:	1.31	0.07	1.25	0.06	1.23	0.08
Plastic/Brittle:	1.32	0.07	1.25	0.04	1.15	-
Elastic:	-	-	-	0.02	0.08	0.08

the energy required to exceed the elastic limit of sodium chloride, and hence initiate plastic deformation, was small. Once this had been achieved lattice distortion would lead to particle-particle bonding. Lattice distortion would arise as a result of energy activation of screw dislocations or vacancies, usually Schottky or Frenkel defects, a schematic drawing of the formation of such defects being shown in FIG.3.12. Schottky defects can be imagined as arising from

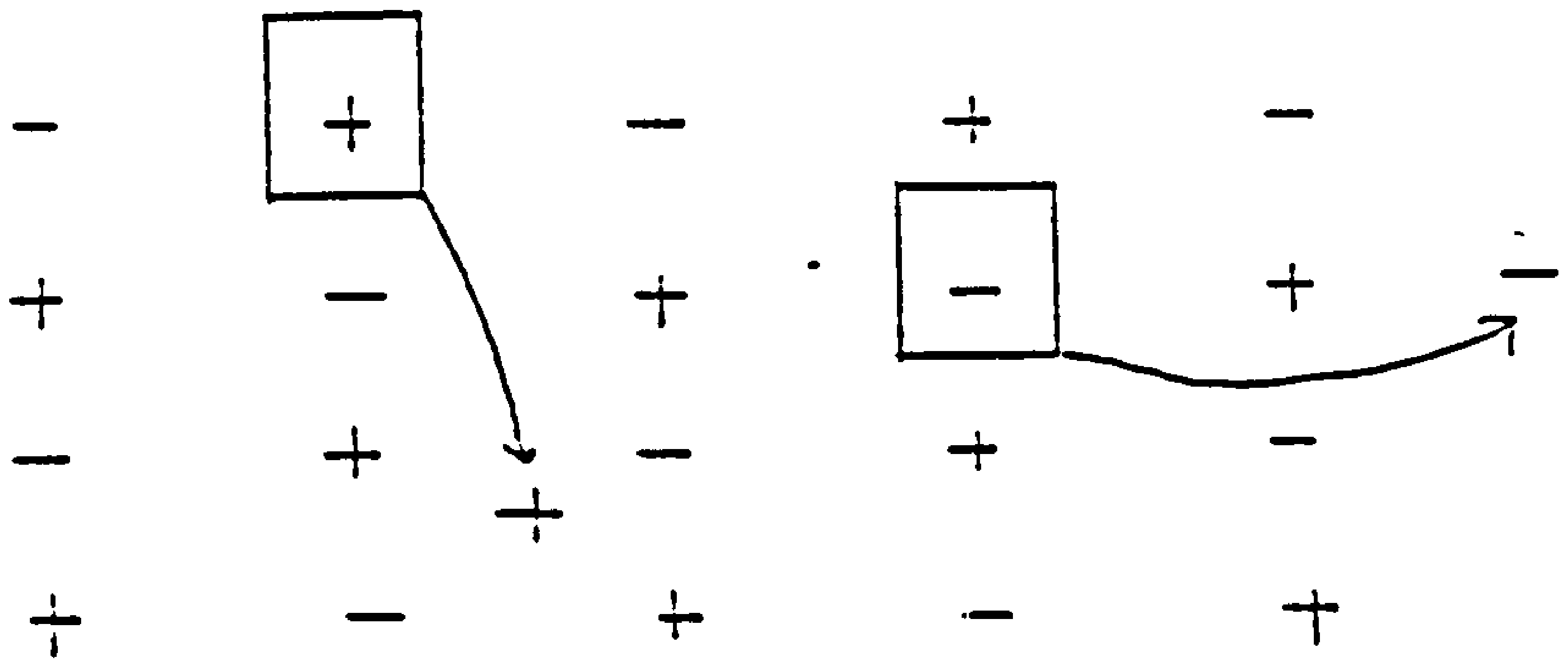


FIG. 3.12. Schematic drawing of the formation of Frenkel and Schottky defects. (After Carstensen 1980).

moving a pair of ions from the interior of the crystal to the surface or of introducing a higher valent ion, such as Ca^{++}, into the lattice. With a crystal considered as a constant volume system, equilibrium would be achieved when the Helmholtz energy is at a minimum, and at equilibrium, there would be a certain number of crystal vacancies such that

$n = N\exp\left(\frac{-E}{kT}\right)$

where n = vacancies formed by moving molecular units to the surface,

N = Lattice unit volume

k = the Boltzman constant

T = Temperature

E = the energy for a pair of ions being moved to the surface or a pair of ions formed in the lattice. It can be visualised that the input of energy during compression would increase n and allow glide planes to be set up within the crystal with short range forming and breaking of bonds until a further stage of equilibrium would be achieved. In the case of interparticle bonding the system can be considered to be, potentially, one single crystal with infinite distance between ions. Cohesion would evolve from a combination of complex electrostatic interactions involving ionic, Van de Waals and London forces. As the interparticle distances were reduced, each type of interaction would play a different part in achieving a stable system. Thus any increase in the energy put into the system would lead to an increase in E in the above equation and hence an increase in n. However, the introduction of polyethylene, a compound of organic structure and one capable of extensive energy absorption giving rise to long range energy diffusion effects, would act as an energy sponge thus reducing that available for sodium chloride bonding. From the data in Table 3.7. energy partition would appear to be overwhelmingly in favour of bonding at cross head speeds of 2 and 10mm min^{-1}. However, at the highest speed (20mm min^{-1}) some effects of reduced dwell time are observed and elastic recovery takes place after both first and second compactions. The manner in which low dwell times accentuate this effect is dealt with in the section on dynamic compaction.

However, further study of the system suggested that, although elastic recovery of polyethylene was not significant when viewed as a function of the force displacement curves its importance in inhibiting interparticle bonding was decisive. Tables 3.8. and 3.9. illustrate the effects of compression variables on diametral crushing strength.

The results indicated that, even at the highest load and lowest dwell-time, the addition of 0.5% polyethylene reduced the crushing strength of sodium chloride to zero. The absence of any measurable energy of recovery would indicate that, under the conditions employed in this study, the viscoelastic

Table 3.8.

Crushing Strength of Tablets after Compaction (6 times at 4KN and 2, 10 and 20mm/min^{-1}) Crushing Strength in Kg.

Sample	4KN/2mm min^{-1}	4KN/10mm min^{-1}	4KN/20mm min^{-1}
Sodium Chloride	3.6	2.8	3.0
Sodium Chloride* + 0.5% Polyethylene	Zero	Zero	Zero
Sodium Chloride** + 1.0% Polyethylene	Zero	Zero	Zero

* At 0.5% polyethylene, tablet integrity was retained on removal from the die but values registered when submitted to diametral testing were less than the minimum registration value of the tester.

**At 1.0% polyethylene, tablets could not be removed from the die without disintegration occurring during the operation.

nature of polyethylene was such that is was able to absorb a very significant proportion of the total energy imparted to the system on compression.

The objectives behind the above static compaction studies were to investigate single component and binary systems of plastic, brittle and elastic materials at low forces and compaction speeds and hence derive information about fundamental compaction mechanisms not overshadowed by factors which would dominate more normal compaction conditions. Such factors.would include low dwell time, higher loads and dual force release (i.e. radial in addition to axial), and the manner in which such factors attain increased importance in the dynamic system becomes apparent in the following section.

Table 3.9.

Energy Distribution during 1st and 2nd Compaction of Sodium Chloride (355-500 microns) - Polyethylene (355-500 microns) Mixtures Compacted at 8KN and 20mm min^{-1}, Energies in Joules x 10^{-2}.

Sample	1st Compaction	2nd Compaction
Sodium Chloride		
Total:	2.23	0.04
Plastic/Brittle:	2.23	-
Elastic:	0	-
Sodium Chloride + 0.5% Polyethylene		
Total:	2.23	0.04
Plastic/Brittle:	2.23	-
Elastic:	0	0.04
Sodium Chloride + 1.0% Polyethylene		
Total:	2.23	0.04
Plastic/Brittle:	2.23	-
Elastic:	0	0.04

* Diametral Crushing Strength (in Kg) were 8, zero and zero for Sodium Chloride alone, 0.5 and 1% Polyethylene respectively.

4. COMPACTION OF POWDERS - The Dynamic System

4.1. Alkali Metal Halides and Polyethylene as Single Components and Binary Mixtures

4.1.1. Single Component Halides

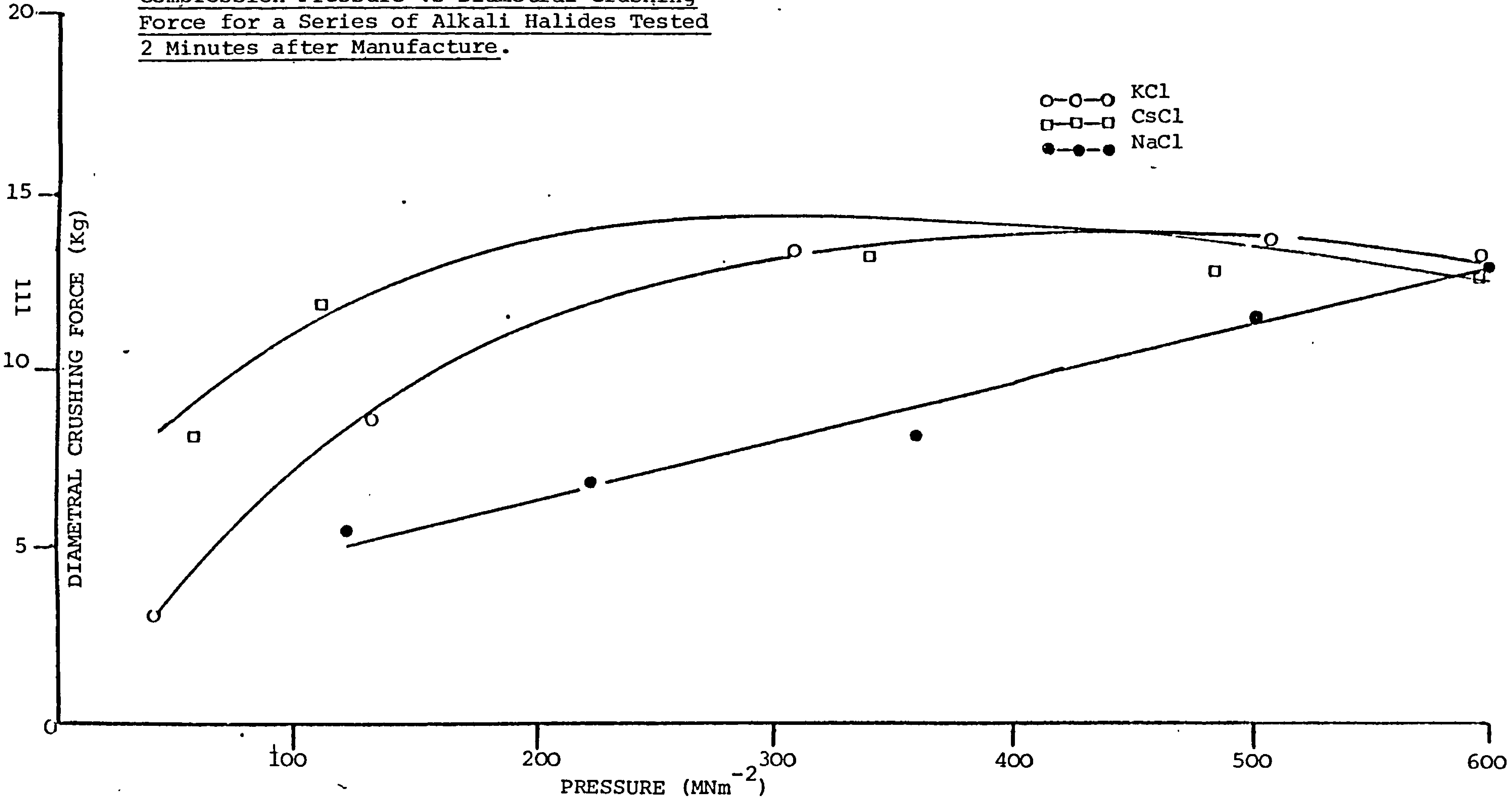
The compaction properties of sodium chloride have been studied by several workers and its behaviour as a material which undergoes plastic deformation when submitted to stress in a confined space has been extensively reported.

By monitoring changes in specific surface area, pore volume and extent of compaction with pressure, Hardman and Lilley (1973) concluded that, unlike sucrose where brittle fracture occurred, sodium chloride compacted via a plastic deformation mechanism. Hersey, Cole and Rees (1974) and Cole, Rees and Hersey (1975) agreed with the above conclusions, extending the concept of plastic deformation to include potassium chloride in addition to sodium chloride. By applying Heckel plots to their data, they decided that, of the two chlorides, potassium deformed more readily than sodium by virtue of its lower yield strength. In the 1975 publication they underlined differences between the two halides by showing how, at the same compaction pressure, potassium chloride suffered a more rapid reduction in pore volume than sodium chloride. Summarising, they stressed the importance of monitoring strength measurements in studies on compaction behaviour as a means of evaluating the degree of bonding.

The results of such an evaluation are shown in FIG.4.1. where variations in diametral crushing strength with punch pressure are compared. Tablet weights were adjusted so that all were compressed to the same thickness, and compaction pressures from 50 - 600MNm^{-2} were chosen since studies involving dilution with an elastic component (see later) were expected to show gross differences in bonding characteristics. Crushing strength was preferred to tensile strength

FIG. 4.1

Compression Pressure vs Diametral Crushing Force for a Series of Alkali Halides Tested 2 Minutes after Manufacture.



as a yardstick for bonding since, at high compaction pressures, stress relaxation would be expected to produce very hard tablets possessing non-idealised breaking behaviour.

Tablet dimensions were monitored, using a micrometer, immediately on ejection and crushing forces were determined either immediately on ejection or after a suitable equilibration period. Crushed tablets were retained for microscopic examination (see later).

All the alkali halides attained similar crushing strengths at the maximum applied force but rates of attainment varied, sodium chloride displaying a linear increase in force with pressure while the remaining two plateaued at lower compaction pressures. The findings agree with those of Cole, Rees and Hersey (1975) with regard to differences in compaction behaviour of sodium and potassium chloride although the compaction pressures they applied were lower. In addition, they tested their crushing strengths after a time lapse of 7 weeks during which strength increase by stress relaxation would have occurred. They explained the difference in behaviour of the two halides in terms of conflicting yield strength but made no attempt to explore the reasons for such differences.

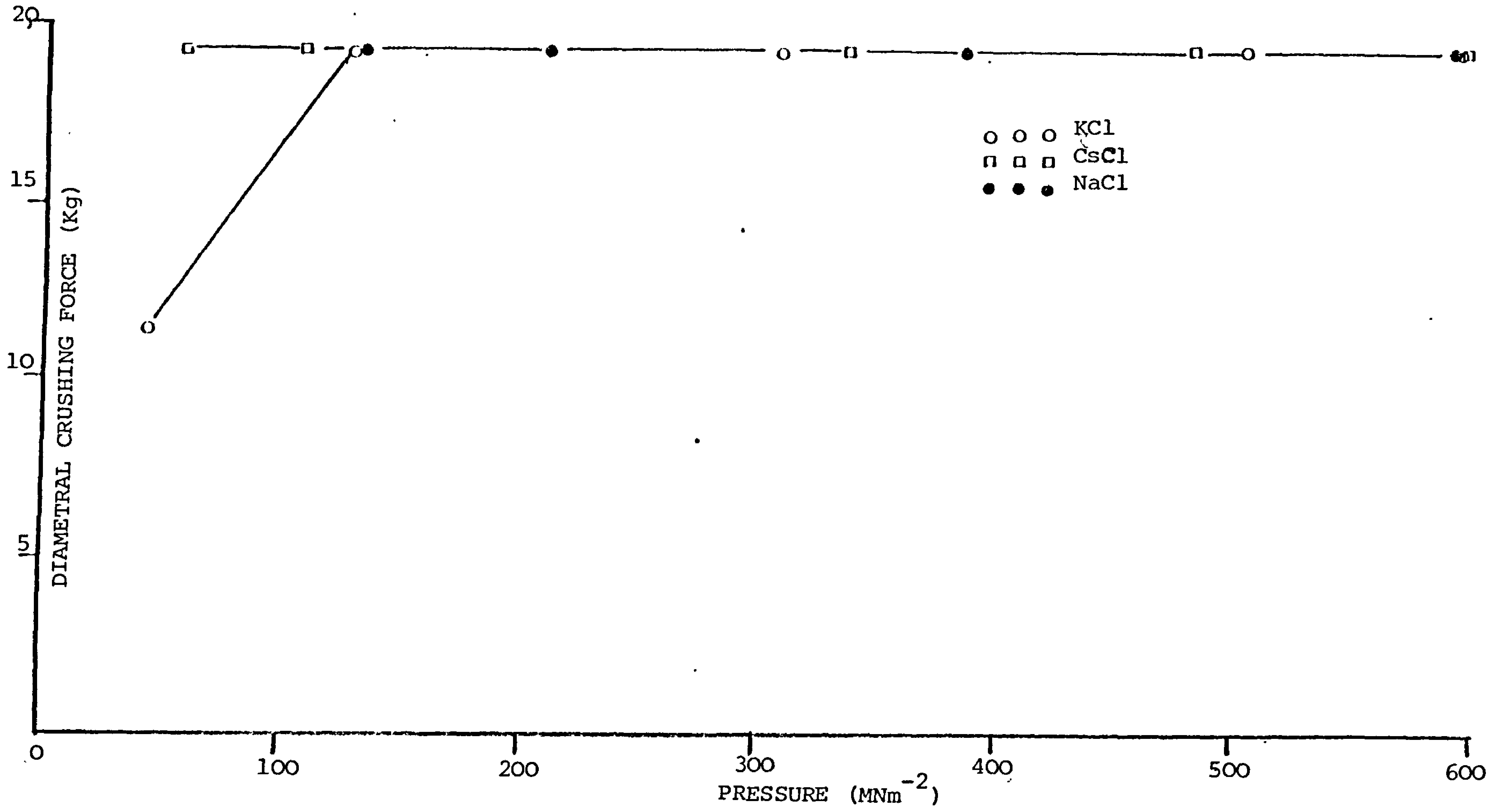
Yield point and yield strength are defined as "the stress at which a marked increase in deformation takes place without increase in the load" and "the stress at which a material exhibits a specified permanent set" respectively (Handbook of Chemistry and Physics, 62 Edition 1981-82). As could be observed from static compression studies detailed in Section 3a yield point would be hard to define although an approximate value could be estimated. Yield strength would be even more difficult to define, especially in the case of alkali halides where strength continued to increase with time. Any difference in behaviour must be a function of lattice alignment and electrostatic interaction during and post compaction although the issue would still be clouded by the extent of lattice dislocation within crystals, such dislocations have a localised energy associated with them made up of an elastic strain energy and a core energy (Johnston 1962) and would be thermodynamically unstable. Thus, ideally, any fundamental study on plastic deformation should be related to single crystal science with the lattice defined before and after. Such a study has yet to be initiated although Burt and Mitchell (1981) have gone some way towards this by studying the effects of crystal defects on dissolution. However, assuming that dislocation content would be essentially the initiation factor for plastic flow, then interionic distance and crystal lattice type could be expected to play a dominant role in lattice and inter particle bonding.

The extent to which a material bonds depends upon the extent to which a balance of attractive and coulombic forces can be achieved. This, in turn, is governed by the ionic radii of both anions and cations present in the lattice. Consequently, it seems probable that, because of their material structures, potassium and caesium chlorides would be more prone to lattice disruption and hence a greater degree of bonding. On the other hand, sodium chloride would be expected to retain its internal structure more easily so that total energy input would be more evenly divided between inter and intra particle bonding.

Alkali halides are known to undergo a time dependent increase in diametral crushing force, such an increase being illustrated by the data shown in FIG.4.2. Very significant increases in strength were observed, on tablets tested after a 10 day storage period, such that compaction pressures greater than 130MNm^{-2} produced tablets whose strength exceeded the measuring capability of the Heberlein testing equipment. Hardening of the same kind has been observed by both Rees and Shotton (1970) and Cole, Rees and Hersey (1975). The latter workers postulated that, in the case of a material such as sodium

FIG. 4.2

Compression Pressure vs Diametral Crushing Force for a Series of Alkali Halides Tested 10 days After Manufacture



chloride which deformed plastically on compaction an outer skin would be formed at the die wall. Energy absorbed by the material, during compaction, would be entrapped within this skin and allow a time dependent stress relaxation influence to operate. Such an effect would give rise to increased hardness. That such an effect does occur has been substantiated, to some degree, by Rue and Barkworth (1980). By comparing an increase in tablet strength with the count rate of acoustic emission activity coinciding with strength increase, they showed that most of the dislocation movement and plastic flow was dissipated within the first few minutes post compaction.

4.1.2. Binary Mixtures of Alkali Halides with Polyethylene

Stress-strain activity of crystalline solids, both during compaction and post ejection, will be conditional upon the amount of energy available to promote lattice movement.

The introduction of a diluent to such a solid, to produce a binary mixture, would succeed in modifying, to a greater or lesser extent, the tableting properties of that solid. Such has been shown to be the case but definitions of character, in more than a strictly empirical sense, have proved tenuous. Thus although Fell and Newton (1970) were able to predict the strengths of tablets prepared from different mixtures of lactose where the form was different but the particle size identical, they were unable to extend their predictions to mixtures containing spray dried and crystalline forms. A failure to predict tensile strengths of mixtures of phenacetin and dicalcium phosphate from a knowledge of those of the individual components led Newton, Cook and Hollebon (1977) to highlight the role played by formation pressures in the compaction process. More recently Sheikh-Salem and Fell (1981) have studied the relationship between tensile strength and densification of mixtures of sodium chloride.

With regard to individual materials they showed that bonding between sodium chloride crystals was stronger than that between lactose crystals. On proceeding to binary mixtures they observed that, irrespective of particle size, an increase in tensile strength of the mixtures was only perceived at sodium chloride concentrations in excess of 80%. The same authors (1981) studied the effect of magnesium stearate on time-dependent hardening of sodium chloride and indicated how a thin layer of lubricant could significantly effect the stress relaxation properties of sodium chloride tablets. This effect has also been observed by other workers (Jackson, Ridgway and Rubinstein, unpublished results).

Thus, addition of a small amount of material having a low Modulus of Elasticity (polyethylene) to a solid which deformed plastically (sodium or potassium chloride) could be expected to extensively reduce the bonding potential of the alkali halides. Such a reduction would be reflected in a corresponding lowering of diametral crushing strength. That this proved to be the case is shown graphically in FIGS.4.3. and 4.4.

At compaction pressures less than 250MNm^{-2} complete disintegration occurred on ejection from the die. Measurable cohesion was retained only at pressures in excess of 300MNm^{-2}. Time dependent stress relaxation did occur when tablet integrity was maintained but the overall strength was very much reduced in comparison to sodium chloride.

Static compression (see Section 3) has shown how, without the contribution of radial relaxation on ejection, similar mixtures had yielded cohesive compacts at very low pressures. By applying much higher pressures a greater degree of intra particle disruption and consequent bonding might be expected. That such was not the case reflected the importance of low dwell time and tablet ejection on

FIG. 4.3

Compression Pressure vs Diametral Crushing Force for Sodium Chloride (355 microns) With and Without 0.5% w/w Polyethylene

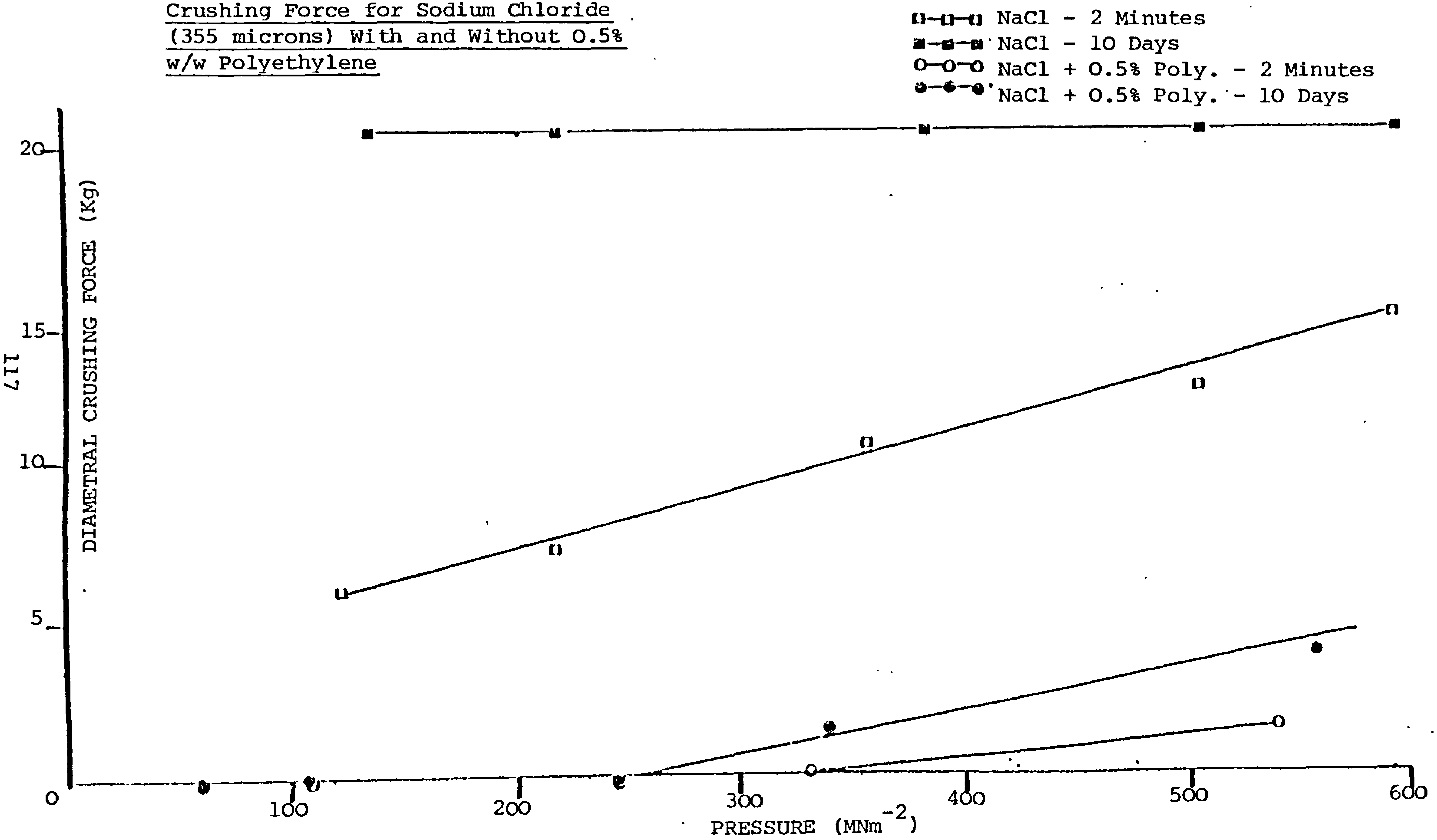
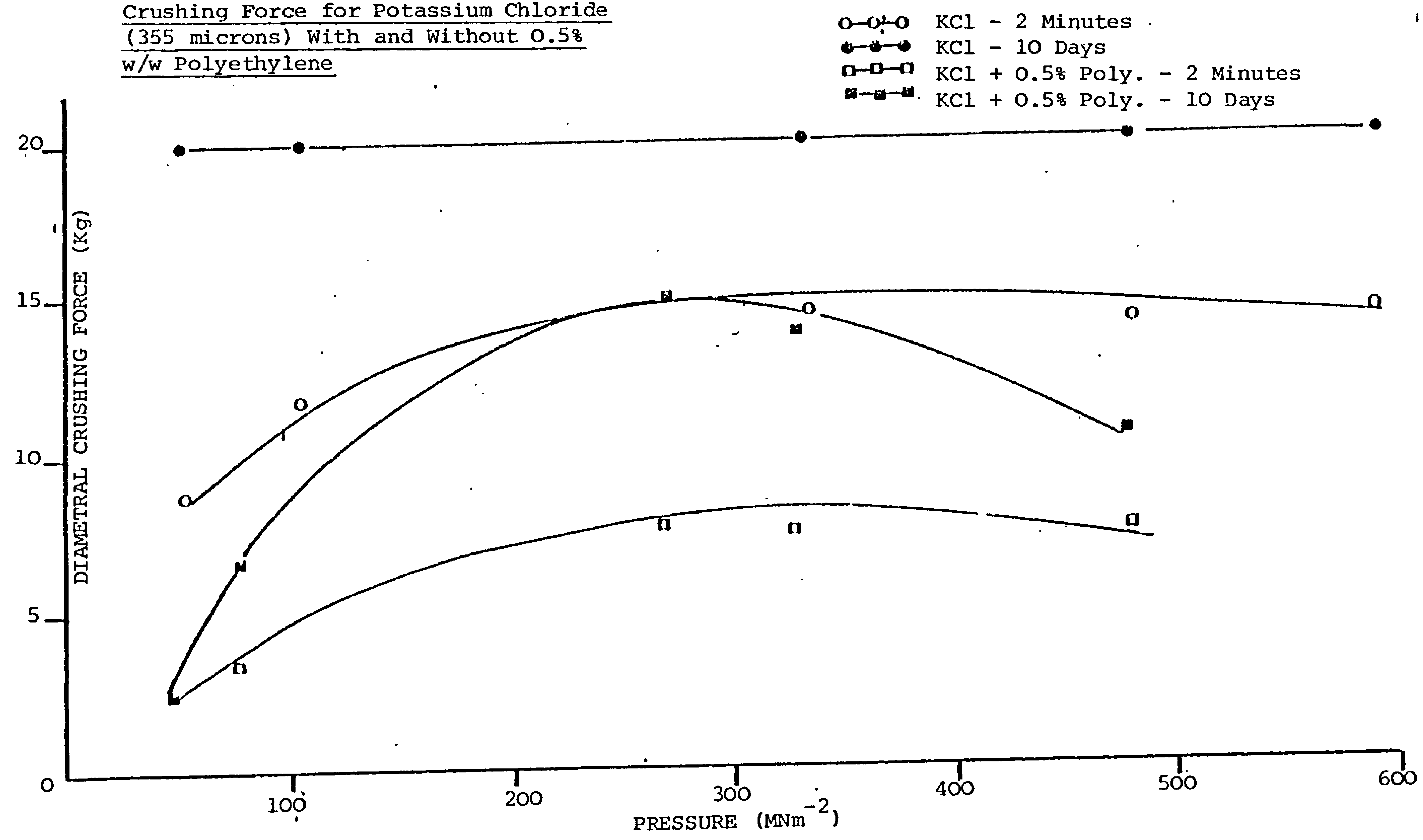


FIG. 4.4

Compression Pressure vs Diametral Crushing Force for Potassium Chloride (355 microns) With and Without 0.5% w/w Polyethylene



tablet cohesion. It seems likely that these two variables in conjunction with high compaction pressures would promote contributions to the overall mechanism. From all three qualifying mechanisms outlined in Section 3. at relatively low dynamic pressures energy absorbed by the viscoelastic component would be released on ejection causing three dimensional eruption of the weakly bonded tablet matrix. Such conditions would not favour either the formation or retention of a continuous outer skin. As compaction pressure increased, a reduction in surface contact of sodium chloride crystals can be envisaged as polyethylene physically deforms. Thus localised areas of weak bonding would exist giving rise to compacts having inherently low strength.

Further increases in compaction pressure eventually produced compacts where sufficient modification of crystal structure had occurred for cohesion to be retained on ejection. Where this was shown to be the case further strengthening of the compact occurred, on storage, as a result of time dependent stress relaxation behaviour.

In the case of potassium chloride, the effects observed were similar to those of sodium chloride except that plateauing noted with potassium chloride alone was mirrored with the addition of polyethylene. The results indicate that, providing sufficient energy has been absorbed, by potassium chloride, during compaction to maintain bonding on ejection, any contained energy will be dissipated to give a time dependent strengthening effect.

At high pressures a decrease in crushing strength of potassium chloride with pressure was consistently observed. Although unexpected it seems probable that potassium chloride suffers some brittle fracture at such pressures.

Scanning electron microscopy on tablets before and after crushing supported the conclusions of Cole, Rees and Hersey (1975) that an outer skin was formed during compaction which reduced elastic recovery. The continuity of such an outer skin is shown in FIG.4.5. Such continuity was not maintained in the presence of polyethylene. All three alkali halides sheared at the die wall in identical manners with consequent dissociation on ejection. The example shown in FIG.4.5. illustrates the surface topography 2 minutes after tablet ejection. No identifiable modification could be observed on storage for various time intervals.

That extensive rearrangement of crystalline structure occurred when sodium chloride was subjected to high loads is illustrated in FIG. 4.6.(a). The tablet depicted was subjected to diametral crushing after storage for 10 days and had experienced considerable work-hardening of the type described by Bowden and Tabor (1964) and Hardman and Lilley (1973). Particle integrity cannot be detected, the whole structure resembling an almost unbroken surface. Opposed to this was the internal structure of a tablet which contained 0.5% polyethylene (FIG.4.6.(b), and had undergone identical treatment to tablets lacking polyethylene. Particle entirety had been retained and although some evidence for changes in particle shape was present, the physical appearance of sodium chloride particles remained essentially constant.

The sequence of events is more ideally illustrated in FIGS.4.7, 4.8 and 4.9. In the case of potassium chloride alone at the highest pressure, almost perfectly aligned slip planes can be perceived. However, at 500MNm^{-2} and in the presence of polyethylene, some

FIG. 4.5

Potassium Chloride Outer Shell

Pressure 250 MNm^{-2} Magnification 200x

FIG. 4.6(a)

Sodium Chloride Internal Structure

Pressure 350 MNm^{-2} Magnification 200x

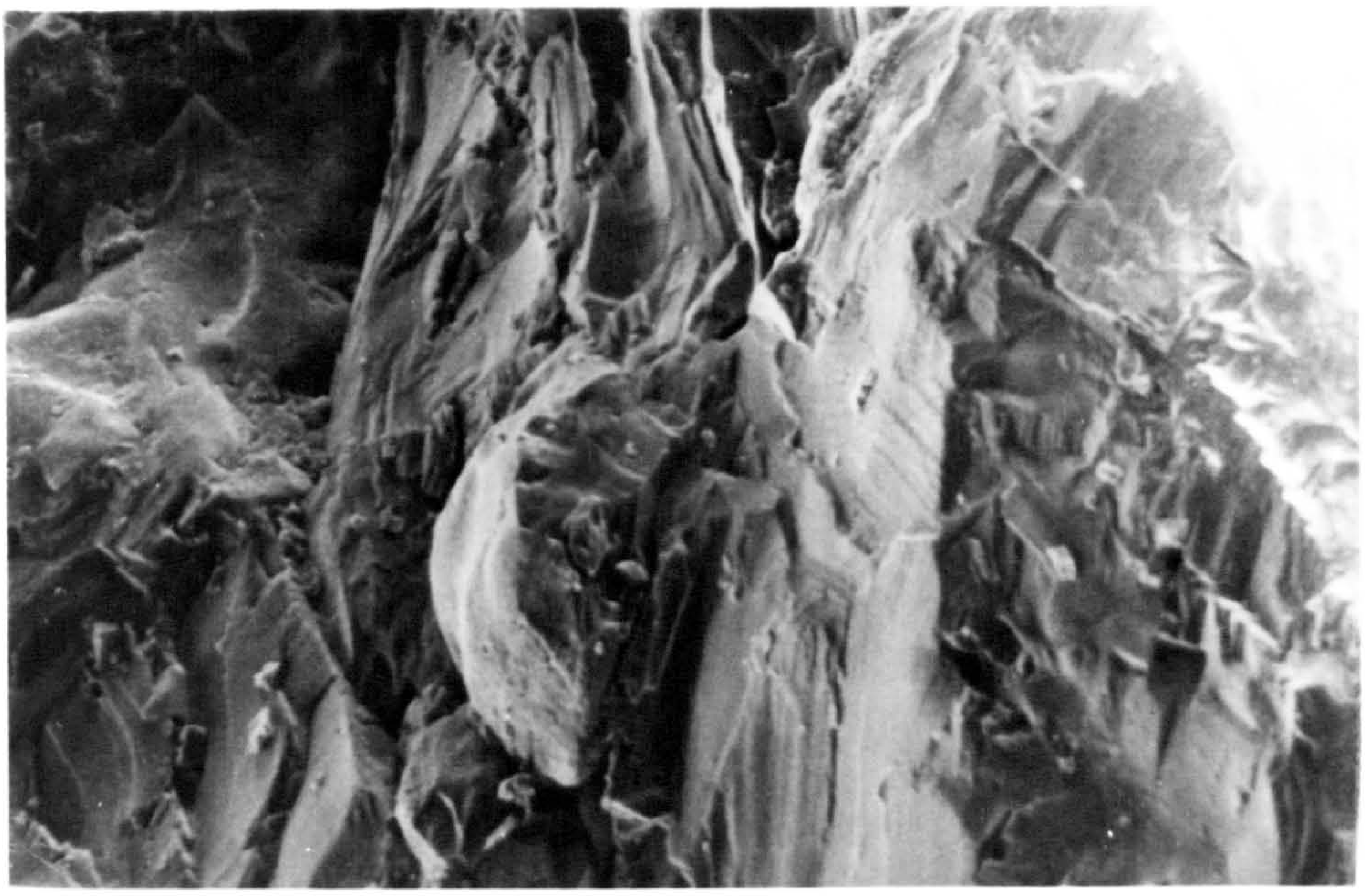


FIG. 4.6(b)

Sodium Chloride plus 0.5% w/w Polyethylene

Pressure 350 MNm^{-2} Magnification 200x

FIG. 4.7(a)

Potassium Chloride plus 0.5% w/w Polyethylene

Pressure 250 MNm^{-2} Magnification 200x

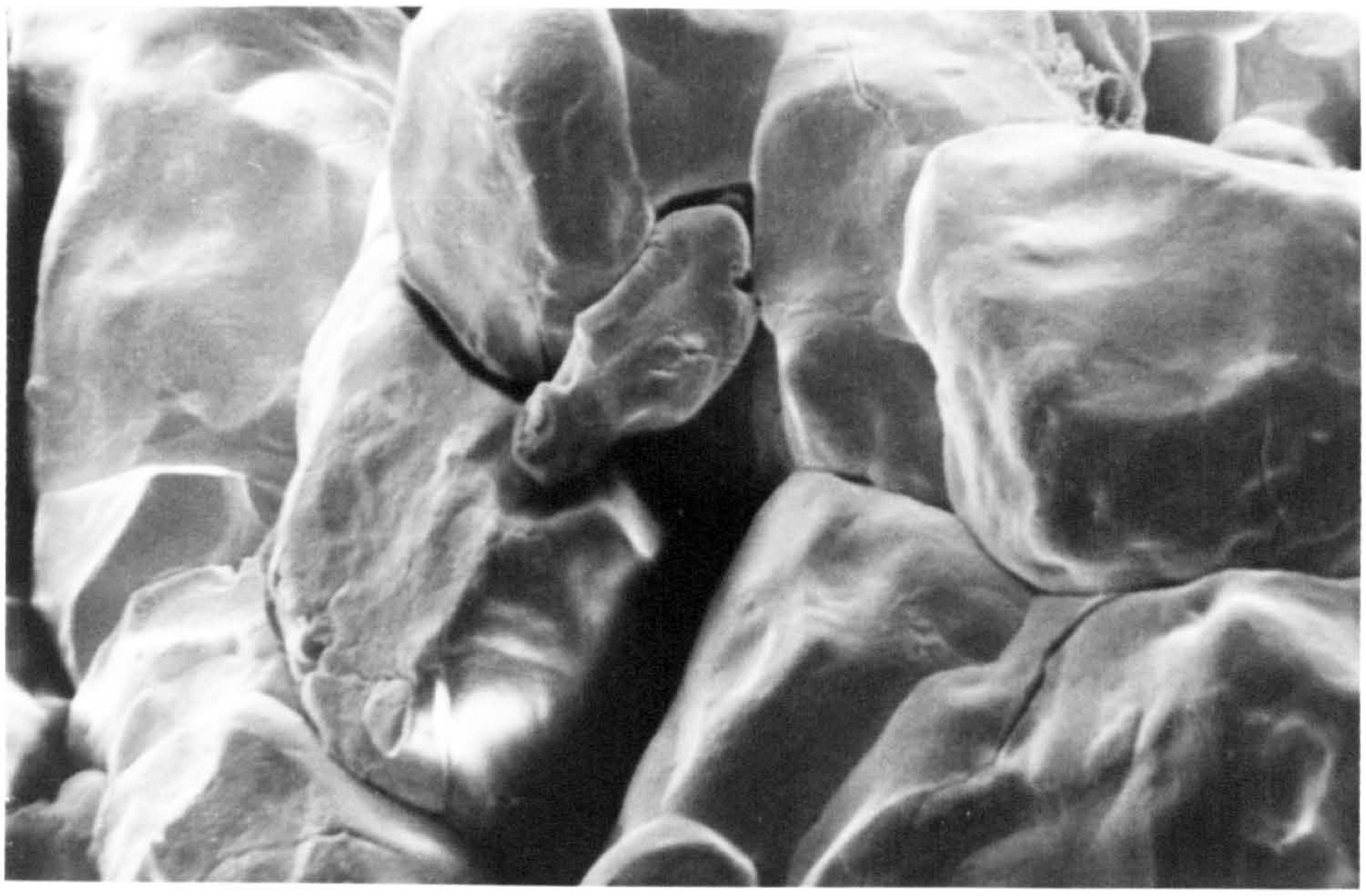


FIG. 4.7(b)

Potassium Chloride

Pressure 250 MNm^{-2} Magnification 200x

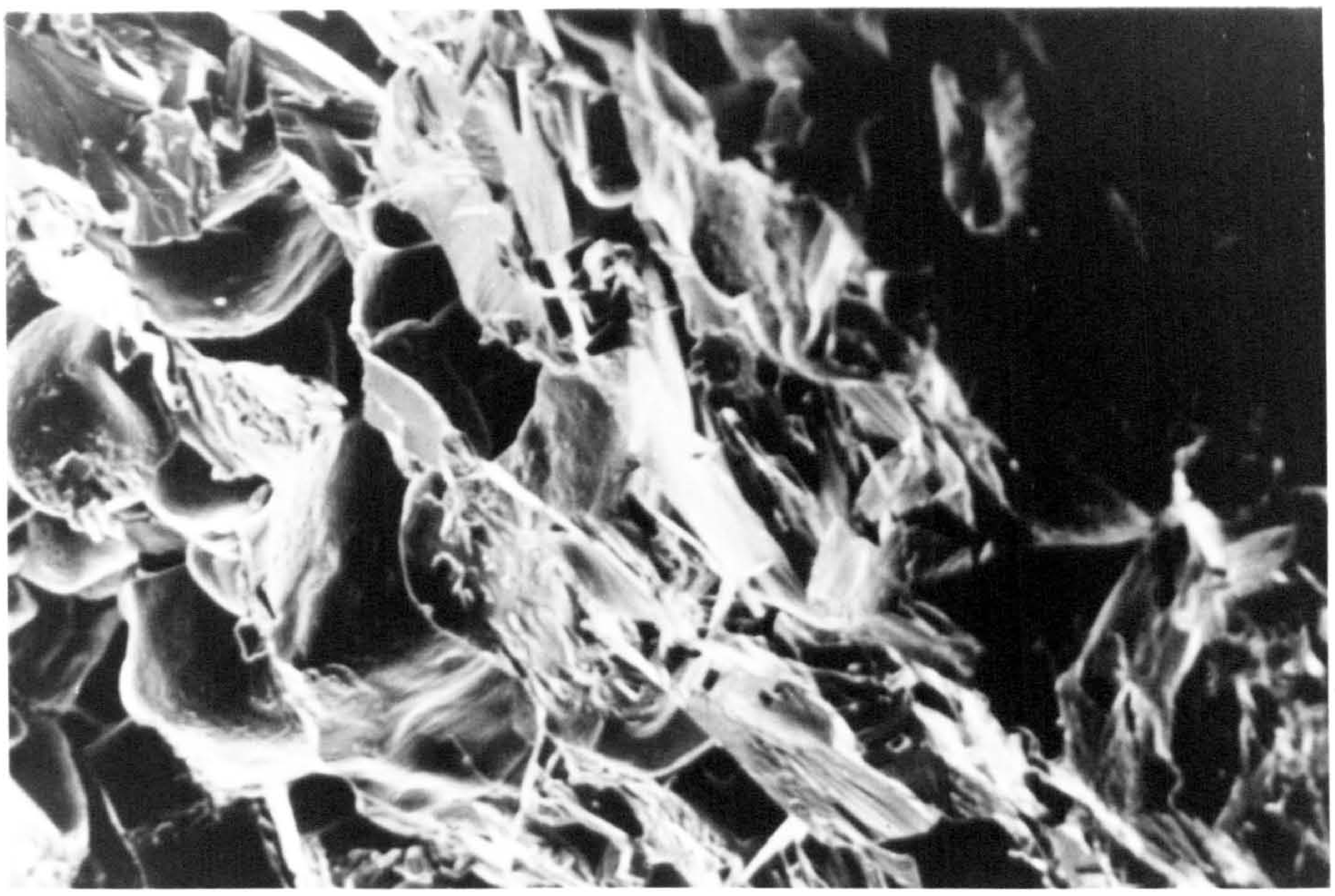


FIG. 4.8(a)

Potassium Chloride plus 0.5% w/w Polyethylene

Pressure 350 MNm^{-2} Magnification 200x

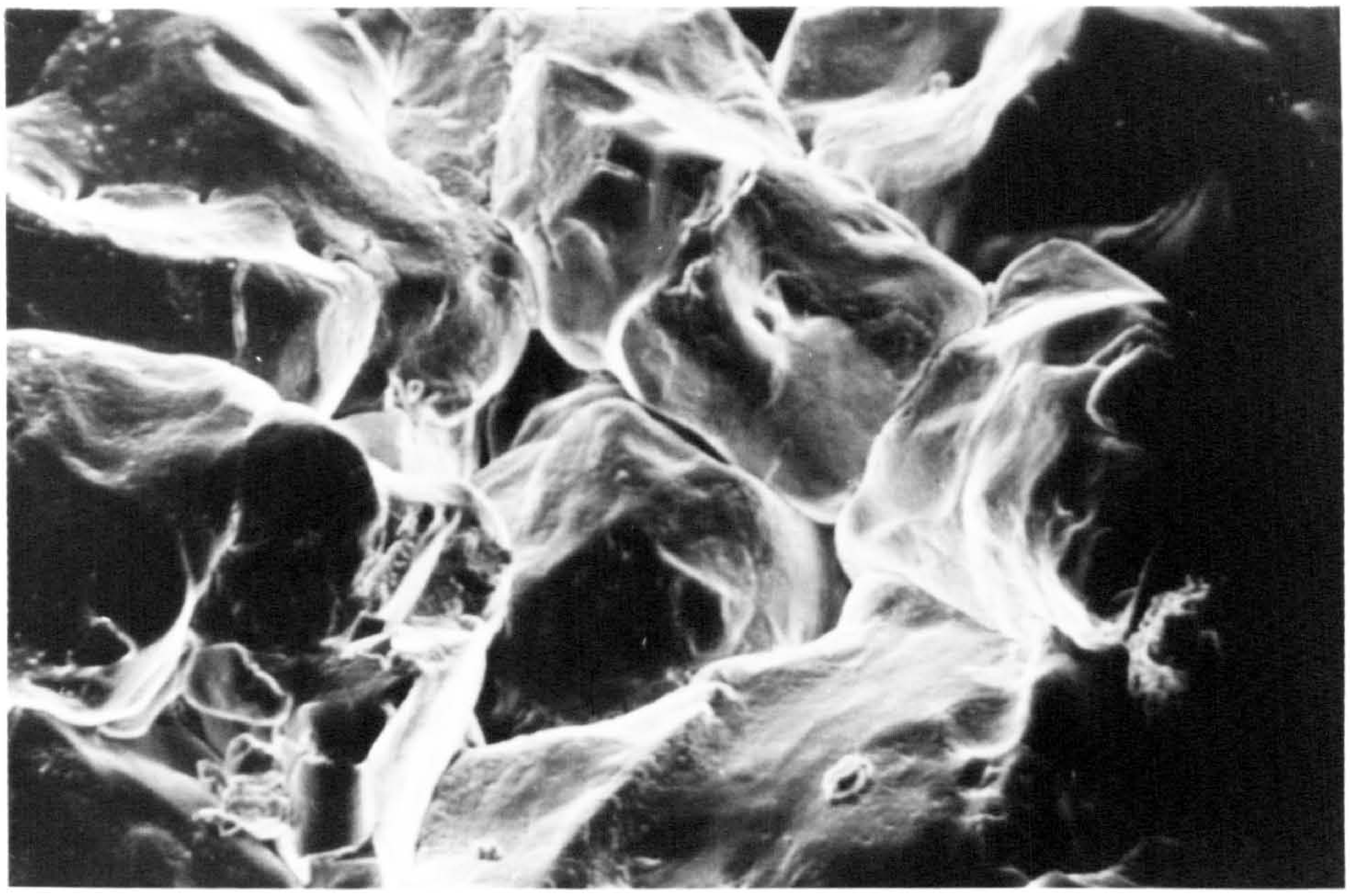


FIG. 4.8(b)

Potassium Chloride

Pressure 350 MNm^{-2} Magnification 200x

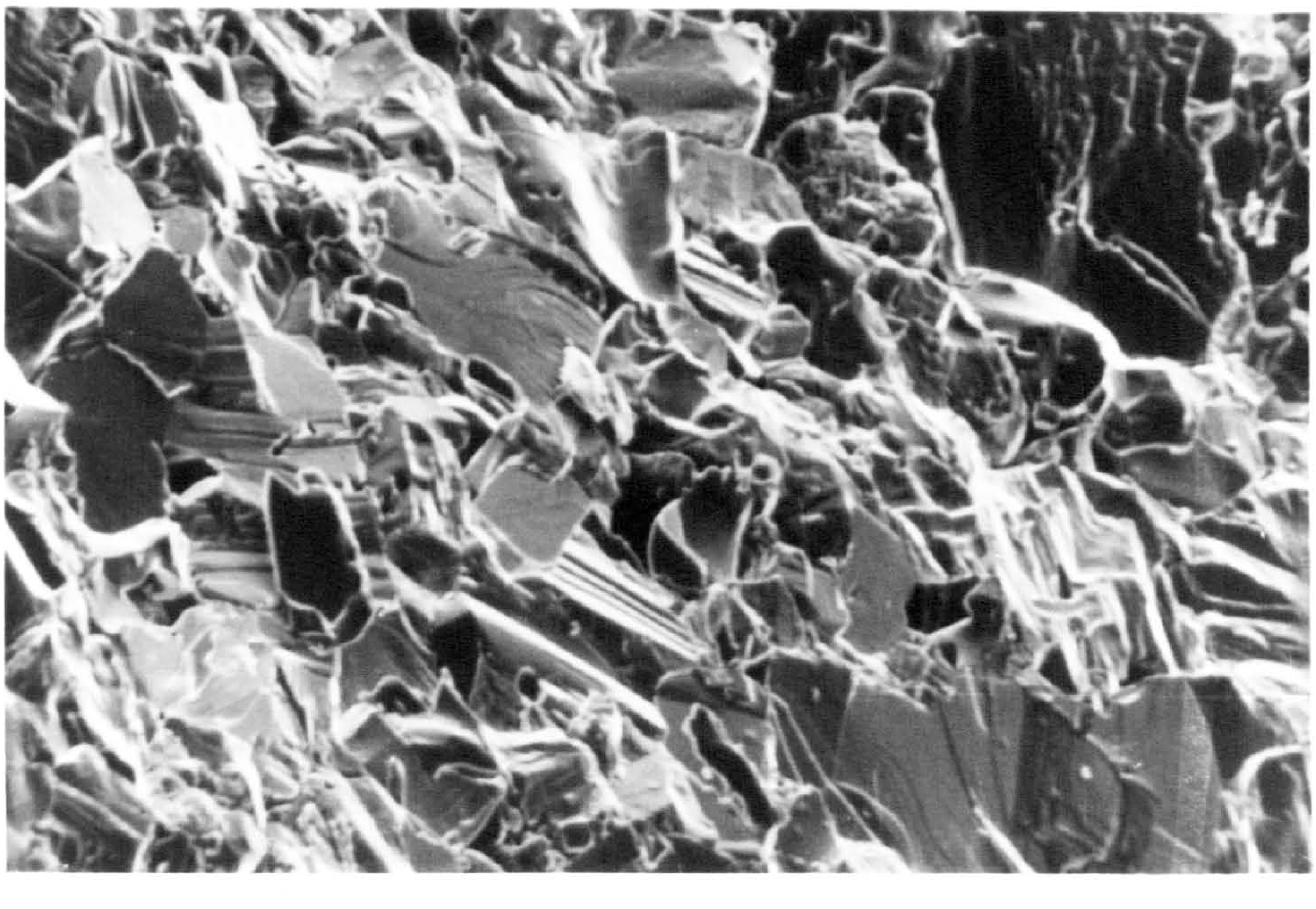


FIG. 4.9(a)

Potassium Chloride plus 0.5% w/w Polyethylene

Pressure 550 MNm^{-2} Magnification 200x

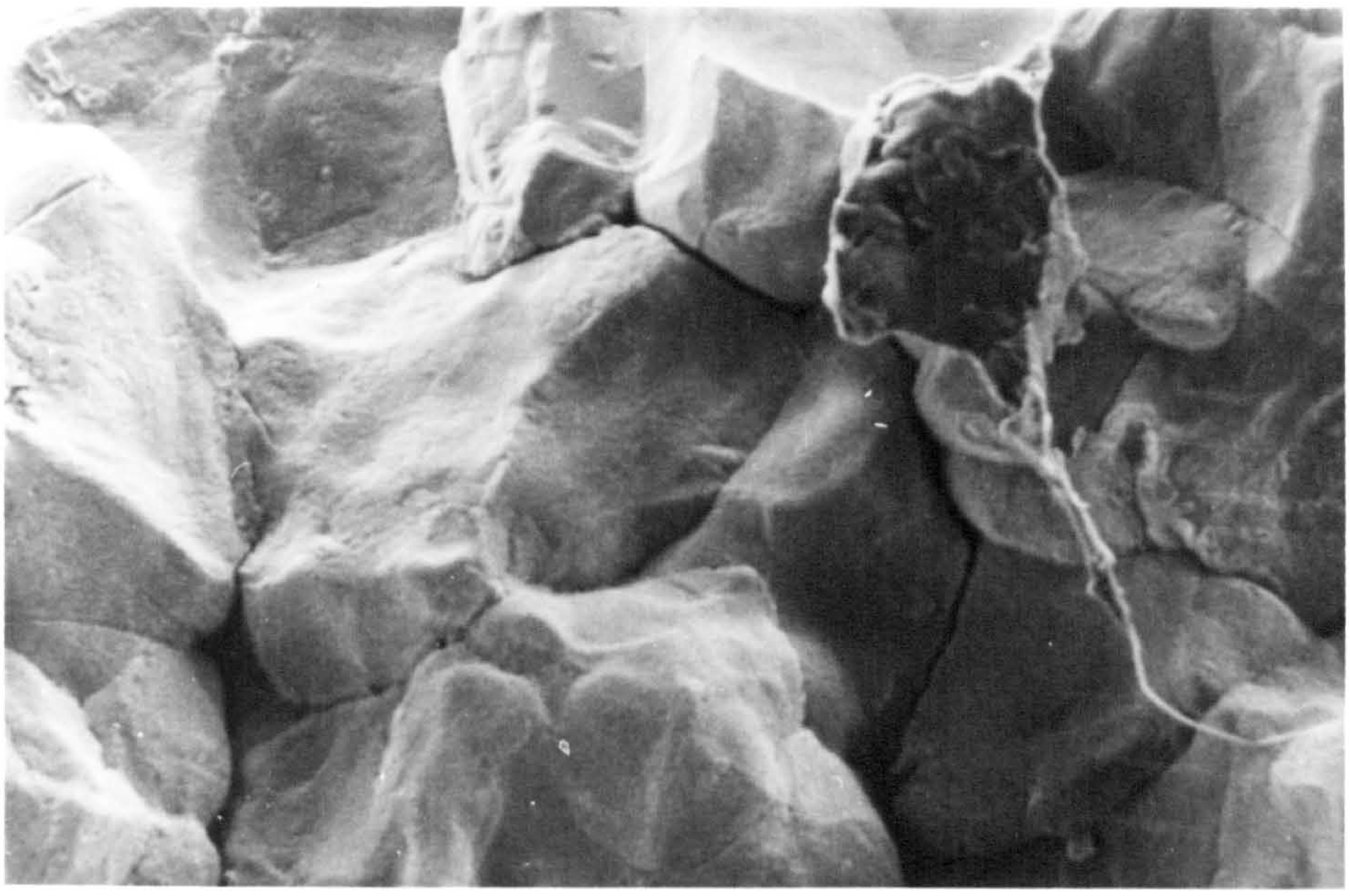
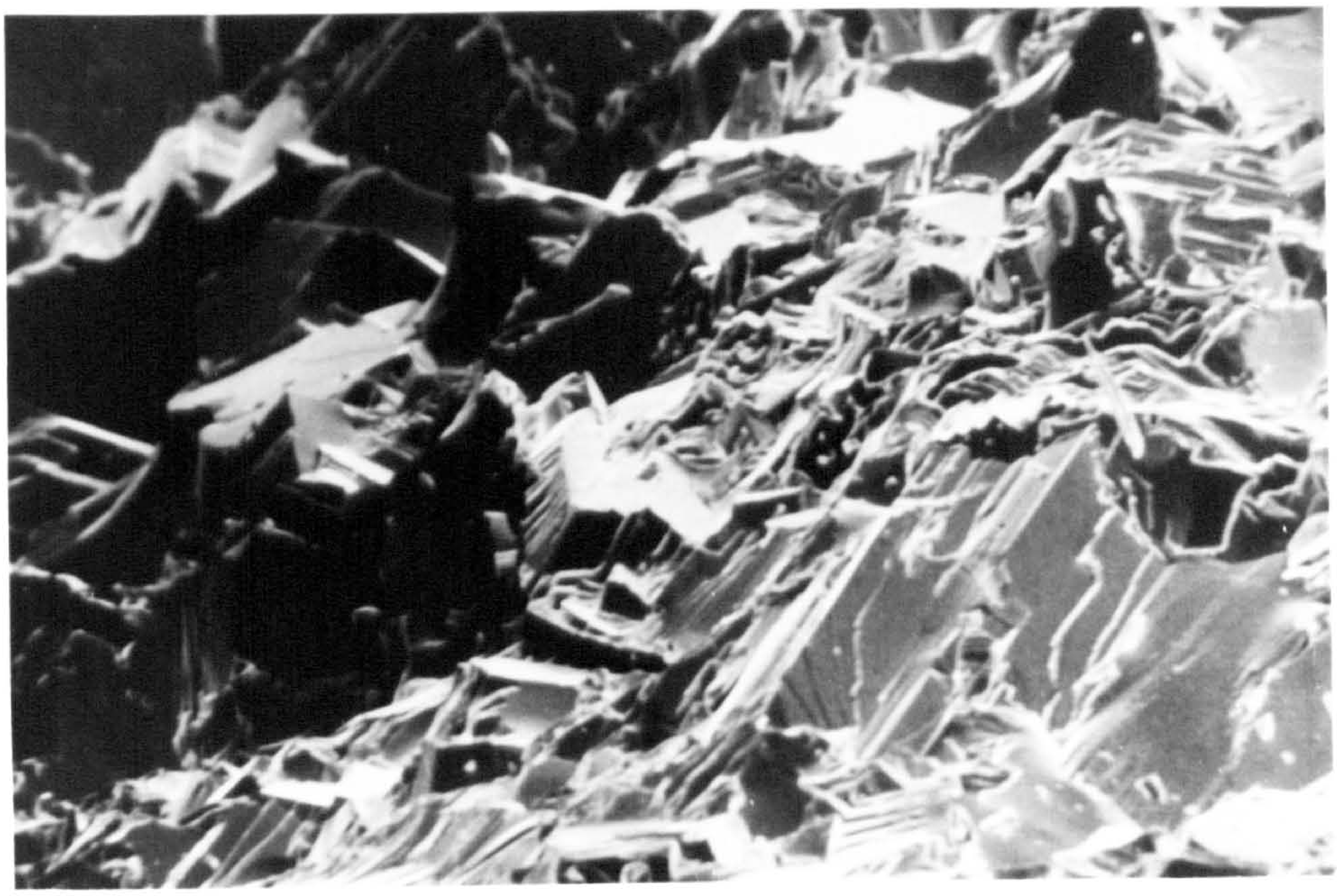


FIG. 4.9(b)

Potassium Chloride

Pressure 550 MNm^{-2} Magnification 200x



evidence for surface fusion was present and reflected the small but defined breaking strength which the compact had attained.

Similar underlying patterns are shown by caesium chloride (FIGS.4.10 and 4.11) but are complicated by what appeared to be excessive entrappment of air giving rise to an excessively porous inner matrix. The picture was further complicated by an apparent fragmentation of large particles (255 micron) to give a munificence of smaller particles, this effect can be observed irrespective of the presence of polyethylene.

4.1.3. The Effect of Particle Size

Gregory (1962) summarised the art of making high-density compacts as the introduction of the highest possible shear strain at the maximum pressure. Once slip planes failed, the upper limit of shear strain had been achieved. He theorised that such a relationship would be most productive as the particle size of the starting material decreased. By grinding samples of anthracite in a ball mill for different time periods followed by compaction at 25 tons/in^2 he was able to produce briquettes from normally unbriquettable material. Since ball milling would produce fine particles, susceptible to plastic deformation under pressure, he considered the finer particles as representing a binding agent microsquashed between the large particles. This contradicted a previous postulate made by Johnson (1958) that, in producing anthracite briquettes, the material behaved as a perfectly elastic body which, under load, attained contact along the peripheries of intimate particles.

Once the load was removed a significant proportion of contact areas were maintained giving rise to sustained cohesion. Johnson's postulate cannot be entertained in the light of present day knowledge of compaction mechanisms but its converse, that elasticity of a diluent

FIG. 4.10(a)

Caesium Chloride plus 0.5% Polyethylene

Pressure 280 MNm^{-2} Magnification 200x

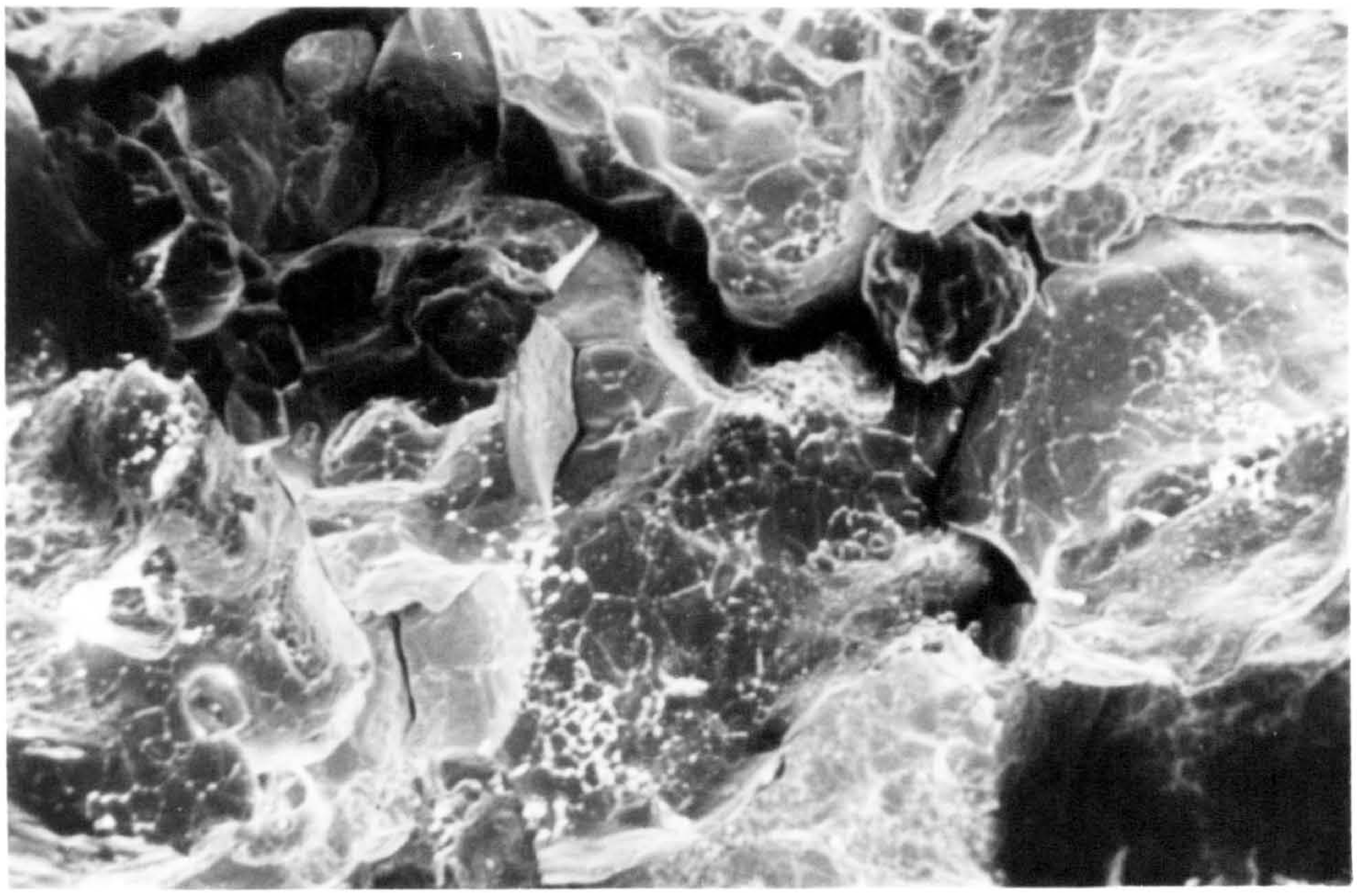


FIG. 4.10(b)

Caesium Chloride

Pressure 280 MNm^{-2} Magnification 200x

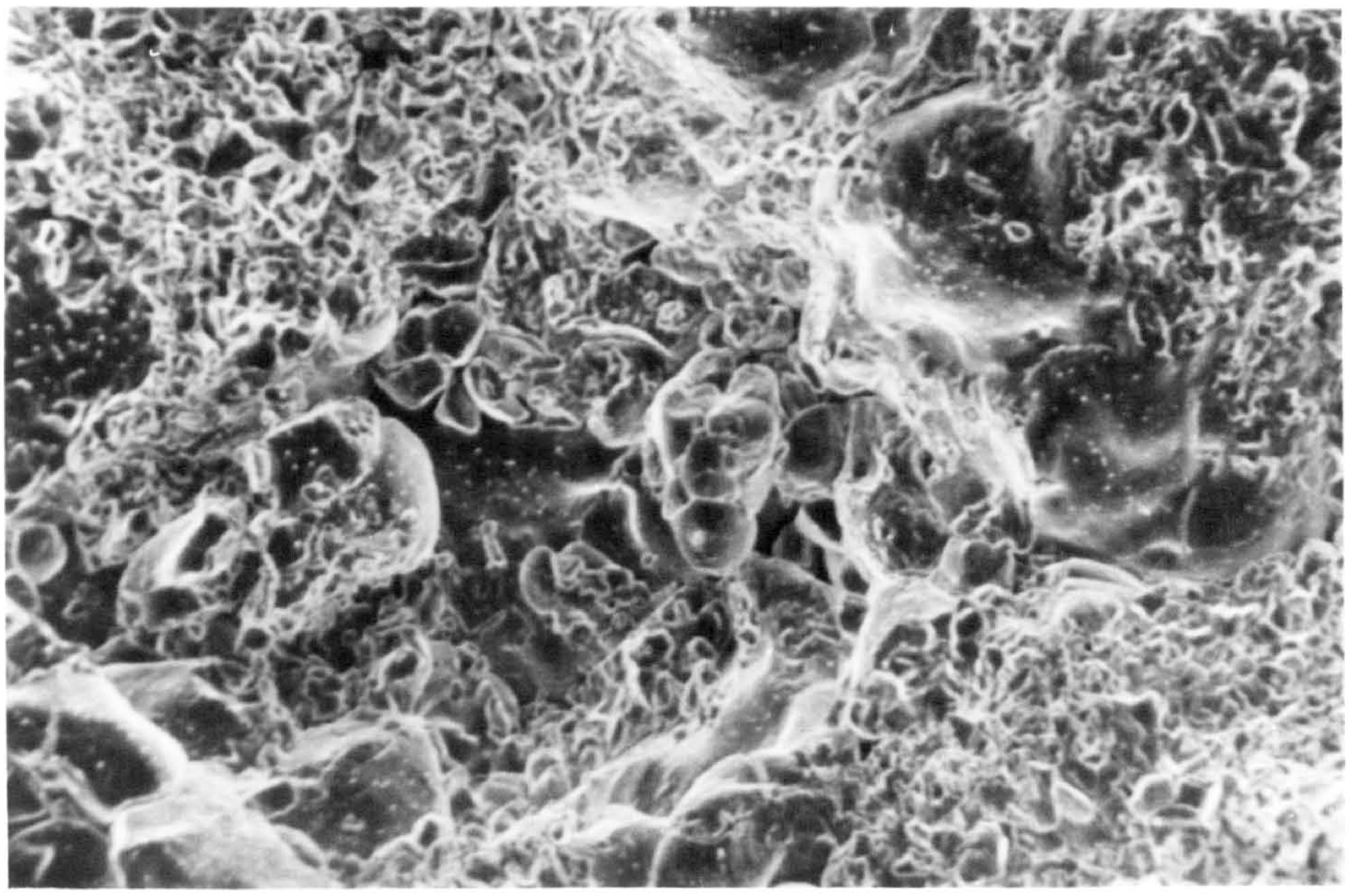


FIG. 4.11(a)

Caesium Chloride plus 0.5% Polyethylene

Pressure 450 MNm^{-2} Magnification 200x

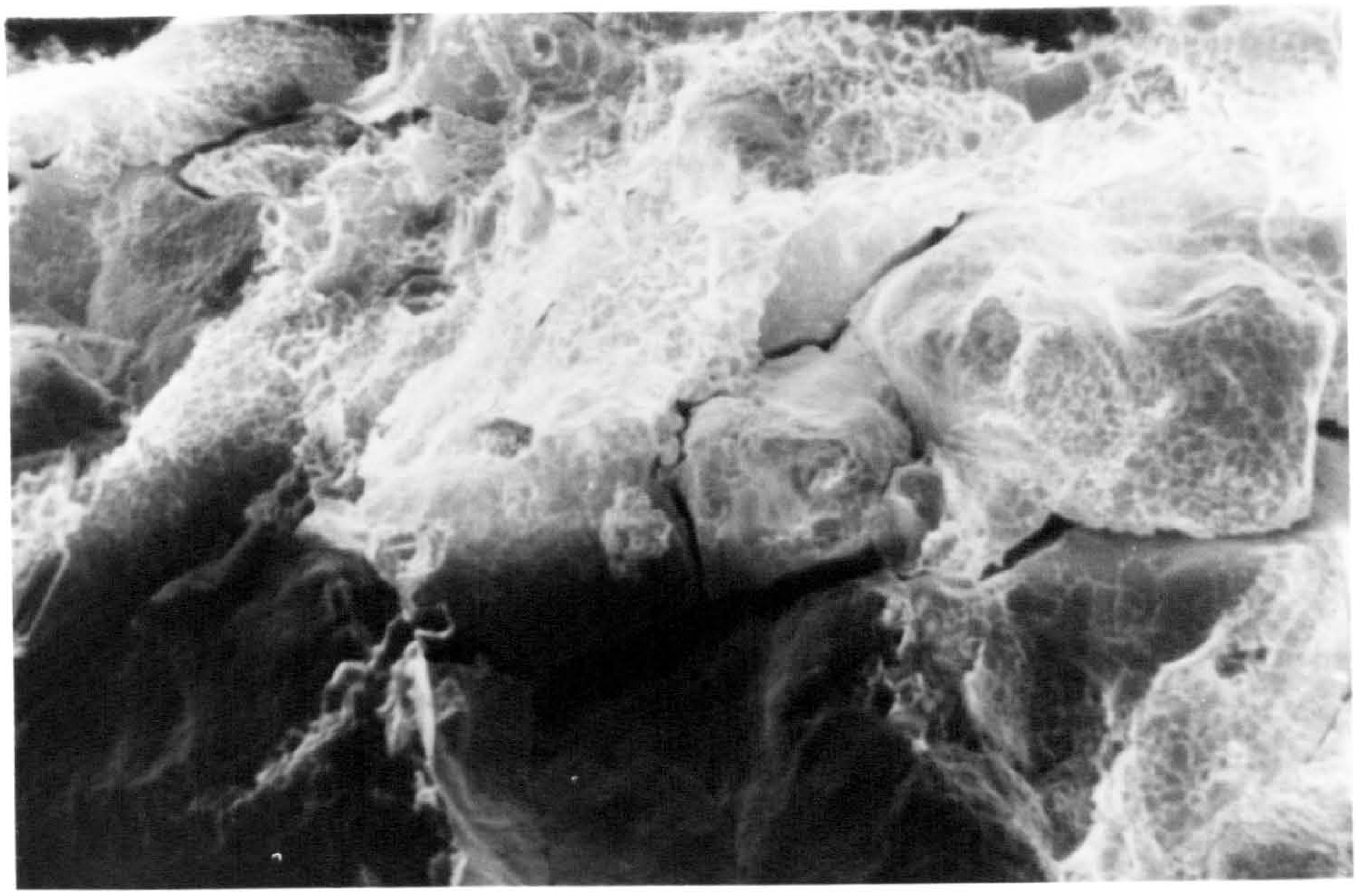
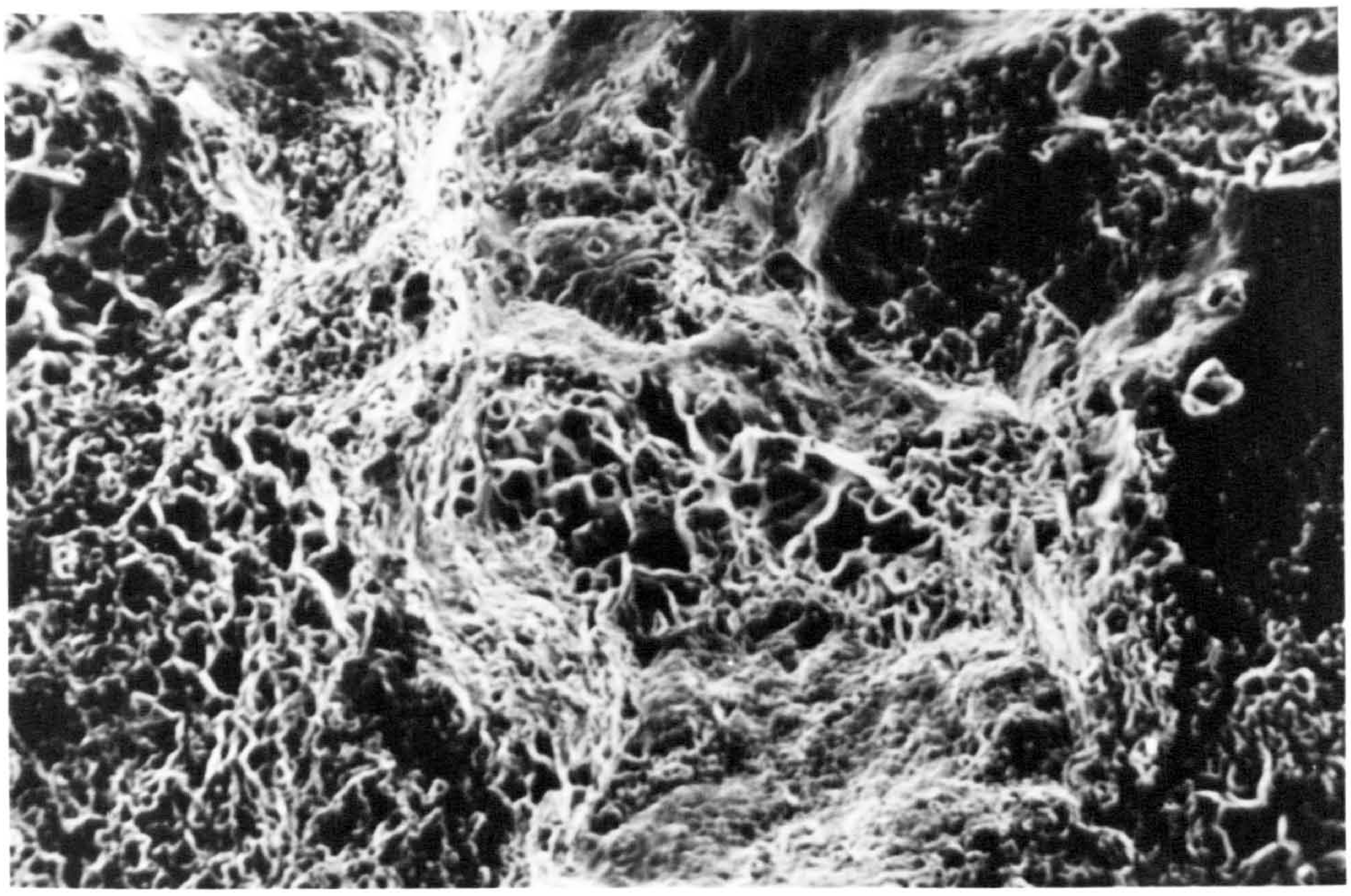


FIG. 4.11(b)

Caesium Chloride

Pressure 450 MNm^{-2} Magnification 200x



can modify interparticle bonding by reducing surface contact of bonding particles as a function of diluent mobility, is being reevaluated by modern investigators.

In the case of a compound which deformed by plastic flow then deviations in particle size would be expected to make significant contributions to tableting behaviour. Since particle-particle contact is directly related to size then, constant axial force and punch displacement with a reduction in particle size would give rise to an initial increase in tablet strength. Since total energy would be constant then surplus energy i.e. that not used for initial bonding would be of a lower magnitude than that available for larger particle sizes. Thus time-dependent stress relaxation would be less, resulting in weaker tablets for smaller particle size starting materials.

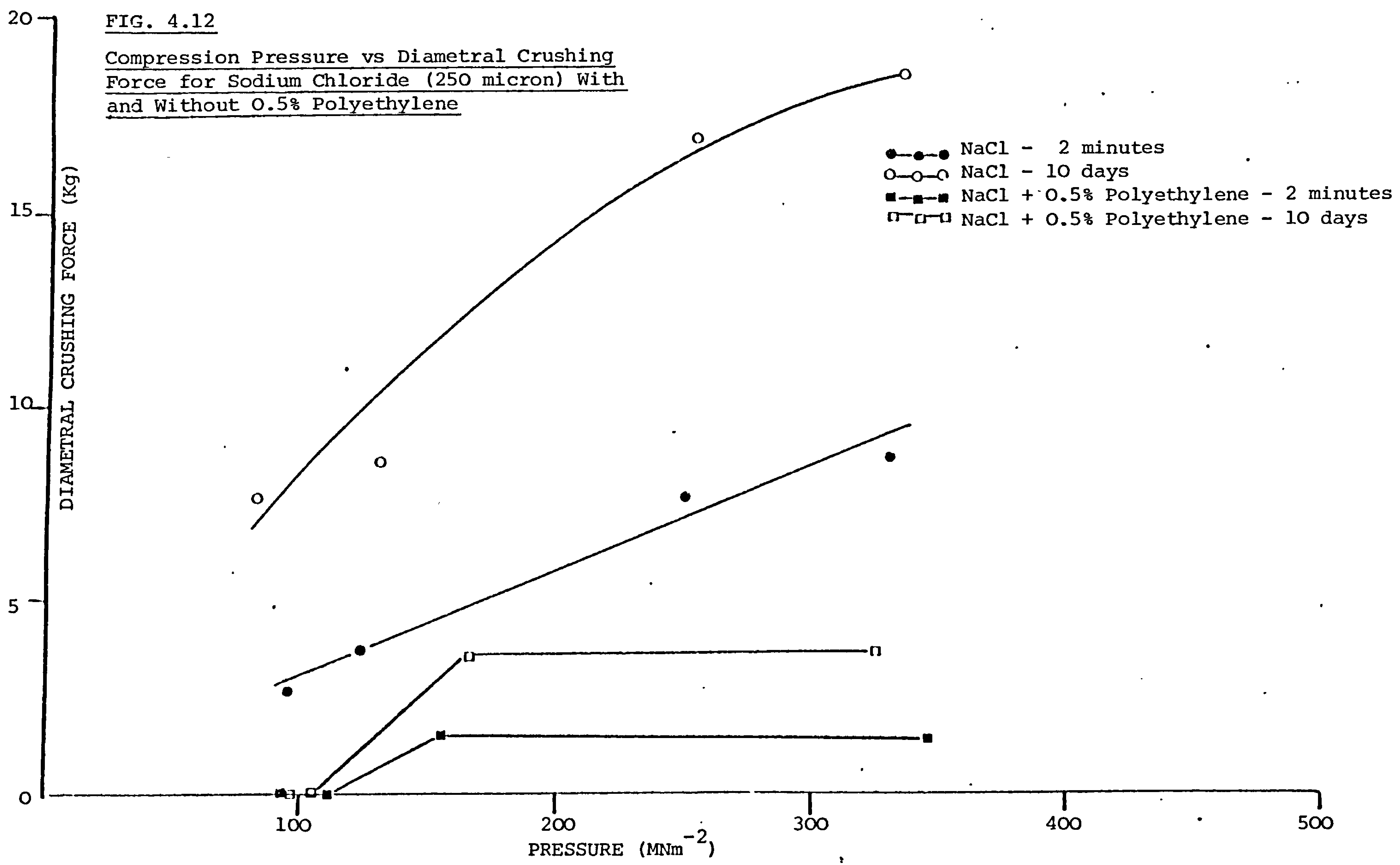
That these conditions hold true is illustrated by FIG.4.12. Although only a slight difference in immediate strength was observed between tablets prepared from 355 micron and 250 micron particles, after storage for 10 days compacts made from the latter were "softer" than those of the former.

On further reduction of particle size the effects observed at the 250 micron level should be even more pronounced with additional increases in initial (2 minute) crushing strength but overall strength, including a stress relaxation component, reduced.

As can be seen from the particle size distribution analysis, discussed in Section 2, sodium chloride contains, in the main, particles of 180 microns and greater. To achieve lower sizes, and thus be comparable with lactose (mean average size of 45 microns), involved size reducing large particles. To achieve this, two approaches were considered, ball milling and crystallisation. In the latter case, an excess of sodium chloride was disolved in water, at 80°C. Ethanol was then added and the solution was crash cooled under agitation. The

FIG. 4.12

Compression Pressure vs Diametral Crushing Force for Sodium Chloride (250 micron) With and Without 0.5% Polyethylene



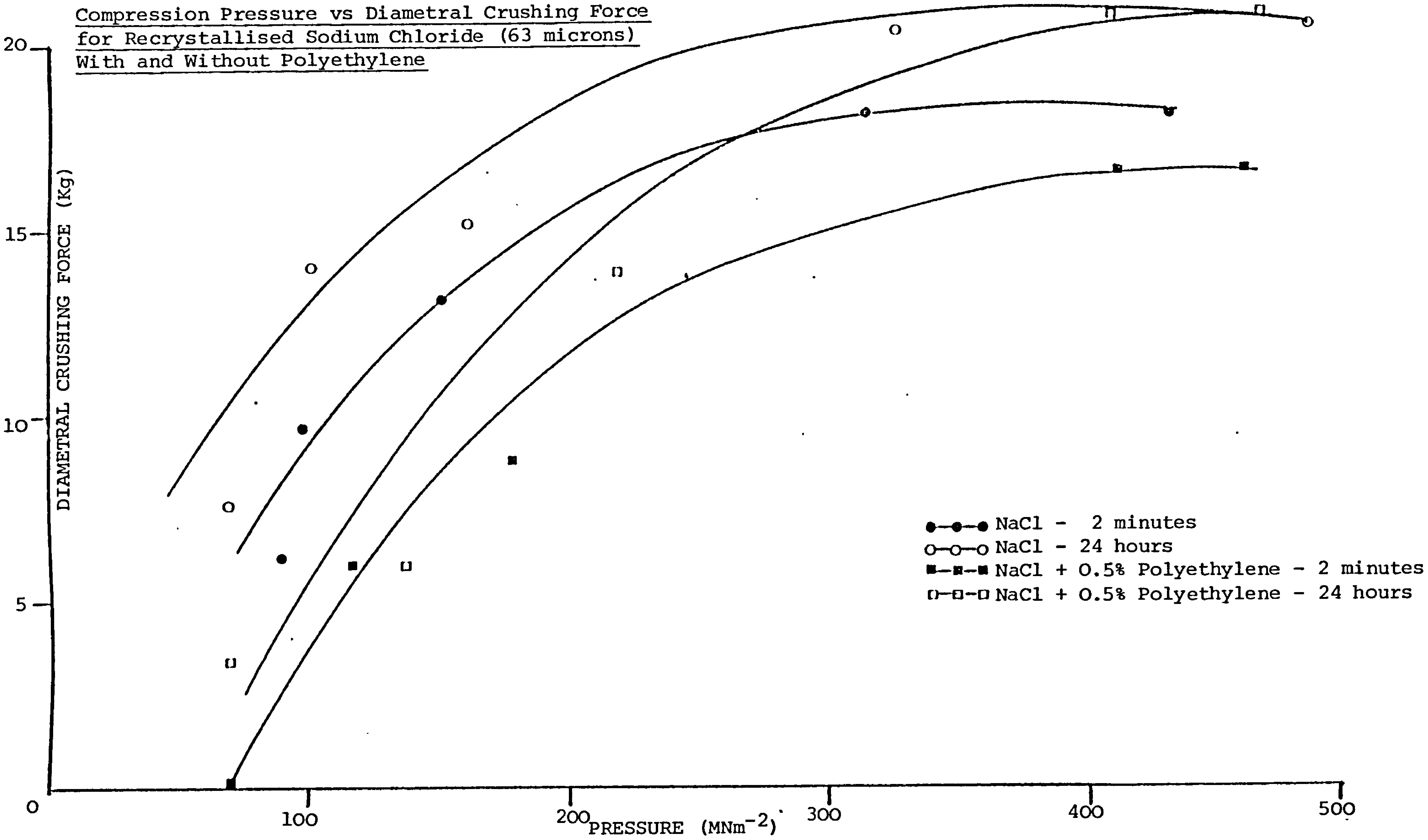
resultant crystals were filtered, dried at 80° for 24 hours under vacuum, sieved and redried. Sieve fractions were stored under silica gel prior to use. Scanning electron microscopy indicated that the crystals chosen for study (63-90 micron fraction) were similar in shape to the starting material.

On compaction the relationship between diametral crushing force and pressure proved to be as expected (FIG.4.13). Intensified point contact heightened initial hardness and reduced time dependent stress relaxation effects. On addition of 0.5% polyethylene behaviour was modified to a very much lesser extent than seen with larger size fractions. Point-point contact would now be so great, relative to large fractions, that the absorption and viscoelastic properties of polyethylene would be overwhelmed. However, under conditions which are less favourable to intensified particle contact i.e. low pressure, significant tablet cohesion was not achieved. In spite of maintaining wholeness on ejection tablets possessed no strength when subjected to diametral crushing immediately post ejection. However, on storage for 24 hours, such tablets did generate, via stress relaxation, sufficient plastic flow to lend significant strength to the matrix.

An alternative method of preparing small crystals from larger ones is that of ball milling, the technique has been used to equate particle sizes of materials whose mean average sizes have been dissimilar. However, Jones (1981) has pointed out that factors such as crystal dislocations and surface microrugosity can affect cohesion, compression, lubrication properties and inherent strength of particles. The process of ball milling would make noteworthy contributions to the modification of such properties. A similar sentiment has been aired by Hüttenrauch (1978) who stated that lattice imperfections are produced by grinding and the intensity of mechanical pretreatment is reflected in the resulting tablet characteristics. He drew attention

FIG. 4.13

Compression Pressure vs Diametral Crushing Force for Recrystallised Sodium Chloride (63 microns) With and Without Polyethylene



to the possibility of particles equal in size having different surface energies.

In the ball milling process it would be impossible to comminute larger particles to smaller ones without producing internal or external artifacts in the shape of lattice dislocations (loss of hydrated water) or surface cracks. Whether such artifacts would be the main outcome of ball milling sodium chloride would be difficult to decide since, in the practical energy expenditure in a ball mill, as shown below, very little is utilised in size reduction.

<u>Practical energy expenditure in a Ball-Mill</u>

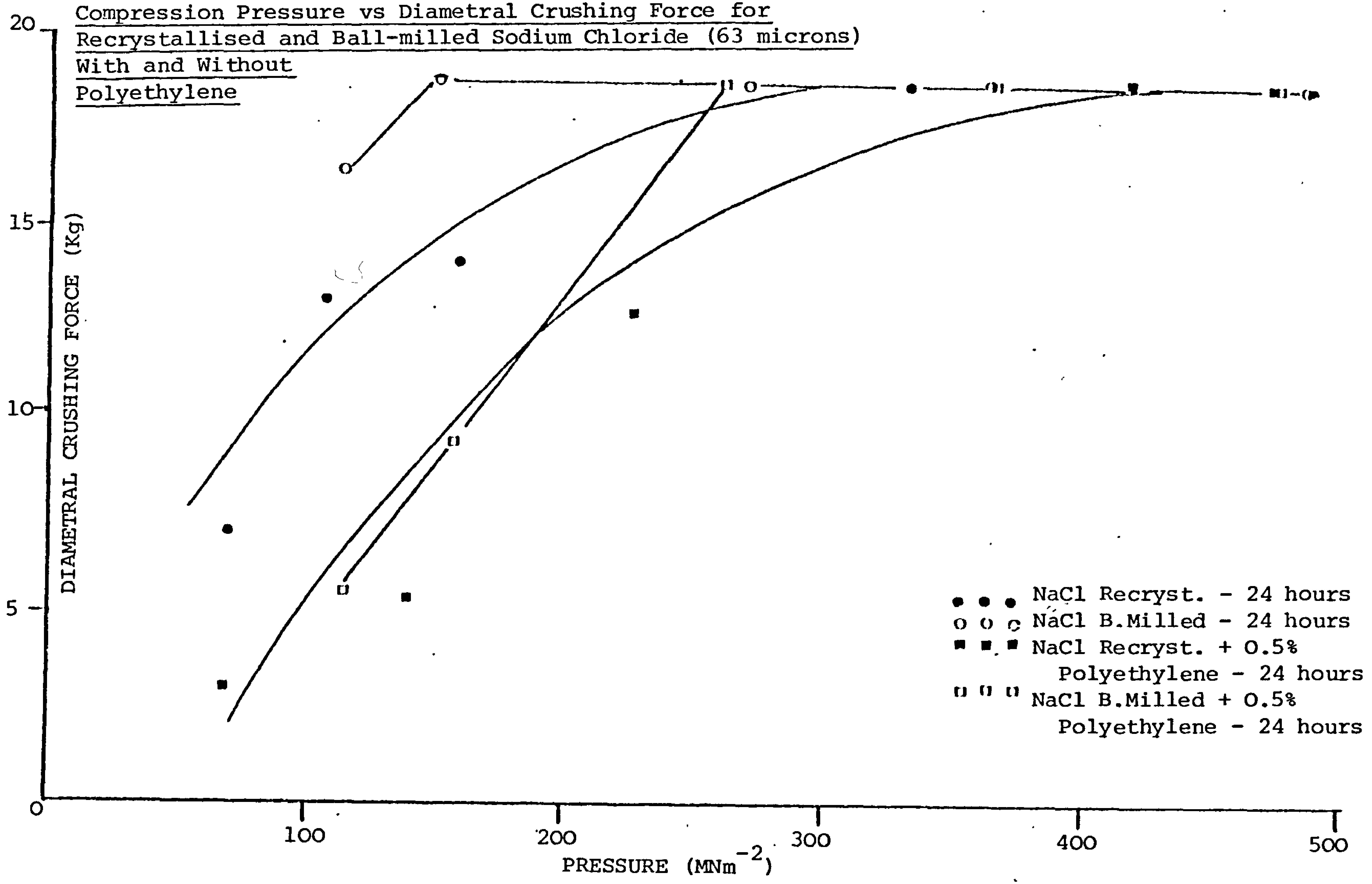
(Parrot,E. 24th Annual National Industrial Pharmaceutical Research Conference, 1982)

Bolt Friction	4.3%
Gear losses	8.0
Heat lost from Drum	6.4
Heat absorbed by air	31.0
Heat absorbed by product	47.6
Energy for size reduction	0.6

If, however, sufficient energy were imparted to the system to produce defects and/or surface activation, then a difference in compaction behaviour would be expected between ball milled and crystallised material of the same particle size. Assuming that, when dealing with particles of the same size range, the same order of particle-particle contact exists, then the presence of induced dislocations in ball milled material should give rise to pronounced slippage during compaction. This will be reflected in greater diametral strength consistent with intensive stress relaxation. Such proved to be the case (FIG.4.14) with ball milled material displaying

FIG. 4.14

Compression Pressure vs Diametral Crushing Force for Recrystallised and Ball-milled Sodium Chloride (63 microns) With and Without Polyethylene



greater strength increases over 24 hours. The inclusion of 0.5% polyethylene produced strength profiles similar in character but reduced in order.

The data outlined in Section 4.1 indicates how the compaction mechanisms of materials which undergo plastic deformation could be modified by the additions of only a very small percentage of a component with a high modulus of elasticity. Explanations were sought and found for the effect of particle size, pressure and material imperfections on such behaviour. It would be anticipated that different mechanisms might be involved in the compaction of a binary mixture which contained an elastic and brittle material, such differences have been observed during static compaction.

The following section extends that study to encompass the dynamic situation.

4.2. Lactose and Polyethylene - Single Component and Binary Mixtures

4.2.1. Compaction of Lactose

Since Hardmann and Lilley (1970-74) published their findings on the compaction mechanisms of sodium chloride (plastic) sucrose (brittle) and coal (intermediate), extensive studies on the behaviour of brittle materials, with particular reference to lactose, have been reported.

Hardman and Lilley assigned to sucrose the following sequence of compacting events. Considerable particle fracture occurred resulting in closer proximity of particles to give a reduced relative volume. They stated that pore filling by particle fragments was an efficient process and at high pressures there was likely to be some plastic flow in very small particles. Similar properties were assigned to lactose. Hersey and Rees (1971) went on to substantiate the basic mechanism of brittle fragmentation using the Heckel equation during compaction, until, above a certain pressure, coincident linear relations were obtained for all particle fractions, such relations were produced as a result of plastic deformation. However, the ability of a powder mass to reduce in volume during compression does not ensure that, on removal of the load, tablet cohesion will be maintained so that the smallest particles will give the strongest tablets. This was illustrated by Fell and Newton (1971) in a comparison of the tensile strength of various particle size fractions of crystalline and spray dried lactose. With respect to the latter, at constant pressure, tablet strength increased as particle size decreased. Such linearity was not observed with crystalline lactose, of the three fractions examined (0-32, 75-104 and 295-410 microns), the middle fraction gave the strongest compacts.

That complicated compaction profiles do exist for lactose is illustrated by FIG.4.15. The data follows a similar order to that of Fell and Newton. Of the three size fractions investigated (45-63, 63-90 and 90-125 microns) the middle fraction produced the strongest tablets. Tablet strengths were determined immediately and after 24, 48 and 120 hours, no increases in strength with time were observed.

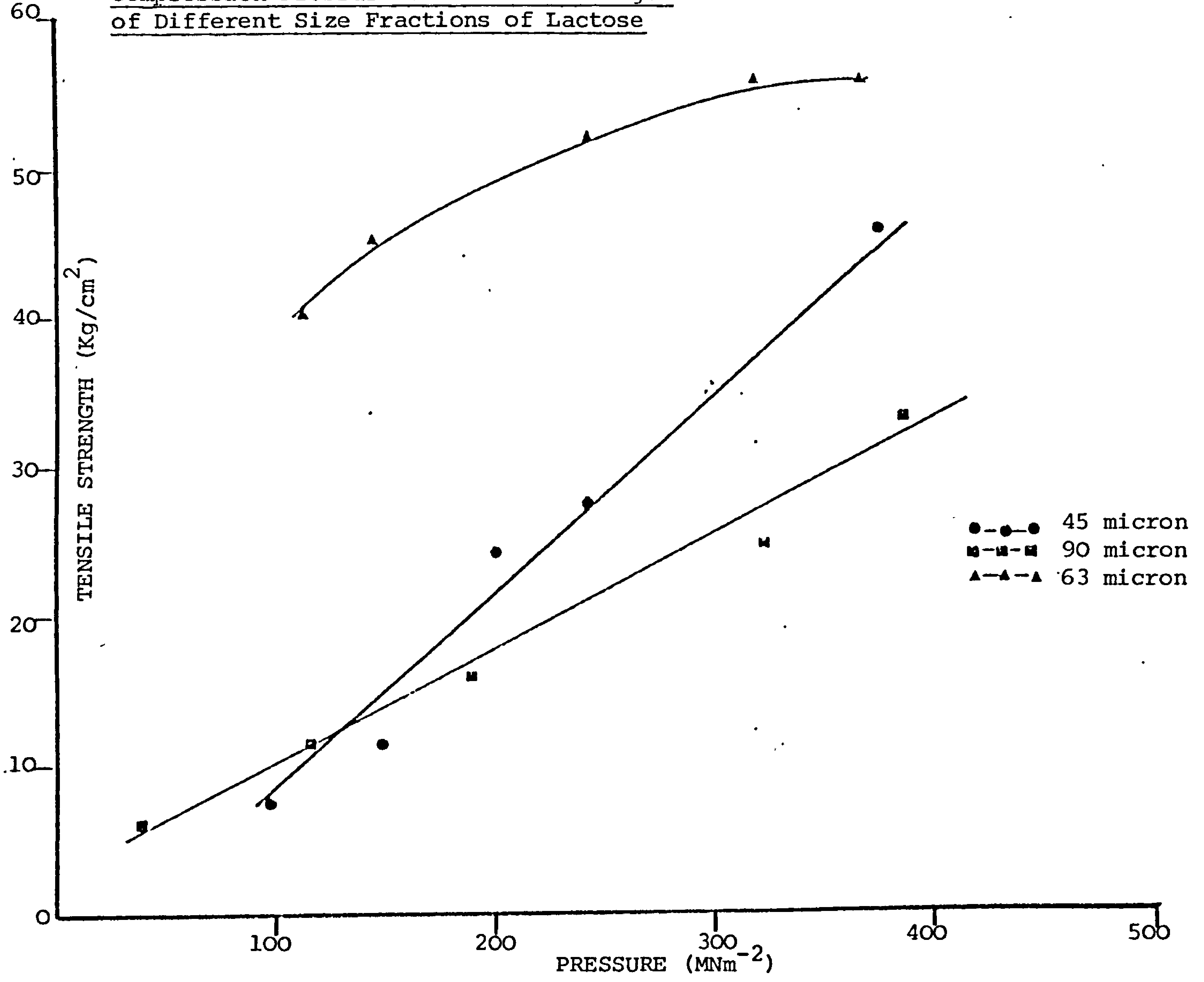
How tablet strength increased with particle size, with a material which underwent brittle fracture on compaction, would depend upon minimising void space and maximising particle contact. Small particles would be less prone to further fragmentation while large particles would probably fragment to produce secondary particles of varying size to give inefficient void filling. Thus, one explanation for the greater strength of tablets produced from intermediate 63-90 micron material could be that on fragmentation of this size range, maximum effective size for void filling and particle proximity occurred.

4.2.2. Binary Mixtures of Lactose and Polyethylene

Arising from the static compression studies described in Section 3 the addition of a small quantity of material having a high modulus of elasticity (i.e. polyethylene) to a powder which undergoes brittle

FIG. 4.15

Compression Pressure vs Tensile Strength of Different Size Fractions of Lactose



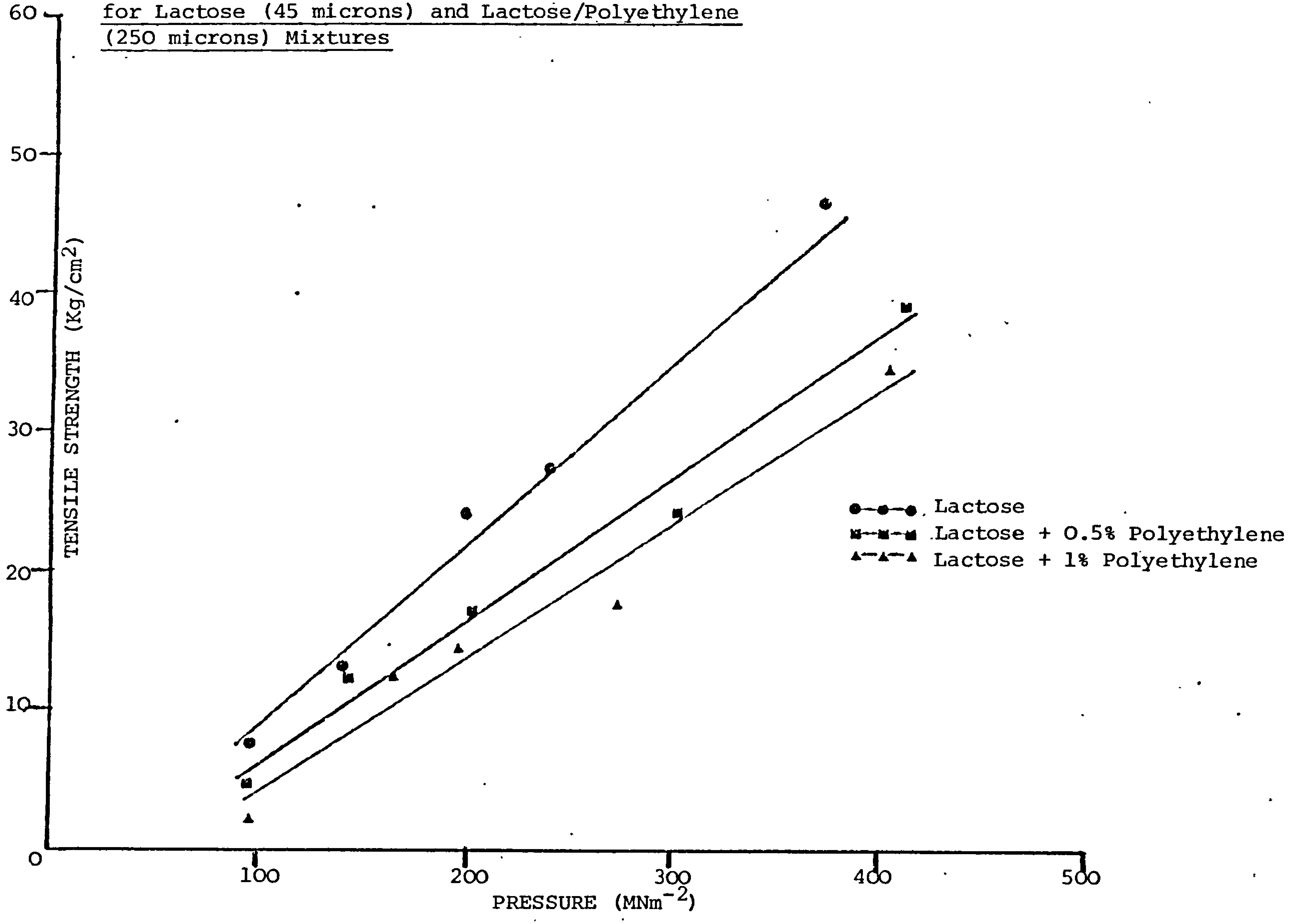
fracture during compaction (i.e. lactose) would be expected to have little effect on the resulting strength of the compact. Unlike the sodium chloride system, where plastic flow properties are extensively compromised by the addition of small quantities of polyethylene, lactose would be expected to overcome any interference in bonding modifications which polyethylene would impart to the system. That lactose can tolerate low levels of polyethylene is illustrated by FIG.4.16, similar quantities added to sodium chloride would reduce tablet cohesion to a minimum except at pressures in excess of 300MNm^{-2}. To achieve bonding, particle-particle contact would be favoured by brittle fracture occurring during the compaction process. The extent to which this occurs, with material of 45-63 micron size, is unknown. Cole, Rees and Hersey (1973) have shown how, during compaction of 250-420 micron lactose at relatively low pressures, very considerable particle reduction occurred to produce a significant (10%) quantity of material less than 75 microns in size. Of greater interest was the spread of size reduction which they obtained in that more than 50% of the starting material was reduced to $<$250 microns during compaction. Thus, it would appear that, during fragmentation, several orders of fracture might arise and the ability to achieve such orders would contribute significantly to final tablet strength.

At compaction pressures in the range investigated in this work fragmentation would be expected to occur extensively, being greater as the pressure increased. Such behaviour would explain the increase in tensile strength with increase in pressure for all systems represented in FIG.4.16.

However, as described during static compression studies, polyethylene would contribute some elastic recovery to the compact on ejection, and discreet pockets of reduced cohesion would exist

FIG. 4.16

Compression Pressure vs Tensile Strength for Lactose (45 microns) and Lactose/Polyethylene (250 microns) Mixtures



throughout the tablet matrix. Such pockets would dictate the final strength of the compact and, since the slopes of the lines for all three systems are essentially similar, it would seem likely that elastic recovery of polyethylene would play the dominating role in controlling tablet strength. Tensile strength was preferred to diametral crushing force in monitoring tablet strength since, on breakage, tablets exhibited near ideal conditions.

On increasing the particle size of lactose to 90-125 microns a similar pattern emerged, with and without the addition of polyethylene, to that of 45-63 micron material (FIG.4.17). Although relative tensile strengths of tablets with and without polyethylene, were greater for the smaller size fraction, compacts containing the viscoelastic component achieved similar strengths, at the highest pressures, irrespective of initial particle size.

On further dilution of lactose with polyethylene, although the tensile strength was greatly reduced, (FIG.4.18) tablet cohesion could be achieved but the viscoelastic component now played the dominating role. With 10% polyethylene, bond formation barely increased on moving from low compaction pressure to high, a similar situation existed with 25% polyethylene except that the influence of the viscoelastic material was more pronounced at a higher pressure (i.e. tablet strength was zero at 150MNm^{-2}). At the higher concentration elastic recovery of polyethylene would be the controlling factor and, even assuming fragmentation of lactose did occur, this would be more than offset by elastic recovery.

On addition of 10% polyethylene to 90-125 micron lactose tensile strength was greatly reduced, the correlation coefficient only just failing to define a linear relationship between strength and pressure. (FIG.4.19). Consequently, no particular emphasis should be placed on

FIG. 4.17

Compression Pressure vs Tensile Strength for Lactose (90 micron) and Lactose/Polyethylene (250 micron) Mixtures.

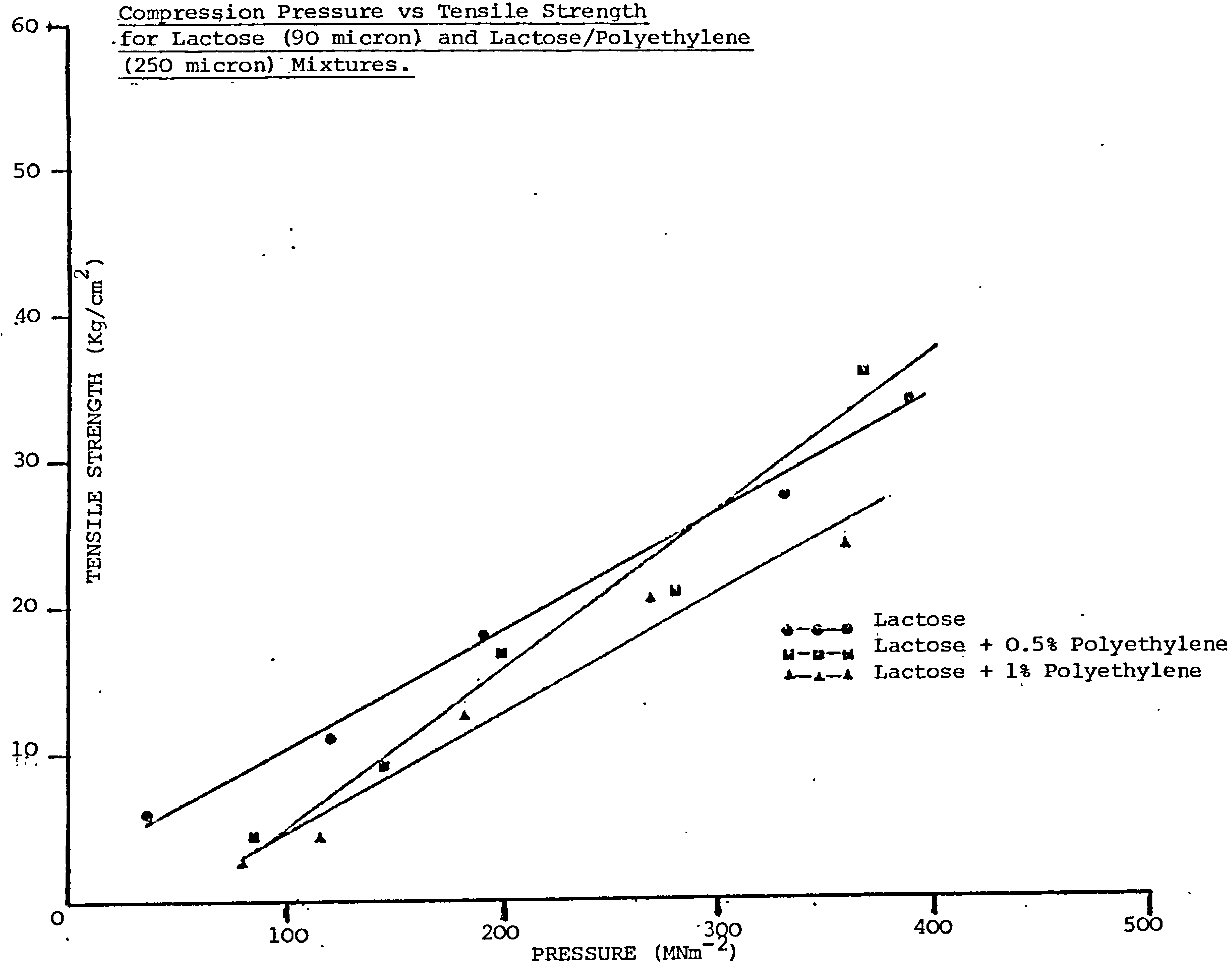


FIG. 4.18

Compression Pressure vs Tensile Strength for Lactose (45 micron) and Lactose/Polyethylene (250 micron) Mixtures

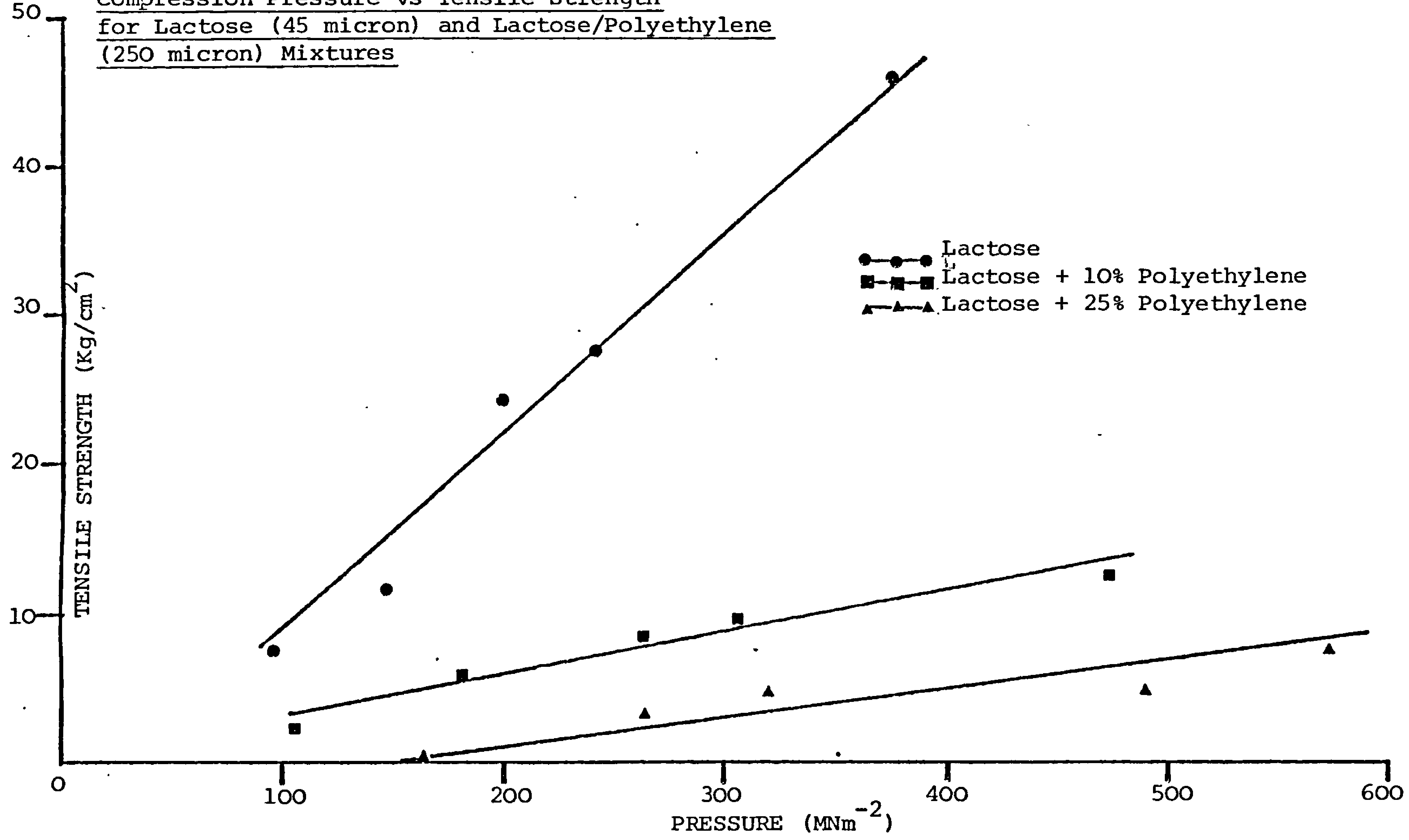
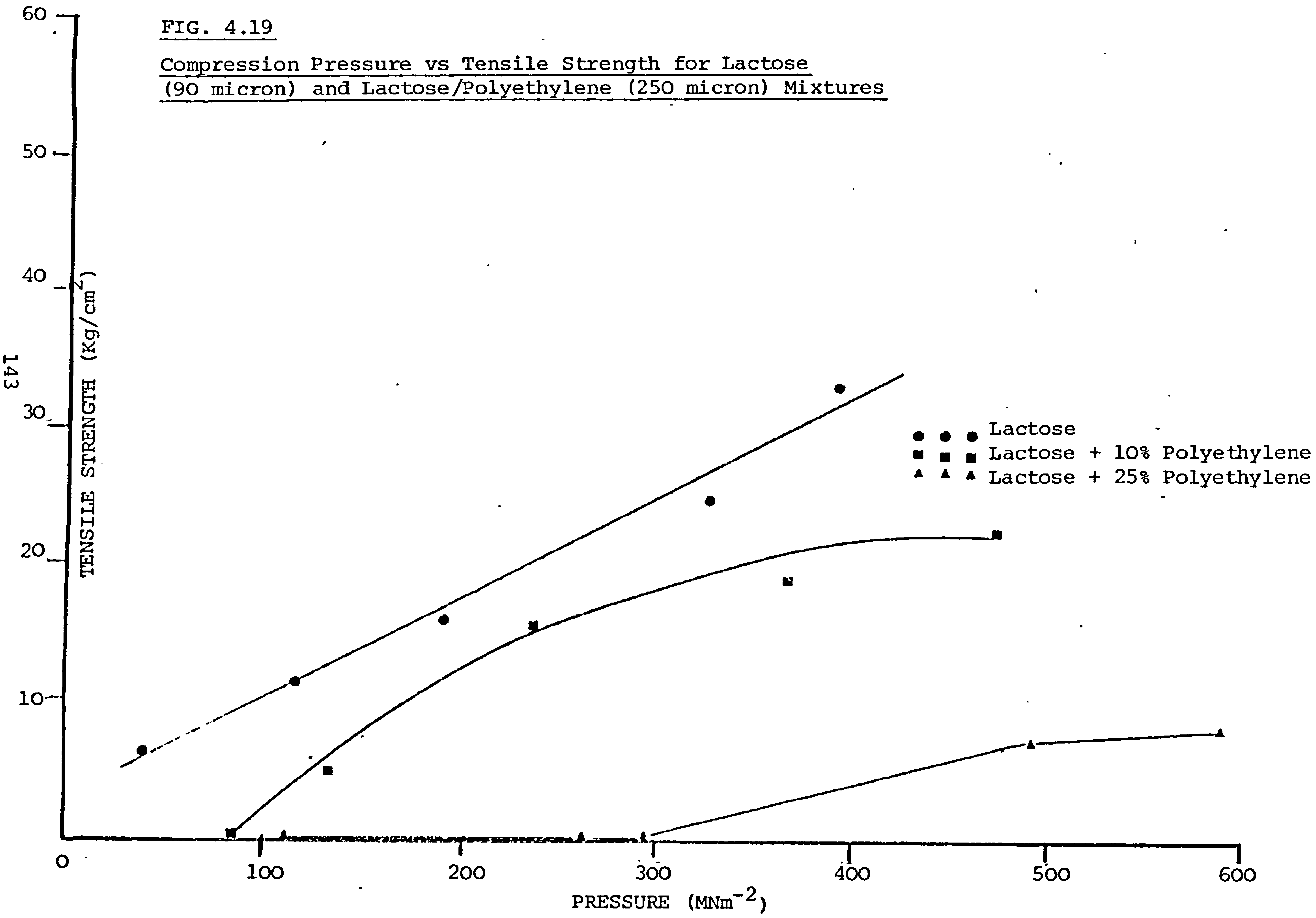


FIG. 4.19

Compression Pressure vs Tensile Strength for Lactose (90 micron) and Lactose/Polyethylene (250 micron) Mixtures



the apparent plateauing at approximately 350MNm^{-2}. On dilution of lactose with 25% polyethylene considerable higher compaction pressures had to be applied, compared with 45-63 micron material, before tablet cohesion could be achieved. As particle size increased the degree of particle-particle contact was lowered and, because of extensive energy absorption of the viscoelastic component leading to substantial elastic recovery less energy was available for particle fracture.

Scanning electron microscopy of tablets prior to breakage illustrated the discontinuity of the outer skins (FIG.4.20(a) and (b), although the outer coating appeared reasonably continuous it lacked the integrated shear structure of sodium chloride tablets. In the presence of 10% polyethylene well-defined fissures can be observed where elastic recovery of polyethylene has influenced the cohesive properties of lactose alone. Whether such stress-relief areas were operating during one or both phases of the compression cycle was not known but their configuration would suggest that localised areas of sustained lactose-lactose bonding were operating.

FIGS.4.21 and 4.22 confirm that, irrespective of compaction pressure, internal structures of tablets prepared from 45 micron lactose are essentially similar, although some fragmentation was observed at both 80 and 150MNm^{-2}. At 90 microns, the effects of increased pressure are more readily discerned, the lower pressure allowed the identity of individual particles to be retained. However, that considerable fragmentation has occurred was verified by comparison with tablets prepared from the same size starting material but containing 10% polyethylene (FIG.4.23 and 4.24). In the presence of the latter the matrix, on breaking, displayed a layer structure whose appearance would suggest that many of the original particles have not been extensively fragmented. Additionally, areas

FIG. 4.20(a)

10% Polyethylene in Lactose Outer

Pressure 220 MNm^{-2} Magnification 50x

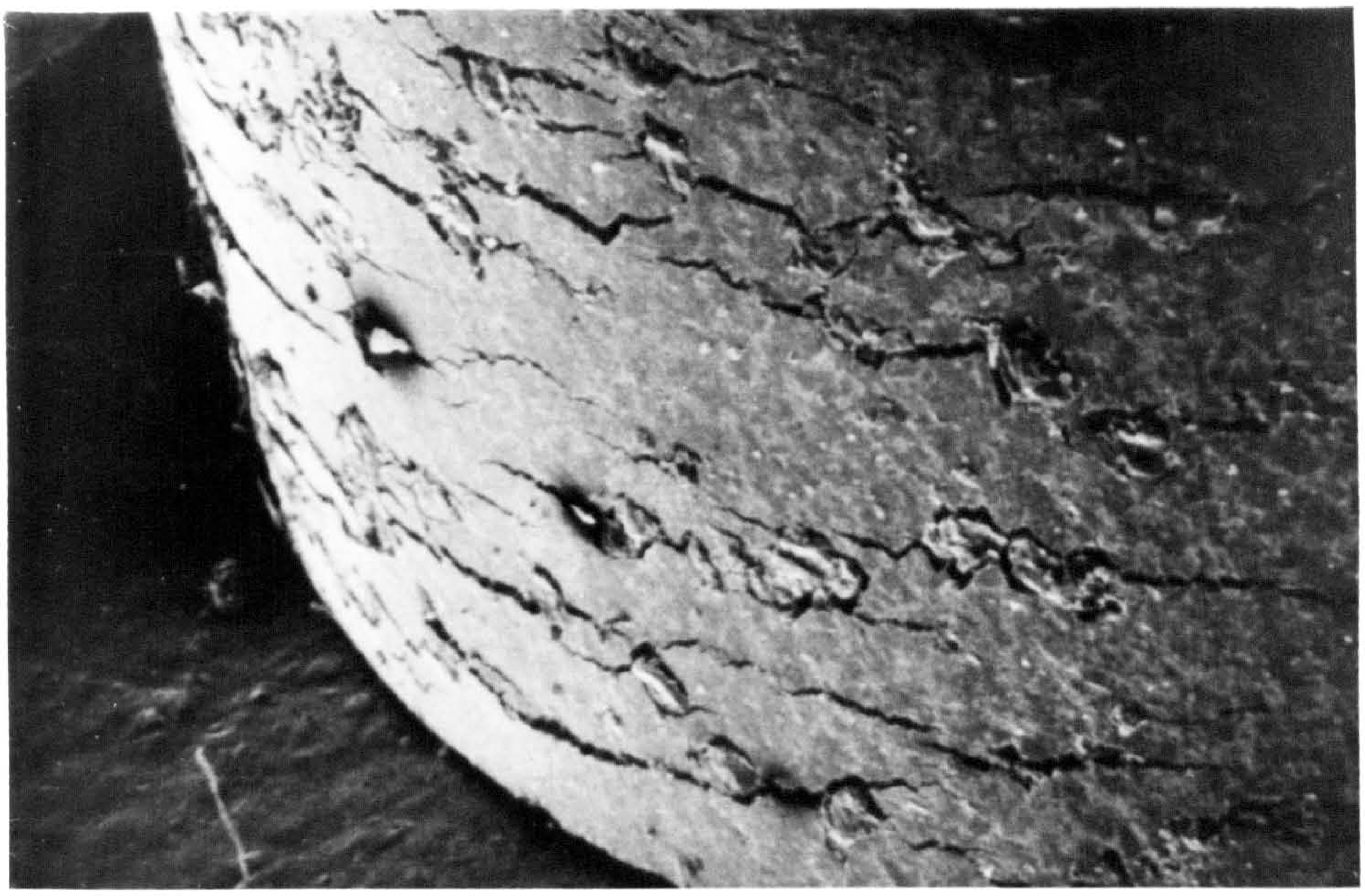


FIG. 4.20(b)

Lactose Outer

Pressure 80 MNm^{-2} Magnification 50x

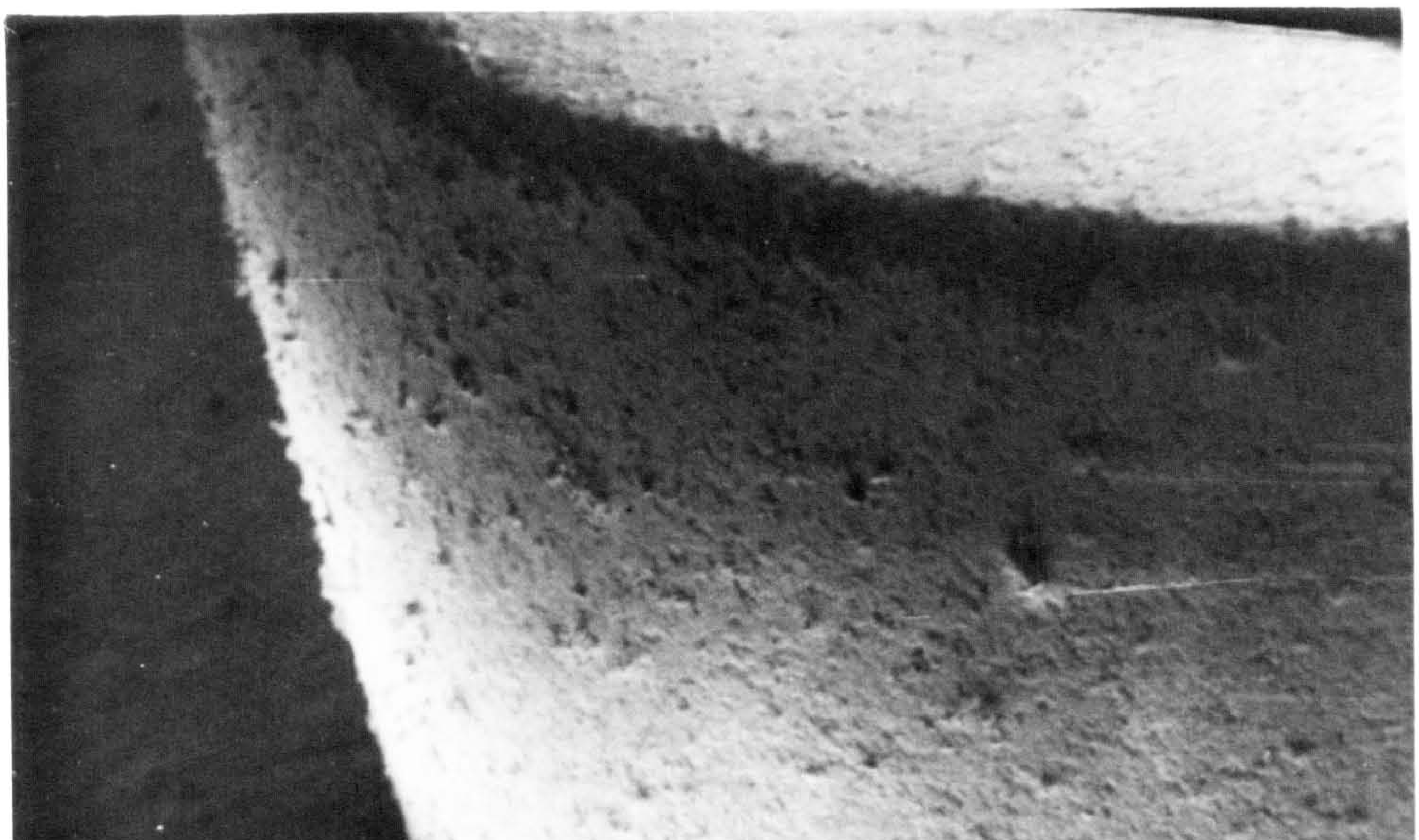


FIG. 4.21(a)

Lactose 45 microns

Pressure 90 MNm^{-2} Magnification 200x

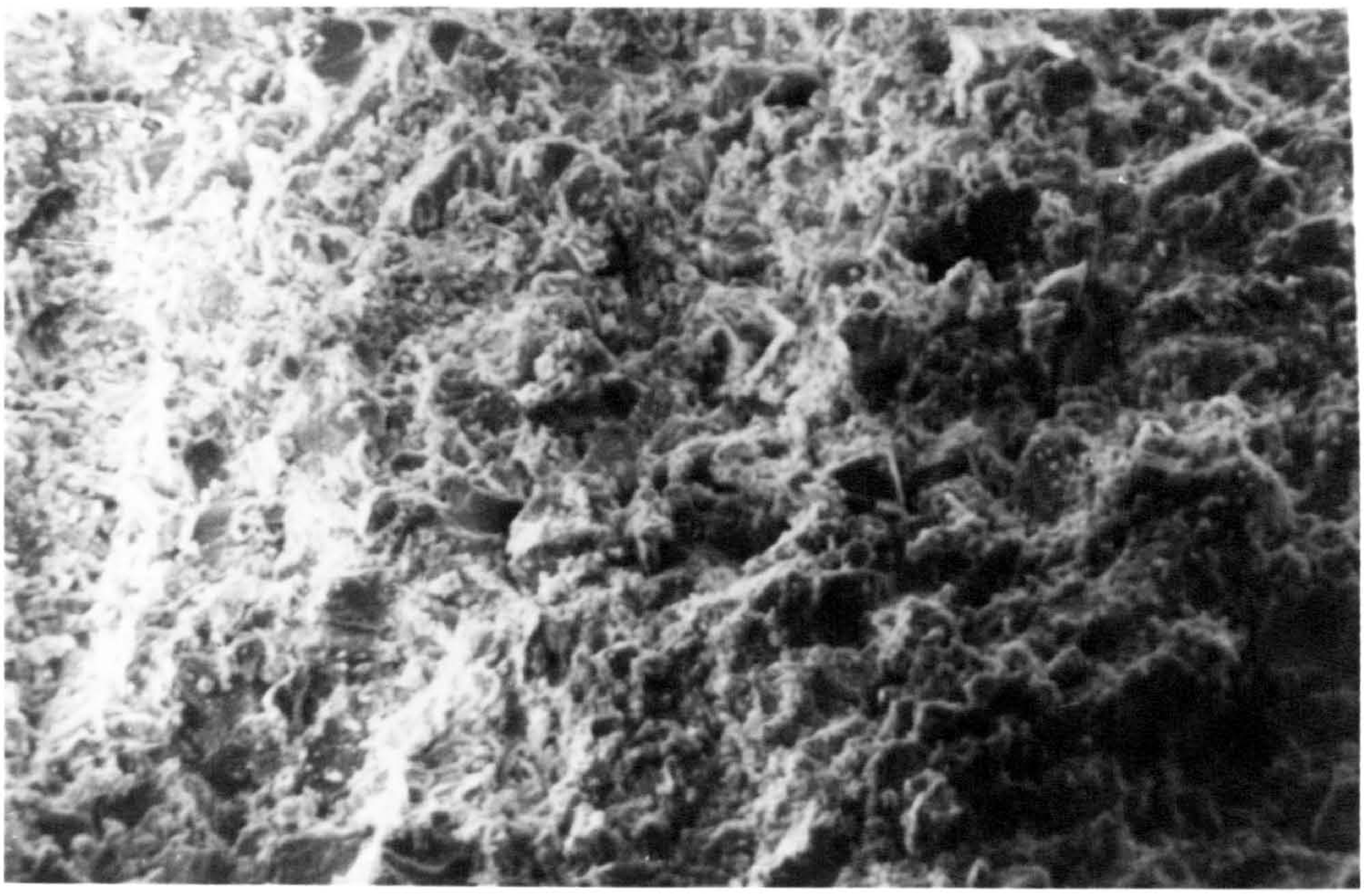


FIG. 4.21(b)

Lactose 45 microns

Pressure 150 MNm^{-2} Magnification 200x

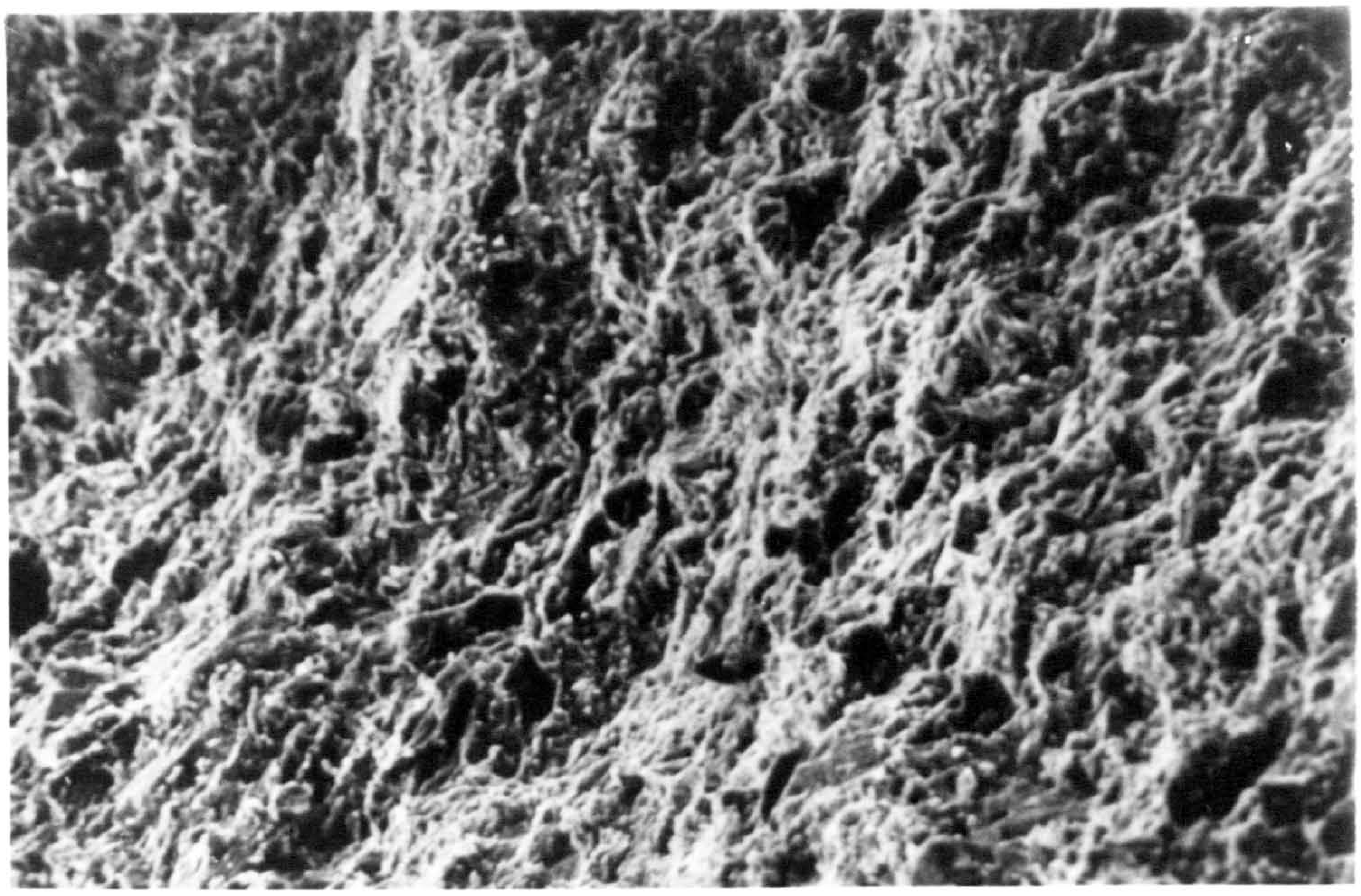


FIG. 4.22(a)

Lactose 90 microns

Pressure 80 MNm^{-2} Magnification 200x

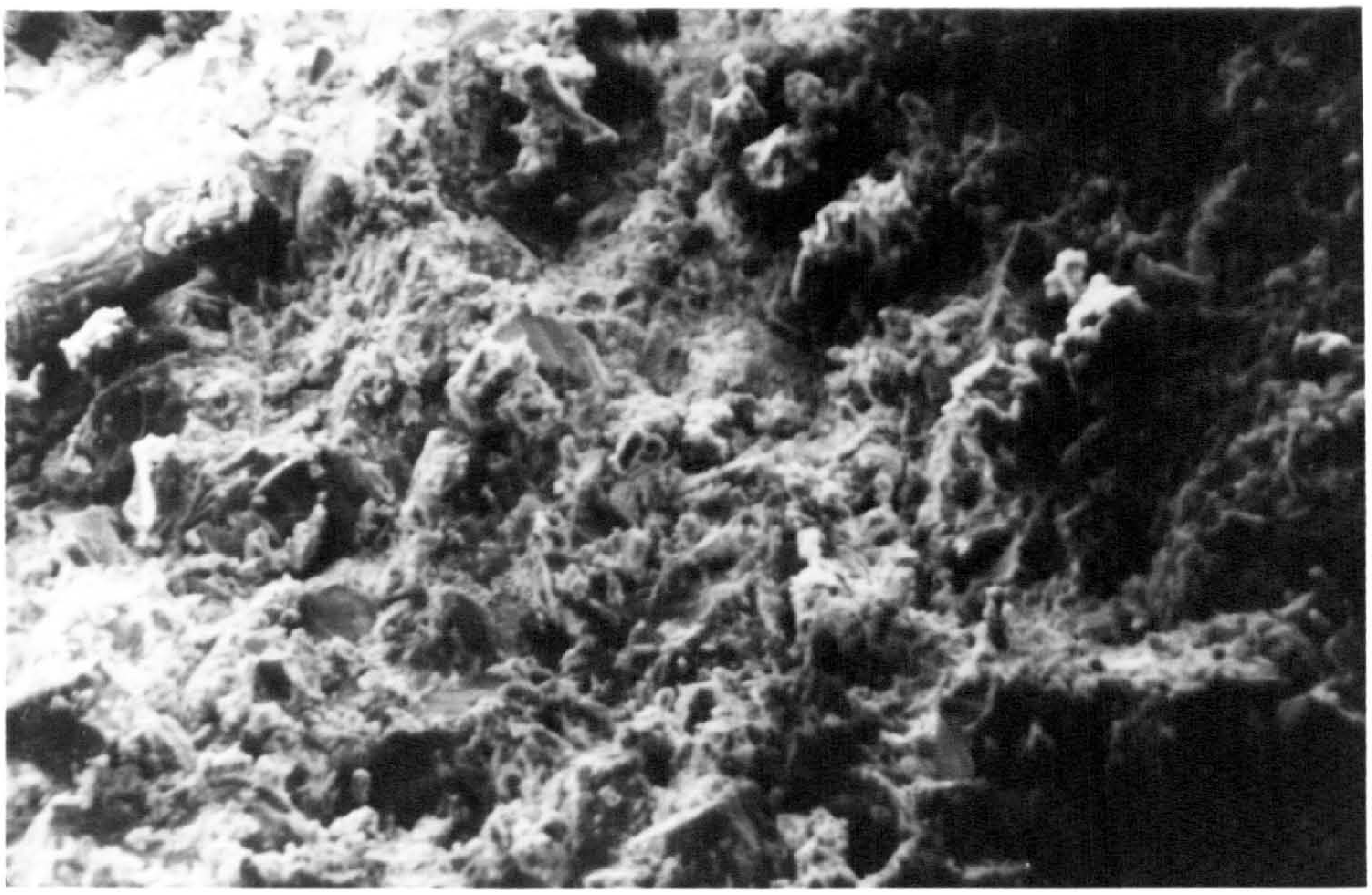


FIG. 4.22(b)

Lactose 90 microns

Pressure 180 MNm^{-2} Magnification 200x

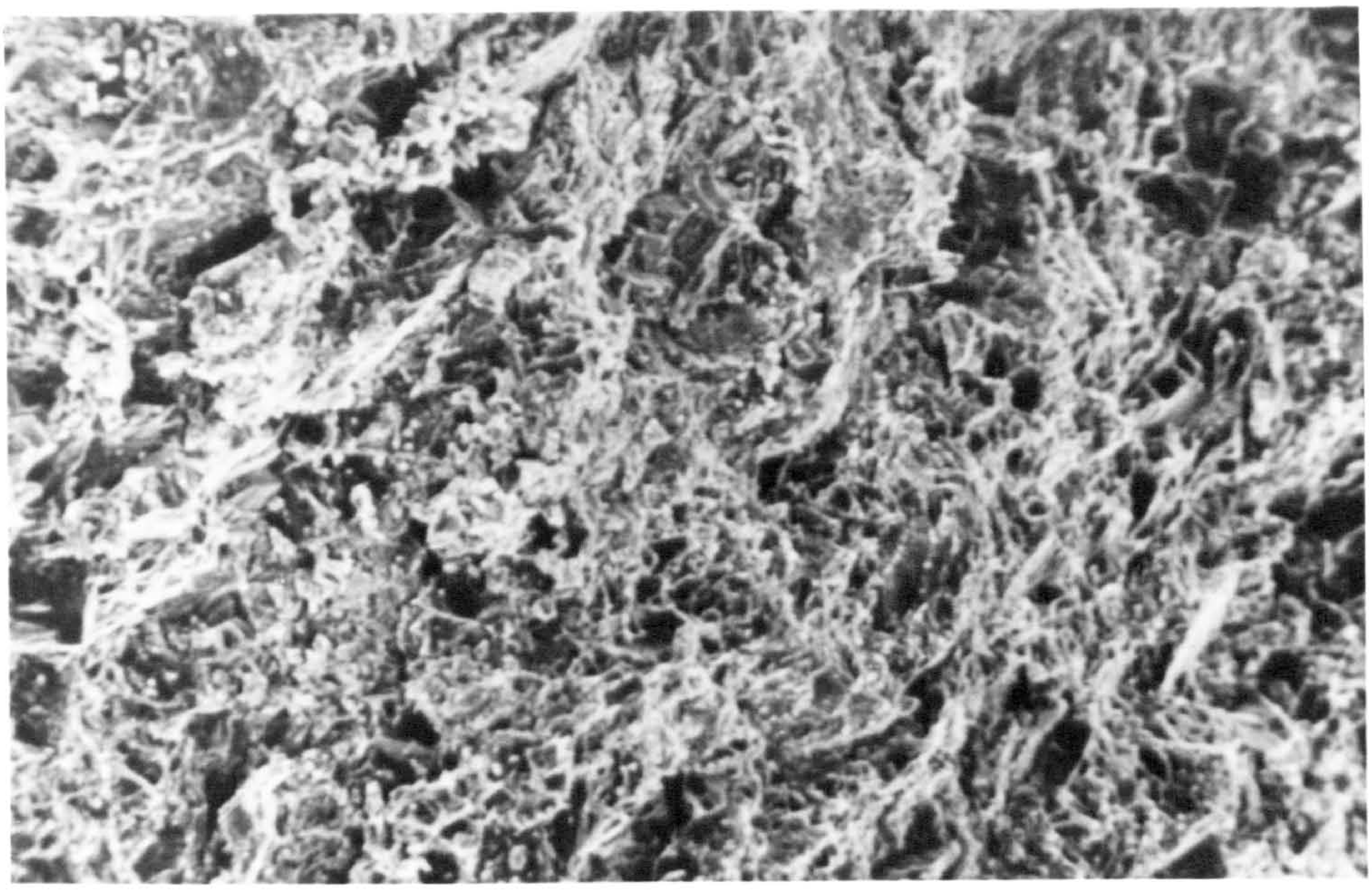


FIG. 4.23(a)

10% Polyethylene in Lactose

Pressure 150 MNm^{-2} Magnification 200x

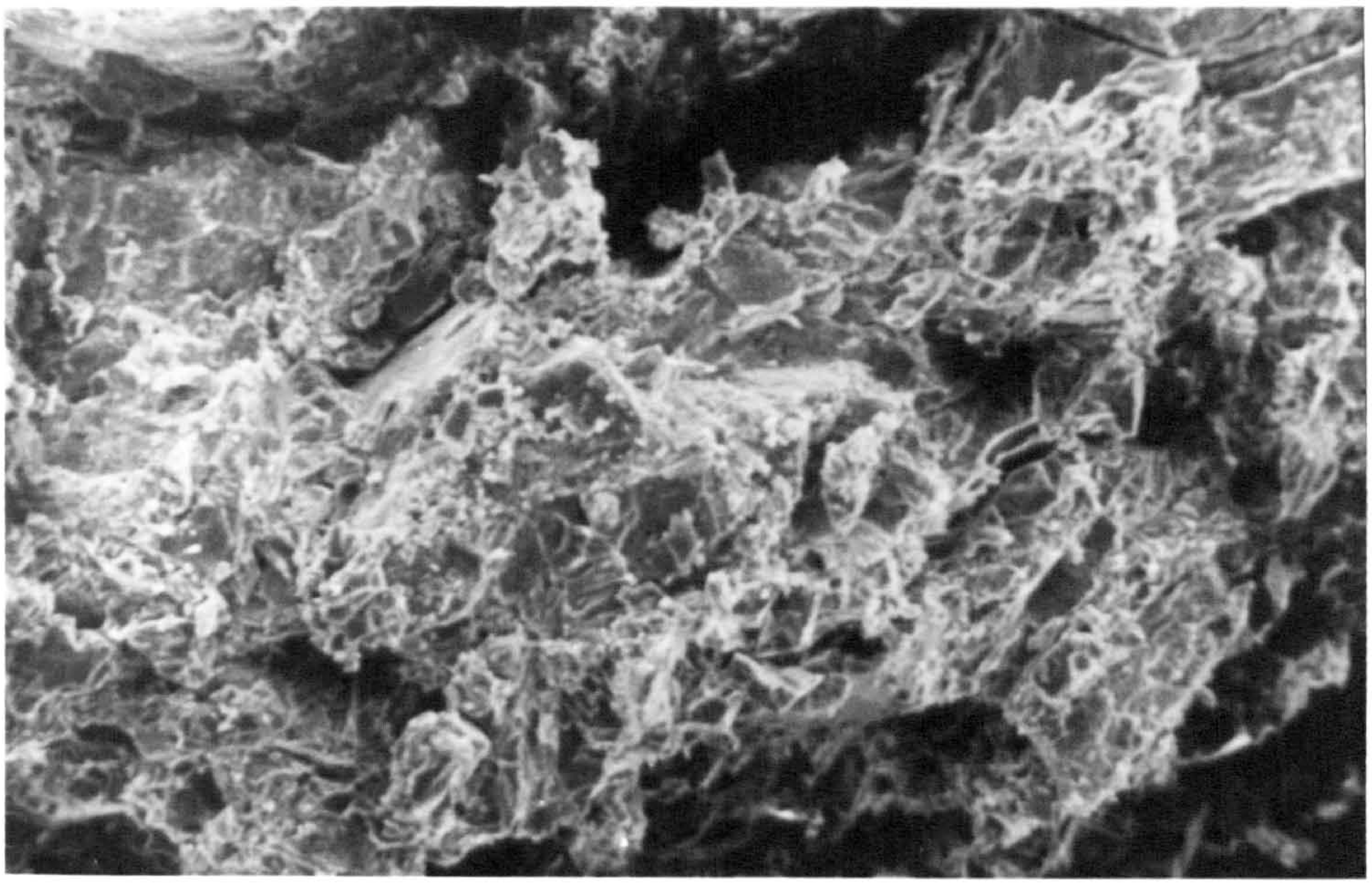


FIG. 4.23(b)

Lactose

Pressure 150 MNm^{-2} Magnification 200x

FIG. 4.24(a)

10% Polyethylene in Lactose

Pressure 175 MNm^{-2} Magnification 200x

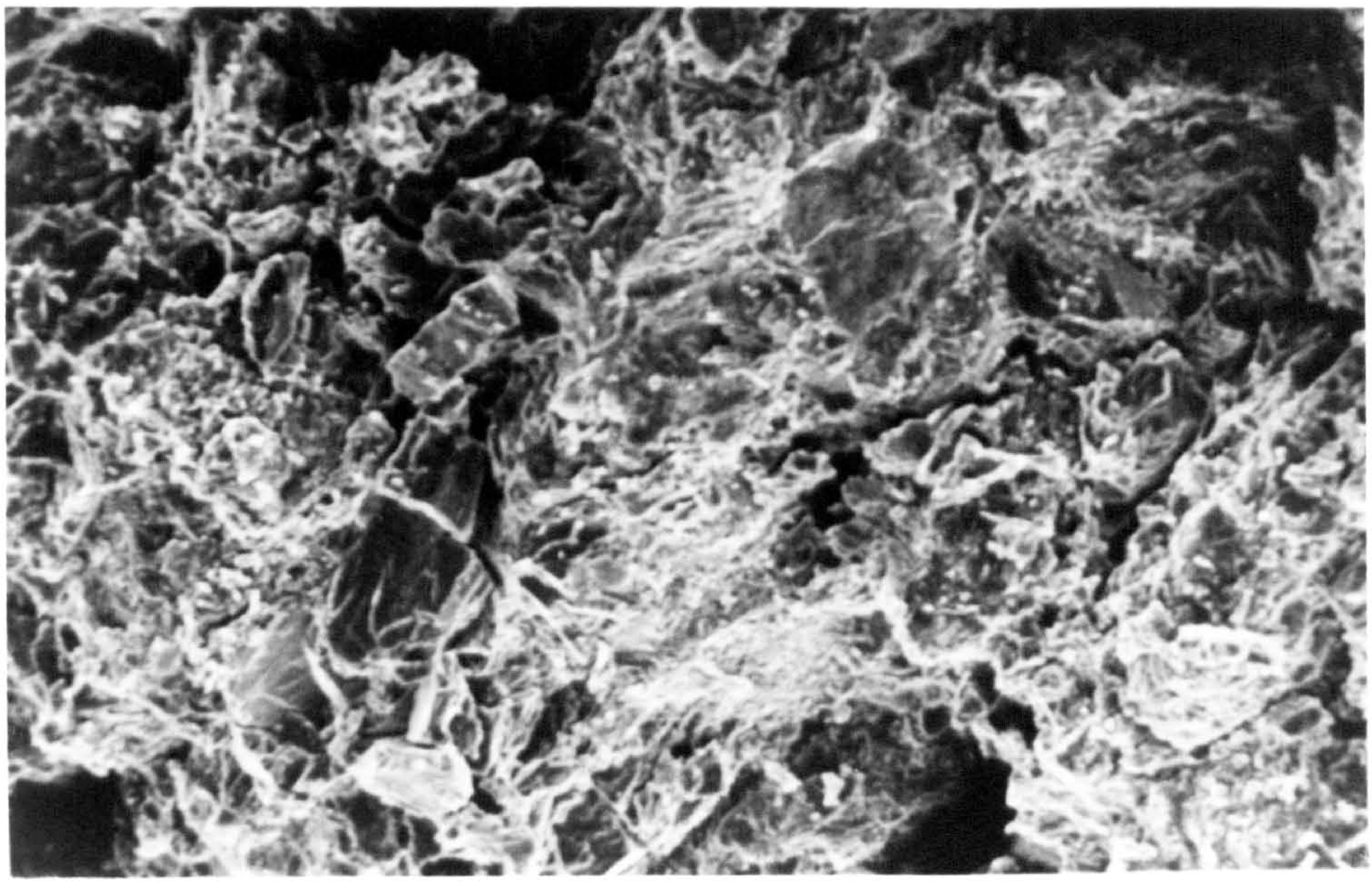
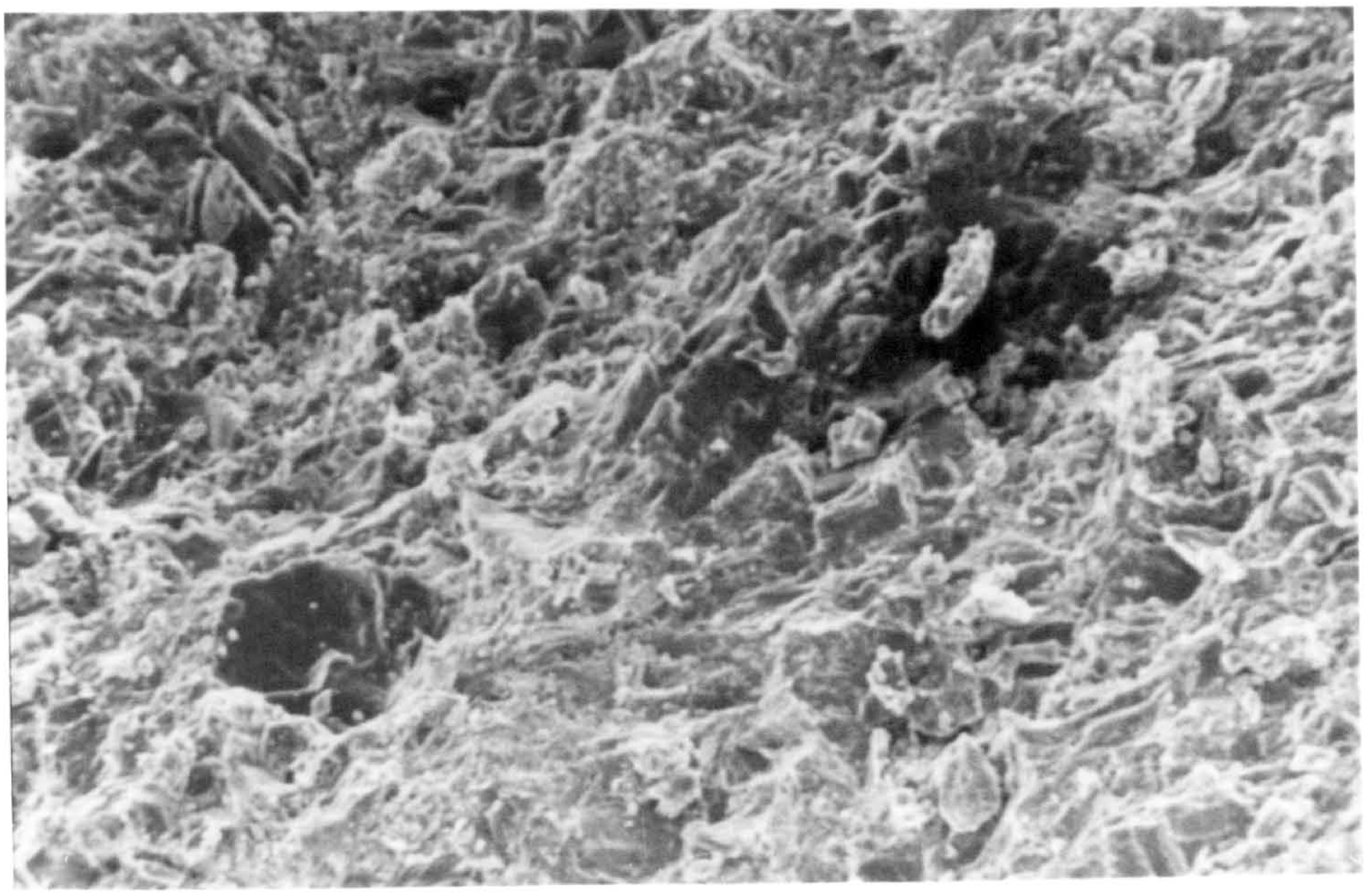


FIG. 4.24(b)

Lactose

Pressure 175 MNm^{-2} Magnification 200x



of emphasized discontinuity can be clearly perceived suggesting that compartments of weak bonding are present prior to diametral crushing.

4.2.3. Particle Size Contributions, to Tablet Strength - A comparison of lactose-polyethylene and sodium chloride-polyethylene systems

Based on static compression studies described in Section 3, the addition of material with a low Modulus of Elasticity to a substance which deforms via brittle fracture should be better tolerated, in terms of resultant compact strength, than would be the case if admixed with a plastically deforming material. To be successful such a prognosis relies, in part, on both materials being comparable in size which, in fact, they are not. Mean particle sizes of sodium chloride (250 microns) and Lactose (45 microns) are very different and the addition of a viscoelastic component to the former would result in a more profound effect on bonding properties than would a similar addition to lactose.

In comparing both lactose (45 microns) and sodium chloride (63 microns) as single component systems, relationships between cohesion and compaction pressure are difficult to rationalize. Because sodium chloride does not exhibit apparent ideal behaviour during diametral failure, crushing force must be used to define compact strength. Post compaction, the influence of stress relaxation on the tablet strength of sodium chloride cannot be ignored and, irrespective of circumstance, will always contribute to the measured strength.

However, as illustrated in FIG.4.13, crushing strength of sodium chloride increased and then plataued whether determined on immediate ejection or on storage. As opposed to this, the tensile strength of lactose continued to increase linearly irrespective of pressure. On addition of polyethylene compact strength was retained for both materials with only slight modifications at all pressures except the lowest where tablet strength was zero for the sodium chloride mixture on immediate ejection.

However, since very profound differences in tablet strength were observed when polyethylene was admixed with 355 micron sodium chloride, a comparison with an identical size of lactose was essential to support the fragmentation theory of bonding.

Lactose EP (Meggle) was available commercially in a variety of particle sizes. Fractions corresponding to sieve ranges 355-500 microns and 45-63 microns were separated and treated as outlined previously in Materials and Methods. To ensure that the Meggle material did not differ in character from that used previously (BDH), the 45 micron fraction was subjected to identical testing procedures to those outlined in Section 4.2.1. As can be seen from FIG.4.25 both materials behaved identically and were indistinguishable in their behaviour on compaction. FIG.4.26 illustrated how lactose, at a particle size of 355 microns, can, unlike sodium chloride, endure dilution with polyethylene and still retain its propensity for cohesion. Such behaviour was undoubtedly due to the tendency of lactose to fragment when subjected to pressure.

From the comparative studies outlined in this section, based on the dynamic compaction of both lactose and sodium chloride, the effect of particle size on cohesive properties has been clearly illustrated (Jackson, Ridgway and Rubinstein (1982, 1983). Low size fractions are able to overcome the presence of a highly elastic component and tablets having acceptable crushing strength can be produced. As the size fraction increases, materials that deform plastically cannot tolerate the introduction of an elastic component whereas the fragmentation deformation of lactose aids its attainment of tablet cohesion.

FIG. 4.25

Comparison of Compression Pressure vs Strength Parameters of Two Types of 45 micron Lactose

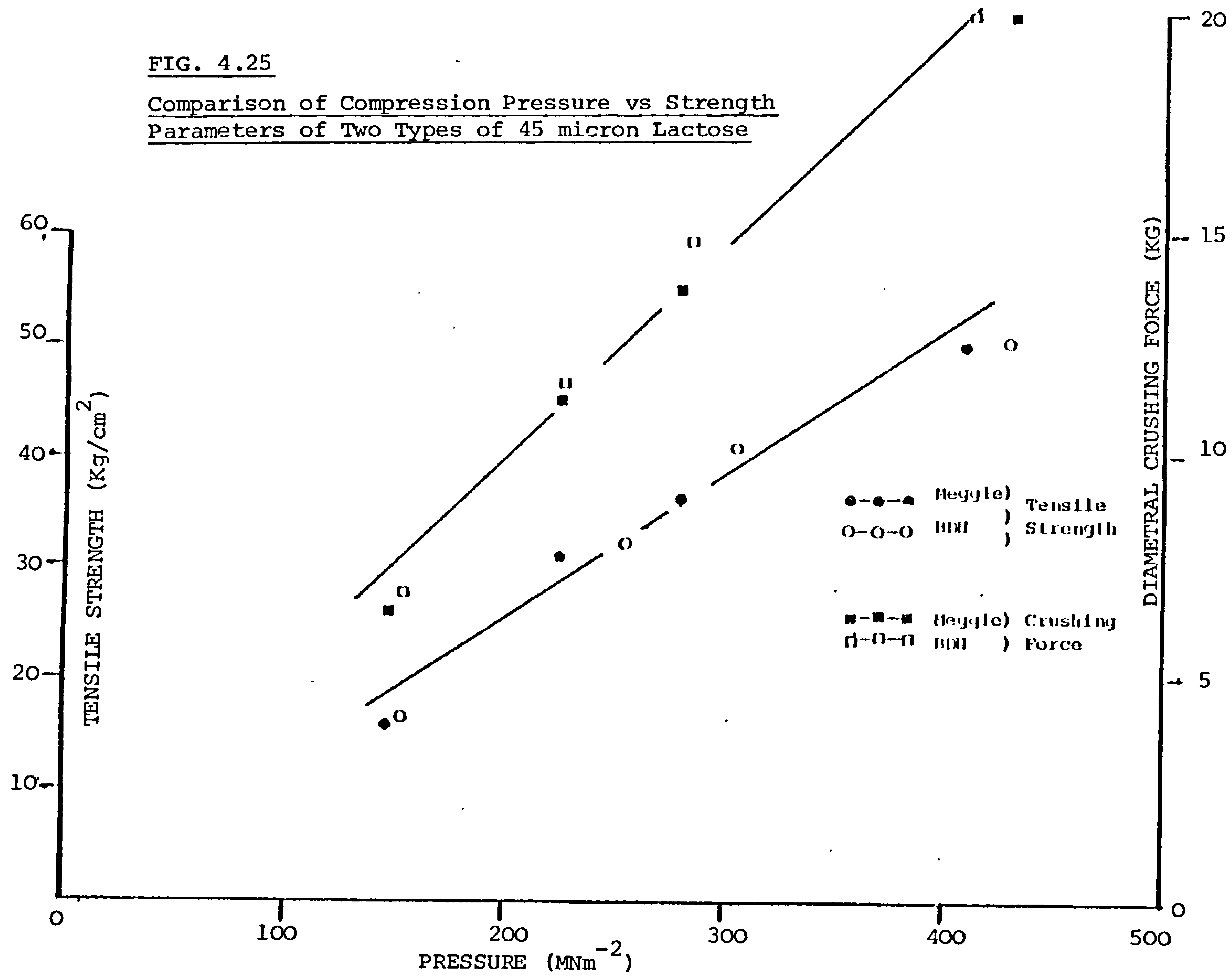
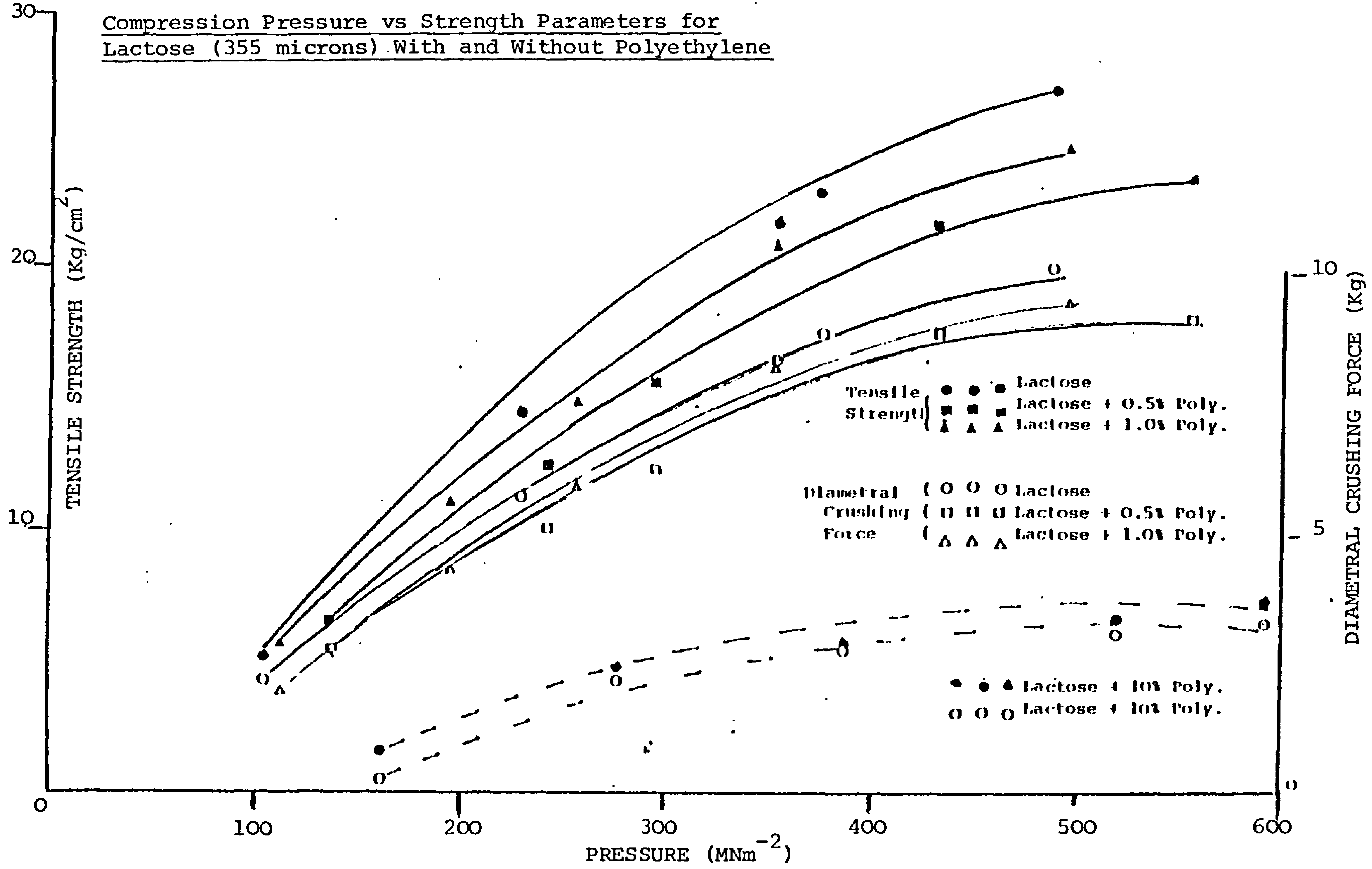


FIG. 4.26

Compression Pressure vs Strength Parameters for Lactose (355 microns) With and Without Polyethylene



5. SODIUM CHLORIDE AND LACTOSE BINARY MIXTURES-DYNAMIC COMPACTION

5.1 Compaction to Similar Thicknesses

Blends containing varying proportions of sodium chloride (355 microns) and lactose (45 microns) were prepared using a Turbula mixer, the relative size fractions being checked both before and after for size modification. No such modifications occurred. Both sodium chloride and lactose were dried pre and post mixing and the resulting mixtures stored over silica gel prior to processing.

After compression to similar thicknesses at relative pressures, breaking strength was monitored both at 2 minutes and 24 hours post ejection, compacts being stored over silica gel in the latter case. Tensile strengths were then calculated from the resulting breaking strengths.

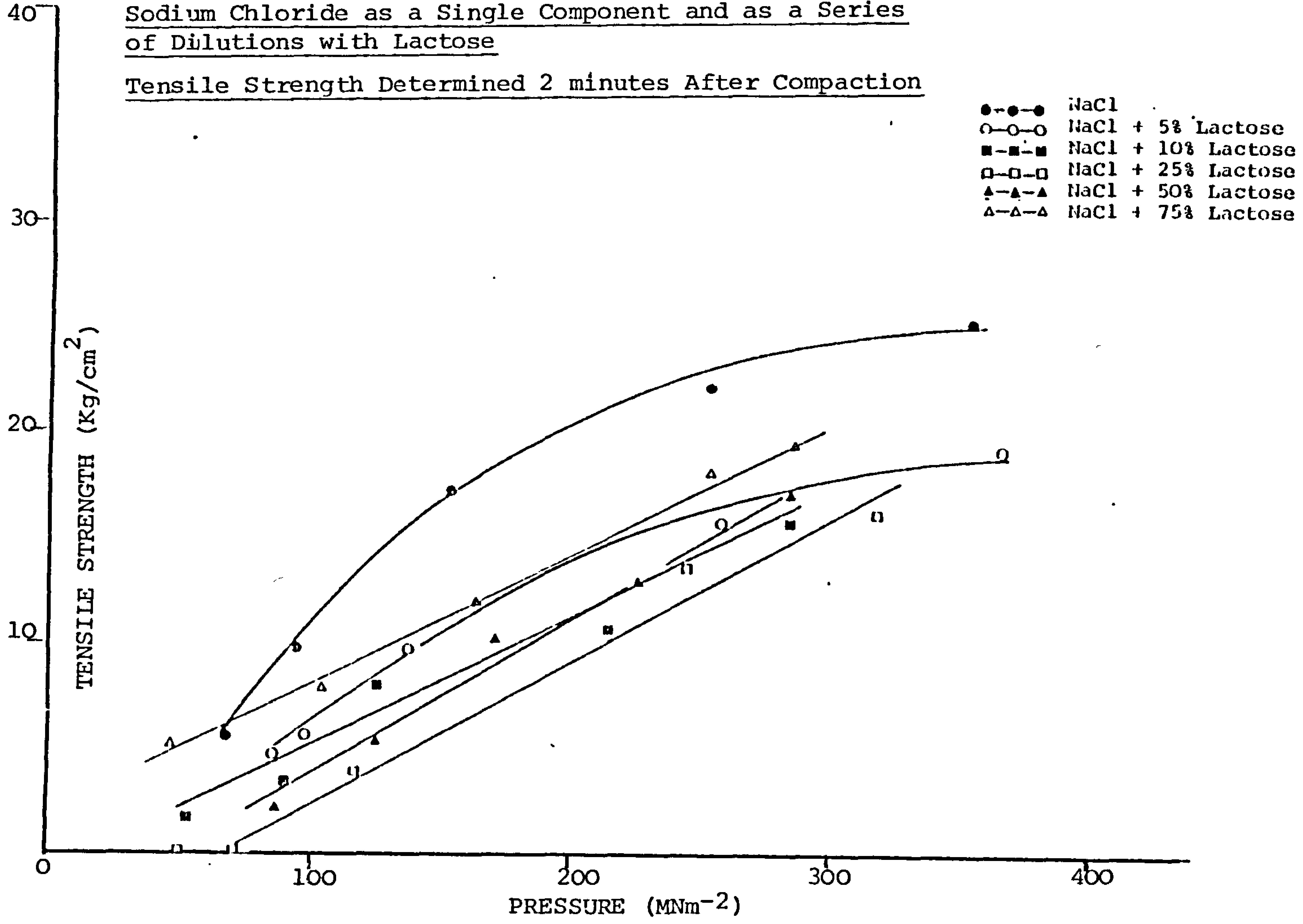
Variations in tensile strength as a function of punch pressure are shown in FIG.5.1 where strengths were ascertained 2 minutes after ejection. In the case of sodium chloride alone, values similar to those obtained previously (see FIG.4.1) were acquired. However, in this instance the correlation coefficient suggested that the relationship between strength and pressure was best characterised by a non-linear rather than linear function. Tensile strength was chosen as a measure of tablet strength since specimens exhibited apparent ideal breaking behaviour under stress. Such behaviour was not observed in the sodium chloride-polyethylene studies where excessive compaction pressures were required to achieve cohesion.

The addition of 5% lactose induced a significant reduction in tensile strength although, relative to sodium chloride alone, a tendency to plateau at high pressures persisted. Prior to compaction, the much smaller lactose particles can be visualised as occupying voids within a body of sodium chloride crystals. On application of pressure, lactose can either be held at site or displaced across

FIG. 5.1

Tensile Strength vs Applied Pressure Relationships for Sodium Chloride as a Single Component and as a Series of Dilutions with Lactose

Tensile Strength Determined 2 minutes After Compaction



solid boundaries. Thus, a reduction in tensile strength can be explained on the basis of an additive effect of two interactions. Firstly, sodium chloride-sodium chloride contacts are reduced with consequent reduction in initial bonding and a lower plastic flow index. Secondly, lactose-lactose bonds are small in number with the inherent elastic component of lactose (outlined in Section 3) serving, on compression, to weaken the internal tablet structure.

The overall effect, but to a very much lesser degree, can be likened to that observed on the addition of polyethylene to sodium chloride. Lactose-sodium chloride bonding can be ignored with tablet cohesion dominated by a plastic flow mechanism.

Assuming the above were the case, then post-compaction hardening, over an extended time period, would be predicted as being similar in nature to that of sodium chloride alone but of a lesser magnitude. Less initial bonding would give rise to a reduction in time-dependent stress relaxation hardening.

FIG.5.2 indicates such to be the case, in that the addition of 5% lactose curtailed plastic flow at the lower pressures. The high tensile strengths achieved at pressures in excess of 250MNm^{-2} resulted from a combination of intensified input energy and a reduction in interparticulate porosity leading to increased numbers of potential bonding sites.

On increasing the lactose content to 10%, significant changes in tensile strength vs pressure relationships were observed. On immediate testing, a linear correlation between strength and pressure was observed although the dimensions of strength were similar to those perceived on the addition of 5% lactose. At the increased lactose concentration it would be expected that the role played by the brittle component would increase in importance as the probability of lactose-lactose bonding increased. Thus, tablet cohesion would be

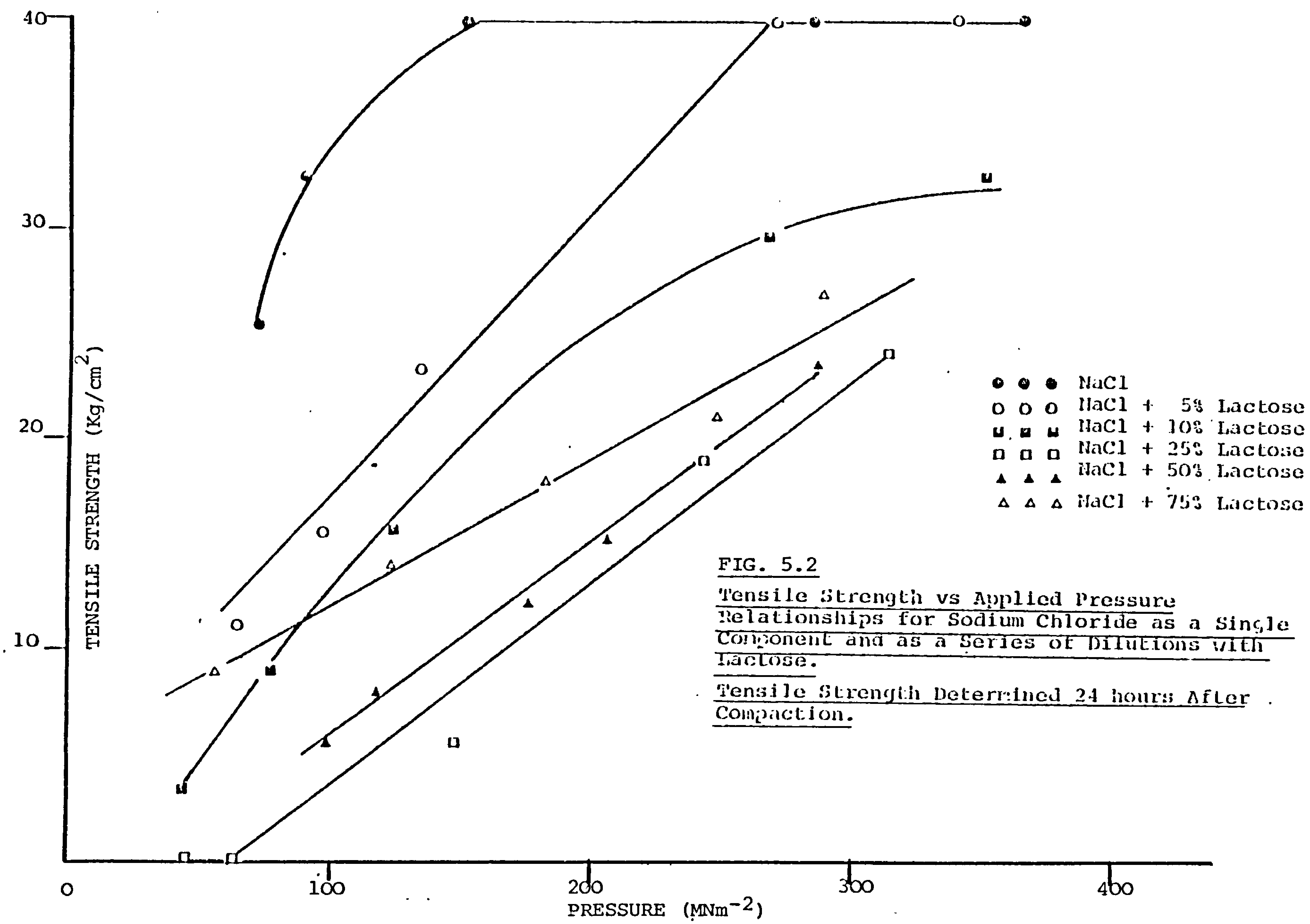


FIG. 5.2

Tensile Strength vs Applied Pressure Relationships for Sodium Chloride as a Single Component and as a Series of Dilutions with Lactose.

Tensile Strength Determined 24 hours After Compaction.

less prone to control via a dominant plastic flow mechanism. That such a prediction was correct is illustrated by long-term testing (FIG.5.2) where, although post-compaction stress relaxation hardening still operated, a further reduction in magnitude occurred. The relationship between strength and pressure also suggested that, at the higher pressures,diminution of hardening also occurred. Such would be expected since, at relatively high pressures, brittle fragmentation of lactose would occur to give smaller particles leading to increased initial bonding. As a consequence, a larger portion of total energy input would be involved in immediate bond formation. At even higher pressures stress-relaxation hardening would plateau or even reduce as minimum porosity was approached and lactose-lactose bonding was maximised.

A further increase in lactose content to 25% indicated that a critical dilution stage had been attained. At lower pressures, concentrations both above and below this critical quantity could be accommodated with one or the other component controlling the extent of bonding.

Thus, at lactose concentrations of 10% the effect of the brittle component on total bonding strength was minimal whereas, on being raised to 50%, compaction behaviour became dependent on lactose behaviour.

At lower pressures, two mechanistic modifications are considered to be operating. Firstly, even though sodium chloride (75% w/w) is in excess by weight, the powder matrix, both before and after compaction, can be visualised as a mixture of random large sodium chloride particles incorporated into, essentially, a lactose continuum. Thus, irrespective of the efficiency of the mixing process, areas of varying lactose density will occur throughout the mix resulting in analogous regions of diversifying bonding.

Consequently, the scatter of lactose particles would now severely inhibit initial sodium chloride bonding resulting in significant reductions in post-compaction plastic flow hardening.

The secondary contributory influence on compaction response at lower pressures, when operating at a lactose dilution of 20% w/w, would arise from the small but significant elastic component of lactose, of the multifarious bonds formed during compaction only lactose-lactose interactions would undergo post compaction elastic recovery. In studies on the static compaction of mixtures of lactose and sodium chloride, Sheikh-Salem and Fell (1981) demonstrated how, at similar pressures, the tensile strength of compacts was minimal at equal dilutions of either component, irrespective of particle size. However, their relatively long dwell-time and static lower punch made comparisons with dynamic conditions unrealistic since the slow consolidation stage and absence of radial relaxation during decompression would favour the production, in the static system, of greater tablet cohesion and mechanical strength. Nevertheless, although the present work did not include compression of lactose alone (it is included in Section 4) the findings do correlate with observations made by the above authors, in that tablets produced from mixtures of materials with different compaction mechanisms can attain lower mechanical strengths than those achieved by compaction of the individual components.

On increasing the pressure, still at 25% w/w lactose, a linear strength-pressure profile emerged irrespective of time lapse prior to testing. The relatively slight but significant strength increase in the 24 hour samples indicated that sodium chloride bonding still had a role to play.

At 50 and 75% dilutions of lactose it became clear that lactose particles were now sufficiently in excess to control the mechanical strength of the compacts produced. At the 75% lactose level, the post-compaction stress relaxation properties of sodium chloride still operated to some degree but the gradient of the strength-pressure curves was reduced with respect to all other lactose concentrations and approached that of the 2 minute test station.

5.2. Compaction to Similar Weights

In the studies described above, a basic starting mass of 500mgs of powder was adjusted, as required, to achieve tablets of comparable thickness irrespective of applied pressure. Independently, mixtures of 355-500 micron sodium chloride and 45-60 micron lactose, at a constant tablet weight of 500mg.± 1% were also evaluated. Top punch displacements were identical to those in the first study but, because of the difference in densities the range of working pressure chosen for study was lower than that for the "constant thickness" evaluations. This adjustment was necessary to compensate for the greater pressures operating as the lactose content increased.

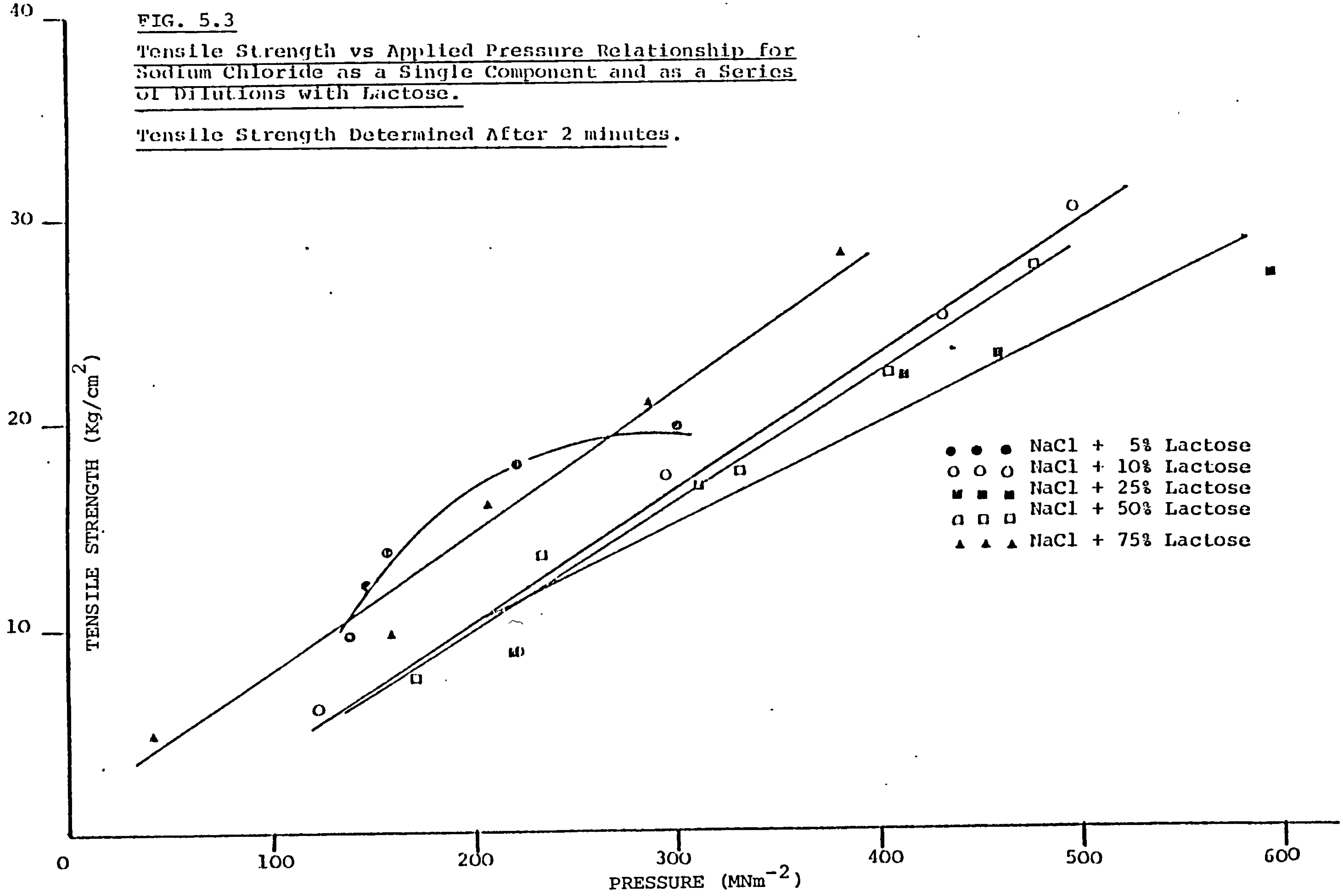
FIG.5.3 shows the strength-pressure relationship when sodium chloride was diluted with 5, 10, 25, 50 and 75% w/w lactose. At the lowest lactose concentration, since the weight was no longer being adjusted, the tensile strength would be expected to be higher initially at similar pressures. A comparison with FIG.5.1 showed this to be the case. As the weight of powder supplied to the die increased, the total energy input would be expected to distribute over a greater area. Thus considerable stress-relaxation hardening would be anticipated but to the same extent as that observed with the thickness adjustment studies. FIG. 5.4 shows this to be correct.

At constant top punch displacement, movement to a higher lactose content (i.e. 10% w/w) resulted in a greater pressure registration on the bottom punch than that observed at constant thickness. However, when pressures were approximately similar (280MNm^{-2}) for both studies, then similar tensile strengths were obtained. As the weight remained

FIG. 5.3

Tensile Strength vs Applied Pressure Relationship for Sodium Chloride as a Single Component and as a Series of Dilutions with Lactose.

Tensile Strength Determined After 2 minutes.



constant but the volume increased, the strength vs pressure relationship remained linear. However, the strength profile was offset to a higher level since at the same displacement, the porosity was reduced and more initial bonding occurred. This was reflected in the greater stress-relaxation hardening observed at the lower pressures when the weights were adjusted. Nevertheless, a similar plateau was observed in both the equal weights and equal thickness studies, as the lactose-lactose interaction began to interfere with the plastic flow properties of sodium chloride.

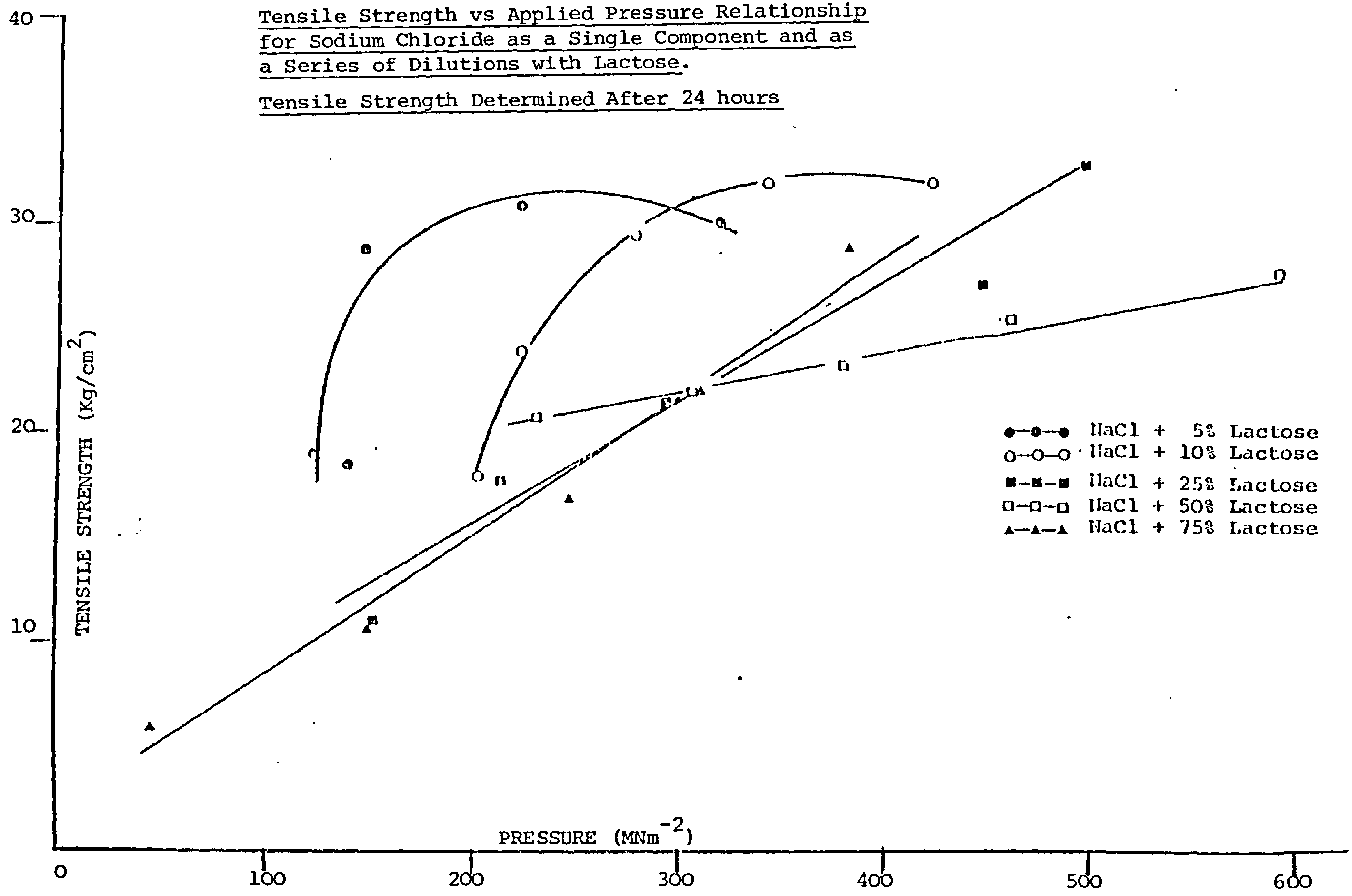
At 25% lactose a drastic reduction in cohesive strength was not observed (FIGs.5.2 and 5.3) although the degree and order of strength remained the same. Any plateauing was now absent and the stress-relaxation properties of sodium chloride were significantly inhibited.

On increasing the lactose content to 50%, an interesting relationship surfaced. Immediate strength determinations indicated a linear correlation between pressure and tensile strength which, when compared with FIG.5.1, suggested that similar initial bonding strength had been achieved irrespective of powder quantity. At 24 hours, the strength vs pressure profiles were quite different (FIG.5.4). At the highest applied pressures appropriate to immediate strength determination ($460MNm^{-2}$) the tensile strength observed was not significantly different from that perceived with stored samples. As opposed to this, on decreasing the applied pressure, the role played by sodium chloride by means of its post-compaction stress relaxation effect remained appreciable, even at 50% dilution with lactose. Since lactose particles will be in considerable excess its presence would almost totally override any interparticle bonding of sodium chloride with a consequent effect on stress relaxation. At the lower pressures filling of voids would be less complete hence increasing the opportunities for sodium chloride particles to interact.

FIG. 5.4

Tensile Strength vs Applied Pressure Relationship for Sodium Chloride as a Single Component and as a Series of Dilutions with Lactose.

Tensile Strength Determined After 24 hours



At 75% w/w lactose such an excess completely swamped any plastic flow bonding potential of sodium chloride and both immediate and time-dependent strengths were comparable. Attempts have been made previously to predict the strength of tablets prepared from components with known strength properties and Fell and Newton (1970) showed such predictions were feasible when applied to mixtures of various types of lactose of approximately equal particle sizes. The same researchers (1971) went on to show that when the different forms of lactose were present in the same crystal then the strength of such tablets, prepared by compaction of such crystals, was not related to the composition of the mixture. Newton, Cook and Hollebon (1977) were the first researchers to attempt to predict the strength of tablets formed from materials which might be expected to compact by different mechanisms. They showed how tablets made from dicalcium phosphate and phenacetin, with 1% magnesium stearate added as lubricant, possessed greater tensile strength than would be anticipated from consideration of the tensile strength of individual components. They stressed the importance of porosity and method of particle consolidation in deriving compaction properties with respect to tablet strength.

The studies reported above involve binary mixtures of plastic and brittle materials which compress to give tablets whose final strength was controlled by varying additions of one or other components. Particle size differences, and hence porosity and density differences, would clearly affect the outcome of strength predictions. The addition to sodium chloride of a material of small particle size and a propensity to further size reduce during compaction will clearly affect the compaction properties of sodium chloride. Such a material is lactose and its energy requirements for bonding during compaction have been shown to effectively reduce the plastic flow behaviour of sodium chloride. However, quite large amounts of the latter would be required to increase the strength of lactose compacts.

6. STRESS RELAXATION BEHAVIOUR

6.1. Introduction

The nature of the internal matrix of a compact, whether composed of single or multiple components, will be a function of interactions occurring during both compression and decompression stages of the compacting process. Among the many factors which contribute to the quality of the final product, of which those such as applied pressure, dwell time and compression speed have been dealt with in previous sections, the utilisation of excess energy, imparted to the system during the compression stage and not employed in the critical bonding function, has been investigated by several researchers. Particular emphasis has been placed on the consequence of stress relaxation or creep, a phenomenon designated by the present author as occurring in that segment of the compaction cycle where external stress is no longer increasing i.e. the instant the load is either held constant or removed.

The importance of separating compression and decompression events is of particular relevance when dealing with materials which deform via a plastic flow mechanism and Jones (1981) has highlighted some of the critical factors involved. He outlined the role played by both contact time and rate of applied force (these two being inseparable) and also the time during which the material was subjected to a maximum force i.e. dwell time. However, since the maximum force would be transient across a powder bed and the dwell time presumably related to the slight pause in motion of the top punch during the compression cycle, such a definition was ambiguous. The inference he made was that slow compression and decompression would allow some degree of stress relaxation to elapse before the maximum load was removed, such a conclusion, being fundamentally correct, underlined the importance of examining the manner in which materials relaxed following stress.

As an alternative, Krycer, Pope and Hersey (1982) related their description of stress relaxation to a decrease in applied force under static compression resulting from plastic deformation of compressed material into interstitial space. This definition was also equivocal, since it assumed that all internal arranging of integral particles ceased the instant the applied load was stopped.

As mentioned earlier, a degree of stress relaxation occurs with certain materials the instant compression ceases or is reversed and, in the case of a material such as sodium chloride, confers a time-dependent strength on compacts of the latter which can be quite substantial. Such an effect has been emphasised both by the present author and by previous researchers (Rees and Shotton: 1970 and Rue and Barkworth: 1980). However, there is little doubt that it is how compacts behave within the die, when subjected to maximum load, which is of major importance and previous attempts to qualify the extent of such importance are highlighted in the following Section.

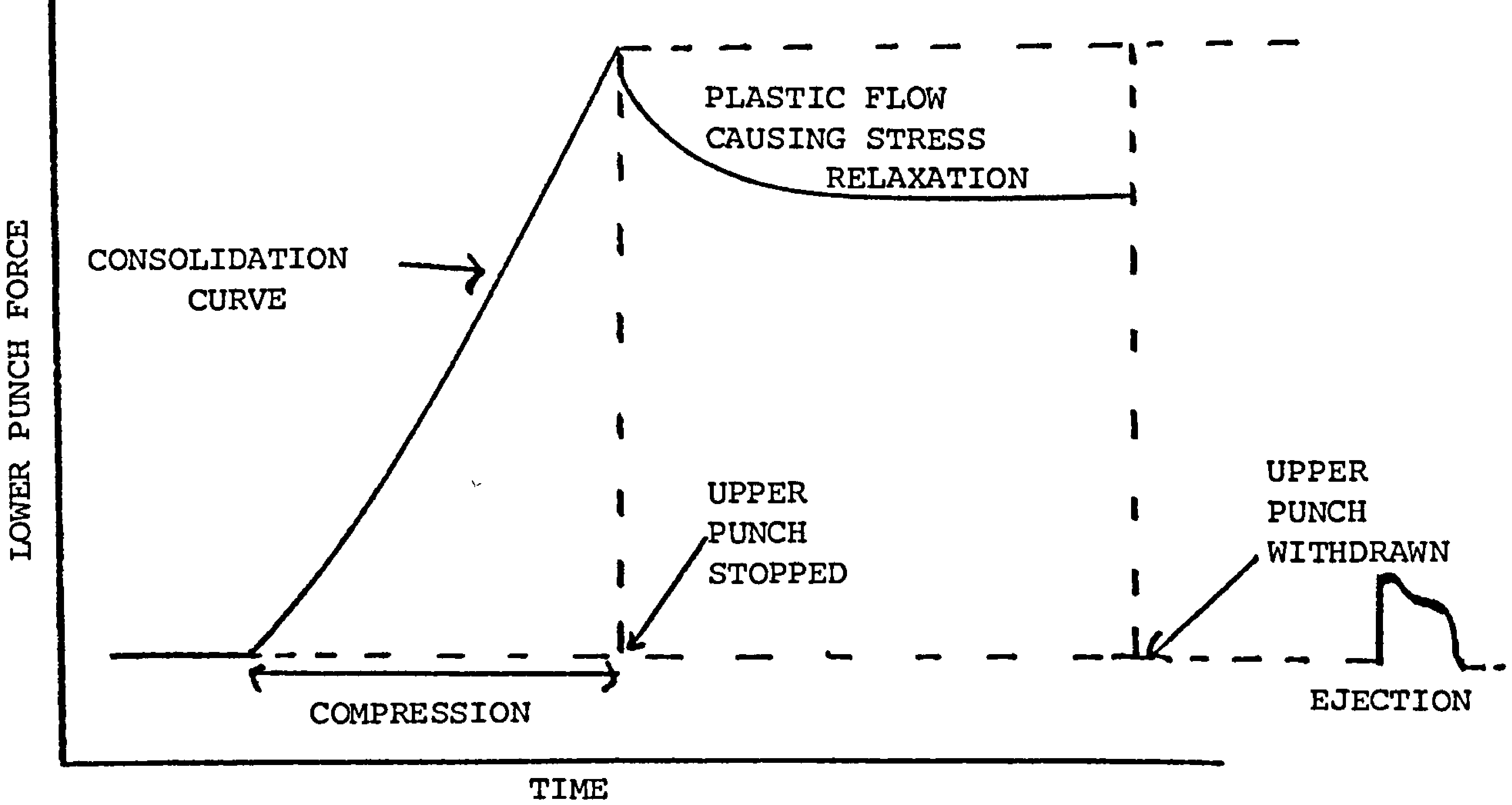
6.2. Stress Relaxation under Static Load

Using an instrumented tablet machine to study stress vs time relationships for various drugs and excipients, Baba and Nagafuji (1965) demonstrated two basic findings, namely that (a) an increase in relaxation coincided with both a reduction in applied pressure and particle size and (b) on tableting, creep recovery led to swelling with tablets containing starch and starch-lactose. Shlanta and Milosovich (1964) also demonstrated a time-dependent effect as did Cole, Rees and Hersey (1975) who measured both the load and resultant deformation of sodium and potassium chloride and potassium citrate by means of an Instron Universal Testing Instrument. They compressed the powder bed at a fixed rate (0.1cm min^{-1}), stopped the upper punch at a preselected maximum load and, without revoking the load, monitored the stress relaxation over 2 minutes.

A typical example of the data generated between onset and completion of compression cycle is shown in FIG.6.1. They assigned their findings to the capability of certain materials to undergo plastic flow.

FIG.6.1.

(From Cole, Rees and Hersey: 1975)



By evaluating the various physical processes involved in tableting Hiestand, Wells, Peot and Ochs (1977) considered the contribution made, to the final identity of the tablet, by each stage of the compaction cycle. As a result, they refocussed the emphasis of tablet control from the compression to the decompression stage. They paid particular attention to the effect of stress relaxation on capping and made the observation that materials known to cap exhibited slower stress relaxation. By eliminating secondary factors such as air entrappment (control experiments were carried out in an evacuated die) the importance of stress relaxation was further concentrated. Overall, their findings clearly designated the time dependent relationship between stress relief and plastic deformation, while rapid decompression produced fractured compacts, extended decompression times resulted in unimpaired compacts.

Ritter and Sucker (1980) supplemented the above concepts, linking capping with stress relaxation by subjecting micronised phenazone to static strain (14 minutes duration) and comparing their findings with tablets ejected immediately post compaction. However, emphasis in their study was placed on the relationship between elastic deformation energy held by the tablet and the interparticulate bonding force. On subjection of static strain, the tendency of phenazone to cap was eliminated.

The most definitive study to date linking the effect of stress relaxation on tablet strength is that of David and Augsburger (1977) whose studies encompassed variations in duration of both the total compression cycle and maximum applied compressive force. They effected the first condition by varying the speed of a rotary press, operating at only a single station, between 0 and 10 seconds, the second was accomplished by retaining the applied pressure at a value which produced tablets of acceptable hardness.

Substances were treated as materials possessing both an elastic and plastic component, the latter concept being treated mathematically as the Maxwell model under constant strain and involving both an elastic and viscous parameter. As a result of such treatment, the following relationship could be derived:

$$\ln \Delta F = \ln \Delta F_o - kt$$

where F = amount of compressional force left in viscoelastic region at time t

F_o = total magnitude of this force at $t = 0$

k = viscoelastic slope, being equal to $\frac{E}{\eta}$

where E = Young's Modulus

η = a viscosity coefficient.

As a result, it was possible to classify the materials under study (a series of direct compression fillers) according to their degree of plastic flow under compaction. By adopting mechanical strength of tablets as a yardstick of ultimate bonding potential, David and Augsburger designated an interdependence between highest attained strength and maximum plastic flow.

Rees and Rue (1978), in a similar study, went on to question some of the conclusions derived by David and Augsburger, since data generated by the former produced conflicting results when subjected to treatment by the Maxwell body concept. Such differences were reflected in the relative findings on the time dependence of stress relaxation, where Rees and Rue's conclusions that stress abatement continued for 30 seconds post compaction contradicted the shorter (10 second) completion time for David and Augsburger. The longer relaxation time was purported to be indicative of static load, a constraint not operating in the David studies. As a result of their findings, Rees and Rue cast doubts upon the usefulness of stress relaxation measurements in the definition of tableting properties.

In the view of the present authors, stress relaxation studies, whether they be concerned with elastic or plastic or combination mechanisms can, when integrated with other parameters associated in defining compression characteristics, usefully contribute to the overall conclusion. The data presented herinafter aids in explaining questions left unanswered in Sections 3,4 and 5 concerning the effect of elastic, plastic and brittle mechanisms on the modification of tablet properties and is concerned, essentially, with that period in a tablet's life between the instant when maximum compression pressure is applied and some following integral of time.

6.3. Materials and Methods

6.3.1. Materials

The materials chosen for study were as outlined in Section 2.1. Particle sizes subjected to testing were as follows:

Sodium chloride:-	355-500 microns
lactose monohydrate:-	45-63 microns
polyethylene:-	180-250 microns

Blends of binary mixtures of different concentrations were prepared using a Turbula mixer. Single components and mixtures were dried and stored over silica gel until compressed.

6.3.2. Methods - Static System

6.3.2.1. Stress Relaxation as a Function of Post Compaction Force/Pressure Decay

The system as described in Section 2.2.2 was employed, a universal force of 8KN ($\equiv 112.6\text{MNm}^{-2}$) being applied at preset speeds of 2, 20 or 50mm min^{-1}. The force-time curve was plotted on a flat bed recorder such that an applied force of 8KN produced an abscissa dimension of 80% full scale. The Instron Universal Testing Instrument can modify compaction loading control in any one of three ways. Firstly, the crosshead can be operated in the "Cycle" mode, thus allowing immediate withdrawal on reaching maximum load. As the name suggests, the load can then be reapplied, if so chosen, on a preset time cycle. Secondly, the load can be held, such that the electronics would maintain the crosshead at the peak load for whatever time desired. Such conditions are unfavourable in studies involving stress relaxation since, in those cases where reduction in tablet dimensions occurred on imposition of peak load (i.e. materials which underwent plastic flow) the load would electronically adjust to account for the slight movement in top-punch position. Finally, the load can be stopped at the instant at which the top punch exerts its maximum pressure on the compacted material. Within the boundaries of the investigation, the third option was chosen as being most favourable for studying the effect of stress relaxation on upper punch force decay.

As mentioned earlier, experimental data was generated at crosshead speeds of 2, 20 and 50mm min^{-1}, as speed increased a machine artefact surfaced, with the electronic cut-out on the "Load Stop" control tending to overshoot. Consequently, as the speed advanced, the registered load exceeded that of the preset upper limit. The effect is illustrated in FIG.6.2 which is a composite of force-time and displacement-time curves generated with the die empty. Calculation of the actual loads operating at the higher two speeds showed them to be 8.20 and 8.25KN respectively, differences which were considered to be sufficiently close to theory to be negligible. It was clear that, once maximum applied load had been attained and the crosshead stopped, force decay was negligible. Thus, on the introduction of a powder into the die, any post compaction deviation from equilibrium between force and time would be a function of the behaviour of the die contents rather than an artefact of the measuring techniques.

6.3.2.2. Stress Relaxation as a Function of Post-Compaction Displacement

By means of an extensiometer attached to the top-punch holder of the jig described in Section 2, a method for measuring

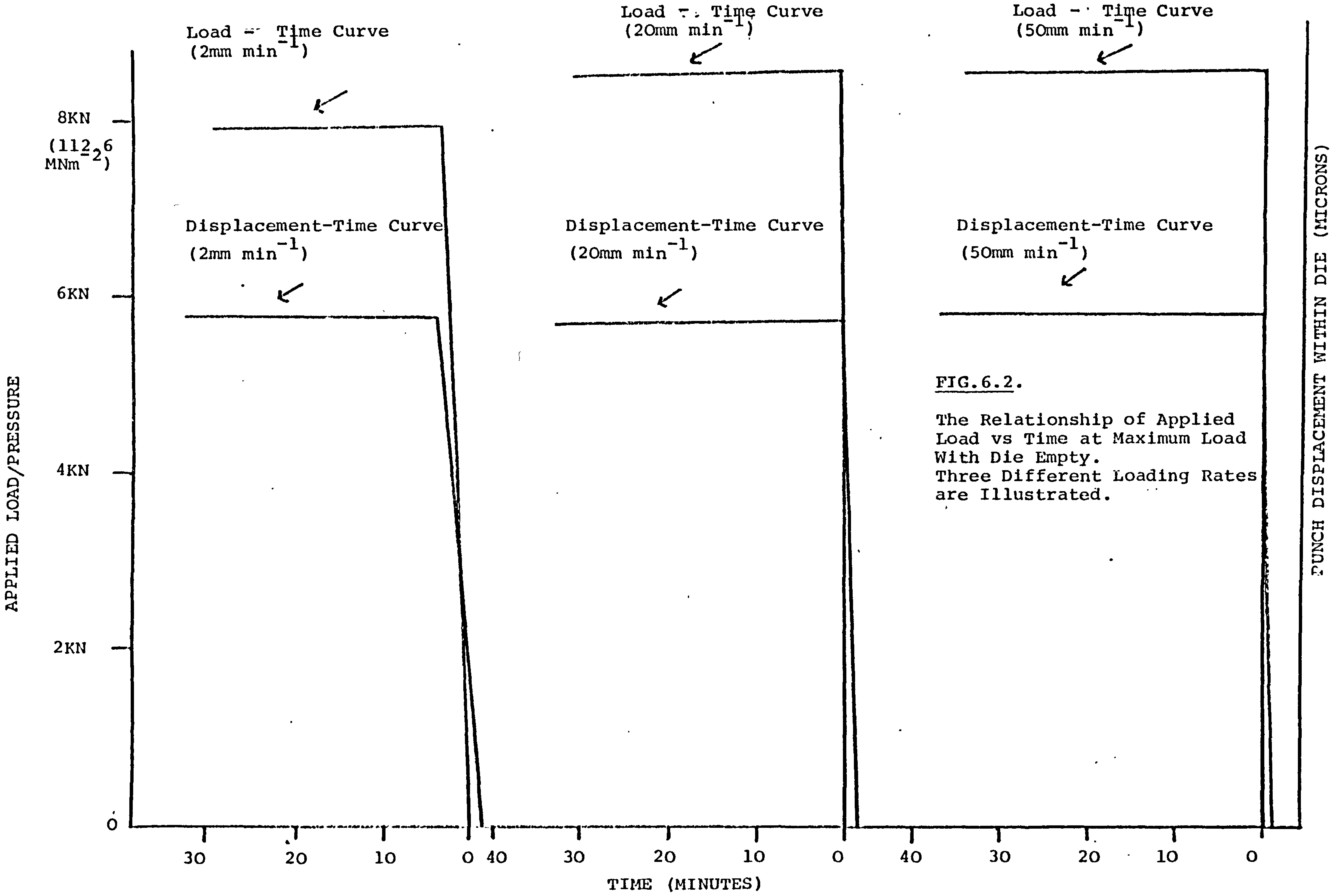


FIG.6.2.

The Relationship of Applied Load vs Time at Maximum Load With Die Empty.
Three Different Loading Rates are Illustrated.

displacement with time was established, both during load increment and throughout the stress relaxation process. Since displacement during the former (and especially when the die contents are undergoing consolidation) was many degrees of magnitude greater than that anticipated for the relaxation event, some capacity for magnifying displacement at maximum load was essential. The incorporation of a 10-stage back-off control, which allowed enlargement of specific peak segments, overcame this difficulty. The units of enlargement were governed by the nature of the sample under investigation and could be regulated so that any requisite fine control could be achieved. To that extent, depending upon the degree of post compaction displacement, (which was anticipated, in the case of sodium chloride, to be of greater magnitude and opposite sign to that of lactose and polyethylene) a smaller or larger portion of the decompression curve could be evaluated against time. By activating the back-off control over an enlarged extension range, stress relaxation displacements of only a few microns could be determined. Precision and reproducibility were acceptable. A preparatory compression, of the material under test, applying normal conditions and measuring total displacement under load, served to define the back-off range requirements.

The magnitude of displacement, both during loading and post compaction, with the die empty, is illustrated in FIG.6.2. Some deformation could be anticipated based on a knowledge of jig geometry. However, being of the order of a few microns, it was considered insignificant alongside the much greater displacement of the material under test. Of greater significance was the punch behaviour once the maximum load had been reached and stopped. Irrespective of applied pressure, punch displacement was negligible over the complete relaxation stage. Thus, the necessity for data correction was obviated.

6.3.3. Stress Relaxation of Powder Mixtures - Pressure Effects

6.3.3.1. Fundamental Responses

Of the three materials under evaluation (sodium chloride, lactose and polyethylene) all would be expected to react differently under the influence of stress relief. The extent to which pressure decay occurred would depend on many factors, among which are, most importantly, those facets of the compression stage outlined in Section 1 (i.e. consolidation, elastic deformation, plastic flow and/or brittle fragmentation) and, under static conditions, specific components of the decompression stage, such as elastic recovery and time-dependent plastic flow.

FIG.6.3. illustrates the pressure decay - time relationships for the three materials under study. Upon attaining maximum applied pressure the compacting mechanisms were then checked such that load cell, upper punch and compact retained contact. All three materials were observed to undergo an immediate pressure decay, the order of magnitude being polyethylene $<$ lactose $<$ sodium chloride. In the case of sodium chloride, a decrease in applied pressure was not unexpected since its deformation mechanism has been well documented. Plastic flow would lend itself to maintained reduction in axial dimension as material flowed interparticularly. Such a reduction would be mirrored by a reduction in force acting on the load cell. However, both

lactose and polyethylene also suffered immediate pressure decays albeit of a much lower magnitude to that observed with sodium chloride. Rees and Rue (1978) also observed upper punch force decay for lactose and reported that decay became minimal after about 30 seconds. A similar duration was observed during the present studies, FIG.6.3 demonstrates the immediate onset of base line decay. Rees and Rue made the somewhat dubious suggestion that the onset of linearity would describe the assumption of a first stress relaxation character of a true Maxwell body.

The third component under study, polyethylene, also exhibited an immediate pressure decay though of a further reduced magnitude. In considering the sequence of events prior to the pressure decay process, a material with a high Modulus of Elasticity would suffer extensive deformation resulting in low pressure-time ratios during the initial stages (see (FIG.6.3.). With increasing pressure the viscoelastic nature of the material would begin to influence compression characteristics and the rate at which material density approached a minimum would also reduce. If only elastic deformation was contributing to material displacement on approaching peak pressure then, once the imposition of increased pressure was halted, the elastic recovery of the polymer would be expected to hold the load at equilibrium with no immediate reduction. Under the influence of a linear increase in load with time, a material under test will deform maximally at pre selected pressures. Within the complex matrix, the overall effect of increasing load will

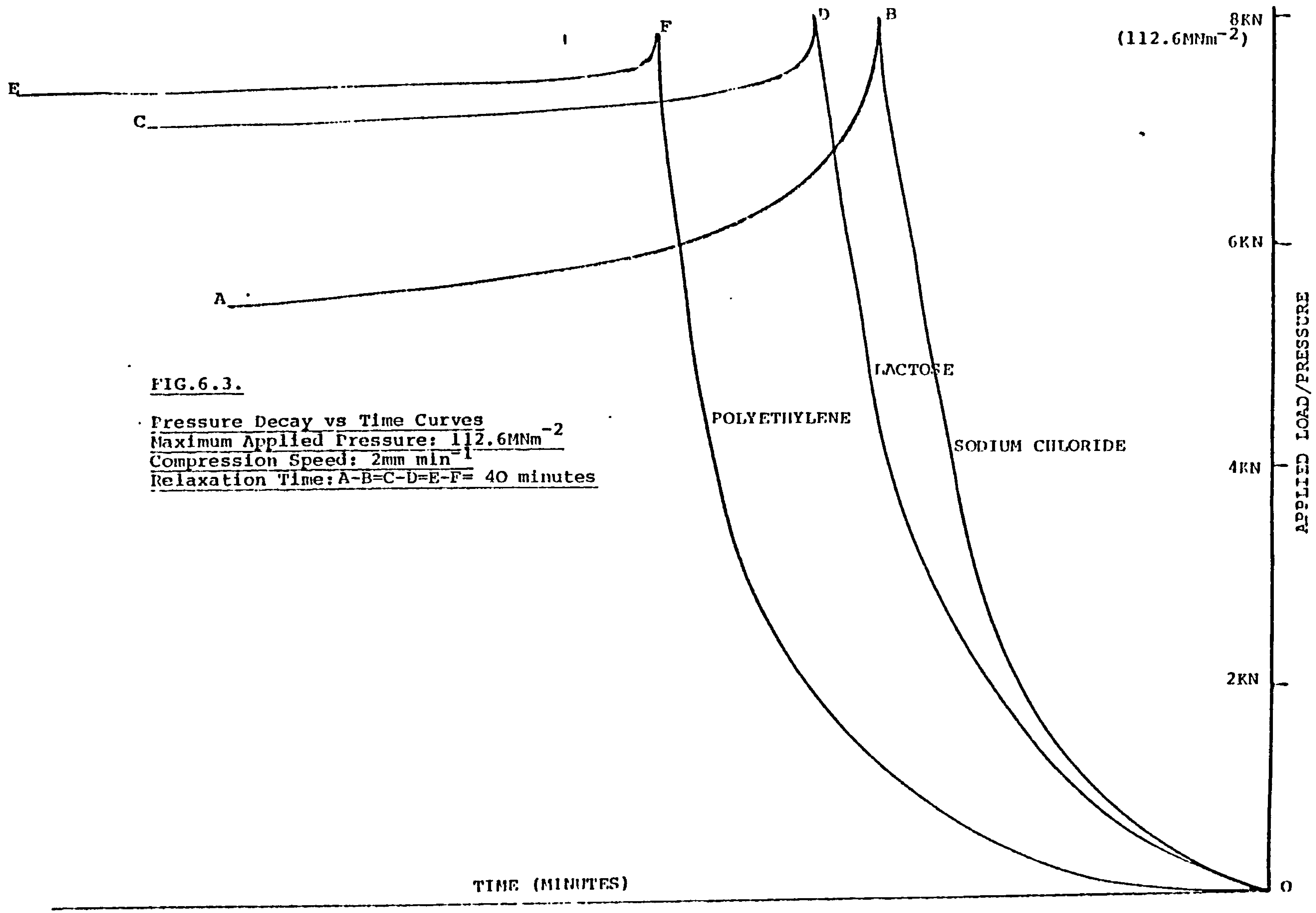


FIG.6.3.

Pressure Decay vs Time Curves
Maximum Applied Pressure: 112.6MNm^{-2}
Compression Speed: 2mm min^{-1}
Relaxation Time: A-B=C-D=E-F= 40 minutes

reduce by a logarithmic relationship, in an axial direction, (i.e. the pressure exerted at the upper tablet extremity will be greater than that at the lower) with the development of a less densely packed structure in direct relationship. Such a conclusion was supported by the physical appearance of the polyethylene plug, after completion of the test, on ejection from the die, with the material adjacent to the upper punch face retaining cohesion to a length of approximately 1mm in 10 mms. The remainder of the compact disintegrated. It seemed likely that, at the maximum applied pressure of 112.6MNm^{-2} employed in the present studies, the material either continued to deform or suffered extended consolidation beyond the apparent instant of pressure stoppage. Such behaviour would suggest a slight overshoot in total pressure, the outcome of which would be an artificial pressure decay.

Events are complicated, however, by the contribution from elastic recovery, which, in the case of polyethylene, should operate the instant a decrease in pressure was induced. That the explanation offered above holds true was supported by the displacement studies discussed later.

The contribution of the above would certainly serve to complicate the issue during compaction of a two-component system. Isolation of "over-shoot" from total effect would be extremely difficult. However, during the compression of two materials possessing quite different compaction mechanisms, such as plastic (sodium chloride) and elastic (polyethylene), the effect described above would be swamped by particles undergoing differing interactions.

This was reflected in the pressure decay profiles obtained on dilution of sodium chloride with polyethylene. In the case of the former material as a single component, a pressure decay of 5-10MNm^{-2} (ca 0.5KN Force) was induced within 15-20 seconds of checking the operation at maximum applied pressure. Pressure then continued to decline over a period of 25 minutes before stabilising. At the end of this time the cumulative decay was in the order of 28MNm^{-2} (ca2KN Force). On increasing the polyethylene content (by successive increments of 0.5; 1; 3; 5 and 10% w/w) both the immediate and total pressure decay reduced, the order of reduction correlated with an increase in viscoelastic component. The extent of the reduction is further illustrated in FIGS. 6.4 a, b and c which differentiate between compression speed and polyethylene content and FIG.6.5 a and b, where a range of polyethylene dilutions compressed at constant applied pressure and speed are depicted. By plotting log$_{10}$ percentage initial pressure against time, overall decay can be clearly observed to consist of two phases, a rapid fall over the first 5-10 minutes followed by a further slow diminution. Such two component behaviour has been previously muted by Rue and Rees (1978) and will be discussed more extensively in a later section.

6.3.4. Stress Relaxation of Powder Mixtures - Displacement Effects

6.3.4.1. Fundamental Responses

When materials under compaction interact via a plastic flow mechanism arising from both intra and interparticle bonding, such bonding being initiated by lattice displacement, then pressure decay and post compaction dimensional changes which

FIG. 6.4(a)

Stress Relaxation (Pressure) of Sodium Chloride Compressed to a Maximum Applied Pressure of 112.6MNm^{-2}.

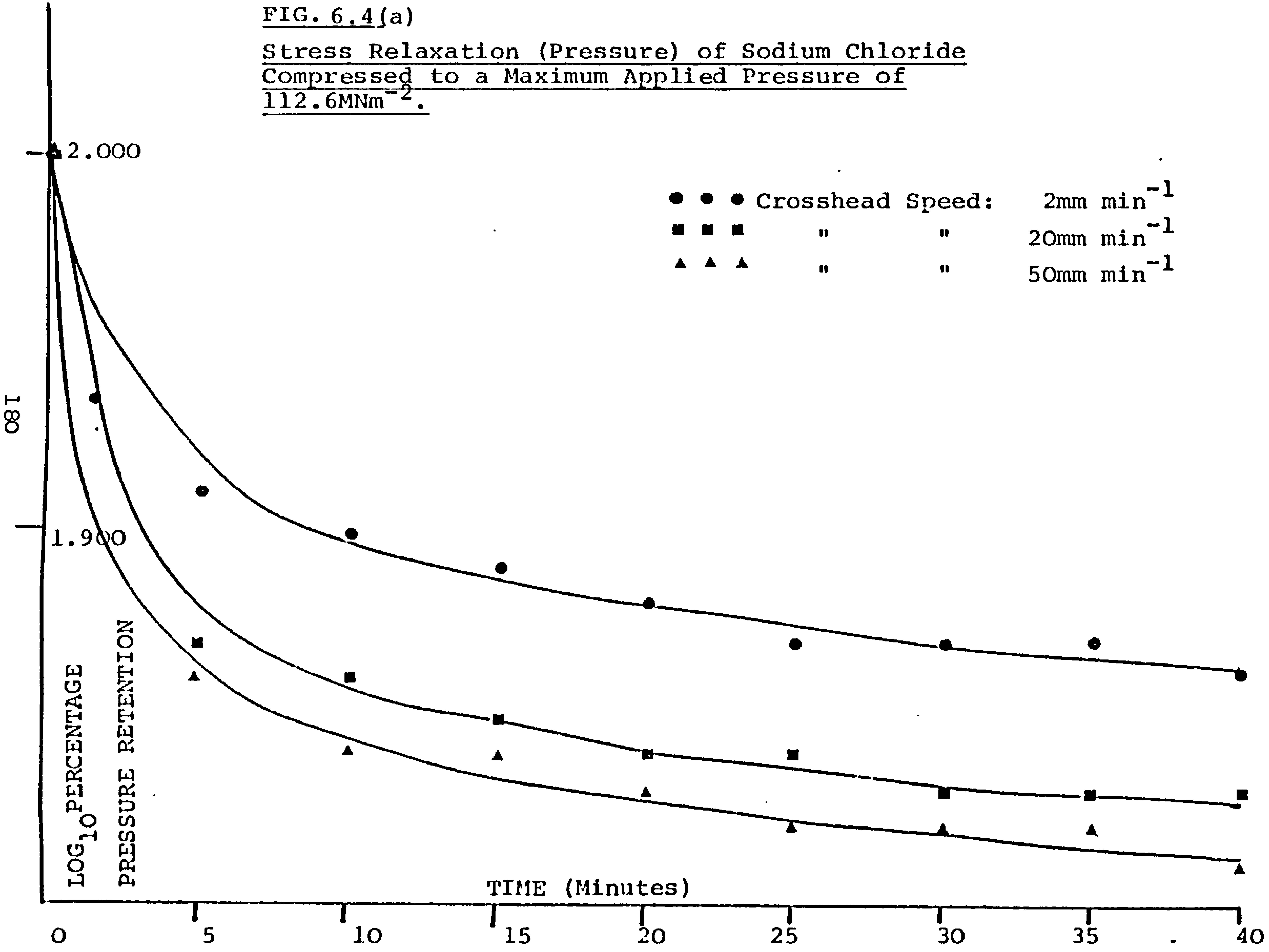


FIG. 6.4(b)

Stress Relaxation (Pressure) of Sodium Chloride plus 3% Polyethylene Compressed to a Maximum Applied Pressure of 112.6MNm^{-2}.

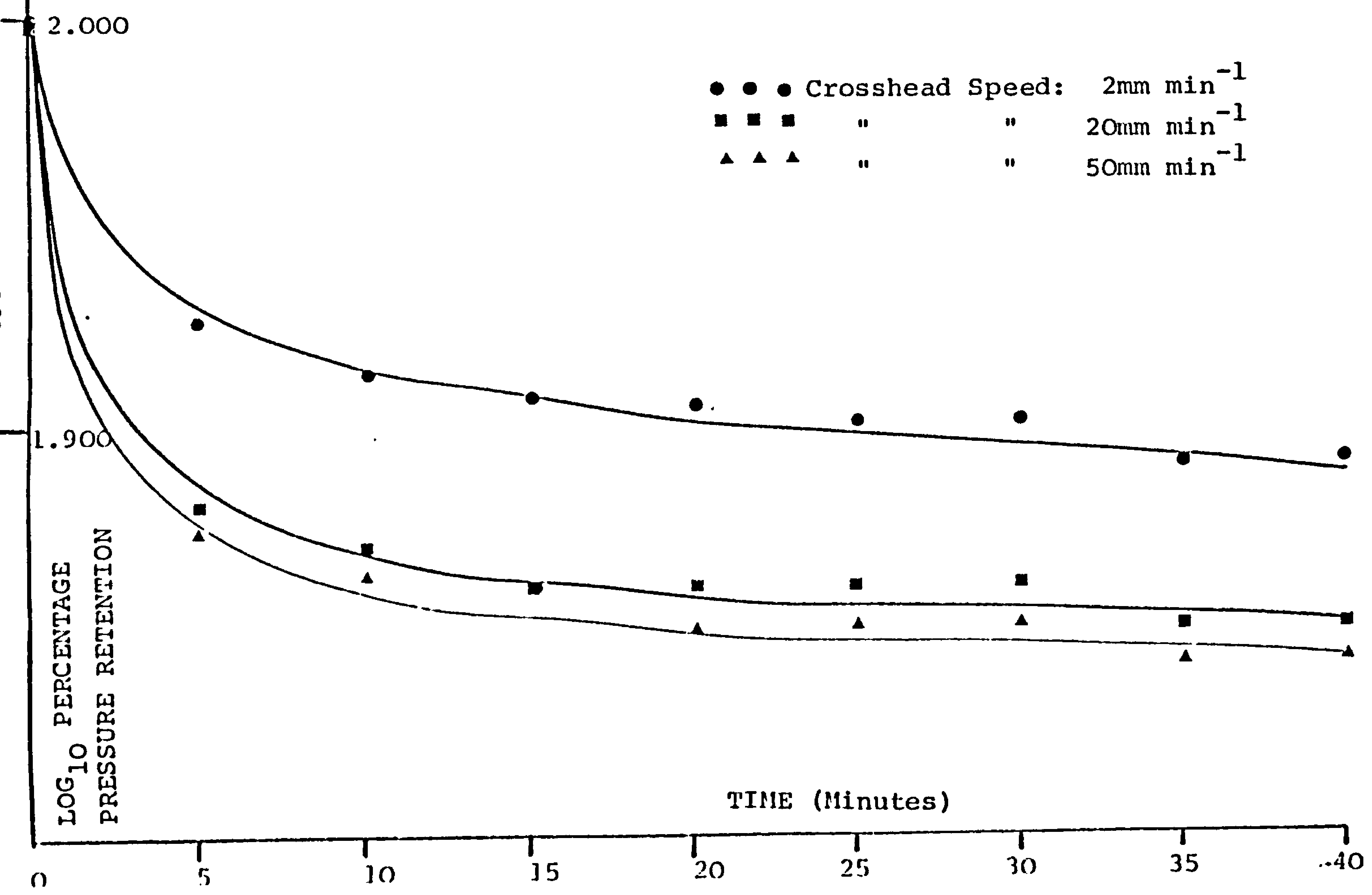


FIG. 6.4(c)

Stress Relaxation (Pressure) of Sodium Chloride plus 10% Polyethylene Compressed to a Maximum Applied Pressure of $112.6 MNm^{-2}$.

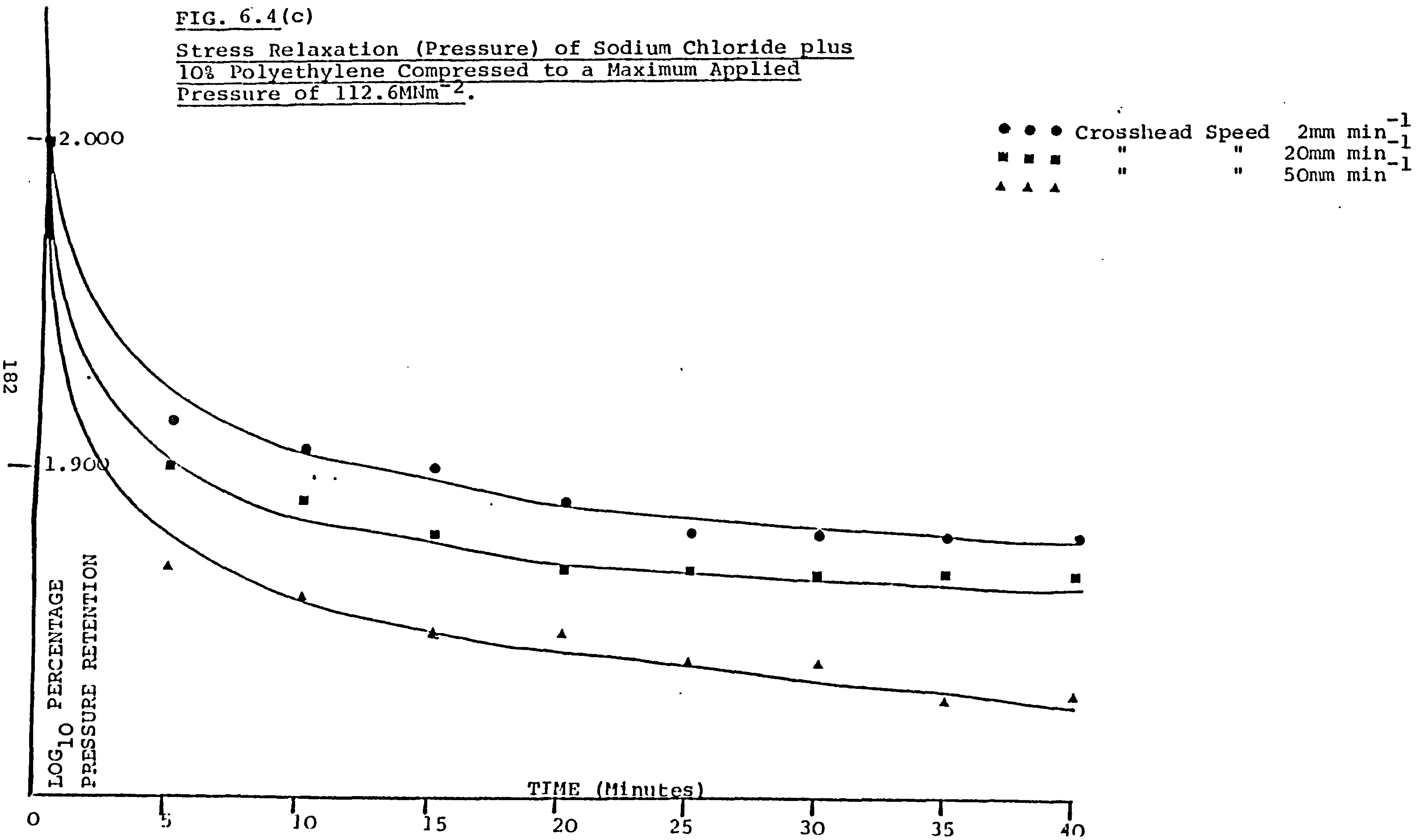


FIG. 6.5(a)

Stress Relaxation (Pressure) of Sodium Chloride With and Without the Addition of Varying Amounts of Polyethylene. All Materials Compressed to a Maximum Applied Pressure of 112.6MNm^{-2} at a Crosshead Speed of 2mm min^{-1}.

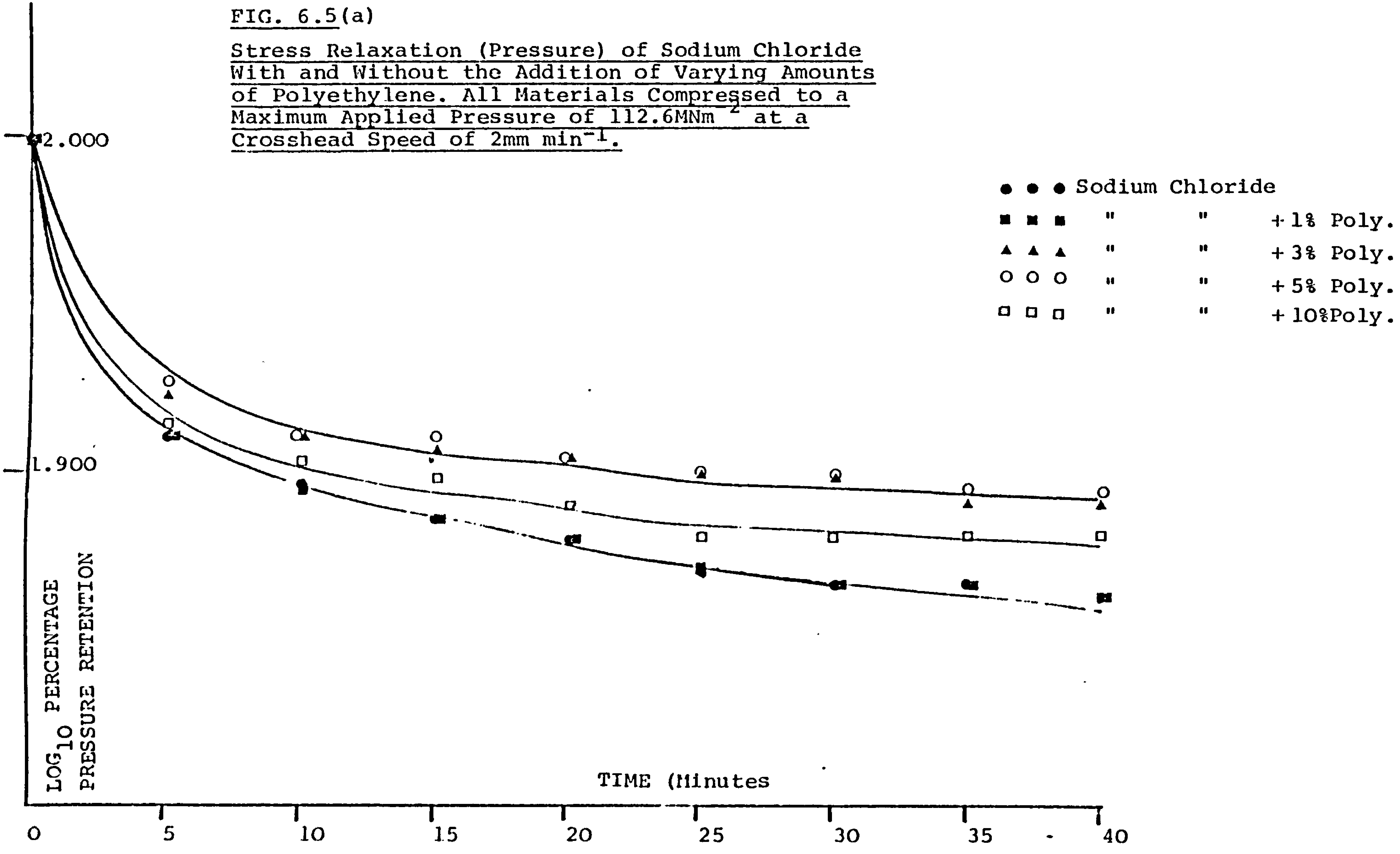


FIG.6.5(b)

Stress Relaxation (Pressure) of Sodium Chloride With and Without the Addition of Varying Amounts of Polyethylene. All Materials Compressed to a Maximum Applied Pressure of 112.6MNm^{-2} at a Crosshead Speed of 50mm min^{-1}

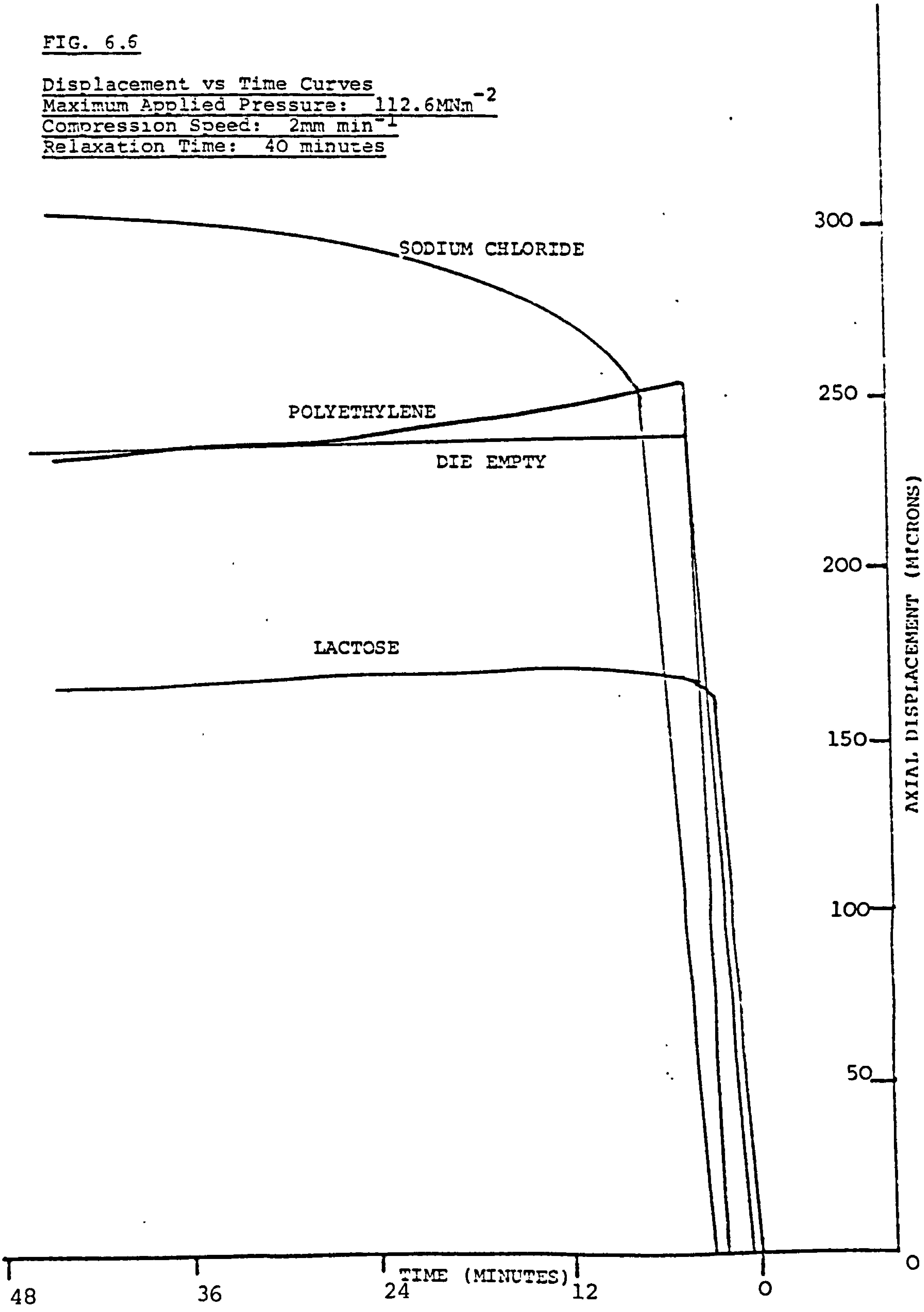
are present, should be directly related. Section 6.3.1. dealt with the fundamental responses of pressure to time-dependent stress relaxation. The volume reduction associated with plastic flow of sodium chloride post compaction is illustrated in FIG.6.6, precise and defined measurement by extensiometer characterising both the degree and direction of displacement. The essential quality of the acquired data indicated that the axial dimension of the compact continued to reduce with equilibrium not being achieved even on termination of the monitoring period (40 minutes). By precisely measuring displacemnt a perspective on plastic flow capability could be accomplished. Turning to lactose as a compound which compacts with a brittle fragmentation pattern, a small further decrease in axial dimension was observed at the instant of halting applied pressure, with a consequent slight tablet expansion as the material underwent elastic recovery.

Finally, in the case of polyethylene, its intrinsic elastic recovery, post compaction, was clearly represented by the displacement curve, showing the material to undergo instant expansion as the applied load was halted. However, as clearly indicated in the previous section, even a viscoelastic material such as polyethylene suffered a slight immediate pressure decay.

The presence of the "over-shoot" component observed in all the experiments described herinafter, has complicated the extrapolation of displacement data. Where feasible, the "over-shoot" contribution has been separated from the main stress-relaxation measurement.

FIG. 6.6

Displacement vs Time Curves
Maximum Applied Pressure: 112.6MNm^{-2}
Compression Speed: 2mm min^{-1}
Relaxation Time: 40 minutes



As a final example in this fundamental section, FIG.6.7 elucidates the modifications of post compaction displacement with the addition of increasing amounts of polyethylene to sodium chloride. As the concentration of the latter increased, the plastic flow component became less dominant.

6.4. The Plastic - Elastic System

6.4.1. Pressure Decay and Displacement Relationship During Stress Relaxation - Qualitative Evaluation

Although the fundamental discussion has dealt with pressure decay and displacement as separate entities, that they are clearly interrelated is illustrated in FIG.6.8 a, b and c, where both are shown as dependents of compression speed and time.

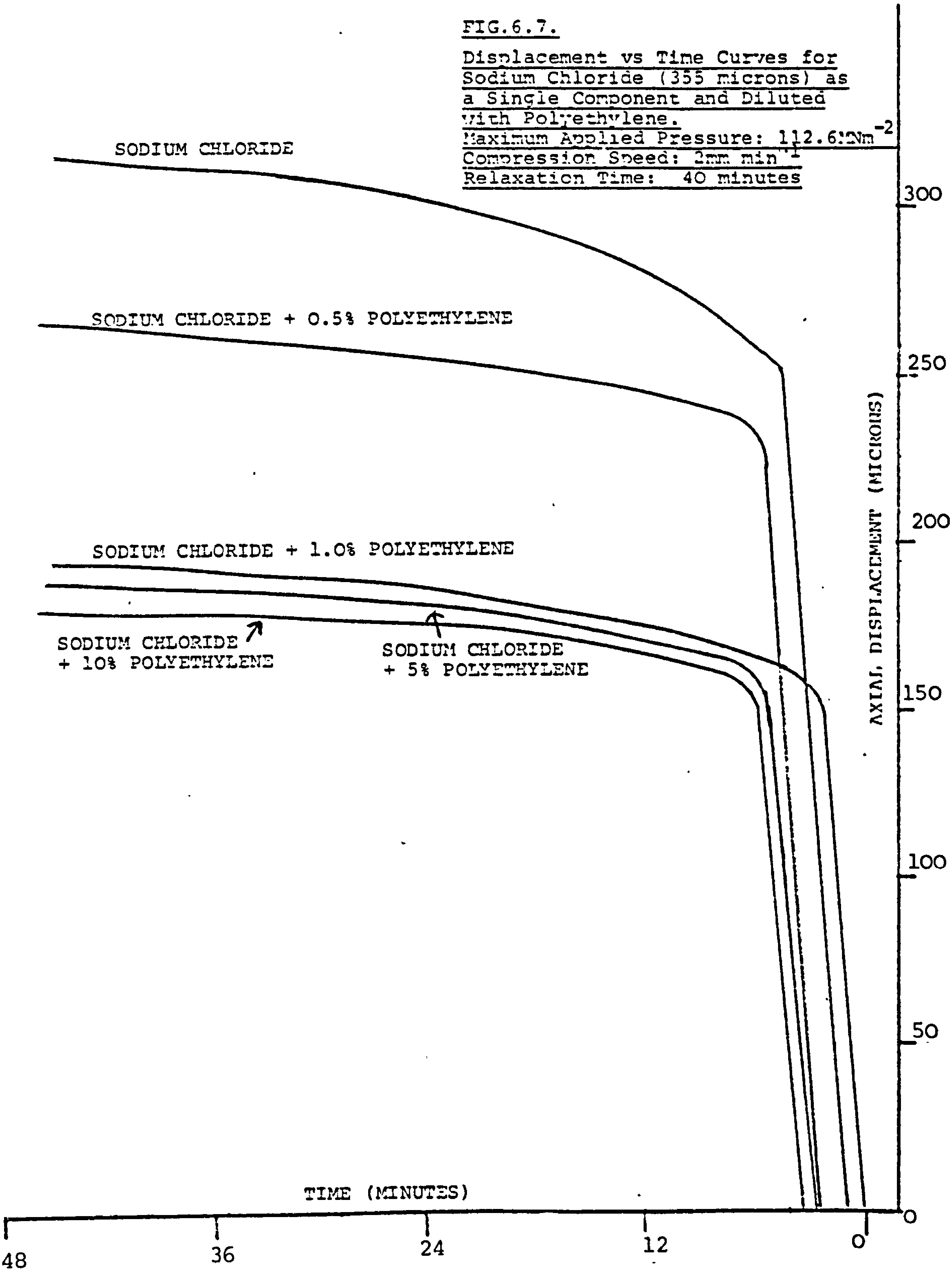
In the case of sodium chloride alone, irrespective of crosshead speed, once the maximum applied pressure had been attained and further application of pressure terminated, a coincidental continuation of axial displacement occurred. Beyond this point, the rate at which plastic flow continued slowed appreciably as did the extent of pressure decay. As has been mentioned previously, a displacement allied with increasing load remained operating even though the maximally applied pressure had been achieved and loading ceased.

Under static conditions, where tablet ejection does not take place at the completion of the compression cycle, consolidation by relatively large sodium chloride particles would serve to fill interstitial holes in the powder body. As more energy was imparted to the system (i.e. as the applied pressure increased) tablet density would increase and bonding would occur with the elastic limit of the material being exceeded. The commencement of plastic flow would then follow.

Because the top punch does not retract at cessation of pressure

FIG.6.7.

Displacement vs Time Curves for Sodium Chloride (355 microns) as a Single Component and Diluted with Polyethylene.
Maximum Applied Pressure: 112.6MNm^{-2}
Compression Speed: 2mm min^{-1}
Relaxation Time: 40 minutes



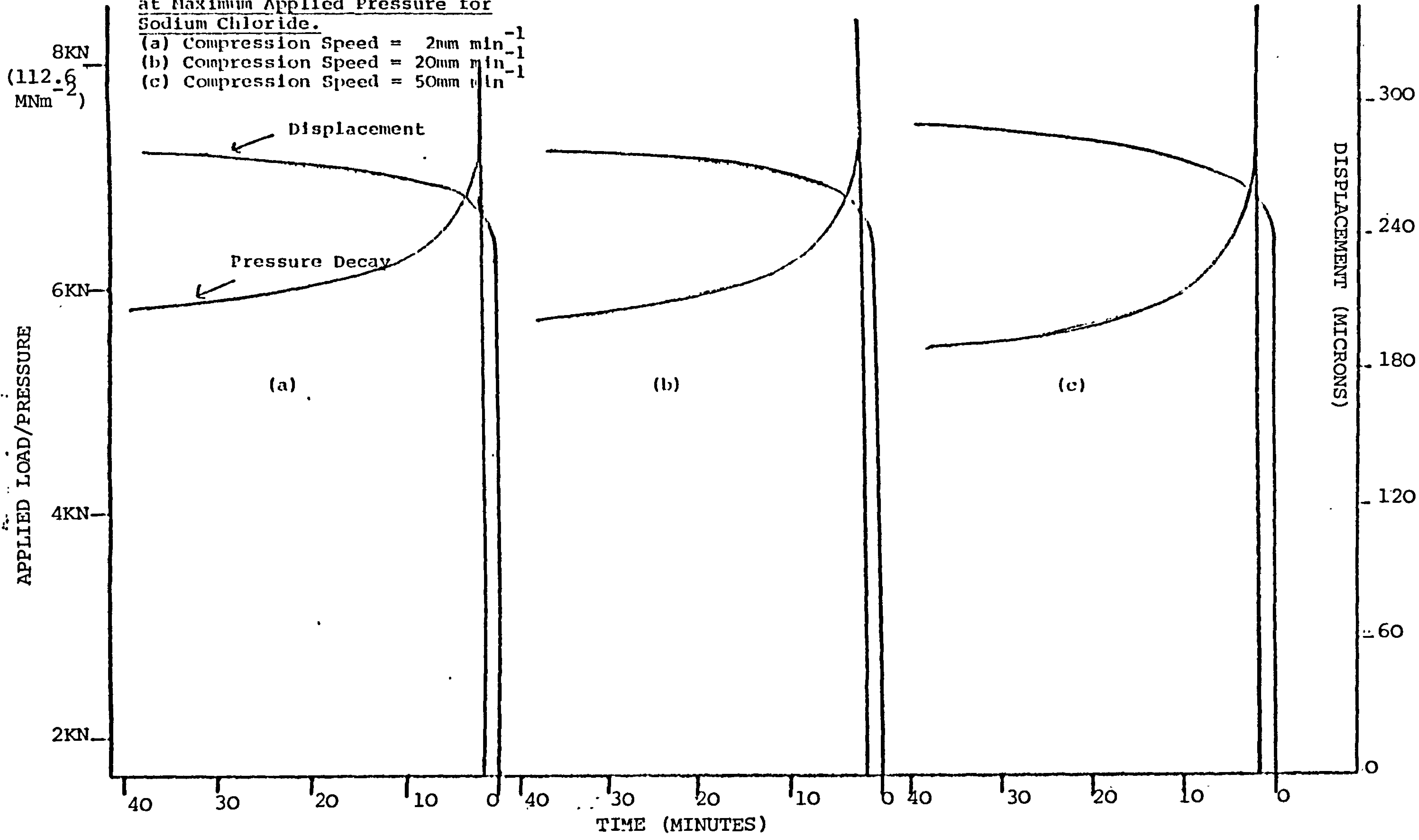


FIG. 6.8(a)

Time Dependent Stress Relaxation at Maximum Applied Pressure for Sodium Chloride.

(a) Compression Speed = 2mm min^{-1}
(b) Compression Speed = 20mm min^{-1}
(c) Compression Speed = 50mm min^{-1}

FIG. 6.8(b)

Time Dependent Stress Relaxation at Maximum Applied Pressure for Sodium Chloride plus 3% Polyethylene.

(a) Compression Speed = 2mm min^{-1}

(b) Compression Speed = 20mm min^{-1}

(c) Compression Speed = 50mm min^{-1}

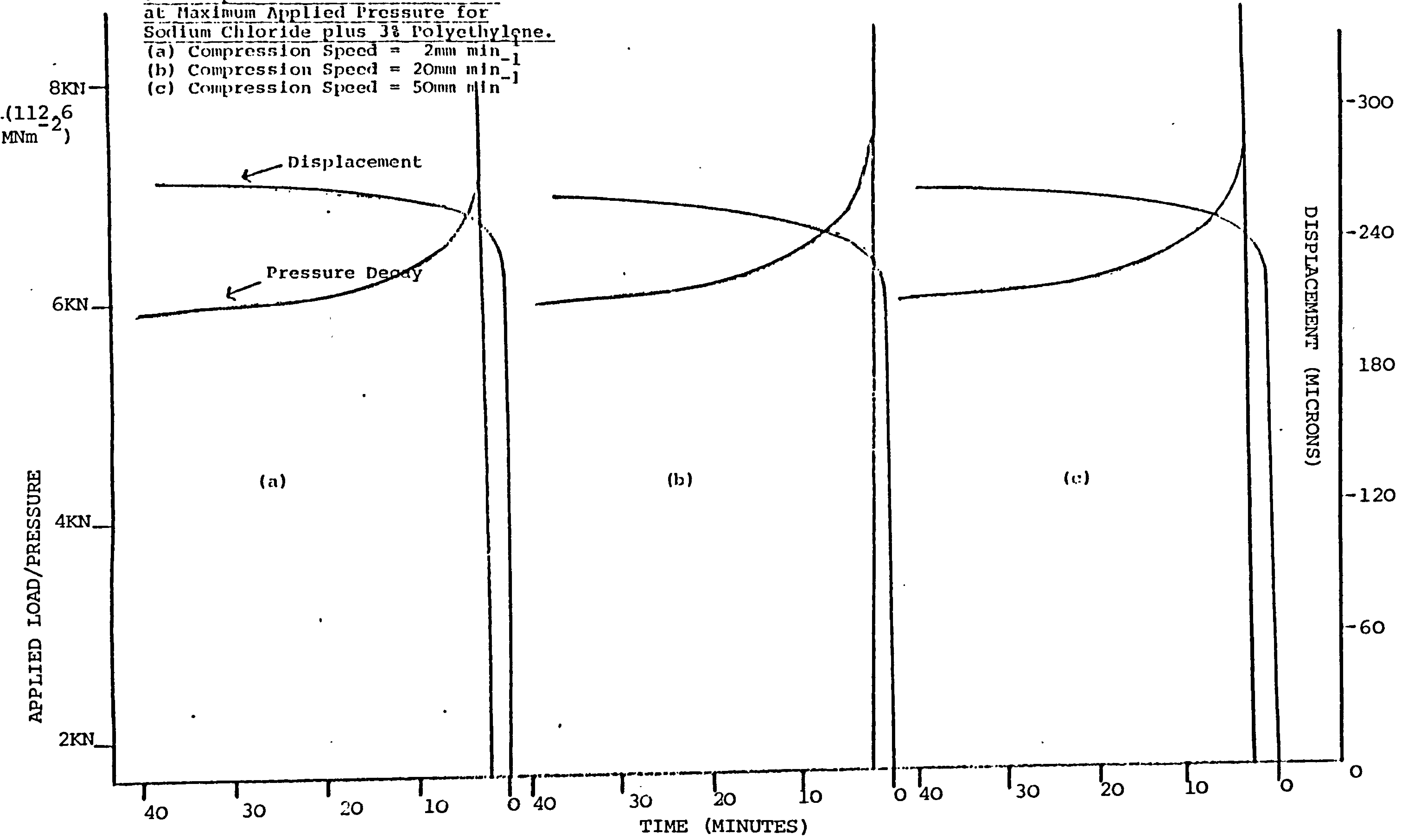


FIG.6.8(c)

Time Dependent Stress Relaxation at Maximum Applied Pressure for Sodium Chloride plus 10% Polyethylene.
(a) Compression Speed = 2mm min^{-1}
(b) Compression Speed = 20mm min^{-1}
(c) Compression Speed = 50mm min^{-1}

increase, with the absence of coextensial upward movement of the bottom punch, it would be unlikely that an instantaneous pause in material displacement with applied load would exist. Such being the case, then an "over-shoot" characteristic would operate where a portion of the apparent post-compaction stress relaxation would overlap from the compression phase. At the relatively low pressures utilised in the present studies it seemed likely that such an event would occur. No attempt has been made to separate the implied effect from the plastic flow contribution, the latter being an additional and, in the case of sodium chloride, an overwhelming source of post compaction displacement. By comparing both displacement and pressure decay curves it was obvious that the intrinsic fall in pressure, once maximum applied pressure was attained, and displacement "over-shoot" were simultaneous events and, in terms of duration, occurred over approximately 1-2 seconds. Nevertheless, even allowing for such an outcome, there were still significant decreases in tablet axial dimension over the initial 20-30 seconds of the stress relaxation event, when interparticulate bonding, dependent upon plastic flow, would be expected to be of considerable magnitude. Prolonged stress-strain recovery over a 40 minute monitoring period resulted in further reduction in tablet volume without equilibrium being achieved.

Variations in post compaction tablet dimensions have been observed by York and Baily (1977), who by the use of a non-contact optical technique, compared changes in the heights and diameters of compacts of sodium chloride and lactose. By monitoring dimensional differences at intervals of 15, 30 and 60 minutes, they inadvertently restricted the scope of their findings which indicated that, in the case of sodium chloride, the greatest dimensional changes occurred after 15 and 20 minutes, with complete recovery at the end of 1 hour. They defined a correlation between reduction in dimension and decrease in porosity. There seemed little doubt that, in the case of sodium chloride, plastic flow would account for such changes. The behaviour of lactose defies explanation.

Long term changes in axial dimensions, assuming the proviso that radial effects are neutralised should, in the case of a material such as sodium chloride, coincide with increased breaking strength, the latter being a function of intensified inter and intraparticle bonding.

With respect to pressure decay, similar findings to those reported herein have been produced by Rees and Rue (1978), wherein they described the effects forthcoming on application of a static load of 20KN, addressed by means of a reciprocating tablet machine, to a powder bed. Although the technique employed (top punch displacement being adjusted by hand until a desired peak force was imparted) was somewhat rudimentary, they observed similar decay patterns to those shown in FIG.6.8. They limited their interest to a 5-6 minute stress recovery period post compaction, although the major stress relief had been effected within this interval the data indicated that terminal decay was not established. Additionally, their representative data, expressed as a series of decay-time relationships, fosters the illusion that initial sightings were taken several seconds after peak force had been applied, they made no reference to an immediate fall in applied pressure. A further singular inference was that, in the case of sodium chloride, 80% of the upper punch force decayed in the first 10 seconds. Based on the premise that such an unlikely event was the result of a pictorial error, then stress relief similar to that described by the present researchers can be assigned.

By increasing compression speed, in the case of sodium chloride alone, corresponding increases in both pressure decay and displacement were observed, both in the immediate and long-term situations. At higher speeds the time between which the top punch makes initial contact with the die contents and completion of the compression stage would be considerably reduced (under static conditions, the classical definition of dwell time becomes disproportionately long with respect to dynamic systems, since the top punch maintains contact with the compact on completion of the applied pressure phase). Uniform powder consolidation gained at low speed would be disrupted resulting in increased carryover mirrored by an evolved increase in immediate displacement. The data represented in FIG.6.11 (see later) reinforced this postulate, the calculated displacement at 20 and 50mm min^{-1} being greater than that at 2mm min^{-1}.

Dilution with polyethylene sustained the correlation between pressure decay and displacement although elapsed effects rather than immediate effects dominated. That substantial stress relaxation did arise, in the presence of relatively high proportions of polyethylene (3% w/w or greater) might suggest that the latter would have little effect on the plastic flow properties of sodium chloride. It has been shown previously (Section 4) that as little as 0.5% w/w polyethylene can serve to negate the cohesive qualities of sodium chloride when compressed under dynamic conditions, the interfering role played by the viscoelastic component being of an uncertain nature. In the static system, at equivalent pressures, no such problem arose until the polyethylene content reached an unacceptably higher concentration. In order to assign the interacting mechanism it is essential to consider the processes (of which there would be several) operating once the maximum applied force has been reached. All processes would be insignificant in comparison to those of elastic recovery (polyethylene) and plastic flow (sodium chloride) both of which would be operative the instance the system sustained, for whatever reason, a fall in applied pressure. The two would be antagonistic with immediate and plastic flow effects affecting elastic recovery. Consequently, an immediate expansion, dependent upon the scope allowed for elastic recovery, would occur which would control the adhesive properties of the compact dependent on removal of restricting boundaries.

In the static as opposed to dynamic environment, such a recovery would be reasonably ordered being fundamentally uniaxial in nature (instrumented by the die geometry) with negligible radial contributions. Within the immediate vicinity of elastic particles strain recovery of such particles would be the overriding influence on compact integrity. Displacement behaviour, while partially modified by the elastic component, would reflect the properties of the remainder of the die contents. The notion that retained energy stored within the compact could be utilized, during strain recovery, in a manner which favoured uniaxial diffusion, was strengthened by the findings that post-compaction plastic flow developed in a similar manner and over a comparable time-scale to that of sodium chloride alone. That uniaxial diffusion compliments enhanced tablet cohesion was also supported by reiterating the decisive role played by the introduction of a radial vector, where a random energy release pattern would be exercised resulting in immediate disintegration. Such distinctions are confirmed by tensile strength relationships generated under varying compaction parameters (see later).

On increasing the polyethylene dilution to 10% w/w, similar outcomes to those described above were observed but to a depreciated extent. Irrespective of compression speed, pressure decay was reduced (FIG.6.9) while displacement interactions were more complex (FIG. 6.11). From the above investigations it can be derived that, over the 40 minute post-compaction study period, plastic flow and pressure decay are inseparable, irrespective of polyethylene content, the evolution of the former being complemented by a decrease in applied pressure.

6.4.2. Pressure Decay and Displacement Relationships During Stress Relaxation - Quantitative Evaluation

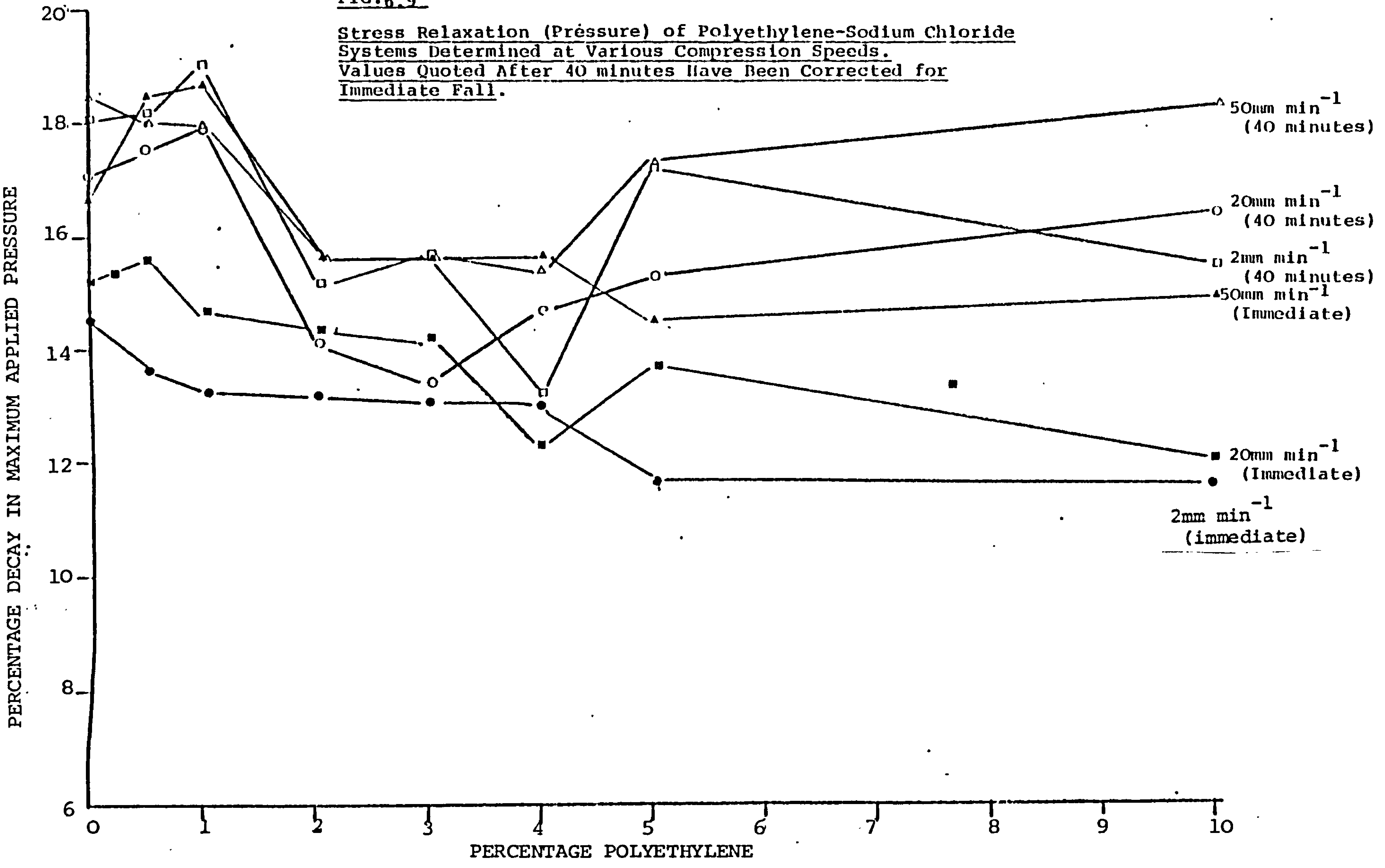
The quantitative relationship between stress-relaxing pressure decay and polyethylene content is illustrated in FIG.6.9. Pressure decay has been expressed as a percentage of maximum applied pressure with, where necessary, a correction to allow for the slightly higher than theoretical pressures imposed at the higher compression speeds. Immediate decay was taken to be that fall in pressure occurring within 1-2 seconds of attaining maximally applied pressure. The time limit constraint was that which coincided with the displacement carry over referred to previously and discussed further below. Additionally, by accelerating the chart speed, the pressure decay-time relationship was calculated to be linear over the first 1-2 seconds for those examples outlined in FIG.6.8 a, b and c.

Quantitative data for relaxation intervals of 40 minutes have been corrected to account for the immediate value.

The resulting data highlighted the emergence of several interesting facets of tablet compaction. Firstly, with respect to the immediate phase of post-compaction stress relaxation, an increase in compression speed coincided with an increased pressure decay, expressed as a percentage of the maximum applied pressure. An advance in rate from 2mm min^{-1} through 20mm min^{-1} to 50mm min^{-1} concurred with respective decays of 14.4, 15.2 and 16.4% for the sodium chloride system. A ready explanation for such effects cannot be offered, very little data having been published concerning the consequences of variable compression speeds (and coincident contact and dwell time) on the compression properties of materials Vezin, Khan and Pang (1983) included a variation of such parameters during an evaluation on tablet tensile strength modification as a function of precompression force and reduced mixing time, being concerned essentially with a binary system of microcrystalline

FIG.6.9

Stress Relaxation (Préssure) of Polyethylene-Sodium Chloride Systems Determined at Various Compression Speeds. Values Quoted After 40 minutes Have Been Corrected for Immediate Fall.



cellulose tablets lubricated with 0.5% w/w magnesium stearate. Their primary interest lay in the causative factors of lamination and capping, a comparison of quality of tablets prepared at 760 min^{-1} and 1000 min^{-1} (i.e. 760 and 1000 tablets per minute) showed them to be indistinguishable. By eliminating the components of compression speed, the improvement in tablet quality introduced by the pre-compression stage could be deduced to arise from two separate compaction events where an intermediate influence, such as stress relaxation, would exert a controlling impetus. A comparison of Vezin et al's findings with those outlined in this report does, of course, suffer limitations, since their mechanics of application (rotary press) would be quite different, in terms of dwell times and compression dynamics, to those operating in the static system.

Earlier, Ritter and Sucker (1980) indicated how the capping tendency of Avicel PH 102 tablets, containing 1% w/w magnesium stearate, increased at varying tableting speed, the applied force being kept constant. As part of the same investigation, they confirmed that the tendency of phenazine to cap on compression was not alleviated in the presence of air or helium. The latter findings should be treated with some reserve since, as has already been pointed out by the present author, compression behaviour cannot be assigned to a single parameter but, rather, will be a composite of several contributions of which one might certainly be dominant. Thus, the test conditions operating in the Ritter and Sucker work were quite different from those partaken in the static system where, under the influence of relatively low applied pressure, slow compression rate and extended dwell time, the importance of air diffusion should not be undervalued.

On addition, since force (KN) and compression speed are related mathematically by the equation

$$1KN = 1000Kg \times m^{-1} \times sec^{-2} = Jm^{-1}$$

then the accuracy of the force applied must be questioned as the speed increased, movement to higher speeds might well influence the actual force applied. It seems likely that events recorded at low pressure and slower compression speeds would be more readily explained, in terms of ordered systems, than would those recorded at fast speeds and high pressures, where, for instance, the expulsion of air may be the most important criterion.

The influence of speed on the static environment was further exemplified by the compression behaviour of sodium chloride diluted with various amounts of polyethylene (FIG.6.9) where the greatest immediate pressure decay derived from the highest compression speed irrespective of polymer content. However, the picture was complicated to some degree at intermediate stages when compared with sodium chloride alone. For instance, the addition of 0.5% polyethylene produced a relative decrease in decay at the low speed (2mm min^{-1}) while relatively large increases were observed at the two higher speeds (20 and 50mm min^{-1}). The introduction of a highly elastic component such as polyethylene, in a system which deformed via a plastic flow mechanism, would lead to significant changes in energy utilisation as the elastic component deformed during compression. At higher compression speeds it seems likely that any resulting slight increases in load would lead to greater non recoverable elastic deformation arising from plastic flow of sodium chloride. At the lowest speed, such an effect would be less critical.

As the polyethylene content was increased further (1% w/w) similar effects to those observed at 0.5% polyethylene occurred.

That a complex post-compaction mechanism was operating, at a preset maximum pressure, could be deduced from the resultant tensile strength data (FIG.6.10). With respect to sodium chloride alone, all compacts displayed identical tensile strengths irrespective of compression speed. At 0.5% w/w polyethylene the lowest compression speed produced compacts of lowest strength, being significantly different to those generated at the two higher speeds. Such a difference would be consistent with a reduced pressure decay arising as a result of both decreased bonding and effective elastic recovery. The highest compression speed generated the hardest compacts both at the immediate and long term testing period. Increasing the polyethylene content to 1% completely negated compact cohesion, irrespective of compression speed, on immediate removal of the compact from the die. Retaining the compact within the die allowed stress relaxing strength to accumulate. Even allowing for zero strength, pressure decay still increased slightly in the immediate region. In order to better assess the mechanisms which operate during this segment of the stress relaxation process, it would be advisable to study increments of polyethylene dilution lying between 0.5 and 1%.

On further increasing polyethylene content, to 3% w/w and above, the elastic component became dominant, correlation between decay and polyethylene content remaining reasonably constant, as a result of punch recoil, over the immediate area.

Once the post compaction monitoring time period was extended, the connection between pressure decay and polyethylene content could be more readily explained. Up to a critical polyethylene content of 2% time dependent stress relaxation continued to play a significant role in both intra and interparticle bonding. Since pressure decay values were similar then it seemed reasonable to expect that comparable matrix properties would exist irrespective of polyethylene content (Note that, over the longer monitoring period, varying compression speed was of little consequence). Because of the apparent similarity

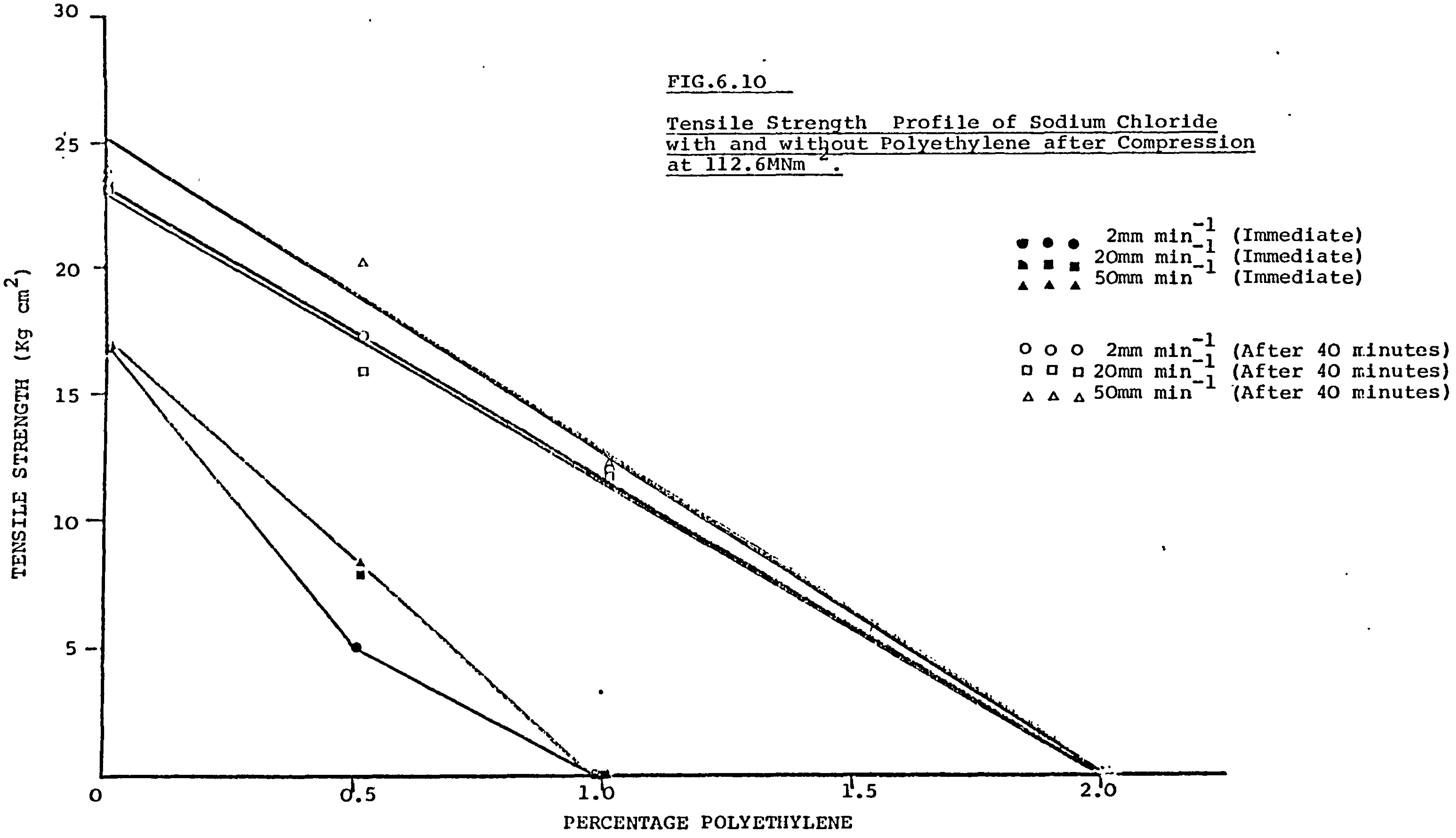


FIG.6.10

Tensile Strength Profile of Sodium Chloride with and without Polyethylene after Compression at 112.6MNm^{-2}.

in pressure decay properties a concomitant correlation of tensile strength would be expected. Such an expectation was not realised and this lack of correlation can be readily explained in terms of the unique static system. Under conditions of static compaction, the degree to which order was retained during the pressure decay interval took precedence over all other parameters. Once the top punch had been subjected to maximum applied pressure, the energy retained within the system would be deployed in a more ordered manner than if either (a) top punch pressure was reduced to zero or (b) the compact was ejected, as in the dynamic situation. As a consequence, while the presence of polyethylene particles would certainly affect immediate bonding and make a significant contribution to the ultimate tensile strength of the compact, areas of ordered sodium chloride not subject to elastic interference from polyethylene would be subject to unhindered plastic flow.

Effectively, whereas in the case of sodium chloride alone, under dynamic conditions, a continuous outer shell was formed during compression which dispersed surplus energy in the form of plastic flow, under static conditions the enclosed intimacy of the encapsulating die served a similar purpose. Clearly any elastic component added to the material which disrupted the continuous outer shell would give rise to energy "waste", and would have a greater effect under dynamic conditions.

The detrimental effects of tablet ejection under dynamic conditions were discussed in Section 5, the data indicating that, at a pressure equivalent to that operating in the static system, a polyethylene content as low as 0.5% would not be tolerated, total compact disintegration occurring on ejection. Provided the particles undergoing time dependent stress relaxation can retain their acquaintance sufficiently to overcome the isolated critical bonding stage, then such a low cohesion threshold can be significantly prolonged.

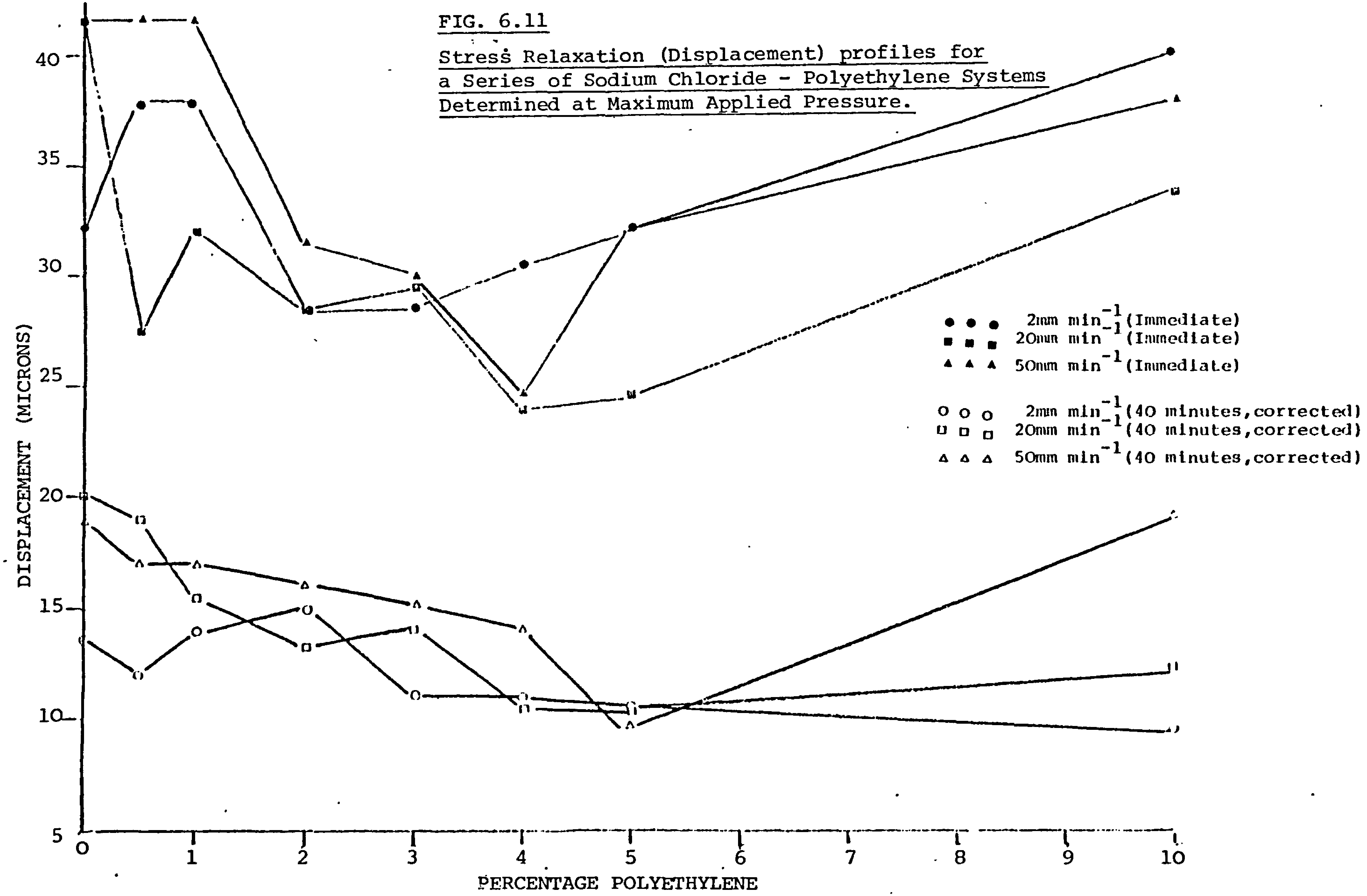
That such a threshold remained severely limited, even in an ordered system, was reflected in the tensile strength properties, only small dilutions of polyethylene being permitted. Thus, at 2% polyethylene, a sharp decrease in pressure decay, originating from an elastically reduced top punch displacement, was allied with instantaneous compact disintegration on removal from the die. However, sodium chloride still retained a significant degree of plastic flow character at dilutions of 2% polyethylene and above, the significance of such behaviour is discussed below.

Comparison of pressure decay with displacement, featured with variable polyethylene contents (FIG. 6.11), highlighted some interesting aspects of the relaxation process. By far the greater proportion of total displacement (i.e. downward movement of the static top punch assembly with reduction in axial length) occurred in the "immediate" region i.e. within 1-2 seconds of stopping the compression at the instant of attaining maximum applied pressure). Of total measured displacement (35-65 microns depending on polyethylene content) between 50 and 75% was determined as "immediate" displacement (to iterate the time scale, "immediate" displacement occurs during "immediate" pressure decay). Displacement-compression speed relationships are more complex than for the corresponding decay patterns but, apart from that of the 0.5% polyethylene mixture at 2.0mm min^{-1}, similarities with pressure decay were noted.

At a critical polyethylene content of 2%, a significant relaxation recovery effect came into operation, confirmed by an analogous reduction in immediate displacement. At this crucial concentration of polyethylene all three variables under study, namely displacement, pressure decay and breaking strength were quantitatively interrelated.

FIG. 6.11

Stress Relaxation (Displacement) profiles for a Series of Sodium Chloride - Polyethylene Systems Determined at Maximum Applied Pressure.



Beyond this dilution, immediate displacement increased as a function of increased elastic deformation, a sequential recovery then occurred.

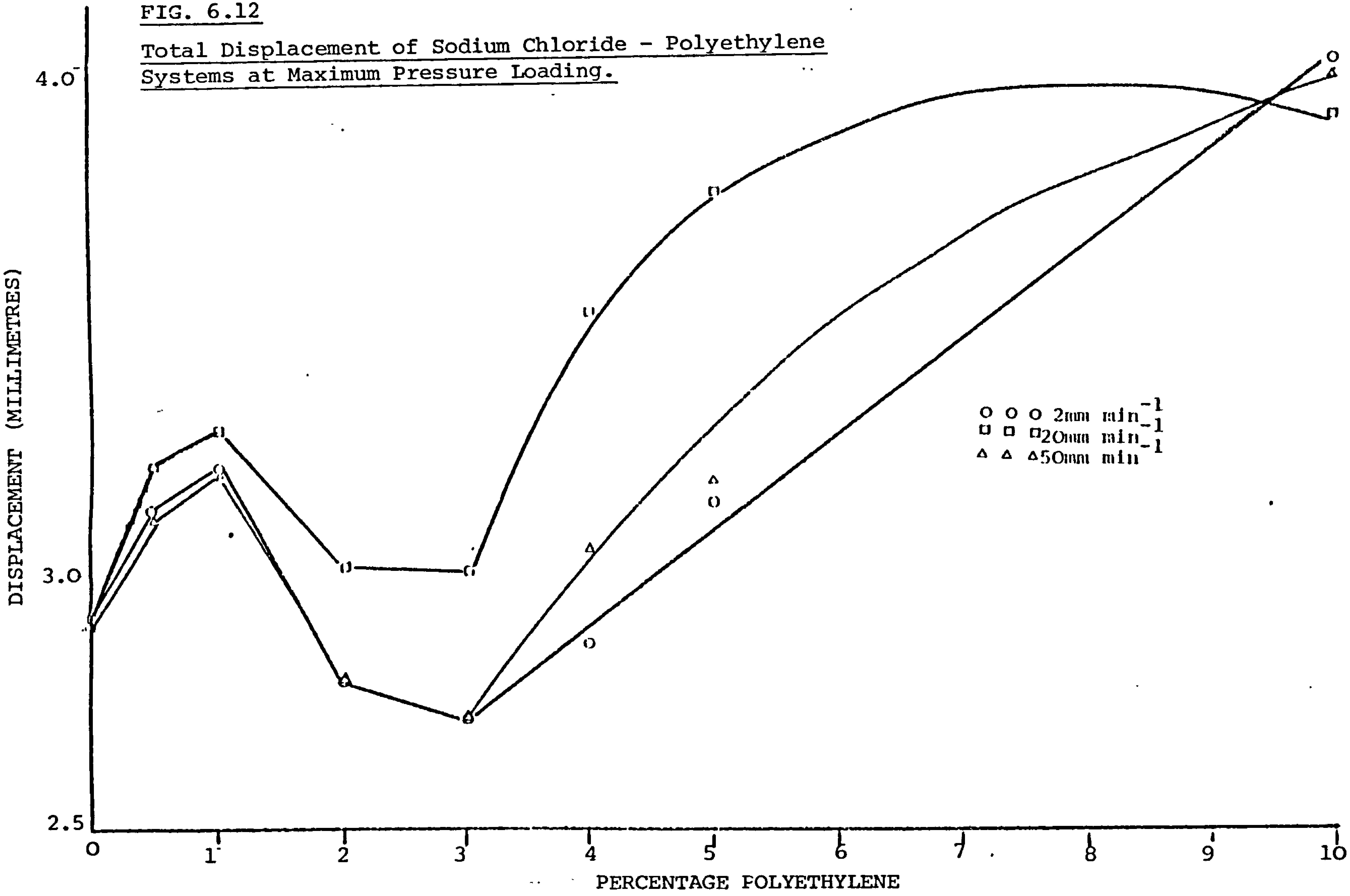
It became clear that, in the immediate case, no pattern could be deduced between displacement and compression speed.

On extending the monitoring period (i.e. the time in which the compact was retained in the die post compaction) and discounting the contribution from immediate displacement a slight reduction in tablet dimensions could be measured, independent of either compression speed or polyethylene content.

That plastic flow was the controlling influence on such a response cannot be doubted, not only with respect to sodium chloride alone but also with small polyethylene dilutions (1-2% w/w). At concentrations of polyethylene of 5-10% it seemed unlikely that decreases in post compaction dimensions would be observed since elastic recovery would be complete within a very short time of compression termination and would result in extensive destruction of particle cohesion. However, since the displacement measurement technique allows microscopic movement to be determined, there can be little doubt that subjection of the compact to displacement, at a dilution of 10% polyethylene, came about as a result of post compaction plastic flow executed at discrete areas within the tablet matrix. That anything resembling an adherent compact reposed in the die after compression of a 10% admixture of polyethylene with sodium chloride cannot be conceived. To illustrate the broad limits attached to post compaction stress relaxation, especially in the case of sodium chloride alone, the total displacement (in millimetres) was determined, with dilutions of polyethylene up to and including 10% w/w (FIG.6.12). At 0.5 and 1% polyethylene increased total displacement can be explained in terms of reduction in

FIG. 6.12

Total Displacement of Sodium Chloride - Polyethylene Systems at Maximum Pressure Loading.



packing density and elastic deformation. On proceeding to concentrations of 2-3% a significant reduction in total displacement coincided with highlighted variations in stress relaxation , displacement and pressure decay parameters. The introduction of such a quantity of viscoelastic material would, while making an enlarged contribution to total displacement with its elastic component, influence the packing properties of sodium chloride particles. Overall, total displacement would be reduced with respect to lower concentrations of polyethylene. At still higher concentrations, total displacement then increased as elastic deformation dominated.

Based on the evidence presented, the mechanism by which a highly elastic component modified the internal binding energy of a sodium chloride compact has been clarified. The mechanism would be equally applicable to other alkali halides and, indeed, to any compound that underwent plastic flow, the alkali halides giving the most exaggerated effects. Under static conditions, it has been shown that an immediate pressure decay occurred once the applied pressure was checked at a preset maximum. Such a decay concurred with a continuing slight reduction in compact axial dimension consistent with a 'snowballing' effect. The compacting technique involves the applied force acting directly on the top punch such that the force still diffusing throughout the system at the instant of stoppage cannot be determined. As Krycer, Pope and Hersey (1982) have emphasized, there would be an anticipated logarithmic decay of applied force in the axial dimension and, since this decay would be related to loss of energy due to particle rearrangement, inter particle friction and particle-die wall interaction (ignored in the pre-lubricated die) then the inestimably small time required for the final applied energy to diffuse across the compact length could well generate a further slight reduction in compact dimensions. Pressure decay would thus continue and be consistent with axial displacement arising from plastic flow of sodium chloride. Of particular significance was the continuation of plastic flow, even though bonding was weak, as witnessed by the immediate disintegration of "compacts" on ejection from the die 40 minutes after the compression phase had ceased. Thus, a considerable amount of energy was implicated in sodium chloride bonding even in the presence of relatively high dilutions of polyethylene.

In the light of the above findings, preferential energy absorption by the viscoelastic component was eliminated as being the controlling factor in effecting non-cohesion of compacts. By specific reference to displacement and pressure decay behaviour, energy partition between sodium chloride and polyethylene occurred during compression, the resulting modifications of material properties contributed to the behaviour of the final product. The mechanism by which a highly viscoelastic component such as polyethylene modified both immediate and stress relaxation bonding was controlled by the deformation of the elastic constituent. Once the maximum applied pressure dropped, elastic recovery produced areas of great structural weakness within the matrix.

Comparison of dynamic and static conditions, dependent upon the boundaries of applied pressure and compression speed imposed by the latter, suggested that a dilution of polyethylene would be attained where plastic flow contributions from sodium chloride would be superseded such that the ultimate apparent strength of the compact would reduce to zero. Such has been accomplished in the dynamic system where the critical dilution was ca 0.5% w/w polyethylene. In the static system, at a similar applied force, the critical dilution was in the order of 2-3% w/w. At such a concentration, the evidence was conclusive. Reduced pressure decay (significant elastic recovery), diminished stress relaxing displacement (plastic flow impaired) and reduced total displacement all correlated with a fall in tensile strength to zero.

That the order in which compact cohesion could be maintained was time-dependent (i.e. post compaction retention time within the die) was not in doubt, reflected in an order of declining tensile strength, such that extended static > immediate static > immediate dynamic. Such a ranking underlined the importance of the radial energy decay vector in the dynamic system.

In the light of the above findings, there can be no hesitation in assuming that the above relationship would always hold and that, at any given pressure and under similar tableting conditions, the same order would be supported. As a consequence, by following a structured sequence of events such that compaction mechanisms (plastic, brittle or elastic) in both immediate and extended static are defined, prerequisits of tensile strength (and, by extrapolation, supportive properties such as friability and disintegration) and compaction pressure, in the dynamic system, can be forecast.

One region which required further clarification is that related to compression speed, although some variations in behaviour patterns are just perceptible, it would appear that, at the relatively low speeds operating in the present study, only slight modifications in compaction counteractions have unfolded. Only by making a comparison of relatively slow and extremely fast speeds could significant differences be anticipated. The Instron measuring device does not lend itself to precise measurements at high compression speeds, such experiments would best be determined on a compaction simulator.

6.5. The Brittle-Elastic System

6.5.1. Pressure Decay and Displacement Relationships During Stress Relaxation – Qualitative Evaluation.

The compression properties of lactose have been demonstrated, by a number of research workers (see Section 1), to be governed by the amount of brittle fracture that occurred during the compression phase. Plastic flow does not occur in the case of lactose, either throughout the compression cycle or even with extended time periods post compaction. That such circumstances exist are endorsed by tensile strength properties where the immediate strength has been shown to remain constant irrespective of time lag between ejection and examination. Consequently, post compaction energy must be expended as alternative work functions, one of which would be elastic recovery on pressure release, an event shown to occur and discussed in Section 3. Particulate interactions originating within the die, once maximum applied pressure has been attained, have been presented previously where an apparent sustained flow was suggested by a fall in applied pressure (FIG.6.3). Although pressure decay was small it was sufficient to satisfy the elastic recovery component of lactose hence allowing upper punch reversal within the die i.e. elastic recovery working against the upper punch assembly "lifted" the latter to yield a measurable displacement on the extensiometer, such a displacement being opposite in sign to that of sodium chloride. The outcome is more satisfactorily described, pictorially, in FIGS. 6.13 a, b and c. Stress relaxation studies were conducted over a 15 minute period although it quickly became evident that matrix modifications had terminated well before 15 minutes had elapsed. Such a conclusion was countenanced from studies outlined in Section 3, where sequential compaction resulted in equilibriated recovery conditions within 5 minutes of load removal.

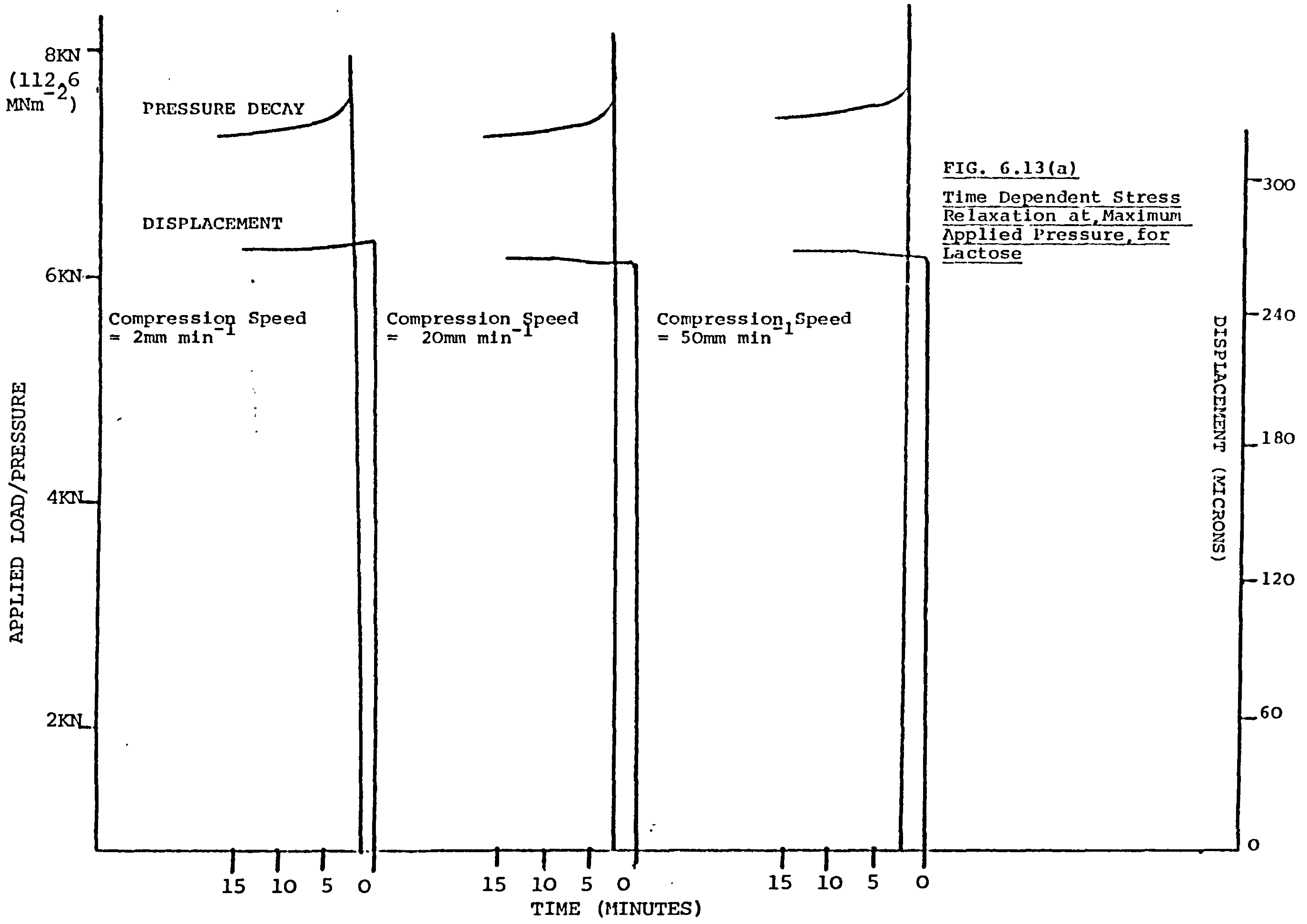


FIG. 6.13(a)

Time Dependent Stress Relaxation at Maximum Applied Pressure for Lactose

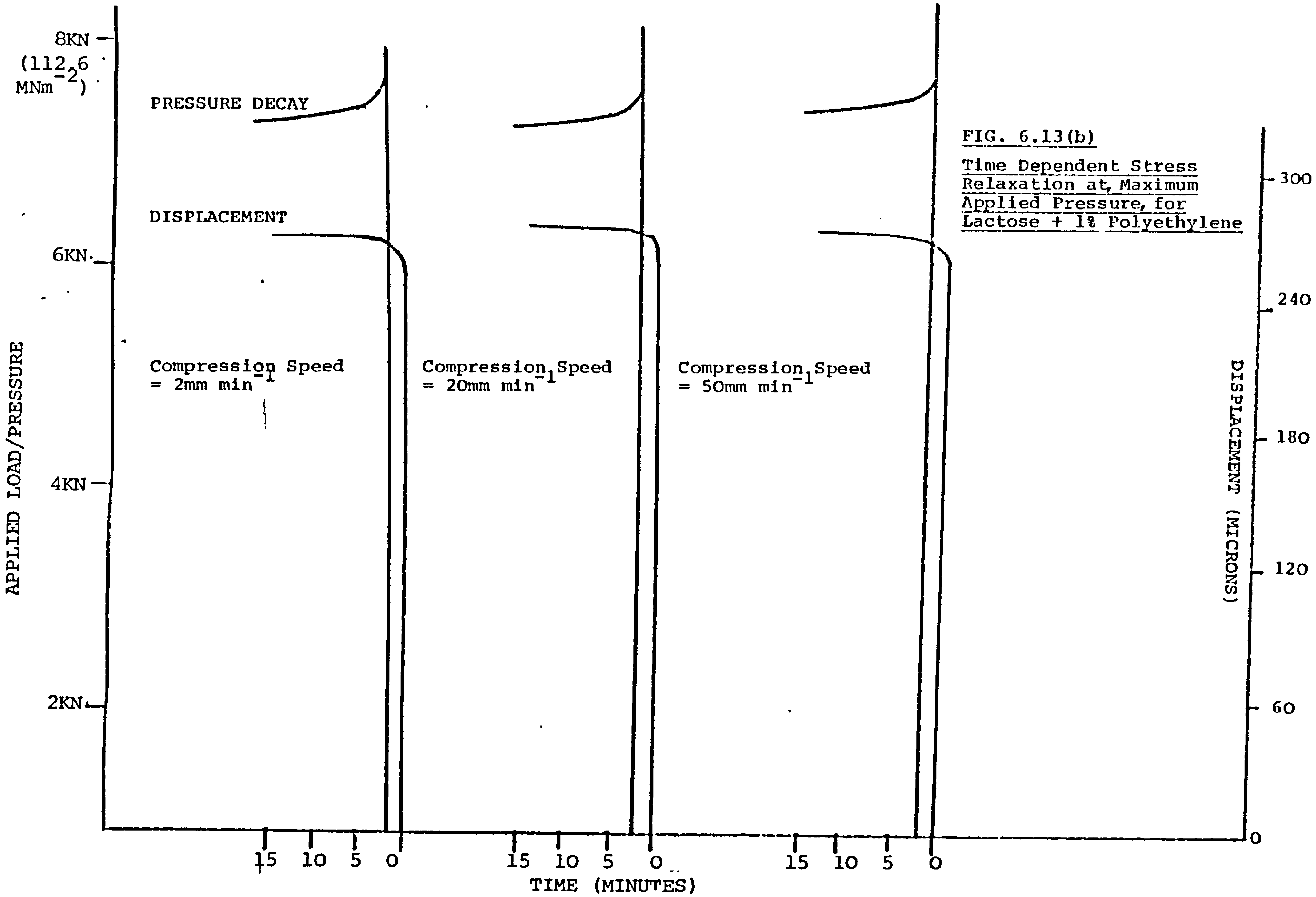


FIG. 6.13(b)

Time Dependent Stress Relaxation at Maximum Applied Pressure, for Lactose + 1% Polyethylene

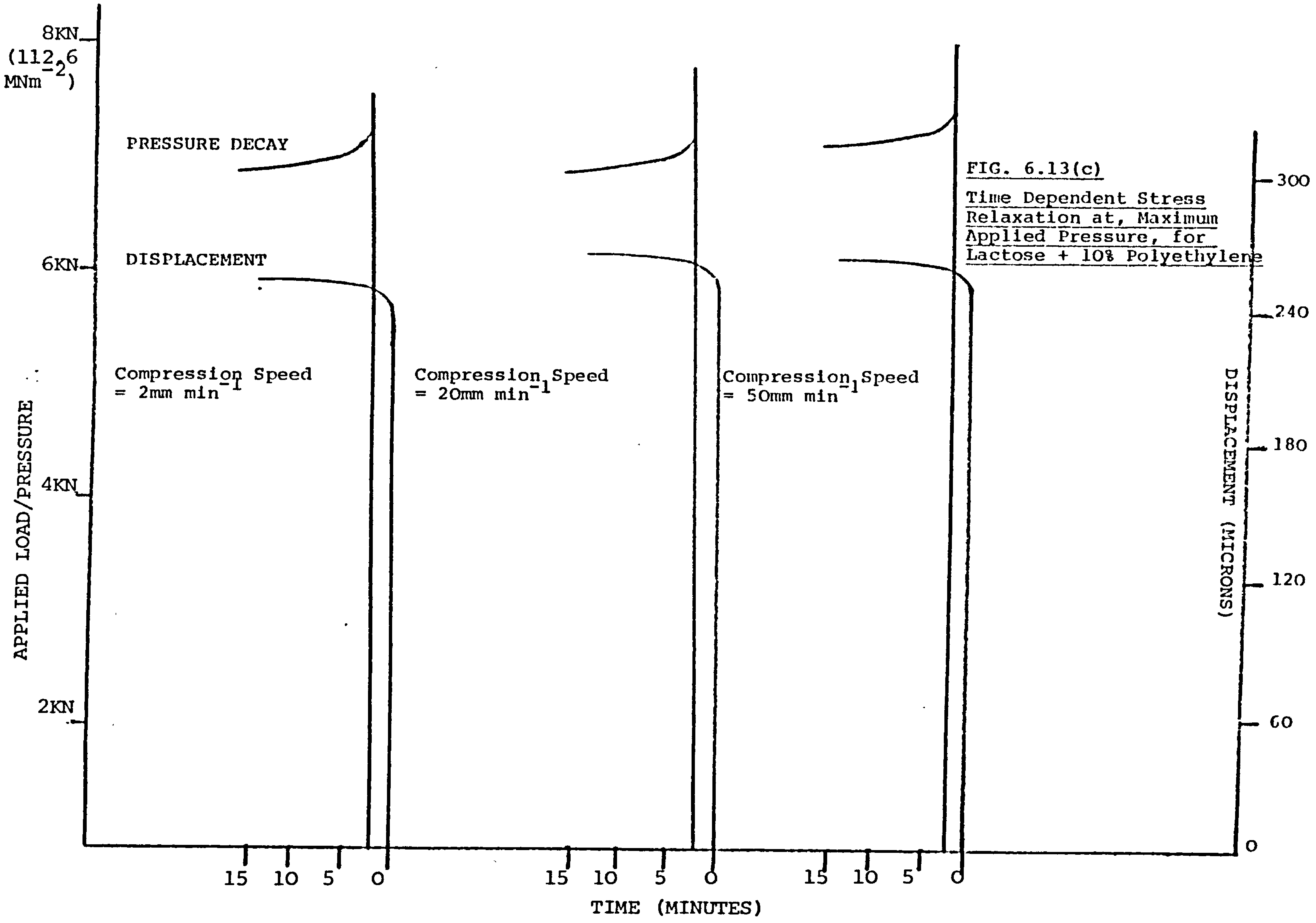


FIG. 6.13(c)

Time Dependent Stress Relaxation at, Maximum Applied Pressure, for Lactose + 10% Polyethylene

Comparison of pressure decay curves for both lactose and sodium chloride featured some important differences between the post compaction behaviour of the two materials.

Firstly, the immediate fall in applied pressure, once maximum pressure had been realised and halted, was very much smaller than that of sodium chloride, this determinant being valid at all three compression speeds. Secondly, pressure decay over the 15 minute monitoring period, when subjected to correction for the immediate effect, plateaued extremely quickly. Within the precision of the technique such a plateauing was complete within the first 2-3 minutes of the stress relaxation events.

Lactose and sodium chloride compress via two quite different mechanisms and one of the most critical precursors controlling the manner and degree of mechanistic behaviour under pressure will be the relative particle sizes of the materials concerned.

The influence of size (and hence, by inference, potential differences in surface variations, bonding sites and bonding strengths), will be perceptible at the consolidation stage and will extend throughout the energy influx period of the compression process. Such differences in properties would be particularly striking at relatively low compaction pressures, at higher loadings extensive brittle fragmentation of particles would potentiate reduced porosity and enhanced interparticular bonding.

Since the particle size of lactose used in the present study was very much smaller (45-63 microns) than that of sodium chloride (355-500 microns), interstitial spaces within a condensing aliquot of sodium chloride would be essentially of large volume and could be occupied either through particle consolidation or plastic flow displacement. On the other hand, spacing within a compacting quantity of lactose would be fundamentally of low volume, remaining, at relatively low pressures, noteworthy but of less significance than that in a sodium chloride system.

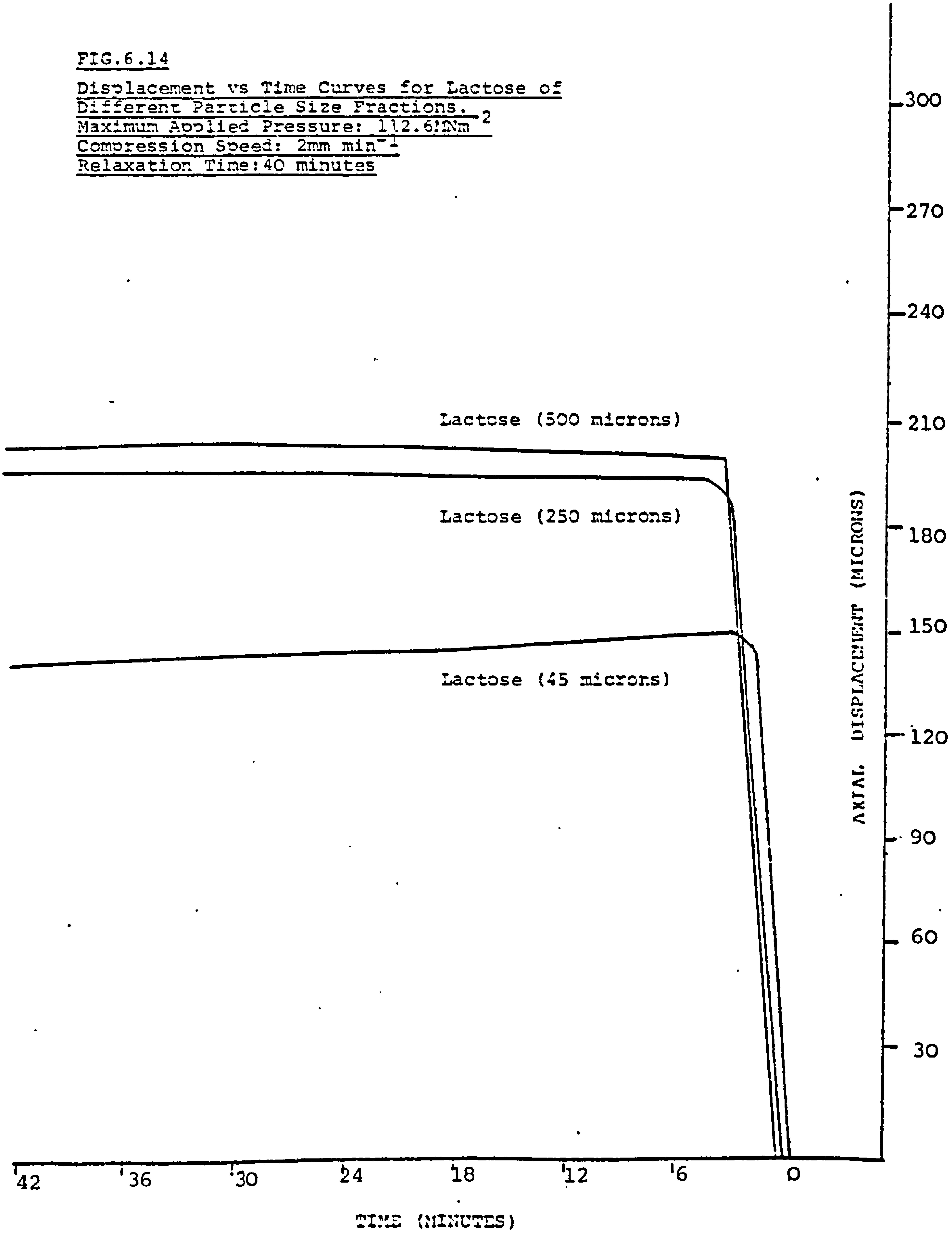
Hence, immediate pressure decay would be occasioned, but to a lesser extent, than that of sodium chloride, findings similar to those previously observed by Rees and Rue (1978). Monitoring stress relaxation over a period in excess of 6 minutes, they perceived a 16% decay in top punch applied pressure with respect to lactose over the first 60 seconds, further losses were negligible. Being essentially concerned with the relationships between stress relaxation and time, their conclusions were based on the premise that the minimal stress relaxation exhibited by lactose, as opposed to sodium chloride, arose as a result of the brittle nature of the material, they proffered no further detail on the decay mechanism, an omission which applied to all the materials they studied, every one exhibited significant immediate decay patterns.

Pressure decay should only be immediate if displacement, however slight, continued on stopping the load at maximum applied pressure. This postulate held in the case of lactose alone even though the displacement was slight at the lowest compression speed. A reversal of this displacement, of opposite sign, then occurred as the compact expanded under the influence of elastic recovery. Such a change in physical dimension, being only of the order of a few microns, was insufficient to register any measureable change in pressure decay over the monitoring period, with the provision of a sufficiently sensitive measuring technique an inflexion would be expected.

That particle size was of considerable importance is further illustrated, (FIG.6.14), for 250 and 500 micron fractions of lactose, a finite slight post compaction displacement (i.e. a reduction in compact volume) occurred with time, this was ascribed to continued settling of the

FIG.6.14

Displacement vs Time Curves for Lactose of Different Particle Size Fractions.
Maximum Applied Pressure: 112.6MNm^{-2}
Compression Speed: 2mm min^{-1}
Relaxation Time: 40 minutes



powder compact causing reduction in particle size through brittle fracture. Cole, Rees and Hersey (1975) have demonstrated very large reductions in the size of lactose particles lying initially in the size range 250-400 microns, such reductions being brought about at pressures much lower than those employed in the present study.

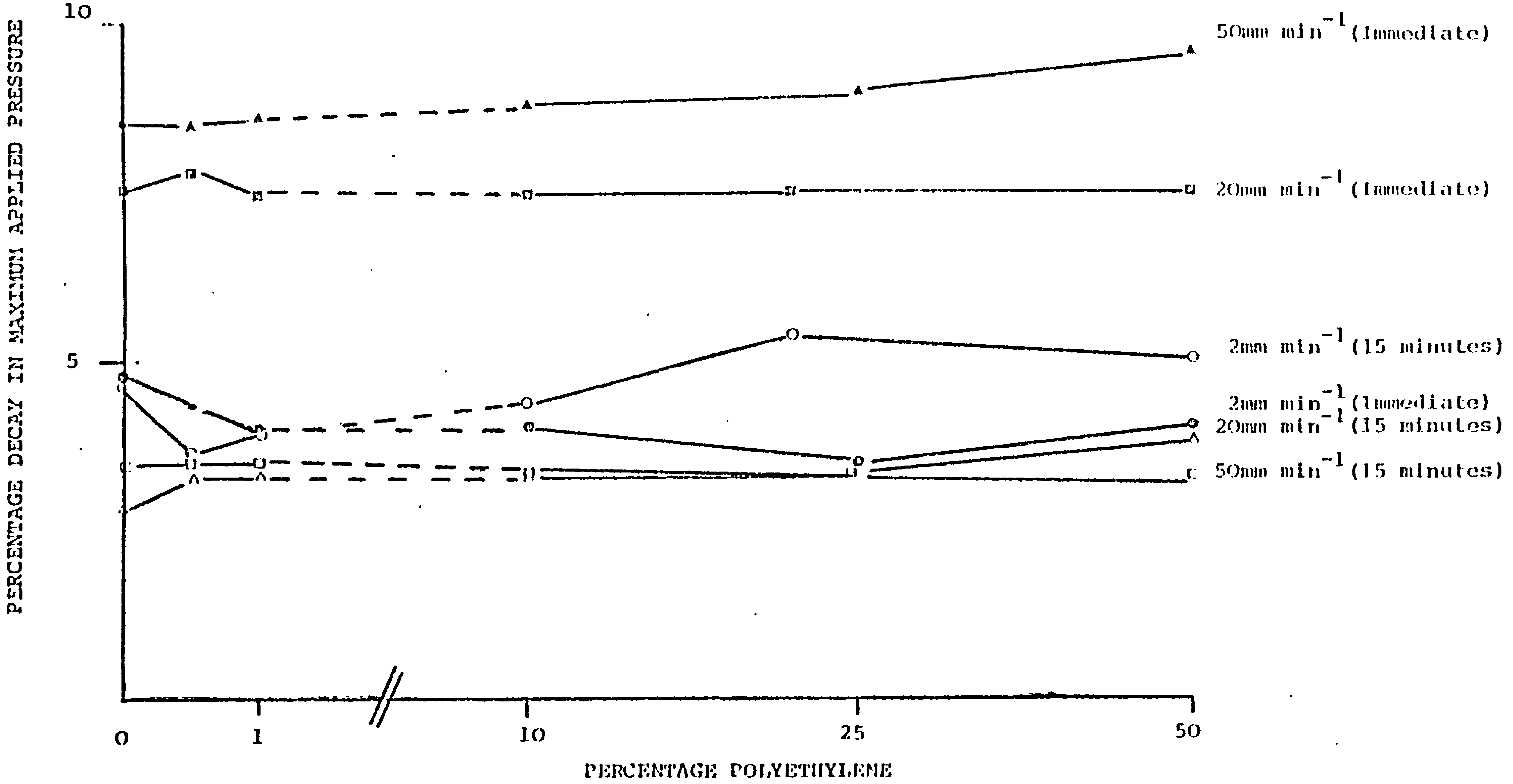
On the addition of polyethylene, pressure decay curves were of a similar nature to those observed with lactose alone, displacements all plateauing after "immediate" changes. The formation of weak bonds by lactose-lactose interactions would not negate the elastic recovery contribution from polyethylene, the compact recovered and held the status quo irrespective of compression speed. The superimposition of decay profiles, without reference to polyethylene content, endorsed such a conclusion.

6.5.2. Pressure Decay and Displacement Relationships During Stress Relaxation - Quantitative Evaluation

The quantitative relationship between pressure decay and polyethylene content is illustrated in FIG.6.15. Monitoring times have been fixed at 15 minute intervals since, with single components and binary systems influenced overwhelmingly by brittle and elastic compaction mechanisms, recovery occurred the instance a reduction in applied pressure was introduced. Dynamic compaction studies (Section 4) have shown how lactose can accommodate a considerable dilution with polyethylene and still retain compact cohesion, the extent of such cohesion controlled by close packing of small particles and multitudinous lactose bonds. Because of this enhanced compatibility with polyethylene, a direct comparison of behaviour at low (0.5 and 1% w/w) and high (10-50% w/w) concentrations of the viscoelastic component was considered sufficient. By comparing the stress relaxation (pressure) data of sodium chloride and lactose (FIGS. 6.9 and 6.15) it was apparent that, although immediate pressure decay was considerably less for lactose,

FIG.6.15

Stress Relaxation (Pressure) of Polyethylene-Lactose Systems Determined at Various Compression Speeds. Values Quoted After 15 minutes Have Been Corrected for Immediate Effect



it remained substantial, particularly at the higher speeds. Such a decay would have two obvious effects on the compact matrix, leading to variations in physico-mechanical properties of the final compacts. Firstly, the operation of an "over-shoot" (i.e. deformation due to powder consolidation continuing for a finite period even as the maximum applied pressure was achieved and application stayed) would be counterbalanced by the contribution from the elastic component of lactose during the stress/strain relaxing period. If, during the "over-shoot", the resultant pressure differential gave rise to weakly bonded areas where elastic recovery played a predominant role then this latent weakness should be reflected in the final strength of the compact, with the systems having the smallest overall pressure drop possessing the weakest tensile strength. However, a second factor must also be considered. Although there can be no doubt that the immediate pressure drop is important and could be affecting the final properties in the manner suggested, the real explanation is probably far simpler with the immediate decay related essentially to "over-shoot" but tensile strength dependent on ordered energy diffusion.

Should the latter be the controlling modus operandi then compression speed becomes important. FIG.6.16 illustrates the relationship between compression rate and tensile strength, the weaker compacts produced at the higher speeds. At the low speed lactose particles are integrated in a relatively ordered manner interstitial movement being favoured with the production of a relatively stable mass. Multiple bonds would be formed with some elastic recovery. As the speed increased, the promotion of a less ordered system, leading to a reduction in interparticle intimacy and coincident reduction in bonding and density, would favour a low tensile strength-high pressure decay interaction.

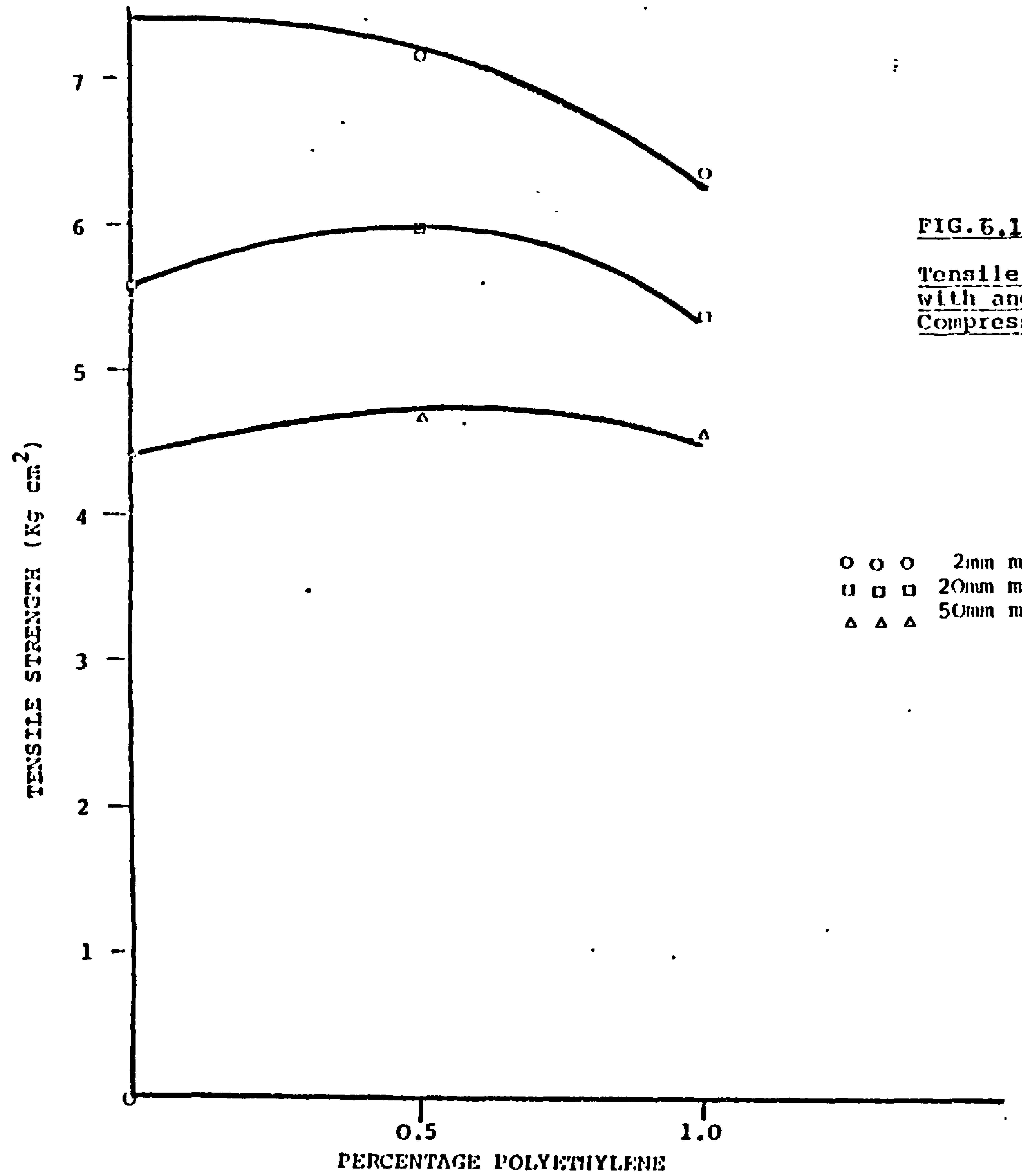


FIG.6.16

Tensile Strength Profile of Lactose with and without Polyethylene after Compression at 112.6 MNm^{-2}

David and Augsburger showed that increasing the duration of the pressure cycle between 0.11 and 10 seconds made no difference to the tensile strength of compacts of compressible lactose containing 0.5% magnesium stearate. However, it seems likely that at the considerably higher applied forces and faster compression cycles they studied, any noteworthy effects would be lost.

The differential in immediate pressure decay, mentioned earlier, was maintained at all polyethylene dilutions up to and including 50% w/w, beyond the "immediate" reaction speed and concentration effects were superfluous. The data suggested that, at concentrations of polyethylene of 10% w/w and above, pressure decay would be more substantive but compensated by instant elastic recovery of the viscoelastic component. That elastic recovery was considerable was reflected in "compact" behaviour when, after completion of the 15 minute retention period, the plug was ejected from the die. On slowly emerging from the die it was obvious that the encapsulating environment had retained cohesion i.e. the compact did not disintegrate during the emerging stage. On finally ejecting, the stored energy escaped as the compact "exploded" out of the die (some energy escaped as sound) with immediate disintegration. At lower concentrations of polyethylene, cohesion was retained. In the latter case, lactose-lactose bonding dominates, not only are dense areas of polyethylene - free lactose available for bonding but particles of polyethylene will, effectively, be coated with layer(s) of lactose particles. Thus, a multitide of weak bonds would be formed which, within the ordered confines of the die, would selectively reduce the recovery capabilities of the viscoelastic component.

A comparison of tensile strength data of lactose-only compacted at similar pressure but under static (FIG.6.16) and dynamic (FIG.4.15) conditions, suggested that increasing the compression speed would make minimal difference to the compaction process, similar strengths being obtained in both cases. However, apart from recognising that the compacts in question were prepared on two different instruments, neither of which was absolutely defined and therefore cannot be directly compared, two major differences between the compacting systems would influence the results. Firstly, the speed of the reciprocating punch machine was very much faster than that of the Instron, even at the highest (50mm min^{-1}) speed of the latter. Secondly, compacts were retained in the die for a period of 15 minutes after completion of load imposition under static dependence, in contrast to undelayed ejection with dynamic control. As a result of immediate ejection, elastic recovery, whether aligned to lactose or polyethylene, would be three-dimensional and randomly distributed, allowing an excess of retained bonds to prevail. Conversely, in the static system, recovery must fully occur within the die confines leading to energy diffusion in a uniaxial direction to give an increase in tablet dimensions. Consequently, in the static system, there will be areas of extreme weakness, proportionally greater than those present on immediate ejection, which will govern tensile strength of the tablet. Such behaviour is of little importance in dealing with lactose or minor dilutions with polyethylene but becomes more influential at higher dilutions. Thus at similar pressures but much greater speeds, 10% polyethylene can be tolerated to give compacts having detailed cohesion.

Turning to displacement as a measure of stress relaxation, only extremely small dimensional changes occurred, within which the precision of the measuring technique may be questionable. A profile of displacement with polyethylene content is illustrated in FIG.6.17. In spite of limitations on precision, unequivocal recoveries in

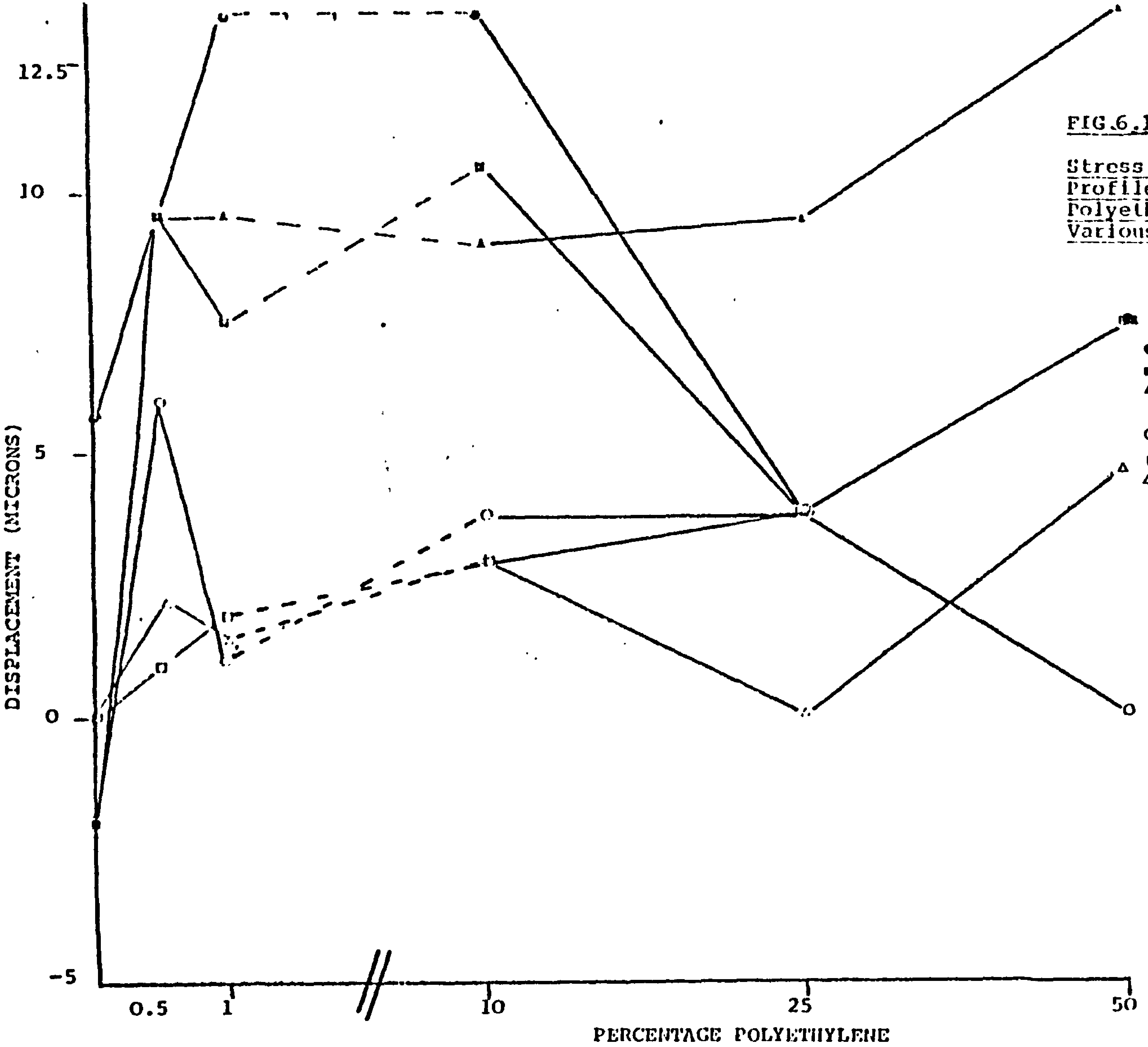


FIG.6.17

Stress Relaxation (Displacement) Profile of a Series of Lactose-Polyethylene Systems Determined at Various Applied Pressure.

uniaxial compact dimensions were observed for lactose alone. Although compact expansion was noted at both 2 and 20mm min^{-1} compression speeds, only at the former were consistent profiles obtained, where repeatability was non-contradictory and expressed in the form of a small apparent 'over-shoot' followed by a recoverable force acting to slightly displace the static top punch in an upward direction (i.e. negative effect). The presence of polyethylene modified compact behaviour, an immediate elastic recovery making variable contributions to the post compaction profile. All displacements are described positively (i.e. further reduction in compact volume) with much the larger proportion of such displacement occurring immediately after the peak of applied pressure.

At high polyethylene content, the circumstances would be further complicated by some contribution to the immediate displacement from a relatively extensive elastic deformation still operating at peak load.

Overall, the stress relaxation profiles of lactose and lactose-polyethylene mixtures indicated that the mechanisms operating post compaction were short-term and predictable. In the lactose system, brittle fragmentation and multi-particle interactions favour a proliferation of bonding sites. The particle size of the starting material(s) would rank highly in factors affecting bonding although, even at relatively low applied pressures, it would be anticipated that large particles (250-500 microns) of lactose would fragment to give reduced multiples. From the findings outlined herein it was apparent that multifarious bonding, initiated by close contact of small particles, would draw extensively on energy supplied to the system throughout the compression cycle. Post compaction equilibration (i.e. energy neutralisation) would be restored by elastic recovery of both lactose and polyethylene. At some critical concentration the highly elastic component, in this case polyethylene, would begin to dominate irrespective of particle size and hence nullify the brittle component.

Any component which compacted via a brittle mechanism can be expected to behave in a similar manner to lactose although, of course, the extent to which it can tolerate other components, especially those possessing of a highly elastic nature, would also be subject to secondary effectation. Such would include aspects of crystal shape (to portend most favourable brittle fragmentation qualities), surface area, surface charge, intraparticle porosity, moisture content and others. However, by applying the type of evaluation outlined, in this thesis, to any given compound, a clear indication of its stress relaxation mechanisms should be capable of forecast and confirmation.

6.6. The Plastic-Brittle System

6.6.1. Pressure Decay and Displacement Study - Composite Conclusions

Where admixtures of plastic and brittle materials are concerned with any elastic contribution either absent or entirely negated, then interactive mechanisms are more easily defined. It has been pointed out previously from dynamic considerations (see Section 5) that the gradation in character of the compact produced as the die contents wholly comprised sodium chloride to lactose could be perceived as a function of two counteractive mechanisms. The same dissimilitude occurred under static conditions, as illustrated in FIGS. 6.18. and 6.19, a single representative compression speed was evaluated since, in the absence of a highly elastic material, differences in compression characteristics would be indiscernible at the relatively low rates acting in the static mode.

There are, to the present author's best knowledge, no published data related to the stress relaxation properties of mixtures consisting of two or more materials compacting by different mechanisms.

FIG. 6.18

Stress Relaxation (Pressure) of Sodium Chloride-Lactose System Compression Speed = 2mm min^{-1}

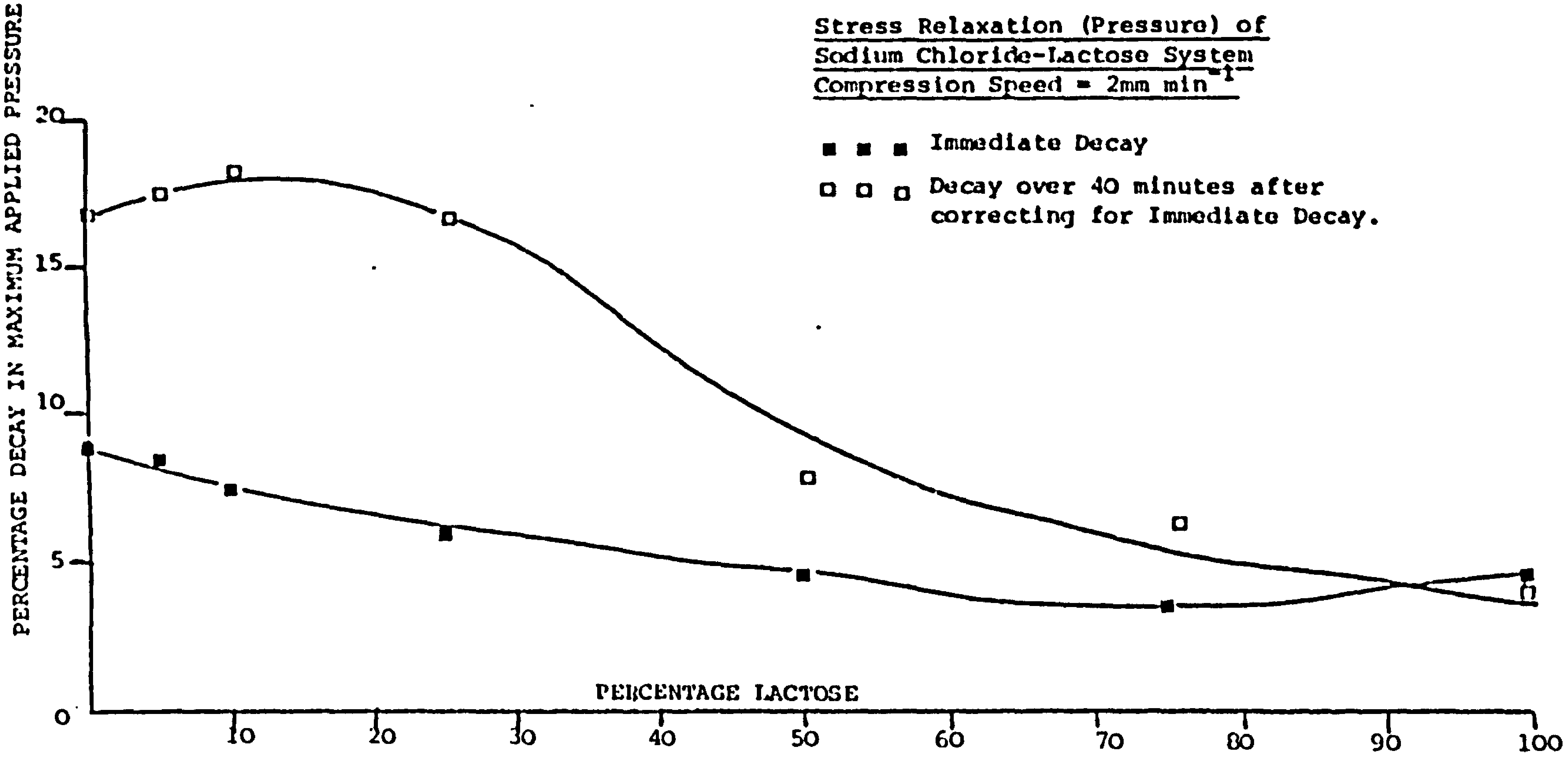


FIG. 6.19

Stress Relaxation (Displacement) of Sodium Chloride-Lactose system at Maximum Applied Pressure. Compression Speed = 2mm min^{-1}

Moreover, no evidence can be found which links the dependence of post-compaction properties (such as strength) on stress relaxation behaviour although researchers have used tensile strength as a yardstick for evaluating the compression characteristics of differing materials. For instance, Newton, Cook and Hollebon (1977) showed how, over a range of applied pressures, the strength of tablets prepared from mixtures of dicalcium phosphate and phenacetin were generally higher than those which would be predicted from the tensile strength of the individual components. They also drew attention to the relationship between tensile strength and tablet composition and how it was influenced by the formation pressure, a facet not observed in previous studies involving one of the researchers(Newton (1971). This interblend of tensile strength tablet composition and formation pressure (applied pressure) has also been shown to exist in the present work (Section 5) with sodium chloride and lactose where a significant reduction in tensile strength of ejected compacts was noted as the ratio of the two components, by weight, approached unity. The importance of this equipart mixture was also reflected under static conditions, reductions in both pressure decay and displacement occurred at this dilution. At higher or lower concentrations of either component, larger displacements were observed when plastic flow dominated without significant lactose impedance whilst, on passing through the intermediate stage, stress relaxation properties were severely modified as a preponderance of lactose restricted plastic flow. That the flow properties of sodium chloride can be extensively qualified by the addition of secondary components has been illustrated conclusively, not only in the present investigations, but also by Sheikh Salem and Fell (1981). In the latter study the secondary component was magnesium stearate (0.1% w/w), the addition of which drastically reduced tensile strength when compared to halide alone.

They proffered two explanations for their findings, either or both of which would exert varying degrees of influence. Either bonding between halide particles was reduced due to surface coating with lubricant or a lesser contribution at the work-hardening stage allowed strain recovery to take place. The nature of the strain recovery remained unexplained but presumably referred to elastic recovery by the lubricant since sodium chloride does not deform elastically to any measurable extent. Compacts formed from lactose containing 0.1% w/w magnesium stearate also exhibited a small decline in strength, being almost certainly due to the elastic recovery of magnesium stearate.

6.6 Conclusions

The findings outlined in Section 6, related to stress relaxation properties of compacts formed under static methods of compaction have highlighted several important hitherto unknown aspects of compaction behaviour. Of these, the most interesting are those that have proved most difficult to define.

Firstly, the stress relaxation relationships between materials having different intrinsic compaction mechanisms became increasingly complex when one component had a low Modulus of Elasticity such that elastic recovery became the controlling factor in post compaction reactions. This constraint on mechanism assessment was particularly conspicuous when observed alongside binary mixtures of plastic and brittle materials where compaction behaviour could be reasonably well defined and predicted.

While bearing in mind that pharmaceutical substances in general are unlikely to have an elastic vector of such magnitude as that of polyethylene, a relatively minor elastic component would certainly influence the compaction properties of materials undergoing plastic flow. By adopting the force displacement methods outlined in

Section 3 and the stress relaxation concepts of Section 6 the elasticity and post compaction behaviour of any tableting material can be assigned.

Secondly, static stress relaxation studies have brought into prominence the immediate pressure decay effects observed with all three types of material (plastic, brittle and elastic) and which are produced to varying degrees depending upon material type. The effect would suggest that all the materials continued to "flow" after maximum applied pressure was achieved, it was considered that this effect was a combination of factors of which one was a physical consolidation of the powder bed as the maximum applied pressure deteriorated across the powder plug.

Thirdly, the dilution of one component with a second having different compaction properties could be tolerated up to a critical point at which tensile strength, pressure decay and displacement strain recovery all correlated to give a quantitative measurement of the critical point.

By applying the test methods outlined in Section 6 to a series of powders of unknown character, pointers as to their post compaction properties would evolve from which their tableting potential can be extrapolated. Such studies are outlined in the following section.

7. EXTRAPOLATION OF STRESS RELAXATION PROPERTIES TO MATERIALS OF INDETERMINATE CHARACTER

7.1. Choice of Constituents

Of the wide choice of drugs, fillers, binders, lubricants and disintegrants available to the pharmaceutical formulator, very few have been defined in terms of absolute compacting mechanisms although a selection have been assigned some properties. In the light of the extensive data now available on both lactose and sodium chloride, both within the published literature and reinforced by the findings in this thesis, there seems little doubt that brittle fragmentation and plastic flow can be assigned, respectively, to these two materials. Additionally, paracetamol has been characterised as having a significant elastic component (Obiorah:1978 and Krycer, Pope and Hersey: 1982), which Nystrom, Mazur and Sjögren (1980) have considered to have real import in affecting capping tendency. Dicalcium phosphate dihydrate, a direct filler, has been demonstrated, by Khan and Rhodes (1975) and de Boer, Bolhuis and Lerk (1978) to have brittle fracture properties while microcrystalline cellulose, an alternative filler, has been apportioned both plastic (David and Augsburger:1977, Ritter and Sucker:1980) and brittle (Sixsmith:1982) qualities. The assigning of specific properties to single components must, of course, always be qualified with caution since there can be little doubt that, in the evaluation of inorganic and organic materials having relatively ordered structures but possessing varying intrinsic energies, contributions, to greater or lesser degrees, will be made by elastic, plastic and brittle influences. By subjecting the three materials, paracetamol, microcrystalline cellulose and dicalcium phosphate dihydrate to precise measurements of stress relaxing pressure decay and displacement, both with and without the presence of polyethylene, a more definitive qualification of compaction properties, with respect to the two contrasting qualities of lactose and sodium chloride, should evolve.

7.2 Materials and Methods

Using a combination of sieving (Endecott and Alpine Air Jet) with Scanning Electron Microscopy, acceptable size fractions of paracetamol (90-180 microns), dicalcium phosphate dihydrate (90-180 microns) and Avicel PH101(45-90 microns) were obtained, the first two proving difficult to clearly define using the techniques employed. However, the final samples were considered sufficiently clean (i.e. free from significant amounts of overlapping sizes) for evaluation. All materials were dried and stored over silica gel prior to use. A single polyethylene dilution (2% w/w) was chosen for study, admixtures of each with polyethylene (180-250 microns) were prepared using a Turbula mixer. Because of the cohesive nature of the materials under test, it was considered expedient to submit each to an identical mixing procedure.

Tablets were prepared, using the Instron test equipment, to the same format as described earlier, all tablets compressed to similar thicknesses. At the maximum applied load (8KN) cohesive tablets were not achieved with paracetamol, in the case of Avicel and dicalcium phosphate no increases in tensile strength were observed when testing was delayed for 3 minutes after maximum pressure had been applied. This was substantiated by both pressure decay and displacement profiles (see later) which indicated that major particle interaction was complete within the "immediate" region.

Since findings with lactose had suggested that strain recovery, post compaction, was completed within a finitely small time of imposing maximum load, greater attention was paid to the 0-2 minute interval immediately following peak loading. However, in as much as plastic flow, of a similar nature to that noted with sodium chloride, could not be disregarded, extended monitoring times, where applicable, were introduced.

7.3 The Paracetamol-Polyethylene System

7.3.1. Stress Relaxing Pressure Decay and Displacement Profiles - Quantitative Evaluation

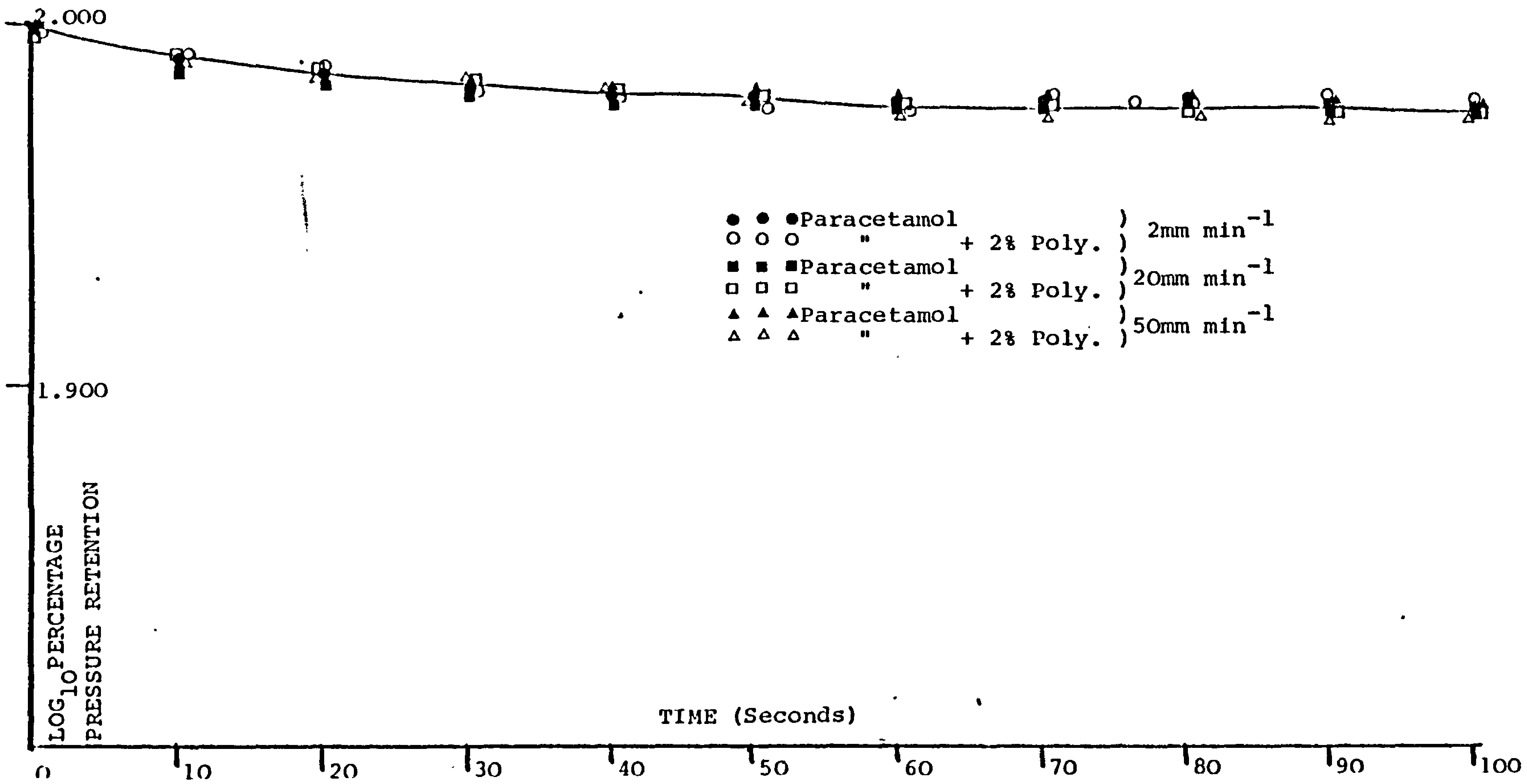
Post compaction behaviour of paracetamol has been studied by several groups of researchers, the material has been classified as possessing a significant elastic component which contributes to bond disruption, thus giving rise to a capping tendency which produces poorly cohesive tablets. Carless and Leigh (1974) measured changes in compact thickness of paracetamol granules both within the die, on reducing the pressure to zero, and on ejection from the die. They found that, as the applied stress increased, axial recovery increased. For instance, at an applied pressure of $88MNm^{-2}$, the percentage recovery within the die was 3.8, on ejection it increased to 7.0. By the addition of a suitable binder (3% polyvinylpyrollidone) relaxation could be significantly reduced. They postulated that, during compression, both elastic potential energy and permanent strain would be induced in the compact, both being detected during the relaxation stage with permanent strain being directly related to residual die wall pressure. During the relaxation process, radial pressure dissipated in three definite stageseach described by a different stress ratio (radial to axial). By assigning a high ratio to the final relaxation stage and correlating it with the increase in axial dimensions discussed above, paracetamol was designated as an elastic material. Unfortunately, sodium chloride also possessed a relatively high final ratio, clearly for a quite different reason, energy was dissipated in the form of plastic flow.

That they also showed an increase in compact size with sodium chloride, during the relaxation stage, must throw their findings into doubt. Nevertheless, the postulate, that a decrease in radial pressure with increasing axial pressure, post compaction, would indicate possible elastic properties, holds firm and was further expanded by Obiorah (1978) in a comparison of paracetamol DC with paracetamol powders. Unsatisfactory tablets produced by the latter were consistent with low residual radial pressure findings, the powder did not give a pressure cycle similar to that of a body with constant yield stress in shear. The distribution and direction of stress relief during recovery would account for capping and lamination. Substitution of paracetamol DC produced satisfactory tablets where radial pressure was retained,to a greater extent, than with paracetamol powder. Tablet dimensions (axial) and residual die wall pressure (RDWP) have also been the basis of two studies by Krycer, Pope and Hersey (1982) in which the relationship between increased height and reduced RDWP served to confirm the elastic properties of paracetamol.

Under the test conditions, utilised in Section 6, the behaviour of an elastic material, post compaction, should mimic that observed with lactose and polyethylene, although such behaviour would be unlikely to compare with that of a highly elastic material such as polyethylene. Consequently, pressure decay should be minimal as paracetamol recovered to hold the pressure constant while displacement should also remain constant. The effects of stress relaxing pressure decay are illustrated in FIG.7.1, a slight decrease in pressure decay occurring over the first 20 seconds to be followed by apparent plateauing. No significant difference was observed either on the addition of 2% polyethylene or on increasing the compression speed. Factors discussed previously such as reduced radial stress,giving rise

FIG.7.1.

Stress Relaxation (Pressure) for Paracetamol, With and Without the Addition of 2% Polyethylene, Compressed at Varying Speeds and to a Nominal Maximal Applied Pressure of 112.6MNm^{-2}



to increased axial stress, would lead to strain release in an axial dimension and hence serve to neutralise any pressure decay observed by the load cell in contact with the upper punch. Both polyethylene and paracetamol would undergo such behaviour, both materials utilizing potential energy to suffer elastic recovery.

That interparticle bonding would be weak was demonstrated by the formation of extremely weak compacts, irrespective of the presence or absence of polyethylene. That cohesion, to a slight extent, had occurred during compaction was witnessed by the production of compacts which retained their integrity on ejection. The mechanisms by which bonding occurs in paracetamol are unknown, attention having mainly been concentrated on elastic properties. That an overwhelming bonding mechanism can operate, such as the plastic flow character of alkali halides or, as in the case of lactose, brittle fragmentation, leading to a multiplicity of electronic bonding, seems unlikely. The polarity and size of the paracetamol molecule would not only limit its energy stabilising interparticle bonding but could well effect intraparticle bonding. Clearly, examination at the molecular level is essential before any postulate on surface bonding becomes feasible but, assuming the above to be the case, then, clearly, energy input will be reclaimed as elastic recovery, the presence of polyethylene making a further contribution to weakening interparticle bonding. TABLE 7.1 depicts the effect of both compression speed and the addition of polyethylene on post compaction displacement of paracetamol. The immediate effect, observed with both sodium chloride and lactose, no longer operates, over the first two minutes of the stress relaxing stage no change in axial dimensions was observed. Such findings correlated with the slight pressure decay discussed above. It was noticeable that, on

Table 7.1.

Stress Relaxation (Displacement), Over Both 2 and 30 minutes Monitoring Periods, as a Function of Compression Speed, for Paracetamol With and Without the Addition of 2% Polyethylene. Displacement Determined from Instant of Attaining Maximum Applied Force (8KN).

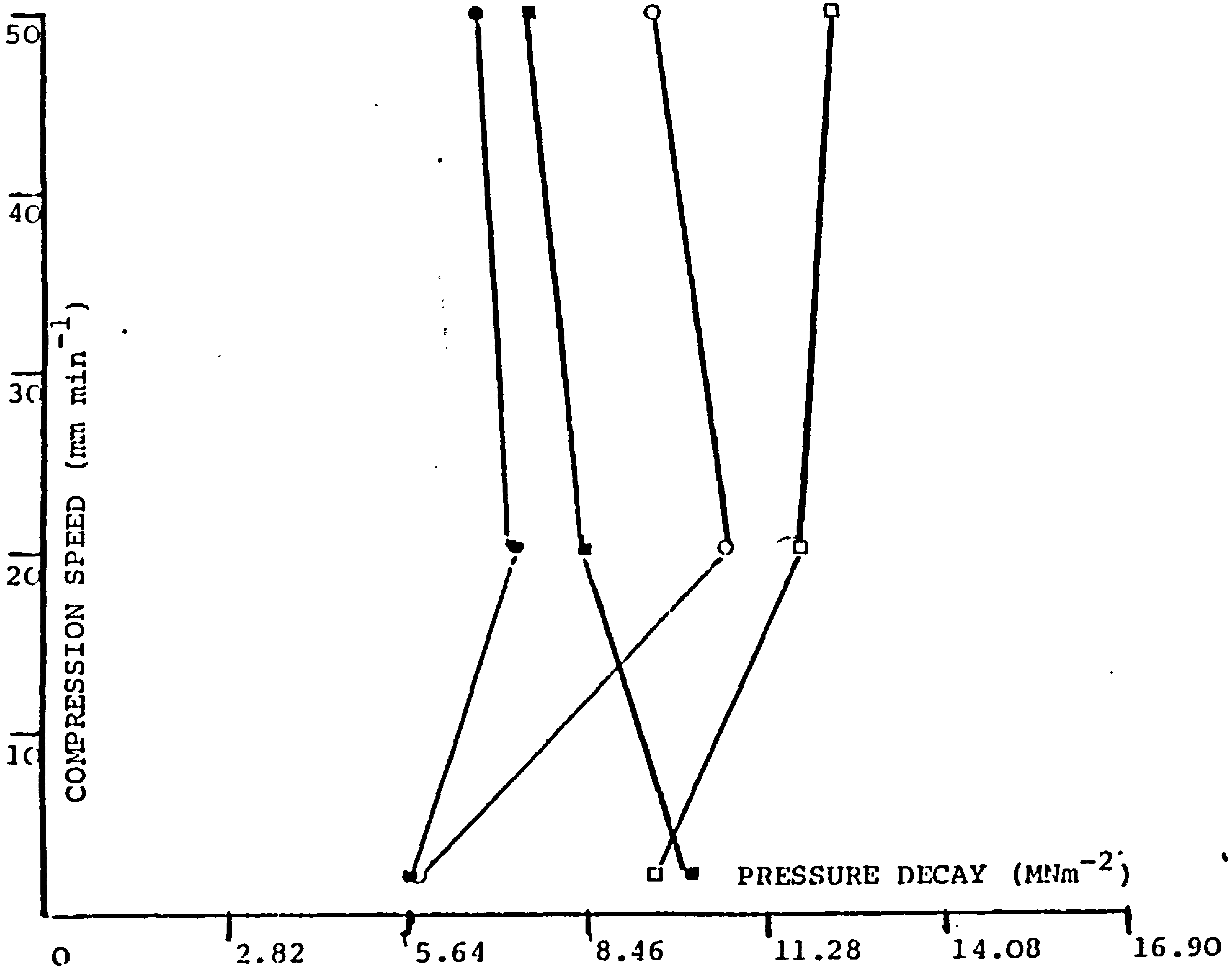
Material	Monitoring Time (Minutes)	Compression Speed (mm min^{-1})	Displacement (Microns) and Nature of Displacement	Time to Achieve Equilibrium
Paracetamol	2	2	Zero	-
		20	Zero	-
		50	Zero	-
	30	2	13.12 - flow	10 minutes
		20	13.12 - flow	10 minutes
		50	14.76 - flow	10 minutes
Paracetamol plus 2% polyethylene	2	2	Zero	-
		20	Zero	-
		50	Zero	-
	30	2	6.56 - flow	10 minutes
		20	8.2 - flow	10 minutes
		50	18.04 - flow	10 minutes

extending the monitoring time, some slight axial displacement was observed, such that the material appeared to flow i.e. the compact underwent a reduction in axial dimension. This apparent reduction stabilised after a 10 minute interval and was consistent irrespective of die contents and speed of compression. It seems likely that, once the die components have recovered elastically with a relatively soft plug retained in the die, the composite effects of the top punch mass and retained pressure is sufficient to promote limited particle consolidation within the die. That such a displacement did occur is suggested in FIG.7.2, which illustrates the slight pressure decay observed once peak pressure had been applied. Thus, in the case of paracetamol alone, percentage decay on applied pressure, over 2 minutes, was of the order of 5%, much less than that observed with sodium chloride.

The above findings, although limited in context, served to further illustrate the elastic properties of paracetamol and could usefully serve as a basis for extending such studies, where materials possessing similar elastic attributes are compressed as admixtures, to systems involving higher compression forces and shorter dwell times. The performance of such mixtures, where "like-with-like" conditions endure, might be visualised as a synchronised event where both materials elastically deform and recover, bonds which are formed during the compacting stage being retained as the whole system recovers. Such an occurrence might produce greater sustained coherence and retained compact strength than that attained with a binary system where energy dissipation, post compaction, was preferentially utilized by one component to give non homogenous structural weaknesses within the final compact.

FIG. 7.2.

Comparative Pressure Decay of Paracetamol, With and Without the Addition of 2% Polyethylene Compressed at Varying Speeds and Over Varying Time Periods.



7.4. The Dicalcium Phosphate Dihydrate-Polyethylene System

7.4.1. Stress Relaxing Pressure Decay and Displacement Profiles - Quantitative Evaluation

The little evidence available, related to the compression characteristics of dicalcium phosphate, is sketchy, although that published would suggest that compaction properties are controlled by, in the main, brittle fracture rather than plastic flow. For instance, Khan and Rhodes (1975) observed a considerable reduction in particle size, from initially 355 to 68 microns, on imposition of $74MNm^{-2}$ pressure. On increasing the pressure to $149.3MNm^{-2}$, particles increased in magnitude to 100 microns. Further increments in pressure coincided with increased particle dimensions, resulting from enhanced bonding, as overall porosity increased. Such behaviour would be consistent with a material undergoing particle fragmentation under stress. Considerable fragmentation was also perceived by de Boer, Bolhuis and Lerk (1978) both with and without the addition of magnesium stearate. By applying the Heckel equation to their data, they derived a non-linear relationship between 1/1-D and force which, based on similar findings with lactose and potassium citrate (Hersey, Cole and Rees: 1972), placed dicalcium phosphate dihydrate alongside those two powders as materials which underwent brittle fragmentation.

The assignment of brittle fracture properties to dicalcium phosphate dihydrate has also been confirmed by Rue and Rees (1978), while deriving their conclusion from reference to the Heckel equation they questioned its utility in designating specific compaction mechanisms based on data generated on a single piece of equipment and emphasized the bias such an exercise might have to any diagnosis. By comparing 1/1-D vs force at different dwell times, with subsequent quantitation of area under the appropriate curve, they suggested that an increase in area with increased dwell time reflected plastic flow properties while little or no change would be indicative of brittle fracture. The technique allowed them to assign the latter property to dicalcium phosphate dihydrate, the former to microcrystalline cellulose.

While the above investigators have been concerned, to a greater extent, with the elucidation of compaction mechanisms, Newton, Cook and Hollebon (1977) attempted to predict the strength of compacts of phenazone and dicalcium phosphate mixtures based on a knowledge of strength patterns of the individual components. Such attempts were unsuccessful and, while they did suggest that the two powders might compact by different mechanisms, they offered no indication as to what such mechanisms might be.

Any attempts to confer specific deformation character to dicalcium phosphate dihydrate based on a knowledge of crystal structure would be extremely difficult since, unlike the reasonably well ordered cubic system of sodium chloride, calcium phosphate possesses the triclinic system. The three cell edges are entirely non specialised in both length and interaxial angles. As a result of such asymmetry there are an infinite number of ways in which the cell can be chosen from the lattice. The cell that is chosen is that which has as edges the three shortest monoplanar translations of the lattice and is called the reduced cell. Buerger (1971) mentions two types of reduced cell, one described by a set of three edges surrounding a corner with three acute angles, the other with three obtuse angles.

In such a relatively disordered system it might be forecast that contributions from plastic flow and elastic recovery would be minimal with brittle fracture being the most dominant mechanism. Compact cohesion would be a function of bonds formed during compression, with indeterminent influences from post compaction stress relief. Assuming brittle fracture to be the major controlling mechanism then the addition of polyethylene should have a notable but not extensive action on tensile strength in a manner similar to that of lactose. However, interparticulate bonding in the latter would be more comprehensive hence reduction in strength of dicalcium phosphate compacts, on addition of polyethylene, should be of a greater order than that for lactose.

The relationship between stress relaxing pressure decay and time for dicalcium phosphate dihydrate with or without polyethylene, compressed at different speeds, is shown in FIG.7.3. Again, by far the greatest percentage pressure decay occurs over the first 10-20 seconds, with the effect of increasing compression speed clearly pronounced. The consequences of increased compression speed would be experienced in two obvious areas. Firstly, the slight increase in applied pressure in increasing the speed would give rise to enhanced interparticulate contact of dicalcium phosphate, the density of the material (2.31gm/cc) being such that slight reductions in porosity would be reflected in increases in tensile strength. Such is shown to be the case in FIG.7.4, the highest compression speed giving the greatest tensile strength. Secondly, as the speed of compression increased, a less ordered compact matrix would evolve. That some particular movement continued at the instant of gaining maximum applied pressure was apparent from the post compaction displacement measurements, where slight flow was observed with immediate pressure decay. (TABLE 7.2). It must be emphasised that only slight positive (i.e. apparent flow) displacement, would generate relatively generous pressure decline. Such is endorsed in FIG.7.5 where percentage decreases, expressed as percentage of applied pressure, are in the order of 7-10% over the first 2 minutes post compaction. Retaining the compact in the

FIG.7.3.

Stress Relaxation (Pressure) for Dicalcium Phosphate, With and Without the Addition of 2% Polyethylene. Compressed at Varying Speeds and at a Nominal Maximal Applied Force of 8KN (112.6MNm^{-2})

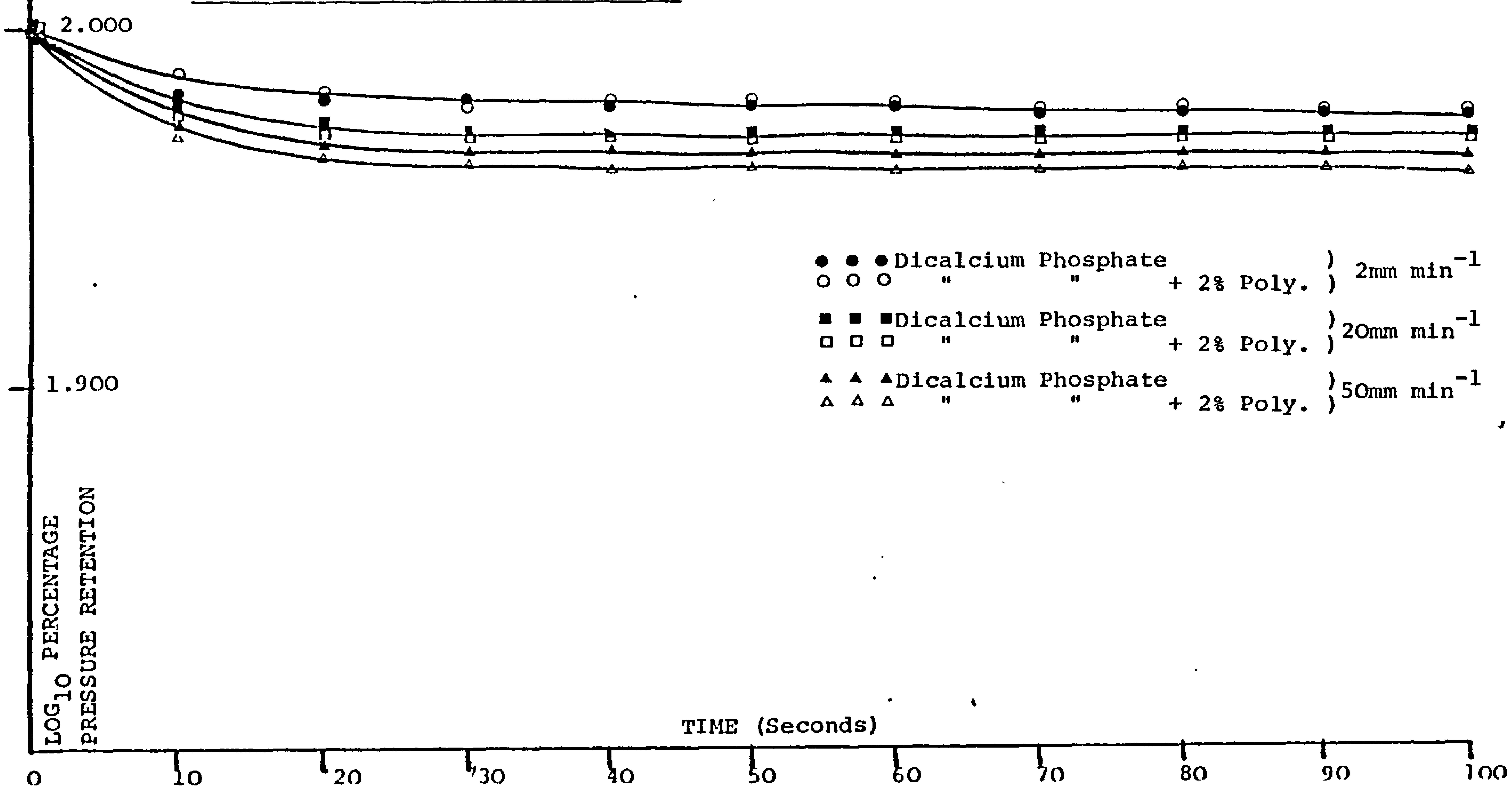


Table 7.2.

Stress Relaxation (Displacement), Over Both 2 and 30 minutes Monitoring Periods, as a Function of Compression Speed, for Dicalcium Phosphate Dihydrate With and Without the Addition of 2% Polyethylene. Displacement Determined from Instant of Attaining Maximum Applied Force (8KN)

Material	Monitoring Time (Minutes)	Compression Speed (mm min^{-1})	Displacement (Microns) and Nature of Displacement	Time to Achieve Equilibrium
Dicalcium Phosphate Dihydrate	2	2	Slight flow	-
		20	Slight flow	-
		50	Slight flow	-
	30	2	8.2 - flow	30 minutes
		20	16.4 - flow	30 minutes
		50	8.2 - flow	30 minutes
Dicalcium Phosphate Dihydrate plus 2% Polyethylene	2	2	4.92 - flow	3 seconds
		20	Slight flow	-
		50	Slight flow	-
	30	2	9.8 - flow	30 minutes
		20	14.8 - flow	30 minutes
		50	11.5 - flow	30 minutes

FIG.7.4.

Tensile Strength as a Function of Compression Speed. Nominal Maximum Applied Force of 8KN (112.6MNm^{-2}Pressure)

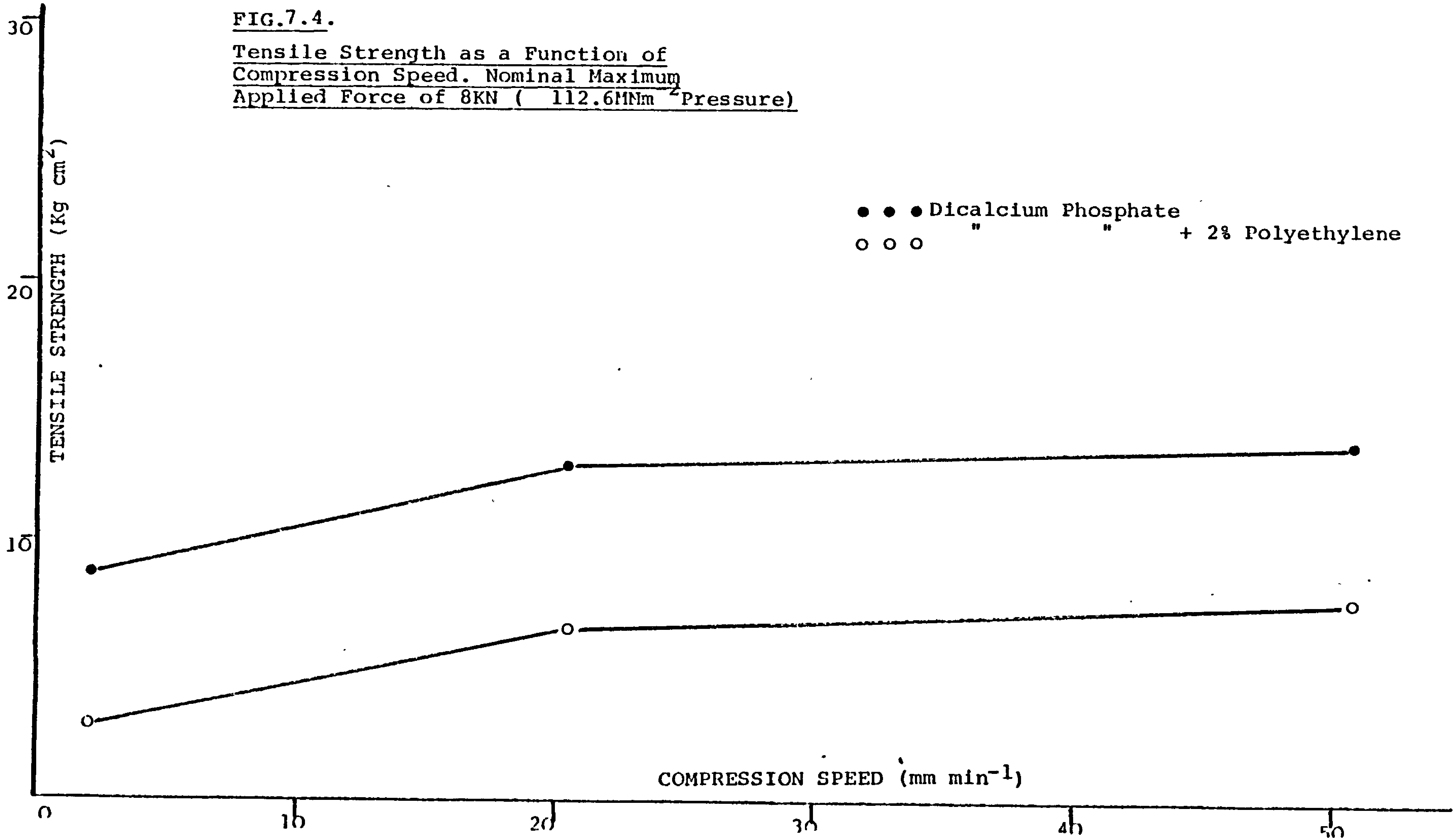
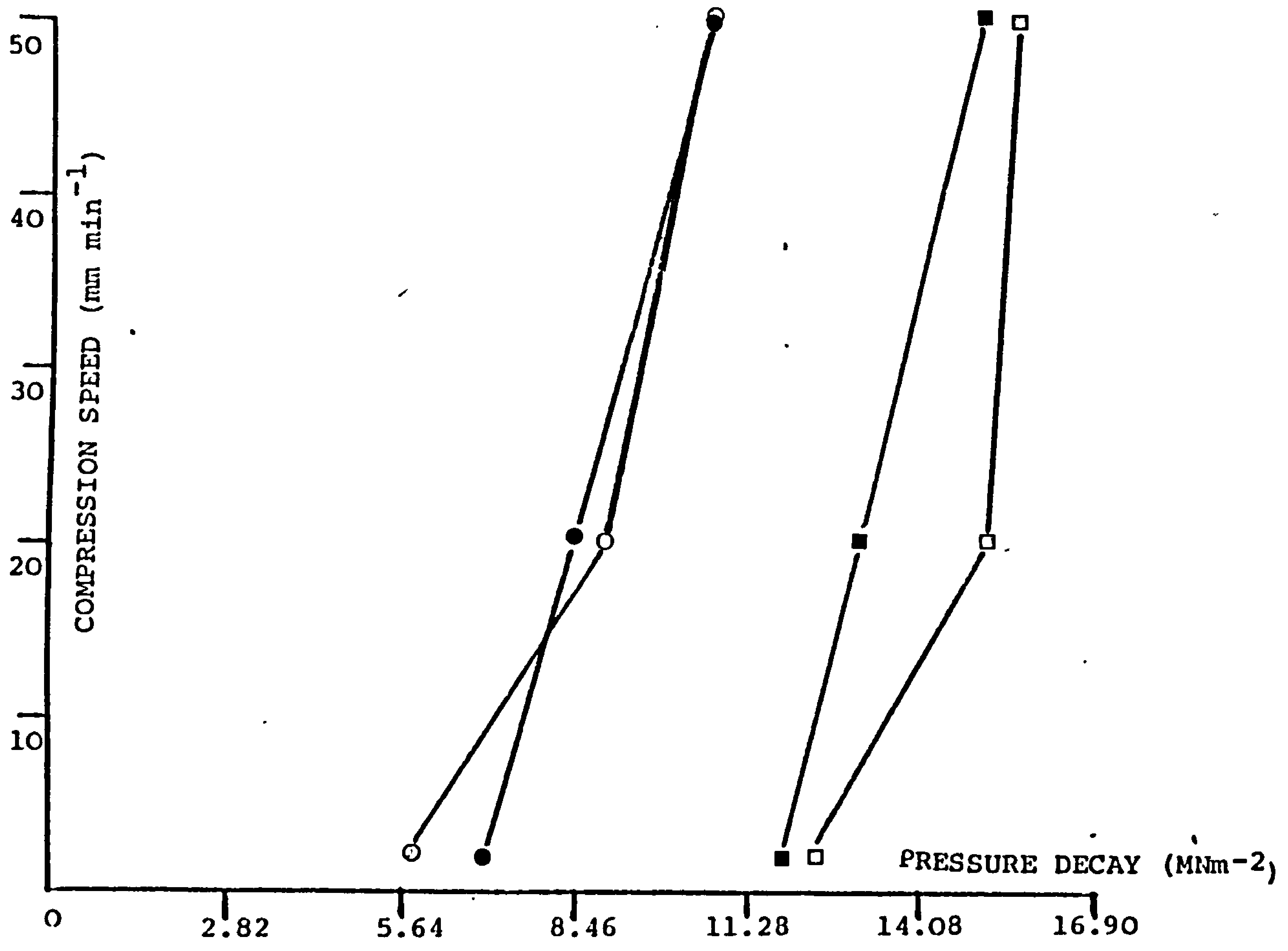


FIG. 7.5.

Comparative Pressure Decay of Dicalcium Phosphate, With and Without the Addition of 2% Polyethylene, Compressed at Varying Speeds and Over Varying Time Periods.



die over an extended time period indicated that further pressure decay occurred accompanied by a reduction in uniaxial dimensions. Tensile strength did not increase during the retaining period and the apparent positive displacement is not attributed to dicalcium phosphate undergoing plastic flow. A more realistic apportioning can be bequeathed to powder consolidation, which is prolonged as the compact remains under load. However, the above postulate is forwarded with some caution since, as can be seen in TABLE 7.2, positive displacement had not stabilised by the completion of the monitoring period, the data would suggest that the assignment of specific compaction mechanisms to the above powder would be a considerable challenge.

Nevertheless, in spite of such misgivings, the stress relaxation data discussed herein would favour brittle fragmentation as being the main contributor to compact cohesion under the static conditions operating such a diagnosis being further endorsed by the ability of dicalcium phosphate to entertain a significant quantity of polyethylene without compact strength being compromised (FIG.7.4).

It would certainly be of considerable interest to assess compaction behaviour under dynamic conditions and imposing much higher pressures.

7.5. The Cellulose-Polyethylene System

7.5.1. Stress Relaxing Pressure Decay and Displacement Profiles - Quantitative Evaluation

The cellulose used in the present study was microcrystalline cellulose AVICEL PH101 (FMC). The powder is formed by breaking the fibrous cell wall of cellulose to give a particular form which is spray dried to produce a granular type material. During processing, through the particular stage, particles aggregate to give crystal bundles each containing very great numbers of dislocations and slip planes. Microcrystalline cellulose particles are held together as a result of hydrogen bonding between hydroxyl groups on adjacent molecules, this bonding is further enhanced by induced plastic flow favoured by the presence of the aforementioned slip planes and dislocations. Extremely large surface-to-surface contact is made between particles of microcrystalline cellulose within a coherent compact. Because of the random and multitudinous centres available for bonding, post compaction energy would be rapidly diffused and equilibrium rapidly attained. Time dependent work hardening, similar to that observed with sodium chloride and dependent upon coulombic repulsion and attraction within a well-defined lattice, should not progress. By similar reasoning, the addition of polyethylene to a system which forms a very great preponderance of hydrogen bonds should have little effect on the tensile strength of the final compact, even accounting for the plastic flow character of the major component.

However, elastic deformation, brittle fragmentation and elastic recovery have all been suggested to play significant roles in the compression behaviour of microcrystalline cellulose. From measurements of surface area on compacts of AVICEL PH101, formed at applied pressures of 100MPa(100MNm^{-2}), Sixsmith (1977) designated a pressure boundary where little change in surface area would occur. Avicel surfaces consisted of essentially internal pores. On increasing the pressure to 125MPa an increase was noticed which he ascribed as arising from elastic recovery of the compact resulting in exposure of previously closed intraparticulate pores.

Sixsmith (1982) extended his studies to encompass the compression behaviour of Avicels PH101, 102 and 103. Compaction profiles (compaction pressure vs radial pressure) indicated that the powders underwent elastic deformation on compression, the elastic limit being in excess of 50MPa and only acquired when particles were subjected to pressures of 60-80MPa. A mathematical treatment, employing the Heckel equation, indicated that, initially, all the microcrystalline cellulose evaluated possessed different bulk densities, as the applied pressure increased, densities became identical. For such an event to occur, beyond the elastic limit, would necessitate particles consolidating predominantly by brittle fracture. Bolhuis and Lerk (1973) had previously adopted force-displacement techniques to assess the percentage of total bestowed energy recovered as elastic energy. For Avicel PH101 this was calculated to be 5% at an applied force of 750Kg.

As opposed to the above, Armstrong, Abourida and Krijgsman (1982) in their sequential compression evaluation of relative force ratios (i.e. the ratio of force exerted on the nth compression to that imparted initially) made no reference to elastic component of Avicel although they did state that microcrystalline cellulose rapidly achieved minimum porosity brought about by the application of only a comparatively small force.

Attention to the behaviour of microcrystalline cellulose during unloading and post compaction periods has been scanty, Rippie and Danielson (1981) adopted a theoretical approach, analysing mechanisms in terms of three dimensional linear viscoelastic theory based on prevailing punch and die wall stresses. They concluded that compacts of Avicel PH101 assumed their final viscoelastic state prior to time of punch separation. Tablets were allowed to remain in the die for several minutes until equilibrium radial stress was preserved. Stresses were monitored every 0.5 m secs of the unloading period (ca.30m secs) and every millesecond of the post compaction event, they separated their data into dilations (considered to be dependent on voids, elastic in all cases) and distortions (described by a Kelvin solid). The elastic moduli were several times larger in dilation than distortion, indicating that particles were more easily sheared than compressed.

Thus, Avicel PH101 should possessdistinctive compression characteristics anticipated to be a composite of elastic and plastic vectors. However, some limiting factors would operate, the first of these being the ability of Avicel to form exceptionally strong compacts at relatively low applied pressures. For this reason a maximum force of 4KN (=56.3MNm^{-2}) was introduced, at this loading prepared compacts approached the maximum limits of the strength testing technique. However, the preponderant cohesive quality permitted lower increments of applied load to be evaluated from which, as discussed below, originated additional useful information.

This is illustrated by FIG.7.6, the stress relaxation profiles for Avicel PH101 compressed at constant speed but at various applied loads. The loads applied were equivalent to pressures of 22.5, 42.2 and 56.3MNm^{-2} all of which, according to Sixsmith (1982) and Aulton, Tebby and White (1974) would be below the predicted (60-80MNm^{-2}) pressure at which the elastic limit of Avicel would be exceeded. The data highlighted several interesting aspects of Avicel compression. Semi-logarithmic plots of retained pressure vs time indicated that a large total stress relaxation occurred with an initial curved section followed by a pseudo first order stress relaxation profile. Such findings were identical to those of Rees and Rue (1978) working with Elcema G250 (similar in identity to Avicel PH101), who compressed to a point force of 20KN. By measuring post compaction pressure decay at incremental pressures and speeds, stress recovery emerged as not only a function of varying applied pressures but also of increasing compression rate (FIG.7.7). A compilation

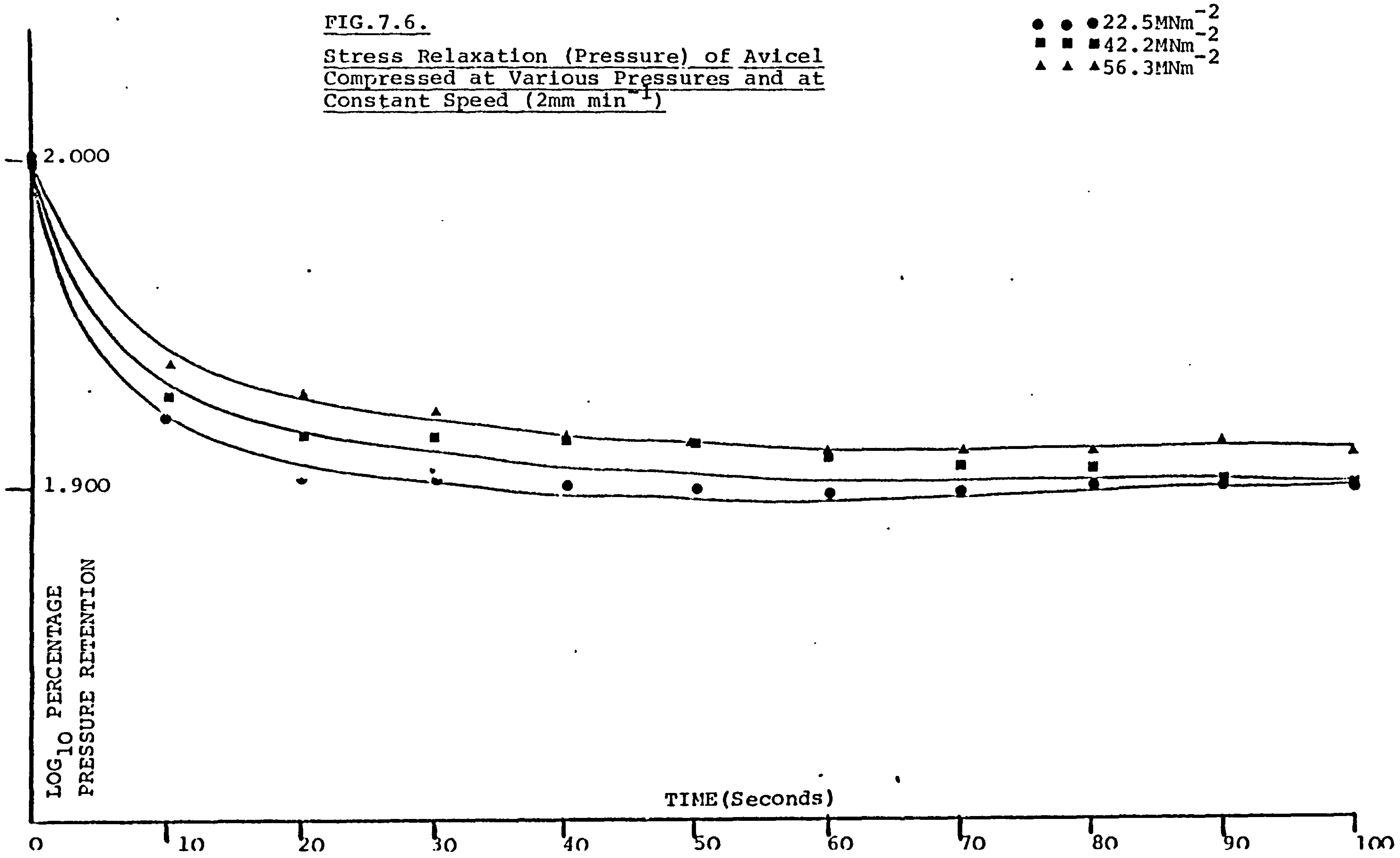
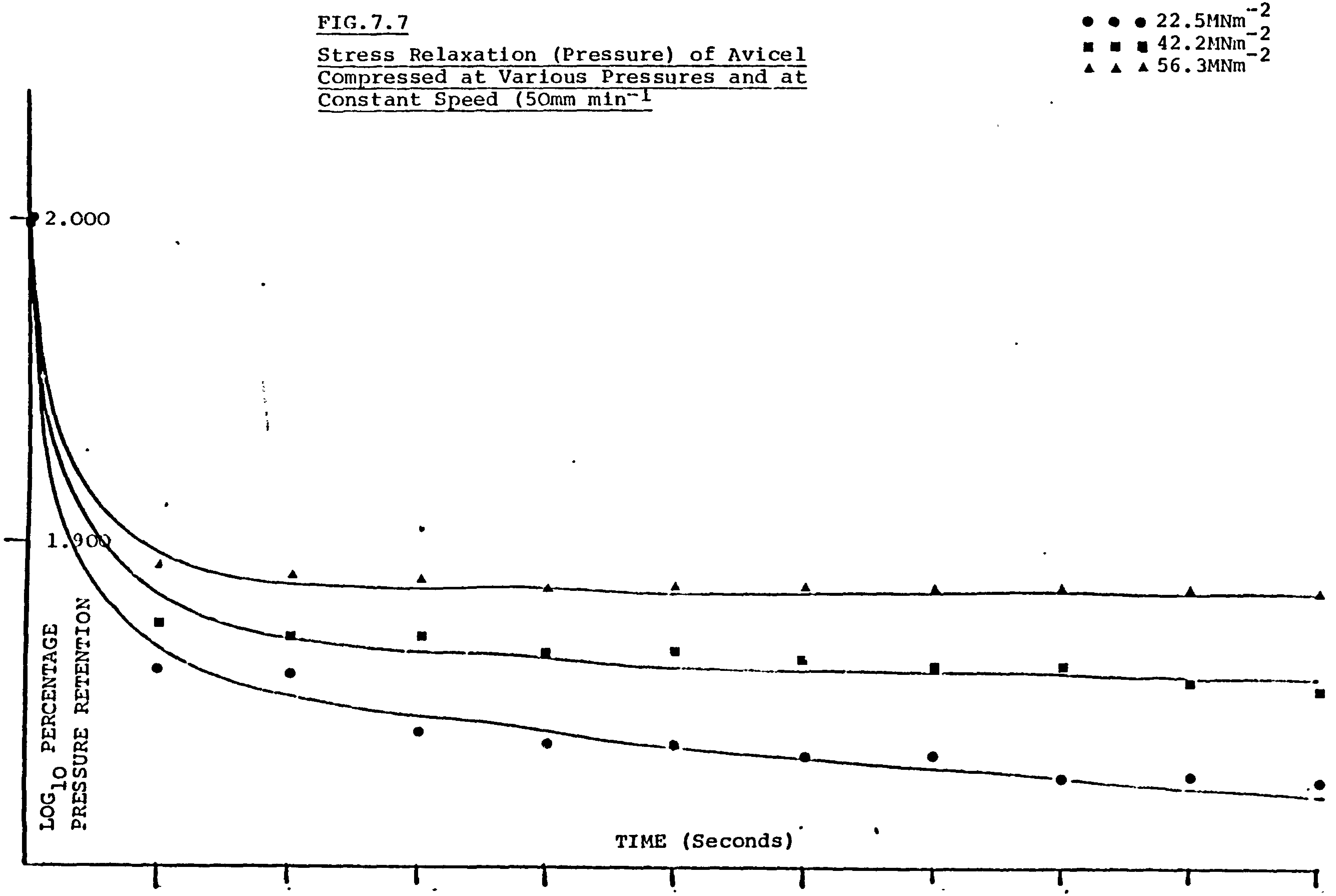


FIG.7.6.

Stress Relaxation (Pressure) of Avicel Compressed at Various Pressures and at Constant Speed (2mm min^{-1})

FIG.7.7

Stress Relaxation (Pressure) of Avicel Compressed at Various Pressures and at Constant Speed (50mm min^{-1}



of both pressure and rate effects is shown in FIG.7.8. The data served to bring into prominence two salient features. Firstly, pressure decay, expressed as a percentage of applied pressure, decreased as the applied load increased. However, in real terms, the actual pressure decay increased as illustrated in Table 7.3(a), representative of the 2 minute die retention operation. Secondly, although a similar decay profile was observed at higher loading rates the rate itself considerably influenced the resultant pressure decay, such that at any applied pressure the decay developed at the high speed was very much greater than that observed at lower speeds (at the relatively low pressures implemented in the Avicel study, no high bias was observed on increasing the speed from 2 to 50mm min^{-1}).

The immediate displacement coincided with an immediate apparent flow specified by the displacement measurement (see later) but it seems likely that such effects of load and loading rate are produced as a result of complex interactions of both physico-mechanical and physico-chemical nature. At such relatively low pressures, retention of the compact under load could maintain consolidation and elastic deformation (providing the powder was below its elastic limit) with the powder also undergoing some degree of plastic flow. The effects of speed appeared the most critical, such exaggerating effects having not been observed within the context of the present studies. However, it seems reasonable that accelerating particles of the nature of microcrystalline cellulose might be expected to continue to interlock and bond, with slight reduction in tablet porosity and volume, even though peak pressure had been attained.

It is worth noting that any elastic recovery which Avicel suffered on pressure reduction would be completely swamped by the strain relief parameters outlined above.

FIGs. 7.9 and 7.10 illustrate the outcome of compressing admixtures

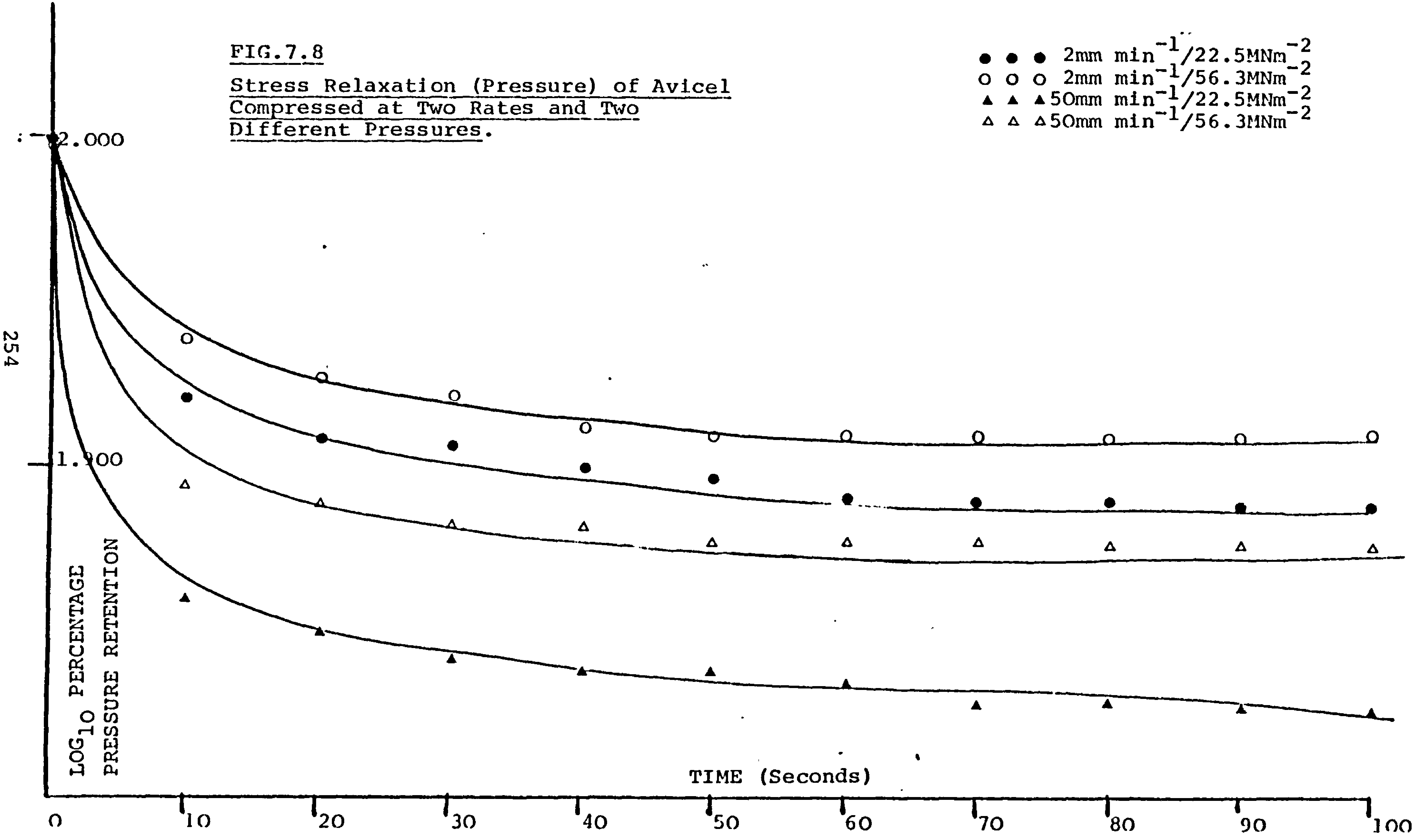


FIG.7.8

Stress Relaxation (Pressure) of Avicel Compressed at Two Rates and Two Different Pressures.

Table 7.3(a)

Stress Relaxing Pressure Decay for Avicel PH101, With and Without the Addition of 2% Polyethylene, as a Function of Compression Speed and Applied Pressure, Compact Retained in Die for 2 Minutes Post Compaction.

Material	Compression Speed (mm min^{-1})	Applied Pressure (MNm^{-1})	Pressure Decay (MNm^{-2} and Percentage)
Avicel	2	22.5	5.18(23)
		42.2	8.73(20.7)
		56.3	10.7 (19)
	50	22.5	7.45(33.1)
		42.2	12.02(28.5)
		56.3	14.6 (26.0)
Avicel + 2% Polyethylene	2	22.5	5.06(22.5)
		42.2	8.44(20)
		56.3	10.4 (18.5)
	50	22.5	6.90(30.7)
		42.2	11.5 (27.2)
		56.3	14.2(25.2)

FIG.7.9

Stress Relaxation (Pressure) of Avicel, With and Without the Addition of 2% Polyethylene. Compressed at a Constant Rate (2mm min^{-1}) and at Two Different Pressures.

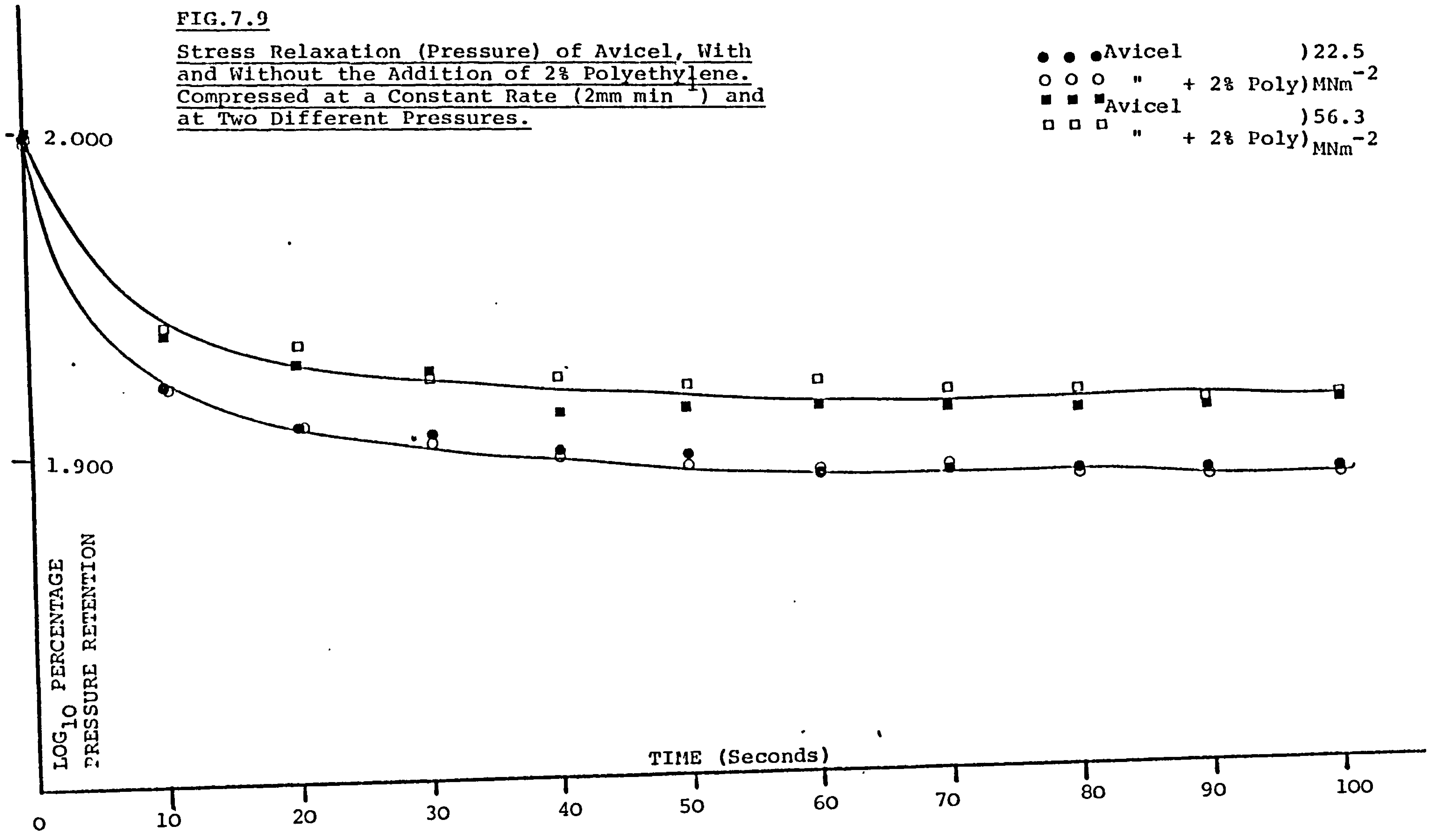
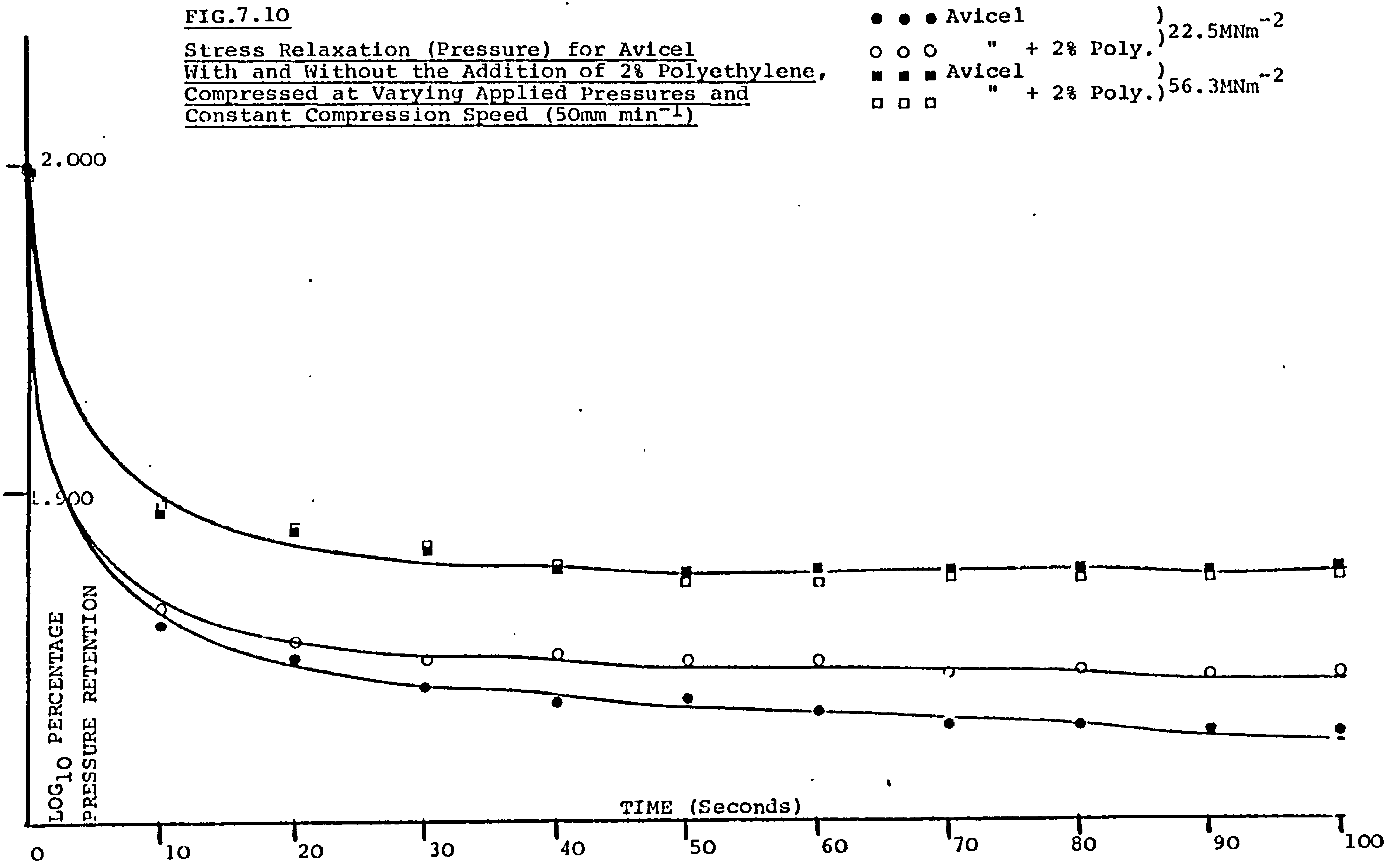


FIG.7.10

Stress Relaxation (Pressure) for Avicel With and Without the Addition of 2% Polyethylene, Compressed at Varying Applied Pressures and Constant Compression Speed (50mm min^{-1})



of polyethylene (2%) with Avicel, at two different speeds and two different pressures. Identical relationships to those observed in the absence of polyethylene evolved, with the addition of the highly viscoelastic component having little apparent effect on the compression behaviour. However, as can be seen in Table 7.3(a) a consistent decrease in pressure decay, irrespective of applied load and loading rate, concurs with the addition of polyethylene. In an already complex matrix the introduction of an elastically deforming material would serve to interfere with the intimate interlocking function of microcrystalline cellulose to reduce the degree of any post compaction effects, whether of a consolidatory or plastic nature. It would certainly be a scientific advantage to study the compression behaviour of Avicel with larger dilutions of polyethylene.

Although all the findings related above describe the first 100-120 seconds of the post compaction phase, pressure decay continued over an extended time period, as illustrated in FIG.7.11 (25 minutes) and Table 7.3(b) (30 minutes). Such behaviour would be consistent with plastic flow, increases were observed both with and without the presence of polyethylene. As an illustration of time and compression rate being influential variables of pressure decay, FIG.7.12 compares selected stations.

Tensile strength, as a function of compression force, with and without the presence of polyethylene, is shown in FIG.7.13. Breaking strengths were determined 45 minutes after peak applied pressure was attained, a comparison of immediate, 2 minute and 30 minute die retention stations indicated that work hardening, as observed with sodium chloride, did not occur. A single loading (1.6KN) point at 20mm min^{-1} has been included for continuity. The data complements the pressure decay data, to some degree, in that up to and including the

Table 7.3(b)

Stress Relaxing Pressure Decay for Avicel PH101, With and Without the Addition of 2% Polyethylene, as a Function of Applied Pressure. Powder Compressed at a Single Compression Speed (2mm min^{-1}) and Compact Retained in Die for 30 Minutes

Material	Applied Pressure (MNm^{-2})	Pressure Decay (MNm^{-2} and Percentage)
Avicel	22.5	6.71(29.8)
	42.2	11.4 (27)
	56.3	13.9 (24.7)
	70.4*	14.4 (20.4)
Avicel + 2% Polyethylene	22.5	6.06(26.9)
	42.2	11.3(26.7)
	56.3	13.5(24)
	70.4	14.1(20)

* A fourth station was included in the study for comparative purposes but no other compression parameters were considered at this relatively high pressure since compact tensile strength was immeasurably elevated.

FIG. 7.11

Stress Relaxation (Pressure) for Avicel With and Without the addition of 2% Polyethylene, Compressed at Varying Applied Pressures and Constant Compression Speed (2mm min^{-1})

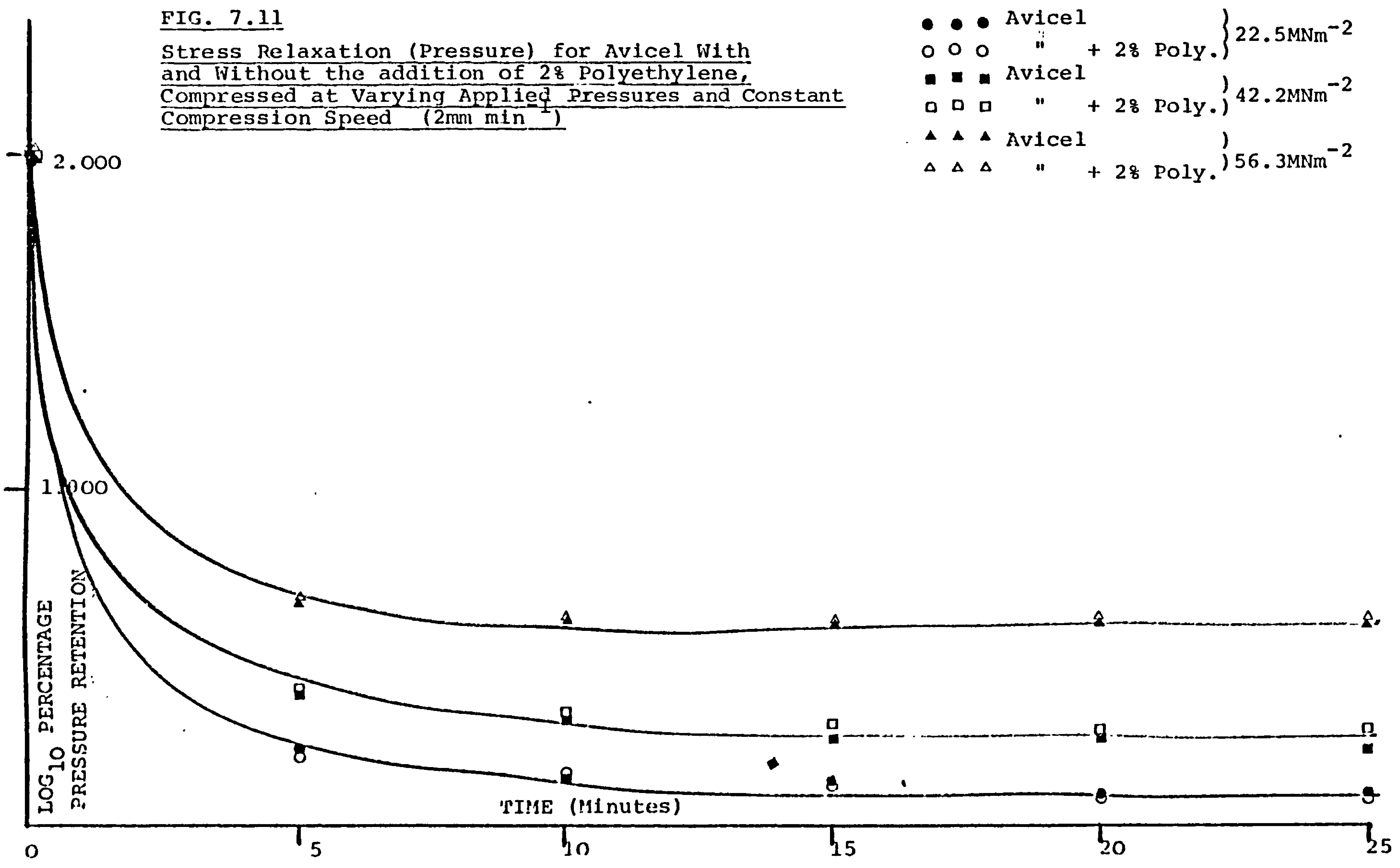
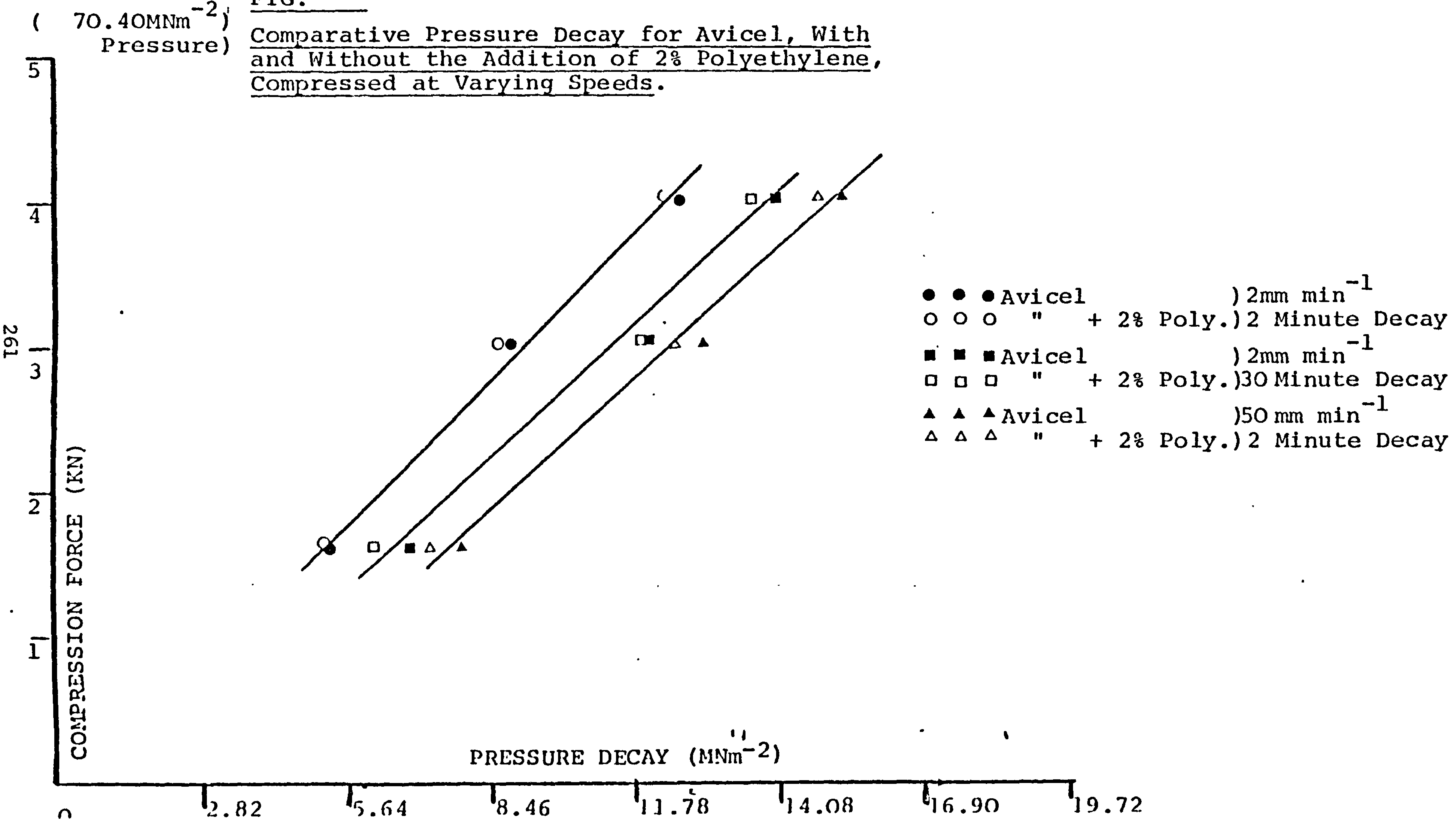


FIG. 7.12

Comparative Pressure Decay for Avicel, With and Without the Addition of 2% Polyethylene, Compressed at Varying Speeds.



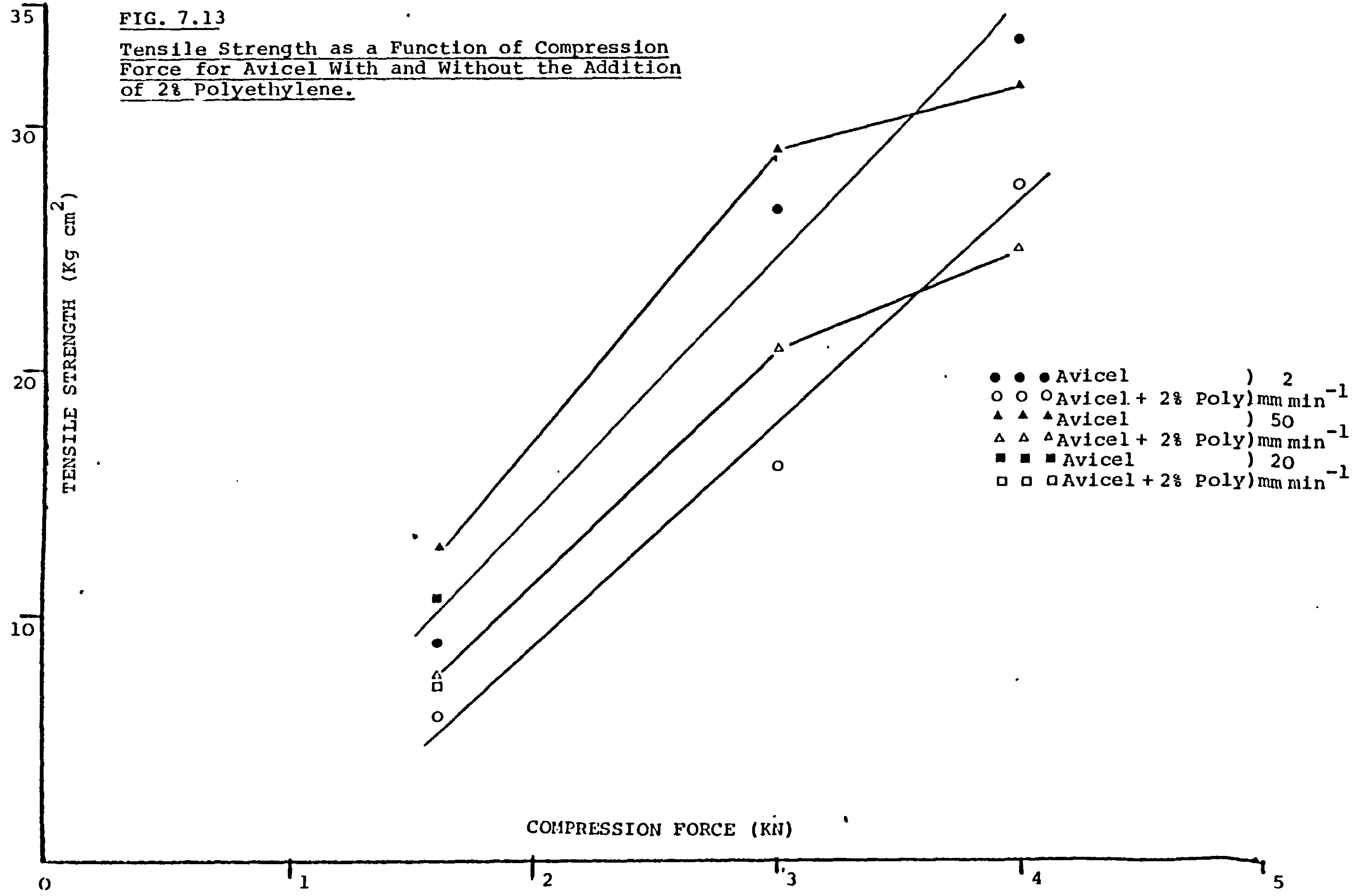


FIG. 7.13

Tensile Strength as a Function of Compression Force for Avicel With and Without the Addition of 2% Polyethylene.

Table 7.4

Stress Relaxation (Displacement), Over a 2 Minute Monitoring Period, as a Feature of Compression Force and Compression Speed for Avicel, With and Without the Addition of 2% Polyethylene. Displacement Determined From Instant of Attaining Maximum Applied Force.

Material	Compression Force (KN)	Compression Speed (mm min^{-1})	Displacement (microns) and Nature of Displacement	Time to Achieve Equilibrium
Avicel	1.6	2	4.92 - flow	5 seconds
		50	Insignificant flow	-
	3	2	9.84 - flow	5 seconds
		50	9.84 - flow	5 seconds
	4	2	13.12 - flow	9 seconds
		50	13.12 - flow	9 seconds
Avicel + 2% Polyethylene	1.6	2	6 - flow	3 seconds
		50	8.2 - flow	2 minutes
	3	2	4.92 - flow	15 seconds
		50	Slight flow	1 minute
	4	2	13.12 - flow	12 seconds
		50	13.12 - flow	12 seconds

3KN loading point, tensile strength increased with increasing load and compression speed. The addition of 2% polyethylene produced a similar picture but at an overall lowered strength. Assuming plastic flow character for Avicel, then addition of a viscoelastic component having a high Modulus of Elasticity would be deleterious to the bonding properties of the former. However, the extensive potential bonding sites of cellulose would serve to maintain its preemminent compacting properties.

Finally, Table 7.4 outlines stress relaxation (displacement) behaviour over the 2 minute monitoring period, beyond this time interval, changes in axial dimensions were insignificant. As can be seen, dimensional changes occurred extremely quickly and were consistent with continued "flow" of the material at the instant of attaining peak applied pressure. The data is in agreement with that for pressure decay.

Clearly, the compaction mechanisms of Avicel PH101 are complex, both during the compression and decompression phases of the compacting process. The data would, however, support the contention, made by other investigators, that it deforms by a plastic flow mechanism although immediate bonding potential is the controlling factor in assessing tablet cohesion. A more extensive evaluation of Avicel using the techniques described herein, is recommended as an objective for further work.

8. CONCLUSIONS

The compression characteristics of plastic, brittle and elastic materials, both as single components and binary mixtures, have been extensively studied under conditions of static and dynamic compaction. Although much published research has centred around investigations related to plastic and brittle materials, very little work has involved studies on materials having low Moduli of Elasticity. In addition, the effects produced when plastic or brittle materials are intimately mixed with varying amounts of an elastic component have also been neglected. Although some studies involving the compression of binary mixtures have been reported where one of the components could be described as being elastic in character (examples of same would be magnesium stearate, Spans and Tweens) none have included a protracted explanation of elastic behaviour. A comprehensive literature review indicated that such a study would make a positive contribution to present day knowledge of compaction mechanisms. This thesis describes such a study and from it the following conclusions can be drawn.

By adapting an Instron Testing Machine to incorporate a special jig whereby, by means of an extensiometer, precise force-displacement relationships can be correlated with force-time data, energy distributions during and post compaction have been assigned. Such profiles have clearly indicated the elastic recovery characteristics of materials which compress via differing mechanisms. Sodium chloride, a material which deforms plastically, does not elastically recover post compaction, the total energy imparted to the system during the compaction process being distributed in the form of plastic flow. As a result, a time-dependent work hardening process operated such that intra and interparticle bonding increased, resulting in increased tablet strength. Sequential compaction indicated that energy requirements were totally satisfied after the first compaction. Lactose, undergoing brittle fracture under the influence of applied pressure, possessed a small but significant elastic recovery component. Sequential compaction showed that, in spite of further small increments of energy being utilised in the form of brittle fracture, the elastic component continued to function in the event of multiple compression. Polyethylene was prone to substantial elastic recovery post compaction and, significantly, of the total energy imparted to the system during compression a considerable portion was retained when the load was removed. However, on second and subsequent compactions both force-displacement and force-time data indicated that the total energy imparted during compaction was recovered post compaction.

Addition of small quantities of polyethylene (0.5 and 1%) to sodium chloride produced similar profiles to those seen with sodium chloride alone, an effect substantiated by the energy distribution data, with a relatively small proportion of the compacted energy required to exceed the elastic limit of sodium chloride. However, in spite of similar energy patterns for both sodium chloride with and without the addition of polyethylene, the importance of the latter in inhibiting interparticle bonding was decisive. Thus, even at the highest load and lowest dwell time studied, the addition of only 0.5% polyethylene reduced the crushing strength of sodium chloride to zero. It was concluded from the absence of any measurable energy of recovery that, under conditions of static compaction, the viscoelastic nature of polyethylene was such that it was able to absorb a very significant proportion of the total energy imparted to the system on compression.

Under similar conditions of compaction, lactose behaved quite differently to sodium chloride, the brittle fracture mechanism controlling the increased quantities of polyethylene which could be accommodated by the system. By plotting the relative total, brittle and elastic energies as a function of polyethylene content, at different loads and various dwell times, not only was it clear that significant amounts of polyethylene could be tolerated by the system but some indication of the point at which the elastic component began to dominate the compaction process could be derived. Thus at approximately equal parts of lactose and polyethylene the elastic recovery of the polyethylene assumed prominence in the compression process. The particle size of lactose has also been shown to be implicated, increases in particle size allowed the polyethylene to assume a more dominant role.

Under conditions of dynamic compression, the effects of low dwell time and immediate post compaction ejection (i.e. the introduction of a radial vector) attained significant importance. Although, under static conditions, retention of a sodium chloride-polyethylene compact, within the die, for an extended period post compaction can assign structure to the compact and further matrix cohesion, no such effect can be achieved in the dynamic system. Only at pressures in the region of 300MNm^{-2} (under static conditions a maximum pressure of 112.4MNm^{-2} was imposed) can an intact tablet be ejected from the die. Attainment of initial bonding lends itself to time-dependent stress relaxation, identified as a function of breaking strength. However, attained strengths are very much lower than those observed with sodium chloride alone and can only be achieved at high pressures.

Other alkali halides have been shown to undergo identical behaviour profiles, the latter being modified by the particle size of the starting material. Sodium chloride particles of similar size to those of standard lactose particles have been produced both by ball milling and recrystallisation and have been shown to increase the plastic deformation capability of the halide in the presence of polyethylene. Initial particle bonding of the halide was vastly increased such that a greater proportion of the applied energy was utilised at the initial stage rather than in the time-dependent hardening process. Scanning electron microscopy of the internal structure of compacts has emphasised how, with plastic deformation of alkali halides, slip planes are produced with compacts possessing well-defined internal symmetry. In the presence of polyethylene, the halide particles tended to retain their initial character.

As in the static system, lactose could tolerate similar quantities of polyethylene to those which destroy the internal structure of sodium chloride. Tensile strength remained unaffected and independent of particle size, lactose of mean size similar to that of sodium chloride (355-500 microns) fractured under the influence of applied pressure to give multiple bonding which counteracted elastic recovery by polyethylene.

Stress relaxation studies, determined under static conditions, have contributed significantly to defining the mechanisms by which plastic, brittle and elastic materials attain internal stability post compaction. By simultaneous measurement of stress relaxation pressure decay and axial displacement all three materials have been shown to undergo an immediate (5-10 seconds) pressure decay concomittant with a reduction in compact height, measured within the die. This has been assigned to sustained powder consolidation within the die immediately after the applied pressure had been maximised. i.e. the powders appeared to flow. Such an effect was very much more marked with sodium chloride than for the other two materials. Once this effect was satisfied, relationships between pressure decay and displacement satisfied the requirements of plastic deformation, brittle fracture and elastic recovery which characterise the three powders.

In the case of lactose, pressure decay and displacement effects were slight, equilibrium being achieved generally within 5 minutes of maximum pressure being applied. Elastic recovery of lactose was observed with the displacement being of opposite sign to that observed with sodium chloride. With respect to the latter, pressure decay and displacement continued for a considerable time post compaction. By expressing log percentage pressure decay as a function of time, then stress relaxation behaviour of sodium chloride could be defined in terms of two distinct phases. The first involved a significant pressure drop over the first 1-2 minutes, the second as an extended slow decay over the next 30 minutes. The addition of increasing quantities of polyethylene, up to and including a maximum of 10% w/w, coincided with comparative reductions in plastic flow. However, even at the highest concentration of polyethylene, post compaction stress relaxation measurements of pressure decay and displacement indicated that plastic flow was maintained, although compact strength was zero. Based on such findings, it was concluded that compact strength was controlled by the elastic recovery effects of polyethylene which produced, post compaction, areas of extreme structural weakness, such areas would negate those regions where plastic flow still operated.

On extrapolating the stress relaxation techniques to the study of microcrystalline cellulose, paracetamol and dicalcium phosphate dihydrate, further contributions to understanding the mechanisms by which each of the above undergoes compaction have been produced. Paracetamol has a relatively low pressure decay profile, consistent with a material possessing a significant elastic component. Dicalcium phosphate can be likened to a material compressing via brittle fracture while Avicel possessed both plastic and brittle properties.

By applying the above techniques to any pharmaceutical compound a measure of excipient/excipient and excipient/drug interaction, under conditions of static or dynamic compaction, can be attained and potential for successful tablet formulation can be derived. The techniques are precise and quantitative and should be introduced at an early stage in any formulation exercise.

RECOMMENDATIONS FOR FUTURE WORK

1. That the techniques outlined in this thesis be used to define the causation of capping with materials such as paracetamol, such studies being visualised as involving the dilution of an elastic component rather than the reverse.
2. That studies involving materials having similar compression characteristics be initiated, especially with regard to mixtures of elastic components. The objectives of such studies would centre around evaluating energy utilisation, between materials of similar character, to produce a stable compact.
3. That the compression characteristics of the materials investigated in the present study be further evaluated as a function of dwell times. Such times should lie between the limits imposed during static and dynamic compression and should include those operating during rotary compression.
4. That the work described in the present study be repeated on materials having less well-defined compression characteristics than those employed herein. The three materials employed in the stress relaxation studies discussed in Section 7 would be suitable choices.
5. That a similar study to that outlined in the present thesis be conducted but substituting polyethylene with a material having a high Modulus of Elasticity. Paracetamol would be an obvious choice.

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