# Reducing Temperature of Fused Deposition Modelling 3D Printing for Linalool Fast Dissolving Oral Films by Increasing Printer Nozzle Diameter

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## Abstract

Oral thrush and throat infections can occur in a wide range of patients. Treatments are available; however, resistance to drugs is a major problem for treating oral and throat infections. Three-dimensional printing (3DP) of fast dissolving oral films (FDFs) of linalool oil may provide an alternative solution. Linalool oil FDFs were printed by fused deposition modelling across 1-18% w/w linalool content range with nozzle diameters of 0.4 or 1 mm at the temperature range of 150°C-185°C. The FDFs were evaluated for physicochemical and mechanical properties. Increasing the printer nozzle diameter to 1 mm allowed reducing the printing temperature from 185°C to 150°C; consequently, more linalool was quantified in the films with improved content uniformity. The higher linalool content in the films increased the film disintegration time and mechanical strength. FDFs containing 10% w/w linalool showed clear antifungal activity against *Candida albicans*. Raman spectroscopy suggested linalool separation from excipients at higher temperature printing. Viscoelastic measurements indicated that to achieve printing; the elastic modulus of molten filament needed to be higher than the loss modulus at low angular frequencies. In conclusion, increasing the printing nozzle diameter may avoid loss of the active ingredient by reducing the temperature of the 3DP process.

Key Words: 3D printing; fast dissolving oral films; linalool, antifungal; Rheological Properties;

## 1. Introduction

*Candida albicans* is associated with candidiasis (known as oral thrush), which is a common fungal infection in the neck and throat region.[1] Oral candidiasis can be treated with drugs such as fluconazole[2] and itraconazole.[3] However, resistance to antifungal drugs is a major problem for treating candidiasis.[4] In addition, swallowing is painful in patients with oral candidiasis.[5] The microbial resistance may be tackled using essential oils. Several studies have demonstrated the antifungal activity of essential oils including thyme[6] and lavender oil.[7] Lavender oil oral capsules are available over-the-counter or as a food supplement. However, many patients including paediatrics and geriatrics cannot swallow large capsules. Therefore, there is a need for an oral formulation, which can be used safely by all patients to target the infected areas and prevent or treat oropharyngeal thrush. There are novel approaches compared to the routine treatment methods, such as oral films,[8-10] oral sprays,[11,12] and employing mucoadhesive particulate formulations e.g. liposomes[13] or nanoemulsions.[14] However, these have their own draw backs for formulation of essential oils such as stability of liposomal formulations.[15]

Fast dissolving oral films (FDFs) are useful for infants,[16] paediatrics, geriatrics, and those that they cannot swallow capsules or tablets easily. FDFs can be formulated by solvent casting method, hot melt extrusion, and 3D printing (3DP).[17] The use of 3DP for pharmaceutical dosage forms is developing rapidly.[18,19] There are several advantages of using 3DP for formulations of FDFs or oral films over solvent casting or hot melt extrusion, as follows. First, 3DP allows for producing multi-layered FDFs,[20] and achieving a desired dose with minimal drying time compared to the solvent casting method.[21] Second, 3DP allows for adjusting the disintegration time of FDFs by printing in mesh or plain-designs.[22] Third, 3DP has provided the opportunity to produce mucoadhesive oral films with unidirectional drug release.[23]

The formulations of linalool (the main ingredient of lavender oil) FDFs were previously reported using fused deposition modelling (FDM) 3DP. [24] In this work, printing of films was possible only at the printing nozzle temperature of 185°C. However, this high printing temperature led to the loss of about 50% linalool content in FDFs. These observations would have been expected due to the volatile nature of linalool. For the first time, this current study aimed to investigate the possibility of printing linalool FDFs by increasing the printer-head nozzle diameter (from 0.4 mm to 1 mm) in FDM 3DP, and if this condition would allow for reducing the printing temperature at the nozzle. The produced FDFs (at different temperatures) were evaluated for physicochemical, and mechanical properties. These included: weight uniformity, content uniformity, disintegration time and employing texture analyser to evaluate the mechanical strength of FDFs. We also investigated using Raman spectroscopy and FTIR to determine that the loss of linalool during printing was due to the evaporation of the active ingredient. Furthermore, we employed rheological measurements of molten linalool filaments to understand the correlation between the printing temperature and printer-head nozzle diameter.

## 2. Materials and Methods

### 2.1. Materials

Linalool, polyethylene oxide (PEO) 100K, and polyvinyl alcohol (PVA, Mw 89,000-98,000, 99% hydrolyzed) were purchased from Sigma-Aldrich (Dorset, UK). Croscarmellose sodium was acquired from Merck-chemicals (Darmstadt, Germany). Kollidon VA 64 and Kolliphor P188 were gifts from BASF (Darmstadt, Germany). Sodium starch glycolate (Explotab®) was kindly supplied by Rettenmaier UK Ltd (Reigate, Surrey). Listerine Breath Strips were obtained commercially. Both nutrient and Sabouraud dextrose agar (dehydrated) were purchased from Thermo Fisher Scientific (Waltham, MA USA).

## 2.2.Methods

### 2.2.1. Preparation of Powder Mixtures

The powder formulations are provided in Table 1. All percentages denote w/w in this paper. The rationale for changing the formulation components' qualities and quantities was to investigate the effects of linalool content on the physicochemical properties of FDFs, as well as reducing the disintegration time and achieving desired antifungal activities.

Since agglomerates formed when linalool was added as a bulk liquid to the powder mixture, different mixing methods were applied to ensure a uniform distribution of linalool in the powder mixture. For formulations F2-F4, the formulation powder was added into a 250 ml glass jar and mixed for 10 min at 42 rpm using a turbula mixer (Type 2B; WAB, Muttenz, Switzerland). As the linalool content was increased in formulations F5-F7, due to the viscose nature of the linalool, the powder formulations were split into 5 portions and each portion was mixed using the turbula mixer as described above. Then all portions were collected in a 1000 mL beaker and hand-mixed using spatula to ensure uniform distribution of linalool in the powder mixture. Only hand-mixing using spatula in 1000 mL beaker was used for formulations F8-F10, as tubular mixing appeared to be ineffective.

### 2.2.2. Filament Preparation

The linalool-loaded filaments were prepared using the holt melt extrusion technique, with the help of the single-screw hot melt extruder (Noztek pro®). The extruder was equipped with a counter-rotating screw with a screw speed of 30 rpm and a brass die containing 1.70 mm hole diameter at the centre to produce filaments. An object with the weight of 11 g was attached to the filament as soon as it formed to elongate the molten filament and produce filaments with

the diameter of 1.75 ± 0.05 mm. Filaments containing PVA were extruded at 180-190 °C, while formulations containing PEO100K were extruded at 80°C.

### 2.2.3. 3D Printing of Films

Square plain films were designed using the SolidWorks® 3DCAD software (Dassault Systèmes SolidWorks Corp., Waltham, MA) with dimensions of 20 mm in length and width, and 0.2 mm thickness, which were saved as stereolithographic format. The films (formulations F1-F7) were printed using the FDM Prusa® i3 MK3S 3D printer (Prague, Czech Republic) with 0.4 mm diameter extruder nozzle and the PrusaSlicer software (version 2.3.3; Prague, Czech Republic). In addition, the PrusaSlicer software was used to create a mesh film design with 50% triangle infill. The printing parameters were 100% infill for plain films and 50% triangles infill for mesh films, two shells, 0.10 mm layer height, and extruder temperature of 185°C. The non-extrusion travel move speed was 60 mm/s, with an infill travel speed of 30 mm/s and a printer bed temperature of 50 °C. Sticky masking blue tape (3M™) was used to help the adherence of printed films to the printer bed. Printing time was about 3 min for plain films, and 2 min for mesh films. Furthermore, plain films (formulations F8-F9) were printed using a RS 3D printer but with 1 mm nozzle diameter and at different printing temperatures: 185°C, 175°C, 165°C, 155°C, and 150°C. Formulation F10 was printed only at 150°C. Formulations F1-F7 were printed both as plain and mesh, and formulations F8-F10 were printed only as plain films.

### 2.2.4. Disintegration Test

The disintegration time of each 3DP film was measured in distilled water at 37 ± 0.5°C using a Copley Scientific disintegration tester DTG 1000 (Copley Scientific, Nottingham, UK). The time that took each film to disintegrate and pass through the wire mesh was recorded. Each experiment was performed in triplicate. The results are given as mean ± standard deviation (SD).

### 2.2.5. Differential Scanning Calorimetry

Differential Scanning Calorimetry (DSC) analysis (DSC 7; Perkin Elmer®, Waltham, MA, USA) was used to analyse the thermal characteristics of powder mixtures, filaments and FDFs. The process involved a nitrogen flow rate of 20 mL/min and a heating rate of $20^0$C/min. The samples were heated up to 220°C. An indium standard was used to calibrate the system. The minimum and maximum values of the endothermic and exothermic peaks, respectively, were used to determine the melting ($T_m$) point.

### 2.2.6. FTIR

FTIR spectra were obtained for powder mixtures, filaments, and films using a Spectrum 100 FTIR spectrometer (PerkinElmer®, USA). The samples were analysed in the 4000-650 $cm^{-1}$ range under ambient conditions. The Spectrum Express programme was used to analyse the spectra.

### 2.2.7. Content Uniformity

The amounts of linalool in each film were determined by applying a previously reported high performance chromatography (HPLC) method.[25] Briefly, an Agilent 1200 series HPLC (Stockport, Cheshire, UK) was used with an RP C-18 column (4.6 x 150mm, 5µm; Waters ®, USA) employing an acetonitrile and water (35/65 v/v) as the mobile phase with a flow rate of 1.0 mL/min. The column temperature was set to 25 °C and the detection spectrophotometer was set at 210 nm, with a sample injection volume of 5 µL. Solutions of linalool (97%) in methanol were used to prepare the calibration curve. Sample solutions were prepared by dissolving one film in deionised water. Each experiment was performed in triplicate. The results are given as mean ± standard deviation (SD).

### 2.2.8. Antifungal Activity

Agar diffusion method was employed to evaluate antifungal activities of linalool films and filaments. Briefly, Sabouraud dextrose plates (10 g dextrose, 2.5 g yeast, 28 g of agar powder per litre) were inoculated with a standardized inoculum of *Candida albicans* under aseptic conditions. Previous work has shown that the linalool antifungal minimum inhibitory concentration was in the range of 256 µg/mL to 512 µg/mL.[26] Then films/filaments comprising linalool each 300 mg were placed on the agar plates and inoculated with 0.2 mL of *Candida albicans*. The plates were incubated at 25°C for three days and examined. Negative control plates did not contain either films or filaments but did contain the microorganism. The experiments were repeated three times.

### 2.2.9. Raman Spectroscopy

An Agilent Resolve handheld Raman spectrometer, which had an 830 nm laser wavelength was used to conduct Raman spectroscopy. Sample holders were not used, to minimise potential interferences. Parameters considered for spectral quality included: the signal to noise ratio (S/N) ratio, spectral wavelength range, maximum peak position and the spectral range of the maximum peak position. Raman spectroscopy was conducted on 10% linalool FDFs printed at different temperatures. Three samples from each temperature set were used and two spectra were taken from each FDF, one from each side. A black plastic cover was placed above the laser to minimise any light interference.

### 2.2.10. Rheological Evaluations

The flow properties of filaments containing 10% linalool were measured using an HR 10 Waters Rheometer at temperatures in the range of 150°C-185°C at two different gaps, 0.4 mm and 1.0 mm, of the Peltier plate. The chosen gaps were based on the printing nozzle diameters. Storage (elastic) modulus, loss modulus, and complex viscosity were measured against angular velocity.

#### 2.2.11. Assessment of FDF Mechanical Properties (the Elongation Test)

The elongation to break mechanical test was performed using a TA-XT-Plus texture analyser (Stable Micro Systems, Godalming, UK) as reported previously.[27] Briefly, the sample film was clamped to a set of tensile grips (A/MTG mini tensile grips). The texture analyzer was adjusted to separate the grips upward at a velocity of 1.0 mm/s. Measurements were recorded when the grips started elongating the sample (triggering force) and stopped when the film ruptured. The applied force (g) was plotted versus the displacement (mm). Exponent software version 6.1.6.0 (Stable Micro Systems, Godalming, UK) was used for data collection and analysis. All experiments were performed in duplicate and at room temperature.

# 3. Results

## 3.1. Morphology of Printed films

Figures 1A and 1B present plain and mesh films, respectively, of 1% linalool (formulation F2) printed by the Prusa 3D printer at 185°C; and Figure 1C shows a plain film (only possible format) of 18% linalool (formulation F10) printed at 150°C by the RS Pro 3D printer with the 1 mm nozzle diameter. Comparing these images indicates that the 18% linalool film printed with the 1 mm nozzle had an acceptable appearance compared to the other films that were printed with the 0.4 mm nozzle diameter.

## 3.2. Disintegration Time of Linalool Films

Figure 2A demonstrates the disintegration time of linalool films for formulations F1 to F7. It is evident that mesh films disintegrated faster than plain films. Only the plain and mesh linalool films of formulation F7 achieved a disintegration time of less than 100 s (56 ± 16 s and 48 ± 4 s, respectively) with minimal differences between the mesh and plain films. Figure 2A also indicates that short disintegration times could not be achieved by PVA films, while changing the formulation excipients to Kollidon VA 64 and Kolliphor P188 significantly

reduced the disintegration time. As 1% linalool films did not present desired anti-fungal activity (see section 3.4), higher linalool content films were developed. Figure 2B compares the disintegration times of plain linalool films (formulations F8 and F9) printed at different temperatures with 1 mm nozzle diameter. This figure shows that by increasing printing temperature, the disintegration time was reduced from 113 ± 8 s at 150°C printing temperature to 64 ± 25 s at 185°C for formulations without disintegrant (F9). Surprisingly, adding the disintegrant (croscarmellose sodium) increased the disintegration time (formulation F8) compared to formulation F9. The disintegration time was 126 ± 11 s for the 18% linalool films (formulation F10) printed at 150°C.

### 3.3. Linalool Content and Weight Uniformity of the Films

Figure 2C illustrates the effects of printing temperature on the linalool content of the films (formulations F8 and F9). The linalool content increased from 4.9 ± 0.9% for printing at 185°C to 6.0 ± 0.2% for printing at 150°C for formulation F8, indicating less linalool loss at the lower printing temperature. A similar trend was observed for formulation F9 as well. This finding may explain the increased disintegration time with decreasing printing temperature (seen in Figure 2B), due to the increased linalool content and more hydrophobic nature of the films. The linalool content was 13.4 ± 0.9% for formulation F10 (initially 18% linalool) printed at 150°C. In this work, different mixing methods had to be employed, depending on the amounts of linalool in each formulation, to ensure uniform distribution of linalool within the powder mixtures. As a result, acceptable content uniformities (<10% deviation) were consistently obtained for the FDFs printed at 150°C (for both F8 and F9 formulation). Printed films showed less than 10% deviations for weight uniformity (Tables S1 and S2) with a trend of lighter FDFs by increasing printing temperatures (Table S2).

### 3.4. Antifungal Activity of Linalool Films

Due to the high disintegration time of formulation F10, only formulations F7-F9 were considered in the following sections. Figure 3 demonstrates the antifungal activities of 5% and 10% linalool films printed at 185°C. Evidently, the 5% linalool films did not show clear antifungal activity, while the 10% linalool films achieved clear inhibition zones. This observation may be speculated that the 5% linalool films did not contain sufficient linalool (due to evaporation/degradation of linalool during printing as indicated in section 3.3) to exhibit clear antifungal activity.

### 3.5. DSC Thermograms, FTIR and Raman Spectra

FTIR spectra (Figure S1) were comparable for the 5% linalool powder formulation (formulation F7), filament, and film (printed at 185°C), suggesting that loss of linalool during printing was mostly due to evaporation of the linalool from the formulation rather than decomposition of the linalool.

DSC thermograms (Figure S2A) presented only major melting points related to the polymers in the powder mixture, filament, and film (printed at 185°C) of formulation F9 (10% linalool). However, the DSC thermograms (Figure S2B) showed small endothermic peaks at temperatures above 130°C for films (formulations F8 and F9) printed at different temperatures (150, 155, and 165°C). These observations suggested the evaporation of linalool from the films, indicating that more linalool might be retained in films printed at lower temperatures compared to those printed at 185°C.

Raman spectra are compared in Figure 4 for 10% linalool (formulation F9) films printed at 185°C (Figure 4A) and 150°C (Figure 4B). Both spectra are similar apart from the Raman shift between 850 $cm^{-1}$ and 1150 $cm^{-1}$, suggesting separation of the linalool from the formulation excipients by increasing the printing temperature.

### 3.6. Mechanical Properties of Linalool Films

Figure 5 compares representative elongation properties of 10% linalool films printed at 185°C (Figure 5A), 150°C (Figure 5B), and for a Listerine Breath Strip (Figure 5C). The films were pulled apart in two different directions:1) parallel to the printing direction (resulting in higher breaking forces) and 2) perpendicular to the printing direction (resulting in lower breaking forces). The insert in Figure 5A shows the main printing direction. It can be seen from Figure 5B that the breaking force (applied parallel to the printing direction) was 8000 g for printing at 150°C, while this decreased to 6000 g for printing at 185°C (Figure 5A). Similarly, the breaking force was 4500 g (opposite to the printing direction) for the linalool film printed at 150°C (Figure 5B), however, this was reduced to 1500 g for the linalool film printed at 185°C (Figure 5A). These observations indicate that printing at a lower temperature led to stronger films, due to higher content of linalool. Figure 5C shows the elongation test of a Listerine Breath Strip, and it can be observed that the 3D printed linalool FDF at 150°C showed higher mechanical resistance compared to the Listerine Breath Strips (3000 g, and only one peak). Based on the above observations, it may be speculated that mesh films would require less breaking force compared to plain films.

### 3.7. Rheological (Viscoelastic) Properties of Linalool Filaments

Figure 6 demonstrates the plots of storage (elastic) and loss moduli against angular velocity for the formulation F8 (9% linalool) filament at 185°C (Figure 6A), 175°C (Figure 6B), and 150°C (Figure 6C) with 0.4 mm gap of the Peltier Plate. The complex viscosities are also shown for all temperatures. It can be seen from Figure 6 that the filaments presented viscoelastic rheological properties at all temperatures. Figure 6A shows that at low angular frequencies the elastic modulus was the dominant feature of the viscoelastic behaviour. However, there was a crossover between the elastic modulus and loss modulus at 1.39 rad/s. This was reduced to 1.07

rad/s at 175°C (Figure 6B). The crossover was not found at 150°C (crossover occurred at angular velocities greater than 100 rad/s) with loss modulus being the dominant viscoelastic behaviour. These observations suggest that at low printing temperatures, the filament had a dominant viscous behaviour. This could be interpreted to mean that the filament was too soft at the printer head and could not push the residue of molten filament in the nozzle chamber. While at higher temperatures such as 185°C, the filament presented an elastic behaviour, resulting in the filament being stiff enough to push parts of the filament in the printer nozzle and therefore enable the flow of the soften filament from the nozzle, allowing printing. These observations may be explained that at higher printing temperatures, linalool evaporated from the softened filaments and caused the molten filaments to present an elastic behaviour. While at low printing temperatures, the linalool content of the molten filament was high, which caused molten filament exhibiting viscous behaviour. In other words, increasing the printing temperature made the filament more suitable for printing by evaporating linalool from the filament.

With the wider Peltier Plate gap (1 mm), there were not significant changes in the viscoelastic behaviours of the molten filaments at the temperature range (Supplementary figures S3-S5), but the complex viscosity decreased from 10 Pa.s at 150°C for the 0.4 mm Peltier Plate gap to about 1 Pa.s for the 1 mm gap. In other words, considerable decrease in the viscosity of the molten filament allowed printing at lower temperatures with the wider nozzle diameter.

## 4. Discussion

This study found that increasing the printing nozzle diameter allowed for obtaining acceptable films (Figure 1). In this work, we had to employ Kollidon VA 64 and Kolliphor P188 to formulate FDFs with shorter disintegration times compared to using PVA (Figure 2A).

Previous studies demonstrated disintegration times in the range of 1-8 seconds for PVA orodispersible films containing aripiprazole, 45 seconds for PVA films prepared by solvent casting method, or FDM 3DP.[28] When linalool FDFs contained Kollidon VA 64 and Kolliphor P188 as excipients, the disintegration times were in the range of 50-140 s. The addition of croscarmellose (used as superdisintegrant) did not reduce the disintegration time. While a disintegration time of 17 s was reported for 3D printed FDFs that contained these excipients and olanzapine as the active ingredient.[29] The differences in disintegration times may be explained due to the coating of excipients by linalool, making them hydrophobic. While olanzapine particles would have been dispersed as distinct units and still allowing the contact of excipients with the aqueous media in the disintegration apparatus. As it has been shown that the surface wettability of films was essential to achieve desired disintegration times.[30] Therefore, further investigations are necessary to reduce the disintegration time of linalool films below 30 s. This may be achieved by the use of microcrystalline cellulose[31], addition of different polymers such as hydroxypropyl methylcellulose E5,[32] hydroxypropyl cellulose ELF,[32] chitosan micro-ribbons,[22] or printing films in other designs such as mesh, as indicated in Figure 2A that design of films affects the disintegration time.

Quantification analysis revealed that about 50% of linalool evaporated during printing at 185°C. In addition, this study found that increasing the printing nozzle diameter allowed for reducing printing temperature of linalool FDFs. As a result, less active ingredient evaporation occurred leading to higher contents of linalool in FDFs (Figure 2C). These observations could explain the increased disintegration time of linalool FDFs by decreasing printing temperature (Figure 2B). As more linalool would have been left in FDFs, which would make FDFs more hydrophobic and consequently prevent the penetration of the aqueous media into the film. We employed different mixing methods to achieve uniform distribution of linalool within the

powder mixture as shown in our previous work.[24] However, only films printed at 150°C showed less than 10% w/w deviation in the linalool content. Increasing printing temperature reduced the content uniformity of the printed films (Figure 2C), which may be explained by the non-uniform evaporation of linalool during printing.

We increased the linalool percentage in the formulations from 1% to 18% (w/w), firstly to achieve desired antifungal effects (Figure 3), and secondly to determine if FDF active ingredient content could be matched with previously published 3D printed FDFs (more than 20% w/w).[20,33] FDFs showed antifungal activities, however, this was evident when the initial linalool content was 10% (w/w) in the formulation (Figure 3). We could not increase the linalool percentage more than 18% (w/w) in the formulations, due to problems associated with mixing high amounts of linalool with other formulation excipients.

Application of Raman spectroscopy showed a minimal change in the spectra by increasing printing temperature (Figure 4), suggesting separation of linalool from formation excipients. A previous work showed formation of active ingredient crystals using selective laser sintering 3DP, which was detected through Raman spectroscopy.[34]

We were able to change the printing nozzle in the RS Pro-Printer, which printed the films in parallel rods (lines), as a result, the films presented two distinct different mechanical properties by applying the elongation test (Figure 5). As expected, the films were easily torn apart, if the shearing force direction was opposite the film's embedded rods. While higher forces were required to break the film, if the shearing force direction was parallel to the printing rods. Increasing the printing temperature reduced the breaking forces in both pulling directions (Figures 5A and 5B). This could be explained by the films printed at 185°C having less linalool content compared to films printed at lower temperatures, and higher contents of linalool functioned as a binder in the films, preventing the deformation of the films. A set of test

procedures was suggested to evaluate the mechanical properties of orodispersible films, including elongation to break.[27] Our mechanical property measurements were close to the previous measurements for the Listerine Breath strips (Figure 5C) in terms of short displacement for the strips before the breakage.[27] Films would have been stronger if printing layers were perpendicular for the 1 mm nozzle diameter, and this would be beneficial for mesh films.

Elbadawi *et. al.* 2020 considered only viscosity as the high throughput screening parameter for printability of pharmaceutical dosage forms.[35] While we observed that it was essential for the elastic modulus to be the dominant figure compared to the loss modulus at quite low angular velocities in order to achieve printing (Figure 6). However, complex viscosity did not change significantly when changing the printing temperature from 150°C to 185°C, but the printing was not possible at 150°C for 0.4 mm nozzle diameter. Furthermore, an elasticity dominant gel-like structure was required for 3D printing of food formulations,[36] thermosets[37], as well as tablets.[38]

This study comes with limitations. First, lower printing temperatures should have been investigated by increasing the printer nozzle diameter to determine the minimum possible printing temperature. Second, the printed films should be evaluated by human subjects to evaluate the acceptable taste and maximum amounts of linalool per film, as well as their antifungal efficacy in clinical applications.

## 5. Conclusion

This study found that increasing the nozzle diameter of printing head produced acceptable linalool films and this allowed to reduce the 3D printing temperature from 185°C to 150°C. The reduction of the printing temperature increased the linalool content of 3D printed FDFs, which also increased the disintegration times and the mechanical strengths of the films. At least

10% w/w linalool was required in the formulation, to observe clear antifungal activity from 3D printed FDFs. For future research directions, the printed films should be evaluated by human subjects for organoleptic properties and antifungal efficacy. Different formulations and film design avenues should be investigated to reduce the disintegration times, which should be evaluated by volunteers.

## 6. Acknowledgment

We are grateful for support of BASF (Darmstadt, Germany) for supplying Kollidon VA 64 and Kolliphor P188. Fazreelia Abu Mohamed was sponsored by British Council Women in STEM Scholarship, and Molly Thompson was supported by LJMU research bursary.

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**Figure 3** Antifungal activity of linalool films and filaments each 300 mg; A) 5% linalool filament, B) 5% linalool film, C) 10% linalool filament, D) 10% linalool film, E) control.

**Figure 4** Raman spectra of 10% linalool films printed A) at 185°C, and B) 150°C. Both spectra are similar apart from the Raman shift between 850 $Cm^{-1}$ and 1150 $Cm^{-1}$, suggesting separation of linalool from the formulation excipients by increasing printing temperature.

**Figure 5** Elongation test of A) a typical 10% linalool film printed at 185°C, B) a typical 10% linalool film printed at 150°C, C) a Listerine Breath Strip. The films broke at two different forces.

**Figure 6:** The viscoelastic behaviours of a typical linalool filament (Formulation F8 with 9% linalool) at 0.4 mm gap of the rheometer Peltier Plate (simulating 0.4 mm printer nozzle diameter), A) 185°C, B)175°C, C) 150°C.

**Table S1:** Weight uniformity of FDFs (formulations F1-F7)

**Table S2:** Weight uniformity of plain FDFs, formulations F8-F10, printed at different temperatures.

**Figure S1** FTIR Spectra for 5% linalool: A) film, B) Filament, C) powder formulation.

**Figure S2** DSC thermograms of 10% linalool: A) powder mixture, a typical filament, and film (printed at 185°C), B) films printed at different temperatures.

**Figure S3-S5**: The viscoelastic behaviours of linalool a typical filament (Formulation F8 with 9% linalool) at 1 mm gap of the rheometer Peltier Plate (simulating 1 mm printer nozzle diameter), S3) 185°C, S4)175°C, S5) 150°C.

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