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*Review*

# Microwave-Assisted Drying and Microwave-Assisted Extraction of *Cannabis sativa* L.: A Mini Review

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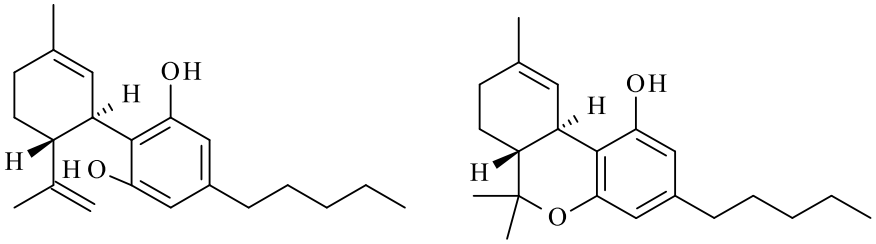
**Abstract:** Phytochemicals that bind to cannabinoid receptors are known as phytocannabinoids. They have pharmacological properties like the plant *Cannabis sativa* L. (Cannabaceae), which produces more than 100 structurally related phytocannabinoids with cannabidiol (**1**, CBD) and $\Delta^9$-tetrahydrocannabinol (**2**, $\Delta^9$-THC or THC) being the two major ones. As phytocannabinoids have remarkable therapeutic and cosmeceutical values, the correct choice of a drying method for harvested *C. sativa* plant materials and an extraction method for extracting phytocannabinoids and other bioactive compounds is essential to maintain the quality of cannabis products. While microwave-assisted drying (MAD) has been found effective for quick drying of *C. sativa* for safe storage and further studies, one of the green extraction methods for selective extraction of various secondary metabolites, including phytocannabinoids from *C. sativa*, is the microwave-assisted extraction (MAE) method, which applies microwaves for heating the solvents and plant tissues in the extraction process. This extraction method increases the kinetics of extraction and offers a shorter extraction time, less solvent, higher extraction rate, and lower cost over the traditional extraction methods of phytocannabinoid extraction. This review article critically appraises microwave-assisted drying techniques and MAE methods of *C. sativa* based on the information available in the published literature.

**Keywords:** microwave; *Cannabis sativa*; cannabis; phytocannabinoids; drying; Marijuana; hemp; processing; extraction

## 1. Introduction

Phytochemicals that bind to cannabinoid receptors are known as phytocannabinoids [1]. *Cannabis sativa* L. of the family Cannabaceae is the major source of well over 100 structurally related phytocannabinoids, but a few other plants from other families, e.g., *Acmella oleracea, Echinacea angustifolia, E. purpurea, Helichrysum umbraculigerum,* and *Radula marginata*, also produce different structural types of phytocannabinoids [1,2]. $\Delta^9$-Tetrahydrocannabinol (**2**, $\Delta^9$-THC or THC) and cannabidiol (**1**, CBD) (Figure 1) are two main phytocannabinoids; the former produces the psychoactive effect, while the latter counteracts this psychoactive property. Phytocannabinoids have therapeutic and cosmeceutical values; cannabis is often indicated for the treatment of pain, glaucoma, nausea, depression, and neuralgia and is used in various cosmeceutical products [1–7]. Cannabis infused food products and beverages have long been used in several cultures globally; for example, 'Bhang', a beverage made from *C. sativa* leaves and flowers, is used in India for religious festivals [8,9]. Because of the medicinal and cosmeceutical importance of *C. sativa* and its phytocannabinoids, as well as for their uses in food products and

beverages, numerous factors relevant to enhancing the efficiency of the cultivation and processing methods of this plant and the extraction of phytocannabinoids from *C. sativa* have been well-researched.




Cannabidiol (**1**)

$\Delta^9$-Tetrahydrocannabinol (**2**)

**Figure 1**. Structures of cannabidiol (**1**, CBD) and $\Delta^9$-tetrahydrocannabinol (**2**, $\Delta^9$-THC)

One of the key steps in processing plant materials, including *C. sativa*, is drying, which involves the removal of moisture to aid preservation and improve storage. While sun-drying and shed-drying in natural air flow are the two most common methods of drying harvested plant materials, other mechanical techniques like hot air flow, oven, and microwave-assisted drying can improve the efficiency of the drying process [10,11]. The extraction of phytochemicals from the dried and ground plant matrices is the next step in medicinal plant research if the aim is to extract various phytochemicals, mainly secondary metabolites, from the matrices [12]. For the extraction of phytocannabinoids [3], several methods, from traditional maceration to modern accelerated solvent extraction [12], are routinely used. However, the trend appears to be the use of environmentally friendly green extraction methods to enhance extraction efficiency and selectivity of phytochemicals, e.g., phytocannabinoids. Before selecting any extraction method for phytocannabinoids, the following points should be considered: the purpose of extraction, quantity of extraction, purification steps to be conducted, the purity level of phytocannabinoids, possible artifact formation, stability and physicochemical properties of target phytocannabinoids, and obviously, the cost and environmental impacts [3].

One of the environmentally friendly extraction methods for selective extraction of various secondary metabolites, including phytocannabinoids from *C. sativa*, is the microwave-assisted extraction (MAE) method, which applies microwaves for heating the solvents and plant tissues in the extraction process [12]. This method increases the extraction kinetics and offers shorter extraction time, less solvent, higher extraction rate, and lower cost than the traditional phytocannabinoid extraction method [3,12]. Although MAE was first introduced in natural products extraction in the early 80s, the use of MAE in phytocannabinoid extraction started not so long ago; through technological developments, it has now become one of the popular and cost-effective extraction methods. Nowadays, several advanced MAE instrumentations and methodologies have become available, e.g., pressurized microwave-assisted extraction (PMAE) and solvent-free microwave-assisted extraction (SFMAE), which not only can enhance extraction efficiency but also improve the quality of the extract. While MAE techniques and instrumentation have been well articulated in several publications [12–14], a schematic representation of a typical microwave extraction unit is presented in Figure 2 for a better understanding of the subsequent sections in this review. This article critically appraises the published literature on the microwave-assisted drying of *C. sativa* and the microwave-assisted extraction of phytocannabinoids from *C. sativa*.

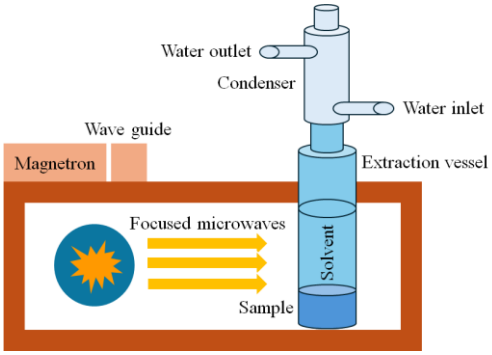



**Figure 2**. A typical microwave extraction unit

## 2. Microwave-Assisted Drying

Drying is an important postharvest step preceding long-term storage of plant materials, and optimized drying conditions are fundamental to secondary metabolite preservation. A quick and dependable drying of plant materials, including cannabis, is essential to ensure high-quality products to meet increasing demands. Microwaves can be used to assist drying plant materials. The use of microwave-assisted drying (MAD) has become popular in recent years, as this technique offers a rapid and efficient method of removing moisture from plant materials [10,11]. This technique leverages the interaction between water molecules and microwaves, resulting in faster drying time, energy efficiency, and better preservation of quality attributes than conventional drying methods. Simply, microwaves penetrate plant materials and cause water molecules to vibrate and generate heat that helps evaporation and moisture removal. However, it should be noted that MAD sometimes may cause uneven heating and destroy or degrade heat-sensitive phytochemicals, and an optimization of microwave parameters is required to obtain the best outcome [15]. Often, 240, 360, 480, and 600 W microwave powers are used in drying plant materials, but higher powers can also be used for thermostable phytochemicals [15,16]. The use of MAD in the processing of *C. sativa* has begun to appear in the literature [17–24]. A summary of available information on MAD of *C. sativa* is presented in Table 1. One of the first reported applications of MAD in *C. sativa* processing was for producing a high concentration of CBD (**1**) from *C. sativa* byproducts, including inflorescences [18]. In that study, as a pretreatment method before hydrodistillation, the plant materials were reduced into small pieces and irradiated with microwaves at 900 and 450 W for 1 and 3 min, respectively, using an internal plate of 32 × 32 cm. The extraction yield for CBD-enriched essential oil ranged from 0.04 to 0.12%, with prolonged microwave heating (3 min) at 450 and 900 W. The highest levels were obtained when the inflorescences were heated with microwaves at 900 W for 1 min and 450 W for 3 min, obtaining 9.0 and 8.9% of CBD (**1**), respectively, corresponding to almost a twofold increase compared to the control. This study demonstrated that MAD could significantly increase the amount of CBD (**1**) in the essential oil extracted from the inflorescences of *C. sativa* by hydrodistillation.

Most of the studies involving MAD were with the inflorescences of *C. sativa* [18–23] (Table 1). The solid-state microwave technique was found to provide faster and uniform drying and higher efficiency for drying cannabis inflorescences than the traditional drying method [19]. It was concluded that this drying method could be used as an effective postharvest step to quickly dry the plant material for improved downstream processing with a minimal negative impact on product quality. In that work, the oven had a specialized closed-loop system with multiple transmitters and receiver antennas to deliver drying energy to the sample load and collect reflections from it. This method used a frequency sweep for the microwave, which was set to a range from 2400 to 2500 MHz, which was generated and amplified by solid-state sources and amplifiers. The technique allowed changes in ion migration and dipole rotation but no changes in molecular structure. The power transmission of each frequency was individually measured and controlled. This drying method also significantly reduced the microbiological load in the inflorescence samples and thus could prevent microbial proliferation and spoilage in the samples. It can be noted that solid-state microwave technology utilizes shifted microwave frequencies, where the hot and cold spot locations change with frequencies [25]. This frequency shifting in solid-state microwave method is different from the frequency variation in magnetron-based ovens, where the dominant frequency is 2.45 GHz but varies randomly within ±50 MHz due to the instability of magnetrons. On the other hand, in solid-state microwave systems, the frequency can be controlled precisely (i.e., between 2.40 and 2.50 GHz with a step of 1 MHz), which helps generate various heating patterns complementing each other to improve heat uniformity.

Addo et al. [20,21] reported the microwave-assisted hot air drying (MAHAD) of *C. sativa* inflorescences and demonstrated that this method could yield a higher phytocannabinoid content than could be achieved by other drying methods. Furthermore, it was observed that the moisture diffusion was significantly affected by the temperature, vacuum, and microwave power and reduced exponentially with time [21]. Greater $\Delta^9$-THC (**2**) content was observed in MAHAD samples than in the fresh, undried, and pre-frozen, undried samples [20]. The MAHAD system used in this study comprised a 2450 MHz microwave generator with adjustable power (0 to 750 W), waveguides, a three-port circulator, a manual three-stub tuner to match the load impedance, microwave couplers to measure forward and reflected power, a carbon load to absorb reflected power, and a microwave cavity made of brass (0.47 × 0.47 × 0.27 m) in which the samples were processed. Approximately 100 g of pre-frozen *C. sativa* inflorescences were dried until the sample reached a dry basis moisture content of 12%. The study aiming at determining the effect of pre-freezing, vacuum, drying temperature, and microwave power on *C. sativa* inflorescences, including drying kinetics, color retention, and moisture diffusivity, and cannabinoid and terpene concentrations, revealed that a microwave power of 2 W/g required only 61 min (with no vacuum) and 57.3 min (under vacuum) at 65 °C to reach the desired final moisture content of 11% dry basis [21]. It was noted that an increase in drying temperature from 35 °C to 50 °C at 1 W/g under vacuum could reduce the drying time by 60.1%

and 68% for pre-frozen and untreated samples, respectively, and reduce by 68% and 65.5% for pre-frozen and untreated cannabis samples, respectively, for samples dried without vacuum.

A coupling between microwave and infrared techniques (MI) was adopted for drying *C. sativa* inflorescences, and the effect on drying characteristics, energy consumption, and quality parameters was assessed [22]. This combined MI technique was efficient and offered a short drying time (16–200 min), high moisture diffusivity of $7.95 \times 10^{-9}$–$8.70 \times 10^{-8}$ $m^2/s$, and low energy consumption of 390.49–1611.42 kJ. This method facilitated the conversion of acidic phytocannabinoids to their neutral forms by decreasing tetrahydrocannabinolic acid ($\Delta^9$-THCA, **4**) from 20.2% to 7.6% and increasing $\Delta^9$-THC (**2**) from 6.3% to 16.7%. This study demonstrated that MI is a rapid and energy-efficient drying method for obtaining high-quality medicinal cannabis. In this study, a lab-scale MI oven dryer (the highest MW power of 700 W, frequency of 2450 MHz, and the highest IR power of 750 W) was used for drying cannabis inflorescence samples (10 g). The equipment was equipped with an automatic intermittent controller to modulate the necessary power for microwave and infrared by cycling the magnetron and halogen lamps on and off, respectively. The halogen lamp helped mitigate uneven heating inside the chamber. The MI power levels were selected based on preliminary trials. The moisture loss due to drying was measured every 2 min interval up to 1 h and 5 min interval for the rest of the time. The average time for taking the sample out of the dryer for weighing and putting it back into the dryer was around 15 s. The drying was continued until it reached a moisture content of around 8–10%.

Continuous microwave (CM) processing, which is an emerging technology because of its short residence time and relatively low environmental footprint [26], has been used for the drying of *C. sativa* inflorescences for CBD (**1**) production [23]. CM processing could achieve a higher yield (92.8%) under milder conditions (90 °C for 30 min) than the batch process (90.3% at 120 °C for 30 min), and for $\Delta^9$-THC (**2**), the continuous process yielded 70.5% under shorter reaction times. Continuous microwave (CM) processing could be an efficient and scalable technology for phytocannabinoid production, addressing the growing global demand for quality industrial hemp products.

Not only the inflorescences of *C. sativa* that were subjected to microwave-assisted drying (MAD), but also the aerial parts [17] and leaves [24] could be processed by MAD. A study evaluating the impact of hot air, 915 MHz microwave and infrared (IR) drying techniques on the color, cannabinoid content and volatile components in hemp aerial parts including inflorescences, revealed a high total color difference between hemp dried with hot air (HA) and IR heat, and hemp dried with HA and IR possessed higher level of CBD (**1**), caryophyllene, and humulene than fresh hemp [17]. However, it was noticed that the total phytocannabinoids and volatiles of hemp dried with IR, MW 2 kW, and MW 3 kW were lower than those of the fresh hemp. An industrial 915 MHz microwave heating system, comprising a microwave generator, control panel, waveguide, and heating zone, was used in this study. Based on the findings, it was suggested that the IR and 915 MHz MW could be employed as effective drying alternatives to dry hemp for specific end-use applications. A vacuum microwave drying method was also applied for drying the leaves of *C. sativa* [24]. This study evaluated the efficiency of the drying methods, convective, vacuum microwave, and combined convective pre-drying and vacuum–microwave finishing drying of hemp leaves on the qualitative and quantitative changes in secondary metabolites, including essential oils, phytocannabinoids, and sterols. The predominant cannabinoids in fresh hemp leaves were CBDA (**3**) 6.05 and CBD (**1**) 2.19 mg/g, and the drying did not cause any change in the cannabinoid profile of the plant material. It can be noted that a vacuum microwave system combines microwave energy with a vacuum environment to dehydrate thermolabile materials rapidly and efficiently.

**Table 1**. Microwave-assisted drying (MAD) of *Cannabis sativa* L.

| Plant Parts | Description of Microwave-Assisted Drying | Outcome | References |
|---|---|---|---|
| Aerial parts and inflorescences | Microwave-infrared drying | The total cannabinoids and volatiles of hemp dried with infrared microwave (2 kW and 3 kW) were lower than those of fresh hemp. | [17] |
| Byproducts and inflorescences | Microwave heat (900 W for 1 min) pre-treatment | Production of high concentration of CBD (**1**) | [18] |
| Inflorescences | Solid-state microwave drying | The solid-state microwave technique was found to provide fast and uniform drying and higher efficiency for drying cannabis inflorescences than the traditional drying method. It was concluded that this drying method could be used as an effective postharvest step to quickly dry the plant material for improved downstream processing with a minimal negative impact on product quality. | [19] |
| | Microwave-assisted hot air drying | A higher phytocannabinoid content than in the other drying methods was observed. | [20] |
| | Microwave-assisted hot air drying | Moisture diffusion was significantly affected by the temperature, vacuum, and microwave power and reduced exponentially with time. | [21] |
| | Microwave-infrared drying | The method was highly efficient, with a short drying time of 16–200 min, high moisture diffusivity, and low energy consumption. | [22] |
| | Continuous microwave processing | For CBD (**1**) production in hemp extracts, the continuous microwave processing could achieve a higher yield (92.8%) under milder conditions (90 °C for 30 min) than the batch process (90.3% at 120 °C for 30 min), and for $\Delta^9$-THC (**2**), the continuous process yielded 70.5% under shorter reaction times. Continuous microwave processing is an efficient and scalable technology for cannabinoid production, supporting the growth of the global industrial hemp market. | [23] |
| Leaves | Vacuum microwave drying | The predominant cannabinoids in fresh hemp leaves were CBDA (**3**) 6.05 and CBD (**1**) 2.19 mg/g, and the drying did not cause any change in the cannabinoid profile of the plant material. | [24] |

### 3. Microwave-Assisted Extraction

Microwave-assisted extraction (MAE) applies microwave energy that rapidly heats solvents in contact with a sample. MAE facilitates the extraction of compounds of interest from the sample matrix into the solvent in a shorter time and with less solvent than conventional methods [12]. This technique typically uses closed vessels, allowing the extraction to take place at an elevated temperature and pressure, which increases the solubility of the target components in the solvent and thus enhances extraction efficiency. The key advantages of MAE include reduced solvent consumption, enhanced extraction rate, rapid extraction, simultaneous and selective extraction, and versatility. MAE has long been used in extracting phytocannabinoids from *C. sativa* [27–44]. Related information on the MAE of *C. sativa* available in the literature is presented in Table 2.

Cannabidiolic acid (CBDA, **3**) and $\Delta^9$-tetrahydrocannabinolic acid ($\Delta^9$-THCA, **4**), which are the carboxylated forms of CBD (**1**) and $\Delta^9$-THC (**2**), respectively, do not bind to the cannabinoid receptors and, therefore, are inactive. Thus, to ensure a high yield of extraction of pharmacologically active CBD (**1**) and $\Delta^9$-THC (**2**), the correct choice of an extraction and processing method of the *C. sativa* plant is important. MAE (2.45 MHz, 400 W) was found to extract CBD (**1**) and $\Delta^9$-THC (**2**) consistently and exclusively, but almost no carboxylated forms, from the flowers of the medicinal cannabis cultivars of *C. sativa* [27]. Temperature and exposure time in the MAE extraction of *C. sativa* could usually convert all acidic phytocannabinoids to their medicinally active decarboxylated forms (Figure 3).

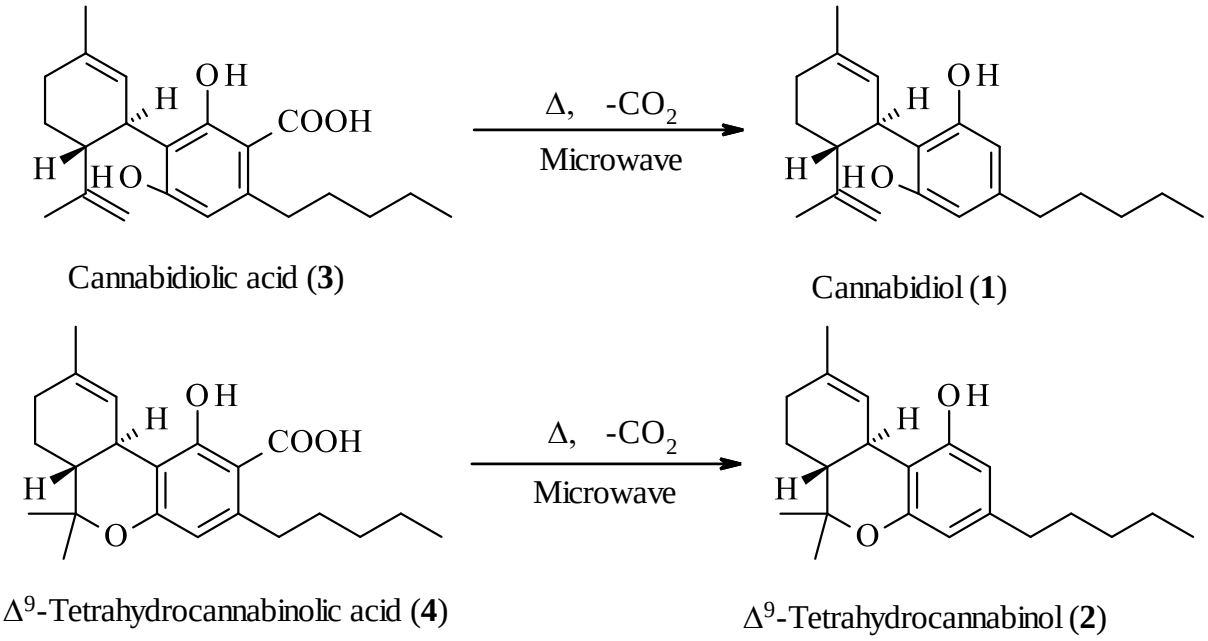



**Figure 3**. Decarboxylation of cannabidiolic acid (**3**) and $\Delta^9$-tetrahydrocannabinolic acid (**4**).

A combination of microwave-assisted hydrodistillation (MAHD), supercritical fluid extraction (SFE), and MAE was used to sequentially extract essential oil, lipids, phenolics, and major phytocannabinoids from the flowers of three varieties of hemp (*C. sativa*) [28]. However, in this combination approach, phytocannabinoids, e.g., CBD (**1**) and $\Delta^9$-THC (**2**), were predominantly obtained by SFE (400 bar, 65 °C and 0.3 kg $CO_2$/h), while MAHD (600 W) extracted volatile compounds and MAE (600 W) extracted bioactive polyphenolics. It can be noted that phytocannabinoids, in small amounts, were present in hydrodistillates and microwave hydrodistillates. CBD (**1**), $\Delta^8$-THC, and $\Delta^9$-THC (**2**) were successfully extracted from the flowers and stems of *C. sativa* by the MAE method employing ethanol (EtOH) as a primary solvent [29]. This study optimized extraction conditions, including solvent choices, and EtOH was the best solvent for extracting phytocannabinoids using MAE.

**Table 2**. Microwave-assisted extraction (MAE) of phytocannabinoids from *Cannabis sativa* L.

| Plant parts | Description | Extracted Phytocannabinoids | References |
|---|---|---|---|
| Flowers | Microwave-assisted extraction (MAE) to consistently produce completely decarboxylated phytocannabinoid extracts. | CBD (**1**) and $\Delta^9$-THC (**2**) | [27] |
| | A combination of microwave-assisted hydrodistillation (MAHD), supercritical fluid extraction (SFE), and MAE were used to sequentially extract essential oil, lipids, phenolics, and major phytocannabinoids from the flowers of three varieties of hemp (*C. sativa*). | CBD (**1**) and $\Delta^9$-THC (**2**) | [28] |
| Flowers and stem | MAE using ethanol as a primary solvent. | CBD (**1**), $\Delta^8$-THC, and $\Delta^9$-THC (**2**) | [29] |
| Biomass | Microwave-assisted sequential extraction of phytocannabinoids aided by a composite design optimization method | CBD (**1**) | [30] |
| Hemp tea | The effect of temperature, irradiation time, and solvent-to-solid ratio on phytocannabinoid extractability of the MAE method was investigated. | Cannabichromene (CBN), CBD (**1**), cannabigerol (CBG), cannabinol (CBN) and $\Delta^9$-THC (**2**) | [31] |
| Inflorescences | MAE and comparison with other extraction methods. | CBD (**1**), CBDA (**3**) and cannabigerol (CBG), | [32] |
| | MAE and comparison with ultrasound-assisted extraction. | CBD (**1**), CBDA (**3**), $\Delta^9$-THC (**2**), $\Delta^9$-THCA (**4**), and cannabinol (CBN) | [33] |
| | An optimized MAE using a central composite design. | CBD (**1**) rich hemp essential oil | [34] |
| | Industrial-scale microwave-assisted highly efficient extraction using 915 MHz microwave. | CBD (**1**) and $\Delta^9$-THC (**2**) | [35] |
| | Microwave-assisted distillation for sequential extraction of essential oil and phytocannabinoids. | CBD (**1**) and $\Delta^9$-THC (**2**) | [36] |
| | Microwave-assisted selective recovery of terpenes, polyphenols, and phytocannabinoids. | CBD (**1**) and $\Delta^9$-THC (**2**) | [37] |
| | MAE and comparison with ultrasound-assisted extraction and dynamic maceration. | CBD (**1**) and CBDA (**3**) | [38] |
| | MAE using response surface methodology. A central composite rotatable design optimized independent factors (sample-to-solvent ratio, extraction time, extraction temperature, and duty cycle). | $\Delta^9$-THC (**2**), $\Delta^9$-THCA (**4**), cannabigerol (CBG), cannabigerolic acid (CBGA), and other phytocannabinoids | [39] |
| | A new prototype microwave reactor (Ethos Lean) was specifically designed for the decarboxylation of the acidic cannabinoids in cannabis inflorescences and subsequent extraction in olive oil. | CBD (**1**) and $\Delta^9$-THC (**2**) | [40] |
| | The study investigates the entrapment of cannabis terpenes in olive oil from inflorescences via stripping under mild vacuum during the rapid microwave-assisted decarboxylation of phytocannabinoids (MW, 120 °C, 30 min) and after subsequent extraction of phytocannabinoids (60 and 100 °C) | Selective extraction of volatile components and phytocannabinoids | [41] |
| | Microwave-assisted hydrodistillation (MAHD) extraction for phytocannabinoids profiling. | CBD (**1**) and $\Delta^9$-THC (**2**) | [42] |
| Nut | MAE using response surface methodology and comparison with other extraction methods. | CBD (**1**), cannabinol (CBN), and $\Delta^9$-THC (**2**) | [43] |
| Total plant (leaves, blossoms, small structural parts of the inflorescence, and bracts) | MAE using various extraction parameters, including ethanol concentration (30, 50, and 70%), extraction time (10, 20, and 30 min), and solid/liquid ratio (5, 10, and 15 g/mL). | CBD (**1**) and $\Delta^9$-THC (**2**) | [44] |

Solvent-free MAE is considered a green extraction method and has become a method of choice for phytochemical extraction, as this method boosts the yield and quality of the extract. A response surface methodology (RSM) [45,46], central composite design-aided optimization of MAE, was applied for recovering essential oil and phenolic compounds from hemp (*C. sativa*) and phytocannabinoids from its terpene-free residual biomass [30]. The residual biomass was the remaining material after the MAE extraction of the essential oil and the removal of the hydrophilic aqueous residue and was found to be an excellent source of phytocannabinoids, e.g., CBD (**1**). After the 18th extraction run, the average amount of CBD (**1**) still present in the residual biomass was equal to 2.35 ± 0.47 g/100 g dry biomass, whereas this amount was 3.10 ± 0.25 g/100 g dry biomass in no MAE-treated samples. However, there was no relationship between the CBD (**1**) in the residual biomass and the MAE experimental parameters. Christodoulou et al. [31] investigated the effect of temperature (50, 65 and 80 °C), irradiation time (4, 7 and 10 min) and solvent-to-solid ratio (20, 30, and 40 mL of methanol/g of hemp tea) on phytocannabinoid (from hemp tea) extractability of an MAE method incorporating a response surface methodology (RSM), e.g., the Box-Behnken Design (BBD) [45,46]. MAE was proven to be a superior technique to other conventional methods for the extraction of CBD (**1**) and cannabinol (CBN).

The MAE extraction of phytocannabinoids from the inflorescences of *C. sativa* and comparison with other available extraction methods have been documented in published papers [32–42] (Table 2). Different extraction methods, dynamic maceration (DM), ultrasound-assisted extraction (UAE), MAE, and SFE, were applied and compared to obtain a high yield of the target analytes from the inflorescences of hemp, also known as the fiber-type *C. sativa* [32]. This study is one of the first few studies conducted with MAE for extracting phytocannabinoids from *C. sativa*, and it used a monomode focused microwave apparatus with a closed-vessel system. A weighed hemp sample (0.25 g) was extracted with EtOH (10 mL) at 60°C for 5 min under stirring. The residue of the first extraction was extracted two more times. The highest content of CBD (**1**) in the extract was found with MAE, which required a short extraction time. This MAE method, which used a high extraction temperature, increased the extraction yield of CBD (**1**), decreased the amount of CBDA (**3**) in the extract, suggesting a partial decarboxylation of this acidic phytocannabinoid **3**. De Vita et al. [33] compared the extraction efficiency of ultrasound-assisted extraction (UAE), MAE, and extraction with Tween 20, a known surfactant, for the extraction of phytocannabinoids from the inflorescences of the commercially available Italian hemp (*C. sativa*). The MAE yield of the Italian variety 'Eletta Campana' was evaluated by analyzing four different parameters: time, temperature, ramping time, and solvent. It was observed that the amount of CBD (**1**) could be increased by increasing both time and temperature at least 4 times more under microwave conditions than the reference extraction. The extraction solvent was also found to influence the MAE efficiency for CBD (**1**) extraction; a better result was observed with olive oil instead of ethanol as an extraction solvent with a shorter ramping time. On the other hand, the trend was just the opposite for the extraction of CBDA (**3**); extraction efficiency decreased with the increase in time and temperature of extraction. As mentioned before, this trend reiterated that MAE accelerates the conversion of CBDA (**3**) to CBD (**1**) through decarboxylation.

To produce CBD (**1**)-rich hemp essential oil, MAE was used in association with a central composite design (CCD) for optimization of extraction conditions, e.g., microwave irradiation power, extraction time, and water added to the plant matrix after moistening [34]. It is noteworthy that hemp essential oil is a popular product with potential applications in pharmaceutical, nutraceutical, cosmeceutical, and agrochemical products. In this study, dry inflorescences of the Italian variety of hemp, Carmagnola Selezionata, were used. A multimode microwave reactor of 2.45 GHz, equipped with two magnetrons with a maximum delivered power of 1800 W (2 × 950 W) and an infrared sensor monitoring the temperature, was employed. The experiments were conducted at atmospheric pressure using a glass reactor closed with a glass cover. It was demonstrated that MAE treatment with high irradiation power and long extraction time considerably increased the CBD (**1**) content in the essential oil while maintaining high oil yield values, and the yield was higher than that of conventional hydrodistillation. An industrial-scale MAE operating with 915 MHz microwaves in continuous flow at atmospheric pressure was used for efficient extraction of CBD (**1**) and $\Delta^9$-THC (**2**) from the inflorescences of *C. sativa* in industrial scale [35]. It was demonstrated that MAE could eliminate additional steps associated with other extraction methods, such as biomass decarboxylation or winterization, and thus, make MAE more time-efficient than other methods. MAE could also achieve high extraction efficiency, up to 95% of phytocannabinoids at an industrial scale.

The use of MAE for the sequential extraction of terpene-rich cannabis oil, phenolic compounds, and phytocannabinoids from the inflorescences of *C. sativa* has become popular in recent years [36,37]. MAE was shown to be particularly useful for the preparation of medical cannabis oil with a high phytocannabinoid and terpene content [36]. It was shown that linking MAE technology to the conventional hydrodistillation process for the inflorescences of *C. sativa* could enhance the extraction efficiency and specificity. Later, Gunjevic et al. [37] designed a fast and cost-efficient microwave-assisted cascade protocol for recovering bioactive compounds,

including phytocannabinoids, from *C. sativa* in a pilot-scale reactor. It was demonstrated that microwave-assisted hydrodistillation (MAHD) could obtain terpene-rich volatile hydrodistillates with a small amount of phytocannabinoids; during this process, phytocannabinoid decarboxylation inside the residual matrix was around 70%, i.e., 69% and 74% for $\Delta^9$-THC (**2**) and CBD (**1**), respectively. MAHD was conducted in an ETHOS X multimode microwave reactor at a maximum delivered power of 1800 W. All extractions were performed in a 12 L vessel, and the temperature was monitored with an infrared sensor. The microwave power for the extractions was set as 500 W for 3 min, 1100 W for 3 min, 1600 W for 14 min, and finally, 1500 W for 90 min. A similar MAHD method has recently been used to extract *C. sativa* inflorescences for phytocannabinoid profiling [42]. Briefly, dried inflorescences were rehydrated with ultrapure water with a 1:3 solid to solvent ratio. After mixing and soaking, the mass was transferred to a 2 L DRY-DIST glass reactor, and each sample was distilled at 620 W for 30 min. A Clevenger-type apparatus was installed outside the microwave system. This study showed the application of a multi-technique approach to tracing the origin of seized cannabis samples. The qualitative and quantitative (volatile fraction and THC/CBD contents), chiral, and isotopic data demonstrated a close correlation between specific samples and helped tentatively group the cannabis samples with common experimental results, suggesting a common origin.

The comparison of an RSM-optimized MAE protocol over UAE and dynamic maceration for the extraction of phytocannabinoids, particularly the nonpsychoactive CBD (**1**) and CBDA (**3**) from the inflorescences of *C. sativa* were reported by Tzimas et al. [38]; the conditions maximizing CBD (**1**), CBDA (**3**), and total CBD (**1**) content and the extraction yield were determined with high desirability (0.97) and were experimentally confirmed. In this MAE method, an accurately weighed amount of inflorescences (400 mg) was transferred to extraction vessels, and 20 mL of EtOH was added. A closed-vessel START E microwave extraction system equipped with a multivessel rotor was used. MAE was performed for 30 min under 80 W irradiation power, and the temperature was set at 40 °C. However, the extraction efficiency of MAE in this study was less than the other two techniques. The relatively poor performance of MAE could be attributed to low microwave power (80 W) during extraction. It was suggested that more microwave power might be needed to adequately use MAE's capability of extraction intensification.

Other recent studies have applied an RSM-optimized MAE extraction of phytocannabinoids from the inflorescences of *C. sativa* [39]. The use of a central composite rotatable design to optimize independent factors like sample-to-solvent ratio, extraction time, extraction temperature, and duty cycle in MAE has become common over the last few years. Optimization of MAE is crucial for enhancing extraction yield and efficiency and, thus, reducing the production cost of phytocannabinoids or phytocannabinoid-rich cannabis oil. RSM-optimized MAE of phytocannabinoids has been shown to have scale-up potential for industrial use [39]. The sample-to-solvent ratio in MAE plays a pivotal role in determining the phytocannabinoid profile of cannabis extract or cannabis oil. In a recent study [39], a positive coefficient value for the sample-to-solvent w/w ratio indicated that increasing the sample-to-solvent ratio from 1:5 to 1:15 could significantly increase phytocannabinoid concentration in extracts by 19.3% (extraction time 10 min at 40 °C). The $\Delta^9$-THC (**2**) content in MAE extracts can be influenced by extraction temperature.

A new prototype microwave reactor (Ethos Leans), equipped with a 1 kW magnetron and an IR pyrometer for temperature measurement, has been specifically designed for the decarboxylation of the acidic cannabinoids in cannabis inflorescences and subsequent extraction in olive oil, where the extraction was conducted in the Ethos Lean's cavity with special accessories such as a rotating drum for the decarboxylation process and a glass reactor with a stirrer for the extraction step [40]. The rotating drum was made of a material that was sensitive to dielectric heating and could operate up to 120 °C. Like any other optimized MAE, the extraction time and temperature were optimized, and the instrument automatically calibrated the power output. The rotating drum assisted the complete, rapid, and homogeneous decarboxylation of phytocannabinoids, e.g., CBDA (**3**) and $\Delta^9$-THCA (**4**) (30 min, 120 °C). It was demonstrated that an exhaustive extraction resulting in 100% yields of both CBD (**1**) and $\Delta^9$-THC (**2**) was possible with MAE with 30 min irradiation at 90 °C. This prototype had distinct advantages, as outlined below. The inflorescences of *C. sativa* come into contact with the internal stainless steel cylinder, which is easy to clean at the end of the decarboxylation process. A pump could provide a continuous flow of air inside the drum to transport the volatile molecules to an aspiration system, such as a fume-extraction unit (used in this study) or an external trap system (not evaluated in this study), and in this way, any unpleasant odor could be avoided. The drum could process a maximum of 150 g of dry matrix per batch, and rotation around its axis ensured continuous mixing to maintain homogeneous conditions throughout the reactor. After the decarboxylation step, the plant matrix and the required volume of solvent could easily be transferred to the glass reactor. Ethos Lean was equipped with two types of glass reactors that could be calibrated to work with different amounts of solvent: a larger one for 25 mL to 1.5 L of solvent and a smaller one for 50–250 mL of solvent. The reactor also included a magnetic stirrer to ensure good mixing of the inflorescence suspension in oil. This MAE setup was easy to use, rapid, and the

extraction yield was slightly higher than under conventional conditions. This specifically designed prototype microwave reactor was shown to intensify the extraction process and save energy to enable environmentally sound processes for phytocannabinoid extraction.

The therapeutic efficacy of *C. sativa* extracts or oils depends on their phytocannabinoid content and profile, especially the amount of acidic phytocannabinoids CBDA (**3**) and $\Delta^9$-THCA (**4**). To obtain their neutral homologues CBD (**1**) and $\Delta^9$-THC (**2**), which have high affinities for the cannabimimetic activity receptor, they are usually decarboxylated via heating during consumption or extraction processes. The decarboxylation step consists of a heating treatment conducted at a temperature above 100 °C, but below 230 °C, to avoid the formation of smoke toxins. A study conducted by Boffa et al. [41] evaluated the entrapment of cannabis terpenes in olive oil from inflorescences via stripping under mild vacuum during the rapid microwave-assisted decarboxylation of phytocannabinoids (MAE extraction time 30 min at 120 °C) and subsequent extraction of phytocannabinoids (60 and 100 °C). This study also used an accurately configured prototype microwave reactor (Ethos Lean), equipped with a 900 W magnetron and IR pyrometer, as discussed earlier.

Although inflorescences of *C. sativa* are the most studied parts for MAE of phytocannabinoids, there are also a couple of reports published in the literature describing the MAE of phytocannabinoids form other plant parts, e.g., hemp nutt and the total plant including leaves, blossoms, small structural parts of inflorescences and bracts [43,44]. An efficient MAE method, optimized by RSM [45,46], for phytocannabinoids CBD (**1**), cannabinol (CBN), and $\Delta^9$-THC (**2**) in hemp nut was developed [43]. The optimal conditions of MAE were as follows: extraction solvent of methanol, microwave power of 375 W, temperature of 109 °C, and extraction time of 30 min. The output of this optimized MAE was compared with that of other extraction methods, including heat reflux extraction (HRE), Soxhlet extraction (SE), SFE, and UAE. MAE was found to achieve the highest extraction yields of total phytocannabinoids in hemp nut (6.09 µg/g for MAE; 4.15 µg/g for HRE; 5.81 µg/g for SE; 3.61 µg/g for SFE; 3.73 µg/g for UAE) with the least solvent consumption and shortest extraction time. This finding demonstrated that MAE could be a rapid, economic, effective, and environmentally friendly extraction method and has the potential for industrial applications. An MAE method having the extraction parameters including ethanol concentration (30, 50 and 70%), extraction time (10, 20 and 30 min) and solid/liquid ratio (5, 10 and 15 g/mL) was optimized by RSM [46], particularly, a Box–Behnken design [45] for the experimental design [45], used for extracting CBD (**1**) and $\Delta^9$-THC (**2**) from the total plant (leaves, blossoms, small structural parts of the inflorescence and bracts) of *C. sativa* [44]. This optimized MAE method afforded $\Delta^9$-THC (**2**) from 0.0339 to 0.0637 mg/mL and CBD (**1**) from 0.2243 to 1.8415 mg/mL and was found to be a simple, efficient, fast, and low environmental impact method for obtaining polyphenols and cannabinoids from *C. sativa* L.

## 4. Conclusions

*Cannabis sativa* L. is the main source of phytocannabinoids. Inflorescences are the main plant part where these phytocannabinoids are concentrated the most. *C. sativa* plant materials can be dried, and phytocannabinoids can be extracted using several techniques, but the yield and profile of phytocannabinoids in the resultant extract depend very much on the drying and extraction method and associated parameters. An efficient drying, extraction, and quantification of phytocannabinoids for medicinal use is essential to achieving the required quality standards and exploiting the entourage effects of the phytocomplex. Drying and extraction techniques for cannabis biomass have evolved over the years, resulting in the emergence of sophisticated and efficient methods with technological and computational advancements. MAD and MAE techniques that offer drying and extraction-process intensification have attracted considerable attention in phytocannabinoid extraction from *C. sativa*. The principle of MAE is different from those of conventional solvent extraction methods because the extraction can occur as the result of changes in the cell structure caused by electromagnetic waves (non-ionizing irradiation); even if cell structure remains unchanged, the instant volumetric heating achieved with microwaves as opposed to transferring heat from the surface, inwards, is more efficient, uniform and less laborious. MAE uses microwaves to create heat and mass gradients. Microwaves increase the kinetic energy of the solvent and improve the rate of penetration of the solvent into the solid matrix. Moreover, the driving force for MAE is not limited to diffusion. MAE, considered as a green extraction technique for phytocannabinoids, is a safe and cost-effective method, as it reduces solvent use and energy consumption, along with various environmental hazards such as chemical wastes. MAE can enrich cannabis oil with certain phytocannabinoids, e.g., CBD (**1**). Over the past few decades, MAE has emerged as a preferred technique for the rapid, scalable, cos-effective, efficient and green method for the sequential extraction of phytocannabinoids and other bioactive compounds from *C. sativa*, and it is particularly useful to enhance almost complete decarboxylation of acidic phytocannabinoids during the extraction process, providing neutral phytocannabinoids e.g., CBD (**1**) and THC (**2**). With the introduction of various computational and mathematical

modelling, it is now possible to fully optimize the MAD and MAE parameters and process to achieve the highest level of efficiency and specificity for phytocannabinoid extraction. MAD and MAE can be successfully used for the drying and extraction of *C. sativa* samples at a laboratory scale and easily scaled up for industrial applications.

## Author Contributions

Both authors contributed equally to retrieving information from the published literature, designing the layout, manuscript preparation and editing. All authors have read and agreed to the published version of the manuscript.

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## Conflict of Interest

The authors declare no conflicts of interest.

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