Cannabis sativa: Release of Volatile Organic Compounds (VOCs) Affecting Air Quality

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Abstract: - This review paper highlights about the emission of volatile organic compounds (VOCs) of Cannabis plants. Volatile organic compounds (VOCs) are a large group of chemicals harmful to human health that are readily released into the atmosphere and participate in atmospheric photochemical reactions. Floral Volatile organic compounds (VOCs) are often involved in defence and pollinator attraction. Cannabis cultivation and consumption may lead to additional environmental impacts. Studies found out that Cannabis plants emit a significant amount of biogenic volatile organic compounds (BVOCs) which could cause indoor air quality issues. Indoor Cannabis cultivation is energy-consuming, mainly due to heating, ventilation, air conditioning, and lighting. Energy consumption leads to greenhouse gas emissions. Common compounds to all the tested hemp cultivars include β-myrcene, ϒ-caryophyllene, α-pinene, β-pinene and limonene, reflecting species specificity in the emission of these compounds. **β-Myrcene** was the most abundant compound in most of the outside hemp cultivars. The **terpenes** had an earthy musky, and fruity smell may contribute to the odour in Cannabis samples at the vegetative stage, flowering stage, and drying/curing stage. All hemp cultivars are the prolific emitters of **terpenoids**. The oxidation of highly reactive Biogenic Volatile organic compounds (BVOCs) from Cannabis plants can lead to the formation of **ozone** and secondary Volatile organic compounds (VOCs) (e.g., formaldehyde and acrolein). In hemp production, considerable odorous emissions occur during field retting. However, more research is needed to address how outdoor air quality is influenced by Cannabis cultivation facilities (CCFs) emissions.

Key Words: Biogenic volatile organic compounds, BVOCs emission, Cannabis cultivation, Carbon footprint, Hemp, Terpens, VOCs emission.

I. Introduction

Cannabis sativa L., belongs to Cannabiaceae family is one of the oldest medicinal plant was found as wild noxious weed particularly in Indian Himalayan Region and other Asian countries, China, Pakistan, Nepal, Bhutan, Afghanistan and Iran, the Persians (1-9, 89-90). Cannabis is known for the accumulation of secondary metabolites, the phytocannabinoids as a part of its own defensive mechanism (1-21). Cannabis spp. are native to the Indian sub-continent and required warm temperatures and high light intensity to achieve good yields (1-25). Humans have a long history with Cannabis sativa, with evidence of cultivation dating back as far as 10,000 years (12, 82). The World Health Organization (WHO) reported that Cannabis is the most widely cultivated, trafficked and abused illicit drug, and it constitutes over half of worldwide drug seizures (1-12). Medical research on Cannabis has primarily focused on isolated THC (Δ9-Tetrahydrocannabinol), and CBD (Cannabidiol) but there are hundreds of other chemical constituents in Cannabis, including Cannabinoids and terpenes (1-21). Phytocannabinoids are naturally occurring Cannabinoids found in the Cannabis plant (1-21, 89-94).

Initial uses of Cannabis date back to almost 5000 years in **India** which was well documented in A***yurveda*** and now cultivated for both medicinal and recreational applications (3-9). Cannabis sativa and Cannabis indica were native of Indian origin found as wild noxious weed in the Indian Himalayan Region and other parts of India (3-9). Since then, hemp consumption has been spurred on by its wide range of properties and uses from **Indian Himalayan civilization** to another civilization through consecutive millennia (3-9, 82-93). Cannabis research work remains years behind than other crops because of the long legacy of prohibition and stigmatization (1-15). Hemp has historically been attractive for its top-quality fibre and edible oil (1-20, 82-93). The uses of Cannabis are economically significant, owing to the various food industry applications and the development of therapeutic and pharmacological applications of phytocannabinoids (1-21, 80-93).

According to the recent literature, over 200 phytocannabinoids have been identified in the Cannabis plant (1-21, 82-94). Cannabis sativa L. plants that contain a large variety of secondary metabolites, including phytocannabinoids, terpenoids, and flavonoids, which have profound anti-microbial activities, in addition to possessing anti-inflammatory, anti-oxidative, and neuromodulatory properties (1-21). They are classified into different subclasses according to their chemical structure, Cannabidiol (CBD), narcotic psychoactive compound, Δ9-tetrahydrocannabinol (Δ9-THC), Cannabigerol (CBG), Δ8-tetrahydrocannabinol (Δ8 -THC), and Cannabinol (CBN) are the most studied (1-21). Cannabis contains a psychoactive compound called Δ9-tetrahydrocannabinol (Δ9-THC), that creates a psychogenic effect (1-21, 82-93). It can be consumed through the respiratory tract and digestive tract through smoking and oral ingesting, respectively (1-21). In contrast, Cannabidiol (CBD), another component derived from Cannabis, is a non-psychoactive Cannabinoid that has gained popularity for its medicinal values and as a supplement (1-21, 82-94).

II. Cannabis sativa: Volatile Organic Compounds (VOCs)

Cannabis sativa L. produces a wide array of secondary metabolites, but it is also a prolific producer of Volatile Organic Compounds (VOCs) (22). One of the study reported the first analysis of Volatile Organic Compounds (VOCs) emitted from hemp, Cannabis sativa cultivars grown in New Zealand (22). This work characterises, for the first time, the Volatile Organic Compounds (VOCs) emissions of six industrial hemp (Cannabis sativa L.) cultivars grown in New Zealand: CFX-2, CRS-1, Ferimon 12, Katani, Futura 75, and Finola (22). All plants release secondary metabolites in the form of volatile organic compounds (VOCs) into the environment (22-37). These compounds mediate ecological interactions between plants and other organisms, e.g., attracting pollinators, acting as cues for foraging herbivores and their natural enemies, or warning neighbouring plants of potential herbivore attack (22-32).

This study identified and quantified thirty-five volatile organic compounds from the headspace of hemp plants, with most of these compounds being monoterpenes and sesquiterpenes (22). Common compounds to all tested cultivars include β-myrcene, ϒ-caryophyllene, α-pinene, β-pinene and limonene, reflecting species specificity in the emission of these compounds (22). **β-Myrcene** was the most abundant compound in most cultivars (22). Myrcene is a plant produced monoterpene, released by multiple species such as bay leaf, juniper, lemongrass, and thyme (22-32).

Myrcene has a multiple ecological roles and industrial applications, with antibiotic and insect repellent properties, and is used for flavours, fragrances, and **polymer** production (22-32). Therefore, high myrcene-producing plants may provide improved defence against pathogens and herbivores, and could be used to produce additional products beyond fibre and seeds (22-32). This study also showed that male plants from dioecious cultivars and monoecious cultivars emit lower amounts of volatiles and do not differ significantly in their volatile emissions (22). In contrast, female plants from dioecious cultivars typically emit significantly more volatiles than their male counterparts or monoecious plants (excluding CFX-2) (22). **β-Ocimene** is a ubiquitous monoterpene volatile compound with multiple biological roles. It is thought to be relevant in pollinator attraction and to play a defensive role by being toxic to herbivores or attracting natural enemies when emitted by vegetative tissue upon herbivore damage (22-32). Although pollinator attraction and plant defence may be the most important functions of Volatile Organic Compounds (VOCs), that they play many other roles in the interaction of plants with their environment (22-39).

According to the study conducted by **Kumeroa et al., in New Zealand,** the female hemp plants produce more volatiles than their male counterparts (and monoecious cultivars) (22). Floral Volatile organic compounds (VOCs) are often involved in defence and pollinator attraction (22-36). Volatile organic compounds (VOCs) are essential in plant-to-plant signalling, allowing other plants to respond to herbivores and activate defences before being attacked (22-36). This is likely due to the presence of stalked glandular trichomes in the female flowers (22). These trichomes produce resin that contains Cannabinoids and other volatile and non-volatile secondary metabolites (22). Trichomes are typically absent from male flowers and leaves, and their abundance and content can be influenced by genetics and the environment (22). Therefore, it is not surprising to find differences in volatile emission among female plants of different cultivars (especially in hemp plants that are selected for their low Cannabinoid content (22). Sexual dimorphism of floral and inflorescence traits is a common among many dioecious plant groups (22-32).

However, in this study, females emitted more volatiles than males, which may be a point of interest and could be explored further (22). Since Cannabis sativa plants do not rely on **insects for pollination**, differences in male and female volatile profiles may reflect their evolutionary history with other insects such as herbivores (22). In this scenario, higher emissions could be a defensive strategy to repel/deter herbivores or recruit their natural enemies to protect costly female flowers (22). The Volatile Organic Compounds (VOCs) emissions of plants can be influenced by environmental conditions (22). For example, temperature, UV-radiation, and soil nutrients have been shown to affect the Volatile Organic Compound (VOCs) emissions of different plant species (native and introduced) occurring in New Zealand (22).

Another study characterized the Volatile Organic Compounds (VOCs) profiles of six hemp cultivars, and explored the influence of cultivar, sex, and site on Volatile Organic Compounds (VOCs) emissions (33-34). This study found that all hemp cultivars are prolific emitters of **terpenoids** (33-34). Abundant compounds such as **β-myrcene** could have important applications in pest management and the production of other products beyond seeds and fibre (e.g., fragrances and flavours) (33-34). Experimental results also showed a marked difference in the volatile emissions between female plants and their male counterparts or monoecious cultivars, with female plants emitting more Volatile Organic Compounds (VOCs) (33-34).

Another parallel study showed that the odour-active constitution of different varieties of industrial hemp flowers is not only composed of **terpenes** but also other key odorants of different substance classes, such as lipid degradation products, methoxypyrazines, sulphur compounds, one ester and even one **pyrrole** (33-34). Nevertheless, the **terpenes** constitute the main part of the volatile fraction, whereby the monoterpenes, α-pinene, myrcene, β-phellandrene, 1,8-cineole and linalool could be analysed as odour-active constituents during GC-O analysis (33-34). Overall, the findings of the study showed that flowers of industrial hemp varieties, as a side product of hemp fibres and the oil production, can be regarded as a valuable source of **aroma compounds**, to be valorised in the development of future food and beverage applications (33-34).

About 200 **scent compounds** have been reported to make up the plants complex aroma. Some compounds that are typically found in high concentrations in Cannabis spp. plants include **β-myrcene, ϒ-caryophyllene, α-pinene, β -pinene, limonene** and **terpineol** (22-32-45). All plants release secondary metabolites in the form of volatile organic compounds (VOCs) into the environment (32-40). One drug-type Cannabis (marijuana) cultivar has elevated levels of terpinolene and **ϒ-limonene**, giving the plant a woody citrus aroma, while one hybrid C. sativa x C. indica cultivar has a floral citrus aroma due to high amounts of **linalool** and limonene (22-32-40). In recent years, researchers have focused on volatile organic compounds (VOCs) as a tool to protect plants from stress and boost crop production (22-25-40). These volatile organic compounds (VOCs) play an essential roles in many ecological functions, such as plant defences to biotic and abiotic stresses, providing information about crop status, mutualists, competitors , and promoting plant growth (22-34-40).

Among all these functions, the most important and understood one is the attraction of pollinators, ensuring the plants reproductive success (22-32). Floral scent promotes **plant–pollinator** specialization, as well as out crossing and reproductive isolation through floral constancy (22-55). Thus, such a **sexual signal** is subject to high selective pressure, being fundamental for plants' evolution and adaptation to the environment (20-57). Volatile Organic Compounds (VOCs) can act as **repellents**, being constitutively emitted or showing an increased emission during herbivory attack (22-50). Volatile Organic Compounds (VOCs) mediate ecological interactions between plants and other organisms, e.g., attracting pollinators, acting as cues for foraging herbivores and their natural enemies, or warning neighbouring plants of potential herbivore attack (22-60). Volatile compounds are emitted from all plant organs (leaves, inflorescences, roots, etc.) and their production and release are highly plastic, responding to biotic and abiotic factors allowing for considerable variation in the quantity and composition of Volatile Organic Compounds (VOCs) blends within and among plant taxa (33-55).

Plants synthesize an amazing diversity of secondary metabolites, which have been selected throughout their evolutionary history as a response to specific needs (22-40). Volatile organic compounds (VOCs) play an important role in plant ecology and can be useful in pest management (22-40). Volatile organic compounds (VOCs) are one of the most important secondary metabolites produced by plants (22-45). These **lipophilic** compounds have a low molecular weight and high vapour pressures at ambient temperature (22-45). More than **1700** Volatile Organic Compounds (VOCs) have been identified in different plant species from both angiosperms and gymnosperms, including a total of 90 families and 38 orders (22-45). Plant Volatile Organic Compounds (VOCs) have effects on plant–pollinator, plant–herbivore, plant–plant and other interactions and, consequently, on fitness (23-40).

Volatile organic compounds (VOCs) are emitted by plants as a consequence of their interaction with biotic and abiotic factors, and have a very important role in plant evolution (22-38). Epigenetic factors, such as DNA methylation and histone modification, which regulate both genes and transcription factors, might trigger adaptive responses to these evolutionary pressures as well as regulating the rhythmic emission of Volatile organic compounds (VOCs) through circadian clock regulation (22-38). Volatile organic compounds (VOCs) emission, especially that of **terpenes**, has been proven to mitigate these stresses, allowing plants to recover rapidly from high temperature exposure or alleviating oxidative stress and consequently increasing plant fitness (22-35). Volatile organic compounds (VOCs) are also crucial in plant defence against herbivores and protection from pathogens (22-39). Volatile organic compounds (VOCs) can act as repellents, being constitutively emitted or showing an increased emission during herbivory attack (22-40). In addition, specific Volatile organic compounds (VOCs) can perform as indirect defences, which can drastically reduce the number of herbivores, especially insects and larvae, by attracting parasitoids and predators (22-40).

In general, plants under attack activate signaling pathways leading to the expression of plant resistance mechanisms (32-78). Gene expression responses and leaf metabolic potential can modify the proportion of Volatile organic compounds (VOCs) biogenesis and emission levels (32-80). The Volatile organic compounds (VOCs) biogenesis can be either constitutive or induced (35-75). The emission of Volatile organic compounds (VOCs) occurs regardless of whether the plant is under conditions of stress (35-81). Therefore, biogenic Volatile organic compounds (BVOCs) can serve as biomarkers to inform about the plant defence mechanisms and resistance levels (35-79). Given the potential to detect Volatile organic compounds (VOCs) rapidly and non-invasively, biomarkers can also assist as a robust phenotyping tool (35-80). Pest attacks on plants can substantially change plants Volatile organic compounds (VOCs) emission profiles (35-75). Comparison of Volatile organic compounds (VOCs) emission profiles between non-infected/non-infested and infected/infested plants, as well as resistant and susceptible plant cultivars, may provide cues for a deeper understanding of plant-pest interactions and associated resistance (35-78). Furthermore, the identification of biomarkers—specific biogenic Volatile organic compounds (BVOCs) associated with the resistance can serve as a non-destructive and rapid tool for **phenotyping** applications (35-80).

Experimental results highlighted that further assessment of Volatile organic compounds (VOCs) emissions from Cannabis cultivation facilities (CCFs) is needed, and this assessment is one of the key factors for developing policies for optimal air pollution control (32-80). The analysis of volatile terpenes at four commercial Cannabis cultivation facilities (CCFs) showed that the most abundant Biogenic Volatile organic compounds (BVOCs) at all facilities are **β-myrcene, D-limonene, terpinolene, α-pinene,** and **β-pinene** (32-36).

It is well-known fact that vegetation is the largest source of atmospheric biogenic volatile organic compounds (BVOCs), contributing a significant fraction (approximately 89%) of the total atmospheric Volatile organic compounds (VOCs) (32-36). Emitted in the air, the Biogenic Volatile organic compounds (BVOCs) react with the hydroxyl radical (HO), ozone (O_3) and the nitrate radical (NO_3) to yield products that react with nitrogen oxides and form pollutants such as **ozone, formaldehyde, acetaldehyde,** and **acrolein** (32-36).

One of the research studies found that Cannabis plants emit a significant amount of biogenic volatile organic compounds, which could cause indoor air quality issues (23-36). Indoor Cannabis cultivation is energy-consuming, mainly due to heating, ventilation, air conditioning, and lighting (23-37). Energy consumption leads to greenhouse gas emissions (22-36). Cannabis cultivation could directly contribute to soil erosion. Meanwhile, Cannabis plants have the ability to absorb and store heavy metals. It is envisioned that technologies such as precision irrigation could reduce water use, and application of tools such as life cycle analysis would advance understanding of the environmental impacts of Cannabis cultivation (22-38). Biogenic Volatile organic compounds (BVOCs) emissions from indoor cultivated Cannabis in Colorado could contribute to ozone formation and particulate matter pollution (35-75). Nevertheless, preliminary findings predicted increases in hourly ozone concentrations, indicating that concentrated indoor cannabis cultivation could influence ozone pollution through Biogenic Volatile organic compounds (BVOCs) emissions (including terpenes), particularly in areas where nitrogen oxides are not limiting factors in ozone formation (40-76). Volatile organic compounds (VOCs) are a large group of chemicals that are readily released into the atmosphere and participate in **atmospheric photochemical** reactions (32-75). Volatile organic compounds (VOCs) can adversely affect air quality, either directly due to their toxicity or indirectly through atmospheric chemical reactions that can lead to ground-level ozone formation and secondary organic aerosol (SOA) formation (35-76).

III. Cannabis Cultivation Methods Influenced Emission

Cannabis cultivation methods have an unavoidable influence on the environment in different degrees (30-81). Outdoor cultivation is the traditional and original method of Cannabis cultivation (23-81). On the contrary, indoor cultivation (including greenhouse cultivation) enables full control over all aspects of the plants, such as light and temperature, but is constrained by higher costs, energy demand, and associated environmental implications (22-80). Hence three primary typologies of legal Cannabis cultivation systems based on existing regulations: indoor, mixed-light, and outdoor (25-80). These three production systems may impact the environment through different pathways (25-80). Indoor and mixed-light Cannabis cultivation systems may require higher external inputs (e.g., energy and fertilizer) but are also associated with higher yields and reduced concerns about ecosystem degradation (27-81). Outdoor farms may require fewer resource inputs, but poor management can disrupt surrounding ecosystems (32-81). Both indoor and outdoor cultivation systems may be associated with air pollution risks from biogenic volatile organic compounds (BVOCs) that can be precursors to ozone formation (25-81). Evidence has emerged that Biogenic Volatile organic compounds (BVOCs) and fertilization may contribute to outdoor air quality issues (30-81). Indoor air pollutants, i.e., Biogenic Volatile organic compounds (BVOCs) emission, mold, pesticide, and chemicals pose a risk of health hazards (30-81). On one side, Cannabis cultivation directly contributes to soil erosion. On the other side, Cannabis has a strong ability to absorb and store heavy metals in the soil (25-81). A third pilot study conducted in four commercial indoor growing facilities in California and Nevada, USA identified β- myrcene, D-limonene, terpinolene, and α- and β-pinenes as the most abundant Biogenic Volatile organic compounds (BVOCs) emitted by Cannabis plants (24-81). This study also found high **butane** concentrations in Cannabis-processing facilities using butane extraction, which could additionally contribute to **ozone formation** (25-81). These results are in line with those of Wang et al., and highlight potential indoor air quality issues in production facilities, which may have consequences for worker safety (32-81).

Trees and other types of vegetation emit Biogenic Volatile organic compounds (BVOCs), such as isoprene, pinenes, and terpenoid compounds (23-45). In recent years, the Cannabis market has increased drastically since the sale of recreational marijuana has been permitted in several states of USA (32-36). The sale of recreational marijuana products has resulted in rapid growth of the commercial Cannabis cultivation and processing industry (32-36). Cannabis facilities are typically built in urbanized areas near automobile roads, which are known areas of high NOx concentration (32-36). At the same time, not much information on Biogenic Volatile organic compounds (BVOCs) emissions from Cannabis industries is currently available (32-36). Therefore, identification of the speculated Volatile organic compounds (VOCs) at commercial Cannabis facilities is needed (32-36). Higher concentrations of VOCs emitted from Cannabis grow facilities can lead to the formation of ozone, secondary Volatile organic compounds (VOCs) (e.g., formaldehyde and acrolein), and particulate matter.

The oxidation of higher molecular weight Volatile organic compounds (VOCs) and Biogenic Volatile organic compounds (BVOCs) produces secondary organic aerosol particles (SOA) that may be even more harmful than ozone (32-36). Some of these pollutants are potentially hazardous compounds (32-36). These facilities can be a source of large amounts of Biogenic Volatile organic compounds (BVOCs) and Volatile organic compounds (VOCs) generated during the production of Cannabis products (32-36). The oxidation of highly reactive Biogenic Volatile organic compounds (BVOCs) from Cannabis plants can lead to the formation of **ozone** and secondary Volatile organic compounds (VOCs) (e.g., formaldehyde and acrolein) (32-36).

Hence Biogenic Volatile organic compounds (BVOCs) emitted by landscaped vegetation contributed significantly to ozone growth rates in the Las Vegas, USA region and should be considered as one of the sources of **ozone air pollution** (32-36). In this pilot study, Biogenic Volatile organic compounds (BVOCs) emissions from Cannabis plants were analyzed at four growth facilities (32-39). The concentrations of measured Biogenic Volatile organic compounds (BVOCs) inside the Cannabis growth facilities were between 110 and 5,500 $\mu g\ m^{-3}$ (32-36). One adult Cannabis plant emits hundreds of micrograms of Biogenic Volatile organic compounds (BVOCs) per day (32-39). This can trigger the formation of **tropospheric ozone** (approximately 2.6 g day^{-1} $plant^{-1}$) and other toxic air pollutants (32-26). In addition, high concentrations of **butane** (1,080– 43,000 $\mu g\ m^{-3}$), another reactive Volatile organic compounds (VOCs) were observed at the facilities equipped with Cannabis oil extraction (32-26).

Little attention has been paid to the possible biogenic volatile organic compounds (BVOCs) emitted from the growing of Cannabis and its impact on indoor and outdoor air quality (30-81). The only studies that have measured the composition of gaseous emissions from Cannabis have been limited to headspace samples above the plants (25-81). These studies have shown high concentrations of Volatile organic compounds (VOCs) such as monoterpenes ($C_{10}H_{16}$), sesquiterpenes ($C_{15}H_{24}$), and Cannabinoids (25-81). These studies also measured **thiols,** a sulfur-containing compound responsible for the characteristic odour of Cannabis species (25-80). The principle (trace) components are reported to be: α- and β-pinene, β-myrcene, d-limonene, cis-ocimene, β-caryophyllene, β-farnesene and α- 68 humulene (32-45). It should be noted that the pharmacologically active ingredients, e.g., Δ9-Tetrahydrocannabinol (Δ9-THC), generally have low volatility and therefore, rarely detected in the gas-phase (32-65).

IV. Volatile Organic Compounds (VOCs) : Adverse Health Effects

However, there are no published studies that systematically addressed health concerns. Cannabis cultivation emissions are still poorly understood (25-81). But all these studies acknowledged that additional data are needed to fully understand the potential risks and implications of indoor Cannabis cultivation on air quality (25-81). Volatile organic compounds, or VOCs are organic chemical compounds whose composition makes it possible for them to evaporate under normal indoor atmospheric conditions of temperature and pressure (25-80). Volatile organic compounds are compounds that have a high vapour pressure and low water solubility (25-81). Volatile organic compounds (VOCs) are gases that are given off by many indoor sources. Concentrations of the most volatile organic compounds are higher in indoor air than outdoor air (25-82). VOCs include a variety of chemicals, some of which may have short- and long-term adverse health effects (27-80). The main concern indoors is the potential for Volatile organic compounds (VOCs) to adversely impact the health of people that are exposed (30-82). Biogenic volatile organic compounds (BVOCs) emitted can also increase the formation of health-damaging pollutants such as ground level ozone (O_3) and particulate matter (PM) (35-78). These Biogenic volatile organic compound (BVOCs) emissions also occur indoors at Cannabis cultivation facilities (CCFs), which may represent an occupational health hazard (60-80). As a result, air quality regulators, public health agencies, and occupational health agencies have begun to explore options for curbing Biogenic volatile organic compounds

(BVOCs) emissions at Cannabis cultivation facilities (CCFs), and the Cannabis research community has identified an urgent need to characterize them (35-81).

Cannabis plants naturally emit **terpenes,** which are volatile organic compounds (VOCs), as they grow (28-80). Marijuana Infused Product (MIP) facilities also emit volatile organic compounds (VOCs) from solvent evaporation during extraction processes (85). Volatile organic compounds (VOCs) react with oxides of nitrogen in the presence of sunlight to create ground-level ozone, a pollutant that is dangerous to human health and the environment (85). Controlling emissions of VOCs from cultivation and Marijuana Infused Product (MIP) facilities helps to improve air quality, which is especially important in urban areas and from May to September, when ground-level ozone levels often exceed health standards (85). The Cannabis industry directly impacts air quality in two predominant operations. 1. Plant growth cultivation 2. Marijuana Infused Product (MIP) facilities (85).

At cultivation facilities, the natural growth of Cannabis plants and other processes emit t**erpenes**, which are Volatile Organic Compounds (VOCs) known for their strong odours (25-80). At Marijuana Infused Product (MIP) facilities, the evaporation of solvents and other processes in the production cycle results in Volatile Organic Compound (VOC) emissions (30-80). Volatile Organic Compounds (VOCs) alone do not typically pose a direct threat to human health or the environment. However, they do contribute to ground-level ozone by chemically reacting with other types of pollution, specifically, nitrogen oxides (NOx) in the presence of sunlight (30-85). **Ozone** is an air pollutant that is harmful to human health and negatively impacts the environment. Therefore, it is important that the Cannabis industry mitigate Volatile Organic Compounds (VOCs) emissions in their processes (35-85).

In Colorado's, USA, Front Range, cultivation and Marijuana Infused Product (MIP) facilities are generally in dense urban areas near heavily trafficked highways and other industrial sources of NOx pollution (85). Because Volatile Organic Compounds (VOCs) required the presence of NOx and sunlight to form harmful ozone, Volatile Organic Compounds (VOCs) from these facilities have a greater impact on ozone formation than facilities in rural areas (85). This makes mitigating Volatile Organic Compounds (VOCs) emissions from the Cannabis industry especially important in these regions. As Cannabis plants grow, they release a distinctive range of odours which are made up of different types of Volatile Organic Compounds (VOCs) called **terpenes** (85). Activities during the cultivation or production cycle that release significant odours also release elevated Volatile Organic Compounds (VOCs) during that time (80-85). Installing control technologies can reduce the amount of Volatile Organic Compounds (VOCs) emissions released from the cultivation process and control the odours in compliance with the Denver city and county odour ordinance (85). Highly reactive, ozone-forming terpenes commonly emitted from Cannabis cultivation include: pinene, limonene, myrcene, and terpinolene (80-84).

Riding the global waves of decriminalization, medical or recreational use of Cannabis (Cannabis sativa spp.) is now legal in more than 70 countries and U.S. states (23-81). As governments regulate this formerly illegal crop, there is an urgent need to understand how Cannabis may impact the environment (25-81). Both monitoring and modeling assessment of odorous emissions from Cannabis cultivation facilities (CCFs) are lacking in the literature (30-81). Moreover, much of the available literature is focused on terpenes when previous research has shown that sulfurous compounds are also present in emissions and can be very odorous (32-81). Although some aspects of indoor air quality have been studied, there is still an opportunity for guidelines dedicated to Cannabis-related terpene exposure (35-80). Importantly, the health effects of exposure to Cannabis-related terpenes for those living near facilities are not yet understood (35-80). Reviews suggested that workers at Cannabis cultivation facilities (CCFs) are exposed to organic dust (molds, pollens, bacteria, other allergens, and bioaerosols), VOCs, fungicides, and pesticides (32-81). An interview of Cannabis cultivation facilities (CCFs) workers found that 71% presented some work-related symptoms, and the majority of symptoms (65%) was **respiratory** (76-80). Workers in indoor cultivation of Cannabis are mostly in contact with "**raw**" material, whereas consumers are exposed to **processed or combusted material** (70-80).

In terms of Volatile Organic Compounds (VOCs) exposures, it is believed that the terpenes, a specific class of Volatile Organic Compounds (VOCs) that are emitted when working with the Cannabis plants, could potentially contribute to the **respiratory** and **dermatological** symptoms among workers (83-84). Terpenes are compounds that are produced by plants and are responsible for the distinct scent and taste of Cannabis (83-84). While low levels of terpenes are unlikely to cause adverse health effects, these compounds have the ability to react with oxidants found in indoor environments and form highly oxidized species which are suspected to cause respiratory tract irritation and airflow limitation (83-84). Studies also indicated that respiratory health effects among workers exposed to terpenes varied among workplace but largely included α-pinene, β-pinene, β -myrcene, β-caryophyllene, and limonen (83-84).

Raw Cannabis material is often composed of larger particles (e.g., organic dust, allergens, impurities) that are filtered by airway defences, while combusted material is composed of smaller particles and gases that are inhaled and penetrate deeper in the respiratory system (70-80). Emissions from Cannabis cultivation facilities (CCFs) may affect public health at the community scale through exposures to: (1) High concentrations of terpene oxidation products, (2) High concentrations of particulate matter and ozone, and (3) Odour. However, studies point to a broad range of symptoms, such **as burning eyes** and **throat, problems sleeping, nausea,** and **headache** (65-80).

As far as health of the people residing near Cannabis cultivation facilities (CCFs) reported **nausea** and **eye irritation** as symptoms caused by strong odours experienced on their properties (35-80). Odour descriptors associated with Cannabis cultivation facilities (CCFs) varied from the typical "**skunky**" to "**citrus**" or "balsamic" (39-79). Some of the studies showed that Biogenic volatile organic compounds (BVOCs) from Cannabis samples also contained small amounts of alkyl pyrazine (0.84%) and Methoxypyrazine (1.25%) (33-81). These compounds have some of the lowest known odour thresholds (0.002 ppb) (33-81). Cannabis odour has also been associated with the presence of dimethylsulfide in trace amounts (33-81). **Dimethyl-sulfide** has a strong **rotten egg** smell with an odour threshold of 3 ppb (35-75). Another study points to 3-methyl-2-butene-1-thiol as the cause of the "skunky" odour in Cannabis (32-79). Nonanal, for example, is expected to have a longer lifetime in the troposphere than most terpenes (32-81). Hence if a sufficient amount is emitted, it could cause a nuisance (32-70). The odour description mainly associated with nonanal/decanol is "citrus" or "greasy", of which the former has been reported for Cannabis smell (35-80, 85).

Volatile Organic Compounds (VOCs) include a variety of chemicals that **can cause eye, nose and throat irritation, shortness of breath, headaches, fatigue, nausea, dizziness and skin problems** (40-81). **Higher concentrations may cause irritation of the lungs, as well as damage to the liver, kidney, or central nervous system** (30-82). Long-term exposure may also cause damage to the liver, kidneys or central nervous system (35-81). Some Volatile Organic Compounds (VOCs) are suspected of causing **cancer** and some have been shown to cause **cancer** in humans. The health effects caused by Volatile Organic Compounds (VOCs) depend on the concentration and length of exposure to the chemicals (35-83).

In hemp production, considerable odorous emissions occur during field **retting,** which refers to the practice of allowing the harvested hemp stems to decompose naturally on the field for several weeks (32-81). The odour concentration and persistence were higher during the first weeks of retting when the stems had been harvested after flowering rather than at seed maturity (32-80). The terpenes that may contribute to the odour in Cannabis samples at the vegetative stage, flowering stage, and drying/curing stage (32-80). The most abundant terpene in all stages, **β-myrcene**, had an earthy "musky", and "fruity" smell (34-78). Other terpenes such as α-pinene and β-pinene smelled like "pine tree", limonene odour was characterized as "citrus", and eucalyptol smelled "minty" (32-81).

Terpenes are the small hydrocarbon compounds that impart aroma and taste to many plants, including Cannabis sativa (86-88). A number of studies have shown that terpenes can produce pain relief in various pain states including chronic neuropathic pain in both humans and animals (86-88). Cannabis is unique in the number of terpenes it contains; while most other plants have two dominating terpene species (86-88). Cannabis contains up to **150 terpenes**, with multiple terpenes acting as the dominant species (86-88). This complexity of the Cannabis chemovar may determine the different biological effects caused by different strains of Cannabis (86-88).

V. Cannabis: Biogenic Volatile Organic Compounds (BVOCs)

Biogenic volatile organic compounds (BVOCs) are low boiling point compounds commonly synthesized by secondary metabolic pathways in plants (32-80). Biogenic volatile organic compounds (BVOCs) produced by plants are involved in plant growth, reproduction and defence mechanism (20-80). They are emitted from vegetation into the atmosphere and have significant effects on other organisms and on atmospheric chemistry and physics (22-69). Climate change strongly influences pest population dynamics that may increase crop damage and new strategies are needed to face challenges from pests and pathogens (25-75). Many vascular plants can discharge Biogenic volatile organic compounds (BVOCs) into the atmosphere (35-75). Biogenic volatile organic compounds (BVOCs) can contribute to the surface **ozone** concentrations (35-68). Biogenic volatile organic compounds (BVOCs) emission to atmospheric ozone and particulate pollution (35-68). Forest is one of the primary sources that can emit Biogenic volatile organic compounds (BVOCs), which occupies about 70 % of the total Biogenic volatile organic compounds (BVOCs) amounts from the vegetation (35-79). Agriculture has been recognized as a major contributor to air pollution through the emission of gases like methane (CH_4), ammonia (NH_3), or nitric oxide (NOx) (35-75). These emissions occur from activities such as inorganic fertilizer amendments, animal husbandry, or transportation associated with food production (35-75). These gases can contribute to the formation of **nitrate aerosols** and fine particulate matter (PM2.5) pollution, which has been linked to severe human health consequences (35-75).

They are fundamentally released from flowers, but also from fruits, leaves, stems and even roots (34-78). Biogenic volatile organic compounds (BVOCs) play an essential role in tropospheric atmospheric chemical reactions (35-76). Biogenic volatile organic compounds (BVOCs) are the main precursors to form tropospheric ozone and atmospheric aerosols, promoting the formation of secondary pollutants such as peroxyacetyl nitrate (PANs), secondary organic aerosols (SOA), particulate matter (PM), aldehydes and ketones (36-78). The ozone is another important pollutant that plagues the urban ambient air quality (35-78). In urban and suburban regions with elevated nitrogen oxides (NOx) concentrations, Volatile organic compounds (VOCs) can undergo photochemical reactions leading to the formation of **ozone** and secondary organic aerosol (SOA), which have adverse effects on human health and ecosystems (35-81). The potential increases in Biogenic volatile organic compounds (BVOCs) emissions due to future urban greening had significant effects on urban air quality that offset the benefits of reducing anthropogenic Volatile organic compounds (VOCs) emissions (32-75).

Biogenic volatile organic compounds (BVOCs) emissions from Cannabis species vary in composition and strength based on the stage of plant growth (35-78). However, emissions due to Cannabis cultivation and processing (drying, sorting, trimming, and curing), which often occur at the same site, are poorly understood due to the limited number of facilities sampled (35-75). According to Wang et al., study, the largest impacts were seen in locations with the highest **terpene** emissions coming from Cannabis cultivation facilities (CCFs), i.e. in Denver County, USA (27, 28, 44-47, 56). Further, Wang et al., study also found that these increases in terpene concentrations affected the local atmospheric chemistry and air quality with ground-level ozone concentrations increasing by as much as 0.34 ppb during the day and 0.67 ppb at night (27, 28, 44-47, 56). Furthermore, the authors also observed that high concentrations of β-myrcene near Cannabis cultivation facilities (CCFs) but did not find high concentrations in other outdoor vegetated areas, suggesting that β-myrcene could be a sensitive tracer of Cannabis cultivation facilities (CCFs) emissions (27, 28, 44-47, 56). More research is needed to address how outdoor air quality is influenced by Cannabis cultivation facilities (CCFs) emissions (27-78).

In one of the study, the concentrations of monoterpenes near Cannabis cultivation facilities (CCFs) are at least four times higher than background, but several times lower than concentrations indoors (27-77). Samples taken indoors during the flowering stage (emissions peak) in four Cannabis cultivation facilities (CCFs) showed that the most of the abundant compounds were β-myrcene, D-limonene, terpinolene, α-pinene, and β-pinene (27-78). For instance, β-myrcene ranged from 4% to 65% of the total Biogenic volatile organic compounds (BVOCs) composition (27-70). **Myrcene** was the dominant compound, present in all strains, in addition to eucalyptol and, to a lesser extent, D-limonene (27-70). Tepenes were also the most abundant chemical family in Biogenic volatile organic compounds (BVOCs) measured from hemp stems harvested after 15 weeks (end of flowering), accounting for 60% of total composition (27-70). Emissions of some compounds were also found to increase with time, particularly those that provide defences against bacteria, including β-caryophyllene, α-humulene, and δ,3-carene (27-70). Compounds such as α-pinene (55%), β-pinene (16%), myrcene (8.3%), and D-limonene (5.4%) dominated the Biogenic volatile organic compounds (BVOCs) in headspace marijuana (27-75).

Biogenic volatile organic compounds (BVOCs) collected and analyzed from male and female plants of two Cannabis species during the flowering stage showed the most abundant compounds to be β- myrcene, (E)-β-ocimene, and terpinolene (27-70). Two compounds are emitted uniquely by female plants: Alkyl Pyrazine and Methoxypyrazine (27-70). A comparison of headspace volatile organic compounds (VOCs) from marijuana, hemp, and other plants found the distinguishing compounds of marijuana to be α-santalene, valencene, and β- bisabolene (27-75). Conversely, compounds such as α-pinene, β- pinene, β-myrcene, β-caryophyllene, and α-caryophyllene were also found in non marijuana samples (21 plant species, including hemp) (27-75).

According to Wang study, (2019) over 100 different compounds have been identified in the headspace above these materials. The most common of which are: monoterpenes ($C_{10}H_{16}$) including a-pinene, b-pinene, b-myrcene, d-limonene, and *cis*-ocimene; sesquiterpenes ($C_{15}H_{24}$) including b-caryophyllene, a-farnesene, and b-humulene; and the terpene alcohols ($C_{10}H_{18}O$) such as linalool, borneol, and terpineol (44-48). Most recently, the Dessert Research Institute measured monoterpene concentrations between 200 ppbv and 10 ppmv from four Cannabis Cultivation Facilities (CCFs) in California and Nevada, USA (44-48). Thus, the **Cannabis industry has higher ozone sensitivity impact**. There are two reasons which cause this phenomenal: the CCFs are located near major highways with massive NOx emission, and the monoterpene is highly reactive biogenic Volatile organic compounds (BVOCs) (44-48).

In general, it is difficult to establish an emissions inventory for Cannabis Cultivation Facilities (CCFs) due to the substantial variability across plant strains, stage-of-life, and different cultivation practices (27-74, 85). **Carbon filters** are the most widely used volatile organic compounds (VOCs) control technology in the greenhouse of Cannabis industry (32-76, 85). Carbon filtration is currently the best control technology for reducing VOC emissions from Cannabis cultivation facilities (85).Carbon filters are simple to install, inexpensive, effective, and reliable when properly maintained and replaced (85). These filters work by using an absorption process where porous carbon surfaces chemically attract and trap Volatile organic compounds (VOCs) along with other gas phase contaminants (85). **Bio-filters** are an emerging odour technology that could proved to be more cost effective and less resource intensive than carbon filtration once it is refined in the future (85). These filters use an organic medium, such as wood chips, that are inoculated with bacteria and consume odorous molecules (85). Odour neutralizer systems are the most commonly used alternative to carbon filtration at Cannabis greenhouses and can be used to complement carbon adsorption systems (44-49, 85).

VI. Conclusion

Cannabis sativa L. produces a wide array of secondary metabolites, but it is also a prolific producer of Volatile Organic Compounds (VOCs). However, there are no published studies that systematically addressed health concerns. Cannabis cultivation emissions are still poorly understood. In general, it is very difficult to establish an emissions inventory for Cannabis Cultivation Facilities (CCFs) due to the substantial variability across plant strains, stage-of-life, and different cultivation practices. However, emissions due to Cannabis cultivation and processing (drying, sorting, trimming, and curing), which often occur at the same site, are poorly understood due to the limited number of facilities sampled. Furthermore, there are many experimental issues and data presented is not enough for the scientific validation. This uncertainty is mainly caused by methodological limitations such as poor study design, relatively small sample sizes, inappropriate outcome measures and primary and secondary end-point selection, and invalid statistical analysis. **Carbon filters** are the most widely used volatile organic compounds (VOCs) control technology in the greenhouse of Cannabis industry. Therefore, future detailed experimental and clinical study is warranted to confirm about how Volatile Organic Compounds (VOCs) affects human health and air quality.

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