Vol. 05, Issue, 04, pp.4402-4405, April 2023 Available online at http://www.journalijisr.com SJIF Impact Factor 2023: 6.599

Research Article



CANNABIS PRODUCTS CONTAMINATION PROBLEMS: A MAJOR QUALITY ISSUE

¹, * Ravindra B. Malabadi, ²Kiran P. Kolkar, ¹Raju K. Chalannavar, ³L**avanya** L, ⁴Gholamreza Abdi, ⁵Himansu Baijnath

¹Department of Applied Botany, Mangalore University, Mangalagangotri-574199, Mangalore, Karnataka State, India. ²Department of Botany, Karnatak Science College, Dharwad-580003, Karnataka State, India. ³Department of Biochemistry, REVA University, Bangalore -560064, Karnataka State, India ⁴Department of Biotechnology, Persian Gulf Research Institute, Persian Gulf University, Bushehr, 7516, Iran. ⁵Ward Herbarium, School of Life Sciences, University of KwaZulu-Natal, Westville Campus, Private Bag X54001, Durban 4000, South Africa.

Received 24th February 2023; Accepted 25th March 2023; Published online 30th April 2023

ABSTRACT

This review paper highlights the recent concerns about the possible contaminations of Cannabis products with **pesticides**, **fungicides**, **insecticides**, **heavy metals**, **microbial pathogens**, and **carcinogenic** compounds during the cultivation, manufacturing, and packaging processes which must be addressed to ensure the safety of consumers. These contaminants are usually introduced during Cannabis cultivation and storage of Cannabis products. Growth enhancers and pest control chemicals are the most common risks to both the producer and the consumer. These contaminants are imminent threats that directly impact public health and wellness, particularly to the immunocompromised and pediatric patients who take Cannabis products as a treatment for numerous human disorders including cancer patients and those suffering from epileptic seizures. For the safety and welfare of all Cannabis users, both medicinal and recreational, there is a necessity for a standardized set of guidelines for cultivation and testing of Cannabis products. This will help to improve the quality based Cannabis products in the market and safe zone for the consumers.

Keywords: Cannabis, cannabidiol (CBD), carcinogens, contamination, heavy metals, hemp, microbes, pesticides, Δ9-Tetrahydrocannabinol (Δ9-THC).

INTRODUCTION

Cannabis is a multi-purpose crop plant with diverse agricultural and industrial applications ranging from the production of paper, wood, and fiber, to potential use in the medicinal and pharmaceutical industries (1-10). However, the Cannabis became controversial owing to some psychoactive components (Δ9-Tetrahydrocannabinol (Δ 9-THC) that have adverse effects on human health (1-10). Cultivation and use of Cannabis plants for recreational, medical, and industrial use were strictly banned and severely limited the scientific research in the field (1-10). Owing to strict legal regulations, the plant remained unexplored for its incredible potential in drug discovery for an extended period until it was legalized for medical use first in California, USA and later in many countries around the globe (1-10). Cannabis legalization fuelled the scientific research in Cannabinoid compounds for potential use in medicinal, pharmaceutical, and neurological applications (1-10). With recent legalization in many more countries are beginning to question the rationale behind criminalizing Cannabis (16, 17). However, many issues have arisen concerning the lack of Cannabis cultivation standards and overall quality control of Cannabis products (11-48).

It has been reported that Cannabis derived products are often contaminated by **microbes**, **heavy metals**, **pesticides**, **carcinogens**, and **debris**, which must be addressed to ensure the safety of consumers (11-25). These contaminants are imminent threats that directly impact public health and wellness, particularly to the immunocompromised and pediatric patients who take Cannabis products as a treatment for numerous human disorders including cancer patients and those suffering from epileptic seizures (10-25). Therefore, there is an urgent Wake up Call to remind hemp

*Corresponding Author: Ravindra B. Malabadi, 1Department of Applied Botany, Mangalore University, Mangalagangotri-574199, Mangalore, Karnataka State, India, producers, manufacturers, medical professionals, and legislators to recognize this risk and establish regulatory measures to educate the public and reduce the adverse effects caused by the contaminants in Cannabis, particularly in Cannabidiol (CBD)-based products (10-25). to consumers has been reviewed and updated by Montoya et al., 2020 and Dryburgh et al., 2018 (16, 17, 25, 26, 27, 37). There are also concerns for edible Cannabis products (e.g., gummies, cookies, etc.) containing under and over reported phytocannabinoid content, specifically Δ 9-Tetrahydrocannabinol (Δ 9-THC) (16, 17, 26, 27). Currently Cannabidiol (CBD)- and Δ9-Tetrahydrocannabinol (Δ9-THC) are the only Cannabinoids required to be labeled, including the profile of acidic forms of Δ 9-Tetrahydrocannabinol (Δ 9-THC) and Cannabidiol (CBD) and some minor cannabinoids such as cannabigerol (CBG), cannabichromene (CBC) on these labels (16, 17, 26-37). These minor cannabinoids are shown to have some therapeutic effects that could be enhanced in combination with other major cannabinoids (16, 17, 25-27).

Cannabis is associated with various types of microbes moulds that have been shown to including harm immunocompromised patients, as well as bacteria and viruses that have the potential of causing harm to humans (10-48). Previous studies have identified several fungal organisms in dispensaryproduced Cannabis including Penicillium sp. (P. paxilli, P. citrinum, P. commune, P. chrysogenum, P. corylophilum, P. citrinum, and P. steckii), Aspergillus sp. (A. terreus, A. niger, A. flavus, A. versicolor, A. ostianus, and A. sydowii), and Fusarium sp. (F. oxysporum) (16, 17, 28-31). Both Penicillium sp. and Aspergillus sp. have been known to produce aflatoxins (e.g., aflatoxin B1) while Fusarium species produce other mycotoxins such as fumonisin (16, 17, 28, 29). Cannabis infected with Aspergillus. Penicilium. or Fusarium can severely affect human health as these toxins can all be carcinogenic, hepatotoxic, neurotoxic or nephrotoxic (16, 17, 28, 29, 30). In addition to pathogenesis in humans by these fungi, Penicillium, Aspergillus, and Fusarium sp. are known to produce both **aflatoxins** and m**ycotoxins** that become especially problematic while drying and storing Cannabis products in humid environments (10-35).

Further, bacterial contamination has also been reported, reviewed and updated by Montoya et al., 2020 and Dryburgh et al., 2018 (10-36). These bacteria contaminate include various species of Pseudomonas, Cellvibrio, Oxalobacteraceae, Xanthomonadaceae, Actinomycetales, and Sphingobacteriales in the examined microbiomes (10-35, 36, 44, 46, 48). While dozens of bacterial species found to be present in Cannabis plants, E.coli, Salmonella, and Clostridium are a few common potential human pathogenic species shown to be associated with Cannabis (10-35, 36, 44). There are also concerns for the contamination of Cannabis food products by potentially harmful bacteria including Listeria (10-35). Viruses found to be associated with Cannabis are purely plant pathogens, and it is not assumed that these could cause human related diseases (10-35, 36, 44). Most of the microbial contamination occurs during the improper preparation and storage of cannabis products. wet, drying and storage under wet, humid conditions can lead to fungal infections such as powdery mildew and botrytis, and budworm or mite infestations (10-48). The carcinogenic load of nonmedicinal Cannabis, particularly when consumed via smoking, is significant (16. 17).

A variety of heavy metals have been found in Cannabis plants and products made with Cannabis (e.g. tinctures and oils) including cadmium, lead, magnesium, copper, and mercury (14-17, 38, 42, 49). Cannabis plants which are used to produce industrial hemp, medical marijuana and Cannabidiol (CBD) oil, among other products have an inherent ability to absorb heavy metals from the soil, making them useful for remediating contaminated sites (10-48). But this ability to soak up toxic metals may also make Cannabis dangerous for consumers who ingest it (10-35). A new meta-analysis, led by researchers at Penn State, USA examines the ability of Cannabis plants to absorb heavy metals and discussed the resulting health impacts on consumers. Furthermore, many heavy metals have been shown to have fatal effects in humans when exposed both acutely or chronically, causing a plethora of diseases, such as, cancers and neurological disorders (10-42). Smoking is the most common recreational consumption technique and involves the combustion of Cannabis and other compounds (10-48). The application of sufficient to Cannabis causes decarboxylation of Δ9-heat tetrahydrocannabinoic acid (THCA) to its active form THC but, concomitantly, the process of pyrolysis transforms some contaminants into more toxic forms (10-48). Heavy metals such as cadmium and arsenic and some pesticides are highly volatile and become carcinogenic under pyrolytic conditions (10-49).

While many claim that Cannabis is naturally a pest resistant crop (1-45), there is still abundant use of various types of pesticides to provide protection, including insecticides, fungicides, and plant growth regulators (14 - 19, 33, 43). As many of these pesticides are lipophilic, they are soluble in the solvents used for extraction of Cannabinoids, including Cannabidiol (CBD) oils and other products using extracted Cannabinoids (1-45). Naturally, this leads to concerns about contamination of Cannabis with pesticides and the potential health risks that would accompany concentrating these pesticides in an extract (10-43). In addition to this, two commonly identified insecticides (Bifenazate, and Abamectin) found on Cannabis products that are known to be harmful to mammals (10-43). Several fungicides have been reported in samples of Cannabis all over the world including known endocrine disruptors and hepatoxic compounds like imazalil and and myclobutanil (10-43). These fungicides should not be considered safe to use for any Cannabis cultivation, and their application should be avoided to protect the health of the consumer (10-43). The toxicity of plant growth regulators (Daminozide and paclobutraxol) are also commonly found in Cannabis, including carcinogens and compounds that have been

shown to be detrimental to mammals (10-43). Polycyclic aromatic hydrocarbons (PAH) are ubiquitous environmental pollutants usually generated by the incomplete combustion of organic materials are also found in some Cannabidiol (CBD) oils and may come either from uptake by the plant during growth or from contaminated carrier oils during product preparation (16, 17). Polycyclic aromatic hydrocarbons (PAH) (benzo anthracene, chrysene, benzo fluoranthene, benzo pyrene) are known to be hazardous, deemed as carcinogens, and can found in Cannabis products worldwide (16, 17). Other debris such as <u>metal fragments, hairs, dusts, machine oils, or insect parts</u> can be found in some Cannabidiol (CBD) oil products as is seen in other foods or food products (10-48).

CONCLUSION

The emerging interest in Cannabis, and Cannabis products is increasing throughout world. However, concerns have arisen about the possible contaminations of hemp with pesticides, heavy metals, microbial pathogens, and carcinogenic compounds during the cultivation, manufacturing, and packaging processes. For nearly a century, Cannabis has been stigmatized and criminalized across the globe, but in recent years, there has been a growing interest in Cannabis due to the therapeutic potential of phytocannabinoids. For the safety and welfare of all users, both medicinal and recreational, there is a necessity for a standardized set of guidelines for cultivation and testing of Cannabis products. The lack of a comprehensive evidence base suggests that the study of cannabis contaminants is an emerging field of clinical pharmacology. Unfortunately, the classification of Cannabis as a schedule 1 drug throughout the world makes the development and implementation of nationwide standards impossible at the moment. Thus, it is imperative to develop universal standards for cultivation and testing of products to protect those who consume Cannabis. International consensus is needed to establish quality control and product standardization. The development of the requisite analytical standards for quality testing of global medicinal cannabis preparations requires a more comprehensive evidence base of the contaminants of cannabis.

ACKNOWLEDGEMENT

We would like to thank and acknowledge, Karen Viviana Castaño Coronado, The Chief Communications Officer (CCO) and CO-Founder of LAIHA (Latin-American Industrial Hemp Association), and CEO-CANNACONS, Bogota, D.C., Capital District, Colombia for encouraging, supporting, promoting and appreciating research work.

REFERENCES

- Hussain T, Jeena G, Pitakbut T, Vasilev N, Kayser O. Cannabis sativa research trends, challenges, and new-age perspectives. IScience. 2021; 24, 103391, December 17, 2021.
- Malabadi RB, Kolkar KP, Chalannavar RK. Cannabis sativa: Ethnobotany and Phytochemistry. International Journal of Innovation Scientific Research and Review. 2023; 5(2): 3990-3998.
- Malabadi RB, Kolkar KP, Acharya M, Chalannavar RK. Cannabis sativa: Cannabis sativa: Medicinal Plant with 1000 Molecules of Pharmaceutical Interest. International Journal of Innovation Scientific Research and Review. 2023; 5 (2):3999-4005.

- Malabadi RB, Kolkar KP, Chalannavar RK. Cannabis sativa: Industrial hemp (fiber type) - An Ayurvedic Traditional Herbal Medicine. International Journal of Innovation Scientific Research and Review. 2023;5 (2): 4040-4046.
- Malabadi RB, Kolkar KP, Chalannavar RK. Medical Cannabis sativa (Marijuana or Drug type); The story of discovery of Δ9-Tetrahydrocannabinol (THC). International Journal of Innovation Scientific Research and Review. 2023; 5: (3):4134-4143.
- Malabadi RB, Kolkar KP, Chalannavar RK. Δ9-Tetrahydrocannabinol (THC): The major psychoactive component is of Botanical origin. International Journal of Innovation Scientific Research and Review. 2023;5(3): 4177-4184.
- Malabadi RB, Kolkar KP, Chalannavar RK. Cannabis sativa: Industrial Hemp (fibre-type)- An emerging opportunity for India. International Journal of Research and Scientific Innovations (IJRSI). 2023; X (3):01-9.
- Malabadi RB, Kolkar KP, Chalannavar RK. Industrial Cannabis sativa (Hempfiber):Hempcrete-A Plant Based Eco-friendly Building Construction Material. International Journal of Research and Innovations in Applied Sciences(IJRIAS). 2023; 8(3): 67-78.
- Malabadi RB, Kolkar KP, Chalannavar RK, Lavanya L, Abdi G. Cannabis sativa: The difference between Δ8-THC and Δ9-Tetrahydrocannabinol (THC). International Journal of Innovation Scientific Research and Review. 2023; 5(4): 4315-4318.
- Ungerleider JT, Andrysiak T, Tashkin DP, Gale RP. Contamination of marijuana cigarettes with pathogenic bacteria – possible source of infection in cancer patients. Cancer Treat Rep. 1962; 66: 589.
- Llamas R, Hart DR, Schneider NS. Allergic bronchopulmonary aspergillosis associated with smoking moldy marihuana. Chest. 1978; 73: 871–2.
- Hamadeh R, Ardehali A, Locksley RM, York MK. Fatal aspergillosis associated with smoking contaminated marijuana, in a marrow transplant recipient. Chest. 1988; 94: 432–3.
- Remington TL, Fuller J, Chiu I. Chronic necrotizing pulmonary aspergillosis in a patient with diabetes and marijuana use. CMAJ. 2015; 187: 1305–8.
- McPartland JM, McKernan KJ. Contaminants of concern in cannabis: Microbes, heavy metals and pesticides. In: Cannabis sativa L – Botany and Biotechnology, eds Chandra S, Lata H, Elsohly M. Cham, Switzerland: Springer, 2017.
- Busse FP, Fiedler GM, Leichtle A, Hentschel H, Stumvoll M. Lead poisoning due to adulterated marijuana in Leipzig. Dtsch Arztebl Int. 2008; 105: 757–62.
- Dryburgh LM, Bolan NS et al., Cannabis contaminants: Sources, distribution, human toxicity and pharmacologic effect. Br. J. Clin. Pharmacol. 2018; 84: 2468–2476.
- Montoya Z, Conroy M, Vanden Heuvel BD, Pauli CS, Park S-H. Cannabis Contaminants: Limit Pharmacological Use of Cannabidiol. Front. Pharmacol. 2020; 11:571832.
- Sullivan N, Elzinga S, Raber JC. Determination of pesticide residues in Cannabis smoke. J. Toxicol. 2013; 1–6.
- McPartland JM, Blanchon DJ, Musty RE. Cannabimimetic effects modulated by cholinergic compounds. Addict Biol. 2008; 13: 411–5.
- Dinis-Oliveira RJ. Metabolomics of Δ9-tetrahydrocannabinol: implications in toxicity. Drug Metab Rev. 2016; 48: 80–7.
- Gartner CE. Mull it over: cannabis vaporizers and harm reduction. Addiction. 2015; 110: 1709–10.
- Tashkin DP. Effects of marijuana smoking on the lung. Ann. Am. Thorac Soc. 2013; 10: 239–47.

- Pizzorno J. What should we tell our patients about marijuana (Cannabis indica and Cannabis sativa)? Dermatol Int. 2016; 15: 8–12.
- 24. Bolan S, Kunhikrishnan A, Seshadri B, Choppala G, Naidu R, Bolan NS, et al. Sources, distribution, bioavailability, toxicity, and risk assessment of heavy metalloids in complementary medicines. Environ Int. 2017; 108: 103–18.
- 25. Tashkin DP. Smoked marijuana as a cause of lung injury. Monaldi Arch Chest Dis. Pulmonary Series. 2005; 63: 93–100.
- 26. Hazekamp A. The trouble with CBD oil. Med. Cannabis Cannabinoids. 2018; 1: 65–72. doi: 10.1159/000489287.
- Vandrey R, Raber JC, Raber ME, Douglass B, Miller C, Bonn-Miller MO. Cannabinoid dose and label accuracy in edible medical cannabis products. JAMA. 2015; 313: 2491– 2493. doi: 10.1001/jama.2015.6613.
- Mcpartland JM, Cubeta MA. New species, combinations, host associations and location records of fungi associated with hemp (Cannabis sativa). Mycol. Res. 1997;101, 853–857.
- Mckernan K, Spangler J, Helbert Y, Lynch RC, Devitt-Lee A, Zhang L. et al. Metagenomic analysis of medicinal cannabis samples; Pathogenic bacteria, toxigenic fungi, and beneficial microbes grow in culture-based yeast and mold tests. F1000Research. 2016; 5: 2471.
- Pitt JL, Basi'Lico JC, Abarca ML, Lopez C. Mycotoxins and toxigenic fungi. Med. Mycol. 2000; 38: 41–46.
- Linger P, Müssig J, Fischer H, Kobert J. Industrial hemp (Cannabis sativa L.) growing on heavy metal contaminated soil: fibre quality and phytoremediation potential. Ind Crops Prod. 2002; 16: 33–42.
- Girdhar M, Sharma N, Rehman H, Kumar A, Mohan A. Comparative assessment for hyperaccumulatory and phytoremediation capability of three wild weeds. Biotech. 2014; 4: 579–89.
- Stone D. Cannabis, pesticides and conflicting laws: The dilemma for legalized states and implications for public health. Regul Toxicol Pharmacol. 2014; 69: 284–8.
- Corroon J, Mackay D, Dolphin, W. Labeling of cannabidiol products: a public health perspective. Cannabis Cannabinoid Res. 2020;1–5.
- Gargani Y, Bishop P, Denning D. Too many mouldy joints marijuana and chronic pulmonary Aspergilliosis. Mediterr J. Hematol Infect Dis. 2011; 3: e2011005.
- Taylor D, Wachsmuth K, Shangkuan Y, Schmidt E, Barrett T, Schrader J, et al. Salmonellosis associated with marijuana. N.Engl J. Med. 1982; 306: 1249–53.
- Bonn-Miller MO, Loflin MJE, Thomas BF, Marcu JP, Hyke T, Vandrey R. Labeling accuracy of cannabidiol extracts sold online. JAMA. 2017; 318: 1708–1709.
- Gauvin DV, Zimmermann ZJ, Yoder J, Tapp R. Marijuana toxicity: Heavy metal exposure through state-sponsored access to "la Fee Verte". Pharmaceut. Reg. Affairs. 2018; 7.
- Daley P, Lampach D, Sguerra S. Testing cannabis for contaminants (Woodlands Hills, CA: BOTEC Analysis Corporation). 2013.
- Jett J, Stone E, Warren G, Cummings KM. Cannabis use, lung cancer, and related issues. J. Thorac. Oncol. 2018; 13:480– 487.
- Lachenmeier DW, Habel S, Fischer B, Herbi F, Zerbe Y, Bock V. et al. Are side effects of cannabidiol (CBD) products caused by tetrahydrocannabinol (THC) contamination? F1000 Research. 2019; 8: 1394.
- 42. Siegel BZ, Garnier L, Siegel SM. Mercury in marijuana. Bioscience. 1988; 38: 619–622.
- Seltenrich, N. Into the weeds: Regulating pesticides in cannabis. Environ. Health Perspect. 2019; 127: 042001.

- Scott M, Rani M, Samsatly J, Charron J.-B, Jabaji S. Endophytes of industrial hemp (Cannabis sativa L.) cultivars: Identification of culturable bacteria and fungi in leaves, petioles, and seeds. Can. J. Microbiol. 2018; 64: 664–680.
- Sarma ND, Waye A, Elsohly MA, Brown PN, Elzinga S, Johnson HE. et al. Cannabis Inflorescence for Medical Purposes: USP Considerations for Quality Attributes. J.Nat. Prod. 2020; 83, 1334–1351.
- Punja ZK, Collyer D, Scott C, Lung S, Holmes J, Sutton D. Pathogens and molds affecting production and quality of Cannabis sativa L. Front. Plant Sci. 2019; 10. doi: 10.3389/fpls.2019.01120.
- Pérez-Moreno M, Pérez-Lloret P, González-Soriano J, Santos-Alvarez I. Cannabis resin in the region of Madrid: Adulteration and contamination. Foren. Sci. Int. 2019; 298, 34–38.
- Sutton S, Lum BL, Torti FM. Possible risk of invasive pulmonary Aspergillosis with marijuana use during chemotherapy for small cell lung cancer. Drug Intell. Clin. Pharm. 1986; 20: 289–291.

- Malabadi RB, Kolkar KP, Chalannavar RK. White and Brown rice- Nutritional value and Health benefits: Arsenic Toxicity in Rice plants. International Journal of Innovation Scientific Research and Review. 2022; 4(7): 3065-3082.
- Malabadi RB, Kolkar KP, Chalannavar RK, Lavanya L, Abdi G. Hemp Helps Human Health: Role of Phytocannabinoids. International Journal of Innovation Scientific Research and Review. 2023; 5 (4): 4340-4349.
- Malabadi RB, Kolkar KP, Chalannavar RK, Lavanya L, Abdi G. Cannabis sativa: Botany, Cross pollination and plant Breeding problems. International Journal of Research and Innovation in Applied Sciences (IJRIAS). 2023; 8(4): 174-190.
