International Journal of Life Science Research Archive
ISSN: 0799-6640 (Online)
Journal homepage: https://sciresjournals.com/ijlsra/

(Review Article)

INDUSTRIAL *CANNABIS SATIVA* (HEMP): BIOPESTICIDE-AN UPDATED REVIEW

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International Journal of Life Science Research Archive, 2026, 11(01), 037–051

Publication history: Received on 12 June 2026; revised on 18 July 2026; accepted on 10 August 2026

Article DOI: https://doi.org/10.53771/ijlsra.2026.11.1.0063

ABSTRACT

This review paper of literature highlights and updates on the use of hemp plant extract and essential oil (EOs) as the biopesticide for the agriculture crop pest management. Industrial *Cannabis sativa* L. (Hemp) belongs to the family *Cannabaceae* is a short-season crop with many applications which is used as a functional food, fibre, 3D printed building material, hempcrete, biopesticide, biochar, bioplastic, paper, textile, biofuel, oil, cosmetics, skincare, animal bedding, ropes, medicine and as a replacement for graphene in supercapacitors. One of the main roles of phytochemicals in plants is to offer a variety of defenses against insects, parasites, and predators. For this reason, plant-based pesticides are emerging as safe, efficient, and environmentally friendly substitutes for chemical pesticides in the fight against plant diseases and arthropods that transmit diseases to humans and animals. Biopesticides are pest management agents and chemicals derived from natural sources such as bacteria, fungi, viruses, plants, animals and minerals. As for hemp, several studies have revealed that aqueous and solvent extracts, as well as essential oils (EOs) and purified phytochemicals from leaves or inflorescences effectively repel and/or inhibit the growth of insects and plant microbial pathogens. Therefore, plant-based biopesticides constitute a small but important group of biopesticides. Many biopesticides are more environmentally friendly than synthetic pesticides. However, there are some limitations that restrict the widespread use of such biopesticides. These limitations include cost, difficulties in production, gentle action, and use of appropriate biopesticide formulations.

Keywords: Biopesticide, *Cannabis sativa*, Essential Oil (EO), Hemp, Pest Management application

1 INTRODUCTION

Cannabis sativa L. belongs to the family *Cannabaceae* was used as a medicine before the Christian era in Asia**,** mainly in India**,** China, Bhutan, Nepal, Afghanistan, Pakistan, Egypt, Africa, Iran, Persians and Latin America [1-59]. *Cannabis sativa* L., is classified into two types as Industrial *Cannabis sativa*, hemp or fibre type and Medical *Cannabis sativa* L. (drug or marijuana) based on its THC content [1-59-60]. Medical *Cannabis sativa* (drug or marijuana) contains a very high levels of THC (above 0.3 to 38% of dry weight) [1-40-57]. On the other hand, Industrial *Cannabis sativa* L. (Hemp) contains very low levels of THC (0 to 0.3% of dry weight) [1-57-61, 118, 119]. Both types medical and hemp are genetically modified and belongs to one genus *Cannabis*. Industrial *Cannabis sativa* L. (Hemp) is a short-season crop with many applications which is used as a functional food, fibre, 3D printed building material hempcrete, biochar, bioplastic, paper, textile, biofuel, oil, cosmetics, skincare, animal bedding, ropes, medicine and as a replacement for graphene in supercapacitors and biopesticide [1-57, 112]. More than 500 compounds including cannabinoids, terpenes, phenolics, phytosterols, and tocopherols are accumulated in leaves, flowers, and seeds, which are typically considered waste products in the fiber industry [1-59,101-114, 118. 119, 120]. However, hemp phytochemicals also find applications in other industrial sectors, including agrochemistry as natural insecticides, cosmetics for skin and hair care, and food and dietary supplements due to their associated health benefits [1-57-87,112, 118, 119, 120].

Biopesticides are pest management agents and chemicals derived from natural sources such as bacteria, fungi, viruses, plants, animals and minerals [101-117]. Also known as biological pesticides, they can provide an alternative to synthetic chemicals used to control pest populations in crop production and other settings [101-114]. Biopesticides can be used by anyone looking for an alternative pest management approach, such as commercial growers, specialty crop growers, ornamental plant growers, or household gardeners [101-117]. Plant-based biopesticides are natural, biodegradable compounds derived from plants that control pests with minimal environmental impact [101-117]. Pests include diseases, insects, mites, and weeds that damage crops and reduce crop yield and quality. Many biopesticides are more environmentally friendly than synthetic pesticides. For instance, many biopesticides target specific pests and have little negative impact on the surrounding ecosystem and human health [101-117]. The commercially used synthetic pesticides have been proven to be toxic not only to humans and other animals, but also to non-target plant, the surrounding organisms around the plant, and the environment [101-117]. There are also increased concerns regarding the development of pest resistance towards these synthetic pesticides [101-117]. As such, biopesticides, which are defined as the certain kinds of pesticides derived from natural sources such as plants, bacteria, fungi, animals and some minerals, are potential alternative pesticides and are gaining increasing attention. Biopesticides are safer and eco-friendly pesticides used for pest management [101-117]. Among these, plant-based biopesticides constitute a small but important group of biopesticides [101-117]. Plant based extracts and essential oils have been particularly used in the management of insects exhibiting a variety of anti-insecticidal mechanisms [101-117]. Their chemical compositions are very complex and acquiring resistance by the pest against such biopesticide is very difficult [101-117]. As far as their mechanism of action is concerned, these can act as insect repellants, insect attractants, or anti-feedants [101-117]. They can also inhibit respiration or they can obstruct the host plant identification [101-117]. These insecticides can inhibit oviposition and decrease adult emergence by ovicidal and larvicidal effects [101-114]. Some of the essential oil based insecticides have even been commercialized for use [101-117]. However, there are some limitations that restrict the widespread use of such biopesticides [101-117]. These limitations include cost, difficulties in production, gentle action, and dearth of appropriate biopesticide formulations [101-114]. As far as their regulations are concerned, it is still a problem in many countries further halting biopesticide use. But one thing is clear that biopesticides do have a promising future due to their eco-friendly nature and unique chemical compositions and unique mode of action [101-117]. Examples include **neem oil** (azadirachtin) for insects, **pyrethrins** (chrysanthemum) as insecticides, **garlic/onion extracts** as repellents, and **essential oils** (thyme, rosemary) for fungal control [101-114]. In the following section the importance of the biopesticides from plant extracts, and esssential oils from hemp has been updated and discussed.

2 INDUSTRIAL *CANNABIS SATIVA* (HEMP): BOTANY AND PHYTOCHEMICALS

Industrial hemp, *Cannabis sativa* L., is an herbaceous, diploid, dioecious plant in the family *Cannabaceae* [1-101-114]. Morphological differentiation of male and female hemp plants becomes evident shortly before the onset of sexual maturation [1-111]. Male plants grow taller, with a more slender appearance, develop fewer fan leaves, and rapidly senesce after pollen shed compared to female plants, which have a shorter, bush-like appearance and an extended reproductive period [1-101-114]. Male inflorescences comprise loose, hanging panicles that bear flowers composed of five sepals [1-111].These sepals act to protect the male reproductive organs [1-111]. Female inflorescences occur at the apical portion of the main stem or leaf and lateral branch axils, depending on plant grooming practices during the vegetative stage [1-111-114]. The female flower is composed of an ovary encapsulated by a perianth and a trichome-dense bract. Floral hemp producers aim to maintain a fully feminized crop, as female flowering structures produce high levels of glandular trichomes [1-111-114]. These trichomes are the site of cannabinoid biosynthesis in hemp plants [1-111]. Fertilization from male plants can significantly reduce the overall concentration of extractable cannabinoids compared to unfertilized females, so male plants are removed if detected. Hemp grown and harvested for seed, grain, and fiber is generally a mix of male and female plants [1-90-112]. The taxonomic status of the genus *Cannabis* has long been in question and is not yet fully resolved. *Cannabis* has been classified as a polytypic genus with at least three distinct species, *C. sativa L., C. indica Lam.,* and *C. ruderalis* Janisch, citing differences in plant height, leaf morphology, leaf arrangement, and hemp pollen grain apertures in support of multiple species [1-90-114].

Cannabinoids are a group of phytochemicals that, together with terpenes, are synthesized and accumulated in the glandular trichomes that coat the inflorescences and most of the aerial parts of the C. sativa plant [1-90-114]. Low amounts of cannabinoids have also been detected in the roots, whereas their presence in the seeds is the result of contamination during the harvesting process, when the seeds can come into contact with the inflorescences and leaves [1-12-112]. The most abundant cannabinoids found in *C. sativa* plants are THC, CBD, CBG and cannabinol (CBN) [1-10-114]. Female inflorescences are the primary source of cannabinoids, making them the ideal starting material for extracting these compounds for use in cannabinoid-based products [1-99-113].

Products derived from hemp seeds and hemp seed oil have become commonplace in grocery stores and cosmetic retailers [1-90]. The recent rise in popularity of plant-based alternatives for traditional animal products has provided a place for hemp-based foods, such as hemp seed milk, butter, and protein powder, to emerge in mainstream markets [1-90-114]. Hemp seeds are a nutritious food source for humans as they provide all nine essential amino acids, high levels of polyunsaturated fatty acids, and a desirable ratio of omega-6 to omega-3 fatty acids [1-90-114]. The bioactive peptide-protein profile of hemp oil has shown to have anti-inflammatory, antioxidant, and antihypertensive properties. Hemp has been grown primarily for its fiber, which has been used for thousands of years for a variety of purposes, including clothing and shoes, ropes and cords, and papermaking; also, hemp seeds have been used as a food ingredient, and leaves as compost, mulch, and animal bedding [1-114].

More than 500 phytochemical compounds have been identified in *C. sativa*, including 125 cannabinoids, 120 terpenes, 42 phenols, and 34 flavonoids [1-5-114]. Tocopherols and phytosterols are also present, albeit in lower amounts [1-5-114]. Cannabinoid compounds found in plants are called phytocannabinoids [1-5-114]. When comparing the aqueous extract of cannabis with the extract in organic solvents in terms of efficacy as a biopesticide, it is understood that both types of extracts show the effects between the scale of not repelling pests at all or killing all pests, so they are similar in effectiveness [1-5-114]. Cannabinoids, naturally occurring compounds found in hemp plants, may have evolved to deter pests from chewing on them, according to experiments that showed higher cannabinoid concentrations in hemp leaves led to proportionately less damage from insect larvae [1-5-114]. According to the recent studies, potentially developing pesticides from cannabinoid extracts, though such uses would be limited to non-edible plants, given the pharmacological properties of the compounds, which include CBDA, THCA and their precursor CBGA [1-5-114]. These compounds are naturally produced by hemp plants and convert to more commonly known CBD, THC and CBG when heated. Researchers have hypothesized that cannabinoids may protect plants from ultraviolet light, pathogens and herbivores [1-5-114]. It has been speculated that they are defensive compounds, because they primarily accumulate in female flowers to protect seeds, which is a fairly common concept in plants [1-5-114]. The potential use of cannabinoids as a pesticide is an exciting area for future research, but there will certainly be regulatory barriers due to pharmacological activity of the compounds, and more studies are needed to understand what pests cannabinoids will be effective against plant pathogens [1-5-114]. Cannabidiol (CBD), cannabigerol (CBG), and cannabichromene (CBC) are three high-value cannabinoids of interest that have led to increased acreage of feminized hemp plants grown solely for trichome-rich inflorescences, commonly referred to as flowering buds [1-5-112]. Cannabinoid-rich oil extracted from flower buds has been used in clinical settings to assist in the treatment of anxiety disorders, posttraumatic stress disorder, schizophrenia, Parkinson’s disease, breast cancer cell development, dystonia, and epilepsy [1-5-114]. However, beyond their potential pharmaceutical applications, hemp phytochemicals are increasingly recognized for their use in agrochemical, cosmetic, and food industries. Hemp phytochemicals are successfully employed in the production of natural pesticides due to their insecticidal properties [1-5-114]. For their antiaging, antioxidant and moisturizing effects, they are used as ingredients in skincare and haircare products [1-8-80]. Additionally, hemp phytochemicals add nutraceutical value and potential health benefits to a range of food products and dietary supplements that contain hemp and its derivatives as ingredients [1-9-113].

3 BIOPESTICIDES

Biopesticides are pest control products derived from natural sources such as microbes, macro-organisms (insects and pathogens), plant extracts, and certain minerals [101-114]. Biopesticides are naturally derived pest control compounds that offer a relatively safer and target-specific complement to conventional chemical pesticides [101-114]. Biopesticides include 1) Biochemicals (plant extracts, biochemicals, microbial extracts/fermentation products, insect growth regulators, compounds synthesized by other organisms, and inorganic compounds), 2) microbial biopesticides (bacteria, fungi, protozoa, viruses, oomycetes, yeast, and algae), 3) macrobials (insect predators, parasitoids, and entomopathogenic nematodes) and classical biocontrol agents [101-114]. Many biopesticides are considered environmentally safe and can complement or substitute conventional chemical pesticides [101-114]. They can also be highly specific or broad spectrum with a unique mode of action controlling a wide range of pest species. Due to their target-specificity and low to no environmental residuality, biopesticides conform to the 3 pillars of Climate-Smart Agriculture, the Sustainable Development Goals, and, ultimately, the Paris Agreement [101-114].

Biopesticides play a crucial role in promoting climate-smart agriculture (CSA) by offering effective pest management solutions, improving crop yield and quality, and reducing pest resistance while minimizing negative impacts on human health and the environment [101-114]. The growing need for biopesticides is partly a consequence of the decrease in the use of conventional pesticides due to farmers increasingly adopting climate-smart agricultural practices and reducing their carbon footprint [101-114]. This shift is driven by several advantages associated with biopesticides, including 1) their ability to slow down the development of pest resistance, 2) low to no toxicity to humans and the environment, hence safeguarding biodiversity, preserving soil health and enhancing food security, 3) their ability to complement chemical pesticides, 4) their low environmental fate, 5) host specificity, 6) biodegradability, 7) minimal risk of post-harvest contamination, 8) resilience against environmental stresses, and 9) compatibility with IPM practices [101-114]. Bopesticides may, however, not be equally effective against all pests, and their efficacy can vary depending on the target species. Additionally, some pests may have natural resistance or tolerance to certain biopesticides [101-114].

Biopesticides offer several advantages over conventional chemical pesticides, including lower toxicity to non-target organisms, reduced environmental impacts, and less likelihood of developing resistance to pests [101-114]. Biopesticides effectively control insects, diseases, weeds, and nematodes, promote plant health, and enhance the productivity and profitability of farmers. Importantly, many of them are non-toxic to beneficial organisms and wildlife [101-114]. Additionally, their biodegradability reduces pollution concerns associated with many chemical pesticides. Due to their targeted action and effectiveness in small quantities, biopesticides are gaining wide application on plants and crops. They are playing an increasingly significant role in agriculture, promoting sustainable practices and a healthier environment, thus complying with the climate-smart agriculture principles (FAO 2017), and, ultimately, the Paris Agreement (United Nations 2015), the Nagoya Protocol of Article 6 [101-114].

Biopesticide is a generic term generally applied to a substance derived from nature, such as a botanical or semiochemical, that may be formulated and applied like a conventional chemical pesticide and that is normally used for short-term pest control [101-114]. Naturally derived or laboratory-made chemicals with structures and functions similar to naturally occurring ones are known as biochemical pesticides. They differ from traditional pesticides in their origin (source) and how they control or kill pests. Microbial pesticides are natural pest control agents harnessing the power of microscopic living organisms [101-114]. These “living bullets” can be either spores or active organisms, often specifically chosen for their pathogenic nature towards targeted pests. Common examples include biofungicides (Trichoderma, Pseudomonas, Bacillus, Colletotrichum), bioherbicides (Phytophthora, Cylindrobasidium, Colletotrichum acutatum), and bioinsecticides (Bt) [101-114]. Microbial biopesticides can originate from naturally occurring or genetically modified bacteria, fungi, algae, viruses, or protozoans. They subdue pests through a diverse range of strategies (toxic metabolites, disease-causing, competitive exclusion, and other modes of action), depending on the specific microbe [101-114].

Despite the benefits, several challenges can hinder the widespread adoption of biopesticides. Novel microbial strain creation with improved features, such as greater efficacy and larger target spectra, should be prioritized in future research and the use of biopesticides [101-114]. To maximize their efficiency and reduce the possibility of resistance, biopesticides’ modes of action must be understood. Along with other tactics, using biopesticides in complete pest management programs can improve overall pest control. The stability, adhesion, and targeted distribution of biopesticides will be improved through improvements in formulation and delivery techniques [101-114]. Risk assessment and regulatory frameworks must be created to guarantee the safety and effectiveness of biopesticides. To encourage knowledge and acceptance of biopesticides, efforts should be made to educate and raise public awareness [101-114]. Collaboration and knowledge sharing among researchers, stakeholders, and regulatory agencies will facilitate progress in the field. By focusing on these recommendations, biopesticides can contribute to sustainable and environmentally safe pest management practices in agriculture [101-114].

4 INDUSTRIAL *CANNABIS SATIVA* (HEMP): BIOPESTICIDES

Pests and diseases have caused significant problems since the domestication of crops, resulting in economic loss and hunger [89-101-114]. To overcome these problems, synthetic pesticides were developed to control pests; however, there are significant detrimental side effects of synthetic pesticides on the environment and human health. There is an urgent need to develop safer and more sustainable pesticides [89-101-114]. The negative factors of synthetic pesticides such as side effects on the environment and humans, resistance development due to high amounts of application, and positive factors of biopesticides such as milder side effect profile, sustainability and cheap and easier extraction formulation possibilities it is understandable that why the balance started to shift towards biopesticides [89-101-114]. Herbal products such as thyme, garlic, cinnamon, and mint are known to be used by the public for protection from mosquitoes and various harmful organisms [89-101-114].

Industrial hemp is a reservoir of compounds that could potentially replace some synthetic bactericides, fungicides, and insecticides [1-89-101-114]. Hemp was also used before the great advent of synthetic pesticides. Repellants obtained from hemp were used against pests such as mites, fleas and mosquitoes that bother people, and against arthropods that feed on plants [68-89-101-114]. In this context, hemp can play a role in the fight against pests in various ways and areas such as planting it together with the crops, by using its fresh or dried parts directly, by applying its water based or various solvent based extracts or by using the oils they contain [1-89-101-114]. There is an urgent need to develop safe, affordable, and effective natural biopesticides, and medicinal plants are a huge reservoir of these potential biopesticides [89-101-114]. Industrial hemp, which contains phytocompounds such as cannabinoids, terpenes, flavonoids, and alkaloids, has been used medicinally for its anti-inflammatory, antimicrobial, and antifungal properties [15–17-114]. However, little is known about its ability to combat plant pathogens. Cannabis essential oils contain sesquiterpenes such as nerolidol, caryophyllene, and caryophyllene oxide, along with monoterpenes such as pinene, linalool, and limonene; all known for their antimicrobial properties [1-18-114]. Pinene inhibits bacterial growth, myrcene disrupts cell membranes, terpineol and linalool have antibacterial activity, limonene exhibits bactericidal and antibiofilm properties, and nerolidol inhibits the growth of various parasites [1-19–22-114]. Caryophyllene, with antioxidant and anti-inflammatory properties, demonstrates antimicrobial activity without cytotoxicity. There is an urgent need to develop safe, affordable, and effective natural biopesticides, and medicinal plants are a huge reservoir of these potential biopesticides. Industrial hemp, which contains phytocompounds such as cannabinoids, terpenes, flavonoids, and alkaloids, has been used medicinally for its anti-inflammatory, antimicrobial, and antifungal properties [15–17-114]. However, little is known about its ability to combat plant pathogens. Cannabis essential oils contain sesquiterpenes such as nerolidol, caryophyllene, and caryophyllene oxide, along with monoterpenes such as pinene, linalool, and limonene; all known for their antimicrobial properties [1-18-114]. Pinene inhibits bacterial growth, myrcene disrupts cell membranes, terpineol and linalool have antibacterial activity, limonene exhibits bactericidal and antibiofilm properties, and nerolidol inhibits the growth of various parasites [1-19–22-114]. Caryophyllene, with antioxidant and anti-inflammatory properties, demonstrates antimicrobial activity without cytotoxicity [1-23,24-114].

Kanyairita et al., (2024) [88] determined the efficacy of industrial hemp extracts against Pseudomonas syringae pv. tabaci (PSTA), Pseudomonas syringae pv. tomato (PSTO), and Erwinia carotovora (EC) [88]. This study by Kanyairita et al., (2024) [88] revealed a minimum inhibitory concentration (MIC) of 2.05 mg/mL and a non-inhibitory concentration (NIC) of 1.2 mg/mL for PSTA, an MIC of 5.7 mg/mL and NIC of 0.66 mg/mL for PSTO, and an MIC of 12.04 mg/mL and NIC of 5.4 mg/mL for EC [88]. Time-kill assays indicated the regrowth of E. carotovora at 4 × MIC after 15 h and P. syringae pv. tomato at 2 × MIC after 20 h; however, P. syringae pv. tabaci had no regrowth [88]. The susceptibility of test bacteria to hemp extract can be ordered from the most susceptible to the least susceptible, as follows: P. syringae pv. tabaci > P. syringae pv. tomato > E. carotovora. Kanyairita et al., (2024) [88], confirmed that hemp extract is a potential source of sustainable and safe biopesticides against these major plant pathogens [88].

The data by the study of Kanyairita et al., (2024**)** [88] showed the susceptibility of the test bacteria to hemp extract, ordered from the most susceptible to the least susceptible, as follows: *P. syringae pv. tabaci > P. syringae pv. tomato > E. carotovora*. This study indicates that hemp extract is effective in controlling *E. carotovora*, *P. syringae pv. tabaci*, and *P. syringae* pv. tomato. However, the hemp extract is more effective against both *Pseudomonas* spp. than *E. carotovora.* More than 50% of the oil content consists of monoterpene hydrocarbons. For example, during the trial of three different biopesticides and cannabidiol on *Sitophilus zeamais, Rhyzopertha dominica, Prostephanus truncatus* and *Trogoderma granarium* beetles has been reported. he major compounds of hemp essential oil were found to be *β*-caryophyllene, myrcene and terpinolene during the trial of hemp essential oil in comparison with *Humulus lupulus* essential oil on *Aedes albopictus* mosquito and *Physella acuta* freshwater snail.

Pellegrini et al., (2021) [105] reported antibacterial activity in the essential oil of Futura 75 inflorescences, a variety of Cannabis sativa L., against *Staphylococcus aureus* and *Listeria monocytogenes*, with an MIC ranging from 1.25–5 μg/mL but ineffective against Salmonella enterica [105]. The oil also exhibited antioxidative properties. In addition, insecticidal activity was observed for some selected insects and they proposed that the insecticidal effect could be attributed to the inhibition of acetylcholinesterase [105]. A study comparing the antimicrobial properties of essential oils from wild hemp inflorescences harvested from northeast Serbia and EU-registered cultivars also highlighted the wide range of CBD concentrations in these wild hemp essential oils (6.9–52.4%) [105]. The wild hemp essential oils assayed showed superior antimicrobial activity against pathogens, including *Staphylococcus aureus, Enterococcus faecalis, Streptococcus pneumoniae, Pseudomonas aeruginosa, Yersenia enterocolitica, Salmonella enterica, Candida albicans, Candida krusei,* and *Candida tropicalis* [105]. Moreover, Naveed et al., (2014) [106] reported the antimicrobial activities of the ethanol extracts of hemp leaf against several pathogenic bacteria using the inhibition zone assay, showing the possibility of using leaf extracts in place of the more commonly used inflorescence extracts controlling bacteria [106]. According to the study reported by, Naveed et al., (2014) [106] none of the studies investigating the antimicrobial activity of hemp extracts reported their activity against the plant pathogens *E. carotovora, P. syringae pv. tomato,* and *P. syringae pv. tabaci* [106]. The great variability in the composition of hemp essential oils probably contributes to contradictory results with respect to antimicrobial activity against the same microbial species [106]. Therefore, more research is needed on the antimicrobial activities of industrial hemp extracts against plant pathogens to improve our understanding of the antimicrobial activities of industrial hemp phytocompounds and their potential for commercial use [106].

Antibacterial activites of industrial hemp phytocompounds against human pathogenic bacteria, very few have examined antimicrobial activities against plant pathogens. Novak et al., (2001) [104] explored the antibacterial properties of essential oils derived from five different cultivars of Cannabis sativa L. containing compounds such as pinene, myrcene, trans-ocimene, terpinolene, trans-caryophyllene, and humulene, with undetectable or extremely low levels of delta-9-tetrahydrocsaannabinol (THC) and other cannabinoids [104]. The study revealed antibacterial activity against some common bacteria, including Staphylococcus aureus, *Acinetobacter calcoaceticus, Beneckea natriegens,* and *Brochothrix thermosphacta* in all five oils [104].

Although various studies have been conducted to determine the antimicrobial activities of industrial hemp phytocompounds against human pathogenic bacteria, very few have examined antimicrobial activities against plant pathogens. Novak et al., (2001) [104] explored the antibacterial properties of essential oils derived from five different cultivars of Cannabis sativa L. containing compounds such as pinene, myrcene, trans-ocimene, terpinolene, trans-caryophyllene, and humulene, with undetectable or extremely low levels of delta-9-tetrahydrocsaannabinol (THC) and other cannabinoids. The study revealed antibacterial activity against some common bacteria, including *Staphylococcus aureus, Acinetobacter calcoaceticus, Beneckea natriegens*, and *Brochothrix thermosphacta* in all five oils [104]. Nissen et al., (2010) [107] discovered antibacterial effects in essential oils of Cannabis sativa L. seeds against Gram-positive bacteria such as *Enterococcus faecium* and *Streptococcus salivarius* at concentrations below 1% (v/v) [107]. However, yeast, which was included in the same study, was unaffected [107]. Zengin et al., (2018) [108] identified the antioxidant properties of hemp essential oils, which show significant antibacterial activity against clinical strains of Helicobacter pylori. The MIC for hemp essential oil was 16–64 μg/mL for Helicobacter pylori and 8 mg/mL for Staphylococcus aureus [108].

Mazzara et al. , (2023) [109] are of the opinion that, the need for sustainable and effective products for mosquito vector control, which can represent a valid alternative to synthetic agents leading to insecticide resistance phenomena, is urgently crucial [109]. In this respect, green pesticides appear to be promising, due to less harmful effects on the environment and the human health, a limited residuality, and fewer resistance issues, with respect to those of the chemical products [109]. Hemp represents one of the most available crops for industrial exploitation due to its several uses in different sectors [109]. In particular, hemp EOs are recognized as safe, and endowed with insecticidal properties which make them exploitable as valuable eco-friendly botanical pesticides [109]. For this purpose, EOs encapsulation in NEs has turned out to be one of the most promising strategies to improve EOs physicochemical characteristics, bioavailability, and administration [109]. According to research, hemp-derived essential oils could be applied against a range of well-known pests across crop types, such as the Egyptian cotton leafworm (*Spodoptera literalis*), tobacco hornworm (*Manduca sexta*) and aphid species including the peach-potato aphid (*Myzus persicae*) [109]. They have also been shown to be effective against insects posing health risks, such as mosquito species from the genus *Anopheles* and the housefly, *Musca domestica*, as well as pests of stored foods such as the Indian meal moth (*Plodia interpunctella*) and *Callosobruchus chinensis,* a type of bean weevil [109].

The latest development on hemp coming from Cornell University (Ithaca, New York) , is that cannabinoids derived from the plant may be the new foundation for natural pesticides [110]. Research conducted by Larry Smart, a plant breeder and professor at the Cornell AgriTech's College of Agriculture and Life Sciences (CALS) (Ithaca, New York), showed that there was fewer damage caused from pests due to the higher cannabinoid concentrations found in hemp leaves [110]. The study was published in the journal Horticulture Research in November 2023 [110]. Data from this study will inspire further research to be done on natural pesticides which would be utilized only on non-edible plants. Research over the years has investigated the cannabinoids found in the cannabis and hemp plants [110]. The theory from researchers is that these cannabinoids may help and provide plants protection from herbivores, ultraviolet light, and pathogens. It has been speculated that they are defensive compounds, because they primarily accumulate in female flowers to protect seeds, which is a fairly common concept in plants," said Lawrence Smart, the senior author of the study [110]. But no one has put together a comprehensive set of experimental results to show a direct relationship between the accumulation of these cannabinoids and their harmful effects on insects [110]. The study gives us insight into how cannabinoids function in natural systems, and can help us develop new tetrahydrocannabinol-compliant (THC-compliant) hemp cultivars that maintain these natural built-in defenses against herbivores [110]

According to the study conduced by Trono (2026) [112], purified hemp phytochemicals, have exclusively focused on cannabinoids and most of them have tested the effect of these compounds on insects harmful to plants [112]. The first study dates back to the 1980s when Rothschild and Fairbairn [71, 112] sprayed the surface of cabbage leaves with 1% CBD or 1% THC and observed that the cabbage butterfly (*Pieris brassicae*) laid 2–3 times less eggs on leaves sprayed with THC than on those sprayed with CBD [71, 112]. The insecticidal and/or anti-feedant activity of cannabinoids against herbivorous insects has also been highlighted by recent studies. The feeding study carried out by Park and coworkers [72] revealed that the addition of 2 mM CBD to the diet of the tobacco hornworm (*Manduca sexta*), a common pest of plants in the *Solanaceae* family, inhibited the growth and development of the larvae and increased their mortality. Similarly, Stack and coworkers [73] observed that the addition of CBDA or CBGA at concentrations ranging from 0.1% to 1.0% to the diet of the cabbage looper (*Trichoplusiani*), a serious pest of cruciferous plants, decreased the growth and survival of the larvae, up to reach 100% mortality at the highest concentration, whereas Abendroth and coworkers [74] observed that the larvae of the fall armyworm (*Spodoptera frugiperda*), a pest that damages a wide variety of crops, showed a dose-dependent decrease in growth and consumption when fed CBD concentrations ranging from 5% to 15% [74, 112]. CBD also showed pesticidal effect against stored product pests [112, 113]. A dose-dependent larvicidal activity was reported for 3% CBD oil against larvae of flou beetle (*Tribolium confusum*), saw-toothed grain beetle (*Oryzaephilus surinamensis*), and meal moth (*Plodia interpunctella*), which infest wheat, rice and corn seeds, with a mortality of up to 100% for the first two and 76% for the third one at the highest dose tested (90 mg mL^{-1}) [112, 113].

Trono (2026) [112] also of the opinion that, it is unclear how exactly CBD affects insects, which are known to lack the canonical cannabinoid CB1 and CB2 receptors [112]. A number of studies have reported the ability of CBD to modulate different biochemical targets in insects, likely through the interaction with other G-protein-coupled receptors. For instance, the reduced growth of *S. frigipeda* larvae fed increasing doses of CBD was found to be accompanied by a decrease in protease and cytochrome P450 activities, which might limit the detoxification response of the larvae by lowering the availability of amino acids required for the biosynthesis of the detoxifying enzymes [112]. Further, CBD-fed M. sexta larvae presented altered signal transduction of the ventral ganglion [33], and down-regulation of genes involved in exoskeleton development, such as cuticle-like and endochitinase, which led to a decrease in the amount of cuticle deposited [112].

Several studies have been carried out on the pesticidal properties of hemp extracts from leaves or inflorescences obtained by using different solvents [68, 112]. As for the insects harmful to humans, the methanolic extract from leaves of cultivar Tango Kush showed a dose-dependent larvicidal effect against the yellow fever mosquito, reaching 100% mortality at 100 μL L^{-1} for both pyrethroid-susceptible and pyrethroid-resistant strains [68, 69, 112]. When the extract was dried and the crude residue was partitioned between methanol and hexane, the larvicidal activity was detected only in the methanolic fraction. The analysis of the phytochemical profile revealed that CBD was the predominant component in the hemp extract and that 80% of this compound was recovered in the methanolic fraction [68, 112]. This prompted the authors to hypothesize that CBD was the main responsible for the observed larvicidal activity [68, 112]. Consistently, authentic CBD produced a concentration-dependent mortality in the mosquito larvae that was indistinguishable from the hemp leaf extract standardized for CBD concentration [68, 112]. Extracts from hemp inflorescences and leaves were also tested against plant pathogens [68- 112]. The ethanolic extract from the inflorescences of the cultivar Cherry Dwarf, containing CBD as the main compound, was found to be toxic against the bacteria Pseudomonas syringae pv. tomato, *P. syringae* pv. tabaci, and *Erwinia carotovora*, which cause diseases in tomato, tobacco, and other crops, achieving 100% growth inhibition at concentrations ranging from 6.5 to 12.5 mg mL^{-1} [68, 112]. Also, an ethanolic extract obtained from the lateral inflorescences of the cultivar Futura 75, in which the polyphenolic component predominated, showed a dose-dependent antifungal activity against fungi responsible for various plant diseases, inhibiting growth up to 75.42–84.79% for *Alternaria alternata, Botrytis cinerea, Colletotrichum coccodes,* and *Trichoderma koningii*, and up to 38.80–72.95% for the *Fusarium* spp. [68, 112]. The ethanolic extract from inflorescences of the cultivar Helena, characterized by the presence of phenolic compounds (4.71 mg g^{-1}) mainly represented by flavonoids (4.40 mg g^{-1}), was found to be effective against the Indian meal moth (*Plodia interpunctella*), a major pest of stored seeds and derived products [68, 112]. At the highest concentration tested (2%), the extract determined a significantly reduced female fecundity (−79%), a prolonged insect's developmental duration (+37%), and up to −81% emerged moths [68, 112]. As emerged from the aforementioned studies, the phytochemical profile of the methanolic and ethanolic hemp extracts includes different classes of bioactive compounds, mainly cannabinoids, terpenes, phenols and flavonoids, which can all contribute to the toxic action of the extract. As for the phenolic compounds, evidence exists that, when used in their pure form, these compounds adversely affect the growth, feeding, oviposition and fecundity of a wide number of insects responsible for plant diseases [112], as well as insects harmful for animal and human health [61]. Similar to terpenes, these compounds act on the nervous system of the insect by negatively affecting the acetylcholinesterase activity [68, 112]. In addition, evidence has been reported on the flavonoid ability to inhibit insect digestive enzymes, such as amylases, glycosidases, proteases, and lipases, which would be responsible for the antifeeding activity of this class of compounds, and to induce oxidative stress through the modulation of the detoxifying enzyme activities [68-112]. Phenolic compounds have also been reported to damage insect DNA by binding covalently to it and causing its fragmentation [68-112].

5 HEMP ESSENTIAL OIL (EO): BIOPESTICIDE

According to the literature survey, numerous studies have highlighted a toxic effect of EOs isolated from different hemp cultivars and tissues on insects and other organisms harmful to humans [112]. Recent studies concluded that cannabis extract removes house fleas and crickets from the environment, while the juice obtained by squeezing the fresh leaves of hemp can affect the earwig insect species [89-101-114]. However, it was observed that the adult forms and larvae of potato beetles disappeared within 45 minutes when hemp aqueous extract was applied in the same way on a potato plant infested by *Leptinotarsa decemlineata* type insects [60-89-101-114]. Wanas and coworkers [75] tested the insecticidal activity of an EO obtained from hemp inflorescences against the yellow fever mosquito (*Aedes aegypti*) and observed that the EO had a biting deterrent activity comparable to that observed for N,N-diethyl-meta-toluamide, one of the most effective insect repellents [75, 112], along with a low LC90 (90% lethal concentration) value (38.7–38.9 ppm) [75, 112]. Interestingly, the authors also found that hemp EO had a significantly greater insecticidal activity than EO from a chemotype II cultivar (LC90 of 40.6–42.6 ppm), whereas EO from a chemotype I cultivar was ineffective [75, 112]. Additionally, EOs derived from the inflorescences of three distinct cultivars, Futura 75, Felina 32, and Kompolti, were found to be effective, albeit to varying degrees, against southern house mosquito (*Culex quinquefasciatus*) larvae (LC90 ranging from 142.3 μL^{-1} to 700.9 μL^{-1}) and housefly (*Musca domestica*) adults (LD90 ranging from 212.9 μg adult $^{-1}$ and 213.5 μg adult $^{-1}$) [75, 112]. The EO derived from the leaves of cultivar Futura 75 was also found to be effective against these two insects, but less so than the EO extracted from the inflorescences of the same cultivar (LC90 of 410.3 μL^{L-1} vs. 199.1 μL^{L-1} for mosquito larvae and LD90 of 428.7 μg adults−1 vs. 212.9 μg adults $^{-1}$) [75, 112]. Other mosquito species highly sensitive to hemp EOs were the malaria vectors *Anopheles stephensi* and *Anopheles gambiae* that, when exposed to 100 ppm EOs from the inflorescences of the monoecious cultivar Felina 32 or from the male and female inflorescences of the dioecious cultivar *Carmagnola selezionata,* showed 82.7–91.6% and 79.6–100% mortality of larvae and pupae, respectively [112, 114]. Albeit with low efficacy (LC90 of 693.999 μL^{L-1}), a commercial EO was found to be effective against the larvae of the Asian tiger mosquito (*Aedes albopictus*) that can transmit several diseases including dengue, chikungunya and Zika [112, 114]. The same EO was successfully tested against the freshwater snail (*Physella acuta*), an intermediate host for nematodes and trematodes that cause diseases in animals and humans, achieving 100% mortality at a concentration of only 100 μL^{L-1} [75, 112].

The toxic activity of hemp EOs against insects and parasites observed in the reported studies may be attributed to α-pinene, myrcene, *β*-caryophyllene, α-humulene and terpinolene that, although at different percentages, have always been detected as the most abundant compounds in the EOs tested [75-112]. This assumption is supported by the numerous observations that, when used as pure compounds, these molecules showed high toxicity against insects and other pests [112]. By way of example, *α*-pinene was found to be toxic against the mosquitos *A. aegypti* [112] and *Culex pipiens* molestus, and together with *β*-caryophyllene demonstrated excellent toxicity against M. persicae [112]. A toxic activity against *A aegypti* was also shown by myrcene , whereas *β*-caryophyllene and *α*-humulene were found to be highly toxic against the tick *H. dromedarii* and the mite *D. gallinae*, which may explain the acaricidal activity shown by the hemp EO on these two ectoparasites [112]. Insecticidal and larvicidal activities were also widely demonstrated for terpinolene [112].

Regarding the mechanism underlying the toxic activity of the EOs against insects and other parasites, several studies have demonstrated that EOs and pure terpenes act by targeting the insect nervous system, thus causing paralysis and death. The most widely studied mechanism is the inhibition of the acetylcholinesterase activity, which is crucial for neuronal transmission [70-112]. However, acetylcholinesterase inhibition does not seem the only neurotoxic action of EOs, and other mechanisms have been proposed through which the EO can modulate the neuronal activity of insects [70-112]. Of these, the most relevant are the ability of EO and its components to act as positive allosteric modulators of GABA receptors and as agonists of the octopamine receptors, the latter being specific receptors for invertebrates including insects [69-112]. Hemp EOs were also tested against ectoparasites of veterinary importance [75, 112]. The same EO from cultivar Felina 32 inflorescences successfully used against housefly and southern house mosquito [78, 79] was found to be effective against the poultry red mite (*Dermanyssus gallinae*) that infests poultry and other birds, and the camel tick (*Hyalomma dromedarii*) that infests camel and cattle, with a LC90 of 493 μg mL−1 and 517 μg mL^{-1} , respectively [78, 79, 112]. A hemp EO containing γ-elemene and caryophyllene oxide as its major components (16.2% and 14.2%, respectively) and a very low amount of monoterpenes showed its toxicity against the cat flea (*Ctenocephalides felis*), a vector of several pathogenic agents to animals and humans, inducing 100% mortality of eggs, larvae and pupae at 200, 400 and 1600 μg cm^{-2} , respectively, and 90% adult mortality at 2000 μg cm^{-2} [112]. An EO extracted from hemp leaves also showed a dose-dependent acaricidal activity against the mite Varroa destructor, an ectoparasite that attacks honeybees, reaching 95.4% mortality at a concentration of 15% [112]. The effectiveness of the hemp EO was found to be higher compared to EOs from sage (*Salvia officinalis*) and laurel (*Laurus nobilis*) that at the same concentration showed an acaricidal activity of 81.08% and 68.96%, respectively [112]. Hemp EOs were also found to be effective against plant pests [112]. The EOs obtained from the inflorescences and leaves of the cultivar Futura 75 and the inflorescences of the cultivar Felina 32, successfully used against the southern house mosquito and the housefly, were found to be effective also against the tobacco cutworm (*Spodoptera littoralis*), with the EO obtained from the inflorescences of the cultivar Futura 75 showing the highest toxicity (LC90 of 89.3 μL L^{-1} vs. 221.5–313.1 μL L^{-1} of the other EOs) [78, 79-85, 112]. The EO from the inflorescences of the cultivar Felina 32 was also found to be highly toxic (LD90 of only 6.2 μL L−1) against the adults of the potato-peach aphid (*Myzus persicae*) [70-112]. Additionally, an EO obtained from the inflorescences of three Polish hemp cultivars was shown to be effective against ornamental plant pests, such as the foxglove aphid (*Aulacorthum solani*) and the two-spotted spider mite (Tetranychus urticae), causing 100% and 98.72% mortality, respectively, at only 0.1% concentration [70-112].

6 CONCLUSION

The *C. sativa* plant produces a unique class of terpenophenolic compounds, called cannabinoids, as well as non-cannabinoid compounds mainly represented by terpenes and phenolic compounds. In addition to this, hemp oil and extracts were also tested as biopesticide for pest management. Biopesticides are natural, biologically occurring compounds that are used to control various agricultural pests infesting plants in forests, gardens, and farmlands. There are different types of biopesticides that have been developed from various sources. Biopesticides are naturally occurring compounds or agents that are obtained from animals, plants, and microorganisms such as bacteria, cyanobacteria, and microalgae and are used to control agricultural pests and pathogens. Products such as genes or metabolites from these biocontrol agents can be used to prevent crop damage. The use of biopesticides is, by far, more advantageous than the use of their counterparts, traditional chemical pesticides, as they are eco-friendly and host specific. The use and application of agro-based chemicals in the agricultural sector to protect crop plants from invading and infecting pests can be greatly improved by employing biopesticides. The chemical pesticides used in crop protection, to reduce the damage caused by pathogens and pests in agricultural fields, pose many long-term threats and risks to living beings due to their harmful side effects. They are known to cause cancers and foetal impairments and they persist in the environment for many years (i.e., they are nonbiodegradable). Furthermore, based on their potential application and strong inhibitory activity against pests, these synthetic pesticides dominate the market and have a significant impact on the manufacture of products. Therefore, adoption of plant based biopesticides is an increasingly popular trend in agriculture due to various environmental, health, and economic benefits. Biopesticides consist of naturally occurring substances, including insects, nematodes, microorganisms, plants, and semiochemicals, along with their by-products, offering a sustainable alternative to traditional chemical pesticides. Hemp plant extract and essential oil are used as biopesticide which are effective in controlling the agriculture pest management.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

Disclosure of conflict of interest

The authors declare no conflicts of interest regarding this manuscript.

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