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John M McPartland
Department of Family Medicine, University of Vermont, Burlington VT, USA

Zahra Sheikh
Department of Medical Entomology and Vector Control, School of Public Health, Tehran University of Medical Science, Tehran, Iran

Correspondence
John M McPartland
Department of Family Medicine, University of Vermont, Burlington VT, USA

A review of *Cannabis sativa*-based insecticides, Miticides, and repellents

John M McPartland and Zahra Sheikh

Abstract
Plant-based pesticides are gaining attention as safe, effective, eco-friendly alternatives to synthetic pesticides. We conducted a literature search regarding the use of hemp (*Cannabis sativa*) as a plant-based insecticide, miticide, or repellent. The search yielded 88 publications, which we grouped into five types of applications: companion planting (17 articles), the use of harvested plant material without any extraction (25 publications), aqueous extracts (20 publications), essential oil extracts (EOs, nine publications), and solvent extracts (17 publications). Few studies chemically analyzed the contents of their extracts, and most studies lacked control comparisons. EO studies were the most rigorous, and yielded the best results. Results with solvent extracts showed moderate efficacy, but little better than aqueous extracts, which lacked tetrahydrocannabinol (THC). Collectively, the studies suggest that EOs (terpenoids) are the primary *Cannabis* constituents responsible for arthropod deterrence. THC exerts nominal deterrence, but is toxic to insects. Mechanisms of action are discussed.

Keywords: *Cannabis sativa*, plant extracts, botanical pesticides, essential oils, tetrahydrocannabinol

1. Introduction
Many arthropods are disease vectors. Mosquitoes (*Culex, Anopheles, Aedes* spp.) vector the causes of malaria, yellow fever, dengue fever, West Nile virus, Zika virus, Chikungunya, and filariasis. Fleas (*Pulex irritans, Xenopsylla cheopis*) vector murine typhus and bubonic plague. Lice (*Pediculus* and *Pthirus pubis* spp.) vector epidemic typhus. Ticks (*Ixodes*, *Amblyomma*, *Dermacentor*, *Rhipicephalus* spp.) spread Lyme disease, babesiosis, anaplasmosis, ehrlichiosis, Rocky Mountain spotted fever, and Q fever. Kissing bugs (*Rhodnius* and *Triatoma* spp.) vector Chagas disease, and sand flies (*Phlebotomus* and *Lutzomyia* spp.) vector leishmaniasis. Arthropod-borne diseases as malaria, Chagas disease, and leishmaniasis account for more than 17% of all infectious diseases, causing more than 700,000 deaths annually [1].
Arthropod pests destroy an estimated 18-26% of annual crop production worldwide. Most of this occurs in the field (13-16%), and the rest is due to post-harvest losses [2]. Household arthropod pests include termites, carpenter ants, fire ants, clothes moths, and cockroaches. Many of these arthropod pests and disease vectors are preventable through informed protective measures.
Prior to synthetic pesticides, plant-based biopesticides were the principal means of repelling arthropods. Plants produce powerful chemicals for defense against phytophagous arthropods. Ancient people used indigenous plants to repel phytophagous arthropods, as well as blood-feeding arthropods and household pests. A century ago synthetics came to dominate the market, because of their greater efficacy, longer duration of action, and more stable shelf life than plant-based products. While this may be true, the widespread use of synthetic pesticides has resulted considerable damage to worldwide ecosystems, and polluted air, water and soil. They may be harmful to non-target species, and directly toxic to users. Widespread usage has led to the development of resistance among the target species.
Plant-based biopesticides can be produced in a sustainable manner, inexpensive to extract, nonirritating to skin, and considered natural. They are culturally acceptable in communities with a tradition of plant use, and they are gaining popularity as substitutes for synthetic pesticides. Spatial repellents derived from *Cannabis sativa* were traditionally deployed against human pests. Targets included mosquitoes, fleas, lice, ticks, bedbugs (*Cimex lectularius*), and scabies mites (*Sarcoptes scabiei*). *Cannabis*-based insecticides and repellents were also traditionally employed to protect crops from phytophagous arthropods [3].
The active ingredient in *Cannabis* that deters arthropods has not been confidently ascertained.

In human medicine, the focus has been on Phytocannabinoids, a class of natural products unique to *Cannabis*. The two best-studied phytocannabinoids are tetrahydrocannabinol (THC) and cannabidiol (CBD). *Cannabis* does not actually biosynthesize THC and CBD. It produces precursor molecules, tetrahydrocannabinol acid (THCA) and cannabidiolic acid (CBDA). These molecules decarboxylate into THC and CBD upon heating (boiling, baking, smoking). The bioactivities of THCA and CBDA are poorly understood, and they differ from THC and CBD. For example, THCA is not psychoactive; it does not bind to the human CB_1 receptor [4].

Terpenoids refer to a class of compounds that includes both hydrocarbon terpenes and their oxygenated derivatives. Terpenoids from other plants are well-known insecticides, such as ryania, azadirachtin, and pyrethrins. Three terpenoids produced by *Cannabis*-limonene, linalool, and pinene—are marketed as insecticides. *Cannabis* biosynthesizes about 140 terpenoids, mostly monoterpenoids ($C_{10}H_{16}$ templates) and sesquiterpenoids (C_{15} H_{24} templates). Collectively, terpenoids constitute the plant's essential oil (EO, also known as volatile oil).

Several other classes of natural products are minor constituents of *Cannabis*, such as flavonoids (quercetin, apigenin, orientin, kaempferol, canniflavone, cannflavin), phenols (eugenol, cannabispiradienone), polyphenols (cannabispirone, canniprene, tannins), phytosterols (camesterol, stigmasterol, *β*-sitosterol), amines (piperidine), lignanamides (cannabisin A-G), and fatty acids in seeds. Many of these compounds show insect repellency [5].

Cannabis produces terpenoids and phytocannabinoids in glandular trichomes, of which there are two main types: sessile glandular trichomes arise on all aerial surfaces throughout the plant's lifespan, except for cotyledons. Their gland heads are 40-50 µm in diameter. Stalked glandular trichomes are largely limited to the flowering tops (perigonal bracts and subtending leaves) of female plants. Their gland heads are at least 70-100 µm in diameter, atop a multicellular stalk usually over 200 µm tall. Potter [6] measured a monoterpenoid-to-sesquiterpenoid ratio of 4:1 in stalked glandular trichomes on flowering tops, and nearly the reverse ratio in sessile glandular trichomes on leaves. The contents of gland heads consist of 90% phytocannabinoids and 10% terpenoids [6, 7].

Gland heads on living plants are "touch-sensitive," burst easily, and release terpenoids and phytocannabinoids. These fluids oxidize and polymerize into a resin on the trichome stalk and leaf surface. The gummy resin physically disables small insects, thereby exerting mechanical control as well as chemical control. Potter [6] photographed cotton melon aphids (*Aphis gossypii*) snared by stalked glandular trichomes. The aphids struggled for a while and then died.

2. Methods

We used three search engines to obtain literature, CAB Direct (https://www.cabdirect.org), PubMed (www.ncbi.nlm.nih.gov/pubmed), and Google Scholar (https://scholar.google.com), using the following boolean search string: (cannabis) AND (insecticide OR aracacide OR pest repellent OR antifeedant). Retrieved articles were screened for supporting citations, and antecedent sources were retrieved.

Publications selected for inclusion included all pre-20th century reports of pesticidal or repellent activity against blood-feeding arthropods and phytophagous arthropods. Publications of the 20th and 21st centuries were limited to first-person accounts in the primary literature. Secondary sources (review articles and textbooks) were excluded, unless: 1. they cited primary sources not available to us; 2. they included experimental data (*e.g.*, LC_{50}, the concentration of a chemical in air or water that kills 50% of arthropods; LD_{50}, the amount of a chemical, given all at once, that kills 50% of arthropods). We also excluded ethnobotanical surveys, which were second-person accounts and lacked experimental data.

Data extracted from publications included plant parts utilized (leaves, flowering tops, seeds, or all aerial parts), targeted arthropod, assay used to measure activity, and experimental results. Activities included acute toxicity (LC_{50}, LD_{50}, or percent killed), repellency, feeding inhibition, and oviposition inhibition. Our narrative review was structured by product application, segregated into five categories:

2.1 *Cannabis* as a companion plant

Companion planting or intercropping describes the sowing of two or more plant species in close proximity. This mimics the biodiversity of natural ecosystems, and enhances crop production via pest control and other mechanisms. Companion plants can be employed in an attract-and-kill (A&K) strategy-pests are lured to an attractant (usually a semiochemical and/or a visual cue), and then killed by a pesticide.

2.2 Recently harvested or dried plants

This category includes the direct usage of plant material without any extraction. In this manner *Cannabis* has found use as a spatial repellent. Recently harvested plants ("fresh," "green") emit volatile compounds—primarily terpenoids. Phytocannabinoids are not volatile. They are present in the fumes of burned plants.

2.3 Aqueous extracts

No studies analyzed the active ingredients in their aqueous extracts. Here we infer their contents: Several classes of *Cannabis* constituents are soluble or miscible in water, including flavonoids, alkaloids, tannins, and amines. Monoterpenes lack solubility. At 25ºC, only 5.0 mg of *α*-pinene is soluble in a liter of water; limonene, 20.4 mg/L; and myrcene, 29.9 mg/L [8]. Conversely, oxygenated monoterpenoids show 60-fold greater soluble: linalool, 1559 mg/L; *α*-terpineol, 1889 mg/L; carveol, 2931 mg/L. Sesquiterpenes are also hygrophobic: (*E*)-caryophyllene, 0.05 mg/L; trans-*α*-bergamotene, 0.03 mg/L [9].

THC is not water soluble: 2.8 mg/L at 23ºC [10]. THCA's carboxylic acid likely makes it more water soluble, but its solubility has not been measured. Aqueous extracts are either infusions (plant material steeped in room-temperature water or heated water) or decoctions (plant material boiled at 100ºC). The difference is an important consideration, because decoctions have lost THCA (decarboxylated into THC) and oxygenated monoterpenoids (which have boiled off).

2.4 Essential oils

EOs are extracted primarily by steam distillation or hydrodistillation. Steam distillation passes steam through a bed of plant material in a closed system. Volatile compounds are carried away in the steam, condensed and separated. Hydrodistillation is an older version of steam distillation, where plant material is soaked in water, then boiled, and

volatile compounds are carried away in the water-oil vapor, condensed and separated.

Benelli [11] described hydrodistillation as "more aggressive" than stem distillation, producing oxidative and hydrolytic reactions. Hydrodistillation shifts the EO profile towards a higher percentage of water soluble terpenoids. Bertoli [12] used hydrodistillation to obtain an EO with an oxygenated terpenoid fraction of 5.67% and 7.46% (cultivar 'Felina 32' grown in two sequential seasons). Benelli [11] steam distilled the identical cultivar in the same region (central Italy), and obtained only 1.6% oxygenated terpenoids.

Phytocannabinoids are not significantly present in steam-distillates. Malingré [7] estimated that 3.3% of phytocannabinoids in plants passed into a steam distillate, whereas 75% of EO passed into a steam distillate. Hydrodistillation is not as selective; Benelli [11] measured 0.1% CBD in steam-distilled 'Felina 32', they compared this with Bertoli [12], who hydrodistilled 1.69% and 1.89% CBD (two seasons).

2.5 Solvent extracts with phytocannabinoids

Phytocannabinoids are extracted with nonpolar solvents (*e.g.*, hexane, chloroform, petroleum ether, supercritical CO_2) or polar solvents (methanol, ethanol, butanol, acetonitrile). The extraction can be done at room temperature, or heated (often using a Soxhlet extractor). Unfractionated (crude) extracts contain phytocannabinoids as well as EOs. Fractionation methods then separate THC, CBD, and other phytocannabinoids.

3. Results and Discussion

The search strategy yielded 88 relevant publications: 17 regarding companion planting, 25 using harvested *Cannabis* plant material without any extraction, 20 using aqueous extracts, nine using EOs, and 17 using solvent extracts. Some studies tested *Cannabis* extracts against phytophagous arthropods known to feed on *Cannabis*, such as *Tetranychus urticae*, *T. cinnabarinus*, *Frankliniella occidentalis*, *Popillia japonica*, *Arctia caja*, *Helicoverpa armigera*, *Spilosoma obliqua*, *Spodoptera frugiperda*, and *Gryllotalpa gryllotalpa* [13].

3.1 Companion plants

Of the 17 publications that described companion planting with *Cannabis*, 13 were observational reports, and four were experimental studies. The observational reports were universally positive, whereas the experimental studies reported mixed results (two positive, two negative).

Eight of the observational reports concern hemp repelling *Pieris brassicae*, the cabbage butterfly. In 1768, Pratje [14] wrote a short article, "Remedy against the cabbage caterpillars," which likely refers to *P. brassicae*. "If one wants to drive the cabbage to safety from the caterpillars, one should sow hemp around the land on which one has been sowed. It will be astonishing to realize that, although all the land lying around is covered with caterpillars, [cabbage] on which hemp is surrounded, not a single one will be seen."

Willich [15] paraphrases Pratje without citing him, "the borders of the ground, where it is intended to plant cabbages, be sown with hemp; and, however the vicinity may be infested with those insects, the ground enclosed will be found to be perfectly free from them." Hamm [16] suggests that the smell of hemp repels egg-laying butterflies, so a ring of plants will protect vegetables and brassicas. Jentink [17] says the interplanting of hemp and cabbage is "a well known fact" among peasants in the Netherlands. D'Arenberg [18] planted hemp in and around cabbage plots to drive away *Piérides du Choux*. He placed cabbage plants in a wire cage with a "tuft of hemp" at one end, and *Piérides du Choux* in the cage massed at the opposite end from the hemp.

Blanchard [19] recommends companion crops of hemp and Jerusalem artichoke (*Helianthus tuberous*) to protect cabbage fields. Linsbauer [20] observed the interplanting of hemp with cabbage to drive away *P. brassicae;* he attributes this effect to odors emitted by "the plant glands." Beling [21] quotes Pratje [14]. However, an actual experiment found no such protective effect against *P. brassicae* [22]. Nevertheless, popular guides still recommend planting hemp to drive off *P. brassicae* (*e.g.*, [23]).

Foy [24] says Egyptian farmers sow *Cannabis* in onion fields. This may have been companion planting; one of onion's rare pests is the onion thrips, *Thrips tabaci*. Potter [6] observed *T. tabaci* becoming ensnared by stalked glandular trichomes in *C. sativa*. Riley [25] "believed" that hemp, *C. sativa*, planted in the midst of cotton reduced damage by the cottonworm, *Alabama argillacea*, as did the neem tree (*Melia azedarach*), pyrethrum plant (*Chrysanthemum* sp.), and dill (*Anethum graveolens*).

Feldt [26] reports that hemp protects plants from the dock aphid, *Aphis rumicis*, as does carrot (*Daucus carota*), parsley (*Petroselinum crispum*), and coriander (*Coriandrum sativum*). Pakhomov and Potushanskii [27] quantified the effects of hemp on the wheat bulb fly, *Delia coarctata*. A control plot of winter wheat showed 31% infestation by *D. coarctata*, whereas a plot bordered by hemp plants showed only 9% infestation.

Stratii [28] reports that when hemp was grown around a potato plot, plants nearest to the hemp were free from infestation by the Colorado potato beetle (*Leptinotarsa decemlineata*) whereas other plants became heavily infested. However, Mackiewicz [29] grew hemp around the edges of a potato field and within the field, and found no effect on *L. decemlineata*. Hemp also had no effect on black bean aphids (*Aphis fabae*) in the beet fields.

3.2 Freshly harvested or dried plants

Of 25 reports that used *Cannabis* plant material without any extraction, 12 reports concerned blood-feeding pests of humans, six targeted storage insects (grain weevils, clothes moths), four concerned phytophagous insects in the field, one study mentioned both blood-feeding and phytophagous insects, one study targeted the varroa mite in honeybee colonies, and one cited nonspecific "bugs" (Table 1). Some of these reports come down to us from secondary sources. The majority (71%) predated the 20th century, and most of them were observational reports. Only five were experimental studies, and they lacked controls. One study compared the efficacy of *Cannabis* to other plants.

Table 1: Reports concerning freshly-cut plants or dried flowers and tops, listed chronologically

Target species, citation	Extracted data
Locusts Rodgers [30]	Ibn Wahshīyah of Iraq fumigated crops infested by locusts with *šāhdānaj* (hemp) and sulfur. Ibn Wahshīyah wrote *Filāha an-Nabātiyya,* the earliest agricultural book in Arabic, between 904 and 931 AD.
Mosquitoes Beckh [31]	The anonymously-written *Geoponika, ca.* 904-959 AD, says "If you lay a flowering branch of *καννάβεως* (green hemp) near you when you go to sleep, *κώνωπες* (mosquitos) will not touch you." Five lines later: "Mosquitos will not bother a person in bed if he puts *καννάβια* (hemp) under him." *Geoponika* attributes this information to Democritus (460-370 BC), whose writings are lost.
Mosquitoes Needham [32]	A passage in *Wù Lèi Xiāng Gǎn Zhì,* written by Zànníng *ca.* 980 AD, recommends burning *má yè* (hemp leaves) to repel mosquitoes.
Bed bugs Ardoini [33]	According to Ardoini, "Hippocrates said: If *herba canapis* (hemp leaves) should be put under the bed, *cimices* shall not come near to him." *Cimices* likely refers to *Cimex lectularius*. To our knowledge, Hippocrates never wrote anything about cannabis in any context.
Mosquitoes Estienne [34]	Estinne translated *Geoponika* from Greek to Latin, but altered the text: *florentes canabis surculi* (flowering cannabis shoots) control *involatia culicum agmina* (hordes of flying mosquitos).
Mosquitoes Ruel [35]	Ruel quotes Democritus in a translation of *Hippiatrica* that includes some passages from *Geoponika*: *cannabis frutices* (hemp flowers) repel *infestis culicibus* (troublesome mosquitoes) from around the bed.
Bed bugs Teodosi [36]	Teodosi likely cribbed Ardoini: *cimices* (bugs) are repelled by the *olent* (smell) of *canabis* [sic] *folia et caules* (hemp leaves and stems)
Fleas Piemontese [37]	Girolamo Ruscelli wrote a "book of secrets" under the pseudonym of "Alessio Piemontese," Spreading *semenza del canape* (hemp seed) around the house will drive away *pulici* (fleas).
Mosquitoes Wecker [38]	A posthumous compilation of writings by the Swiss alchemist states that *mouscheros* (mosquitoes) will not annoy a person who places *chanvre* (hemp) under his bed
Bed bugs and caterpillars Chomel and Bradley [39]	Bradley translated and revised *Dictionnaire œconomique* by Noël Chomel. His revision makes comments that do not appear in Chomel's original. "Take some ox-gall and hemp-oil, mix the whole together, rub the joints and bedstead therein, and the bugs will never touch the places you have rubbed." Regarding caterpillars in crops, "Some burn hemp-sheaves, as they are called, being the stalk of the hemp, near their gardens, and it's very good to kill them."
Grain weevils Walpole [40]	A British diplomate in Munich reports that Bavarians repel "flying weevils" by mixing green hemp into piles of stored grain.
Clothes moths Anonymous [41]	"*Moist* [*i.e.,* fresh] hemp and tobacco leaves preserves all sorts of cloaths from moths and worms."
Mosquitoes Darwin [42]	Erasmus Darwin, grandfather of Charles, says the "musquito, *Culux pipiens*… may be driven away by smoke, especially… by that of cannabis, hemp."
Bugs Rafinesque [43]	"Bugs are killed by the smoke of the cayenne pepper, the infusion of the *Acorus* or sweet flag, and of the hemp seeds."
Bed bugs King [44]	King recommends placing "green plants collected in the spring" around the bed to rid the room of bedbugs
Grain weevils Riley and Howard [45]	Leaves gathered from wild-type *Cannabis* in South Africa were placed among bags and heaps of grain for protection from "grain weevils."
Fleas Chopra and Badhwar [46]	"Hemp (*Cannabis sativa* L.), if spread under a bedsheet, affords ample protection against fleas which disturb sleep at night in many of the hill stations of India."
Ticks Reznik and Imbs [47]	Larvae of *Ixodes redikorzevi*, *Haemaphysalis punctate*, *Rhipicephalis rossicus*, and *Dermacentor marginatus* exposed to powdered leaf were killed in 10, 18, 8, and 21 minutes, respectively. Exposure to fresh whole leaf killed larvae in 50, 68, 50, and 72 minutes, respectively.
Sitophilus oryzae Khare [48]	300 adult weevils were placed into an olfactameter, with wheat mixed with powdered *Cannabis*, 1% w/w. After 24 hours, only 1.66% of weevils were found in the grain, the rest were repelled. *Cannabis* was more effective than *Acorus calamus* or *Physalis minima*.
Leptinotarsa decemlineata Stratii [28]	When flowering hemp plants were torn up and waved over infested potato plants, adult beetles fell to the ground paralyzed.
Spilosoma obliqua Deshmukh [49]	When 6th instar larvae were fed a no-choice diet of freshly-harvested *Cannabis* leaves, 50% died after 24 days.
Arctia caja Rothschild [50]	Larvae fed a no-choice diet high-THC *Cannabis* leaves did not survive beyond the third instar. Those fed high-CBD leaves pupated successfully.
Sitophilus oryzae Prakash [51]	Dried leaves mixed into rice, 2% w/w, gave 59% protection against adult weevils in the laboratory. This dose failed to provide adequate protection under natural storage conditions (Prakash *et al.* 1982)
Varroa jacobsoni Surina and Stolbov [52]	Honeybee mites were partially controlled by vapors from fresh leaves and stems, reduced to a powder. Inner walls of the hive were rubbed with 10-12 g powder per bee family.
Phthorimaea operculella Kashyap [53]	A 2 cm layer of dried, powdered leaves over piles of potatoes protected them from larvae of the tuber moth for up to 120 days. Of eight plants tested, *Cannabis* tied for second place.

Cannabis may employ an A&K strategy: Deshmukh [49] gave 6th instar larvae of the jute hairy caterpillar, *Spilosoma obliqua,* a choice of 16 plants from 12 plant families, and *Cannabis* was among the six favorite. But when larvae were fed a no-choice diet of fresh *Cannabis* leaves, 50% died after 24 days. Surviving larvae did not pupate. Rothschild [50] raised larvae of the garden tiger moth, *Arctia caja*, on fresh leaves of either high-CBD (Turkish) or high-THC (Mexican) landraces of *C. sativa*. Larvae reared on high-THC leaves did not survive beyond the third instar. Those fed high-CBD leaves pupated successfully. But in a feeding choice experiment, caterpillars showed a definite preference for high-THC leaves. "Should these compounds exert a fatal fascination for tiger caterpillars it suggests another subtle system of insect control

by plants." Larvae of *Arctia caja* fed *C. sativa* passed THC into the frass (3.0 mg/g), or sequestrated THC in the exoskeleton (1.4 mg/g). The exoskeleton accumulated up to 0.07 mg THC per caterpillar-enough to cause psychoactivity in a caterpillar-eating mouse. This is analogous to larvae of the monarch butterfly, *Danaus plexippus,* which accumulate toxic glycosides in their exoskeleton.

3.3 Aqueous extracts

Studies on aqueous extracts (n=20) rarely described their extraction techniques, whether infusions (either cold or heated), or boiled decoctions. Three reports were observational, the rest were experimental studies. Few experimental studies had control arms, but several studies compared *Cannabis* to other plants.

Only three reports predated the 20th century, and these were the observational reports. Piemontese [54] boiled *semenza del canape* (hemp seed) in seawater, and poured the decoction around the house to get rid of *pulici* (fleas). Buc'hoz [55] killed underground nests of *courtillières* (mole crickets, *Gryllotalpa* spp.) by flooding them with water suffused with hemp seed oil. This causes them to flee from their holes, blacken, and die.

Culpeper [56] says "juice" squeezed from fresh leaves dropped into the ears "draweth forth earwigs" which have gotten into them. It is well-known that Culpeper revised information regarding earlier authors without cited them. Regarding earwigs, Culpeper likely revised Pliny (*ca.* 23-79 AD), who says juice of hemp seed (*semen cannabis*) "drives out of the ears the worms and any other creature that has entered them" [57]. Pliny in turn plagiarized Dioscorides (*ca.* 20-70 AD), who instilled "juice of *χλωρός καρπόν*" (fruit when green) to treat ear aches (nothing about worms) [58].

Mackiewicz [59] sprayed potato plants in the laboratory with a water extract of hemp, which had no repellent effect on ovipositing potato beetles, *Leptinotarsa decemlineata*, and did not affect larval development. In contrast, Stratii [28] sprayed a decoction of boiled hemp flowers on infested potato plants, and no living beetles or larvae of *L. decemlineara* remained after 45 minutes. Kurilov and Kukhta [60] repeated the study in laboratory and field tests. Aqueous extracts of neither leaves nor flowering tops had any effect on larvae or adults of *L. decemlineara.* Adding sunflower oil to the extract caused young adults to drop to the ground, but they returned to plants in 5-10 minutes and resumed feeding.

Fenili and Pegazzano [61] reported that leaf extracts of *Cannabis sativa* (preparation details not given) were toxic to all stages of the spider mite *Tetranychus urticae*. Bajpai and Sharma [62] sprayed a 20% w/v cold water extract of *bhang* to reduce oviposition by the spotted stalk borer, *Chilo partellus.* Plants sprayed with the extract averaged 110 eggs, and control plants averaged 765 eggs.

Rothschild and Fairbairn [63] evaluated the cabbage butterfly, *Pieris brassicae*, in a free-choice test of oviposition deterrence. Cabbage leaves were sprayed with either tap water, aqueous extracts of Mexican (high-THC) *Cannabis,* or Turkish (high-CBD) *Cannabis*. Extracts were prepared at room temperature, 5 g leaves in 5 Imperial oz water (*i.e.*, 3.4% w/v). Given the choice of leaves sprayed with tap water versus Mexican extract, butterflies laid 1418 eggs and 135 eggs, respectively, on the two choices. Offered tap water versus Turkish extract, they laid 1421 eggs and 773 eggs, respectively. Butterflies could also distinguish between the two extracts: they laid 510 eggs on the Mexican extract versus 1691 eggs on the Turkish extract.

Then Rothschild and Fairbairn heated the extracts in a steam bath for 30 minutes to remove volatiles. The loss of volatiles resulted in a reduction in oviposition deterrence. Given the choice of Mexican unsteamed versus Mexican steamed, they laid 72 eggs and 683 eggs, respectively. Given the choice of Turkish unsteamed versus Turkish steamed, they laid 319 eggs and 405 eggs.

Sharma [64] tested a 2% leaf extract (preparation details not given) against the potato tuber moth, *Phthorimaea operculella.* Dipping eggs in the extract for two minutes extract reduced egg hatching by 13.7%. Potato leaves dipped in the extract for 2 minutes deterred egg laying by 41.7%. Out of ten plant species tested, *Cannabis* ranked 5th in oviposition deterrence, and tied for 6th in ovicidal mortality.

Masih and Singh [65] tested a leaf extract (1% w/v) on three lepidopteran borers, *Chilo partellus* on maize, *Helicoverpa armigera* on gram, and *Leucinodes orbonalis* on eggplant. They evaluated mortality on the 2nd, 4th and 6th days after treatment: *C. partellus* (37.5, 17.5 and 7.5%, respectively), *H. armigera* (55.0, 27.5 and 5.0%), and *L. orbonalis* (30.0, 20.0 and 7.5%).

Sharma *et al.* [66] tested ovicidal effects against eggs masses of the diamondback moth, *Plutella xylostella*, using five dilutions of an aqueous leaf extract. Egg hatch was 90.9% (distilled water), 86.5% (1% extract), 79.9% (2.5% extract), 88.8% (5% extract), 84.4% (8% extract), and 82.2% (10% extract). Extracts from all other plants showed greater ovicidal effects (*Melia azedarach, Lantana camara, Artemisia annua*). Kumar *et al.* [67] republished the data, with clarifications regarding methods: The dilutions came from a 20% w/v stock solution of leaves that were air-dried for 6-7 days. Egg masses were on cauliflower leaves; they were dipped for 10 seconds in each test solution.

Bhattacharyya *et al.* [68] collected ruderal plants in Bengal, and prepared room-temperature aqueous extracts from dried leaves. Extracts were sprayed on mustard (*Brassica juncea*) to test repellency against the mustard aphid *Lipaphis erysimi*. Three days later, control plants harbored a mean of 21.25 aphids, and plants sprayed with 6000 ppm cannabis extract had a mean of 35.41 aphids (1.7-fold increase). In contrast, plants sprayed with *Parthenium hysterophorus* extract showed a 3.4-fold decrease.

Sharma *et al.* [69] tested oviposition deterrence in the tobacco cutworm, *Spodoptera litura*. Leaves were dried in a 30ºC oven for 24 hours (therefore likely devoid of monoterpenoids, and THCA decarboxylated into THC, and possibly oxidized into CBN). Four concentrations of aqueous extracts were tested. Egg laying was reduced by 11.9% (1% extract), 15.5% (2.5% extract), 18.5% (5% extract), and 18.1% (10% extract). Extracts from all other plants showed greater oviposition deterrence (*M. azedarach, L. camara, Azadirachta indica, Nerium indicum, Rininus communis, Solanum nigrum, Eucalyptus* sp.).

Sharma *et al.* [70] tested larvicidal effects against the tobacco cutworm, *Spodoptera litura*, and the cabbage worm, *Pieris brassicae* (extract preparation details not given). Second-instar larvae were placed on leaves dipped in aqueous extracts (castor leaves for *S. litura,* cabbage for *P. brassicae*). Mortality assessed at 24 hours. For *S. litura* the results were 6.2% (1% extract), 23.8% (2.5% extract), 23.8% (5% extract), and 9.5% (10% extract). Extracts from *M. azedarach, A. indica, N. indicum, R. communis,* and *S. nigrum* caused greater mortality, *L. camara* and *Eucalyptus* sp. caused less.

Sharma and Gupta [71] tested antifeedant and toxic effects on second instar larvae of *Pieris brassicae*. They dipped cabbage leaves in extracts prepared at room temperature from flowers, fruits, and leaves (10% w/v), and recorded antifeedant effects (percentage of leaf area not eaten) after 24 hours. Four concentrations were tested (10, 5, 2.5, and 1%), with a mean antifeedant effect of 25.8%-the least efficacy of eight plant species tested. Mortality response, corrected for control mortality, averaged 15.8%-*Cannabis* ranked third, after *Melia azedarach* (19.6%), *Nerium indicum* (19.6%), and *Azadirachta indica* (18.5%).

Zia *et al.* [72] tested the effects of ten plants on the stored cowpea bruchid, *Callosobruchus chinensis.* Aqueous extracts were prepared by boiling 1g dried leaf material in 100 mL of water for 10 minutes. They placed ten pairs of *C. chinensis* in a container (who mated and laid eggs) with 40 g cowpeas, and a cotton swab injected with 1 mL of extract. Parameters included: 1. number of days to 100% mortality, 2. feeding damage (number of holes/cowpea), 3. feeding damage (weight loss of cowpea) 4. extent of oviposition, 5. percent of egg hatching, 6. mortality of F-1 generation. Four plants of ten plants outperformed the *Cannabis* extract: *Piper nigrum*, *Syzygium aromaticum*, *Azadirachta indica*, and *Allium sativum*.

Sattar *et al.* [73] prepared aqueous extracts of leaves or seeds of *Cannabis*, at three concentrations described as 50%, 33%, and 25%. Filter paper was injected with 0.2 mL of each concentration, placed in a petri dish with 4th-5th instar termites of *Microtermes obesi* and *Odontotermes lokanandi.* On days 1-3, the seed extract caused greater mortality than the leaf extract for both species. After 11 days, 95-100% of *M. obesi* died at all concentrations for both leaf and seed extracts. *O. lokanandi* mortality was 80-100%, significantly higher at 50% and 33% than 25%, but no difference between leaf and seed.

Yadav and Patel [74] tested five plant extracts on mortality of third instar larvae of tobacco caterpillar (*Spodoptera litura*) and mustard sawfly (*Athalia proxima*), feeding on leaves of castor and mustard, respectively. Fresh leaves (250 g) were added to 500 mL water, and boiled down to half the original volume. Leaves of castor and mustard were dipped in three extract concentrations (1, 3, and 5%). Mortality of *S. litura* at 72 h was 73.3%, 76.7%, and 86.7%, respectively. At 5%, *Cannabis* tied for first with *Solanum nigrum*. Mortality of *A. proxima* at 72 h was 73.3%, 73.3%, and 80.0%, respectively. *Cannabis* ranked last.

3.4 Essential oils

We identified nine studies of EOs. Most authors described their extraction technique (*i.e.*, steam distillation or hydrodistillation), but few analyzed the content of their EOs (Table 2). All were experimental studies; few had control arms, several compared *Cannabis* to EOs from other plants, and in one case, a synthetic pesticide.

Table 2: Studies of *Cannabis* essential oils, listed chronologically

Target species, citation	EO extraction method, Analysis[1]	Assay, activity[2]
Culex tritaeniorhynchus, *Aedes aegypti*, *Anopheles stephensi*, *Culex quinquefasciatus*, Thomas *et al.* [75]	hydrodistillation of ruderal plants in Delhi, bioassay using WHO protocol	Four concentrations of EO (0.06, 0.1, 0.12 and 0.2 ml/litre) added to water with larvae of four mosquito species. Rank order of LC_{50}: *C. tritaeniorhynchus* (0.0101), *A. aegypti* (0.026), *A. stephensi* (0.0273), *C. quinquefasciatus* (0.0919)
Mosquito *Culex quinquefasciatus* Pavela 2009 [76]	EO purchased in USA	Fourth instar larvae exposed 24 h to doses, LC_{50} =127.3 μg/mL. Out of 22 plant species, *Cannabis* ranked 10th (*Thymus vulgaris* best, 32.9 μg/mL)
rosy apple aphid *Dysaphis plantaginea* Górski *et al.* [77]	steam distillation of Polish fiber hemp cultivars, with water emulsifier RO-1 (which caused no mortality alone)	Mortality from two EO concentrations (0.05 and 0.1%) sprayed on apple trees at rate of 750 L/ha. After 24 hours, mortality 93.0% (with 0.05%) and 93.5% (with 0.1%). Mortality similar to Mospilan 20 SP insecticide at rate of 0.125 kg/ha
Spider mites *Tetranychus urticae* *Tetranychus cinnabarinus* Fiedler *et al.* [78]	Same as above (emulsifier Triton), cucumber leaves naturally colonized by spider mites	*T. urticae:* mortality after 14 days from spraying leaves with 0.5% EO, nymphs 82%; adults 91% *T. cinnabarinus:* mortality after 14 days from dipping leaves in 0.5% EO, nymphs 75%; adults 87%.
Spider mite *Tetranychus urticae;* foxglove aphid *Aulacothum solani* Górski *et al.* [79]	Same as above (emulsifier RO-1) S 50.9%, M 49.3%	*T. urticae:* mortality on bean leaves dipped in 0.02%, 0.05%, or 0.10% EO. After 24 hours, mortality 43.6%, 60.3%, and 71.1% respectively. After 48 hours 66.6%, 71.4%, and 79.8%. After 72 hours 83.3%, 95.8%, and 98.7%. *A. solani:* mortality on eggplant dipped in same three concentrations. After 24 hours, mortality 22.3%, 27.5%, and 23.9%, respectively. After 48 hours 29.4%, 25.9%, and 57.3%. After 72 hours 98.2%, 100%, and 100%.
Termite, *Reticulitermes virginicus*; fruit fly, *Drosophila melanogaster* Prabodh & Setzer 2014[80]	EO from leaves of a Nepali plant, S 68.1%, M 11%, CBD 1.6%, THC 0.4%	*R. virginicus:* worker larvae mortality after 24 h exposure to filter paper w/ 1% EO at three concentrations: LC_{50} =354 μg/mL. *D. melanogaster* mortality after 24 h exposure to 1% EO at 20 μL or 150 20 μL, LC_{50} =500 μg/mL
Mosquito *Aedes albopictus*, Bedini *et al.* [81]	EO purchased in Italy, M 58.6, S 39.0	Fourth instar larvae exposed 24 h to doses from 25 to 500 μL/L, LC_{50} =301.6 μL/L
Mosquito, *Culex quinquefasciatus*; House-fly, *Musca domestica;* Tobacco cutworm *Spodoptera littoralis* Benelli *et al.* [82]	hydrodistillation of monoecious 'Futura 75', flowering tops (M 37.9, S 47.7, CBD 11.1) or leaves (M 5.3, S 75.0, CBD 10.0)	*C. quinquefasciatus*: WHO protocol, larvae exposed 24 h to doses from 30 to 500 μL/L; leaf LC_{50} =152.3 μL/L, flower LC_{50} =124.5 μL/L. *M. domestica:* adult females, 2-5 days old, topical application of 1 μL EO in acetone, range of doses 0-90% EOs; leaf LD_{50} = 305.2 μg/adult, flower LD_{50} =122.1 μg/adult.

		S. littoralis: early 3rd instar larvae, topical application of 1 μL EO in acetone, range of doses 30-500 μg/larvae; leaf LD_{50} =112.8 μg/larvae, flower LD_{50} =65.8 μg/larvae
Mosquito, *Culex quinquefasciatus*; House-fly, *Musca domestica;* Tobacco cutworm *Spodoptera littoralis* Green peach aphid *Myzus persicae* Benelli *et al.* [11]	steam distillation of flowering tops, monoecious 'Felina 32' (M 54.2, S 45.6, CBD 0.1), protocols similar Benelli *et al.*[82]	*C. quinquefasciatus* larvae: LC_{50} =252.5 mL/L *C. quinquefasciatus* adults: LC_{50} =500 $\mu g/cm^2$ *M. domestica* adults: LD_{50} =43.3 μg/adult *S. littoralis* larvae: LD_{50} =152.3 μg/larvae. M. *persicae*: four concentrations sprayed on cabbage leaves, adults placed on leaves and mortality at 48 h: LC_{50} =3.5 mL/L.

1. Analysis of EO, if performed: M, monoterpenoid percentage; S, sesquiterpenoid percentage
2. Assay: WHO, World Health Organization

In Table 2, note that Benelli *et al.* [82] found that a monoterpenoid-dominant EO (from flowers) was more potent than a sesquiterpenoid-dominant EO (from leaves) in three different insect species. In addition to mosquitos, Bedini *et al.* [81] tested a nontarget species, the mayfly *Cloeon dipterum*, with a LC_{50} = 282.2 μL/L. They also compared *Cannabis* EO to *Humulus lupulus* EO, which was more toxic to *C. dipterum* (LC_{50} = 219.8 μL/L). Benelli *et al.* [82] tested two nontarget species. They exposed the multicolored Asian lady beetle, *Harmonia axyridis*, to various EO concentrations (0.6, 1.25, 2.5, and 5.5 mL/L sprayed on cabbage leaves). Adults showed no mortality, and 3rd instar larvae showed only 3.3% mortality at the highest concentration. In comparison, 0.005% α-cypermethrin killed 100% of larvae and adults. They exposed *Eisenia fetida* earthworms to various EO concentrations (50, 100, and 200 mg/kg of soil), with no mortality after a week, whereas α-cypermethrin (250 μL/kg soil) killed 100%.

3.5 Solvent extracts with phytocannabinoids

Seventeen studies used solvent extracts. All were experimental studies; few had control arms, several compared *Cannabis* to extracts from other plants. No studies chemically analyzed the constituents in their solvent extracts, we assume the presence of phytocannabinoids and terpenoids. Two studies used purified cannabinoids (THC, CBD, or THCA).

Table 3: Studies of *Cannabis* solvent extractions, listed chronologically

Target species, citation	extraction method, Analysis[1]	Assay, activity[2]
Japanese beetle, *Popillia japonica* Metzger and Grant [83]	Pharmaceutical (U.S.P.) EtOH diluted to 1/64	Repelled adult beetles. They made extracts from 390 plant species, and only 56 showed any repellency.
Mosquito *Aedes aegypti* Abrol and Chopra [84]	EtOH of leaves, 20% solution	A spray repelled mosquitos but caused no toxicity
Cabbage butterfly *Pieris brassicae* Rothschild and Fairbairn [63]	Egg laying, free choice test, spraying cabbage leaves with water or EtOH solutions of purified THC 1% or CBD 1%	Choice of THC, 1301 eggs; vs. CBD, 3261 eggs. Choice of water, 2211 eggs; vs. THC, 1119 eggs. Choice of water, 2739 eggs; vs. CBD, 3859 eggs. Choice of Mexican extract, 0 eggs, vs. THC, 83 eggs.
Spotted stalk borer *Chilo partellus* Bajpai and Sharma [62]	PE extract of leaves, 20% w/v	Extract killed 40% of borers, and this toxicity persisted for four days.
Anopheles stephensi, Culex quinquefasciatus, Aedes aegypti Jalees *et al.* [85]	EtOH of leaves, 4% solution	Extracts added to water in the laboratory killed all mosquito larvae within 24 hours, LC_{50} = 1000 mg/L (*A. stephensi*), 1400 (*C. quinquefasciatus*), 5000 (*A. aegypti*)
Termite *Reticulitermes speratus* Lajide *et al.* [86]	MeOH extract from *Xylopia aethiopica*, which contained cannabisin B and D	Feeding deterrence at 10,000 ppm.
Potato tuber moth *Phthorimaea operculella* Sharma *et al.* [64]	EtOH, PE, benzene, and acetone extracts of leaves, 2%. Ovicidal effects by dipping eggs in extract for 2 min. Oviposition deterrence on potato leaves dipped in extract for 30 sec, 1 min, or 2 min	Reduction in egg hatching: Ethanol 13.7% > PE 13.3% > Benzene 10.4% > Acetone 6.7%. Mean of four extracts, *Cannabis* ranked 6th out of 10 tested plants. Reduction in egg laying: Ethanol 35.7% w/30 sec, 42.7 w/1 min, 43.3% w/2 min, > Acetone 31.3% w/30 sec, 40.0% w/1 min, 41.9% w/2 min, > PE 30.0% w/30 sec, 35.5% w/1 min, 42.4% w/2 min. Mean of four extracts, *Cannabis* ranked 5th out of 10.
Asian blue tick *Rhipicephalus microplus* Mansingh and Williams [87]	EtOH of leaves, topical application on engorged ticks	Acaricidal index (ranged from 50 to 100), *Cannabis* = 58, ranked 24th out of 29 plants tested
Swarming non-biting midge *Chironomus samoensis* Roy and Dutta [88]	EtOH of wild-type leaves in a refluxing apparatus. Last-instar larvae incubated in 200 mL phosphate buffered saline (PBS)	PBS with 2 mL DSMO (1%), plus 5, 10, or 20 mg dried crude extract per mL PBS. Paralysis and death in 82-100, 66-80, and 36-48 minutes, respectively. Controls (DSMO only) moulted into normal adults. Microscopy (SEM) showed damage to body cuticle, especially sensilla trichoidea, suggestive of neurotoxicity
Mustard aphid *Lipaphis erysimi* Srivastava & Guleria [89]	PE extract, 200 g leaves in 500 ml PE, Soxhlet at 40-60ºC	Mustard leaf dipped in extract diluted to 1% extract, adult aphids placed on leaves; 22.2% mortality. *Cannabis* tied 8th out of 34 tested plants
Fall armyworm *Spodoptera frugiperda* Sirikantaramas *et al.* [90]	Insect cell culture, Sf9 cell line, 24 hour exposure to THCA at 50 μM	THCA induced cell death via apoptosis as demonstrated by trypan blue staining

Tobacco cutworm *Spodoptera litura* Singh *et al.* [91]	Acetone, EtAC, and EtOH extracts	Antifeedant activity (preference index value) rank order: acetone (0.46), EtAC (0.5), EtOH (0.5)
Tobacco cutworm *Spodoptera litura* Singh *et al.* [92]	Acetone, EtAC, and EtOH extracts, assayed three paramters	Shortened larval period: acetone 12.2 days, EtAC 13.8 days, EtOH 14.5 days. Percent pupation: acetone 73.3%, EtAC 83.3%, EtOH 83.3%. Adult emergence: acetone 23.3%, EtAC 30.0%, EtOH 23.3%. Rank order: *Azadirachta indica* > *Datura alba* > *Cannabis* > seven other plants
Diamondback moth *Plutella xylostella* Sharma *et al.* [66] (method clarifications in Kumar *et al.* [67]).	EtOH leaf extract, Soxhlet apparatus. Ovicidal effects of eggs on califlower leaves dipped in test solutions for 10 sec.	Egg hatch 97.7% (distilled water), 81.1% (1% extract), 93.2% (2.5% extract), 91.1% (5% extract), 77.8% (8% extract), and 75.5% (10% extract). Extracts made from *Melia azedarach*, *Lantana camara*, and *Artemisia annua* showed greater ovicidal effects.
Mosquito *Culex quinquefasciatus* Maurya *et al.* [93]	CT, PE, MeOH leaf extracts, Soxhlet apparatus, WHO protocol, 3rd instar larvae	LC_{50} (ppm) after 24 hours: CT (88.5) > MeOH (160.8) > PE (294.4). After 48 hours: CT (68.7) > MeOH (71.1) > PE (73.32). Extracts from *Aloe barbadensis* more effective
Two spotted spider mite, *Tetranychus urticae*; Wheat aphid, *Schizaphis graminum*; Western flower thrips, *Frankliniella occidentalis* Taisiya *et al.* [94]	EtOH flower extract, 30 g in 300 EtOH for 3 days, sonicated, evaporated. 1% emulsion made with Tween. Leaf dipped in emulsion, then pests introduced.	Adult female spider mites counted after seven days on bean leaves, 50–80% lethality. Adult female aphids counted after 24 hours on wheat leaves, 50–80% lethality. Early 2nd instar thrips larvae counted after 5 days on bean leaves, 0–20% lethality
Pulse beetle, *Callosobruchus chinensis* Thakur and Devi [95]	Acetone and MeOH, room temperature extraction of leaves, assayed mortality, oviposition deterrence, and F1 adult emergence	Acetone 20% extract 100% mortality took 7 days, 10% extract took 9 days, 5% extract took 10 days. MeOH 20% extract 100% mortality took 8 days, 10% extract took 10 days, 5% extract took 11 days. Number of eggs laid: acetone 20% extract 4.1, control 36.0; methanol 20% extract 5.4, control 38.6. Number F1 adult emerged: acetone 20% extract 1.7, control 26.0; methanol 20% extract 2.3, control 27.5.

Extraction method: carbon tetrachloride, CT; ethanol, EtOH; ethyl acetate, EtAC; methanol, MeOH; petroleum ether, PE

Two studies compared aqueous extracts to solvent extracts. They suggest little difference in efficacy. Sharma *et al.* [64] assayed ovicidal activity and oviposition deterrence in the potato tuber moth, *Phthorimaea operculella.* A 2% aqueous extract reduced egg hatching by 13.7%, identical to a 2% ethanol extract, and marginally superior to PE extract (13.3%), benzene extract (10.4%), and acetone extract (6.7%). Potato leaves dipped in a 2% aqueous extract for 2 minutes deterred egg laying by 41.7%, marginally inferior to ethanol extract (43.3%), PE extract (42.4%), and acetone extract (41.9%).

Sharma *et al.* [66] assayed ovicidal activity in the diamondback moth, *Plutella xylostella*, and compared extracts at several dilutions. They reported ethanol extracts showing greater ovicidal activity than aqueous extracts at 10%, 8%, and 1% concentrations, but the reverse was found at 2.5% and 5% (data repeated in Kumar *et al.* [67]). They did not run statistics; our paired *t* test of their data showed no significant difference.

The study by Rothschild and Fairbairn [63] is particularly instructive. Aqueous extracts with terpenoids (cold extracts) were more effective than aqueous extracts lacking terpenoids (heated extracts), and extracts made from pure THC or CBD were even less effective. CBD was actually an oviposition attractant. The authors summarized, "the butterfly is sufficiently sensitive to differentiate between purified THC and CBD-two substances which taste and smell alike to the human observer."

Thomas *et al.* [75] compared their EO results with those of Jalees *et al.* [85], who used ethanol extracts. Both groups tested the same insects, in the same laboratory (one co-author in common). The EO extract was more effective than the ethanol extract. They suggested that hydrodistillation retained an active ingredient lost or reduced in the ethanol extract.

3.6 Mechanism of action

THC's mechanism of action in arthropods is not mediated by cannabinoid CB_1 receptors-its primary target in vertebrates. Arthropods do not express CB_1 receptors [96]. The spectrum of activity of THC is similar to that of rotenone: little or no repellency, but notable toxicity. Rotenone and THC do not share a mechanism of action. Rotenone potently inhibits the mitochondrial Complex I electron transport system. This inhibition has been measured in rat liver mitochondria and *Spodoptera frugiperda* Sf9 cells, with an IC_{50} of 19.3 and 21.0 nmol/L, respectively [97]. THC only inhibited Complex I activity 11% in pig brain mitochondria, at a thousand-fold greater dose (50 μmol/L) [98].

Organophosphate pesticides inhibit acetylcholinesterase (AChE) activity, whereas THC does not inhibit AChE activity [99]. AChE activity is inhibited by EOs extracted from *Azadirachtina*, *Mentha*, and *Lavendula* [99]. Surprisingly, EOs extracted from *Cannabis* show little AChE inhibition, with an IC_{50} = 4.0 mg/mL [82]. Benelli and colleagues [82] noted that individual terpenoids in *Cannabis* EO show potent AChE inhibition, such as α-farnesene, β-pinene, terpinolene, and (*E*)-caryophyllene. They concluded that the complex mixture in *Cannabis* EO was competitive, rather than synergistic. Rather than AChE inhibition, they suggest that *Cannabis* EO targeted insect octopamine or GABA receptors.

Octopamine receptors in insects are equivalent to norepinephrine receptors in vertebrates. Octopaminergic toxicity is elicited by EOs extracted from *Citronella*, *Pinus*, *Cendrus*, and *Eucalyptus* [100], as well as amitraz. Octopaminergic activity by *Cannabis* EO or phytocannabinoids has not been assayed.

The monoterpenoid thymol (present in the EO from *Thymus vulgaris*) antagonizes the insect GABAergic system [100], as does the insecticide fipronil. THC impacts the GABAergic system in vertebrates, although its direct effects are difficult to assess, because CB_1 receptors are localized on GABAergic neurons, where CB_1 activation decreases GABAergic activity. However, one study showed that THC decreased locomotion,

nociception, body temperature in knockout mice with a deletion of CB_1 in GABAergic neurons [101]. This suggests that THC may be a mechanism imparting toxicity in insects. GABAergic effects by *Cannabis* EO have not been measured.
Several pesticides target voltage-gated sodium channels in nerve axons. Pyrethrins, sabadilla, and DDT depolarize axon membranes. Indoxacarb and metaflumizone block sodium channels [102]. THC also depresses voltage-gated sodium channels [103], so THC may also affect insects via this mechanism.

4. Conclusions

Companion planting showed the least robust evidence of the five types of applications. Most publications were anecdotal. The two experimental studies diverged: one showed efficacy, the other did not. The use of harvested plant material, without any extraction, has an ancient anecdotal history. Experiments with this material successfully repelled or killed pests, at least in under laboratory conditions.
Aqueous and solvent extracts showed similar efficacies. Both extracts produced a wide range of outcomes, from no repellency to total mortality. Ten studies with aqueous extracts compared *Cannabis* with other pesticidal plants, and *Cannabis* ranked in the top half four times. In seven studies with solvent extracts, *Cannabis* ranked in the top half four times.
Experiments with EO extracts were the most rigorous, and yielded the best results. However, these studies evaluated small arthropods with thin cuticles (mosquitos, aphids, spider mites, termites). Studies with aqueous and solvent extracts tested a greater percentage of Lepidoptera and Coleoptera. The two EO studies with Lepidoptera showed only moderate toxicity.
Collectively, the studies point to terpenoids as the primary *Cannabis* constituents responsible for arthropod deterrence. EO extracts-nearly pure terpenoids-worked the best. Aqueous and solvent extracts have lesser amounts of terpenoids, and lesser efficacies. Freshly harvested plant materials outgas terpenoids, not cannabinoids, and they repelled or killed arthropods, especially in closed laboratory conditions. Terpenoids dissipate outdoors, and this may explain poor results seen in companion plant experiments.
Cannabis-based pesticides show promise in repelling pests of humans and crop plants. Surprisingly, some even showed efficacy against arthropods that attack *Cannabis* crops. No toxicity was seen in three non-target organisms, which is remarkable, to say the least. The mechanisms of action of *Cannabis* EO and THC remain to be elucidated.

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