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Inhibitory Effect of *Satureja* on Certain Types of Organisms

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Abstract: This review focuses on inhibitory effect of *Satureja* species on certain organism types. For this purpose; Web of Science, PubMed, Scopus, and Google Scholar databases were searched up to 24th December 2013. The search term was only "*Satureja*" without narrowing or limiting search elements. Once all reports obtained from databases (total number is about 610), author keywords and keywords plus sections, in addition to their full texts, were carefully checked out to find the active plant species related to the topic of this review. By this way, errors based on overlooks were eliminated. Forty-three reports, published between 1991-2013, were reviewed for their insecticidal, larvicidal, acaricidal, antiviral, anti-leishmanial, anti-protozoal, trypanocidal, nematicidal, ovicidal, molluscicidal, anti-helmintic and amoebicidal activities.

Keywords: *Satureja*; inhibitory effect; herbal medicine; extract; essential oil.

1. An Overview to Genus *Satureja*

Satureja species are food plants for the larva of some Lepidoptera (butterflies and moths). Caterpillars of the moth *Coleophora bifrondella* feed exclusively on winter savory (*S. montana*). Savory may be grown purely for ornamental purposes; members of the genus need sun and well-drained soil. Both summer savory and winter savory are used to flavor food. Cooks prefer the former, but as an annual is only available in summer; winter savory is an evergreen perennial. Savory plays an important part in Bulgarian and Italian cuisine, particularly when cooking beans. It is also used to season the traditional Acadian stew known as fricot. Savory is also a key ingredient in *sarmale*, a stuffed cabbage dish in traditional Romanian cuisine. The modern spice mixture Herbes de Provence has savory as one of the principal ingredients. Yerba buena (Spanish: "good herb"; *S. douglasii*) is used to make an herbal tea in the western United States [1].

Satureja species are native to warm temperate regions and may be annual or perennial [1]. The genus *Satureja* L. includes about 200 species of herbs and shrubs, often aromatic, with a center of distribution in the Mediterranean Basin. Many of these species from genus *Satureja*, with a high content of essential oil up to 4%, are widely applied in ethno medicine and ethno botany. Significant proportions of *Satureja* species are plants that have an important role in the pharmaceutical industry. The essential oils isolated from various *Satureja* species have shown various biological activities [2].

In recent years, plant species has been in the focus of scientific researches due to their unique phytochemical contents. As well known, these compounds have excellent pharmacological properties.

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There is a growing amount of information on the biological activity potential of *Satureja* members and new ones are continues to be added to this area day by day. As far as my literature survey could ascertain, the scientists have evaluated many aspects of these species. Many groups identified essential oil composition and phytochemical content of the extracts of these species. The oldest source that can be achieved in this area is belonging to the year 1981.

Biological properties of *Satureja* species, reported so far, can be given as following: Antibacterial, antifungal, antioxidant, cytotoxic, insecticidal, antidiabetic, anti-leishmanial, insect repellant, hepatoprotective, antiviral, anti-cholinesterase, hypolipidemic-hypoglycemic, anti-inflammatory, anti-nociceptive, nematicidal, anti-proliferative, genotoxic, anti-genotoxic, neuroprotective, ovicidal, anti-biofilm, molluscicidal, antihelmintic, herbicidal, anti-epilepsy, anti-Alzheimer, amoebicidal, nephroprotective, anti-lipase, wound healing, trypanocidal/anti-protozoal, enzyme inhibition, anti-spasmoidal, vasodilatory-vasorelaxant, antitumoral and diuretic activities.

Additionally effect of these species on; fertility treatment, blood level of sex hormones, sperm characteristics, DNA integrity, chromation quality, prophage induction, reproductive stimulation, premature ejaculation, human ulcerative colitis, serum lipid profile, peripheral blood temperature, hydatic cysts, DXR gene expression, periodontitis, productive performance, treatment of thrombosis and cardiovascular diseases, pathology of chronic age-related diseases and cytokine-induced cell activation have also been investigated in details.

This review is especially focused on inhibitory effect *Satureja* genus on certain organism types. For this purpose, forty-three reports, published between 1991-2013, were screened. We are aware of the existence of many other valuable activity data reported for this genus. We think to evaluate the rest of data as the issues of other review articles under consistent titles with them. Therefore, in this review, insecticidal, larvicidal, acaricidal, antiviral, anti-leishmanial, anti-protozoal, trypanocidal, nematicidal, ovicidal, molluscicidal, anti-helmintic, amoebicidal activities and insect repellence of *Satureja* species are evaluated.

2. Insecticidal, Larvicidal and Acaricidal Activities

Synthetic chemical insecticides play an important role in modern agriculture. These agricultural chemicals preferably administered as repeated doses for getting more effective results. Consequently, overdose usage of these chemicals has led to the development of resistance in insects and pollution problems on the environment [3]. As well known, plant secondary metabolites have been formed as a result of the interaction between plants and environment during the long evolutional periods. Insect active agents derived from plant secondary metabolites may lead to less or slower resistance development and lower pollution [4]. In recent years, discovery of new chemicals having insecticidal activity from plants and molecular structure modifications of these compounds has become one of the areas of interest [5].

According to literature data, insecticidal activity of the members of *Satureja* is being investigated since 1993. Within these reports, *S. hortensis*, *S. thymbra*, *S. spinosa*, *S. parnassica* subsp. *parnassica* and *S. montana* have proven to have insecticidal activity. Most of these studies have focused on *Satureja hortensis*, which is followed by *S. thymbra*. In the majority of studies, essential oils were used as insecticidal, larvicidal and acaricidal agents. When compared, in general, essential oils of these species have shown to be more efficient on insects than those of extracts.

Insecticidal activity potential of the members of *Satureja* are presented in table 1. As far as my literature survey could ascertain, plant species have been evaluated against twenty-one different insect species. As can be seen from the table, *Ephestia kuehniella* is the most commonly tested organism [6-9]. Data reported by Karaborklu et al. [6], Ayvaz et al. [8] and Sarac and Tunc [9] are directly concerned with the activity of the essential oil of *S. thymbra*. According to Karaborklu et al. [6], essential oil of *S. thymbra* was found rich in linalool as the major compound. LC_{50} and LC_{99} values of the oil were determined as 3.27 and 5.13 μL/L air, respectively. On the other hand, according to another study carried out by Ayvaz et al. [8], in the presence of *S. thymbra* essential oil, of which main compounds is carvacrol, 100% mortality observed after 24 h at 25 μl /l air on *E. kuehniella*. Sarac and Tunc [9] also tested essential oil of this plant species against *E. kuehniella*. According to this report, essential oil exhibited high toxicity (over 94%). Doses in the range of 108-135 μl /l air and at exposure periods varying between 24-144 h, *S. thymbra* oil showed high toxicity against *E. kuehniella*. Essential oil of *S. hortensis* has also tested against the same organism for its insecticidal activity by Maedeh et al. [7]. According to this study, after 9 h of exposure, the LC_{50} value of the essential oil was determined as 80.9 μL/L. The oil also showed contact toxicity against this organism with an IC_{50} value of 0.27 μl/cm^2.

According to data obtained from literature survey, *E. kuehniella* is followed by *Culex quinquefasciatus* for its sensitivity against *S. hortensis* (Table 1). Three different reports, carried out by the same research group, have focused on the insecticidal activity of this plant [10-12]. In two of these studies, extracts obtained by *S. hortensis* were used as the insecticidal agent [11-12], while Pavela [10] studied only the essential oil as observed commonly. Pavela et al. [11] evaluated the acute toxicity of *S. hortensis* extracts (obtained with supercritical CO_2 and by traditional extraction techniques) on larvae of *C. quinquefasciatus*. Supercritical CO_2 extract encoded with SFE2 found as the most efficient one within this study with the LC_{50} and LC_{90} values of 45 and 53 mg/ml, respectively. Pavela [12] also studied the extract of this species against the same organism. According this report, *S. hortensis* showed larvicidal effect after 24 h of exposure in a maximal dose of 500 ppm. It also displayed larvicidal effect at a dose of LD_{50} 28 ppm. Mortality of *S. hortensis* essential oil, as underlined above, also studied by Pavela [10]. In this study, major compounds of the oil were determined as carvacrol and γ-terpinene (48.1 and 36.7%, respectively), as seen commonly. According to this study, essential oil showed mortality with an IC_{50} value of 36 μg/ml. The oil showed excellent effectiveness with respect to mortality and percentage of adult emergence upon short-term exposure. In the presence of this oil, 16% adult emergence was observed. Additionally, 100% deterrence of female oviposition was determined at 0.02% oil concentration [10].

One another member of *Culex* (*C. pipiens* biotype *molestus*) was also evaluated for its sensitivity against the essential oils of three different *Satureja* species (*S. spinosa, S. parnassica* subsp. *parnassica, S. thymbra, S. montana*) [13] (Table 1). According to this report, major compounds of the essential oils were determined as monoterpene hydrocarbons and phenolic monoterpenes. The oils of all species presented within this study possessed significant larvicidal activity.

Toxicity of the essential oil vapour of *S. hortensis* was evaluated against cotton whitefly, *Bemisia tabaci* Gennadius (Homoptera: Aleyrodidae), by two different research groups [14,15] (Table 1). According to data reported by Zandi-Sohani [14], the essential oil vapour caused the highest mortality in 2 μL/L air dose and 24 h of exposure time. Mortality rate increased time and dose dependently. The mean mortality caused by the essential oil was calculated as 53.47%. Findings reported by Aslan et al. [15] are highly in agreement with that of Zandi-Sohani [14]. According to the report of Aslan et al. [15], *S. hortensis* exhibited considerable insecticidal effect.

Essential oil of *S. hortensis* was also tested for its insecticidal activity against cowpea seed beetle, *Callosobruchus maulatus* (Fabricius) (Table 1) [16,17]. According to the study reported by Ebadollahi et al. [16], the essential oil showed high fumigant activity on the insect. The LC_{50} value of the essential oil was measured as 68.728 μL/L air. Additionally, the oil showed low toxicity. Heydarzade and Moravvej [17] showed gender-specific susceptibility of *C. maculatus* against the same oil. In this report, males were more susceptible to the oil than females. Toxicity of the oil against male and female adults of *C. maculatus* was calculated as 535.69 and 640.99 μL/m^2 (LC_{50}). The oil showed also considerable persistence. The researchers attributed high persistence of the oil to the presence of high oxygenated-monoterpenes proportion [17].

Leptinotarsa decemlineata (Colorade potato beetle) is another species, of which susceptibility was tested against *S. hortensis* (Table 1). As far as my literature survey could ascertain, only two studies are available in the literature concerning this topic [11,18]. Unlike other studies discussed above, extract of this plant species was tested against this organism instead of essential oil. The same group, Pavela et al, carried out both studies. In the first case [18], toxicity and anti-feedant effect of the extract of *S. hortensis* was evaluated. In this report, extract caused mortality in 24 h after its topical application. The lethal dose was calculated as 22 μg. Extract also showed strong deterrent effect against larvae. The consumption of leaf discs treated with extract was significantly lower than that of control. In the latter case, Pavela et al. [11] evaluated the acute toxicity of *S. hortensis* extract obtained with supercritical CO_2 and by traditional extraction techniques on larvae of *L. decemlineata*. Supercritical CO_2 extract encoded with HD found as the most efficient one with LC_{50} and LC_{90} values of 22 and 52 μg/mL, respectively.

Susceptibility of Indianmeal moth, *Plodia interpunctella* (Hubner) was also investigated for its susceptibility against *S. hortensis* and *S. thymbra* essential oils [7,8] (Table 1). According to Maedeh et al. [7], after 9 h of exposure, LC_{50} value of the essential oil was determined as 139.8 μL/L. The oil also showed contact toxicity against this organism with an IC_{50} value of 0.19 μL/cm^2. On the other hand, according to another study carried out by Ayvaz et al. [8], in the presence of *S. thymbra* essential oil, of which main compounds found as carvacrol, 100% mortality observed after 24 h at 9 μL/L air on *P. interpunctella*.

Due to page limitations, it is not possible giving all details of the studies here. Activity potentials of the *Satureja* species against *Acanthoscelides obtectus, Bruchus dentipes, Camptomyia corticalis, Drosophila melanogaster, Hyalomma marginatum, Lipaphis pseudobrassicae, Musca domestica, Sitophilus granaries, S. oryzae, Spodoptera littoralis, Tetranychus urticae, Tribolium castaneum* and *T. confusum* are summarized in table 1 [7-9,11,15,19-24].

3. Insect Repellency

Table 2 presents the repellence potential of *Satureja* species. As can be seen from the table, repellence of *Satureja* species against nine different insect species (*A. fabae, B. brassicae, E. kuehniella, F. occidentalis, P. interpunctella, S. oryzae, T. infestans, T. castaneum* and *T. confusum*) has been reported elsewhere [7,25-28]. As underlined above, in the majority of studies, *S. hortensis* was the major plant used as insect repellent agent. In all studies, essential oils were used as sample.

As can be seen from table 2, data obtained within this area is commonly originated from the essential oil of *S. hortensis*. Nottingham et al. [28] has studied the repellence effect of oil against *A. fabae* and *B. brassicae*. According to results obtained from behavioural and electrophysiological studies, *S. hortensis* volatile repelled these organisms effectively. Maedeh et al. [7] also found the repellence of this oil excellent against *E. kuehniella*, *P. interpunctella* and *T. castaneum*.

Picard et al. [25] has done an interesting study on *S. montana* essential oil against *F. occidentalis*. At a concentration of 0.5%, essential oil exhibited repellence. The incorporation of alginate and methylcellulose polymers into treatment solutions containing 0.5% concentration of essential oil resulted in remarkable repellence. High repellency was maintained for 4 days when a 0.5% concentration of the alginate was used in combination with a 0.5% concentration of essential oil.

S. thymbra oil was also tested against the insect species by Sarac and Tunc [27]. According to this report, essential oil effectively repelled *S. oryzae* adults in food preference tests. In the presence of oil, only 5.2-17.4% of the insects settled in the treated food. On the other hand, in area preference test with *T. confusum* adults, repellence over or about 50% were retained for 2 weeks with the oil. Essential oil gave repellence falling into the range of promising repellents, that is, presumably, 40.1-60% repellence as an overall average of an 8 weeks exposure.

In the literature, only one report is available concerning the insect repellence effect of *S. parvifolia* [26]. According to this report, essential oil showed excellent properties with repellence values between 60 and 100%.

4. Antiviral Activity

Currently, there are serious limitations in the use of antiviral drugs due to their narrow spectrum of activity, limited therapeutic usefulness, and variable degrees of toxicity. Therefore, attempts to find new and alternative antiviral agents have gained momentum. The majority of the studies regarding the development of new antiviral agents have focused on synthetic substances [29,30]. Recently studies are especially focused on the antiviral activity of phytochemicals obtained from plant species. Currently, the scientists are trying to isolate and characterize novel compounds that could inhibit virus replication and/or treat viral infection, or even serve as models for new molecules [31-37]. In recent years, several plant species used traditionally in the treatment of diseases by the public worldwide have been tested for their antiviral activity against DNA and RNA viruses [38-50].

Data reported on the antiviral activity potential of *Satureja* species are presented in table 3. As can be seen from the table, most of studies have focused on *Herpes simplex* virus type 1 (HSV-1). Parainfluenza virus type 3 (PI-3), tobacco mosaic virus (TMV), cucumber mosaic virus (CMV), severe acute respiratory syndrome coronavirus (SARS-CoV), vesicular stomatitis virus (VSV), poliovirus type 1 (PV-1) and human immunodeficiency virus type 1 (HIV-1) are other viruses evaluated within these reports [51-56]. Among the plant species evaluated, *S. thymbra* is the most predominant one [53,56]. There is an important point to be noted here; as underlined in the table, nearly half of the studies were carried out with extracts. This point also emphasized by Yamasaki et al [55]. According to this report, the active components in the extract samples were described as water-soluble polar substances, not non-polar compounds such as essential oils. Abad et al. [54] has also demonstrated the similar findings related to polar phytochemicals.

Susceptibility of HSV-1 to *Satureja* species is presented in table 3. Extracts and/or essential oils of *S. thymbra, S. cuneifolia* and *S. boliviana* have been evaluated against this organism [51,53,54,56]. Saab et al. [56] and Loizzo et al. [53] have reported antiviral activity of *S. thymbra*. In the first case, *in vitro* antiviral activity of the ethanol extract of *S. thymbra* was investigated against HSV-1 infection on monkey kidney cells [56]. In this study, cytotoxicity was also determined by MTT assay in Vero cells. *S. thymbra* extract showed high selective index (SI) value and thus it is expressed that the extract can have potential use in the treatment of HSV-2. In the latter case, essential oil of *S. thymbra* was screened against HSV-1 replication *in vitro* by visually scoring of the virus-induced cytopathogenic effect post-infection [53]. In the presence of essential oil, IC_{50} and selectivity index (SI) values were determined as 220 ± 1.6 and 4.5, respectively.

Antiviral activity of *S. cuneifolia* was also evaluated against HSV-1 [51]. In this study, essential oil of *S. cuneifolia*, as well as the widely encountered components in essential oils, were assayed for their antiviral activity. According to the results, essential oil and components, in general, displayed strong antiviral effect against HSV-1, ranging between 0.8 and 0.025 μg/mL.

One another species assayed for its antiviral activity is *S. boliviana* against HSV-1. According to Abad et al. [54], ethanolic and aqueous extracts of this plant species used in the traditional medicine of Bolivia was evaluated. According to this study, the aqueous extract showed better antiviral activity than that of ethanolic one against HSV-1. The same research group also screened the antiviral activity of *S. boliviana* against vesicular stomatitis virus (VSV) and poliovirus type 1 (PV-1). Similar results were observed concerning this plant species especially for the aqueous extract.

As well known, human immunodeficiency virus type 1 (HIV-1) is probably among the most critical viruses from which the humanity suffers. *S. montana* extract was tested against HIV-1 induced cytopathogenycity in MT-4 cells by Yamasaki et al. [55]. As indicated in this report, *S. montana* showed great anti-HIV-1 activity with an ED of 16 μg/mL. According to this report, active components in the extract were found to be water-soluble polar substances. Additionally, the aqueous extract inhibited giant cell formation in co-culture of Molt-4 cells with and without HIV-1 infection and exhibited inhibitory activity against HIV-1 reverse transcriptase.

Among the virus types studied by the researchers, severe acute respiratory syndrome coronavirus (SARS-CoV) found as the most interesting one. According to a study carried out by Loizzo et al. [53], essential oil of *S. thymbra* showed no activity against this virus.

Antiviral activities of *Satureja* species were also tested against the plant pathogens. According to a study reported by Dunkic et al. [52], essential oil of *S. montana* L. ssp. *variegata* was tested against tobacco mosaic virus (TMV) and cucumber mosaic virus (CMV). In the presence of essential oil, number of local lesions on both TMV and CMV infected plants (*Chenopodium amaranticolor* and *C. quinoa*) was reduced for 29.2% and 24.1%, respectively. In this study, individual essential oil components, thymol and carvacrol, were also tested. Thymol was more effective in reducing CMV infection (33.2%), while carvacrol was more effective in reducing the TMV infection (34.3%). Additionaly, thymol and carvacrol exhibited no synergistic effect.

Susceptibility of parainfluenza virus type 3 (PI-3) against *S. cuneifolia* essential oil was reported by Orhan et al. [51]. In this study, essential oil of *S. cuneifolia*, as well as the widely encountered components in the oil, were assayed for their antiviral activity. According to the results, the oil and the components, in general, displayed moderate antiviral effect against PI-3 ranging between 1.6 and 0.2 μg/ml.

5. Anti-leishmanial Activity

Leishmaniasis is a disease caused by protist parasites from the genus *Leishmania*. It is transmitted by the bite of a female phlebotomine sand fly. Leishmaniasis can occur as three different forms: cutaneous, mucocutaneous and visceral leishmaniasis. In the world, in every 20 seconds, one person becomes infected by cutaneous leishmaniasis. The disease is endemic in 82 countries of tropical and subtropical areas around the world, and 10 million people suffer from cutaneous leishmaniasis today [57]. As in other areas, studies in this area have focused on phytochemicals to find new and alternative therapeutics agents.

Majority of the work carried out in this area has focused on *L. major*. Activities of essential oils and/or extracts of *S. khuzestanica, S. bakhtiarica* and *S. hortensis* have been evaluated against *L. major* [58-61]. This organism is followed by *Plasmodium falciparum*. Essential oils and/or extracts of *S. parvifolia* and *S. thymbra* were screened for their possible activity potentials on three different strains of *P. falciparum* (D10, W2 and K1) [62,63]. Susceptibility of other two *Leishmania* species, *L. donovani* and *L aethiopica*, was tested against *S. punctata* ssp. *punctata* by Tariku et al. [64]. In addition to these findings, Sulsen et al. [65] has determined the inhibitory effect of *S. parvifolia* extract. As seen in antiviral activity section, in almost half of studies, extracts were used instead of essential oils and researchers have observed interesting findings.

As seen from table 4, susceptibility of *L. major* has been evaluated against *S. hortensis*, *S. bakhtiarica* and *S. khuzestanica* [58-61]. According to literature data, both essential oil and extract of *S. khuzestanica* were evaluated in terms of their activity potential [60,61]. According to study carried out by Sadeghi-Nejad et al. [60], ethanolic and methanolic extract of *S. khuzestanica* obtained from the leaves of this plant was tested against *L. major*. The extracts inhibited the parasite development after 24 h of incubation, which gave IC_{100} = 2.4 and 4.8 mg/mL and IC_{50} = 0.3 and 0.6 mg/mL, respectively. The authors claimed that *S. khuzestanica* leaf extracts contain active compounds, which could serve as an alternative agent in controlling of cutaneous leishmaniasis. On the other hand, interesting findings were obtained with essential of same plant species [61]. According to this report, lesions' size in essential oil treated mice groups was restrained but not significantly different from the control group that might be due to the low sample size or concentration of the oil. The mortality rate in treated groups was clearly less than control. According to the authors, the oil has an effect on preventing death in infected mice.

Mohammadpour et al. [59] has evaluated the essential oil of *S. bakhtiarica* against *L. major*. According to this report, the oil of *S. bakhtiarica* showed higher activity than standard anti-leishmania drug, glucantime. The authors claimed that, due to the high concentration of phenolic compounds in the oil, all the parasites were killed after 24 hours and the oil is a potential plant drug against leishmaniasis.

Extract of *S. hortensis* obtained by maceration in hydroalcoholic solution was also screened against *L. major* [58]. *S. hortensis*, displayed high anti-leishmanial activity (IC_{50} 15.625 ± 3.76 μM) and was toxic against the J774 macrophage cell line at higher concentrations than those needed to inhibit the parasite cell growth (IC_{50} 100.44 ± 17.48, μM). According to the authors, *S. hortensis* extract contains active compounds, which could serve as alternative agents in the control of cutaneous leishmaniasis.

Tariku et al. [64] have studied the leishmanicidal activity of *S. punctata* ssp. *punctata* essential oil against promastigote and axenic amastigotes of *L. donovani* and *L. aethiopica* including toxicity studies on human monocytic leukemia cells (THP-1) and erythrocytes *in vitro*. The oil showed effect on promastigotes (MIC 76.5 to 312.5 nL/mL) and amastigotes (EC_{50} 4.06 to 131.00 nL/mL) of *L. donovani* and *L. aethiopica*, and varying toxicities on THP-1 cells (CC_{50} 0.013 to 350 nL/mL with selectivity index between 0.001 and 28) and erythrocytes (with LC_{50} 0.35 to 1.52 μL/mL).

6. Anti-protozoal Activity

Another organism, of which susceptibility was tested against *Satureja* species, is *P. falciparum*. As far as my literature survey could ascertain, essential oils and/or extracts of *S. thymbra* and *S. parvifolia* have been tested for their activities against D10, W2 and K1 strains [62,63]. According to a study, in which essential oil of *S. thymbra* tested for its larvicidal and adulticidal activities on *Anopheles gambiae* susceptible strains D10 and W2 [62], the oil rich in thymol, found as the most effective agent against *P. falciparum* with an inhibitory activity independent from the time of collection (IC_{50} 17-26 μg/mL on D10 and 9-11 μg/mL on W2). Then, the oil has been further fractionated to obtain a thymol-enriched fraction. This fraction showed excellent activity on both strains (IC_{50} 20-22 μg/mL on D10 and 8-10 μg/mL on W2) and thymol was confirmed as mainly responsible for this activity (IC_{50} 19.7 ± 3.0 and 10.6 ± 2.0 μg/mL on D10 and W2, respectively). According to this report, the oil showed also larvicidal and adulticidal activities. The larvicidal activity, expressed as LC_{50}, was 0.15 ± 0.002; 0.21 ± 0.13; and 0.15 ± 0.09 μg/mL depending on the time of collection: before, during and after flowering, respectively.

van Baren et al. [63] have evaluated susceptibility of *P. falciparum* K1 strain against *S. parvifolia*. This study, in which individual phytochemicals were screened, is extremely important in the field. According to this study, bioassay-guided fractionation of *S. parvifolia* MeOH extract led to the isolation of eriodictyol, luteolin and ursolic and oleanolic acids. As clearly stated in the report, ursolic acid showed an IC_{50} of 4.9 μg/mL, luteolin 6.4 μg/mL, oleanolic acid 9.3 μg/mL and eriodictyol 17.2 μg/mL. Additionally, eriodictyol showed moderate activity on the parasite but was the most selective compound as a result of its rather low cytotoxicity (IC_{50} 174.2 μg/mL) on the mammalian KB cell line.

7. Trypanocidal Activity

Organic and aqueous extracts of *S. parvifolia* were tested by Sulsen et al. [65] for their *in vitro* trypanocidal activities on epimastigote forms of *Trypanosoma cruzi*. According to this report, the aqueous extract showed trypanocidal activity with a percentage of growth inhibition higher than 70% at a concentration of 100 μg/mL.

8. Nematicidal Activity

In this review, nematicidal, ovicidal, molluscicidal, anti-helmintic and amoebicidal activities of the members of *Satureja* genus are also presented. As far as my literature survey could ascertain, I reached a limited number of reports concerning the activities presented under this topic. Among these, the most widespread one is nematicidal activity.

According to my literature survey, three-research groups [66-68] have reported the nematicidal activity of *Satureja* species. In these reports, *Bursaphelenchus xylophilus* was used as the target organism. In all of these studies, only essential oil of *S. montana* was used for its nematicidal potential.

According to the first study [66], acetone was investigated and found to be an appropriate alternative to Triton X-100 as a solvent of essential oil in bioassays aimed to investigate its effect on pinewood nematode mortality. The essential oil was highly effective, resulting in more than 90% pinewood nematode mortality at 2 mg/ml. The LC_{100} values ranged between 0.50 mg/mL and 0.83 mg/ml for the essential oil of *S. montana*.

Barbosa et al. [67] has also studied the oil of *S. montana* against the same organism. According to this report, high nematicidal activity was achieved with essential oil. The oil had an estimated minimum inhibitory concentration ranging between 0.097 and 0.374 mg/mL and a lethal concentration necessary to kill 100% of the population (LC_{100}) between 0.858 and 1.984 mg/mL.

I finally would like to mention about the report of Faria et al. [68] as the last study for the nematicidal potential of the oil of *S. montana*. The oil showed a mortality ≥ 96% at 2 μL/mL. The oil also showed lethal concentration (LC_{100}) < 0.4 μl/ml. According to this report, fractions enriched with the oxygen-containing molecules showed corrected mortality ≥ 96% did not always show LC_{100} value similar to the corresponding oil, suggesting additive and/or synergistic relationships among fractions. Additionally, decoction water (remaining hydrodistillation waters) revealed 100% mortality at a minimum concentration of 12.5 µL/mL. As a result, the authors claimed that, *S. montana* oil is a potential environmentally friendly alternative to control *B. xylophilus* due to its high nematotoxic properties.

9. Anti-helmintic Activity

My literature survey resulted in only one report concerning antihelmintic activity of *Satureja* species. Urban et al. [69] has studied the antihelmintic activity of ethanolic extract of *S. hortensis* against eggs *Ascaris suum* and infectious larvae *Trichostrongylus colubriformis*. According this report, the extract did not showed strong activity against the organisms. On the other hand, an effect against the infective third-stage larvae in comparison with synthetic anthelmintic Zentel (albendazole), have been obtained for the extract.

10. Ovicidal Activity

Ayvaz et al. [70] has reported ovicidal activity of the essential oil vapour of *S. thymbra* against two stored-product moths namely the Indian meal moth *P. interpunctella* and the Mediterranean flour moth, *E. kuehniella*. According to results obtained, the oil produced 100% mortality on the eggs of both *E. kuehniella* and *P. interpunctella*. The mortality caused by the oil was measured as 42.50% for *E. kuehniella* eggs and was 57.50% for *P. interpunctella* eggs, respectively. Additionally, at the moderate dose (50 µL/L air) the LT_{99} value of the oil was 158.50 and 81.88 h for the eggs of *E. kuehniella* and *P. intetpunctella*, respectively.

11. Molluscicidal Activity

While doing literature search, I could reach only one report for the molluscicidal activity of *Sature* species [71]. The target organism used in this study was *Arion lusitanicus*, which causes significant crop damage in some parts of Poland. Within this study, a palatability index (P.I.) and a consumption index (C.I.) were determined for *S. hortensis*. As result, *S. hortensis* found as palatable to the slug.

12. Amoebicidal Activity

In this review, finally, amoebicidal activity potential of *S. cuneifolia* will be discussed. Our research group reported this study in 2012 [72]. In this study, we evaluated the methanolic extract of this plant against *Acanthamoeba castellanii* trophozoites and cysts. In the presence of methanolic extract (ranging from 1.0 to 32.0 mg/mL), numbers of viable *A. castellanii* trophozoites and cysts decreased during the experimental process. Extract showed a time- and dose-dependent amoebicidal action on the trophozoites and cysts. In the presence of 32 mg/mL extract, no viable trophozoites were observed within 24^{th} h of experimental procedure. At the same concentration value, the extract was found effective against the cysts at a rate of 46.3% within 72^{nd} h of the experimental process. At 16 mg/mL extract concentration, no viable trophozoites were observed in the 24^{th} hour of the experiment.

13. Conclusion

As can be seen from the tables, in some cases, essential oil composition of *Satureja* species have not been reported by the authors. For establishing a chemical profile on the members of this genus, the whole genus was screened for its major volatiles and the distribution of compounds tried to be explained. As expected, thymol and carvacrol are found as the main compounds for many *Satureja* members. Additionally, *p*-cymene- γ-terpinene, linalool and borneol were determined as the other main compounds. On the other hand, some species exhibited unusual oil profile. For example, piperitone, piperitenone and piperitenone oxide are, in general, determined as the major compounds for *S. parvifolia* and *S. fruticosa* [26, 73-78]. Camphor and isomenthone were also found as the main volatiles for *S. visianii* and *S. boliviana* essential oils, respectively [79-81]. However, essential oil chemotypes suggested by the authors should also be underlined here. Chemotypes suggested in the papers are as following: carvacrol, thymol, linalool and carvacrol/*p*-cymene chemotypes for *S. montana* and *S. thymbra* [82-84], α-eudesmol, β-eudesmol and spathulenol chemotypes for *S. subspicata* [82], linalool, borneol, α-pinene and borneol/ α -pinene chemotypes for *S. coneifolia, S. biflora, S. subspicata* subsp. *subspicata* and *S. subspicata* subsp. *liburnica* [85-87] and bicyclic or isomenthone chemotypes for *S. douglasii* [88].

Table 1. Insecticidal, larvicidal and acaricidal activities of *Satureja* species

Insect	Plant species	Main compounds	Short explanation	References
Acanthoscelides obtectus	*S. thymbra* (Essential oil)	Carvacrol	*A. obtectus* was found as tolerant species against essential oil.	[8]
Bemisia tabaci	*S. hortensis* (Essential oil)	Not reported	It caused the highest mortality in 2 µL/L air dose and 24 h of exposure time. The mean mortality caused by the essential oil was calculated as 53.47%.	[14]
	S. hortensis (Essential oil)	Linalool	The amount of essential oil applied was 1.56, 3.125, 6.25 and 12.5 µl corresponding to 0.39, 0.782, 1.563 and 3.125 µL/L air. *S. hortensis* exhibited considerable effect.	[15]
Bruchus dentipes	*S. hortensis* (Essential oil)	Carvacrol, γ-terpinene, p-cymene, α-terpinene	The oil found as toxic to adults. Insect mortality increased with increasing concentration of oil. The oil (20 pi dose) brought about 100% mortality in 36 h.	[21]
Callosobruchus maulatus	*S. hortensis* (Essential oil)	Not reported	The essential oil had high fumigant activity on the insect. The LC_{50} value of essential oil was measured as 68.728 µL/L air. Additionally, the oil showed low toxicity.	[16]
	S. hortensis (Essential oil)	Carvacrol, thymol	Males were more susceptible to essential oil than females. Toxicity of the essential oil against male and female adults of *C. maculatus* was calculated as 535.69 and 640.99 $\mu l/m^2$ (LC_{50}). The oil showed also considerable persistence.	[17]
Camptomyia corticalis	*S. hortensis* (Essential oil)	Not reported	The LC_{50} value of essential oil was between 0.61-0.99 mg/cm^3.	[19]
Culex quinquefasciatus	*S. hortensis* (Essential oil)	Carvacrol, γ-terpinene	Essential oil showed mortality with an IC_{50} value of 36 µg/ml. In the presence of this oil, 16% adult emergence was observed. Additionally, 100% deterrence of female oviposition was determined for the oil in concentration of 0.02%	[10]
	S. hortensis (Supercritical CO_2 extract)	Not reported	Supercritical CO_2 extract encoded with SFE2 found as the most efficient one within this study with the LC_{50} and LC_{90} values of 45 and 53 mg/ml, respectively.	[11]
	S. hortensis (Methanol extract)	Not reported	*S. hortensis* showed larvicidal effect after 24 h of exposure in a maximal dose of 500 ppm. It also displayed the larvicidal effect at a dose of LD_{50} 28 ppm.	[12]
Culex pipiens biotype *molestus*	*S. spinosa, S. parnassica* subsp. *parnassica, S. thymbra, S. montana* (Essential oil)	*p*-cymene, γ-terpinene, thymol, carvacrol, β-caryophyllene	Major compounds of the essential oils were determined as monoterpene hydrocarbons and phenolic monoterpenes. The oils of all species discussed within this study possessed significant larvicidal activity.	[13]
Drosophila melanogaster	*S. hortensis* (Essential oil)	Carvacrol, thymol, γ-terpinene, *p*-cymene	*S. thymbra* found as effective as an insecticide. Carvacrol found to be more toxic than thymol. The toxicities of carvacrol and thymol did not show correspondence to their participation in the essential oil.	[24]
Ephestia kuehniella	*S. thymbra* (Essential oil)	Not reported	LC_{50} and LC_{99} values of this essential oil were determined as 3.27 and 5.13 µL/L air, respectively.	[6]
	S. hortensis (Essential oil)	Not reported	After 9 h of exposure, the LC_{50} value of the essential oil was determined as 80.9 µL/L. The oil also showed contact toxicity against this organism with an IC_{50} value of 0.27 $\mu l/cm^2$.	[7]
	S. thymbra (Essential oil)	Carvacrol	In the presence of *S. thymbra* essential oil, of which main compounds is carvacrol, 100% mortality observed after 24 h at 25 µL/L air on *E. kuehniella*.	[8]
	S. thymbra (Essential oil)	Not reported	Essential oil exhibited high toxicity (over 94%). Doses in the range of 108-135 µL/L air and at exposure periods varying between 24-144 h, *S. thymbra* oil showed high toxicity against *E. kuehniella*.	[9]
Hyalomma marginatum	*S. thymbra* (Essential oil)	Carvacrol, γ-terpinene	Mortality increased with concentration and exposure time. Ticks exposed to vapors from cotton wicks containing at least 40 µL/L resulted in complete (100%) mortality at 3 h. Knockdown was observed only in the carvacrol ang g-terpinene treatments.	[22]

Table 1. *Continued*

Insect	Plant species	Main compounds	Short explanation	References
Leptinotarsa decemlineata	*S. hortensis* (supercritical fluid, benzene and ethanol extracts)	Not reported	Extract caused mortality in 24 h after its topical application. The lethal dose was calculated as 22 µg. Extract also showed strong deterrent effect against larvae. The consumption of leaf discs treated with extract was significantly lower than that of control.	[18]
	S. hortensis (Supercritical CO_2 extract)	Not reported	Acute toxicity of *S. hortensis* extract obtained with supercritical CO_2 and by traditional extraction techniques on larvae of *L. decemlineata* was evaluated. Traditional extract encoded with HD found as the most efficient one with the LC_{50} and LC_{90} values of 22 and 52 mg/ml, respectively.	[11]
Lipaphis pseudobrassicae	*S. hortensis* (Essential oil)	Carvacrol, γ-terpinene	Essential oils were directly applied to aphid females in randomized blocks at concentrations of 0.0, 1.0, 2.5, 5.0 and 10.0 mg/l. Aphids were quickly incapacitated and killed by aliphatic aldehydes, phenols and monocyclic terpenes contained in the oil at applied concentrations as low as 0.3 to 1.0 mg/ml.	[23]
Musca domestica	*S. hortensis* (Supercritical CO_2 extract)	Not reported	Acute toxicity of extract obtained with supercritical CO_2 and by traditional extraction techniques was evaluated on larvae and adults. Traditional extract encoded with HD found as the most efficient one on adults with the LC_{50} and LC_{90} values of 35 and 45 mg/ml, respectively.	[11]
Plodia interpunctella	*S. hortensis* (Essential oil)	Not reported	After 9 h of exposure, the LC_{50} value of the essential oil was determined as 139.8 µL/L. The oil also showed contact toxicity against this organism with an IC_{50} value of 0.19 µl/cm^2.	[7]
	S. thymbra (Essential oil)	Carvacrol	In the presence of *S. thymbra* essential oil, of which main compounds is carvacrol, 100% mortality observed after 24 h at 9 µL/L air on *P. interpunctella*.	[8]
Sitophilus granarius	*S. hortensis, S. spicigera* (Essential oil)	Not reported	Treatment with the essential oils leads to a high mortality on adults. The mortality rates after 96 h of treatment with maximum dose (20 µL/L) of essential oils of *S. hortensis* and *S. spicigera*, was determined as 100 and 94.27%, respectively.	[20]
Sitophilus oryzae	*S. thymbra* (Essential oil)	Not reported	Essential oil showed high toxicity as vapour with doses in the range of 108-135 µL/L air and at exposure periods varying between 24-144 h.	[9]
Spodoptera littoralis	*S. hortensis* (Supercritical CO_2 extract)	Not reported	Acute toxicity of extract obtained with supercritical CO_2 and by traditional extraction techniques was evaluated on larvae. Supercritical CO_2 extract encoded with SFE2 found as the most efficient one on larvae with the LC_{50} and LC_{90} values of 31 and 52 mg/ml, respectively.	[11]
Tetranychus urticae	*S. hortensis* (Essential oil)	Linalool	The amount of essential oil applied was 1.56, 3.125, 6.25 and 12.5 µl corresponding to 0.39, 0.782, 1.563 and 3.125 µL/L air. *S. hortensis* exhibited considerable effect.	[15]
Tribolium castaneum	*S. hortensis* (Essential oil)	Not reported	After 48 h of exposure, the LC_{50} value was calculated as 192.35 µL/L.	[7]
Tribolium confusum	*S. thymbra* (Essential oil)	Not reported	Essential oil showed moderate toxicity as vapour with doses in the range of 108-135 µL/L air and at exposure periods varying between 24-144 h.	[9]

Table 2. Insect repellence potential of *Satureja* species[1]

Insect	Plant species	Main compounds	Short explanation	References
Aphis fabae *Brevicoryne brassicae*	*S. hortensis* (Essential oil) *S. hortensis* (Essential oil)	Not reported	According to the results obtained from behavioural and electrophysiological studies, *S. hortensis* volatile repelled *A. fabae* and *B. brassicae* effectively.	[28]
Ephestia kuehniella	*S. hortensis* (Essential oil)	Not reported	Repellency of this oil against *E. kuehniella* found as 6.40 µL/L air (average repellency 85%, repellency class V).	[7]
Frankliniella occidentalis	*S. montana* (Essential oil)	Not reported	At a concentration of 0.5%, essential oil exhibited repellency. The incorporation of alginate and methylcellulose polymers into treatment solutions containing 0.5% concentration of essential oil resulted in remarkable repellency.High repellency was maintained for 4 d when a 0.5% concentration of the alginate was used in combination with a 0.5% concentration of essential oil.	[25]
Plodia interpunctella	*S. hortensis* (Essential oil)	Not reported	Repellency of this oil against *P. interpunctella* found as 6.40 µL/L air (average repellency 80%, repellency class IV).	[7]
Sitophilus oryzae	*S. thymbra* (Essential oil)	Not reported	Essential oil effectively repelled adults in food preference tests. In the presence of oil, only 5.2-17.4% of the insects settled in the treated food.	[27]
Triatoma infestans	*S. parvifolia* (Essential oil)	Piperitone, piperitenone, *cis*-piperitenone epoxide, piperitenone oxide	Essential oil showed excellent properties with repellency values between 60 and 100%.	[26]
Tribolium castaneum	*S. hortensis* (Essential oil)	Not reported	Repellency of this oil against *T. castaneum* found as 6.40 µL/L air (average repellency 92.5%, repellency class V).	[7]
Tribolium confusum	*S. thymbra* (Essential oil)	Not reported	In area preference test with adults, repellencies over or about 50% were retained for 2 weeks with the essential oil. Essential oil gave repellency falling into the range of promising repellents, that is, presumably, a 40.1-60% repellency as an overall average of an 8 weeks exposure.	[27]

[1] Essential oils of the plant species given in the table were used as the insect repellence agent.

Table 3. Antiviral activity potential of *Satureja* species

Virus	Plant species	Main compounds	Short explanation	References
Herpes simplex virus type 1 (HSV-1)	*S. thymbra* (Ethanol extract)	Not reported	Extract showed high selective index (SI) against HSV-1.	[56]
	S. cuneifolia (Essential oil)	Not reported	Essential oil displayed strong antiviral effect against HSV-1, ranging between 0.8 and 0.025 µg/ml.	[51]
	S. thymbra (Essential oil)	α-pinene, sabinene, β-pinene, *p*-cymene, γ-terpinene	IC_{50} and selectivity index (SI) values were determined as 220 ± 1.6 and 4.5, respectively in the presence of essential oil against HSV-1.	[53]
	S. boliviana (Aqueous extract)	Not reported	The aqueous extract showed better antiviral activity than that of ethanolic one against HSV-1.	[54]
Parainfluenza virus type 3 (PI-3)	*S. cuneifolia* (Essential oil)	Not reported	Antiviral activity of the essential oil ranged between 1.6 and 0.2 µg/ml.	[51]
Tobacco mosaic virus (TMV) Cucumber mosaic virus (CMV)	*S. montana* ssp. *variegate* (Essential oil)	Carvacrol, thymol	In the presence of essential oil, the number of local lesions on both TMV and CMV infected plants was reduced for 29.2% and 24.1%, respectively.	[52]
Severe acute respiratory syndrome coronavirus (SARS-CoV)	*S. thymbra* (Essential oil)	α-pinene, sabinene, β-pinene, *p*-cymene, γ-terpinene	The essential oil showed no antiviral activity against SARS-CoV.	[53]
Vesicular stomatitis virus (VSV) Poliovirus type 1 (PV-1)	*S. boliviana* (Aqueous extract)	Not reported	The aqueous extract showed better antiviral activity than that of ethanolic one against VSV.	[54]
Human immunodeficiency virus type 1 (HIV-1)	*S. montana* (Aqueous extract)	Not reported	The extract showed potent anti-HIV activity with an ED value of 16 µg/ml and showed inhibitory activity against HIV-1 reverse transcriptase.	[55]

Table 4. Anti-leishmanial, anti-protozoal and trypanocidal activities of *Satureja* species

Organism	Plant species	Main Compounds	Short explanation	References
Leishmania major	*S. hortensis* (Ethanolic extract)	Not reported	The extract displayed high anti-leishmanial activity (IC_{50} 15.625 µM). It was also found toxic against the J774 macrophage cell line (IC_{50} 100.44 µM).	[58]
	S. bakhtiarica (Essential oil)	Thymol, *p*-cymene	The essential oil showed higher activity than that of standard anti-leishmania drug, glucantime. All the parasites were killed after 24 hours.	[59]
	S. khuzestanica (Ethanolic and methanolic extracts)	Not reported	The ethanolic and methanolic extracts inhibited the parasite after 24 h incubation (IC_{100} 2.4 and 4.8 mg/ml, IC_{50} 0.3 and 0.6 mg/ml).	[60]
	S. khuzestanica (Essential oil)	Carvacrol, tetradecane, hexadecane 5 butyl	The lesions size in essential oil treated animals was restrained but not significantly different from the control group due to the low sample size or concentration of essential oil.	[61]
Plasmodium falciparum (D10 and W2 strains)	*S. thymbra* (Essential oil)	Thymol, carvacrol, terpinen-4-ol	The essential oil of savory, rich in thymol, was the most effective against P. falciparum with an inhibitory activity independent from the time of collection (IC_{50} 17-26 µg/ml on D10 and 9-11 µl/ml on W2). Thymol was confirmed as mainly responsible for this activity (IC_{50} 19.7 ± 3.0and 10.6 ± 2.0 µg/ml on D10 and W2, respectively).	[62]
Plasmodium falciparum K1	*S. parvifolia* (Bioassay-guided fractionation of MeOH extract)	Triterpenic acids (ursolic acid, oleanolic acid), Flavonoids (eriodictyol, luteolin)	Constituents of the extract were determined as ursolic acid, luteolin, oleanolic acid and eriodictyol (IC_{50}: 4.9, 6.4, 9.3 and 17.2 µg/ml, respectively).	[63]
Leishmania donovani *Leishmania aethiopica*	*S. punctata* ssp. *punctata* (Essential oil)	Geranial, neral, α-bisabolol, (E)-nerolidol	Essential oil showed effect on promastigotes (MIC 76.5 to 312.5 nl/ml) and amastigotes (EC_{50} 4.06 to 131.00 nl/ml) of *L. donovani* and *L. aethiopica*, and varying toxicities on THP-1 cells (CC_{50} 0.013 to 350 nl/ml with selectivity index between 0.001 and 28) and erythrocytes (with LC_{50} 0.35 to 1.52 µl/ml).	[64]
Trypanasoma cruzi	*S. parvifolia* (Aqueous extract)	Not reported	Aqueous extract showed trypanocidal activity with a percentage of growth inhibition higher than 70% at a concentration of 100 µg/ml.	[65]

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