An Update on Pharmacology of *Satureja* Species: From Antioxidant, Antimicrobial, Antidiabetes and Anti-hyperlipidemic to Reproductive Stimulation

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**Abstract:** Since ancient, the genus *Satureja* L. is well recognized for its therapeutic values. Only recently, scientists have been aware of its new medicinal aspects. In our last review, we evaluated existing scientific data about this genus. Regarding ongoing reports and new multi-functional properties of this plant we were interested to update pharmacology of *Satureja*. Data were gathered using scientific books, journals, articles and websites including Pubmed, Scopus and Google Scholar up to 25th April 2010. Of initial search, 1540 records were reviewed for inclusion or exclusion in study, of which 71 publications were included. Different species of *Satureja* are famous for their analgesic, antiseptic, antimicrobial, antiviral, antioxidant, antiproliferative, antiprotozoal, antifungal, antidiarrheal, anti-inflammatory, anti-nociceptive, anticholinesterase and vasodilatory activities. The valuable therapeutic aspects of this genus are mostly correlated to the existence of essential oils, flavonoids and triterpenoids. The combination of two or more subspecies acting by different mechanisms to produce a synergistic effect should be considered. Based on the conducted assessments so far, antibacterial, antifungal, antiviral, antioxidant, anti-diabetic, vasodilatory and analgesic activities are characterized as the most applicable properties of *Satureja* subspecies. Further studies are needed to confirm novel pharmacological aspects of this genus in both animal and human.

**Key words:** *Satureja*, pharmacology, toxicology, animal, human

**INTRODUCTION**

Accessibility and affordability of the medicinal herbs have made them as fundamental part of many people’s life all over the world. The selection of medicinal plants is a conscious process, which has led to an enormous number of medicinal plants being used by the numerous cultures of the world (Heinrich *et al.*, 2004). Surveys conducted in Australia and US indicate that almost 48.5 and 34% of individuals used at least one form of unconventional therapy, including medicine, respectively (Kim *et al.*, 2007). According to the World Health Organization (WHO), about 65-80% of the world’s population in developing countries, due to poverty and lack of access to modern medicine, depends essentially on plants for their primary health care (Calixto, 2005). Regarding the lack of safe modern drugs, evaluation of effective plants for diseases like diabetes has been recommended by WHO (Kim *et al.*, 2007). In the recent years, efficacy of herbal medicines in diseases like inflammatory bowel disease (Rahimi *et al.*, 2009; Rezaie *et al.*, 2007), obesity (Hasani-Ranjbar *et al.*, 2009a), diabetes (Rahimi *et al.*, 2005), pancreatitis (Monfared *et al.*, 2009), inflammatory and oxidant-related diseases (Hasani-Ranjbar *et al.*, 2009b; Rahimi *et al.*, 2010) has been systematically reviewed. It is estimated that close to 25% of the active compounds in currently prescribed synthetic drugs were first identified in plant resources (Halterstein, 2005) and 20000 plants have been used for medicinal purposes, which, 4000 have been used commonly and 10% of those are commercial.

The genus *Satureja* L. (savory) belonging to the family Lamiaceae (labiatae), subfamily Nepetoideae and tribe Mentheae contains about 200 species of aromatic herbs and shrubs that are grown in Middle East, Mediterranean region to Europe, West Asia, North Africa, the Canary Islands and South America. Over 30 species of this genus are distributed in eastern parts of Mediterranean area (Cantino *et al.*, 1992). The known characteristic of the subfamily Nepetoideae is that its representatives contain more than 0.5% of essential oil. Moreover, remarkable differences between and within the

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chemical composition of the essential oils of Satureja subspecies has been found (Slavkovska et al., 2001). Phytochemical studies have revealed volatile oils, terpenes, phenolic compounds, steroids, acids, gum, mucilage and pyrocatechol as the main components of Satureja species. The major constituents of the essential oils from savory species are phenols, carvacrol, thymol and flavonoids (Sefikdon et al., 2004). Regarding existence of high amount of thymol and carvacrol in Satureja species, good smelling and simple cultivation, they are used as a flavoring compound in food, pharmaceutical and cosmetic industries. Savory species have been traditionally used as muscle pain reliever, tonic and carminative in treating stomach and intestinal disorders such as cramps, nausea, indigestion and diarrhea (Zargari, 1990). In the last five years, other properties of Satureja species such as antibacterial, antifungal, antioxidant, anti-diabetes, anti-HIV, anti-hyperlipidemic, reproduction stimulatory, expectorant and vasodilatory activities have been demonstrated (Abdollahi et al., 2003; Amanlou et al., 2005; Basir et al., 2007; Deans and Svboda, 1989; Hajhashemi et al., 2000; Sahin et al., 2003; Yamasaki et al., 1998; Vagionas et al., 2007; Vosough-Ghanbari et al., 2008).

An extensive review of the literature regarding biological and composition of Satureja species has been already published. The aim of this review is to complete on previous data specially those provided since the publication of the above-mentioned reviews. The present work is an update on pharmacology of Satureja up to May 2010.

MATERIALS AND METHODS

The data presented in this review were collected using all scientific data come from encyclopedia books, journals, articles and websites Pubmed, Scopus, Scirus and Google Scholar up to 25th April 2010. Of initial search, 1540 records were reviewed for inclusion or exclusion in study, of which 71 publications were included.

RESULTS AND DISCUSSION

As Satureja sp. are consumed commonly, their possible beneficial health effects have faced a great deal of attention. Recently, the consumption of natural antioxidant that occur in all higher plants and in all parts of them, has risen up regarding the side effects of synthetic ones (Bakkali et al., 2008). Antioxidant activity of Satureja subspecies have been confirmed in many studies (Exarchou et al., 2002; Madsen et al., 1998; Radonic and Milos, 2003). The oils of genus Satureja are being filled with isopropenoids such as carvacrol, thymol, flavonoids, β-caryophyllene, γ-terpinene, p-cymene and limonol, which are expected to possess strong antioxidant effects (Ruberto and Baratta, 2000). The constituents containing hydroxyl group exhibited relatively strong antioxidant effect in S. Montana (Radonic and Milos, 2003). Newly, S. khouzestanica essential oils (SKEO) was found to protect rat reproductive system from toxicity of cyclophosphamide that is currently used an anticancer alkylating agent having adverse effect on male reproductive tract (Rezvanfar et al., 2008). In a related study, SKEO protected rats from cyclophosphamide-induced Hemorrhagic Cystitis (HC) by reduction of free radical-induced toxic stress (Rezvanfar et al., 2010). Interestingly, the essential oil of S. ciliaca has been suggested for usage as a natural antioxidant and aroma agent in butter in a dose dependent manner (Ozkan et al., 2007).

Generally, production of essential oils by plants is a source of self protection against environmental pathogens. Antibacterial activity of essential oils depends on the type, composition and concentration of the oil, the type and concentration of the target microorganism, the composition of the substrate and the processing/storage conditions (Baydar et al., 2004). The concentration of essential oils in S. thymbra and S. pannassica is known to be fluctuated. Those oils which were obtained during the flowering period were found the most potent in exhibiting the lowest Minimum Inhibitory Concentration (MIC) values and retaining considerable antibacterialic properties (Chorianopoulos et al., 2006).

As yet, carvacrol and thymol play the fundamental roles in antimicrobial activity of this genus. In an interesting study in Turkey, carvacrol the major constituent of the essential oil of S. spicigera was tested against 25 phytopathogenic bacterial strains and exhibited potent antibacterial activity over a broad spectrum of the bacteria. Their results demonstrated that S. spicigera oil could be used to control agricultural plant pathogenic bacteria and as a seed disinfectant (Kotan et al., 2010). Of fifty-five compounds isolated from the oil of S. cuneifolia, linalool and α-pinene were found to be the dominant compounds. The oil exhibited a complete inhibition of the growth of mostly all tested microorganisms at the lowest supplied concentration.

Antifungal activity of the different species of savory have been reported frequently (Boyrac and Ozcan, 2006; Sokovic et al., 2002). Potent antiviral activities of S. boliviana (against viruses-HSV-1 and VSV) and S. montana (against HIV-1) have been proven by Abad et al. (1999) and Yamasaki et al. (1998), respectively.

Up to date, limited investigations have noticed to the anti-diabetes effects of Satureja sp. Anti-diabetic activity of S. khouzestanica has been proven in several studies.
It is thought that this activity is mostly mediated through antioxidant potential of this genus (Basiri et al., 2007; Saadat et al., 2004). The antioxidant property of S. khuzestanica is also known as a reasonable explanation for its triglyceride-lowering effects (Abdollahi et al., 2003). The investigation showed that carvacrol, thymol and flavonoids (the main constituents of S. khuzestanica essential oil) are responsible to marked reduction of serum cholesterol levels in diabetic patients. Confirming those findings, Mchedlishvili et al. (2005) explained flavonoids isolated from S. hortensis responsible for reduction of cholesterol level in rabbits. Study on the effect of SKEO on male rat fertility has revealed significant improvements in potency, fecundity, fertility index and litter size. Additionally a significant decrease in post implantation loss has been observed (Haeri et al., 2006).

Lamiaceae is well recognized as a family with great antispasmodic and pain reliever properties. Due to the broad distribution of the species of the genus Satureja, various compounds are recognized responsible for its analgesic effect. For instance, three known flavonoids (naringenin, eriodictyol and luteolin) isolated from S. obovata exhibited significant laxant effects and (De Rojas et al., 1999) while eriodictyol (5,7,3,4 -tetrahydroxyflavanone) isolated from same species showed slight vasodilatory activity in rats and (De Rojas et al., 1999). Two studies clarified SKEO has beneficial anti-inflammatory effects comparable to those of prednisolone, indomethacin and morphine (positive controls) (Amanlou et al., 2005; Ghazanfari et al., 2006). In contrast, some species does not show any anti-inflammatory effects. The essential oil of S. thymbra L. did not show any anti-inflammatory effect while it caused central analgesic activity in mice and rats (Karabay-Yavasoglu et al., 2006).

Despite the contradictions about the safety and toxicity of various species of Satureja, many people are consuming the subspecies as herbal tea, spices and additives every day worldwide. As earlier mentioned it is necessary to differ between the cytotoxic effects of the subspecies on microorganisms and its toxic effects in eukaryotic cells. The essential oils of S. hortensis and S. khuzestanica exhibited protective effects against the toxicity of hydrogen peroxide and malathion in rats, respectively (Behravan et al., 2006; Basiri et al., 2007). Another study revealed that SKEO protects reproductive system from toxicity of cyclophosphamide. Co-administration of SKEO significantly improved cyclophosphamide-induced changes in plasma testosterone, sperm quality, spermatogenesis, fertility, toxic stress and DNA damage (Rezvanfar et al., 2008). The biological activities and the major components isolated from the most common species of Satureja. have been depicted in Table 1.

<table>
<thead>
<tr>
<th>Botanical and species</th>
<th>Local name</th>
<th>Therapeutic indications</th>
<th>Effective component</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. acinos L.</td>
<td>-</td>
<td>-</td>
<td>Triterpenes, oleastoinic, unsolytic, estragole, naringenin, rutinoside and eriodictyol</td>
<td>Escudero et al. (1985)</td>
</tr>
<tr>
<td>S. antiquedensis</td>
<td>-</td>
<td>Antibacterial</td>
<td>Carvacrol and p-cymene</td>
<td>Aziz et al. (2005)</td>
</tr>
<tr>
<td>S. backianica</td>
<td>Marzeh</td>
<td>Antifungal</td>
<td>Carvacrol, γ-terpinene and p-cymene</td>
<td>Sefidkon et al. (2004)</td>
</tr>
<tr>
<td>S. balsamita Husskn. ex Boiss.</td>
<td>-</td>
<td>Flavouring</td>
<td>Carvacrol, γ-terpinene and p-cymene</td>
<td>Kurkcuoglu et al. (2001)</td>
</tr>
<tr>
<td>S. boiviniana Briq.</td>
<td>-</td>
<td>Antiviral</td>
<td>P-terpinene, β-caryophyllene and germacrene D</td>
<td>Laurent et al. (1997), Vittero et al. (2000)</td>
</tr>
<tr>
<td>S. corola Janka</td>
<td>-</td>
<td>Wild savory or cureate Turkish savory</td>
<td>Germacrene-D</td>
<td>Tunen et al. (1998)</td>
</tr>
<tr>
<td>S. edmondii</td>
<td>Marzeh</td>
<td>Antioxidant</td>
<td>Carvacrol and thymol</td>
<td>Sefidkon et al. (2004)</td>
</tr>
<tr>
<td>S. forbesi (Benth.) Briq.</td>
<td>-</td>
<td>-</td>
<td>Geranial, nerol</td>
<td>Oret et al. (2009)</td>
</tr>
<tr>
<td>S. gilosii</td>
<td>-</td>
<td>Antiprotozoal</td>
<td>Mono and sesquiterpene peroxides</td>
<td>Labbe et al. (1993)</td>
</tr>
<tr>
<td>S. gulgula (Michx.) BRIQ.</td>
<td>Smooth savory</td>
<td>-</td>
<td>Germacrene D, isomenthone, menthone and limonene</td>
<td>Duke and Beckstorn-Sternberg (2001)</td>
</tr>
<tr>
<td>S. grandiflora L.</td>
<td>French savory</td>
<td>-</td>
<td>Germacrene D, isomenthone, pulegone and methanol</td>
<td>Duke and Beckstorn-Sternberg (2001), Hajhashemi et al. (2002), Zargari (1990), Gulluce et al. (2003), Sahin et al. (2003), Behravan et al. (2006), Mchedlishvili et al. (2005)</td>
</tr>
<tr>
<td>S. hortensis L.</td>
<td>Summer savory</td>
<td>Analgesic Antibacterial Antifungal Antoxidant Anti-inflammatory</td>
<td>Carvacrol, γ-terpinene, thymol and p-cymene</td>
<td></td>
</tr>
<tr>
<td>Botanical and species</td>
<td>Local name</td>
<td>Therapeutic indications</td>
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<tr>
<td><em>S. icerica</em> P.H. Davis</td>
<td>-</td>
<td>Antibacterial</td>
<td>Carvacrol</td>
<td>Tunen et al. (2000)</td>
</tr>
<tr>
<td><em>S. intermedia</em> C.A. Mey.</td>
<td>-</td>
<td>Antibacterial</td>
<td>Thymol, γ-terpinene and p-cymene</td>
<td>Sefidkon and Jamzad (2004)</td>
</tr>
<tr>
<td><em>S. khusenitica junzad.</em></td>
<td>-</td>
<td>Antibacterial</td>
<td>P-cymene and carvacrol</td>
<td>Haert et al. (2006), Stadlat et al. (2004)</td>
</tr>
<tr>
<td><em>S. kusheis</em> Wierzb. ex Hadr.</td>
<td>-</td>
<td>Antifungal</td>
<td>p-cymene, geraniol and β-elemene</td>
<td>Azar et al. (2005), Sefidkon and Jamzad (2004)</td>
</tr>
<tr>
<td><em>S. macrantha</em> C.A. Mey.</td>
<td>-</td>
<td>Antibacterial</td>
<td>Carvacrol, p-cymene, limonene and thymol</td>
<td>Amer et al. (2006), Sefidkon and Jamzad (2004)</td>
</tr>
<tr>
<td><em>S. montana</em> L.</td>
<td>Winter savory</td>
<td>Antiinflammatory Antioxidant Anticonvulsant</td>
<td>Thymol, p-cymene, carvacrol, γ-terpinene, flavonoids, triterpenes</td>
<td>Mastelic and Jekovic (2002)</td>
</tr>
<tr>
<td><em>S. parvissalis Heldr.</em> and <em>S. Sart ex Boiss.</em></td>
<td>-</td>
<td>Antibacterial</td>
<td>Caryophyllene, carvacrol, caryophyllene oxide, spathulenol, p-cymene and limonol</td>
<td>Chorianopoulos et al. (2006), Tzikou and Skalitsa (2003)</td>
</tr>
<tr>
<td><em>S. pilosa</em> Velen.</td>
<td>Pampa savory</td>
<td>Antibacterial</td>
<td>-</td>
<td>Tunen et al. (2000)</td>
</tr>
<tr>
<td><em>S. punctata</em></td>
<td>-</td>
<td>Antiprotozoal</td>
<td>-</td>
<td>Taran et al. (2010)</td>
</tr>
<tr>
<td><em>S. sahendica</em></td>
<td>Culinary herbs</td>
<td>Antibacterial</td>
<td>Thymol, p-cymene and γ-terpinene</td>
<td>Sefidkon et al. (2004)</td>
</tr>
<tr>
<td><em>S. spicigera</em> (C. Koch) Boiss.</td>
<td>-</td>
<td>Antibacterial</td>
<td>Thymol, p-cymene and γ-terpinene and carvacrol</td>
<td>Azar et al. (2005), Elbekhar et al. (2009)</td>
</tr>
<tr>
<td><em>S. spinosa</em> L.</td>
<td>-</td>
<td>Antifungal</td>
<td>Monoterpenoid hydrocarbons and phenolic monoterpenes</td>
<td>Chorianopoulos et al. (2004)</td>
</tr>
<tr>
<td><em>S. subspicata</em> Vis.</td>
<td>-</td>
<td>Antibacterial</td>
<td>Carvacrol, α-pinene, p-cymene, γ-terpinene and thymol methyl ether</td>
<td>Skocibasic et al. (2008)</td>
</tr>
<tr>
<td><em>S. widmanianum</em> (Lallem.) Velen.</td>
<td>-</td>
<td>Antibacterial</td>
<td>Carvacrol, thymol, p-cymene and γ-terpinene</td>
<td>Bas et al. (2001)</td>
</tr>
</tbody>
</table>

CONCLUSIONS

Clearly, herbal-based pharmaceuticals, cosmetics and flavoring are more welcoming every day. Numerous studies have been conducted to brighten both theoretical and practical aspects of the traditional usage of *Satureja* sp. There are remarkable varieties in chemical composition and therapeutic values of different species of this plant. In a recent investigation in Ethiopia, the oil of *S. punctata* contained 67 compounds of which geraniol and neral were the main components with significant antiprotozoal activities (Taran et al., 2010). Similarly, these compounds were the major constituents of the essential oil of *S. forbesii* with potent antioxidant activity (Ortet et al., 2009). Sefidkon et al. (2009) presented carvacrol and p-cymene as the most frequent component in *S. bacthiarica* oil while carvacrol and thymol were the most fluctuated elements in the oil of *S. mutica*. Their results showed the high antibacterial effect of these oils. Based on the conducted assessments so far, antibacterial, antifungal, antiviral, antioxidant, anti-diabetic, vasodilatory and analgesic activities are characterized as the most applicable properties of *Satureja* subspecies. In 2009 the inhibitory activity of acetyl- and butyrylcholinesterase by *S. montana* extracts was assessed as a potential indicator for the control of Alzheimer's disease. The result indicated a significant anticholinesterase activity of this species (Silva et al., 2009).

According to the literature reviews, more than 90% of the present investigations only emphasized on the antibacterial activities of savory sp. while the other biological effects also seem promising. Monitoring and standardization is needed to direct studies passing
through clinical trials. Various molecular, cellular and whole animal models should be used to demonstrate more valuable significance of *Satureja* sp. Future exploration are critical to assess the synergistic effects, efficacy and edibility of these essential oils.

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