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CHEMICAL CONSTITUENTS AND BIOLOGICAL ACTIVITIES OF SOME IRANIAN *STACHYS* SPECIES

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ABSTRACT

Stachys is one of the largest genera in the flowering plant family Lamiaceae. Estimates of the number of species in the genus vary from about 300, to about 450. The type species for the genus is *Stachys sylvatica*. *Stachys* is in the subfamily Lamioideae. Generic limits and relationships in this subfamily are poorly known. The distribution of the genus covers Europe, Asia, Africa, Australasia and North America. Common names include hedgenettle, heal-all, self-heal, woundwort, betony, and lamb's ears. Wood betony, *Stachys officinalis*, was the most important medicinal herb to the Anglo-Saxons of early medieval Great Britain. The Chinese artichoke (*St. affinis*), is grown for its edible tuber. Several species are cultivated as ornamentals. Woolly Betony (*St. byzantina*) is a popular decorative garden plant. *Stachys* was named by Linnaeus in Species Plantarum in 1753. The name is derived from the Greek word σταχυς (*stachys*), meaning "an ear of grain", and refers to the fact that the inflorescence is often a spike. The name woundwort derives from the past use of certain species in herbal medicine for the treatment of wounds. *Stachys* species are used as food plants by the larvae of some Lepidoptera species, including the moths *Coleophora auricella*, *C. lineolea*, and *C. wockeella*, all recorded on *St. officinalis*. They are also widely used by the European wool carder bee (*Anthidium manicatum*), which scrape the hairs from the plant in order to use them for building their nests. The present review descripts the chemical and biological activities of some Iranian *Stachys* species, *Stachys acerosa* Boiss., *Stachys asterocalyx* Rech. f., *Stachys byzanthin* C. Koch., *Stachys inflata* Benth., *Stachys lavandulifolia* Vahl., *Stachys multicaulis* Benth., *Stachys obtusicrena* Boiss., *Stachys persica* Gmel., *Stachys pilifera* Benth., *Stachys turcomanica* Trautv. and *Stachys schtschegleevii*.

KEYWORD: Iranian *Stachys* Species, Lamiaceae, Constituents and Biological Activities.

INTRODUCTION

The genus *Stachys* comprises more than 270 species and is considered one of the largest genera of the family Lamiaceae. There are 34 *Stachys* species, growing in Iran, 13 of these which are endemic [1], [2]. Some species, such as *St. recta* and *St. alpine* are highly polymorph, with a number of intraspecific taxa. Plants of this genus have long been applied in folk medicine to treat genital tumors, sclerosis of the spleen, inflammatory tumors, cough and ulcers.[3]

The extract obtained from the non-flowering aerial parts of *St. inflata* have been used in Iranian folk medicine in infective asthmatic, rheumatic and other inflammatory disorders.[4]

Since ancient times the crude herbal extracts of aromatic plants have been in use for different purposes, such as food, drugs and perfumery. These extracts have recently gained popularity and scientific interest in biologically active compounds isolated from plant species for the elimination of pathogenic microorganisms because of the resistance that they have built against antibiotics.[5] Plant products would be useful in preserving food storages from contamination[6], whereas the synthetic antioxidants that have been used previously are now toxicologically suspecting.[7],[8]

Stachys acerosa Boiss.

The oil obtained by hydro-distillation of the aerial parts of *Stachys acerosa* Boiss., which is endemic to Iran, was analyzed by GC/MS. There were twenty components including cis-chrysanthenyl acetate (41.0%) and linalool (23.5%), comprising 92.1% of the total oil detected. The oil was richer in oxygenated monoterpenes than sesquiterpenes.[9]

In another study, the essential oil of the aerial parts of *Stachys acerosa*, which belongs to the Lamiaceae family and grows in central Iran, was obtained by a hydro-

distillation method and analyzed by GC and GC-MS apparatus. Fourteen compounds representing 98.8% of the oil were identified. Among them N-methylisatin (30%), α-pinene (25%), sabinene (12.3%), and 2-hydroxyacetophenone (11.2%) were the major constituents of the oil, which were obtained in 0.1% yield.[10]

***Stachys asterocalyx* Rech. f.**

Water-distilled essential oil from the aerial parts of *Stachys asterocalyx* Rech. f. which is endemic to Iran was analyzed by GC and GC/MS. The major components of the oil of *St. asterocalyx* were α-bisabolol (25.1%) and linalool (18.0%).[11]

***Stachys byzanthin* C. Koch.**

The chemical composition of the oil obtained by hydro-distillation of the aerial parts of *Stachys byzanthin* C. Koch. was investigated by GC and GC/MS analysis. Twenty-four components representing 88.5% of the total oil were identified, of which sesquiterpenes; α- copaene (16.5%), spathulenol (16.1%), β- caryophyllene (14.3%) and β- cubebene (12.6%) were the major components.[12]

In another study, the oils obtained by hydro-distillation and steam distillation of the aerial parts of *St. byzanthin* C. Koch. grown in Iran were analyzed by GC/MS. Both hydro-distilled and steam distilled essential oils of the aerial parts of *St. byzantina* were rich in sesquiterpenes such as α-copaene (16.6% and 10.4%), spathulenol (16.1% and 18.5%) and β-caryophyllene (14.3% and 13.5%), respectively.[13]

In another study, from the aerial parts of *Stachys byzanthina* C. Koch., an acyclic diterpene ester, phytyl nonadecanoate, was isolated for the first time. In addition, two normal alkanes, one fatty acid and two sterols were also identified. Structures were established by conventional methods of analysis and confirmed by ^{1}H, ^{13}C NMR and mass spectral analysis. Anti-inflammatory effects of acetone and methanolic extracts of aerial parts of *Stachys byzanthina* C. Koch. were investigated in this study. For assessment of anti-inflammatory properties, two well-characterized inflammatory models, formalin test and carrageenan-induced paw edema were used. Intraperitoneal injections of either acetone or methanolic extract of *Stachys byzanthina* C. Koch. (50, 100 and 200 mg/kg), 30 min before formalin injection, had no effects against the first phase of the formalin-induced pain, but all three doses caused a significant blockade on the second phase ($p < 0.01$). The recording of the early phase started immediately after formalin injection and lasted for 10 min (0–10 min).[14]

***Stachys benthamiana* Boiss.**

The composition of the essential oil from *Stachys benthamiana* Boiss. obtained by hydro-distillation was analyzed by GC and GC/MS. Twenty compounds were identified in the oil of *St. benthamiana*, representing 91.2% of the total oil, with germacrene D (16.8%), linalool (16.6%) and β-caryophyllene (11.0%) as the major constituents. The endemic oil of *St. benthamiana* consisted mainly of sesquiterpenes.[15]

***Stachys inflata* Benth.**

The essential oils obtained by hydrodistillation of three different stages of growth, per-flowering, flowering and post-flowering of *Stachys inflata* Benth. were analyzed by GC and GC-MS. Twenty-eight components were identified in the pre-flowering oil and flowering oil, and twenty-four components in the post-flowering oil, representing 98.3 %, 91.9 % and 90.1 % of their total oils, respectively. All three samples were characterized by higher amounts of germacrene-D (30.3 %, 32.9 % and 15.4 %) and limonene (16.4 %, 15.6 % and 13.1 %), respectively. The other main component in the pre-flowering oil was α-pinene (18.5%) and in the post-flowering oil, bicyclogermacrene (14.3%), spathulenol (13.6%) and α-pinene (12.1%) were predominated.[16]

In another study, Composition and antioxidant and antimicrobial activities of essential oil and methanol extract polar and nonpolar sub fractions of *Stachys inflata* were determined. GC and GC/MS analyze of the essential oil showed 45 constituents representing 95.46% of the oil, the major components linalool (28.5%), α-terpineol (9.4%), spathulenol (8.4%) and (2*E*)-hexenal (4.6%) constituted 51.0% of it. Essential oil and extracts were also tested for their antioxidant activities using 2, 2-diphenyl-1-picrylhydrazyl (DPPH) and β-carotene/linoleic acid assays. In the DPPH test, IC_{50} value for the polar sub fraction was 89.5µg/ml, indicating an antioxidant potency of about 22% of that of butylated hydroxytoluene (IC_{50} = 19.72 µg/ml) for this extract. In β-carotene/linoleic acid assay, the best inhibition belonged to the nonpolar sub fraction (77.08%). Total phenolic content of the polar and nonpolar extract sub fractions was 5.4 and 2.8% (w/w), respectively. The plant also showed a week antimicrobial activity against three strains of tested microorganisms. Linalool and α-terpineol were also tested as major components of the oil and showed no antioxidant but considerable antimicrobial activities.[17]

***Stachys lavandulifolia* Vahl**

The constituents of the oil obtained by hydrodistillation of *Stachys lavandulifolia* Vahl. grown in Iran were analyzed using GC (retention indices) and GC/MS. Fifty-five compounds were observed, of which 44 could be identified. The major components found in the oil were α-pinene (20.1%), β-pinene (12.1%) and spathulenol (7.2%).[18]

***Stachys multicaulis* Benth**

Water-distilled essential oil from the aerial parts of *Stachys multicaulis* Benth. Growing Wild in Iran was analyzed by GC and GC/MS. Bicyclogermacrene (23.0%), spathulenol (20.7%), germacrene D (12.4%)

and caryophyllene oxide (11.1%) were the predominant compounds in the oil of *St. multicaulis*.[11]

***Stachys obtusicrena* Boiss**

Water-distilled essential oil from the aerial parts of *Stachys obtusicrena* Boiss. which is endemic to Iran was analyzed by GC and GC/MS. In the oil of *St. obtusicrena*, α-pinene (34.6%), germacrene D (8.0%) and bicyclogermacrene (7.8%) were found to be the major constituents.[11]

***Stachys persica* Gmel**

The oils obtained by hydro-distillation and steam distillation of the aerial parts of *Stachys persica* Gmel. grown in Iran were analyzed by GC/MS. The essential oil obtained by hydro-distillation of the aerial parts of *St. persica* was characterized by a high amount of non-terpenoid components of which methyllinoleate (27.7%), hexadecanoic acid (9.8%) and 6,10,14-trimethyl-2-pentadecanone (9.2%) were the major constituents, whereas the steam distilled oil of the plant contained hexadecanoic acid (27.2%), carvacrol (9.4%) and eugenol (5.2%).[13]

***Stachys pilifera* Benth**

The oil obtained by hydrodistillation of the aerial parts of *Stachys pilifera* Benth. which are endemic to Iran, was analyzed by GC/MS. Thirty compounds representing 88.9% of the oil of *St. pilifera* were identified, among them *cis*-chrysanthenyl acetate (25.2%) and *trans*-verbenol (19.7%) being the major ones. The oil was richer in oxygenated monoterpenes than sesquiterpenes.[9]

***Stachys turcomanica* Trautv**

The composition of the essential oil from *Stachys turcomanica* obtained by hydro-distillation was analyzed by GC and GC/MS. Twenty-eight compounds were identified in the oil of *Stachys turcomanica* representing 93.0 % of the total oil with germacrene D (17.4 %), 7-epi-α-selinene (10.5 %), βelemene (9.2 %) and β-pinene (8.6 %) as the major constituents.[19]

Stachys schtschegleevii

The composition of the essential oil obtained by hydro-distillation from the leaves of *Stachys schtschegleevii* Sosn. before the flowering stage was analyzed by GC and GC-MS. Forty-five compounds representing 98.7% of the total oil were identified, of which α-pinene (36.4%), germacrene-D (18.6%), limonene (8.2%), and piperitone (6.2%) were the major constituents. Furthermore, antibacterial activity of the entire oil and its two main monoterpenes was evaluated against six Gram-positive and Gram-negative bacteria. The oil exhibited moderate activity against the tested bacteria.[20]

In another study, the results showed the various *Stachys* species (especially *St. byzantina* and *St. persica*) are valuable sources of natural compounds with important biological properties. Nine *Stachys* plants were collected from different regions of Iran. Cytotoxic activities of methanol, 80% methanol and dichloromethane (DCM) extracts of these plants were assessed on three human cancer cell lines (HL-60, K562 and MCF-7 cells) with the MTT assay, while antioxidant and antimicrobial activities were determined on methanol extracts by DPPH and nutrient broth micro-dilution assays, respectively. DCM extract of *St. pilifera* Benth. had the lowest IC50 in three cancer cell lines ranging from 33.1 to 48.2 µg/ml, followed by the 80% methanol extract of *St. persica* S.G.Gmel. ex C.A.Mey. (IC50 range: 62.1–104.1 µg/ml) and DCM extract of *St. byzantina* C. Koch (IC50 range: 62.7–131.0 µg/ml). *St. byzantine*, *St. lavandulifolia* Vahl., *St. acerosa* Boiss., *St. obtusicrena* Boiss. and *St. persica* showed lowests IC50 values in the DPPH scavenging assay (135.1, 162.6, 164.7, 169.4 and 172.4 µg/ml, respectively), while their total phenolic contents were 23.9, 18.2, 18.6, 20.4, 27.8 mg equivalent of Gallic acid in 1 g dry plant, respectively. The methanol extracts of *St. byzantina* and *St. persica* inhibited all six tested Gram-negative and Gram-positive bacterial strains.[21]

CONCLUSION

As mentioned in this review Constituents and Biological Activities of Some Iranian *Stachys* Species including *Stachys acerosa* Boiss., *Stachys asterocalyx* Rech. f., *Stachys byzanthin* C. Koch., *Stachys inflata* Benth., *Stachys lavandulifolia* Vahl., *Stachys multicaulis* Benth., *Stachys obtusicrena* Boiss., *Stachys persica* Gmel., *Stachys pilifera* Benth., *Stachys turcomanica* Trautv. and *Stachys schtschegleevii*.

Some species, such as *Stachys recta* and *Stachys alphina* are highly polymorth, with a number of intraspecific taxa. Plants of this genus have long been applied in folk medicine to react genial tumors, sclerosis of the spleen, inflammatory tumors, cough and ulcers.

Stachys species produce cis-chrysanthenyl acetate, linalool, α- bisabolol, α- copaene, spathulenol, β-caryophyllene, α- pinene, β- pinene, germacrene-D and bicyclogermacrene.

In fact the Iranian *Stachys* species has yielded a considerate amount of interesting terpenoids.

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