THE PHARMACOLOGICAL IMPORTANCE OF ANTIRRHINUM MAJUS- A REVIEW

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ABSTRACT

Antirrhinum majus (common snapdragon) is a species of flowering plant belonging to the genus Antirrhinum. It was used traditionally as a diuretic, for treatment of scurvy, liver disorders and tumors. The leaves and flowers were used as antiphlogistic, resolvent, stimulant and as poultices on tumours and ulcers. Antirrhinum majus contained amino acids, pigments, oils, anthocyanidins, flavonols, flavones, aurones, flavanones, cinnamic acids and many other compounds. The recent studies showed that Antirrhinum majus possessed antimicrobial, insecticidal, cytotoxic, antioxidant, central and peripheral nervous system effects, and many other biological activities. This review highlights the chemical constituents and biological effects of Antirrhinum majus.

Key words: Antirrhinum majus, Anthocyanidins, Biopesticides.

INTRODUCTION

Herbal Medicine is the oldest form of medicine known to mankind. Each population in the world developed its own traditional medical knowledge and experiences. Recent studies showed that plants are a valuable source of a wide range of secondary metabolites, which are used as pharmaceuticals, agrochemicals, flavours, fragrances, colours, biopesticides and food additives [1-61]. Antirrhinum majus a member of the genus Antirrhinum contained amino acids, pigments, oils, anthocyanidins, flavonols, flavones, aurones, flavanones, cinnamic acids and many other compounds. The recent studies showed that Antirrhinum majus possessed biological effects. This review was designed to highlight the chemical constituents and pharmacological effects of Antirrhinum majus.

Synonyms


Taxonomic classification

Kigdom: Plantae; Divison: Tracheophyta; Subdivision: Spermatophytina; Class: Magnoliopsida; Superorder: Asteranae; Order: Lamiales; Family: Scrophulariaceae Juss.; Genus: Antirrhinum L.: Species: majus [64].

Common names

Arabic: anf Al thwor, anf al ejil, lesan al saba, halq al saba, hink al saba, abo fam, fam al samaka; Brazilian: boca de leao; Czech: Hledík větší; Dutch: Grote leeuwebek; English: Snapdragon, lion’s mouth, rabbits mouth, toad’s mouth, dragon’s mouth; Estonian: Suur lõvilõug; Esperanto: Antirino granda, Antirino maja, Leonfaŭko granda; Finnish: Iso jalopeuran kita, Leijonankita; French: grand muffler, gueule de lion, gueule de loup; German: Löwenmaul; Italian: bocca di leone commune; Spanish: boca de dragon; Swedish: lejongap; Turkish: aslariagzi [62-63].

Distribution: It was distributed in Africa (Algeria, Libya, Morocco and Tunisia); Asia (Palestine, Lebanon, Syria, Iraq and Turkey); Europe (Albania, Croatia, Greece, Italy, Malta, Serbia, France, Portugal and Spain). It was now widely cultivated in temperate regions in gardens in many color and habit varieties [63, 65].

Description

Antirrhinum majus, or Common Snapdragon, is an annual, erect perennial plant. Plants usually reach a height of 2-3 feet (0.6-0.9 m) in containers and the landscape. Some plants can attain a height of up to 6 feet (1.8 m) if
planted in the landscape. Leaves are lanceolate to oblong-lanceolate to 3 inches (7.6 cm) long. There are many fancy and Latin named cultivars available, classified by size and color groupings. Snapdragons have a long been used in gardens and in the cut flower industry. They are easy plants to grow, whether in container or in the landscape. Flowers are borne in terminal racemes and will bloom in most areas from late spring into fall. In warmer areas, they bloom in the spring and again in the fall. Individual flowers reach from 1.5-2 inches (3.8-5.1 cm) long. When in flower they are very showy [65, 67].

Uses
The cultivated snapdragon, *Antirrhinum majus* was used as a model for biochemical and developmental genetics. It emerged as a model organism during early studies of inheritance and mutation because of its diploid inheritance, ease of cultivation, and variation in morphology and flower color [68].

However, for medical purposes, it was used traditionally as a diuretic, for treatment of scurvy, liver disorders, tumors and as a detergent and astringent. The leaves and flowers were used as antiphlogistic, resolvent and stimulant. They were also employed in poultices on tumours and ulcers. The plant was also used in the treatment of all kinds of inflammation and in haemorrhoids [69-70].

Chemical constituents
*Antirrhinum majus* contained 2.79-5.69% free amino acids, 2.15-4.69 % soluble sugars and carotenoids 0.22-0.27%. Application of the amino acids phenylalanine and tryptophan (each at the ratio of 50 or 100 ppm), applied separately or in combinations of the different concentrations increased free amino, soluble sugars and carotenoids [71].

*Antirrhinum majus* contained anthocyanidins, flavonols, flavones, aurones, flavanones, and cinamic acids. Geissman *et al* found that flavone, flavonol, aurone, and anthocyanin glycosides were present in *Antirrhinum majus* color types. Aurone pigment is produced in the flower petals only, the other pigments are found in flowers, stems, and leaves. However, Harborne isolated five flavones from the flowers of *Antirrhinum majus*, namely: apigenin 7,4′-diglucuronide, luteolin 7-glucuronide, chrysoeriol 7-glucuronide, kampferol 3-glucoside and kampferol 3,7-diglucoside. A new aurone, bracteatin 6-glucoside, was also isolated [65, 72-74].

Proanthocyanidins, flavonols and anthocyanidins were quantified in fruit during fruit growth and ripening. The concentrations of proanthocyanidins and total flavonols were highest in flower ovaries and earliest fruit development stages. Proanthocyanidins declined rapidly during ovary development and growth and then increased slightly during fruit ripening. Flavonols exhibited a less pronounced decline from levels in flowers and early fruit set stages, and also increased slightly during fruit ripening. The major flavonol glycosides were quercetin-3-galactoside, quercetin-3-arabinofuranoside, quercetin-3-rhamnoside, quercetin-3-(6″-benzoyl)-β-galactoside, methoxyquercetin pentoside, and quercetin-3-(6″-coumaroyl)-β-galactoside [75].

*Antirrhinum majus* also contained four tertiary alkaloids, one of which has been identified as 4-methyl-2,6-naphthyridine. A water-soluble base has been identified as choline [76]. It was also contained four major iridoid compounds (antirrhinoside, antirrhide, 5-glucosyl-antirrhinoside and linarioside) [77-78].

*Antirrhinum majus* was also rich in monoterpenes [79]. Three chalcones have been found in yellow flowers of *A. majus*, two of which have been identified as chalcononaringenin 4′-glucoside and 3,4,2′,4′,6′-pentahydroxychalcone 4′-glucoside [80]. There were a great seasonal differences in the total iridoids in *Antirrhinum majus*. The total contents of iridoids ranged 9.16 - 107.98 mg /g dry weight. The amount of Antirrhinoside, Antirrhide, 5-Glc-antirrhinoside, Linarioside were also differ. Their relative amounts (%) were (69.87-93.33%), (2.57-19.84%), (1.61-14.19%) , (0.00-2.97%) respectively [81].

There was seasonal and diurnal variation in the content of the four iridoids (antirrhinoside, antirrhide, 5-glucosyl-antirrhinoside and linarioside) found in cultivars of *Antirrhinum majus*. The seasonal variation in total iridoid content showed a marked bimodal distribution with high total values (around 100mg/g dry matter) early and late in the season and a very low content of all iridoids coinciding with the onset of flowering at the beginning of August. The relative contribution of antirrhinoside was significantly higher before flowering than after bud break. The relative decrease in antirrhinoside was counteracted by an increase of antirrhide, which was significantly higher after the onset of flowering than before. The diurnal variation showed a variation between 20 and 60mg/g dry weight, but there was no relation to light/darkness conditions, temperature patterns or water content [78].

The floral scent of snapdragon flowers consists of a relatively simple mixture of volatile organic compounds (VOCs). The three major snapdragon floral volatiles were myrcene, (E)-beta-ocimene, and methyl benzoate [82].

n-Hexane extract of *Antirrhinum majus* contained: 1-Methoxybutane, 3-Methylcyclohexanone, 4-Methyl lonone, 3,8-Dimethylundecanone, (E,E)-3,5-Octadien-2-one, Hene decane, trans-p-Menta-2,8-dien-1-ol, 2-Ethyl hexanoic acid, Carvomenthone, trans-1,3, cis-1,4-Menthol, 4-Methyldecan, 6-isopropyl-3-methylcyclohexen -2-one, Ethyl undecanoate, Eicosane, Octadecanoic acid ethyl ester, Hexadecanoic acid methyl ester and Protoverine [83].

Lipid classes fatty acids phytosterols and tocopherols composition of snapdragon (*Antirrhinum majus* seed) oil were determined by Ramadan and El-Shamy. They found that *Antirrhinum majus* seeds were a
good source of oil (12.3%). The amounts of neutral lipids in the oil were the highest, followed by glycolipids and phospholipids. Linoleic and oleic accounted for 88% of the total fatty acids. Snapdragon seed oil was characterized by a relatively high amount of phytosterols, wherein the sterol marker was β-sitosterol. All tocopherol isomers were present, where in γ-tocopherol constituted 81% of the total tocopherol content followed by β–tocopherol (ca. 14.3%) [84]. However, the occurrences (%) of volatile organic compounds in two *A. majus* subspecies was determined by Suchet *et al.*, as shown below in the table 1 [85].

Pharmacological effects

**Antimicrobial effect**

The antimicrobial assay of different concentrations of plant extract and fractions was studied against selected microorganisms. The results showed that when the concentration of plant extract and fraction was increased the antimicrobial activity also increased. The plant samples exhibited considerable antimicrobial activity against most of the bacterial and fungal strains. Disc diffusion method measured in inhibition zone (IZ) indicated that absolute methanol extract has significant inhibitory activity at the concentration of 10 mg/mL against bacterial strains such as *S. aureus* (IZ = 33.60 mm), *B. subtilis* (IZ 31.40 mm), *P. multocida* (IZ 29.40 mm), *E. coli* (IZ 30.50 mm) and against fungal strains *R. solani*, (IZ 31.10 mm), *A. niger* (IZ 30.30 mm), *A. alternata* (IZ 27.20 mm) and *A. flavus* (IZ 25.30 mm). The n-hexane extract (extracted by soxhlet) showed less activity against all the tested bacterial and fungal strains. It was observed that when the concentration of plant extract and fraction increased to 5 mg/mL some of the strains also inhibited which were resistant at 1 mg/mL concentration. The n-butanol fraction was unable to inhibit the growth of *E. coli*. The chloroform fraction was also unable to inhibit the growth of *S. aureus*, *B. subtilis*, *A. alternata* and *A. niger*. The ethyl acetate fraction showed significant activity as compared to the other fractions [83].

**Insecticidal effect:**

The iridoid glucoside, antirrhinoside, is constitutively distributed throughout *Antirrhinum majus* L. in a manner consistent with its possible role as an allelochecmochemical. However, the insect herbivory of iridoid glucoside, antirrhinoside was studied. Two generalist herbivores, *Lymatrina dispar* L. (gypsy moth) and *Trichoplusia ni* Hübner (cabbage looper) were chosen for feeding trials on excised whole leaves of *A. majus* and in artificial diet assays. In leaf excision feeding trials, fourth instar gypsy moth rejected, without sampling, the leaves of *A. majus* regardless of what node the leaf was excised from. In contrast, fourth instar cabbage looper readily fed on the excised leaves, and antirrhinoside was not found in their bodies or feces (frass) as determined by thin layer and high-pressure liquid chromatography. In the leaf and diet assays, a second major leaf iridoid in *A. majus*, antirrhize, was found in both cabbage looper and gypsy moth frass. In diet feeding assays, the growth of gypsy moth and cabbage looper were not inhibited by methanol extracts, iridoid fractions, or pure antirrhinoside at concentrations of 0.6% in diet, but cabbage looper growth was enhanced. At an antirrhinoside concentration of 3.3% in diet, gypsy moth growth was reduced, whereas cabbage looper growth again increased significantly relative to the control. It is likely that antirrhinoside functions as defense against herbivory for one generalist insect herbivore but also, at low concentrations, enhances the growth of another [86].

**Cytotoxic effect**

The cytotoxic effect of the plant extract and its fractions was studied by haemolytic activity against human red blood cells (RBCs) using Triton X-100 as positive control (99.78). The percentage lysis was evaluated by comparing the absorbance of sample with the Triton X-100 as positive control. The percent lysis red blood cells was observed after treatment with Snapdragon absolute methanol extract and its fractions as follows: absolute methanol extract (4.89 ± 0.04), n-butanol (4.14 ± 0.05), chloroform (3.18 ± 0.02), ethyl acetate (2.23 ± 0.03) and n-hexane extract (extracted by soxhlet) (2.45 ± 0.02). The study showed that the percent lysis of human erythrocytes resulted in less than 5.0 % for all samples, thus these findings indicate minor cytotoxicity of the plant [83].

**Antioxidant effects**

The radical scavenging activity (RSA) toward 1,1-diphenyl-2-picrylhydrazyl (DPPH) radicals and galvinoxyl radicals of *A. majus* oil were higher than those of extra virgin olive oil [84]. The antioxidant activity of absolute methanol extract and its fractions from the snapdragon (*Antirrhinum majus*) plant was evaluated. The presence of total phenolics content, IC₅₀ and the % inhibition in linoleic acid oxidation were evaluated. The antioxidant activity of plant extract and fractions was also studied using sunflower oil as an oxidative substrate. Peroxide value (PV), free fatty acids (FFA), conjugated dienes (Cd), conjugated trienes (CT) and para-anisidine values were also determined by stabilising the sunflower oil as oxidation substrate. Moreover, it was observed to provide a protective effect in *H₂O₂* -induced oxidative damage in plasmid pBR322 DNA, indicating that the plant has antioxidant properties. Accordingly, the authors revealed that snapdragon plant may be considered as a good source of natural antioxidants [83].

**Effect on central and peripheral nervous system:**

Aurones belong to the family of flavonoids, structurally isomers of flavones, were synthesized in *Antirrhinum majus* [75, 87]. They were named as benzylidenebenzofuran-3(2H)-ones. Aurones and extracts comprising them were useful in the prophylactic and/or
therapeutic treatment of an animal (including a human) with a phosphodiesterase (PDE) dependent disease or condition of the central nervous system. Among the diseases and conditions of the nervous system to be treated prophylactically or therapeutically, neurodegenerative disorders, such as Parkinson’s disease, Alzheimer’s disease, age related dementia or dementia in general, neurological trauma including brain or central nervous system trauma, depression, anxiety, psychosis, cognitive dysfunction, mental dysfunction, learning and memory disorders, and ischemia of the central and/or peripheral nervous systems [88].

Other biological effects
The iridoid glucoside, antirrhinoside, is constitutively distributed throughout Antirrhinum majus L. in a manner consistent with its possible role as an allelochemical. In diet feeding assays, the growth of gypsy moth and cabbage looper were not inhibited by methanol extracts, iridoid fractions, or pure antirrhinoside at concentrations of 0.6% in diet, but cabbage looper growth was enhanced. At an antirrhinoside concentration of 3.3% in diet, gypsy moth growth was reduced, whereas cabbage looper growth again increased significantly relative to the control. It is likely that antirrhinoside functions as defense against herbivory for one generalist insect herbivore but also, at low concentrations, enhances the growth of another [89].

The volatile organic compounds (VOCs) inhibited Arabidopsis root growth. Out of the three major snapdragon floral volatiles, myrcene, (E)-beta-ocimene, and methyl benzoate (MB), MB was found to be primarily responsible for the inhibition of root growth. Ten micromoles MB reduced root length by 72.6% [82].

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<tr>
<th>Table 1. Volatile organic Chemical of A. majus</th>
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<tr>
<td>Fatty acid derivatives</td>
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<tr>
<td>Aldehydes</td>
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<tr>
<td>2-Methyl-propanal</td>
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<td>3-Methyl-butanal</td>
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<td>Pentanal 100</td>
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<td>β-Pinene</td>
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<tr>
<td>p-Cymene</td>
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<tr>
<td>Limonene</td>
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<tr>
<td>γ-Terpenes</td>
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</tbody>
</table>

Non-cyclic

| β-Myrcene  | 100  | 100  |
| (Z)-β-ocimene | 100 | 77   |
| (E)-β-ocimene | 100 | 100  |
| 3,4-Dimethyl-2,4,6-octatriene | 75 | 40   |
| (E,E)-2,6-dimethyl-1,3,5,7-octatetraene | 48 | 20   |

Irregulars

<table>
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<th>6-Methyl-5-hepten-2-one</th>
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<th>97</th>
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<tr>
<td>Benzenoids</td>
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<td>0.18±0.08 (Emission rate, μg gDW⁻¹ h⁻¹)</td>
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<td>Acetophenone</td>
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<tr>
<td>Total</td>
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<td>150.24</td>
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</tbody>
</table>

CONCLUSION

Antirrhinum majus (common snapdragon) contained amino acids, pigments, oils, anthocyanidins, flavonols, flavones, aurones, flavanones, cinnamic acids and many other compounds. The recent studies showed that Antirrhinum majus possessed antimicrobial, insecticidal, cytotoxic, antioxidant, central and peripheral nervous system effects, and many other biological activities. This review highlight the chemical constituents and biological effects of Antirrhinum majus.

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