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A Review on Pharmacological Activities of Agastache rugosa

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ABSTRACT: This article provides an overview on the pharmacological effects, phytochemical constituents of Agastache rugosa. Short notes on taxonomy, synonym Korean mint plant; a plant belonging to the Lamiaceae family has many therapeutically active phytochemicals. Agastache rugosa is an aromatic herb in the mint family used as a remedy for different health disorders. This article gives a board review on various pharmacological activities of Agastache rugosa such as antifungal, anti-inflammatory, antioxidant, anti HIV, anti-diarrhea, anticancer, gastric diseases, abdominal pain, in treating common cold, vomiting, and coagulation.

KEYWORDS: Agastache rugosa,

I. INTRODUCTION:

Herbal medications have been used for the treatment of variety of ailments by a huge number of people in the world. Many medicinal plants and their formulations are used for ethno-medicinal practices. At present many compounds have been isolated from plants for treating numerous diseases. Medicinal plant research has succeeded in overwhelming the problems associated with synthetic drugs in maintaining low toxicity and less side effects[1]. The plant from family "Lamiaceae" or (Labiatae) provides many medicinal constituents include the strong aromatic essential oil, tannins, saponins and organic acids[2]. Some examples from this family include mints, thymes, tulasi, spearmint and coleus.

DESCRIPTION OF PLANT:

Agastache rugosa, the Korean mint, also known as[3] wrinkled giant hyssop, purple giant hyssop, Indian mint, blue licorice, and Chinese patchouli is an aromatic herb in the mint family, native to East Asia (China, Japan, Korea, Russian Primorye, Taiwan, India, and Vietnam.[4] Agastache rugosa is a perennial plant growing up to 40-100 cm (16-39) in tall, with square stalks that branch at the upper part.[5] The oval cordate leaves are oppositely arranged, 5-10 cm (2-4) in long and 3-7 cm broad, with coarsely serrated margins. Some leaves have hair and/or touches of white on the underside. From July to September in the Northern Hemisphere, purple bilabiate flowers bloom in verticillasters that are 5-15cm (2-6) in long and 2 cm broad. The calyx is 5-6 mm (0.20-0.24) in long, with five narrow triangular lobes. The petals are 8-10 mm (0.31-0.39) in long, lower ones longer and the ones inside serrated. The stamens are didynamous, long, and exposed. The fruit is schizocarp, with obovate elliptical mericaps of 1.8mm.

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TAXONOMY:

Kingdom: Plantae

Clade: Tracheophytes

Clade: Angiosperms

Clade: Eudicots

Clade: Asterids

Order: Lamiales

Family: Lamiaceae

Genus: Agastache

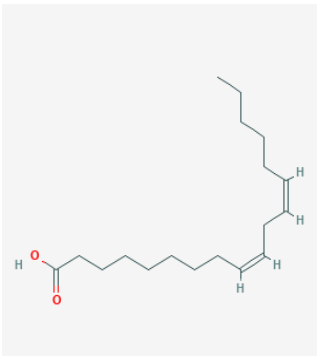
Species: rugosa

CULTIVATION:

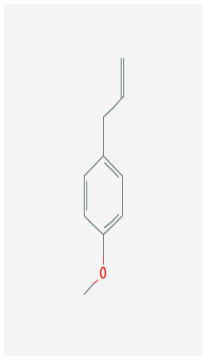
Korean mint grows well in fertile, moisture-retentive soils and good sunlight[6]. The aroma becomes weaker in shady conditions. Korean mint can be propagated by both sexual and asexual means. [7]The seeds gathered in autumn can be sown in the spring. One can also dig out the plant in autumn or early spring, divide the roots, and plant them at intervals of 30 centimeters.[8]

Chemical compounds found in the plant include Estragole- plant, [10][9]p-Anisaldehyde- plant, 4-methoxycinnamaldehyde-shoot, Pachypodol-leaf, [10]Methylchavicol, d-Limonene, Caryophyllene,[11] Hexadecanoic acid, Linoleic acid,[12] Octahydro-7-methyl-methylene-4-(1-methylethyl)-1H-cyclopene(1,3)cyclopropa(1,2)benzene[13].
Detailed structures of these chemical constituents are taken from https://pubchem.ncbi.nlm.nih.gov

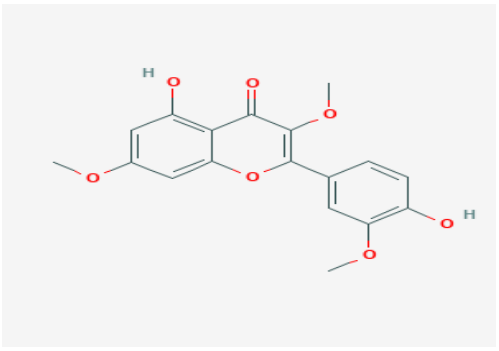
CHEMICAL CONSTITUENTS:



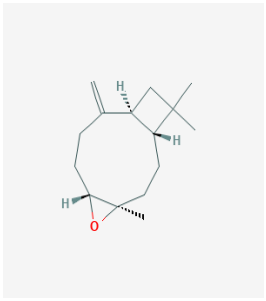
Linoleic acid



Estragole



Pachypodol



Caryophyllene

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Traditional Usages:

Agastache rugosa has been used in folk medicine to treat a variety of diseases, including cholera, vomiting, miasma and other intestinal disorders[14][15]. According to Traditional Chinese Medicine theory, A . rugosa is classified as an aromatic and damp dissolving herb. [16]Thus it has been widely used as an effective herbal drug to cure the disease of human pathogenic summer heat and dampness virulence in clinical in china[17]. Its thermal properties are slightly warm with the channel affiliations entering the spleen, stomach and the lungs according to Korean traditional medicine theory[18][19].

Reported Activities:

Antibacterial and antifungal activity[20]

Antibacterials destroy or inhibit only the growth of bacteria. The inhibitory potential of EOF, EOL, aqueous extracts and alcohol extracts of different parts against growth of three different bacterial was assessed of minimum inhibitory concentration (MIC) and minimum bacterial concentration (MBC) using broth microdilution techniques following clinical and laboratory standard institute methods. The essential oils, aqueous extracts and alcohol extracts were added aseptically to sterile melted Mueller Hinton Broth medium (Sabouraud's Broth medium for B.albicians) to produce the concentration range of 5.25-336 microgram/ml for EOF, range of 4.72-302microgram/ml for EOL, range of 3.125-2000 mg/ml for aqueous extracts, range of 1.563-100mg/ml for alcohol extracts. For the determination of MIC, MBC. Standard reference antibiotics (penicillin, gentamycin, flucanazole) were used as positive control. The MIC was defined as the lowest concentration that completely inhibited growth of the organism, as detected by the unaided eye after incubation for 24h. The MBC was defined as the lowest concentration at which no microorganism's growth was detected on the agar plate. S.aureus and E.coli were incubated at 37c, and C.albicans was incubated at 25oc.

Anti-inflammatory Activity:[21][22]

The cytotoxicity of Agastache rugosa extracts on RAW 264.7 cells were deterimined using a cytotoxicity assay. The cells were treated with Agastache rugosa extracts at concentration of 100 and 200 microgram/ml with LPS (1microgram/ml). There was no significant effect on cell viability with Agastache rugosa treatment or LPS activation. The inhibitory effects on inflammatory reactions of Agastache rugosa were measured by NO production in RAW 264.7 cells. NO production was significantly increased by LPS treatment alone compared to normal controls, but a reduction of NO was observed in the cells pretreated with Agastache rugosa extracts in a dose dependent manner compared to the control. Expression of inflammatory proteins iNOS and p-NFkB was analysed by western blot assay. Although the levels of iNOS and p-NFkB p65 were significantly increased in LPS control, the levels of inflammatory proteins decreased by Agastache rugosa extract treatment in a dose dependent manner. Thus, the extract was used at concentration of 100 and 200 microgram/ml for subsequent anti-inflammatory activity analysis.

Antibiofilm Activity:[23][24][25]

The flower and leaf of examined plants were separated and dried in shadow at room temperature, and submitted 100grams to hydro distillation with 1L of distilled water in a Clevenger-type apparatus for 6 hours. At the end of each distillation the oils were collected, dried with anhydrous sodium sulfate prior to analyses, measured, transferred to glass flasks and stored at 4 degree Celsius until the moment of analysis. The oils were distilled with dimethylsulfoxide (DMSO) as the stock solution for antibiofilm activity. 10µL of DMSO loaded on three sterile blank disks was placed on the agar plates and was then incubated at 37c for 24h. There was no antibacterial activity on the plates and so DMSO was selected as a safe diluting agent for the oil. Each oil dilution was followed by sterilization using a 0.22 micrometer membrane filter. The solvent served as control.

The assay was performed in 96 well microtiter plates, and to each well were added the bacterial suspension (5× 10^6 CFU/ml, S.aureus, E.coli, C. albacians) the EOF and the essential oil of leaf at concentrations less than MIC (10-fold dilution from 0.1 to 0.0000006). Then the microplates were incubated at 37˚C for 24h under aerobic condition. After this incubation period, the culture medium was removed and rinsed with sterile distilled deionized water (six rinses). Then the biofilm was fixed with 150µl of methanol (PA) for 15min, stained with crystal violet 0.1% (v/v) and rinsed with water. Biofilm formation was evaluated by adding 150µl of 95% ethanol to the wells, and the plates were subjected to spectrophotometric reading at 620nm. The results were expressed as

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percent inhibition of biofilm formation, considering the absorbance of the positive control (no potential antibacterial agent was added) as 0% inhibition. At least three replicate experiments were performed for each concentration of EOF and essential oil of leaf that was tested.

Antimicrobial activity:[26]

The in vitro antibacterial activities of EOF and essential oil of leaf from Agastache rugosa against the microorganisms were qualitatively and quantitatively assessed by the MIC values. The results were obtained and screening of the antibacterial activity of essential oil of Agastache rugosa. With the broth dilution method, the MIC values for EOF and essential oil of leaf were in the range of 21-42 µg/ml and 9.4-37.8µg/ml, respectively. The essential oil of flower and leaf of Agastache rugosa was found to have moderate to high antimicrobial activity. It showed strong inhibition against E.coli for essential oil of leaf. And it showed low activity against C. albicans for essential oil of flower and leaf. The results of MIC values indicated that E . coli was inhibited at lower concentrations by essential oil of leaf than S. aureus, in which the lowest MIC value is 9.4 µg/ml. The essential oil of leaf was sensitive than essential oil of flower in fungicidal activity. The antibacterial activity showed by the essential oil of leaf may be due to the chemical composition of the extract, which is rich in p-Methan-3-one. When the oils were added to the culture medium, the growth rates of tested organisms were found to significantly decrease as compared to the control cultures. In some cases, the oils showed the same type of antimicrobial activity compared to the penicillin, while the oils showed high activity in some other cases than the standard reference antibiotics.

Anti-atherogenic activity:[27]

The adhesion of monocytes to the vascular endothelium and their subsequent recruitment into the artery wall are key features in the pathogenesis of atherosclerosis. Vascular cell adhesion molecule-1 (VCAM-1) an adhesion molecule expressed on the endothelial cell surface may be partly responsible for the recuirtment of monocytes during atherogenesis. VCAM-1 expression has been demonstrated in human coronary atherosclerotic plaques, and this is consistent with the belief that this adhesion molecule plays a role in the disease. Nuclear factors- κB (NF-κB) is a heterodimer of two proteins, p50 and p65, that are localized in the cytoplasm of unstimulated cells in an inactive form. On stimulation of cells, for example by tumor necrotic factor-α (TNF-α), the hetero dimer translocates to the nucleus and transactivates gene expression. The VCAM-1 promoter consists of two NF-κB binding sites. The cell-surface expression of VCAM-1 correlates with an increase in mRNA levels, which indicates transcriptional activation of this gene by TNF-α. Flavonoids, such as PD 098063 (2-(3-amino-phenyl)-8-methoxy-chromene-4-one),and gallates , have been shown to block the TNF-α- stimulated NF-κB activation, transcription, and cell- surface expression of VCAM-1 in the endothelial cells. The plant species of Agastache rugosa contain several kinds of flavonoids (acacetin-7-O-β-D-glucopyranoside (ti-lianin), acacetin, linarin, and agastachoside) and tilianin is a main constituent of Agastache rugosa. Both the extract and the constituents of this plant have a variety of physiological and pharmacological activities on inflammatory immune responses such as anti-complement and the inhibition of Haemophilus influenza adhesion to human cells.

HIV Integrase Inhibitory Activity:[28]

Recombinant HIV-1 integrase was expressed in Escherichia coli and purified using a nickel- chelated column in one step manner. Aliqouts of HIV-1 integrase of 0.5 mg/ml as stock solution were stored at -60˚C until used. Two 20-mer olidonucleotides whose sequences resemble the end of U5-LTR were obtained. The oligonucleotides were purified using 20% polyacrylamide gel before use. The labeling reaction was subjected to 10Mm EDTA and heated to 85˚C for 15 min to inactivate T4 PNK. After the addition of complementary oligonucleotide K16(30pmol), the reaction mixture was boiled for 3 min and cooled slowly. Labeled substrate was separated from unincorporated nucleotide by passage through a Biospin 6 instrument. A standard reaction assay of endonucleolytic activity was carried out in the presence of potential inhibitor containing 0.1 pmol of duplex oligonucleotide substrate and 15pmol of HIV-1 integrase in 15Mm Tris-HCL(Ph 6.4), 100 mm NaCl, 1 mm imidazole in a total volume of 10ml. Inhibitors or plant extracts were dissolved in 100% DMSO and added to the reaction mixture. Reaction mixtures were incubated at 33˚C for 90min and stopped by the addition of 4ml 95% formamide, 20mm EDTA, 0.05% bromophenol blue, and 0.05% xylene cyanol FF. The reactions were heated to 90˚C for 3 min and subjected to electrophoresis on a 20% denaturing polyacrylamide gel. Reaction products were visualized by autoradiography of the

wet gel. The IC-50 values were calculated by scanning bands on a phosphoimage analyzer. The methanol extract of A. rugosa which showed significant inhibitory activity against HIV integrase. Acacetin and tilanin were simple and easy to operate. They might have a good pharmaceutical prospect. Being cheap, safe and effective, they can meet requirements of today's market about antithrombotic drugs.

Coagulation activity:[29]

Agastache rugosa extract shows procoagulation activity while acacetin tilianin identified as the main components of A. rugosa had a significant anticoagulant activity in vitro. As a novel, effective and promosing drug for the treatment of various coagulation disorders. A. rugosa may be beneficial for the individual with the high risks of with hemophilia and other bleeding disorders.

Antioxidant activity:[30]

Antioxidant related properities of A.rugosa extracts were reported. A. rugosa leaf extract protects RAW264. Macrophage cells from hydrogen peroxide- induced injury via the induction of protein kinase G- dependent heme oxygenase-1, which proposes one of action mechanism of the extract as an antioxidant

Barrier Protective activity:[31]

Skin barrier protective function has been regarded as one of crucial targets in the manufacture of functional cosmetics. Barrier function and hydration of psoriatic skins are defective and secondary structure in C proteins is altered in the involved psoriatic skin. Acute psychological and sleep deprivation stress disrupt skin barrier function in women, which results from stress induced changes in cytokine secretion. Dietary glucosylcermide improves the skin barrier function through the reinforcement of CE formation via transglutaminase expression and involucrin production in the epidermis mediated by sphingoid bases its metabolites.A. rugosa possess barrier protective activity through upregulating the UV-B flaggrin and caspase-14 in HaCaT Keratinocytes.

II. CONCLUSION:

From this review, Agastache rugosa is an important medicinal herb and extensively used in treating various diseases. The difference parts of the plant such as leaf, bark, root are used to cure variety of diseases. The Agastache rugosa has Anti bacterial, Anti fungal, Anti inflammatory, Anti biofim, Anti microbial, HIV integrase inhibitory, Coagulation, Antioxidant, Barrier Protective activites.

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