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The Formulation, Evaluation and Pharmacological Properties of Rosemary Plant

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ABSTRACT

Rosemary (Rosmarinus offcinalis). is one of the most economically important species of the family Lamiaceae. Native to the Mediterranean region, the plant is now widely distributed all over the world mainly due to its culinary, medicinal, and commercial uses including in the fragrance and food industries. Rosemary used as a medicinal and aromatic herb for thousands of years. The chemical composition of rosemary essential oil and extract includes several compounds that are known to be strong antioxidants. Rosmarinus officinalis in view of its medicinal, aromatic and socio-economic interests in order to evaluate his tolerance to salts by applying four saline treatments: 0; 2; 5 and 8 g / l of NaCl. The search terms were "Rosmarinus officinalis", "therapeutic", "and pharmacological". Various studies have shown that Rosmarinus officinalis possess anti-inflammatory effect, antioxidant effect, hepatoprotective activity, anti-obesity, radioprotective effect, anti - androgenic activity, memory improvement, antimicrobial, antibacterial and antifungal activities, antiplatelet activity, anti-anxiety, anti- Alzheimer, anticancer, antidermatophytic activity, anti-tumour activity. Rosmarinus officinalis was shown to possess lots of healing activity. Medicinal properties of its extract, essential oils, its stems and leaves should be further examined to be able to diagnose other useful and unknown properties of this valuable plant.

KEYWORDS: *Rosemary, Phenolic compounds, Antioxidant, Antimicrobial, Rosmarinus officinalis, Carsonic acid, Anti-diabetic activity*

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INTRODUCTION

Rosemary (Rosmarinus officinalis Linn. Fam. Labiatae) is an evergreen branched bushy shrub, attaining a height of about one metre with upright stems, whitish-blue flowers and dark green leaves which are small with edges turned over backward. It grows wildly along the north and south coasts of the Mediterranean sea, and also in the sub-Himalayan areas6-8 it has been cultivated since ancient days in England, Germany, France, Denmark and other Scandinavian countries, Central America, Venezuela and the Philippines.[1] Rosemary extracts have been used in the treatment of diseases, due to its hepatoprotective potential therapeutic potential for Alzheimer's disease and its antiangiogenic effect.[2]

Rosemary, *Rosmarinus officinalis* L. (Labiatae) has been used in folk medicine to alleviate several diseases including headache, dysmenorrhea, stomach-ache, epilepsy, rheumatic pain, spasms, nervous agitation, improvement of memory, hysteria, depression, as well as physical and mental fatigue.[3] The major use of rosemary is in the perfumery industry where the essential oils are employed as natural ingredients of fragrances.[4] The extract is produced mainly from the leaves. Solvents used for extraction include ethanol, acetone and hexane, and extraction by means of supercritical CO2 is also popular. Extracts contain considerable amounts of biologically active substances. e.g. phenolic acids,

flavonoids, terpenes.[5] This has been one of the reasons for the growing use of herbs as low-risk, affordable, and inexpensive natural ingredients in the treatment of bacterial infections compared to synthetic antibiotics. Also, these herbal remedies are more popular with people. The role of natural products in drug production is increasing, not only when bioactive compounds are used directly as therapeutic drugs, but also when used as a raw material for drug synthesis, or as a model the base is used for new biologically active compounds.[6] Among the phenolic acids in rosemary extract, researchers have managed to isolate caffeic acid, 4-hydroxybenzoic acid, p-coumaric acid, and Rosmarinus acid (0.14 mg/g).[7] Cedarwood, lavender, thyme, and rosemary oils have been used anecdotally for over 100 years to treat hair loss. Other medicinal herbs have also been explored for their potential in enhancing hair growth. Current literature reviews suggest that oleogel is a promising base for various drugs to design topical formulations.[8] Rosemary also in Persian as is used a soil for preventing hair fall, nourishing the hair roots, sciatic and joint pains, rheumatoid arthritis, and used as anti-inflammatory.[9] Rosemary achieves an appropriate physiological state for harvest before blooming. Furthermore, new buds are harvested when they only have a length between 10 and 20 cm. New or young shoots that are harvested have more turgidity and hence a higher water content in the cellular structures.[10] The essential oil secreted by glandular trichomes is mainly located in leaves and the flowers; the highest quality essential oil is obtained from the leaves.[11] Rosmarinus officinalis L. essential oil and three of its main components 1,8-cineole (27.23%), α-pinene (19.43%) and β-pinene (6.71%) were evaluated for their in vitro antibacterial activities and toxicology properties. R. officinalis L. essential oil possessed similar antibacterial activities to α-pinene, and a little bit better than β-pinene, while 1, 8-cineole possessed the lowest antibacterial activities. R. officinalis L. essential oil exhibited the strongest cytotoxicity towards three human cancer cells. Its inhibition concentration 50% (IC_{50}) values on SK-OV-3, HO-8910 and Bel-7402 were 0.025‰, 0.076‰ and 0.13‰ (v/v), respectively. The cytotoxicity of all the test samples on SK-OV-3 was significantly stronger than on HO-8910 and Bel-7402.[12] Several flavonoids and phenolic compounds such as hispidulin, cirsimaritin, apigenin, genkwanin, naringin, caffeic acid and rosmarinic acid are also present in rosemary extracts (Jasim, 2017). It has been considered as one of the most effective herbs for treating inflammatory diseases, headaches, poor circulation, headaches, and physical and mental fatigue (Eilyad et al., 2012). Rosemary extracts and its components have anti lipid peroxidant activities and free radical scavenging by various in vitro antioxidant assays (Bilto & Alabdallat, 2015).[13] Furthermore, the ethnopharmacological uses of tea, infusions, alcoholic extract and oil of *R. officinalis* include the treatment of several disorders, such as inflammatory diseases, physical and mental fatigue, and treatment of nervous agitation and depression, among other applications (Balmé, 1978, Duke, 2000, Heinrich et al., 2006).[14] The bioactive components of REs exhibit potent antioxidant activities reduce lipid peroxidation in heart and brain (cortex and hippocampus) inhibit the production of reactive oxygen species and suppress inflammatory response It has been reported that REs can be useful in the prevention of disorders due to angiogenesis and atherosclerosis.[15] Distribution**:** Rosemary is an aromatic herb exported by Colombia. It is a perennial aromatic bush that can grow up to 2 m high. Its leaves are narrow, thin, shiny and strongly scented; the stemware woody and resinous, branched and slightly bitter. The mechanical behaviour of rosemary leaves corresponds to a viscoelastic, anisotropic and highly variable material.[16] r. *Rosmarinus officinalis* L. (rosemary) is an important medicinal plant from Lamiaceae family originated from Mediterranean region and has been cultivated for long time in Iran. It is traditionally used as a spice in foods and beverages and as alternative herbal medicine for GI ailments including flatulence and dyspepsia, and various spasmodic conditions such as renal and biliary colic.[17] Rosemary (Rosmarinus officinalis) is one of Household herbs that contains a number of phytochemicals, including rosmarinic acid, camphor, caffeic acid, ursolic acid, betulinic acid, and the antioxidants carnosic acid and it used in traditional medicine to treat a variety of disorders. The rosemary extract containing 40% carnosic acid was purchased from Hunan Geneham Biomedical Technological Company of China, (RAP20-110401).[18] The long slender branches bear many sessile opposite leaves, smooth and green, woolly whitish and glandular beneath, 24 cm long, almost cylindrical and folded inwards flowers are situated in small clusters towards the ends of the branches; the calyx is 2- lipped, with an upper single broad oval lobe and a lower two segmented triangular lobe; the corolla is two lipped with two violet stamens and a long style projecting from it; fruit is an oval 4 sectioned cremocarp (Joy et al., 2001).[19]

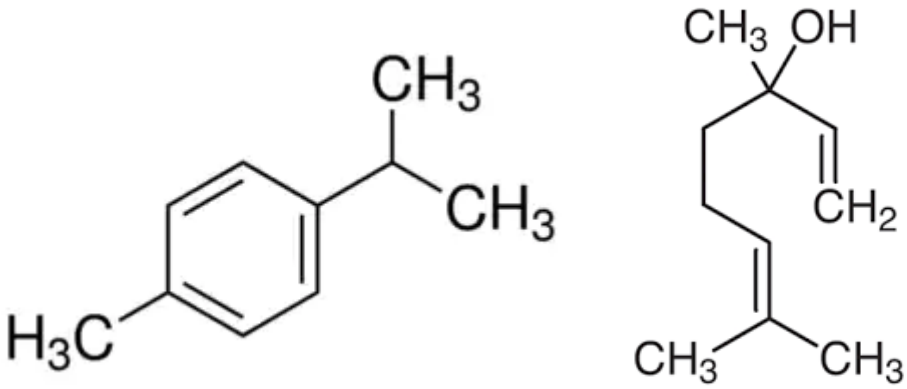
Classification of Rosemary plant:

Sr. No.	Kingdom	Plant/Plantae
1.	Sub Kingdom	Tracheobionta
2.	Super Division	Spermatophyta
3.	Division	Magnoliophyta
4.	Class	Magnoliopsida
5.	Sub class	Asteridae
6.	Order	Lamiales
7.	Species	Officinalis
8.	Family	Lamiaceae
9.	Genius	Rosemarinus.L

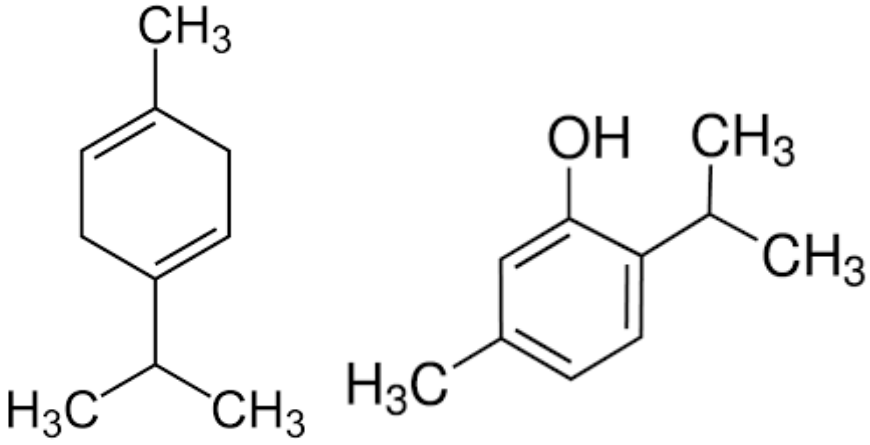
Fig. Rosemary plant

Different Names:

Common name (some European countries): Romero (Spanish), alecrim (Portuguese), rosemary (English), rosmarin (French and German), rosmarino (Italian), and δενδρολι΄βανο (Greek).[20]



Structure of p-cymene Structure of linalool



Structure of gamma-terpinene Structure of thymol

Figure: Structure of *Rosmarinus officinalis*:

Essential oil of Rosemary: Rosemary (*Rosmarinus officinalis* L.) is of considerable importance in term of its great an important medicinal and aromatic value. Rosemary herbs have been widely used in the traditional medicine and cosmetics. *Rosmarinus officinalis* essential oil is also important for its medicinal uses and its powerful antibacterial, cytotoxic, antimutagenic, antioxidant, antiphlogistic and chemopreventive properties. The major components determined in *R. officinalis* essential oil were 1,8-cineol (38.5%), camphor (17.1%), α-pinene (12.3%), limonene (6.23%), camphene (6.00%) and linalool (5.70%).[21] After this period, mice were sacrificed, Sustainability 2022, 14, 3927 5 of 15 and the blood was subjected to biochemical analysis by assaying biochemical markers such as aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP), blood uric nitrogen (BUN), total protein (TP), glucose (GLU), total bilirubin (T-BIL), creatinine (Crea) and total cholesterol (T-CHO).[22]

Pharmacological Properties:-

Anti-Inflammatory Effect: It is probable that the anticonvulsant effects observed in the former studies occur with the same mechanisms as rosemary's effects on reducing insomnia in this study. An investigation by Hosseinzadeh *et al*. 2006, showed that rosemary can decrease muscle jerks produced by morphine withdrawal syndrome. These beneficial properties of the plant might be attributed to psycho-stimulant and anti-inflammatory effects. [23] The roots of Diospyros lotus L., traditionally used in several diseases, including pain syndromes and sleep disorders, were studied by Uddin et al. (2014), and it was concluded that the antinociceptive and anti-inflammatory effects of the roots of D. lotus appear to be partially attributed to the analgesic properties of some compounds, such as diospyrin and 8-hydroxyisodiospyrin, thus supporting the ethnopharmacological uses of D. lotus L. as antinociceptive, anti-inflammatory, and sedative.[24] The *in vitro* anti-inflammatory activity of supercritical rosemary (*Rosmarinus officinalis* L.) extracts (rosemary A and B) is been reported in this study. To achieve that, THP-1 macrophages were activated using lipopolysaccharide or human ox-LDL and secretion and gene expression of TNF-α, IL-1β, IL-6.[25]

Antioxidant Effect: Rosmarinus officinalis, an antioxidative polyphenolics producing plant, is characterized for the presence of some prominent ortho-dihydroxyl bearing antioxidant flavonoids. The aqueous-ethanolic extract of the plant was fractionated with CH2Cl2 and n-BuOH. Cellulose CC fraction of each partition gave a fluorescent band, and each was eluted and collected separately under UV light and antioxidant activity of each fraction was determined against DPPH free radical at 518 nm. The flavonoids from prominent antioxidative

fractions were characterized by UV, 1HNMR and MS studies. Two antioxidative flavonoids, luteolin-5-O- ß-D-glucopyranoside and hispidulin-7-O-(6"-Ocaffeoyl)-glucopyranoside were characterized from the plant first time.[26] Rosemary's sedative effects are possibly due to its antioxidant property.[27] The antioxidative activity of rosemary extracts has been evaluated using different solvents. In this regard, Inatani et al. reported that rosmanol, showed an antioxidant capacity four times higher than BRT and BRA (synthetic antioxidants) in both linoleic acid and lard. In addition, this study reported the antioxidant activity of carnosol and rosmanol by TBA and ferric thiocyanate methods. They reported the correlation between activity and chemical structure as an antioxidant. Aruoma et al. studied the antioxidant and prooxidant properties of rosemary. The main constituents with antioxidant properties are carnosic acid and carnosol that are responsible for 90% of the properties. Both are inhibitors of lipid peroxidation in liposomal and microsomal systems, they are good scavengers of CCl3O2 (peroxyl radicals), reduce cytochrome c and scavenge hydroxyl radicals. Specifically, carnosic acid scavenges H2O2, but could also act as a substrate for the peroxidase system.[28] The antioxidant feature of rosemary extract on rat testicular tissue after exposure to the electromagnetic field.[29] Among natural antioxidants, rosemary has been widely accepted as one of the species with the highest antioxidant activity. Rosemary has long been recognised as having antioxidant molecules, such as rosmarinic acid, carnasol, rosmaridiphenol and these have found in ethanol-soluble fraction.[30]

Antidiabetic Activity: *Rosmarinus officinalis* is an aromatic evergreen shrub used as a food additive and medicine, which has been extensively used to treat hyperglycaemia, atherosclerosis, hypertension, and diabetic wounds. A great deal of pharmacological research showed that rosemary extract and its phenolic constituents, especially carnosic acid, rosmarinic acid, and carnosol, could significantly improve diabetes mellitus by regulating glucose metabolism, lipid metabolism, anti-inflammation, and anti-oxidation, exhibiting extremely high research value.[31]

In vivo investigation of the antidiabetic effect of Rosmarinus officinalis (Linn.) essential oil in Animals

Male Swiss-Webster mice, 12 to 16 weeks of age, were kept in adaptation environment for a period of 1 week prior to initiation of the experimental procedure. The adaptation environment was similar to the conditions previously described.8 The mice were kept in individual cages at room temperature of 22 ± 1°C and a light/dark cycle of 12 hrs each. The animals had free water access and were fed with standard pellets of proteins (20%), fats (5%) and multivitamins (1%). Sixteen hrs prior to experimentation, feeding pellets were removed from the cages in order to make the mice fast. However, the free access to water was kept. Experimentation 5 on animals and animal care were all done according to the regulations of the Lebanese Ministry of Higher Education and the animal experiment legislation and with the approval code (2016A-0035-P-M-112) of the Institutional Review Board of Beirut Arab University.[32]

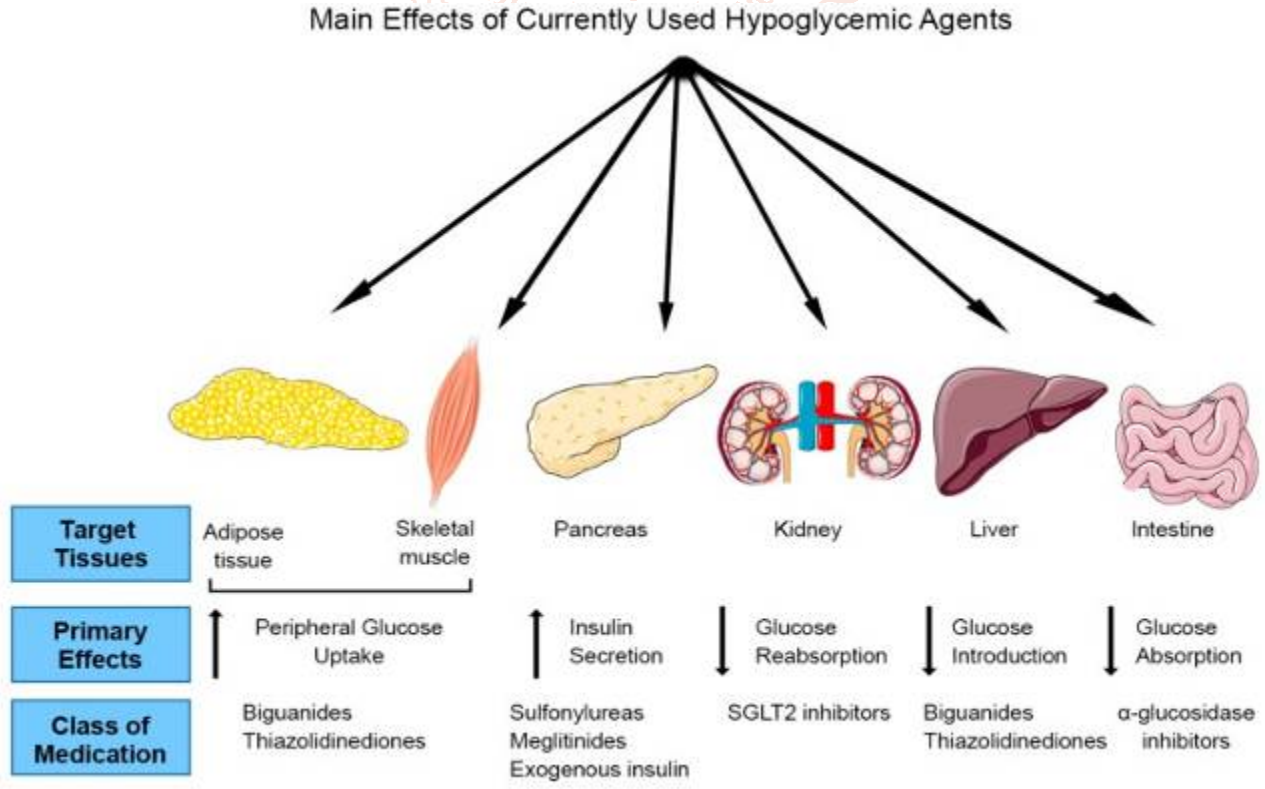


Figure: Target tissues and mechanism of action of current anti-diabetic drugs. [33]

Anti-obesity Activity: While only three studies reported anti-obesity activities of *Rosmarinus officinalis*, their findings are very noteworthy. All three found rosemary to effectively limit weight gain, but each study identified a different mechanism to explain this response. In one study, extracted carnosic acid was found to suppress adipocyte differentiation. This inhibition of adipogenesis can promote sustainable weight loss. In another study, rosemary extract prevented weight gain by limiting lipid absorption in the intestine. This was made possible through the inhibition of pancreatic lipase activity. Finally, the third study found rosemary extract to inhibit lipid synthesis through the suppression of diacylglycerol acyltransferase (DGAT), the main enzyme responsible for the production of triglycerides. The results of all three studies indicate that *R. officinalis* has great potential as an effective treatment against obesity and other metabolic disorders.[34]

Antiproliferative Activity: *Rosmarinus officinalis e*ssential oil was solubilized in DMSO and then diluted in culture media for use. The human breast cancer (MCF-7) and fibroblast (NIH-3T3) cell-lines were maintained in Dulbecco's Minimum Essential Medium (DMEM), while hormone dependent prostate carcinoma LNCaP was cultured in RPMI 1640 medium. Both media were supplemented with 10% heat-inactivated fatal calf serum, 1% L-glutamine, 1% penicillin/streptomycin. Cells (104/well) were cultivated in 96 well plates for 24h before the test compounds were added. Essential oils dilutions (10–500 µg mL-1) were added to triplicate wells and cells were incubated for further 24 h. DMSO was tested as a solvent control while Doxorubicin as a reference standard. Cell viability was evaluated by the MTT assay and the percent inhibition of cell viability was calculated using cells treated with DMSO as control. The IC50 values (concentration at which 50% of cells were killed) were calculated.[35]

Anticancer Activity: These studies provide evidence for the role of RE as an anticancer agent in colon cancer cells, capable of consistently inhibiting cell growth and viability at relatively low concentrations in the 20–100 µg/mL range.[36] The anticancer activity of rosemary and its main derivatives has been correlated with diverse actions, including antioxidant effects, antiangiogenic properties, epigenetic action, the regulation of immune response and anti-inflammatory response, alteration of hormone signalling, modification of specific metabolic pathways and increased expression of oncosuppressor genes.[37]

Anti–Anxiety: Anxiety is an emotional state composed of two components; psychological and physiological which are responsible for the stimulating performance, the term of anxiety represent a feel of displease that is comprised of feelings of fear and concern, insecurity, or changes in the states of alert and awake. Normal anxiety is a normal response ("flight or fight" response) which helps us how react to the dangers because it prompts humans either to escape from the danger or fight. It has been found that peoples with a reduced levels of anxiety are more susceptible to the risk of death comparing to those with a normal level. But when it becomes excessive, it will be considered as a disorder of anxiety. The anxiety disorders have found to be more in patients with a family history.[38]

Antidepressant Activity: There is an ongoing need to discover new therapeutic targets for the development of novel, more effective, and safer drugs with antidepressant- and anxiolytic-like properties that can ameliorate mood disorders of psychosocial nature. Given the suggestive evidence of OXT dysregulation in depression and anxiety, there has been growing interest in exploring novel com- pounds that can induce endogenous OXT release. In a recent study, authors showed that exposure to the aroma of certain essential oils such as lavender, neroli, jasmine absolute, roman chamomile, clary sage, and Indian sandalwood increases salivary OXT concentration. We investigated antidepressant- and anxiolytic-like activities of RE on behavioral paradigms in two different rodent models. TST is one of the most widely used models for assessing antidepressant-like activity in rodents and is suggested to have better sensitivity compared to other behavioral tests, namely the forced swimming test (FST) EPMT post-LPS injection is a highly validated method for assessing the anti- anxiety effect. Both TST and EPMT behavior paradigms are stan-dardized and comprehensive to study neural mechanism of depression and anxiety tress-induced control groups, suggesting significant antidepressant-and anxiolytic-like activities of RE.[39]

Antimicrobial Activity: The antibacterial effect of rosemary has been widely demonstrated in several food studies: beef meatballs cooked beef and in pork sausage. Gomez-Estaca et al. Reported that rosemary oil inhibited the growth of common food bacteria contributing to food spoilage.[28] The significance of rosemary's antibacterial effect does not end there, however. According to one study, rosemary has the potential to inhibit the drug resistance of some bacteria by overcoming and reducing the impermeability of these bacteria's membranes. This

impressive antibacterial activity makes R. officinalis a strong defense against common food pathogens and a promising new preservative that could replace artificial additives.[40]

Conclusion:

Rosmarinus officinalis (rosemary) has displayed exciting potential as both a natural food preservative and a therapeutic agent in the literature recieved for this project. It has also been tested for anxiety- as an alternative to the available antianxiety and antidepressant. It has be toxicity level ''It is a rich source of antioxidant, antibacterial and antifungal activities of plant extract for make rosemary It is an effective for food preservative with fever side effects than artifical additives It's extract found in the strong antoxidant Compound, and nosemary's biological activities for many essential oil account. Antidiabetic and Anticances it's also include. It has eight species of Labiatae herbs. The nasemary had feesh and commerical. it as highest phenolic content and antioxidant activity.''

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