SALVIA
Kornati

DALMATIAN SAGE

Salvia Officinalis

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History and traditional use of sage

Sage is a plant that, throughout the centuries, has gained the reputation of one of the most exquisite plants on Earth. The oldest known medicine record on sage dates back **more than 4.000 years in the past**. From the ancient Egypt through Greece and the Romans to this day, sage has remained and still is one of the most prized plants on Earth.

Old civilizations used sage as a remedy for almost all health issues. Sage had the status of a holy plant and was gathered for ceremonies as a symbol of fertility, good health and longevity.

Sage has deserved its Latin name *Salvia*, which comes from the Latin word *Salvus* which means "*being saved*", "*healthy*". The addition *officinalis* in the name denotes the exact species, which is a Latin adjective designated exclusively for plant species of exceptional medicinal properties.

Ancient Egyptians used sage mostly as a cure for infertility, but also in the treatment of severe diseases and epidemics such as plague. It was used in the pharaonic tombs as one of the main ingredients of the embalming mixture. Therefore no Egyptian pharaoh could go in the afterlife without this special plant.

Since sage is one of the oldest and most important medical herbs, it was mentio-

ned by all ancient medical writers. At that time, they used it as a remedy for almost all illnesses: high body temperature, headache, inflammation of the throat, oral cavity and respiratory tract treatment, urinary tract and bladder infections. It has also been used in the treatment of intestine, stomach, liver, gallbladder, urinary tract inflammations and many other diseases.

The ancient Romans considered sage to be the holy plant and a special ceremony had to be performed before its harvest. They used a special iron free knife in order not to react with sage. Collectors had to be dressed in clean clothes and have clean feet. Before they started they had to offer a sacrifice in the food as well.

Thanks to the Virgin Mary, sage was considered a plant that gives eternal life. According to the legend, the Virgin Mary had been hidden from Herod in a sage bush during Egypt's escape with Jesus. After the danger passed the Mother of God said to the sage:

"From now on and forever you will be people's favorite flower. I will give you the power to cure every illness and save people from death as you saved me".

Sage also had a great reputation **during the Middle Ages**. It is a well-known fact that Charlemagne, one of the greatest medieval rulers in Europe, appreciated sage. This can be seen in his strict laws, or "capi-

tulars", in which the great ruler commands all state properties (mostly monasteries) to plant one hundred medicinal herbs, sage being stated in the first place.

The reputation of sage and the faith in its healing properties may best be described by the axiom created in Salerno, which says: "*Why should a man die whilst sage grows in his garden?*".

It is interesting that the Salerno Medical School, founded in 984. in Salerno, southern Italy, was the first European medical school, the strongest western medical center in the Middle Ages and the forerunner of the medical university.

Modern scientific research has proven many beneficial effects of sage which is one of the few plants that can successfully replace antibiotics. No wonder people have given so much credit to the sage in the past. How much it was appreciated in all parts of the world could be illustrated in the fact that 17th century Chinese had even traded 3 chests of their tea for 1 chest of sage.

Just like in the previous centuries, sage is being successfully used in folk medicine today to cure many health problems. Antibacterial, antiviral and anti-inflammatory effects of sage are the main reasons for its success.

Likewise, **sage is traditionally used** to cure

various problems within the oral cavity such as: general inflammation, gum inflammation and throat inflammation. It is also beneficial for treating various inflammatory processes on the skin such as acne, eczema, herpes zoster, and also for treating female hormonal disorders.

In recent years, this plant has been the subject of an intensive scientific research created to document its traditional use, but in the process new biological effects were also revealed. These studies have revealed a wide range of pharmacological activities involving anticancer, anti-inflammatory, antinociceptive, antioxidative, antimicrobial, antimutagenic, antidementative, hypoglycemic and hypolipidemic effects.

Analysis and chemical composition

This versatile plant contains a number of compounds and substances that help combat many diseases and disorders and thus produce a positive synergetic effect on the entire organism. Thus in sage we can find the following groups of compounds:

- *phenolic acids*
- *flavonoids*
- *polysaccharides*
- *terpenoids*

Apart from already mentioned, here we will highlight some of the most important

pharmacological effects of these compounds:

Phenolic acids are herbal metabolites widespread throughout the plant kingdom. The interest in phenolic acids derives from the potential protection against oxidative diseases (eg. coronary heart disease, stroke and cancer). Phenolic acid function is very broad and is associated with various roles including nutrition, protein synthesis and allelopathy. It also provides many health benefits of important biological and pharmacological properties, especially anti-inflammatory, antioxidative, antimutagenic and anticarcinogenic[57].

Flavonoids are compounds also widely present in nature. Their extensive beneficial bioactive effects include antiviral, antibacterial, anti-inflammatory, cardioprotective, anti-diabetic, anti-cancerous and anti-aging effects, and have long received great attention and confirmation in numerous scientific studies[56].

Water-soluble ***polysaccharides*** derived from sage posess immunomodulatory activity[58], so arabinogalactan improves immune system[59,60], alleviates allergies[61,62], helps fight cancer[59,61], helps fight pathogens[61,63], and helps reduce pain[64].

Terpenoids are one of the largest active compounds that can often be found in various essential oils. Thus, in the sage we can find the following compounds:

The camphor exhibits many biological properties such as: antimicrobial, antiviral, anticancer and antinociceptive action. The skin easily absorbs it and it serves as an ingredient that facilitates the penetration of the substance through the skin[78].

It stimulates nerve endings that are sensitive to heat and cold, creating a warm feeling when it is absorbed deep into the skin or a cold feeling when applied gently to the skin surface. Also, its action on nerve endings creates minor local analgesic effects[79,80,81]. It is used as a cough suppressor because it facilitates breathing and helps in the treatment of colds and inflammatory conditions[82].

Eucalyptol (*1.8 cineol*) is one of the main compounds of many essential oils. It is known for its mucositic effect - it works directly on the mucus, breaks it down, dilates it and makes it easier to cough. Likewise, 1.8 cineol is also known for its spasmolytic effect, i.e. suppressing cough. It also demonstrated therapeutic benefit in inflammatory airway illnesses, such as asthma and chronic obstructive pulmonary disease[77].

α-thujone and β-thujone Clinical data show that thujone has positive effects in the treatment of acute colds and coughs. It has also been shown that thujone has antibacterial activity against bacteria such as *E. coli, K. pneumonia, S. Aureus* and *P. aeruginosa*[99]. Thujone is a GABA receptor antagonist, which means that inhibits the activati-

on of GABA receptors. Inhibiting the GABA receptor thymus reduces GABA's slowing effect and allows neurons to be more easily interconnected. In extreme quantities, thujone is neurotoxic and therefore sage essential oil should be used with extra caution[100].

α-pinene and β-pinene - studies have shown intense antimicrobial potential of α-pinene and β-pinene that significantly inhibit the growth and cellular vitality of potential infectious endocarditis causing gram-positive bacteria[55]. Also, the results indicate that β-pinene produces a similar effect to antidepressants through interaction with a monoaminergic system[20,21,55,67].

Borneol is being used as a topical analgesic for millennia in the traditional Chinese medicine. In modern clinical trials, borneol showed analgesic, anti-inflammatory and antibacterial properties. In clinical studies on humans, it was shown that topical application of borneol significantly alleviates pain. Such results support the therapeutic potential for painful and inflammatory disorders[53,54].

Healing properties

Because of all the above mentioned compounds and their mutual synergy, here are stated some of the scientifically proven effects of sage:

Antioxidant activity

Antioxidants are substances that can prevent or slow down the oxidative damage of the body. When our cells use oxygen, they produce free radicals (by-products) that can cause harm to the organism. As we know oxidative stress plays an important role in initiating and advancing several diseases like cancer, cardiovascular disorders, diabetes and neurological diseases[24,25,26,27].

Antioxidants act as free radical cleaners, thus preventing and repairing the damage caused by free radicals. Evidences from several studies have shown that medicinal sage has strong antioxidant activity. The most effective antioxidant ingredients are carnosine, rosemary acid and carnosic acid, then caffeic acid, rosmanol, rosemary, genkwanine and cirsymethystine[23].

Antibacterial and antiviral activity

The study on antibacterial effects of sage against selected nutrients *in vitro* suggests that the sage water extract had significant antibacterial activity and was most effective against *Bacillus mycoides, Bacillus subtilis, Enterobacter cloacae* and *Proteus sp.*[37]. The essential oil of medicinal sage is thus a good alternative to traditional antibiotics as well as food preservatives[38].

The results show that the hydroalcoholic extract of sage has an inhibitory effect on growth of specific dental caries caused by bacteria such as *Streptococcus mutans, Lactobacillus rhamnosus* and *Actinomyces*

viscosus. Based on this study and global interest in using traditional treatments instead of chemical solutions, sage with its bactericidal effect can be a natural remedy for the treatment of diseases affecting mouth and teeth.

A study on antibacterial activity of sage essential oil showed that the higher concentrations of essential oil showed better efficacy than antibiotics[38].

It has been shown that the aqueous extract of sage also has a good antiviral effects[37,52]. In several studies, the antiviral effects of sage were studied and its efficacy was confirmed[66].

Antifungal activity

Antifungal activity was reported against *Botrytis cinerea, Candida glabrata, Candida albicans, Candida krusei* and *Candida parapsiloza*[39,40]. Sage essential oil shows high antifungal capacity and can be used as an ecological fungicide against pathogenic or fungi such as *Verticillium dahliae* and *Penicillium aurantiogriseum*.

Previous studies have shown that the antifungal effect is not only caused by one large specific compound but by the synergy of other compounds in small quantities[49].

Memory and cognitive functions

Many studies have shown that sage affects mood, memory, attention and cognitive functions. By increasing dosage it increases

mood, satisfaction as well as wakefulness and calmness.

A randomly controlled study by Akhondzadeh and his associates showed that 4-month treatment with hydroalcoholic extract of sage improved cognitive function in patients with mild to moderate Alzheimer's disease[1,2,3,4,5,22].

Anti-inflammatory and antinociceptive - analgesic effects

Pharmacological studies have shown that healing sage has an anti-inflammatory and antinociceptive effect[43,44,45,46,47,48].

Mansourabad and associates reported that flavonoids extracted from sage reduce inflammation and induce analgesic effects in a dose-dependent manner.

In the treatment of throat inflammation and the effect of the liquid extract of sage, it has been shown to reduce the throat pain within 2 hours of the application[6,7].

Anticancerogenic effects

It was noted that drinking sage tea prevents the initial stages of carcinogenesis of the colon[28].

Also, sage extracts showed proapoptotic and inhibitory activity on breast cancer cell lines (*MCF-7*), cervical cancer adeno (*HeLa*), colorectal cancer (*HCT-116, HCT15, C115, HT29*), insulin (*RINm5F*), laryngeal can-

cer (*Hep-2*), lung cancer (*A549*), melanoma (*A375, M14, A2058, B16*) and squamous cell carcinomas[29,30,31,32,33,34,35].

These effects may be related to the presence of several cytotoxic and antitumor compounds in sage. It has been shown that caryophyllens and α-humulens are isolated from sage, thus preventing the growth of tumor cells[30].

Among flavonoids, rosemary acid has been extensively studied for its anti-tumor effects. It inhibits the growth of various human cancer cells, including breast adenocarcinoma, colon cancer, chronic myeloid leukemia, prostate cancer, hepatocellular carcinoma and small lung cancer[34,36].

Antimutagene effects

Sage reduces DNA oxidation damage induced by hydrogen peroxide and dimethoxy-1,4-naphthoquinone in HepG2 cells. The antimutagenic effect of sage is mainly attributed to monoterpene compounds such as tuwon, camphor, limonene and 1,8-cineol[10, 11, 12, 13]. The protective effect of sage on DNA can be explained by its antioxidant activity[14,15].

Sage is also a natural source of flavonoids and polyphenolic compounds that have strong antioxidative and antibacterial activity[16].

Antidiabetic effects

In many countries sage was used as a tradi-

tional anti-diabetic medicine because of its impact on glucose reduction.

The sage tea has been as effective as metformin, an oral antidiabetic drug used to treat *type II* diabetes and works by reducing the production of glucose in the liver and increasing the activity of insulin[18].

The effects on glucose and lipids - reduces the level of total cholesterol, triglycerides, LDL and VLDL in the blood, so-called *bad cholesterol*; while simultaneously leading to an increase in HDL, so-called *good cholesterol*, and leads to a reduction in blood glucose levels[8,9].

Hormone-regulating effects in women
Menopause is considered a physiological process of adaptation to an altered hormonal balance.

Sage is traditionally used to relieve menopausal symptoms such as increased sweating and menopausal heat waves as well as alleviating other menopausal symptoms. The efficacy of sage for the treatment of menopausal symptoms has been shown to be accurate in multiple clinical trials in various research centers. It also relieves menstrual cramps and regulates the menstrual cycle[41,42].

Anti-diarrheal effects
Based on the use of sage in diarrhea and abdominal cramps, the raw extract of sage was tested for its antidiuretic and antispa-

smodic activity using *in vitro* and *in vivo* assays. The study has shown that the crude extract provides a protection against diarrhea through its inhibitory effect on the mobility of the intestine by the presence of some components for the intestinal relaxation[50].

Effects against dental plaque

Dental caries is a widespread oral disease, especially in developing countries. *Streptococcus mutans* (SM) is the main bacterium in the dental plaque, responsible for the caries process.

A double blind clinical study was performed showing that rinsing with the extract of sage effectively reduced the number of *Streptococcus mutans* bacteria in dental plaques, thereby helping to fight the emergence of caries[51].

REFERENCES

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