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Rosmarinus officinalis L.: an update review of its phytochemistry and biological activity

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ABSTRACT

Herbal medicine is one of the oldest valuable bestowals that were given to mankind. Many plants and herbs hold their prestigious position in the field of medicine. The worldwide interest in the use of medicinal plants has been growing, and its beneficial effects being rediscovered for the development of new drugs. Based on their vast ethnopharmacological applications, which inspired current research in drug discovery, natural products can provide new and important leads against various pharmacological targets. This work pioneers an extensive and an updated literature review on the current state of research on *Rosmarinus officinalis* L., elucidating which compounds and biological activities are the most relevant. According to these references, there has been an increasing interest in the therapeutic properties of this plant, regarding carnosic acid, carnosol, rosmarinic acid and the essential oil. The present manuscript provides an updated review upon the most reported activities on *R. officinalis* and its active constituents. This knowledge about the medicinal plants usage can also be extended to other fields like field of pharmacology. In view of the nature of the plant, more research work can be done on humans so that a drug with multifarious effects will be available in the future market.

Keywords: *Rosmarinus officinalis,* phytochemicals, carnosic acid, rosmarinic acid, neuroprotective activity, anti-diabetic activity.

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INTRODUCTION

Medicinal plants have been used worldwide by indigenous populations, playing an important role in the treatment of human and animal diseases. More recently, the majority of modern drugs have been developed from isolated compounds of medicinal plants, based on their ethnopharmacological uses/applications. The role of natural products on drug development has been increasing, not only when the bioactive compounds are directly used as therapeutic agents but also when they are used as raw material for drug synthesis, or as a base model for new biologically active compounds. However, validating and using plants as a phytopharmaceutical requires a great deal of basic and applied research, in order to set this resource at the same level of importance of conventional pharmaceutical products. Moreover, only about 10% of 250,000 species of plants estimated worldwide have been scientifically studied with potential use in healthcare. Also, around 60,000 species will probably become extinct by the year of 2050, so it is urgent to search for new compounds with therapeutic interest. Medicinal plants have remained the major sources of drugs; in fact many of the currently available drugs were derived either directly or indirectly from them. The approach to new drugs through natural products has proved to be the single most successful strategy for the discovery of new drugs. In the past decade, research has been focussed on the scientific evolution of traditional drugs of plant origin for the treatment of various diseases.

Rosmarinus officinalis L. is a medicinal plant that belongs to the Lamiaceae family and is commonly known as rosemary. Besides the culinary uses due to the characteristic aroma, this plant is also widely employed by indigenous populations, where it grows wild[1,2]. *R. officinalis* is a woody, perennial herb with fragrant, evergreen, needle like leaves and white, pink, purple or blue flowers. This is a powerful herb that originates from Mediterrean region. It is derived from the latin word ros (dew) and marinus (sea) which means 'dew of the sea'. Forms range from upright to trailing: the upright forms can reach 1.5 m (5ft) tall, rarely 2 m (6ft 7 in). The leaves are evergreen, 2-4 cm (0.8-1.6 in) long and 2-5 mm broad, green above and white below, with dense, short, woolly hair. Rosemary has a tendency to flower out-side, its normal flowering season; it has been known to flower as late as early December, as early as mid-February. The taxonomic classification and anatomy of this plant were well documented and discussed by many researchers. It contains triterpenoids, diterpenoids, flavonoids, phenolic acids. Usage of herbal plants is as common as old ages. The current researchers are more focused on natural chemicals than the synthetic chemicals due to their environmental, economical and health benefits plants produce many chemical compounds for its biological activities including defensive mechanism against microbes, insects and herbivorous animals and these chemicals are called as phytochemicals. Herbal plants are a natural source of many important phytochemicals and widely used in pharmaceutical, food and cosmetic industries. A wide variety of herbal plants are available in the Indian subcontinent and they are the backbone of Indian traditional medicinal system, Ayurveda and Siddha[3].

Rosemary has been named the herb of the year in 2001 by the international herb association. It was introduced to Britain by the Romans and is still particularly loved today by the Italians and the British, who use it frequently in their cooking. In ancient Greece and Rome rosemary was believed to strengthen the memory, which accounts for its been known as the herb of remembrance and fidelity. Rosemary was an essential part of the apothecary's repertoire during the Renaissance. Hippocrates, Galen, Dioscorides prescribed rosemary for liver problems. Rosemary is not a popular plant in India. It was introduced by the Europeans as a garden plant due to its present fragrant scented leaves. Medicinal plants are the native heritage with the universal importance. The actual amount of constituents present varies according to the stage of development, variety of plant, season harvested, origin of leaves, extraction methods. As accordingly, the crude extracts are used for biosynthetic preparations of new drugs. In ancient medical system, various parts of plants such as stem bark, root bark, aerial roots, vegetative buds, leaves, fruits and latex are used to cure various ailments. Herbal medicines are very much secured than the others. Medicinal plants are the sources of a large number of combinations of herbs and modern medicine. Indian people have an incredible passion for medicinal plants and they use them for a lot of health related applications. Approximately, 25000 plant based formulations are available in the ethnic medical texts. Also, the modern medicine contains minimum 25% drugs produced from plants and many others which are artificial drugs manufactured on original compounds isolated from plants. India is one of the richest medicinal herbal granaries in the world that is of remarkable modern application, ensuring health security to millions of people[4].

Rosmarinus officinalis is a species within the *Rosmarinus* (genus) and the Lamiaceae family. There are many common names, it is so commonly called as rosemary it is found throughout India, it is known for its various uses in the fields of medicine and agriculture. *R. officinalis* is distributed in Southern Europe, Meditterean basil, Northern Africa and Southern Asia. The herb has been hailed since ancient times for its medicinal properties, rosemary was traditionally used to help alleviate muscle pain, improve memory, boost the immune and promote the hair growth. Leaves are used as culinary condiments, to make bodily perfumes and for its potential health benefits. Flowers are considered useful for making of sachets. Rosemary has been found to be a stimulant and mild analgesic, for skin tumours[4].

Figure 1: *Rosmarinus officinalis* plant

Figure 2: ***Rosmarinus officinalis***

Other names

Sanskrit: Satapatri, Satapatrika, Rusmari

Hindi: Gul mehandi

Maharastra: Shatavari

Latin: Rosa damascene

English: Persian rose

Tamil: Marikkolundu

Malyalam: Poovaamkurunthal

Telugu: Davanamu vantti vokka chettu

Taxonomy

Kingdom: Plantae, herb

Subkingdom: Viridiplantae, green plants

Infra kingdom: Streptophyta

Super division: Embryophyta

Division: Tracheophyta, vascular plants

Sub division: Sprematophytina, seed plants

Class: Magnoliopsida

Sub-class: Asteridae

Super order: Asteranae

Order: Lamiales

Family: Lamiaceae

Genus: *Rosmarinus*

Species: *R. officinalis*

Botanical distribution

Rosmarinus officinalis is commonly known as Rosemary; Rosemary is evergreen, usually erect, bushy shrub up to 2m tall and wide. Stem indistinctly quadrangular finely grey pubescent. Leaves opposite, tufted on the branches, sessile to short, petiolate, blade linear, 1-5cm×1-2mm, base attenuate, margin entire but revolute, apex obtuse, leathery, dark glossy, sea green and sub glabrous above, white felted tomentose beneath, aromatically fragrant when crushed. Inflorescence Racemose, axillary 5-10 flowered, 0.5-2.5 cm long, terminating short lateral branches, pedicle 2-5mm long, calyx campanulate, 2-lipped, 5-6mm long, densely stellate tomentose, upper lip small and 3 dentate, lower lip 2–lobed, corolla tabular, 2 lipped, 10- 13 mm long, pale blue or white, upper lip or recurved , 2-lobed, ovate, about 4mm long, lower lip 3-lobed above 7mm long, with large concave middle lobe; 2 anterior stamens perfect, 7-8 mm long, ascending under the base of the upper lip, two posterior stamens reduced to hardly visible staminodes, pistil with deeply 4-parite ovary style incurved, 1.5 cm long ending into 2 short, unequal branches with stigma. Fruit composed of 4 sub-globose to obovoid nut-lets, above 2mm long, glabrous and smooth[72].

Phytochemical studies

The characteristic aroma of camphor[4,5,6,8]. The main constituents of the rosemary essential oil are camphor (5.0–21%), 1,8-cineole (15–55%), α-pinene (9.0–26%), borneol (1.5–5.0%), camphene (2.5–12%), β-pinene (2.0–9.0%) and limonene (1.5–5.0%) in proportions that vary according to the vegetative stage and bioclimatic conditions[4]. Regarding the extracts, the phytochemicals mainly present in *R. officinalis* are rosmarinic acid, camphor, caffeic acid, ursolic acid, betulinic acid, carnosic acid and carnosol[4,7]. Therefore, *R. officinalis* is mainly composed of phenolic compounds, di and triterpenes and essential oils[9,10].

In traditional medicine, the leaves of *R. officinalis* are used based on their anti-bacterial activities, carminative and as analgesic in muscles and joints[4]. Also, rosemary's essential oils and extracts obtained from flowers and leaves are used to treat minor wounds, rashes, headache, dyspepsia, circulation problems, but also as an expectorant, diuretic and anti-spasmodic in renal colic[4,7]. Polyphenols are anti-oxidant chemical compounds primarily responsible for the fruit colouring, which are classified as phenolic acids, flavonoids and non-flavonoids[11]. In addition to their antioxidant properties, they play a very important role in the plant defences against herbivores, pathogens and predators; therefore, they have an application in the control of infectious agents in humans[11]. In *R. officinalis*, the most common polyphenols are apigenin, diosmin, luteolin, genkwanin and phenolic acids (>3%), especially rosmarinic acid, chlorogenic acid and caffeic acid[3,5].

Other major compounds common in rosemary are terpenes, usually present in essential oils and resins, which include over 10,000 compounds divided into mono, di, tri and sesquiterpenes, depending on the number of carbon atoms and isoprene groups (C_5H_8)[11]. It is possible to find in rosemary terpenes such as epirosmanol, carnosol, carnosic acid, ursolic acid and oleanolic acid (triterpenes)[3,4,7]. However, the carnosic acid, which is converted to carnosol by oxidation, has physicochemical, thermal and photo-labile properties, which can be avoided by a supercritical fluid extraction (low temperature operation)[12]. In 2014, five new compounds were identified in an ethanolic extract of *R. officinalis*, the officinoterpenoside A_1 and A_2 (diterpenoid glycosides), officino-terpenoside B and C (triterpenoid glycosides) and officinoterpenoside D (normonoterpenoid)[13]. Regarding the most studied compounds from *R. officinalis* and their biological activities, the increased pharmacological potential is clear for carnosic acid and the essential oil of rosemary.

Pharmacological value

Rosemary oil is used as a food seasoning[14], due to its chemical compound constituents responsible for the anti-bacterial, anti-fungal and anti-oxidant properties. Traditionally, rosemary oil has been shown to possess a number of applications in managing or curing many diseases such as inflammatory diseases[15] and diabetes mellitus[16]. On the other hand, the bioactivities of rosemary extracts include properties such as anti-inflammatory[17], anti-diabetic[18], hepatoprotective[19] and anti-microbial activity[20]. These bioactivities are related to the phenolic compound constituents (mainly caffeic acid, rosmarinic acid and carnosic acid).

Anti-oxidant activity

The anti-oxidative activity of rosemary extracts has been evaluated using different solvents. In this regard, Inatani et al.[21] reported that rosmanol, showed an antioxidant capacity four times higher than BRT and BRA (synthetic anti-oxidants) 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 anti-oxidant. Aruoma et al.[22] studied the anti-oxidant and pro-oxidant properties of rosemary. The main constituents with anti-oxidant 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 CCl_3O_2 (peroxyl radicals), reduce cytochrome c and scavenge hydroxyl radicals. Specifically, carnosic acid scavenges H_2O_2, but could also act as a substrate for the peroxidase system. The anti-oxidant properties depend on fruiting stages: the increase in concentration of polyphenols, which include carnosol, rosmarinic acid and hesperidin, during the fruiting stage, is directly related to the improvement of the extract anti-oxidant capacity. This statement is supported by scientific papers previously published by Cui et al.[23] and Kontogianni et al.[70], who consider lactone carnosol as the main property responsible for this activity. Likewise, rosmarinic acid and hesperidin have been cited in literature as important free radical scavengers[24,25]. One of the most significant aspects of the anti-oxidant activity of rosemary is the relationship between diterpenes and radical-scavenging activity. The anti-oxidant activity of rosemary through animal diet has been reported in additional studies by: Lopez Bote et al.[26] with 500 mg kg−1 in broiler diets; Descalzo et al.[27] in feed of cattle; Petron et al.[28] in lamb, in pork meat[29], turkey meat products[30,31], chicken meat[26], hen's meat[32,33], cooked sausages[34]. Generally, the addition of rosemary extract into the meat products or through animal feed improved the meat lipid stability. On the contrary, O'Grady et al.[36] and Galobart et al.[37] included that feeding animals with rosemary did not improve the lipid stability of meat or eggs. As previously reported, the antioxidant effect of rosemary is due to the polyphenols present in the leaves (mainly rosmarinic acid, carnosol and carnosic acid), which accumulate in the fatty membranes of cells where the anti-oxidant effect is required[31].

Anti-microbial activity

The anti-bacterial effect of rosemary has been widely demonstrated in several food studies: beef meatballs[39], cooked beef[40] and in pork sausage[41], and the anti-bacterial activity of rosemary oil against *E. coli, Bacillus cereus, Staphylococcus aureus*[37], *Staphylococcus aureus, Clostridium perfringens, Aeromonas hydrophila, Bacillus cereus* and *Salmonella choleraesuis* was reported. This essential oil was incorporated into meat reporting anti-bacterial activity against *Brochothrix thermosphacta* and *Enterobacteriaceae*[38].

Anti-proliferative activity

The crude ethanolic rosemary extract has differential anti-proliferative effects on human leukemia and breast carcinoma cells. The 50% inhibitory concentration (IC50) was estimated at 1/700, 1/400, 1/150 and 1/500 dilutions, for the HL60, K562, MCF7 and MDA-MB-468 cells, respectively[44,46,70].

Hepatoprotectivity

The hepatoprotective effects of the aqueous extract of the Egyptian rosemary against CCl_4-induced hepatotoxicity. Rosemary inhibited and reduced the CCl_4-induced hepatotoxicity in rats possibly by scavenging or blocking the formation of free radicals generated during CCl_4 metabolism. These improving effects of rosemary could be attributed to the bioactive constituents that alleviated the deleterious effect of CCl_4 either by the well-known scavenging action or the anti-oxidant properties that inhibited lipid per-oxidation, stabilized the reactive radicals, preserve the cellular integrity and restrain the severity of CCl_4[25,43].

Anti-cancer activity

Many studies have reported on the anticancer mechanisms of *Rosmarinus officinalis*. Rosemary has displayed significant anti proliferative activities against several human cancer cell lines. Major compounds in the plant's extract, such as carnosic acid, carnosol, and rosemarinic acid, have been shown to induce apoptosis within these cancer cells, possibly through the production of nitric oxide[44-46]. Carnosic acid appears to be the strongest promoter of apoptosis[44,46]. Rosemary extract also has intriguing anti-tumorigenic activity. In one study, the extract was found to strongly inhibit skin tumorigenesis in mice by preventing carcinogens from binding to epidermal DNA[47]. This anti carcinogenic effect is caused by the extract's antioxidant activity[48]. These anti proliferative and anti tumorigenic activities of *R. officinalis* can possibly be utilized in future cancer treatments and warrant further investigation.

Anti-diabetic activity

Diabetes mellitus is a growing worldwide disorder. By 2025, an estimated 300 million people will be diabetic, and global costs of treating the disease could reach US $1 trillion annually[49]. The development of diabetes is often fostered by high oxidative stress; pancreatic β-cells are especially vulnerable to reactive oxygen species, leading to decreased insulin secretion and higher blood glucose levels[4]. This information has prompted new diabetes treatments to focus on natural anti-oxidants, particularly those found in plants. Not surprisingly, multiple studies have identified *Rosmarinus officinalis* as a promising anti diabetic agent. Rosemary's anti-oxidant properties execute several anti diabetic and hypoglycemic mechanisms. In one study, rosemary extract lowered blood glucose levels in normoglycemic, hyperglycemic, and diabetic rabbits. By inhibiting lipid peroxidation and activating antioxidant enzymes, the extract also promoted insulin secretion[49]. Rosemary was also found to alleviate delayed wound healing, a serious complication of diabetes[50]. These anti diabetic activities are attributable to the body's improved antioxidant status after administration of rosemary[51].

Anti depressant activity

The potential use of *Rosmarinus officinalis* as an anti depressant was the focus of many research articles reviewed for this project[24]. The majorities of these studies involved two tests that are used to model anti-depressant like effects in mice-the Tail Suspension Test (TST) and Forced Swimming Test (FST). The administration of rosemary continuously decreased the immobility time of mice in both the TST and the FST, indicating an anti-depressant like effect. Rosemary's anti-depressant potential was further bolstered when it was found to decrease exploratory and anhedonic-like behavior in bulb ectomized mice[52]. There is much evidence that the antidepressant activity of *R. officinalis* depends on interactions with the monoaminergic system. Rosemary is believed to enhance dopaminergic, serotonergic, noradrenergic, and cholinergic functions within the brain, possibly explaining its antidepressant effects. Rosemary has also been found to increase the concentration of neurotransmitters in the brains of mice[53]. Several compounds in rosemary extract and essential oil are responsible for its anti depressant activity, including carnosol, betulinic acid, ursolic acid and polyphenols[53-55].

Neuroprotective activity

Remarkably, *Rosmarinus officinalis* has demonstrated significant neuroprotective effects against neurodegenerative diseases such as Alzheimer's disease and dementia. Rosemary has displayed inhibitory activities against the two enzymes in the brain responsible for the breakdown of Acetylcholine-Cholinesterase (AChE) and Butyryl Cholinesterase (BChE). These anti-AChE and anti-BChE activities are likely caused by rosemarinic acid and terpene compounds in the plant's essential oil[56,57]. By increasing total choline levels in the brain, rosemary could attenuate not just Alzheimer's disease, but also memory loss, anxiety, and depression[58,59]. Two more studies highlight the neuro-protective ability of *R. officinalis.* In the first, polyphenols present in rosemary extract were found to inhibit stress proteins, which play a role in the neurodegenerative process[60]. The second study concluded that rosemary promotes the production of Nerve Growth Factor (NGF), a protein vital to the growth and maintenance of nerve tissue. Increased NGF levels can help alleviate Alzheimer's disease, dementia, and other neurodegenerative diseases[61]. Both these studies clearly demonstrate rosemary's growing potential as a neuroprotective.

Anti-inflammatory activity

Rosmarinus officinalis displayed potent anti-inflammatory mechanisms in several of the reviewed studies[17]. Rosemary essential oil and extract were found to significantly inhibit leukocyte migration *in vivo*[62]. This reduced the number of leukocytes (White Blood Cells) at the site of inflammation, resulting in an anti-inflammatory response[63,64]. Rosemary extract also inhibited other proinflammatory substances, such as nitric oxide and inflammation associated genes[64-65]. While carnosol and carnosic acid appear to be particularly important, the anti-inflammatory activity of rosemary most likely depends on a synergistic mechanism between many of its components[62,63]. These studies suggest that the anti-inflammatory effect of *R. officinalis* is rather strong; in fact, the anti-inflammatory activities of pure carnosol and carnosic acid were found to be nine times higher than that of Indomethacin, a common anti-inflammatory drug agent[63].

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[66]. 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[67]. 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[68]. The results of all three studies indicate that *R. officinalis* has great potential as an effective treatment against obesity and other metabolic disorders[66-68].

Ulcerative colitis

Excessive accumulation and activation of phagocytes in the gut may cause severe damage and may be reduced by anti-oxidant. This study was carried out to investigate the effects of rosemary leaves hydroalcoholic extract (RHE) and essential oil (REO) in a well-defined model of experimental colitis induced by trinitrobenzene sulfonic acid (TNBS) in rats. Different doses of RHE (100, 200 and 400 mg/kg) and REO (100, 200 and 400 μl/kg) were administered orally and intraperitoneally (100, 400 mg/kg and 100, 400 μl/kg) to male Wistar rats (n=6), 6 h after colitis induction and continued for 5 days by intracolonic instillation of 0.25 ml TNBS (80 mg/kg)/ethanol 50% v/v. Wet colon weight/length ratio was measured and tissue damage scores as well as indices of colitis were evaluated both macroscopically and histopathologically. RHE and REO at all test doses used were effective to reduce colon tissue lesions and colitis indices while greater doses were significantly effective to diminish histopathologic parameters irrespective to the route of administration. Administration of oral prednisolone, Asacol (mesalazine microgranules) and parenteral hydrocortisone acetate were effective to reduce colon tissue injures as well. These data suggest that RHE and REO are both effective to possess anti-colitic activity, and reinforce the use of this plant as a remedy for inflammatory bowel diseases in traditional medicine[69].

Table 1: Pharmacological value of *R. officinalis*

Sl. No.	Tissue	Extract	Activity
1	Leaves	Super critical CO_2	Anti-tumor activity
2	Leaves	Methanol extract	Anti-inflammatory effect
3	Leaf	aqueous extract	Anti-pyretic, improve circulation
4	Whole plant	Methanol extracts	Anti-microbial activity
5	leaves	acetone extract	Food additive
6	Whole plant	Aqueous Extract	Choleretic and hepatoprotective activities
7	Leaf	Ethanol extract	Anti-cancer activity
8	Whole plants	n-hexane extract	Anti-oxidative activity

DISCUSSION

Rosmarinus officinalis, an evergreen perennial shrub commonly known as rosemary, is garnering considerable attention from the food and medical industries due to its wide array of biological activities. Rosemary has been used as a source of traditional medicine for centuries, but its potential as a natural food preservative has only recently been investigated. Studies have shown that the strong antioxidant and antimicrobial activities of the plant's extracts make rosemary an ideal replacement for more toxic artificial food additives. As concern over these potentially harmful additives has grown, so has the demand for natural preservatives such as rosemary. While rosemary is beginning to be used as a preservative around the globe, more can be done to maximize the plant's potential. Additional research is needed to identify the extracts and essential oils of rosemary that have the most potent preservative activities. Toxicity levels and potential side effects of rosemary must also be constantly monitored. Assuming it remains less toxic, *R. officinalis* should continue to replace artificial additives in many preservative applications, thereby reducing risk to consumers.

Rosmarinus officinalis has also displayed many intriguing therapeutic properties. Rosemary's anti-microbial, anti depressant, neuroprotective, anti-inflammatory and anti-obesity activities all have potential in the treatment against various diseases. However, it is the anticancer and anti diabetic mechanisms of rosemary that warrant the most attention. Oxidative stress has been shown to contribute to the progression of diabetes mellitus and many forms of cancer. It is not surprising, then, that the strong anti-oxidant activity of rosemary extract and essential oil represents a promising new strategy in the treatment of both diseases. The plant's ability to promote insulin secretion in diabetic patients and induce apoptosis within cancer cells is particularly intriguing. While these initial results have been encouraging, more clinical studies are needed before rosemary can be regularly used in humans. If it continues to display such promising anti-diabetic and anti-cancer activities with few side effects, *R. officinalis* could eventually provide an innovative treatment in the fight against these two serious diseases.

CONCLUSION

Rosmarinus officinalis (Rosemary) has displayed exciting potential as both a natural food preservative and a therapeutic agent in the literature reviewed for this project. The low toxicity levels and strong anti-oxidant, anti-bacterial, and anti-fungal activities of the plant's extract make rosemary an effective food preservative with fewer side effects than artificial additives. The strong anti-oxidant compounds found in its extract and essential oil account for many of rosemary's biological activities, including its anti diabetic and anticancer mechanisms. Rosemary has also been found to alleviate depression, neurodegenerative diseases, inflammation and obesity. While the initial results have been encouraging, additional research is needed to confirm the safety and efficacy of *R. officinalis* as a preservative and therapeutic agent. More studies are strongly recommended to establish the mechanisms are involved and the active constituents which are really responsible for its beneficial pharmacologic actions.

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