REVIEW ARTICLE

A Review on Therapeutic Potential of *Rosmarinus* officinalis L.

Bhaskar Raju V1, Supriya T1, Srinu P2*, Nandhini GVSR3, Uma Devi M4, Sharmani R4

¹Sri Vasavi Institute of Pharmaceutical Sciences, Pedatadepalli, Tadepalligudem, Andhra Pradesh, India.

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Abstract: Rosemary (Rosmarinus officinalis L.) is an aromatic evergreen shrub with a long history of culinary and medicinal applications. This review aims to provide a comprehensive overview of the therapeutic potential of rosemary and its bioactive constituents. The plant's essential oil and extracts are rich in potent antioxidant compounds, including carnosic acid, carnosol, rosmarinic acid, and ursolic acid. These phytochemicals have been extensively investigated for their diverse biological activities. Numerous studies have demonstrated the remarkable antioxidant, anti-inflammatory, and antimicrobial properties of rosemary extracts, attributable to their ability to neutralize reactive oxygen species and inhibit pathogenic microorganisms. Moreover, rosemary has shown promising anticancer effects, inducing apoptosis and inhibiting the proliferation of various cancer cell lines, including breast, colon, and leukemia. Emerging evidence also highlights the potential of rosemary in managing metabolic disorders, such as diabetes and hyperlipidemia. Its bioactive compounds have been found to modulate glucose and lipid metabolism through the activation of AMPK and PPAR pathways, thus improving glucose homeostasis and lipid profiles. Moreover rosemary has garnered significant interest for its neuroprotective and cognitive-enhancing properties. Compounds like rosmarinic acid have exhibited cholinergic and neuroprotective effects, inhibiting acetylcholinesterase activity and mitigating oxidative stress in the brain, thereby potentially benefiting neurodegenerative disorders like Alzheimer's and Parkinson's diseases. This review discusses about the vast therapeutic potential of rosemary and its constituents, highlighting the need for further research to elucidate their mechanisms of action, bioavailability, and potential synergistic effects, paving the way for their future application in modern medicine.

Keywords: Rosemary; Antioxidant activity; Antimicrobial activity; Anticancer activity; Neuroprotective activity; Metabolic disorders

1. Introduction

Rosemary (*Rosmarinus officinalis* L.) is an evergreen aromatic shrub belonging to the Lamiaceae family, native to the Mediterranean region. Its culinary and medicinal uses date back to ancient civilizations, where it was revered for its therapeutic properties. Throughout history, rosemary has been utilized for various purposes, including flavoring food, producing fragrances, and treating a wide range of ailments. [1,2] In traditional medicine, rosemary has been employed as an antispasmodic agent for treating renal colic and dysmenorrhea, alleviating respiratory conditions, and promoting hair growth. Its therapeutic potential can be attributed to its rich phytochemical composition, which includes a diverse array of bioactive compounds, such as terpenoids, flavonoids, phenolic acids, and essential oils.

Among the most notable bioactive constituents of rosemary are the diterpenes carnosic acid and carnosol, as well as the phenolic compounds rosmarinic acid, ursolic acid, and betulinic acid. These compounds have garnered significant scientific interest due to their remarkable biological activities, particularly their potent antioxidant and anti-inflammatory properties. Antioxidants play a crucial role in neutralizing reactive oxygen species (ROS) and preventing oxidative stress, which is implicated in the pathogenesis of various chronic diseases, including cancer, cardiovascular disorders, neurodegenerative diseases, and metabolic disorders. [3] Rosemary's antioxidant potential has been extensively studied, with numerous in vitro and in vivo studies demonstrating its ability to scavenge free radicals and inhibit lipid peroxidation.

Furthermore, rosemary has exhibited significant antimicrobial activity against a wide range of pathogenic microorganisms, including bacteria, fungi, and viruses. This antimicrobial property has been attributed to the presence of various bioactive compounds, such as terpenoids and phenolic acids, which can disrupt the cellular membranes and inhibit the growth of microbes. [4] In addition to its antioxidant and antimicrobial activities, rosemary has shown promising potential in the management of various chronic diseases. Numerous studies have highlighted its anticancer, anti-diabetic, neuroprotective, and anti-inflammatory effects, among others. These therapeutic properties have been linked to the modulation of various molecular pathways and biological processes by

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^{*} Corresponding author: Srinu Pappu

rosemary's bioactive constituents. [5] With the increasing global burden of chronic diseases and the growing interest in natural and sustainable therapeutic solutions, rosemary has emerged as a promising candidate for further research and development. This review aims to provide a comprehensive overview of the therapeutic potential of rosemary, highlighting its bioactive constituents, mechanisms of action, and current research findings, while also exploring future directions and potential applications in modern medicine.



Figure 1. a. Whole plant of Rosmarinus officinalis L b. leaves c. flowers

2. Plant profile

2.1. Botanical classification

Kingdom: Plantae Division: Magnoliophyta Class: Magnoliopsida Order: Lamiales Family: Lamiaceae Genus: Rosmarinus Species: Rosmarinus officinalis L.

2.2. Common names

Rosemary, Compass Plant, Polar Plant, Old Man

2.3. Description

Rosemary (*Rosmarinus officinalis* L.) is an aromatic, evergreen, perennial shrub that can grow up to 2 meters in height. The plant is native to the Mediterranean region and is widely cultivated in many parts of the world for its culinary, medicinal, and ornamental purposes. Rosemary has a distinct, pungent, and somewhat piney aroma, which is due to the presence of volatile essential oils, primarily composed of monoterpenes such as α -pinene, camphene, and 1,8-cineole. The taste of rosemary is slightly bitter, warm, and astringent, with a woody and resinous undertone [6,7]

2.4. Morphology

2.4.1. Stems

The stems of rosemary are woody, branched, and covered with short, dense, grayish-green or whitish hairs.

2.4.2. Leaves

The leaves are oppositely arranged, sessile (without a petiole), linear to lanceolate in shape, and have a leathery texture. They are typically 2-4 cm long and 2-5 mm wide, with rolled-under margins and a distinctive aroma when crushed. [8]

2.4.3. Flowers

Rosemary produces small, blue or white, bilateral, and zygomorphic flowers that are arranged in short, axillary racemes or terminal panicles. The flowers have two-lipped corollas, with the upper lip being entire and the lower lip being three-lobed. [9]

2.4.4. Fruits

The fruits of rosemary are small, smooth, and ovoid nutlets, each containing a single seed.

2.4.5. Roots

The root system of rosemary is extensive and deep, allowing the plant to thrive in dry and rocky habitats.

2.5. Cultivation and Habitat

Rosemary is a hardy plant that thrives in well-drained, sandy, or rocky soils and prefers full sun exposure. It is drought-tolerant and can withstand high temperatures and low humidity. The plant is widely cultivated in Mediterranean regions, as well as in other parts of the world with similar climatic conditions. [10]

2.6. Traditional and Culinary Uses

Rosemary has been used for centuries in traditional medicine and culinary applications. In folk medicine, it has been employed for its purported therapeutic properties, including as an antispasmodic, diuretic, and tonic for the nervous system. It has also been used to alleviate respiratory problems, improve digestion, and stimulate hair growth. In culinary applications, rosemary is widely used as a flavoring agent in various dishes, particularly in Mediterranean cuisine. Its needle-like leaves are used to season meats, vegetables, breads, and sauces, imparting a distinct aroma and flavor. Rosemary is also used in the production of cosmetics, perfumes, and insect repellents. [11]

2.7. Phytochemical Composition

Rosemary is a rich source of various bioactive phytochemicals, including:

2.7.1. Terpenoids

Carnosic acid, carnosol, ursolic acid, betulinic acid, and their derivatives.

2.7.2. Phenolic compounds

Rosmarinic acid, caffeic acid, and other phenolic acids and flavonoids.

2.7.3. Essential oils

Monoterpenes like α -pinene, camphene, 1,8-cineole, and others

3. Pharmacological activities

3.1. Antioxidant activity

Rosemary is renowned for its remarkable antioxidant properties, which can be attributed to its rich phytochemical composition, particularly the presence of phenolic compounds like rosmarinic acid, carnosic acid, and carnosol. These compounds have been extensively studied for their ability to scavenge free radicals and inhibit oxidative stress, which is a major contributing factor to various chronic diseases. *In vitro* antioxidant assays have demonstrated the potent antioxidant capacity of rosemary extracts and their bioactive components. [12,13] For instance, rosmarinic acid has exhibited excellent free radical scavenging activity against reactive oxygen species (ROS) such as superoxide, hydroxyl, and peroxyl radicals. Carnosic acid and carnosol have also shown remarkable antioxidant potential in various *in vitro* assays, including DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging, ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) radical cation decolorization, and inhibition of lipid peroxidation. In vivo studies have further corroborated the antioxidant effects of rosemary and its constituents. Administration of rosemary extracts or its isolated compounds has been found to increase the levels of endogenous antioxidant enzymes, such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), in various animal models. [14, 15] Additionally, rosemary supplementation has been shown to mitigate oxidative stress markers, including malondialdehyde (MDA) and protein carbonyl levels, in various tissues and organs, thereby protecting against oxidative damage.

3.2. Antimicrobial activity

Rosemary has exhibited potent antimicrobial properties against a wide range of pathogenic microorganisms, including bacteria, fungi, and viruses. The antimicrobial activity of rosemary is primarily attributed to its essential oil components and phenolic compounds, which can disrupt the cellular membranes and inhibit the growth and proliferation of microbes. [16]

3.2.1. Antibacterial effects

Rosemary essential oil and extracts have demonstrated significant antibacterial activity against both Gram-positive and Gramnegative bacteria, such as Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, and Klebsiella pneumoniae. The antimicrobial effects have been linked to the ability of rosemary's bioactive compounds to disrupt cell membranes, inhibit enzyme activity, and interfere with bacterial quorum sensing mechanisms. [17]

3.2.2. Antifungal effects

Several studies have reported the antifungal potential of rosemary against various fungal species, including Candida albicans, Aspergillus niger, and Penicillium chrysogenum. The antifungal activity is primarily attributed to the disruption of fungal cell membranes and inhibition of ergosterol biosynthesis, which is essential for maintaining the structural integrity of fungal cell walls. [18]

3.2.3. Antiviral effects

While research on the antiviral properties of rosemary is relatively limited, some studies have suggested its potential against certain viruses. For instance, rosemary extracts have shown inhibitory effects against the human immunodeficiency virus (HIV) and the herpes simplex virus (HSV), possibly by interfering with viral entry, replication, and assembly processes. [19]

3.3. Anticancer activity

Rosemary has gained significant attention for its potential anticancer properties, with numerous studies investigating its cytotoxic effects on various cancer cell lines and exploring the underlying mechanisms of action. Rosemary extracts and their bioactive compounds, particularly carnosic acid, carnosol, and ursolic acid, have exhibited potent cytotoxic effects against a wide range of cancer cell lines, including breast, colon, liver, and leukemia cells. These compounds have been shown to selectively induce apoptosis (programmed cell death) in cancer cells while exhibiting minimal toxicity towards normal, healthy cells. [20]

The anticancer effects of rosemary are mediated through various mechanisms, including the induction of apoptosis, cell cycle arrest, inhibition of angiogenesis (formation of new blood vessels), and modulation of signaling pathways involved in cell proliferation and survival. Carnosic acid and carnosol have been reported to induce apoptosis in cancer cells by activating caspase cascades, disrupting mitochondrial membrane potential, and regulating the expression of pro-apoptotic and anti-apoptotic proteins. Additionally, rosemary compounds have been found to inhibit the activity of key enzymes involved in cancer progression, such as matrix metalloproteinases (MMPs), which play a crucial role in tumor invasion and metastasis. [21] Additionally, rosemary extracts have demonstrated anti-angiogenic properties by inhibiting the production of vascular endothelial growth factor (VEGF) and blocking the signaling pathways involved in angiogenesis. While most anticancer research has been conducted using in vitro models, some in vivo studies have also provided promising results. For instance, administration of rosemary extracts or its bioactive compounds has been shown to suppress tumor growth, inhibit metastasis, and enhance the efficacy of conventional chemotherapeutic agents in various animal models of cancer. [22]

3.4. Antidiabetic and metabolic effects

Rosemary has garnered significant interest for its potential in managing metabolic disorders, particularly diabetes and associated complications. Several studies have investigated the effects of rosemary on glucose and lipid metabolism, as well as its ability to modulate key metabolic pathways. [23]

3.4.1. Effects on glucose metabolism

Rosemary extracts and their bioactive compounds, such as carnosic acid and rosmarinic acid, have been found to exhibit hypoglycemic (blood glucose-lowering) effects in various animal models of diabetes. These compounds have been shown to improve insulin sensitivity, enhance glucose uptake in peripheral tissues, and inhibit the activity of enzymes involved in carbohydrate metabolism, such as α -amylase and α -glucosidase.

3.4.2. Effects on lipid metabolism

In addition to its effects on glucose metabolism, rosemary has also demonstrated beneficial effects on lipid metabolism. Studies have shown that rosemary supplementation can improve lipid profiles by reducing total cholesterol, triglycerides, and low-density

lipoprotein (LDL) levels, while increasing high-density lipoprotein (HDL) levels. These effects are attributed to the ability of rosemary compounds to inhibit lipid absorption, modulate lipid metabolism enzymes, and enhance the expression of genes involved in lipid homeostasis.

3.4.3. Modulation of metabolic pathways

Rosemary's bioactive compounds have been found to modulate several key metabolic pathways involved in energy metabolism and glucose homeostasis. For instance, carnosic acid and carnosol have been shown to activate the AMP-activated protein kinase (AMPK) pathway, which plays a crucial role in regulating cellular energy balance and glucose and lipid metabolism. Additionally, rosemary compounds have been reported to activate the peroxisome proliferator-activated receptors (PPARs), which are nuclear receptors involved in regulating gene expression related to lipid and glucose metabolism

3.5. Neuroprotective and Cognitive-Enhancing Effects

Rosemary has gained increasing attention for its potential neuroprotective and cognitive-enhancing properties, which have been attributed to its bioactive compounds, particularly rosmarinic acid and other phenolic constituents. [24]

3.5.1. Cholinergic and neuroprotective activity

Rosmarinic acid has been identified as a potential inhibitor of acetylcholinesterase (AChE), an enzyme responsible for the breakdown of acetylcholine, a neurotransmitter crucial for cognitive function. By inhibiting AChE, rosmarinic acid can enhance cholinergic transmission and potentially improve cognitive performance. Additionally, rosemary extracts and their compounds have exhibited neuroprotective effects by scavenging free radicals, reducing oxidative stress, and modulating various signaling pathways involved in neuronal survival and function.

3.5.2. Effects on neurotransmitters and signaling pathways

Rosemary has been shown to modulate the levels and signaling of various neurotransmitters, including acetylcholine, dopamine, serotonin, and gamma-aminobutyric acid (GABA). These neurotransmitters play crucial roles in cognitive processes, mood regulation, and neuronal communication. Furthermore, rosemary compounds have been found to modulate signaling pathways involved in neuronal plasticity, such as the MAPK (mitogen-activated protein kinase) and PI3K/Akt (phosphoinositide 3-kinase/protein kinase B) pathways, which are essential for neuronal growth, survival, and synaptic function

3.5.3. Cognitive enhancement and memory improvement

Cognitive enhancement and memory improvement: Several preclinical studies have demonstrated the potential of rosemary extracts and their bioactive compounds in enhancing cognitive function and improving memory performance. In animal models, rosemary supplementation has been shown to improve spatial memory, learning abilities, and working memory. These effects are believed to be mediated through the modulation of neurotransmitter systems, reduction of oxidative stress, and enhancement of neuronal plasticity.

3.6. Anti-inflammatory Activity

Rosemary has been extensively studied for its potent anti-inflammatory properties, which can be attributed to its ability to modulate various inflammatory pathways and mediators.

3.6.1. Inhibition of inflammatory mediators

Rosemary extracts and their bioactive compounds, such as carnosic acid, carnosol, and rosmarinic acid, have been found to inhibit the production and activity of several pro-inflammatory mediators, including prostaglandins, leukotrienes, cytokines (e.g., interleukin-6, tumor necrosis factor-alpha), and nitric oxide. These compounds have demonstrated the ability to suppress the activity of enzymes involved in the inflammatory cascade, such as cyclooxygenase (COX), lipoxygenase (LOX), and inducible nitric oxide synthase (iNOS).

3.6.2. Modulation of inflammatory pathways

Rosemary compounds have been shown to modulate various signaling pathways involved in the inflammatory response, particularly the nuclear factor-kappa B (NF-xB) pathway. NF-xB is a transcription factor that regulates the expression of numerous genes involved in inflammation, immune response, and cell survival. Rosemary compounds have been found to inhibit the activation of NF-xB, thereby suppressing the downstream production of inflammatory mediators. [25]

3.7. Other activities

3.7.1. Cardioprotective effects

Several studies have suggested that rosemary possesses cardioprotective properties. Rosemary extracts and their bioactive compounds have been shown to improve endothelial function, reduce oxidative stress in the cardiovascular system, and exhibit antihypertensive and hypolipidemic effects. These actions may contribute to the prevention and management of cardiovascular diseases, such as atherosclerosis, hypertension, and ischemic heart disease.

3.7.2. Hepatoprotective effects

Rosemary has demonstrated potential hepatoprotective effects, primarily attributed to its antioxidant and anti-inflammatory properties. In various animal models of liver injury, rosemary extracts and compounds have been found to protect against hepatotoxicity induced by chemicals, drugs, or environmental toxins. These effects are mediated through the modulation of oxidative stress, inflammation, and apoptotic pathways in liver cells. [26]

3.7.3. Skin protective effects

Rosemary has gained attention for its potential applications in skin care and protection. Its antioxidant and anti-inflammatory properties make it a promising candidate for the prevention and treatment of various skin conditions, such as photoaging, skin cancer, and inflammatory skin diseases. Additionally, rosemary extracts have been explored for their potential in promoting wound healing and protecting against UV-induced skin damage.

4. Conclusion

Rosemary (*Rosmarinus officinalis* L.) is a remarkable herb with a wide range of pharmacological activities that hold immense therapeutic potential. This comprehensive review highlights the plant's rich phytochemical composition, particularly the presence of bioactive compounds such as carnosic acid, carnosol, rosmarinic acid, and ursolic acid, which contribute to its various biological effects. The antioxidant, antimicrobial, anticancer, anti-diabetic, neuroprotective, and anti-inflammatory properties of rosemary have been extensively investigated and documented through numerous in vitro and in vivo studies. The mechanisms underlying these activities involve modulation of various signaling pathways, inhibition of inflammatory mediators, induction of apoptosis in cancer cells, and regulation of metabolic pathways. While preclinical research has provided substantial evidence for the therapeutic potential of rosemary, clinical studies in humans are still limited. Future well-designed, large-scale clinical trials are warranted to validate the efficacy and safety of rosemary extracts or isolated compounds for specific therapeutic applications.

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