



## The Pharmacological and Nutritional Properties of *Rosmarinus officinalis*: A Comprehensive Review

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### ABSTRACT

*Rosmarinus officinalis*, commonly called rosemary is an aromatic plant native to the Mediterranean region. It has been employed in traditional medicine for its diverse therapeutic benefits. Contemporary research has validated its pharmacological potentials, attributing its efficacy to its rich phytochemical profile. This review explores the pharmacological and nutritional properties of rosemary, with particular focus on its bioactive compounds, including carnosic acid, carnosol, and rosmarinic acid. A comprehensive literature search across multiple databases yielded a robust dataset on the composition and biological activities of rosemary. The nutritional profile, encompassing essential oils, flavonoids, triterpenic acids, vitamins, minerals, and macronutrients, was meticulously examined. In addition, the review elucidated advanced extraction techniques for optimal bioactive compound recovery. By unraveling the mechanisms underlying the health-promoting effects of rosemary, this study provided adequate information that could guide the clinical applications and nutritional use of rosemary especially within the context of functional foods.

**Keywords:** *Rosmarinus officinalis*, Rosemary, Pharmacological potential, Nutritional benefits, Anti-inflammatory effects, Anticancer activities.

### Introduction

*Rosmarinus officinalis* L., commonly known as rosemary, is a prominent aromatic plant native to the Mediterranean region and cultivated extensively around the globe.<sup>1</sup> Rosemary is historically used in traditional medicine, and has garnered significant scientific interest due to its diverse therapeutic properties. It has a wide range of pharmacological activities, including anticancer,<sup>2</sup> anti-inflammatory, and antioxidant activities.<sup>3</sup> The bioactive components of *Rosmarinus officinalis* essential oil (ROEO), particularly phenolic diterpenes and triterpenes, exhibit remarkable pharmacological effects.<sup>4</sup>

Recent research has accentuated the potential of rosemary extracts (REs) and their primary polyphenols, such as carnosic acid, carnosol, and rosmarinic acid, in demonstrating a wide range of biological activities. These compounds affect multiple pathways and regulate several transcription factors.<sup>5</sup> Additionally, *Rosmarinus officinalis* demonstrates antifungal,<sup>6</sup> antiviral,<sup>7</sup> antibacterial,<sup>8</sup> antithrombotic,<sup>9</sup> antinociceptive, antidepressant,<sup>10</sup> and antiulcerogenic properties. Traditional uses of rosemary include use in alleviating symptoms associated with renal colic,<sup>11</sup> dysmenorrhea, muscle spasms, and other conditions.<sup>12</sup>

The review comprehensively explored the biological properties and therapeutic potential of rosemary. It examined isolated compounds, extracts, and essential oils, highlighting the plant's diverse applications and bioactive constituents. The study highlighted major bioactive compounds including carnosic acid, carnosol, and rosmarinic acid.

Various extraction methods, such as Soxhlet extraction, maceration, decoction, infusion, hydrodistillation, distillation, and supercritical fluid extraction, were examined to assess their efficacy in isolating these compounds. Additionally, the nutritional composition of *Rosmarinus officinalis* was evaluated, focusing on its essential oils, flavonoids, triterpenic acids, vitamins, minerals, and macronutrients. The review thoroughly investigated the impact of these nutritional components on human health, particularly within the context of functional foods.

This review aims to comprehensively examine the pharmacological and nutritional properties of *Rosmarinus officinalis*, with a particular focus on its bioactive compounds. Through a detailed analysis of its biological activities, this review will provide a thorough understanding of the mechanisms by which rosemary exerts its health-promoting effects. Ultimately, the review intends to contribute to the body of knowledge on *Rosmarinus officinalis*, facilitating its integration into clinical practice and daily nutrition for improved health outcomes.

### Materials and Methods

This review investigated the pharmacological, nutritional, and chemical properties of *Rosmarinus officinalis* through a comprehensive analysis of existing literature.

The search strategy was designed to ensure a thorough and systematic exploration of a wide array of relevant studies published in English, Spanish, French, and Portuguese. Key databases such as Science Direct, Web of Science, Medline, BVS Regional Portal, SciELO, Embase, Capes Periodicals, and Google Scholar were used. The primary keywords employed in the search included "*Rosmarinusofficinalis*", "Rosemary", "Rosmarinic acid", "Carnosol", "Carnosic acid", "Essential oil", "Anti-inflammatory", "Antioxidant properties", "Pharmacological potential", "Nutritional benefits", "anti-inflammatory effects", and "Anticancer activities".

To ensure scientific rigor, only peer-reviewed research was included. The review process involved a meticulous evaluation of titles and abstracts, followed by in-depth analysis of selected full-text articles. Key data were systematically extracted and categorized based on study type, bioactive compounds, extraction methods, and observed therapeutic effects. Emphasis was placed on the pharmacological

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activities of *Rosmarinus officinalis*, such as anticancer, anti-inflammatory, antioxidant, antifungal, and antiviral effects, among other health-promoting benefits.

## Results and Discussion

### Botanical description

#### Lamiaceae family

The Lamiaceae family, which includes rosemary, is one of the most extensive families of flowering plants. This family comprises 236 genera and more than 7,000 species globally.<sup>13</sup> This family was originally known as Labiatae due to the characteristic morphology of the flowers, which typically exhibit petals fused into upper and lower lips, the contemporary botanical nomenclature predominantly uses the term Lamiaceae.

Members of the Lamiaceae family are renowned for their production of biologically active essential oils. They are widely cultivated for both ornamental and culinary applications, and they consist of a diverse array of species, including basil, lavender, mint, sage, thyme, and rosemary. These plants are characterized by a rich phytochemical profile, notably containing terpenes, iridoids, flavonoids, and phenolic compounds.

#### Ethnobotany of *Rosmarinus officinalis* Linnaeus

*Rosmarinus officinalis* L., an aromatic perennial shrub endemic to the Mediterranean Basin, belongs to the Lamiaceae family. Historically valued for its culinary, medicinal, and ornamental attributes, rosemary has garnered significant ethnobotanical interest.

This evergreen shrub typically reaches heights exceeding one meter with a dense, branched architecture.<sup>14</sup> Its woody stems, commonly erect and brown, occasionally adopt a prostrate growth pattern. Characteristically, rosemary leaves are sessile, coriaceous, and linear to linear-lanceolate, measuring 1–4 cm in length and 2–4 mm in width.<sup>15</sup> Reproductive structures of *R. officinalis* are distinctive, consisting of small, bilabiate flowers arranged in an axillary verticillasters, typically bearing few flowers. The corolla displays a coloured spectrum ranging from blue-white to pale pink, facilitating pollinator attraction. The androecium comprises two prominent lateral stamens, each filament adorned with a small lateral tooth.<sup>16</sup>

This species is well-adapted to the Mediterranean climate, but thrives in environments with moderate humidity. *R. officinalis* exhibits less resilience in anaerobic or waterlogged soils with remarkable tolerance to drought and salinity. While adaptable to various soil types, optimal growth is achieved in well-drained conditions.

The phenological cycle of rosemary is characterized by flowering and fruiting periods, generally occurring from May to June. During this period, the plant produces schizocarpic fruits, which subsequently divide into four nutlets. This reproductive mechanism ensures efficient seed dispersal and population expansion within its native habitat.

#### Extraction techniques and phytochemical profile

To unlock the therapeutic potential of *Rosmarinus officinalis*, a variety of extraction methods have been employed targeting diverse plant parts, including leaves, roots, stems, and flowers. These processes, relying on selective solvents and standardized protocols, yield complex mixtures in various forms such as liquids, semisolids, or dry powders. The efficiency of extraction is contingent upon several factors, including plant characteristics, solvent selection, temperature, pressure, and extraction duration.<sup>17</sup>

Traditional extraction techniques, such as Soxhlet extraction, maceration, decoction, and infusion, have been employed due to their simplicity and effectiveness in isolating a wide variety of compounds. In recent times, modern methods, such as supercritical fluid extraction and solid-phase micro-extraction have also been developed. Specifically, maceration, hydrodistillation, distillation, and supercritical fluid extraction are extensively used for extracting bioactive compounds from *Rosmarinus officinalis*.<sup>18</sup> Maceration, which involves soaking plant material in a solvent at room temperature, allows for the diffusion of compounds into the solvent. On the other hand, hydrodistillation and distillation, both utilizing heat, are particularly effective for obtaining essential oils and other volatile substances.

Modern techniques like supercritical fluid extraction (SFE) and solid-phase micro-extraction (SPME) offer more advanced and efficient approaches. SFE uses supercritical fluids, typically CO<sub>2</sub>, which act as

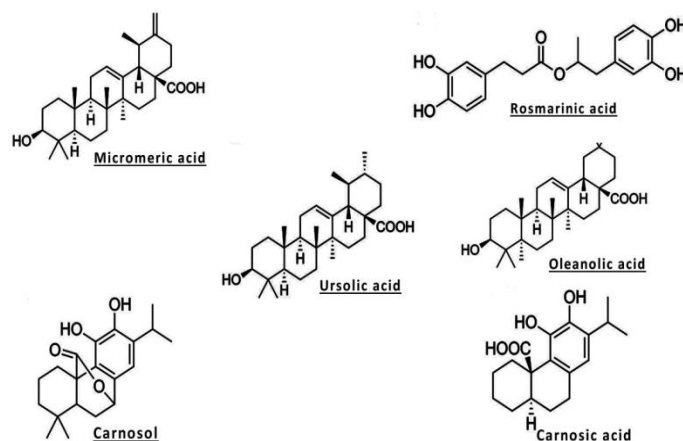
solvents to extract bioactive compounds under specific temperature and pressure. This method is particularly advantageous for its ability to selectively extract compounds without the use of organic solvents, making it environmentally friendly. SPME, on the other hand, employs a coated fiber to adsorb volatile and semi-volatile compounds directly from the sample matrix, which are then desorbed for analysis. This technique is valued for its rapidity and minimal solvent requirement.

Rosemary essential oil, a complex mixture of volatile compounds, including monoterpenes, sesquiterpenes, and their derivatives, is primarily obtained through steam distillation of the leaves. The resulting oil, characterized by a distinct camphor aroma, is colourless to light yellow and immiscible with water. Key constituents of rosemary essential oil are 1,8-cineole (15–55%),  $\alpha$ -pinene (9.0–26%), camphor (5.0–21%), borneol (1.5–5.0%), camphene (2.5–12%),  $\beta$ -pinene (2.0–9.0%), and limonene (1.5–5.0%).<sup>19</sup> However, the composition can fluctuate based on plant developmental stage and environmental conditions.<sup>19</sup>

The phytochemical profile of *R. officinalis* extracts is rich and diverse. Principal compounds include camphor, rosmarinic acid, ursolic acid, caffeic acid, betulinic acid, carnosic acid, rosmanol and carnosol (Figure 2). Phenolic compounds, renowned for their antioxidant properties, constitute a significant proportion of the plant's phytochemistry and are instrumental to its antioxidant defense mechanisms. Major polyphenols in rosemary include apigenin, diosmin, luteolin, rosmarinic acid, genkwanin, caffeic acid, and chlorogenic acid. Furthermore, the plant contains an array of terpenes, including epirosmanol, carnosol, oleanolic acid, carnosic acid, and ursolic acid. Notably, carnosic acid, a precursor to carnosol, retains its properties when preserved using supercritical fluid extraction. The phytochemical reservoir of rosemary is further enriched by officinoterpenosides A1, A2, B, C, and D, classified as diterpenoid, triterpenoid, and normonoterpenoid glycosides, respectively.<sup>20,21</sup>



**Figure 1:** *Rosmarinus officinalis* L.; a. Whole plant, b. leaves



**Figure 2:** Chemical composition of Rosemary (*Rosmarinus officinalis*)

#### Nutritional composition of *Rosmarinus officinalis*

Functional foods provide considerable physiological benefits and essential nutrients, contributing to body function and offering additional health advantages. It can be described as whole foods, including fortified, enhanced, and enriched varieties that produce beneficial health effects when consumed regularly. They are of increasing

importance due to the prevalence of lifestyle-related diseases like obesity, cancer, diabetes, and cardiovascular issues.

*Rosmarinus officinalis* is renowned for its rich content of bioactive compounds, including terpenes, rosmarinic acid, and carnosic acid (Table 1), which contribute to its diverse applications and benefits. In addition to these compounds, rosemary possesses a nutritional profile consisting of essential oils, flavonoids, triterpenic acids, vitamins, minerals, and macronutrients, thereby enhancing its value as a dietary component.<sup>22</sup>

*Rosmarinus officinalis* essential oil contains compounds such as 1,8-cineole,  $\alpha$ -pinene, camphor, linalool, and camphene, providing a unique fragrance and therapeutic properties.<sup>23</sup> Additionally, rosemary is a source of vitamins like vitamin A, thiamine, riboflavin, niacin, vitamin B6, and vitamin E, which support immune function, provide antioxidant defense, and enhance metabolic processes.<sup>24</sup> The herb is also a rich source of minerals such as calcium, magnesium, potassium, and iron, which are essential for bone health, enzymatic reactions, and overall physiological balance. Rosemary's notable vitamin C content and dietary fiber complement its established health benefits.<sup>25</sup> Research has demonstrated that rosemary leaf extract standardized to carnosic acid can attenuate body weight gain, fat accumulation, hyperglycemia, and hypercholesterolemia when administered to a high-fat diet animal model, suggesting its potential as a preventive intervention for metabolic disorders.<sup>26</sup> In the context of dairy farming, rosemary supplementation has been shown to positively influence milk production, protein content, and other metabolic indicators in dairy ewes, thereby presenting opportunities for enhancing organic production quality. Moreover, the incorporation of rosemary distillation residues and linseed into the diets of cull ewes has been found to favourably modify the fatty acid profile of goat meat, specifically by increasing n-3 polyunsaturated fatty acids, thereby augmenting its nutritional value.

#### Composition and chemotypes of *Rosmarinus officinalis* essential oil

*Rosmarinus officinalis* essential oil (ROEO) is a commercially valuable product with applications spanning the pharmaceutical and food industries. This colourless to pale yellow liquid is characterized by a pungent, spicy aroma. Its typical constituents include 1,8-cineole,  $\alpha$ -pinene, camphor, bornyl acetate, borneol, camphene,  $\alpha$ -terpineol, limonene,  $\beta$ -pinene,  $\beta$ -caryophyllene, and myrcene (Figure 3). However, the precise chemical composition of ROEO is influenced by a myriad of factors, including geographical origin, climatic conditions, plant part used, and extraction method. For instance, supercritical CO<sub>2</sub> extraction has been shown to yield higher concentrations of verbenone and bornyl acetate compared to traditional hydrodistillation.<sup>29, 32</sup> The phenological stage of the plant is another critical determinant of essential oil yield and composition. Plants in the flowering phase produce significantly higher oil yields than those in the vegetative stage, with summer harvests often doubling winter production. Moreover, the specific plant part employed for extraction influences the oil's chemical components. While leaves are the most commonly used part, 1,8-

cineole predominates in leaf-derived oil, caryophyllene in stem-derived oil, and caryophyllene oxide in flower-derived oil.<sup>30</sup>

Terpenes, the fundamental component of essential oils, are responsible for the characteristic aroma and flavour of aromatic plants. ROEO contains a diverse array of terpenes, including monoterpene hydrocarbons, oxygenated monoterpenes, and sesquiterpenes. Monoterpene hydrocarbons such as  $\alpha$ -pinene and camphene are typically predominant, while oxygenated monoterpenes like 1,8-cineole and camphor are also significant constituents. Sesquiterpenes, with  $\beta$ -caryophyllene as a key representative, contribute to the overall composition. Based on their dominant chemical component, ROEO samples can be classified into chemotypes, such as cineoliferous (1,8-cineole), camphoriferous (camphor), and  $\alpha$ -pinene chemotypes.

The terpene profile of ROEO is extensive, encompassing compounds such as 1,8-cineole,  $\alpha$ -pinene, camphene,  $\beta$ -pinene, camphor, borneol, bornyl acetate, p-cymene,  $\beta$ -myrcene, limonene,  $\alpha$ -terpinene, verbenone,  $\beta$ -terpineol, linalool, and terpinen-4-ol. These monoterpenes, derived from two isoprene units, serve as characteristic markers for ROEO and are intricately involved in plant metabolism. Biosynthetic pathways for these compounds include the epoxidation of  $\alpha$ -terpineol to form 1,8-cineole, the cyclization of  $\alpha$ -terpineol to produce  $\alpha$ -pinene, and the oxidation of borneol to generate camphor.

#### Pharmacological Potentials of *Rosmarinus officinalis*

*Rosmarinus officinalis* has been employed both culinarily and medicinally for centuries to enhance flavour and address ailments such as colds, rheumatism, and musculoskeletal pain. This plant serves as a rich source of bioactive compounds, exhibiting a broad spectrum of pharmacological activities, including antibacterial, antidiabetic, anti-inflammatory, antitumor, and antioxidant activities.<sup>7,21,33-35</sup>

The pharmacological potential of *R. officinalis* is underscored by the growing body of research focused on carnosic acid and essential oils. The plant's bioactive properties are primarily attributed to its volatile and phenolic compounds, including flavonoids, rosmarinic acid, and diterpenes derived from carnosic acid and carnosol. These constituents collectively contribute to the anticancer, antioxidant, and antimicrobial effects of rosemary. Furthermore, emerging evidence supports the effect of the plant on the central nervous system (CNS), resulting in antidepressant, neuroprotective,<sup>36</sup> and cholinergic activities, in addition to its anti-inflammatory and analgesic properties.

The chemical composition of *R. officinalis* essential oil exerts a substantial influence on its biological activities.<sup>31</sup> Key constituents such as 1,8-cineole, camphor, and  $\alpha$ -pinene contribute to its pharmacological properties. Notably, 1,8-cineole is linked to antidepressant, antimicrobial, antioxidant, anti-allergic, smooth muscle relaxant, and anti-inflammatory effects. Similarly,  $\alpha$ -pinene is recognized for its antioxidant, antifungal, antibacterial, and anti-inflammatory properties, while camphor is known for its antimutagenic, antioxidant, anti-allergic, and anti-inflammatory activities (Table 2).

**Table 1:** Nutritional and Chemical Composition of *Rosmarinus officinalis*

S/N	Category	Component	Reference
1	Macronutrients	Carbohydrates, Dietary Fiber, Lipids (Fat), Protein, Water	27
2	Fatty Acids	Saturated, Monounsaturated, Polyunsaturated	28
3	Vitamins	Ascorbic Acid, Folate, Niacin, Riboflavin, Thiamin, Vitamin A, Vitamin B12, Vitamin B6, Vitamin D (D2 + D3), Vitamin E	24
4	Essential Oils	1,8 Cineole, 3-Carene, $\alpha$ -Pinene, $\alpha$ -Thujene, $\beta$ -Pinene, Borneol, Camphene, Campholenal, Camphor, Iso-Pinocamphone, Limonene, Linalool, Myrcene, Myrtenol, p-Cymene, Terpineol, Verbenone	29-32
5	Minerals	Aluminum, Arsenic, Barium, Bismuth, Boron, Cadmium, Calcium, Chromium, Cobalt, Copper, Iron, Lead, Lithium, Magnesium, Manganese, Nickel, Phosphorus, Potassium, Selenium, Silver, Sodium, Strontium, Titanium, Vanadium, Zinc	25

**Table 2:** Bioactive properties of Rosemary and its major constituents

S/N	Major constituents of Rosemary	Biological activities
1	Rosemary	Rosemary has been shown to reduce total cholesterol, fasting plasma glucose, LDL-C (low-density lipoprotein cholesterol), and triglyceride levels, while simultaneously increasing HDL-C (high-density lipoprotein cholesterol) levels. <sup>26</sup> Additionally, it exhibits antidepressant properties, offering potential benefits in the management of depressive symptoms. <sup>37</sup> Furthermore, rosemary is beneficial in treating coughs and various digestive disorders, such as spasms, diarrhea, and flatulence. <sup>20</sup>
2	Carnosic acid	Carnosic acid has been demonstrated to inhibit the secretion of allergic inflammatory mediators and decrease atopic dermatitis. <sup>21,34</sup> It also inhibits platelet aggregation, <sup>38</sup> and has shown a protective effect against melanoma. <sup>39</sup>
3	Rosemary extract	Rosemary extract has demonstrated a range of beneficial properties, including anti-inflammatory activity, <sup>40</sup> and the reduction of cancer metrics such as tumor number, weight, and diameter, as well as their occurrence. <sup>41</sup> It hinders the initial activation of the allergic signalling pathway, including NF-kappaB, <sup>42</sup> and significantly impedes the messenger RNA for various pro-inflammatory chemokines and cytokines, such as IL-6, TNF, and IL-13. <sup>43</sup> Additionally, rosemary extract extends the latency period of cancer, <sup>44</sup> It also inhibits fungal growth, <sup>45</sup> promotes hair growth, <sup>24</sup> improves cell protection against UV radiation, and reduces skin damage caused by the sun. <sup>46</sup> Moreover, rosemary extract inhibits the production of nitric oxide (NO) within activated macrophages, <sup>47</sup> and exhibits emulsion stabilizing properties. <sup>38</sup>
4	Rosmarinic acid	Rosmarinic acid has demonstrated chemoprotective properties, <sup>48, 49</sup> exhibits neuroprotective and cholinergic effects, and has the ability to inhibit acetylcholinesterase. <sup>50</sup>
5	Rosemary oil	Rosemary oil has been shown to promote healing, angiogenesis, and improvements in granulation tissue, <sup>51</sup> and it accelerates wound healing. <sup>52</sup> The monoterpenes present in rosemary oil enhance cutaneous absorption. <sup>38</sup> Additionally, rosemary oil exhibits antifungal properties, <sup>53</sup> and enhances the survival and viability of tissues while reducing tissue necrosis. <sup>54</sup> Traditionally, it has been used to relieve dysmenorrhea, renal colic pain, and respiratory disorders due to its antispasmodic properties. <sup>55</sup> Rosemary oil nanoparticles improve hydration and elasticity of the skin. <sup>56</sup> Moreover, rosemary essential oil preserves colour, flavour, and nutrient content, effectively delaying rancidity. <sup>27</sup> It also exhibits notable antibacterial activity against both Gram-negative and Gram-positive bacteria, demonstrating potent inhibitory effects even against highly resistant bacterial strains. <sup>53,57</sup>

#### Anticancer activity

Dietary substances exert a substantial influence on cancer risk, with certain constituents exhibiting both prophylactic and deleterious effects. Chemoprevention, a long-term pharmacological approach to cancer risk reduction, has stimulated extensive research into the anticancer properties of plant-derived compounds.<sup>7</sup>

Rosemary, renowned for its antioxidant capacity to inhibit genotoxicity and protect against carcinogens and toxins, has emerged as a focal point of investigation. Despite the plant's promising attributes, the adverse side effects associated with conventional cancer therapies underscore the importance of innovative treatment and prevention strategies.<sup>2</sup>

Polyphenols, capable of modulating cell growth and differentiation, play a pivotal role in impeding tumorigenesis and progression. Given the abundance of phenolic compounds in rosemary, numerous studies have explored its anticancer potential. Diterpenes such as carnosic acid and carnosol, prevalent in dried rosemary leaves, have shown particular promise as anticancer agent. In recent times, there has been a surge in the investigations into the anticancer effects of these compounds, alongside rosmarinic acid and ursolic acid.<sup>48</sup>

Extensive research has elucidated the antitumor mechanisms of *Rosmarinus officinalis*.<sup>58</sup> Rosemary has demonstrated potent antiproliferative effects against multiple cancer cell lines. Key constituents of the extract of the plant, comprising rosmarinic acid, carnosic acid, and carnosol, have demonstrated the capability to induce apoptosis in cancer cells, potentially facilitated by the production of nitric oxide. Among these compounds, carnosic acid has been identified as the most potent inducer of apoptosis.

Rosemary extract has also exhibited notable antitumorigenic activity by strongly inhibiting skin tumorigenesis through the prevention of carcinogen binding to epidermal DNA. This anticarcinogenic effect is attributed to the extract's antioxidant properties. The antiproliferative and antitumorigenic activities of *R. officinalis* hold significant promise for future cancer treatments and warrant further exploration. Breast, melanoma, colon, liver, and leukemic cancers have been the primary focus of these investigations.<sup>59,60</sup> *In vitro* studies have demonstrated the cytotoxic effects of carnosol and carnosic acid on various human cancer cell lines, including those resistant to

conventional therapies, suggesting their potential as complementary anticancer agents.<sup>60</sup> *In vivo* experiments have corroborated these findings, revealing that rosemary extract, particularly through its carnosic acid content, can prevent gastric lesions and inhibit experimental mammary tumorigenesis.

Rosemary extracts exhibit pronounced cytotoxic effect on a range of cancer cell lines, including colon, prostate, and others. Studies indicate that rosemary extracts exert stronger cytotoxic effects on colon cancer cells at 48 hours compared to 24 hours, with HT-29 cells demonstrating the highest resistance.<sup>61,62</sup> IC50 values decreased with prolonged treatment, suggesting increased efficacy over time. Methanol extracts, particularly those rich in carnosic acid, exhibited potent activity against colon cancer cells, while individual compounds like carnosic acid and rosmanol induced apoptosis and inhibited cell proliferation.<sup>63</sup>

In prostate cancer, rosemary extracts suppressed cell proliferation and reduced tumor growth. The extracts also decreased androgen receptor expression and modulated endoplasmic reticulum stress in cancer cells. Carnosic acid and carnosol were particularly efficacious, inducing apoptosis and inhibiting key signalling pathways involved in cancer cell survival and proliferation.<sup>64</sup>

Apart from colon and prostate cancers, rosemary extracts also exhibit cytotoxic effect against various other cancer types, including bladder, breast, cervical, leukemic, liver, lung, ovarian, and pancreatic cancers. Rosemary's chemopreventive benefits encompass enhancing the efficacy of anticancer drugs and reversing multidrug resistance. Rosemary phytochemicals, such as diterpenes and triterpenes, possess abundant antioxidant properties and show promise as dietary chemopreventive agents.<sup>49</sup>

#### Antioxidant properties of *Rosmarinus officinalis*

The burgeoning interest in plant-derived natural antioxidants has underscored their significance across diverse fields, including nutrition, food science, and preventive medicine.<sup>65</sup> Antioxidants function as crucial defense mechanisms against reactive oxygen species (ROS),

deleterious byproducts of metabolic processes or exogenous substances. Chronic ROS exposure contributes to cellular damage, aging, and the pathogenesis of various diseases, including diabetes and cancer. This oxidative imbalance, termed oxidative stress, has emerged as a pivotal factor in numerous pathological conditions.

*Rosmarinus officinalis* has attracted attention for its potential to mitigate oxidative stress by counteracting free radicals and reactive oxygen species. The plant's robust antioxidant properties underpin its therapeutic applications. The primary contributors to rosemary's antioxidant efficacy are phenolic diterpenes such as carnosic acid, carnosol, and rosmarinic acid, predominantly found in its essential oil and extracts. These compounds exert their antioxidant effects through multiple mechanisms, including direct free radical scavenging, inhibition of lipid peroxidation, and enhancement of endogenous antioxidant enzymes. *In vitro* studies have substantiated the antioxidant potency of rosemary's bioactive compounds. Employing assays such as the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay, researchers have quantified the antioxidant capacity of rosemary extracts and isolated compounds.<sup>66</sup> Furthermore, the ability of carnosol, rosmanol, and epirosmanol to inhibit lipid peroxidation has been demonstrated through superoxide anion scavenging and Rancimat assays. These findings underscore the multifaceted antioxidant properties of rosemary phytochemicals, extending beyond free radical scavenging to cytoprotective and anticancer effects.<sup>67</sup>

*In vivo* investigations have corroborated the *in vitro* findings. For example, studies on Wistar rats have demonstrated the ameliorative effects of rosemary essential oil supplementation on oxidative stress biomarkers, including enzymatic activities such as glutathione peroxidase, catalase, nitric oxide synthase, and superoxide dismutase alongside the levels of lipid peroxidation within brain and heart tissues.<sup>68</sup> These results highlight rosemary's capacity to attenuate oxidative damage *in vivo*. The combined *in vitro* and *in vivo* evidence supports the use of rosemary essential oil as a functional food ingredient. Its antimicrobial and antioxidant attributes, coupled with other beneficial properties, contribute to its extended shelf life and reduced toxicity. Moreover, the anti-inflammatory potential of ROEO aligns with the emerging concept of preventive nutrition, suggesting its role in mitigating metabolic disorders such as obesity, metabolic syndrome, and diabetes.<sup>69</sup>

#### Anti-infective activity of *Rosmarinus officinalis*

*Rosmarinus officinalis* L. has attracted significant attention for its potent antimicrobial properties, attributed to its secondary metabolites. The increasing global prevalence of multidrug-resistant microorganisms, driven by the overreliance on antibiotics, necessitates the discovery of novel antimicrobial agents. Rosemary essential oil emerges as a promising candidate, exhibiting robust antibacterial activity and serving as a natural food preservative.<sup>70</sup> Studies have demonstrated the efficacy of rosemary essential oil in inhibiting the growth of pathogenic bacteria such as *Escherichia coli*, *Listeria monocytogenes*, and *Staphylococcus aureus*. Moreover, it has shown potential in overcoming bacterial drug resistance by disrupting membrane permeability.<sup>71</sup> This strategy offers a promising approach to combating resistant strains. Additionally, rosemary oil can enhance the susceptibility of certain bacteria to conventional antibiotics, further augmenting its antimicrobial potential. Besides its antibacterial properties, rosemary essential oil exhibits insecticidal, antiparasitic, and antifungal activities, contributing to its overall anti-infective efficacy.<sup>72</sup> Major compounds of rosemary, including carnosic acid, carnosol, rosmarinic acid, oleanolic acid, and ursolic acid, have demonstrated pronounced antimicrobial activity against a broad spectrum of pathogens, comprising both Gram-positive and Gram-negative bacteria, as well as fungi.<sup>73</sup> A recent study highlighted the antibacterial efficacy of a rosemary oil-based nanoemulgel, with potent activity against *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and Methicillin-resistant *Staphylococcus aureus* (MRSA).<sup>57</sup>

#### Anti-inflammatory and analgesic activities of *Rosmarinus officinalis*

Plants constitute a rich repository of anti-inflammatory compounds, presenting promising avenues for the discovery of novel therapeutic agents, especially within species possessing a historical record of

medicinal use. Anti-inflammatory pharmacotherapy primarily focuses on modulating the release of inflammatory mediators. Inflammation and pain are intricately connected to wound healing and oxidative stress, processes exacerbated by free radical generation. Oxidative stress are central to the pathogenesis of cardiovascular and neurodegenerative diseases; however, plant-derived polyphenols offer potential protective effects.<sup>74</sup>

Rosemary, traditionally employed to alleviate abdominal pain and respiratory inflammatory conditions such as bronchial asthma, has been extensively studied experimentally. Its essential oil and bioactive terpenes, including ursolic acid, carnosic acid, betulinic acid, rosmanol, carnosol, rosmarinic acid, and oleanolic acid, have demonstrated notable anti-inflammatory and analgesic properties. The antinociceptive efficacy of these compounds has been shown to be comparable to ketorolac, a nonsteroidal anti-inflammatory drug.<sup>75-77</sup>

*In vitro* investigations have primarily centered on assessing anti-inflammatory and analgesic activities by examining the expression of inflammatory cytokines (e.g., IL-1 $\beta$ , IL-6, TNF- $\alpha$ ), COX-1/COX-2 enzymes, iNOS, and nitric oxide production in RAW 264.7 macrophage cells. Additionally, research has explored rosemary's potential anti-atherosclerotic effects, emphasizing its capacity to impede the movement and activation of matrix metalloproteinases in vascular smooth muscle cells, specific compounds have been investigated. Notably, carnosic acid has exhibited the capability to inhibit the expression of matrix metalloproteinase-9 through the downregulation of NF- $\kappa$ B, thereby diminishing the migration of smooth muscle cells.<sup>78</sup>

The anti-inflammatory and analgesic properties of rosemary have been thoroughly investigated, with a particular focus on elucidating the mechanisms of action of various compounds, particularly carnosol. Preclinical studies have further validated the efficacy of rosemary essential oil in mitigating muscular and rheumatic pain, as evidenced by its ability to reduce edema and pleural exudate volume in carrageenan-induced inflammation models in rats. These observations underscore the oil's dual anti-inflammatory and antinociceptive properties.<sup>76</sup>

Carnosol, a major compound of *Rosmarinus officinalis*, has been a primary focus in the investigations of the analgesic mechanisms of the plant. Preclinical studies have employed models of carrageenan-induced pleural and paw edema to evaluate the analgesic effect of rosemary essential oil. These experiments have consistently demonstrated significant reductions in edema and pleural exudate volume, thereby confirming the oil's potent analgesic properties.<sup>76</sup>

#### Endocrine system activities

*Rosmarinus officinalis* L. has emerged as a potential alternative therapeutic agent for the management of diabetes mellitus. A recent study by Kabubiet *et al.*<sup>79</sup> investigated the antidiabetic properties of rosemary leaf powder (ROP) in streptozotocin-induced diabetic Wistar rats. Diabetic rats were subjected to dietary supplementation with ROP at varying concentrations (3%, 6%, and 12%) for a six-week period. A comprehensive assessment of metabolic parameters, including food intake, body weight, organ weights, blood glucose, lipid profile, and liver enzymes, was conducted. The findings demonstrated that ROP supplementation significantly attenuated hyperglycemia while concomitantly improving lipid profiles. Specifically, the treatment group exhibited reductions in total cholesterol, low-density lipoprotein cholesterol, and total triglycerides coupled with an elevation in high-density lipoprotein cholesterol. In addition, ROP administration led to a significant reduction of liver enzyme and creatinine levels. These findings collectively suggest that *Rosmarinus officinalis* L. possesses promising antidiabetic and hypolipidemic properties.<sup>79</sup>

#### Central nervous system activities

The prevalence of chronic, incurable central nervous system (CNS) disorders, including depression, Parkinson's, and Alzheimer's disease, has spurred research into potential novel treatments. Among the promising candidates is *Rosmarinus officinalis*, a plant with a growing body of evidence supporting its neuroprotective and cognitive-enhancing properties. Preclinical studies have demonstrated the antidepressant potential of *R. officinalis*. For instance, research has indicated that the plant can reduce immobility time in animal models

while concurrently modulating neurotransmitter levels (dopamine, norepinephrine, serotonin, acetylcholine) and gene expression (TH, PC, MKP-1) in the brain. These findings suggest potential antidepressant effect of rosemary. Furthermore, *R. officinalis* has emerged as a promising candidate for the management of neurodegenerative diseases. Rosmarinic acid, a major constituent of rosemary, has exhibited cholinergic and neuroprotective effects, in part through its inhibition of acetylcholinesterase. Clinical trials, such as the randomized, placebo-controlled, double-blind crossover study by Pengelly *et al.*<sup>80</sup> have demonstrated the acute cognitive benefits of rosemary leaf powder, suggesting its potential use in ameliorating cognitive decline associated with aging. The neuroprotective properties of rosemary extend to conditions such as Alzheimer's disease and dementia. The plant has been shown to inhibit both acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), enzymes responsible for acetylcholine breakdown. By increasing overall choline levels in the brain, rosemary may offer a potential therapeutic strategy for mitigating cognitive decline, anxiety, and depression associated with Alzheimer's disease.<sup>80</sup> Additional studies have delved deeper into the underlying mechanisms of rosemary's neuroprotective effects. Research has demonstrated that polyphenols in rosemary extract can inhibit stress proteins implicated in neurodegeneration. Rosemary has been shown to stimulate the production of nerve growth factor (NGF), a crucial protein for neuronal growth and maintenance. These findings have collectively demonstrated the potential of *R. officinalis* as a neuroprotective agent.

#### Cognitive health

Natural interventions for cognitive decline associated with aging, such as Alzheimer's disease (AD), are gaining attention due to the oxidative stress underlying these conditions. Studies have highlighted the potential of herbal ingredients, particularly those from rosemary, in mitigating cognitive deficits through their antioxidant properties. Oxidative damage, driven by free radicals, is the hallmark of aging and neurodegenerative diseases. When the body's endogenous antioxidants fail to counteract this damage, plant-based antioxidants become crucial. Farr *et al.*<sup>82</sup> demonstrated that rosemary extract, rich in carnosic acid, and spearmint extract, containing rosmarinic acid, improved memory in mice over 90 days.<sup>81</sup> This indicates that such compounds could enhance cognitive functions by inhibiting prolyl oligopeptidase (POP), an enzyme linked to memory processes.<sup>82</sup> Rosmarinic acid, administered in varying doses (1-8 mg/kg), showed significant cognitive improvements in mice by inhibiting POP activity over both short and longer periods. Similarly, Song *et al.*<sup>84</sup> found that rosemary extract with 20% carnosic acid improved cognitive deficits in rats, likely through its antioxidative and anti-inflammatory actions, including reduced levels of ROS and inflammatory cytokines in the hippocampus.<sup>83</sup>

#### Protective and therapeutic effects of ROEO against hexavalent chromium-induced hepatotoxicity

Hexavalent chromium (Cr VI) is a well-recognized potent hepatotoxin in both human and animal systems, primarily exerting its toxic effects through oxidative stress mechanisms. In an *in vivo* investigation aimed at assessing the protective and therapeutic capabilities of ROEO against hepatotoxicity induced by Cr VI, male Wistar rats were segregated into five uniform groups: a control cohort, a group receiving ROEO (0.5 mL/kg BW), a cohort exposed to Cr VI (2 mg/kg BW), a group pre-treated with ROEO before Cr VI administration, and a cohort receiving Cr VI followed by ROEO treatment over a three-

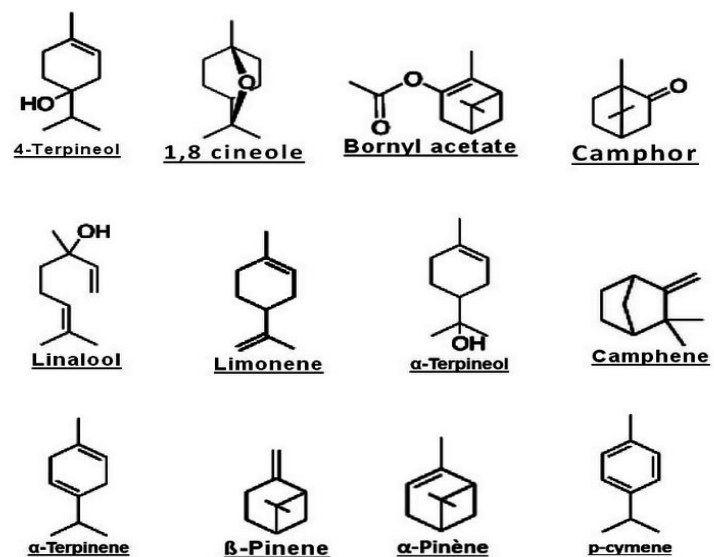
week period. The findings revealed significant hematological parameter alterations following Cr VI exposure, heightened levels of oxidative stress markers such as protein carbonyl, TBARS, and H<sub>2</sub>O<sub>2</sub>, and a significant depletion in glutathione (GSH) level. Concurrently, there was a marked decrease in enzymatic antioxidants (SOD, CAT, GPx, and GST), transaminases (AST and ALT), alkaline phosphatase (ALP), total protein, and albumin levels. Furthermore, serum biomarkers indicative of liver function displayed significant elevations. Histopathological and immunohistochemical analyses of PCNA expression further confirmed these biochemical findings, revealing pronounced hepatic alterations. Administration of ROEO, either prior

to or following Cr VI exposure, effectively ameliorated the aforementioned parameters, restoring them closer to control values. Particularly, ROEO independently attenuated lipid peroxidation and enhanced antioxidant status.<sup>84</sup>

#### *Rosmarinus officinalis* essential oils as biopesticides

The potential of plant-derived essential oils (EOs) as sustainable alternatives to synthetic pesticides has been demonstrated. A study investigated the effects of *Eucalyptus globulus* Labill and *Rosmarinus officinalis* L. EOs in the management of German cockroach (*Blattella germanica* L.). The results showed lethal dose (LD50) values of 9.27%, 10.54%, and 3.23% for rosemary, eucalyptus, and their combination, respectively. A corresponding increase in LD95 values was observed for all treatments. In addition, the repellent efficacy of the EOs was assessed. The mixture of eucalyptus and rosemary oils demonstrated superior repellency, achieving a 98.9% repellency at 3% concentration, surpassing the individual performance of rosemary (93.3%) and eucalyptus (90%) at 5% concentration.<sup>85</sup>

The chemical composition of these EOs was determined through gas chromatography-mass spectrometry (GC-MS) analysis following hydro-distillation of dried leaf material. The primary constituents identified in rosemary oil were  $\alpha$ -pinene, borneol, camphor, camphene, 1,8-cineole, and limonene (Table 3).



**Figure 3:** Major compounds in Rosemary essential oil (ROEO).

**Table 3:** Comparative Chemical Composition of *Rosmarinus officinalis* Essential Oil

S/N	Constituents identified in rosemary	Percentage Composition
1	$\alpha$ -pinene	20.67%
2	Camphor	10.69%
3	1,8-cineole	9.38%
4	Borneol	9.02%
5	Camphene	7.15%
6	Limonene	4.88%

## Conclusion

The review of *Rosmarinus officinalis* highlights its extensive pharmacological potential attributed to a rich profile of bioactive compounds, including carnosic acid, carnosol, and rosmarinic acid. Experimental evidence supports rosemary's significant antioxidant and anti-inflammatory properties, which are crucial in mitigating oxidative stress and inflammatory responses associated with chronic diseases such as neurodegenerative disorders, cardiovascular diseases, and cancer. The neuroprotective effects of rosemary are particularly promising, suggesting its potential role in preventing cognitive decline and supporting brain health. This is complemented by its antimicrobial properties, which provide a natural solution against a broad spectrum of pathogens, including antibiotic-resistant strains. In addition, the anticancer activity of rosemary further validates its therapeutic promise, with studies demonstrating its ability to inhibit cancer cell proliferation and modulate key signalling pathways involved in tumour progression. Rosemary has also been shown to exhibit beneficial effects on cardiovascular and metabolic health, indicating its potential as a natural intervention for managing cholesterol levels, blood glucose, and other metabolic parameters. These findings align with the traditional uses of rosemary and underscore its relevance in modern therapeutic applications.

However, the review identifies the need for standardized extraction methods and comprehensive clinical trials to confirm the efficacy and safety of rosemary in human populations. Understanding the molecular mechanisms of its bioactive compounds and exploring their synergistic effects with other treatments are essential steps for advancing rosemary's application in integrative medicine.

## Conflict of Interest

The authors declare no conflict of interest.

## Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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AbdelhayBenaich contributed to the literature search, drafted the manuscript, and gave final approval of the version to be published. Mustapha Aksissou provided additional data and illustrations, participated in the revision and editing of the manuscript, and also gave final approval of the version to be published.

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