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An Overview and Renewed Emphasis on Ethnopharmacology of Rosemary (*Salvia rosmarinus*)

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Abstract

Medicinal herbs have been employed to treat a wide range of illnesses and as an approach to maintain excellent health since ancient times. Substantially, their efficacies have been methodically investigated to guarantee the high standards of medicinal plant-derived products. This review focuses on Rosemary (*Salvia rosmarinus*), formerly referred as *Rosmarinus officinalis*, an aromatic evergreen shrub in the Lamiaceae family. Our goal is to compile all ethnobotanical applications of the herb, as well as relevant phytoconstituent, *in vivo*, and *in vitro* studies, and to thoroughly outline its potential use in contemporary herbal-based medicine. Using popular search engines, multiple sources were successfully identified. Moreover, the search for published materials such as books, articles, and conference proceedings from today to the previous eras was prioritized. The most notable findings about this herb's ethnopharmacological actions include the inhibition of Dipeptidyl Peptidase (DPP-4), the most pertinent enzyme in Type 2 Diabetes Mellitus (T2DM), as well as its anticancer activity, particularly the overall inhibition actions of its active compounds on endothelium and cancer cell proliferation. In a broad sense, it is a good medicinal plant with a lot of potential for improving human health.

Keywords: Anticancer, anti-inflammatory, antimicrobial, antioxidant, hepatoprotective, phenolic compounds

1. Introduction

Generally, plants have always played an essential role in the history of medicine. As a result, they have made a significant contribution to the development of contemporary medicine (Labiad et al., 2020). *Salvia rosmarinus*, originally *Rosmarinus officinalis* and popularly identified as rosemary, is a perennial evergreen herb with aromatic, needle-shaped leaves and blue, white, purple, or pink flowers that is endemic to the Mediterranean region. *Salvia rosmarinus* has been demonstrated to have a lot of therapeutic properties, which are mostly attributable to its aromatic essential oils (Berdahl and Mckeague, 2015; Miraj, 2016). Various studies have revealed that *Salvia rosmarinus* has anti-Alzheimer, anti-androgenic, anti-anxiety, antibacterial, anticancer, anti-dermatophytic, antifungal, anti-inflammatory, antimicrobial, anti-obesity, antioxidant, antiplatelet, anti-tumor, hepatoprotective, memory-improving, and radioprotective properties (Miraj, 2016). Furthermore, *Salvia rosmarinus* essential oil (SREO) has been found to have anticancer and antibacterial properties, as well as being a brain and nerve tonic and a treatment for mental weariness (Sadeh et al., 2019). *Salvia rosmarinus* has a lengthy culinary history and its intense aroma has restricted its culinary application to substantially flavored foods like meats, where its strong flavor is partially concealed (Berdahl and Mckeague, 2015).

Salvia rosmarinus extracts (SREs) contain a wide spectrum of phenolic compounds, including abietane diterpenes, carnosol, and ursolic acid, which may have antimicrobial effects in addition to their antioxidant activity. Antioxidants in spices, particularly rosemary, are well known. From time immemorial, spices and shrubs have been used for seasoning, to serve as preservatives, to enhance the sensory characteristics of food, and for their nutritious and healthy properties. Additionally, *Salvia rosmarinus* is acknowledged as a source of various dietary compounds, particularly diterpenes, with carnosol as the leading polyphenol utilized to standardize SREs accepted as a food preservative, but currently, SREs are not approved as a food preservative (Vemu et al., 2021).

SREs and SREOs from leaves and flowers are employed in Indian traditional medicine to treat several disorders, including diseases of the cardio-vascular system, the central nervous system, and some genito-urinary conditions (Fernández et al., 2014). Moreover, essential oils are combinations of volatile substances extracted from medicinal and aromatic plants, primarily through steam distillation. The *Lamiaceae* family is one of the most significant in the production of antioxidant and antibacterial essential oils (Nieto, 2017). SREOs have thoroughly investigated in terms of their chemical composition as well as their biological activities (Satyal et al., 2017).

The current review highlights and evaluates available studies on the use of *Salvia rosmarinus* in the cure of numerous illnesses in all regions of the world. Because it contains several active compounds, acknowledging its medicinal advantages and curative actions based on methodically documented reports will greatly lead to the creation of innovative and suitable herbal-based medicinal products. The desire to keep up with new information on the ethnomedicinal use of *Salvia rosmarinus* was also a primary motivation for writing this review. We helped to fill a gap in the literature engendered by the recent change in genus membership from *Rosmarinus* to *Salvia*.

2. Methodology

For the bibliographic search, several eminent search engines were used (The search period was from January 1, 2005, through December 31, 2021.), amongst others; PudMed (https://pubmed.ncbi.nlm.nih.gov), SciFinder (https://sso.cas.org), Web of Science (https://www.webofknowledge.com), Embase (https://www.otago.ac.nz), Google Scholar (https://scholar.google.com) and Scopus (https://www.scopus.com). This review prioritized recent published materials in high-quality peer-reviewed journals as well as by reputed academic publishers. A total of 53 reference sources were compiled in this review.

3. Botanical description

Salvia rosmarinus is a Mediterranean woody evergreen shrub that is now used as an ornamental plant all over the world. It can flourish up to an altitude of 1500 m above the sea level. The plant grows to a height of 60–

200 cm and is a pointed, dense, evergreen perennial herb. The leaf's upper surface is dark green or blue, while the underside is white; the leaves are resinous. Its needle-shaped leaves are waxy and somewhat curved (Figure 1) (Elamrani et al., 2000; Begum et al., 2013; Berdahl and Mckeague, 2015). The trunks are brown, square, and woody, with tight branches and scratched bark. It is characterized by cymose inflorescences with whitish, blue (Figure 2), or purple flowers (Elamrani et al., 2000; Sasikumar, 2012; Begum et al., 2013).

Figure 1. Rosemary (*Salvia rosmarinus*) leaves.

It got its name from the fact that it is very common on the seashore and flourishes in the sea climate. It is one of the Mediterranean region's distinctive plants (Sasikumar, 2012; Begum et al., 2013). Although it grows naturally along Turkey's western and southern coasts, it is widely cultivated in countries such as France, Italy, Spain, Portugal, and Greece (Malayoğlu, 2010). It can averagely withstand salt and drought stress. Cultivated *Salvia rosmarinus* is produced from transplanted cuttings, which means it is costly than productions employing direct seeding. *Salvia rosmarinus* can be harvested three to four times a year, and *Salvia rosmarinus* stands can last for up to seven years. Carnosic acid is mostly found in *Salvia rosmarinus* chloroplasts, where it assists in the protection of the photosynthetic machinery and chloroplast membrane against oxidative stress (Berdahl and Mckeague, 2015). *Salvia rosmarinus* belongs to xeromorphic species which thrives naturally on cliffs, sand, and stony zones close to the sea across the globe, including Africa, Europe, and Asia (Santos et al., 2015).

Figure 2. Rosemary (*Salvia rosmarinus*) flowers.

4. Chemical compounds

Later, in the 1960's, researchers advanced the extraction process for the antioxidant compounds from *Salvia rosmarinus*, as well as removing a part of the essential oils to make the extracts taste less harsh. The following is a list of some of the antioxidant compounds found in *Salvia rosmarinus*; carnosic acid, carnosol, methyl carnosate, rosmanol, epirosmanol, isorosmanol, 12-*O*-methyl carnosic acid, rosmanol-7-ethyl ether, dimethoxy-rasmanol, rosmadial, rosmariquinone (miltirone), rosmaridiphenol, rosmarinic acid, luteolin, luteolin-7-O-glucoside and homoplantaginin (Berdahl and Mckeague, 2015). It was reported by Kontogianni et al. (2013) that SREs contain about twice the amount of diterpenoid phenolics, essentially carnosic acid plus carnosol. Thus, many studies consider carnosic acid to be the most compelling antioxidant in *Salvia rosmarinus*. It should be mentioned that there has been confirmation of compelling variations in the chemical makeup of SREOs. Several factors have been highlighted to influence the makeup of essential oils, such as geographic origin, parts of plants, harvesting season, and stage of maturity, as well as the isolation method (Teixeira et al., 2013). According to Rašković et al. (2014), there are three main chemotypes. The main chemotype, which includes Tunisian, Turkish, Moroccan, and Italian oils, has more than 40% 1,8-cineole, whereas the second chemotype, which includes French, Greek, and Spanish oils, contains the same amount of α-pinene, camphor, and 1,8-cineole (20-30%). Finally, South America has a myrcene-rich rosemary oil chemotype.

Hussain et al. (2010) reported that different biological activities might result due to the country of origin of collected essential oils. According to Rašković et al. (2014), essential oils distilled from *Salvia rosmarinus* had a variable yellow tint color and a strong smell, and the acquired yield of the essential oil had approximately 1.03% (v/w) of dry matter. In terms of chemical components, the *Salvia rosmarinus* essential oils are primarily made up of oxygenated monoterpenes (approximately 63-67%), followed by monoterpene hydrocarbons (approximately 26-31%). Table 1 shows details of all chemical constituents of SREOs, with three distinctive chemical compound groupings (monoterpene hydrocarbons, oxygenated monoterpenes, and sesquiterpene hydrocarbons) standing out (Hussain et al., 2010; Rašković et al., 2014). Furthermore, from the identified chemical constituents distinct chemotypes (infraspecific chemical variations) of essential oils were discovered, including the 1,8-cineole chemotype, the myrcene chemotype, the α-pinene/verbenone/bornyl acetate chemotype, the 1,8-cineole/α-pinene/camphor chemotype, and the 1,8-cineole/borneol/p-cymene chemotype (Santos et al., 2015).

It's imperative to understand the distribution of bioactive compounds in *Salvia rosmarinus* plants that are responsible for a whole range of biological effects (Moreno et al., 2006). The polyphenol composition of *Salvia rosmarinus* flowers, fresh leaves, and branches following a methanol extraction was investigated using HPLC chromatography by the same authors. Leaf extract contained carnosol, rosmarinic acid, and carnosic acid in its chromatographic profile. In comparison to flowers, leaves had a larger amount of carnosic acid and rosmarinic acid, whereas branches had no notable presence of these polyphenol compounds. The main active polyphenols were found in the highest concentrations in leaves and flowers. Furthermore, they conducted several extraction processes using organic solvents and discovered that acetone and methanol extracts displayed major peaks matching to rosmarinic acid, carnosol, and carnosic acid, with 52.2 and 36.5 percent ratios, respectively. Extraction of phytochemical components by supercritical fluid and extraction by hydro-distillation utilizing liquid solvents such as hexane and ethanol are the most popular methods. For instance, supercritical fluid technology is used to recover a number of antioxidants from *Salvia rosmarinus* (Vicente et al., 2013). SREOs can be extracted using hydro and steam distillation processes, according to Santos et al. (2015). Hydro-distillation was employed by Hussain et al. (2010) to extract essential oil from air-dried and finely chopped leaves. Although bioactive compounds have a broad spectrum of polarity and their solubility in extraction media varies, they can pose a few challenges during extraction (Berdahl and Mckeague, 2015).

5. Antioxidant activity

Antioxidants extracts are beneficial to human health because they suppress or delay the oxidation mechanism by limiting the beginning or spread of oxidative sequences. They play an essential task in preventing a range of diseases, like aging, atherosclerosis, cancer, and ischemia (Moreno et al., 2006; Nieto et al., 2018). Several researchers have developed and employed distinct in vitro chemical-based approaches to evaluate the antioxidant activity (AOA) of SREOs and their individual compounds. And ones the most used is DPPH (2, 2-diphenyl-1-picrylhydrazyl and/or 1, 1-diphenyl-1-picrylhydrazyl) and ABTS (2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) radical scavenging assay. Thus, DPPH is a steady free radical that has been utilized to replicate the antioxidant action of active compounds found in essential oils, extracts, and other natural products. (Hussain et al., 2010; Karadağ et al., 2019; do Nascimento et al., 2020).

Table 1. Major volatile constituents of *Salvia rosmarinus* essential oils (SREOs).

Identification Method	Potency Level - Identified compounds	Oxygenated Monoterpenes	Monoterpene Hydrocarbons	Sesquiterpene Hydrocarbons	References
GC-MS analysis	Potency Level	(67.0%)	(26.0%)	(N/A)	(Hussain et al., 2010)
	Identified compounds	• (+)-Camphor, • 1,8-Cineol, • Borneol, • Isoborneol, • Linalool, • α-Terpineol	• Camphene, • Limonene, • α-Phellandren, • α-Pinene, • β-Myrcene, • β-Pinene, • γ-Terpinene	• Verbenone, • β-Caryophyllene, • β-Farnesene, • γ-Muurolene	
GC-FID and GC-MS analysis	Potency Level	(63.88%),	(31.22%)	(4.77%)	(Rašković et al., 2014)
	Identified compounds	• 1,8-Cineole, • Borneol, • Bornyl acetate • Camphor, • Isoborneol, • Linalool, • Terpinen-4-ol, • α-Terpineol, • γ-Terpineol,	• Camphene, • Limonene, • p-Cymene, • Sabinene, • Tricyclene, • α-Phellandrene, • α-Pinene, • α-Terpinene, • α-Terpinolene • α-Thujene, • β-Myrcene, • β-Pinene, • γ-Terpinene, • δ3-Carene,	• Germacrene D, • Longifolene, • α-Copaene, • α-Humulene, • β-Caryophyllene, • δ-Cadinene	

GC-MS: Gas Chromatography associated with Mass Spectrometric detection
GC-FID: Gas Chromatography associated with Flame Ionization detection

Through this DPPH assay and for medicinal research, a strong AOA of *Salvia rosmarinus* and its potential as an anti-inflammatory agent and cell protector in heart illness, cancer, pathological liver conditions, neurodegenerative diseases, and other diseases were confirmed (Vicente et al., 2013; Rašković et al., 2014; Habtemariam, 2016; Yimam et al., 2017). While in food industry, antioxidants are often employed in the food industry to prevent food degradation, and the high applicability of rosemary extracts arises from their ability to control oxidation in foods and beverages, which is facilitated by a diverse variety of antioxidant phenolic compounds with distinct chemical properties (Moreno et al., 2006; Berdahl and Mckeague, 2015).

Salvia rosmarinus contains numerous compounds with AOA, the majority of which are polyphenols. Carnosic acid and carnosol are likely accountable for the majority of the activity (Moreno et al., 2006; Jiang, 2019). Other phenolic diterpenes (methyl carnosate and rosmanol) and phenolic acids (caffeic acids and rosmarinic) are the two most abundant antioxidant phenolic substances in *Salvia rosmarinus* (Vicente et al., 2013). Most of extracts are obtained from wild *Salvia rosmarinus* in country like Morocco, as well as cultivated *Salvia rosmarinus* in France, Romania, Spain, and the United States (Berdahl and Mckeague, 2015). When assessing a fresh SRE, the most important factor to consider is the process of extraction and the type of solvent employed, as these will impact the antioxidant attributes (Nieto et al., 2018). The mode of action of these compounds has been described in countless ways in the literature. The antioxidant capabilities of *Salvia rosmarinus* were found to be due to its high content of isoprenoid quinones, which function as free radical chain terminators and chelators of reactive oxygen species (ROS). Thus, the phenolic compounds found in commercial SREs work as main antioxidants when they react with hydroxyl and lipid radicals to convert them to stable molecules. Furthermore, it was proposed that these compounds could operate as metal ion (Fe^{+2}) chelators, limiting the production ratio of reactive species from oxygen (Nieto et al., 2018). According to Habtemariam (2016), carnosic acid and carnosol's antioxidant mechanisms are based on the eprivation of hydrogen from their phenolic hydroxyl groups, resulting in the production of quinone derivatives. In vitro and in vivo, this antioxidant system protects brain cells from oxidative injury.

For instance, Hussain et al. (2010) used a DPPH radical scavenging assay to validate the AOA of SREOs. They measured the percent inhibition of peroxidation in the linoleic acid system and found that SROEs had the highest inhibition compared to the individual and main components of the oil. This demonstrates a synergistic impact of certain minor components found in SREO. The scavenging activities in both DPPH$^{\cdot}$ and $^{\cdot}$OH were evaluated and only rosmarinic acid had the highest AOA among the twelve compounds isolated from *Salvia rosmarinus* ethanol extract (SREE), according to Nei et al. (2019). Similarly, Moreno et al. (2006) used the DPPH method to assess AOA in aliquots of extracts from rosemary branches, leaves and flowers. It was discovered that leaves and flowers had a high AOA, whereas branches had a low activity. Furthermore, they utilised HPLC chromatography fractions following partition of the methanol extract of leaves to evaluate AOA and discovered that fractions comprising rosmarinic acid, carnosol, and carnosic acid had a high AOA. Antioxidant activity was also tested in acetone, methanol, and water SREs using a micro titer model system. AOAs were found to be higher in methanol and acetone extracts. Water extract, on the other hand, demonstrated lower AOA. *Salvia rosmarinus* diterpenes have also been shown to have protective effects in neurodegenerative diseases like Alzheimer, comprising lipid peroxidation and cell protection from oxidative cell death. For instance, carnosic acid has been found to protect neuronal cells from ischemic injury by scavenging reactive oxygen species (ROS) (Habtemariam, 2016).

Rašković et al. (2014) investigated at rosemary's AOA and its role in treatment of various pathological liver disorders. In vivo tests in rats were conducted to examine the preventive impact of SREO against carbon tetrachloride-induced liver injury, and they confirmed that SREO prevented the rise in lipid peroxidation caused by carbon tetrachloride in liver homogenates. Additionally, pre-treatment with the tested essential oil for a few days dramatically reduced the activity of antioxidant enzymes such as catalase, glutathione peroxidase, peroxidase, and glutathione reductase in liver homogenates, particularly at 10 mg/kg dosage. Bakırel et al. (2008) revealed that SREs had antidiabetic properties, including the ability to suppress lipid peroxidation and activate antioxidant enzymes like superoxide dismutase (SOD) and catalase (CAT), which are involved in the direct removal of ROS. Recently, DPPH and ABTS methods were employed to assess the antioxidant potential of the SRE fractions. According to Karadağ (2019), the ethyl acetate fraction of *Salvia rosmarinus* has a stronger AOA than the n-hexane fraction. Taking everything into account, more research on Rosemary's antioxidant activity is needed strong reliance on a range of factors, including the plant maturity, presence of an inhibitor, presence of a synergistic effect among several constituents, and the concentration of active constituents in the extract (Nieto et al., 2018).

6. Antimicrobial activity

The most well-known species is *Salvia rosmarinus*, sometimes known as "rosemary" (Drew et al., 2017). As the aerial part of these plants has been widely utilized as natural preservatives since ancient times. The essential oils derived from *Salvia rosmarinus* have been reported in various studies for their antibacterial and antifungal characteristics (Borges et al., 2019; Pieracci et al., 2021). It was reported that the combination of SREE with cefuroxime demonstrated synergistic antibacterial effect against all methicillin-resistant Staphylococcus aureus (MRSA) (Jarrar et al., 2010). Other research has found that rosemary oil has antibacterial activity against *Aeromonas hydrophila, Bacillus cereus, Clostridium perfringens, E. coli, Staphylococcus aureus, and Salmonella choleraesuis* (Sirocchi et al., 2013; Nieto et al., 2018). In a previous study, rosemary was identified as a good broad-spectrum antibacterial agent (Abers et al., 2021). Another study investigated the antimicrobial activity of five *Salvia rosmarinus* species and found that they had a mild antibacterial effect on the tested bacteria strains (Pieracci et al., 2021).

A recent study observed the antibacterial activity of rosemary extracted in ethanol using an agar well diffusion assay against 10 multidrug-resistant (MDR) clinical isolates, human type culture pathogens, and meat-borne bacterial isolates. The findings suggested that *Salvia rosmarinus* could be a good source as an antimicrobial agent for treating drug-resistant bacteria and meat-borne pathogens (Manilal et al., 2021). *Salvia rosmarinus* has also been recommended for use as a natural antibacterial in food processing (Saricaoglu and Turhan, 2018). The antibacterial and antifungal properties of rosemary's principal components, such as 1,8-cineol, α-pinene, camphor, carnosol, and carnosic acid, make it efficient against a wide range of infections (Nieto et al., 2018).

Antibiotic use has increased dramatically in medicine, agriculture, and livestock, resulting in an increase in multidrug-resistant bacteria (Qabaha, 2013). Antimicrobial resistance is a global public health concern, and researchers have been focusing more on this field in order to find new antimicrobial effective bioactives (Petrolini et al., 2013). SREOs include insecticidal, antiparasitic, and antifungal characteristics in addition to antibacterial properties, which are useful for the control of microbial illnesses in humans (Andrade et al., 2018). *Rosemary* spp. has a bright future in medicine and food science. As a result, additional reliable trials are needed in the future to assess *Salvia rosmarinus*'s antibacterial capabilities and undiscovered phytocompound activity, as well as its safety and efficacy.

7. Antidiabetic activity

Type 2 Diabetes Mellitus (T2DM) is a metabolic condition that results in hyperglycemia due to pathophysiological reasons and may induce various health problems (Galicia-Garcia et al., 2020). The first step in managing this illness is to keep blood glucose levels under control. As reported by the World Health Organization and the International Diabetes Federation (IDF), T2DM is expected to impact over 439 million persons by 2030 (Naimi et al., 2017). Dipeptidyl Peptidase (DPP-4) is the most significant enzyme in mellitus T2DM (Röhrborn et al., 2015). *Salvia rosmarinus* has been found to inhibit the DPP-4 enzyme, resulting in a diabetic impact without any negative health implications (Salim et al., 2017).

A Turkish study looked at the effects of an ethanolic extract of *Salvia rosmarinus* leaves on glucose homeostasis and antioxidant defense in rabbits and found that SRE has a significant anti-diabetic impact (Bakırel et al., 2008). Rosemary extract, as well as the rosemary extract polyphenols carnosic acid and rosmarinic acid, have been demonstrated to have insulin-like effects in insulin target cells in vitro, as well as strong anti-diabetic benefits in various animal models of T2DM in vivo (Naimi et al., 2017). These positive results from in vivo animal experiments show that *Salvia rosmarinus* and its polyphenolic ingredients could be useful in the treatment of diabetes and management of blood sugar levels. It is also shown that the SRE has outstanding hypoglycemic and antihyperglycemic action as a result of its various effects involving both pancreatic and extra-pancreatic mechanisms (Bakırel et al., 2008). However, more research is needed to fill in the gaps in the literature and to assess the efficacy and safety of *Salvia rosmarinus*' antidiabetic activities.

8. Anticancer activity

Herbs and plants contain chemicals that may have anticancer properties and can halt the progression of carcinogenesis at various levels (Allegra et al., 2020). Because of its antioxidant potential, *Salvia rosmarinus* has been considered as a significant anticancer medication. In fact, It can function on free radicals and safeguard DNA, lipids, and proteins from oxidative deterioration (Xiang et al., 2013). Some angiogenic properties of endothelial cells, such as differentiation, proliferation, migration, and differentiation capacity, are blocked by carnosic acid and carnosol. Numerous studies have found that their effects on endothelium and cancer cell proliferation might be connected to programmed cell death stimulation. In vivo studies verified the inhibition of angiogenesis in vitro by *Salvia rosmarinus* compounds (López-Jiménez et al., 2013).

According to the systematic review, SRE includes several polyphenols, with carnosic acid and rosmarinic acid having the largest amounts, and they have diverse powerful and effective anticancer activities (Moore et al., 2016). *Salvia rosmarinus* was found to have antitumoral activity, which could be linked to an antioxidant mechanism (Choukairi et al., 2020). In recent years, the focus has switched to developing new targeted cancer medicines that can modify specific cancer pathways that are frequently altered. There have been few studies on the signaling molecules and pathways that SRE targets. Animal studies must be conducted in a more methodical manner before human trials can begin (Moore et al., 2016). As a result, the use of *Salvia rosmarinus* and its derivatives in cancer therapy is a fascinating topic of research. Large, well-designed studies are needed to conclusively determine the true influence of this substance in clinical practice in the future.

9. Anti-inflammatory properties

Inflammation is presently thought to have a key role in the pathophysiology of depression (Miller and Raison, 2016). SREs, the key active ingredients isolated from *Salvia rosmarinus*, have sparked widespread interest due to their anti-inflammatory properties. *Salvia rosmarinus* demonstrated a potent anti-inflammatory effect, particularly in vivo, where SREO and SRE were demonstrated to significantly suppress leukocyte migration (de Melo et al., 2011). This lowered the amount of leukocytes (white blood cells) at the inflammatory site, giving rise in an anti-inflammatory reaction (Benincá et al., 2011; de Melo et al., 2011; Mengoni et al., 2011). Other pro-inflammatory components, like nitric oxide and inflammation-related genes, were similarly hindered by SRE (Benincá et al., 2011; Mengoni et al., 2011; Yu et al., 2013). Although carnosol and carnosic acid tend to be essential, rosemary's anti-inflammatory effect is most probably due to a synergistic process involving a number of its constituents (de Melo et al. 2011; Mengoni et al., 2011; Yu et al., 2013). These investigations indicate that *Salvia rosmarinus* has a considerable anti-inflammatory impact; in particular, the anti-inflammatory activities of pure carnosol and carnosic acid were shown to be nine times greater than those of indomethacin, a popular anti-inflammatory medicine (Mengoni et al., 2011). SREs inhibited gut microbiota dysbiosis, depressive-like behaviors, and inflammatory reaction activation in the hippocampus and serum of CRS mice, as well as inflammatory reaction activation in BV-2 microglia cells caused by lipopolysaccharide (LPS). Likewise, another study conducted by (Guo et al., 2018) revealed that SRE may reduce the variety of gut microbiota, reduce the sequencing percentage of both Proteobacteria and Bacteroidetes, and increase the affluence of Lactobacillus and Firmicutes, suggesting that the anti-depressant effects of RE arise from gut microbiota rebalancing. (Borges et al., 2019) reviewed and highlighted the role of SREO. The studies confirmed the application of SREOs in diseases associated with inflammation and their future potential as a muscle relaxant and anti-inflamatory oils. This anti-inflammatory action of SREO can be attributable mostly to 1,8-cineole and -pinene, which are frequently found in higher concentrations and whose mechanisms are well characterized (Borges et al., 2019). However, more research and clinical trials are required to determine the direct impacts of RE and its polyphenolic contents in certain cells and tissue types as well as their mode of action particularly in humans.

10. Conclusion

This review article corroborates that the plant's extracts contain high antioxidant, antimicrobial, and antibacterial properties, making *Salvia rosmarinus* a perfect replacement for more hazardous artificial food supplements. Furthermore, it has shown great promise as a natural food preservative as well as a medicinal agent. Many of its significant biological properties, including anti-diabetic and anticancer processes, are attributed to the powerful antioxidant chemicals contained in its extract and essential oil. If it persists to exhibit such potent anti-diabetic and anticancer properties with minimal side effects, *Salvia rosmarinus* could potentially provide a unique therapy addressing these two critical diseases. *Salvia rosmarinus* has also been highly beneficial in the treatment of depression, neurological diseases, obesity, and inflammation. The findings pave the way for a prospective expansion in the use of supercritical SREs in food formulations for inflammatory disease mitigation or prevention. Although the preliminary findings are promising, more study and research are needed to validate its safety and efficacy as a therapeutic and preservative agent. Although preliminary findings are encouraging, more research and study are required to corroborate its safety and potency as a medicinal and preservative agent.

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Author Contribution

The study and design were conceptualized and designed by FS and GZ. The first draft of the manuscript was written collaboratively by FS, GZ, and FN. The work was revised critically by FS. All authors read and approved the final manuscript.

Conflicts of Interest

The authors have no relevant financial or non-financial interests to disclose. The authors also declare that no funds, grants, or other support were received during the preparation of this manuscript.

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