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# An Evidence-Based Review on Herbal Remedies of *Rosmarinus officinalis*

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**ABSTRACT**

*Rosmarinus officinalis is a perennial herb with fragrant, evergreen, needle-like leaves and white, pink, purple, or blue flowers, native to the Mediterranean region. It is a member of the mint family Lamiaceae. The aim of this study is to overview phytochemical compound as well as Herbal Remedies of Rosmarinus officinalis. This review article was carried out by searching studies in PubMed, Medline, Web of Science, and IranMedex databases up to 2016. In this study 123 articles found, and 87 articles were included. The search terms were "Rosmarinus officinalis", "therapeutic", "and pharmacological". Various studies have shown that Rosmarinus officinalis possess anti-inflammatory effect, antioxidant effect, hepatoprotective activity, anti-obesity, radioprotective effect, anti-androgenic activity, memory improvement, antimicrobial, antibacterial and antifungal activities , antiplatelet activity, anti-anxiety ,anti-Alzheimer ,anticancer, antidermatophytic activity, anti-tumor activity. Rosmarinus officinalis was shown to possess lots of healing activity. Medicinal properties of its extract, essential oils, its stems and leaves should be further examined to be able to diagnose other useful and unknown properties of this valuable plant.*

**Keywords**: Rosmarinus officinalis, therapeutic, pharmacological, phytochemical

## INTRODUCTION

It is proved that herbal medicine is effective in the treatment of many disease [1-21]. Rosmarinus officinalis, commonly known as rosemary, is a woody, perennial herb with fragrant, evergreen, needle-like leaves and white, pink, purple, or blue flowers, native to the Mediterranean region[22, 23]. It is a member of the mint family Lamiaceae, It is native to the Mediterranean and Asia, but is reasonably hardy in cool climates. It has a bitter, astringent taste and a characteristic aroma which complements many cooked foods. Rosemary essential oil is used as a preservative in the food industry for its antioxidant[24] and antimicrobial properties[25]. Rosemary extract has been shown to improve the shelf life and heat stability of omega 3-rich oils which are prone to rancidity. In traditional medicine of India, extracts and essential oil from flowers and leaves are used to treat a variety of disorder including disease involved in central nervous system, cardio vascular system, genito urinary conditions, liver treatments, reproductive system and respiratory system.

The volatile oil of the plant is used in oils and lotions for the treatment of various ailments like arthritis, gout, and muscular pain, neuralgia, wound and rubbed into hair for stimulating the hair bulbs to renewed activity, to prevent premature baldness [26, 27].it is used as an antispasmodic in renal colic and dysmenorrhea, in relieving respiratory disorders and to stimulate growth of hair [28]. Extract of rosemary relaxes smooth muscles of trachea and intestine, and has choleretic, hepatoprotective [29] and antitumerogenic activity [30]. The most important constituents of rosemary are caffeic acid and its derivatives such as rosmarinic acid. These compounds have antioxidant and antimicrobial [31] effect. rosemary and its constituents especially caffeic acid derivatives such as rosmarinic acid have a therapeutic potential in treatment or prevention of bronchial asthma, spasmogenic disorders, peptic ulcer, inflammatory diseases, hepatotoxicity, atherosclerosis, ischemic heart disease[32], cataract, cancer[33] and poor sperm motility, Alziethmer, and can act as antidepressant and anxiolytic properties [34, 35].

**Pharmacological properties**
**Anti-inflammatory effect**
the anti-inflammatory properties of rosmarinic acid and of an extract of R. officinalis in local inflammation [carrageenin-induced paw oedema model in the rat]was evaluated .Administration of rosmarinic acid and extract at the dose of 25 mg/kg reduced paw oedema at 6 hr by over 60%, exhibiting a dose-response effect. For the first time, the anti-inflammatory potential of rosmarinic acid has been identified, as it causes a substantial reduction in inflammation, and we speculate that it might be useful in the pharmacological modulation of injuries associated to inflammation [36].

**Antioxidant effect**
The antioxidant activity of sunflower oil-oleoresin rosemary [Rosmarinus officinalis L.] blends [SORB] was assessed .The multivariate kinetic approach effectively screened SORB1500 as the best blend conferring the highest oxidative stability to sunflower oil. This approach can be adopted for quick and reliable estimation of the oxidative stability of oil samples [37].

Selected components of plant essential oils and intact Rosmarinus officinalis oil [RO] were investigated for their antioxidant, iron-chelating, and DNA-protective effects. It was observed that whereas eugenol, carvacrol, and thymol showed high antioxidative effectiveness in all assays used, RO manifested only antiradical effect and borneol and eucalyptol did not express antioxidant activity at all. DNA-protective ability against hydrogen peroxide [H2O2]-induced DNA lesions was manifested by two antioxidants [carvacrol and thymol] and two compounds that do not show antioxidant effects [RO and borneol]. Borneol was able to preserve not only DNA of HepG2 cells but also plasmid DNA against Fe[2+]-induced damage. This paper evaluates the results in the light of experiences of other scientists [38].

The bioaccumulation potential of cadmium in liver, kidney, gills and muscles of freshwater fish, Nile tilapia Oreochromis niloticus and the changes in oxidative stress indices in liver and kidney with or without simultaneous treatment with waterborne vitamin C and rosemary leaf extract was assessed. Reduction in Cd induced oxidative stress and bioaccumulation was comparable between the two antioxidant treatments, Vitamin C and rosemary leaf extract. The key findings suggest that both the antioxidants used showed ameliorative potential to reduce tissue accumulation of Cd and associated oxidative stress in fresh water fish, Nile tilapia [39].

The bioactive compounds from these three plants were first extracted and thereafter assayed for total phenols, 2, 2-diphenyl-1- picrylhydrazyl [DPPH] radical scavenging activity, total antioxidant capacity [TAOC] and reducing power. There was a direct relation between total phenolics and antioxidant activities of extracts. Results showed that these three natural extracts and their combination can be effectively used as a substituent of synthetic antioxidant BHT [40].

the effects of endurance exercise training accompanying Rosmarinus officinalis Labiatae [rosemary] leaves extract on lipid peroxidation and antioxidative systems in the blood of rats with streptozotocin-induced diabetes was analyzed.These data demonstrated that the levels of lipid peroxidation in the erythrocyte of diabetic rats were high, whereas there was a decrease in the basal antioxidant enzyme activities. However, rosemary extract with endurance exercise may attenuate oxidative stress by enhancing antioxidant enzyme activities and decreasing lipid peroxidation levels in experimental rats with diabetes [24].

Four diterpenoids, carnosic acid [1], carnosol [2], rosmanol [3], and epirosmanol [4], were isolated as antioxidative agents from the leaves of Rosmarinus officinalis by bioassay-directed fractionation. These diterpenoids inhibited superoxide anion production in the xanthine/xanthine oxidase system. Mitochondrial and microsomal lipid peroxidation induced by NADH or NADPH oxidation were also completely inhibited by these diterpenes at the concentration of 3-30 microM. Furthermore, carnosic acid protected red cells against oxidative hemolysis. These phenolic diterpenes were shown to be effective to protect biological systems against oxidative stresses[41].

The effect produced by a methanolic extract of Rosmarinus officinalis on CCl[4]-induced liver cirrhosis in rats was investigated .When the cirrhosis by oxidative stress was evaluated as an increase on liver lipoperoxidation, total lipid peroxides, nitric oxide in serum, and loss of erythrocyte plasma membrane stability, R. officinalis was shown to prevent such alterations. On cirrhotic animals treated with CCl[4], histological studies showed massive necrosis, periportal inflammation and fibrosis which were modified by R. officinalis. These benefits on experimental cirrhosis suggest a potential therapeutic use for R. officinalis as an alternative for liver cirrhosis[42].

The absorption, distribution and elimination of carnosic acid, the main antioxidant found in rosemary was studied, in vivo, in rats. The recovery of carnosic acid in the feces, 24 h after oral administration, was 15.6 ± 8.2%. Carnosic acid is absorbed into the bloodstream after oral administration in rats and is therefore bioavailable. It was found that carnosic acid in vivo is present in its free form and that its main elimination route is the fecal route[43].

These data suggest that phenolic compounds from rosemary ameliorate the antioxidant defense in different tissues and attenuate oxidative stress in diet-induced hypercholesterolemic rats, whereas the serum lipid profile was improved only in rats that received the aqueous extract[44].

The possibility of coal tar creosote to induce oxidative stress and biochemical perturbations in rat liver and the role of rosemary [Rosmarinus officinalis] in ameliorating its toxic effects was investigated. Rosemary pretreatment to coal tar creosote-treated rats decreased LPO level and normalized GPx, GR, SOD, CAT, and GST activities, while GSH content was increased. Also, liver AST, ALT, AlP, and LDH were maintained near normal level due to rosemary treatment. In conclusion, rosemary has beneficial effects and could be able to antagonize coal tar creosote toxicity[45].

The protective effect of rosemary essential oil on carbon tetrachloride - induced liver injury in rats and to explore whether its mechanism of action is associated with modulation of hepatic oxidative status was evaluated. results demonstrate that rosemary essential oil, beside exhibiting free radical scavenging activity determined by DPPH assay, mediates its hepatoprotective effects also through activation of physiological defense mechanisms[29].

**Hepatoprotective activity**

The effect of water extract [200 mg/kg body weight] of Rosmarinus officinalis L. in streptozotocin [STZ]-induced diabetic rats for 21 days was examined. This study revealed that rosemary extracts exerted a hepatoprotective effect. The results indicate that the extract exhibits the protective effect on tissues and prove its potentials as an antidiabetic agent[46].

Lyophilised ethanol and aqueous extracts of Rosmarinus officinalis young sprouts and total plant have been evaluated for choleretic and hepatoprotective activities in the rat. R. officinalis ethanol extracts prepared from young sprouts show a significant dose-related choleretic activity and are more active than the total plant extract. Aqueous extracts of young sprouts show a significant hepatoprotective effect on plasma GPT levels when given as pretreatment before carbon tetrachloride intoxication while the whole plant extract was inactive. Both sprouts and whole plant aqueous extracts were ineffective when given after carbon tetrachloride administration[47].

The phytochemical analysis of the methanol extract of Rosmarinus officianalis leaves [MEROL] and its efficacy against CTX-induced hepatotoxicity was investigated. Pretreatment with 100 mg/kg MEROL for 16 d ameliorated CTX-induced hepatotoxicity represented in lowering the levels of the aspartate aminotransferase [AST] and lipid profile and minimizing the histological damage. Conclusions Pretreatment with 100 mg/kg b.w. MEROL mitigated CTX-induced hepatotoxicity due to its antioxidant activity[48].

The effect of oral administration of Rosmarinus officinalis L. [Lamiaceae] on CCl[4]-induced acute liver injury was investigated. Histological evaluation showed that Rosmarinus officinalis partially prevented CCl[4]-induced inflammation, necrosis and vacuolation. Rosmarinus officinalis might exert a dual effect on CCl[4]-induced acute liver injury, acting as an antioxidant and improving GST-dependent[49]

The hepatoprotective and antimutagenic effects of the rosemary essential oil and the ethanolic extract were investigated .The potential hepatoprotective and antimutagenic activities of the rosemary ethanolic extract and essential oil, respectively, are attributed to the presence of a relatively high percentage of phenolic compounds with high antioxidant activity [according to our chemical studies][50].

The expression of the subunits NR1, NR2A and NR2B of the glutamate receptor in rat prefrontal cortex in a model of hepatic damage induced with carbon tetrachloride after a treatment with Rosmarinus officinalis L was evaluated. Treatment with extract of Rosmarinus officinalis L. in cirrhotic animals modifies the expression of subunits of the NMDA receptor due to an improvement in hepatocellular function in the presence of antioxidant compounds and flavonoids[51].

**Anti-obesity**

The effects of rosemary [Rosmarinus officinalis L.] leaf extract [RE] on the prevention of weight gain and associated metabolic disorders in mice fed a high-fat diet was investigated. While glucose tolerance and fasting glycaemia were not affected by RE treatment, hepatic triglyceride levels were decreased by 39% in RE-treated mice. Administration of the lower dose of RE [20 mg/kg BW] was ineffective on all the parameters measured. In conclusion, our results demonstrate that consumption of 200 mg/kg BW of RE can limit weight gain induced by a high-fat diet and protect against obesity-related liver steatosis[52].

Plasma alanine aminotransferase was lower with these diets at the end of the ongrowing period. Rosemary extract reduced the plasma levels of glucose and triglycerides on week 4 and glucose and HDL/LDL cholesterol ratio on week 12, suggesting better transport and energy metabolism of the lipids. Overall, the most evident effect of rosemary extract was observed with the 600 mg kg[-1] dose[53].

The effects of rosemary extract on metabolism was investigated and demonstrated that rosemary extract significantly increased glucose consumption in HepG2 cells. the PPARγ-specific antagonist GW9662 diminished rosemary's effects on glucose consumption. Overall, our study suggested that rosemary potentially increases liver glycolysis and fatty acid oxidation by activating AMPK and PPAR pathways[54].

**Radioprotective effect**

Radioprotective effect of leaves extract of Rosemarinus officinalis [ROE] has been studied against 6 Gy gamma-radiations in the liver of Swiss albino mice at various post-irradiation intervals between 12 h and 30 days. ROE significantly delayed and inhibited the rise in these biochemical parameters. Almost normal values of such constituents were regained by day 30th in experimental animals; whereas in control animals, normal values were not ever attained. In control animals, there was an elevation in lipid peroxidation [LPx] and a decrease in glutathione [GSH] in blood and liver; whereas in experimental group, decline in LPx accompanied by an increase in GSH concentration was observed[55].

**Anti-androgenic activity**

The antiandrogenic activity mechanism of RO-ext was investigated. As an active constituent of 5α-reductase inhibition, 12-methoxycarnosic acid was identified with activity-guided fractionation. These results suggest that they inhibit the binding of dihydrotestosterone to androgen receptors. Consequently, RO-ext is a promising crude drug for hair growth[56].

**Memory improvement**

The effects of subchronic [28-fold] administration of a plant extract [RE] [200 mg/kg, p.o.] on behavioral and cognitive responses of rats was assessed. The passive avoidance test results showed that RE improved long-term memory in scopolamine-induced rats. The extract inhibited the AChE activity and showed a stimulatory effect on BuChE in both parts of rat brain. Moreover, RE produced a lower mRNA BuChE expression in the cortex and simultaneously an increase in the hippocampus. The study suggests that RE led to improved long-term memory in rats, which can be partially explained by its inhibition of AChE activity in rat brain[57].

**Antimicrobial, antibacterial and antifungal activities**

Antifungal activity of oil of T. vulgaris and O. majorana was assessed. Additionally, antibacterial and antioxidant activities were evaluated. Oils of T. vulgaris and O. majorana showed growth inhibition activity against dermatophytes, especially T. vulgaris oil, which completely inhibited growth of all tested dermatophytes. The oils also showed bioactivity against bacteria, with minimum inhibitory concentration [MIC] values between 62.5 and 500 μg/mL. The antioxidant activity of the oils was low, with effective concentration [EC50] values <250μg/mL. The major components in the oils were as follows: T. vulgaris, o-cymene, μ-terpinene, thymol and carvacrol; R. officinalis, terpinen-4-ol and 1,8-cineole; O. majorana, terpinen-4-ol and thymol[58].

The antibacterial activity of the crude hydroalcoholic extracts, fractions, and compounds of two plant species, namely Rosmarinus officinalis and Petroselinum crispum was evaluated, against the bacteria that cause urinary tract infection. The fractions and the pure compound rosmarinic acid did not furnish promising results for Gram-negative bacteria, whereas fractions 2, 3, and 4 gave encouraging results for Gram-positive bacteria and acted as bactericide against S. epidermidis as well as E. faecalis [ATCC 29212] and its clinical isolate. R. officinalis led to promising results in the case of Gram-positive bacteria, resulting in a considerable interest in the development of reliable alternatives for the treatment of urinary infections[59].

The relationship between the concentrations of these components affects their antioxidant and antibacterial activities was investigated. In extracts with similar rosmarinic acid contents but differing proportions between carnosic acid and carnosol, the two diterpenes were seen to equally affect the in vitro antioxidant activity; however, and related with the antibacterial efficiency, this biological activity improved when carnosol was the major diterpene component[60].

Rosmarinus officinalis L. essential oil and three of its main components 1,8-cineole [27.23%], α-pinene [19.43%] and β-pinene [6.71%] were evaluated for their in vitro antibacterial activities and toxicology properties. The cytotoxicity of all the test samples on SK-OV-3 was significantly stronger than on HO-8910 and Bel-7402. In general, R. officinalis L. essential oil showed greater activity than its components in both antibacterial and anticancer test systems, and the activities were mostly related to their concentrations [61].

The antimicrobial activity was investigated by the disc diffusion and broth dilution methods against six microbial species, including gram-positive bacteria [Staphylococcus aureus and Bacillus subtilis], gram-negative bacteria [Escherichia coli and Pseudomonas aeruginosa], a yeast [Candida albicans], and a fungus [Aspergillus niger]. The most active fraction was the one obtained in experiment 4 [4% ethanol as modifier; extraction pressure, 25 MPa; extraction temperature, 60 degrees C]. S. aureus was found to be the most sensitive bacteria to the rosemary extracts, whereas the least susceptible was A. niger. alpha-Pinene, 1,8-cineole, camphor, verbenone, and borneol standards also showed antimicrobial activity against all the microorganisms tested, borneol being the most effective followed by camphor and verbenone. In that way, it was confirmed that essential oil from experiment 4, with the best antimicrobial activity, presented the highest quantity of camphor, borneol, and verbenone[62].

The antimicrobial activity and chemical composition of the essential oils [EOs] of Thymus algeriensis, Eucalyptus globulus and Rosmarinus officinalis from Morocco was reported.for the first time ,that minimum inhibitory and bactericidal concentration values have been reported for Eucalyptus globulus EO. Result support the possible use of this EO as well as Thymus algeriensis EO, as potential natural agents in preservatives for food and pharmaceutical products [63].

The in vitro inhibitory activity of crude EtOH/H2O extracts from the leaves and stems of Rosmarinus officinalis L. was evaluated .The bioassay-guided fractionation of the leaf extract, which displayed the higher antibacterial activity than the stem extract, led to the identification of carnosic acid [2] and carnosol [3] as the major compounds in the fraction displaying the highest activity, as identified by HPLC analysis. Rosmarinic acid [1], detected in another fraction, did not display any activity against the selected microorganisms. HPLC Analysis revealed the presence of low amounts of ursolic acid [4] and oleanolic acid [5] in the obtained fractions. The results suggest that the antimicrobial activity of the extract from the leaves of R. officinalis may be ascribed mainly to the action of 2 and 3 [64]

The antibacterial effect of rosemary on S. iniae was studied. Activity of rosemary cultivar Israel was reduced during the winter, but there was no significant change in cultivars Oranit and Star. Storage of powdered rosemary leaves at 50 degrees C resulted in fourfold and eightfold higher MIC [24 h] values after 3 and 4.5 months, respectively. Storage at -20 degrees C, 4 degrees C and 25 degrees C and autoclaving [120 degrees C] each resulted in a twofold increase in MIC [24 h]. Repeated exposures of S. iniae to rosemary did not affect minimal inhibitory concentration, suggesting no development of resistance to rosemary [65].

The aerial parts of Rosmarinus officinalis were assessed for their antibacterial activities against strains of Staphylococcus aureus possessing efflux mechanisms of resistance. Compound 1 was evaluated against a strain of S. aureus possessing the NorA multidrug efflux pump and was shown to inhibit ethidium bromide efflux with an IC50 of 50 microM, but this activity is likely to be related to the inhibition of a pump[s] other than NorA. The antibacterial and efflux inhibitory activities of these natural products make them interesting potential targets for synthesis [66].

The essential oil of Rosmarinus officinalis L. [rosemary] was and its major constituents was tested against the some microorganisms.The essential oil displayed low activity against the selected microorganisms. In the present study, the pure major compounds were more active than the essential oil. Among all the microorganisms tested, the pathogen S. mitis was the most susceptible and E. faecalis was the most resistant to the evaluated samples. This is the first report on antimicrobial activity of the major components of rosemary oil against oral pathogens [67].

The antiproliferative, antioxidant and antibacterial activities of Rosmarinus officinalis essential oil, native to Pakistan was investigated and compared. t the major components determined in R. officinalis essential oil were 1,8-cineol [38.5%], camphor [17.1%], α-pinene [12.3%], limonene [6.23%], camphene [6.00%] and linalool [5.70%]. The antiproliferative activity was tested against two cancer [MCF-7 and LNCaP] and one fibroblast cell line [NIH-3T3] using the MTT assay. It is concluded from the results that Rosmarinus officinalis essential oil exhibited antiproliferative, antioxidant and antibacterial activities [68].

The essential oils of rosemary [Rosmarinus officinalis L.] and sage [Salvia officinalis L.] were tested for their antimicrobial and antioxidant activities. Investigated essential oils reduced the DPPH radical formation [IC50 = 3.82 microg/mL for rosemary and 1.78 microg/mL for sage] in a dose-dependent manner. Strong inhibition of LP in both systems of induction was especially observed for the essential oil of rosemary [69].

The antimicrobial and antifungal tests showed a weak activity of Sardinian rosemary. On the other hand, an inductive effect on fungal growth, especially toward Fusarium graminearum was observed [70].

**Antiplatelet activity**

The antiplatelet activity of carnosic acid. Carnosic acid was investigated. In contrast to the inhibition of arachidonic acid-induced platelet aggregation, carnosic acid had no effect on the formation of arachidonic acid-mediated thromboxane A2 and prostaglandin D2, thus indicating that carnosic acid has no effect on the cyclooxygenase and thromboxane A2 synthase activity. Overall, these results suggest that the antiplatelet activity of carnosic acid is mediated by the inhibition of cytosolic calcium mobilization and that carnosic acid has the potential of being developed as a novel antiplatelet agent[71].

**Anti-Anxiety**

The effect of the hydroalcoholic extract ofRosmarinus officinalisL. on anxiety in mice was evaluated. The rosemary extract, similar to the standard drug diazepam, showed an anti-anxiety effect. This effect is probably due to the presence of flavonoids in this plant and their antioxidant property [23].

**Anti-Alzheimer**

The therapeutic potential of these compounds for Alzheimer's disease [AD] is studied. The multifunctional nature of the compounds from the general antioxidant-mediated neuronal protection to other specific mechanisms including brain inflammation and amyloid beta [Aβ] formation, polymerisation, and pathologies is discussed[34].

**Anticancer**

The anticancer effects of rosemary was reported and it was demonstrated molecular mechanisms related to these effects and the interactions between rosemary and currently used anticancer agents. The possibility of using rosemary extract as a complementary agent in cancer therapy in comparison with its isolated components is discussed[72].

Carnosic acid, carnosol, and rosmanol with promising results of anti-cancer activity was evaluated. These studies have provided evidence of diterpenes to modulate deregulated signaling pathways in different solid and blood cancers. Rosemary extracts and the phytochemicals therein appear to be well tolerated in different animal models as evidenced by the extensive studies performed for approval by the EU and the FDA as an antioxidant food preservative. This mini-review reports on the pre-clinical studies performed with carnosic acid, carnosol, and rosmanol describing their mechanism of action in different cancers [73].

In vitro and in vivo studies carried out towards understanding the molecular mechanisms of carnosic acid and carnosol leading to inhibition of prostate cancer was examined. The reported findings suggest that these polyphenols target multiple signaling pathways involved in cell cycle modulation and apoptosis. Further work is required to understand its potential for health promotion and potential drug discovery for prostate cancer chemoprevention [74]. The genotoxic and mutagenic potential of essential oil of R. officinalis in rodents, using comet, micronucleus and chromosome aberration assays was investigated. Based on the comet assay, all three doses of rosemary oil induced significant increases in DNA damage in the mouse cells. There was a significant increase in micronucleated cells and chromosome aberrations only at the two higher doses. We conclude that rosemary essential oil provokes genotoxic and mutagenic effects when administered orally [75].

The expression of bcl-2 and bax genes in the liver cancer cell line HepG2 after apoptosis induced by essential oils from Rosmarinus officinalis was investigated. Essential oils from Rosmarinus officinalis can affect the pattern of bcl-2 and bax genes expressions, and this may increase the apoptosis of liver cancer cell line HepG2 [76].

Anti-tumour, anti-diabetic, antibacterial and neuroprotective properties of Salvia fruticosa [Cretan sage] and Rosmarinus officinalis [Rosemary] was investigated. S. fruticosa and R. officinalis were searched for cytochrome P450 [CYP] encoding genes potentially involved in the synthesis of the first phenolic compound in the CA pathway, ferruginol. Three candidate genes were selected, SfFS, RoFS1 and RoFS2. Using yeast and N. benthamiana expression systems, all three where confirmed to be coding for ferruginol synthases, thus revealing the enzymatic activities responsible for the first three steps leading to CA in two Lamiaceae genera [77].

**Antidermatophytic activity**

It was investigated that whether a Rosmarinus officinalis extract could improve the skin flap survival. In this study, 21 Wistar albino rats were divided into three groups. The mean percentage of the flap survival areas and vessel diameters were significantly greater in the Groups II and III than in the control group [$p < 0.05$]. The results revealed that the topical use of the Rosmarinus officinalis extract can increase the flap survivability[78].

the efficacy of a combination of rosemary [R. officinalis] and grapefruit [C. paradisi] in decreasing the individual susceptibility to UVR exposure [redness and lipoperoxides] and in improving skin wrinkledness and elasticity was investigated.The long-term oral intake of Nutroxsun™ can be considered to be a complementary nutrition strategy to avoid the negative effects of sun exposure. The putative mechanism for these effects is most likely to take place through the inhibition of UVR-induced reactive oxygen species and the concomitant inflammatory markers [lipoperoxides and cytokines] together with their direct action on intracellular signalling pathways[79].

The antifungal activity of hydroalcoholic extracts from R. officinalis and T. riparia against strains of Trichophyton rubrum, T. mentagrophytes and Microsporum gypseum was investigated. Both extracts showed good action against dermatophytes, inhibiting fungal growth and causing alterations in their hyphae. Therefore, R. officinalis and T. riparia are potential sources of new compounds for the development of antifungal drugs[80].

the effect of essential oil of Rosmarinus officinalis L. [Lamiaceae] on the transdermal absorption of Na diclofenac from topical gel was investigsted .This study proved the enhancing effect of 0.5 and 1% of rosemary essential oil on diclofenac percutaneous absorption[81].

The effects of extracts and purified compounds from fresh leaves of Rosmarinus officinalis L. was evaluated. In vitro, we showed that ethanolic extract, carnosic acid and carnosol significantly inhibited the overproduction of nitric oxide [NO] in a dose-dependent manner in the RAW 264.7 murine macrophage cell line. For the first time in vivo, we showed that CA and CS differentially regulate the expression of inflammation-associated genes, thus demonstrating the pharmacological basis for the anti-inflammatory properties reported for CA and CS[82].

**Anti-tumor**

A rosemary extract standardized to carnosic acid was evaluated for its potential in disrupting the endoplasmic reticulum machinery to decrease the viability of prostate cancer cells and promote degradation of the androgen receptor. The results are especially significant as it is becoming more likely that individuals will be receiving standardized rosemary extracts that are a part of a natural preservative system in various food preparations. Taken a step further, it is possible that the potential benefits that are often associated with a "Mediterranean Diet" in the future may begin to extend beyond the Mediterranean diet as more of the population is consuming standardized rosemary extracts[83].

The modulatory effects of R. officinalis was monitored on the basis of the average latency period, tumor incidence, tumor burden, tumor yield, tumor weight and diameter as well as lipid peroxidation and glutathione level. The results indicate that R. officinalis leaves extract could prolong the latency period of tumor occurrence, decrease the tumor incidence, tumor burden and tumor yield. The average weight and diameter of tumors recorded were comparatively lower in the rosemary extract treated mouse groups. The level of lipid peroxidation was significantly reduced in blood serum and liver. Furthermore, depleted levels of glutathione were restored in RE-administered animal groups. Thus, at a dose rate of 500 mg/kg body wt/mouse, the oral administration of rosemary extract was found to be significantly protective against two-stage skin tumorigenesis.[84]

Antioxidant, anti-inflammatory, cytostatic, and cytotoxic activities of crude extracts or of pure components of Rosmarinus officinalis was examined. Main components of rosemary extract were identified by liquid chromatography coupled to tandem mass spectrometry [LC/ESI-MS/MS] and the effect of the crude extract or of pure components on the proliferation of cancer cells was tested by MTT and Trypan blue assays. The effect on cell cycle was investigated by using flow cytometry, and the alteration of the cellular redox state was evaluated by intracellular ROS levels and protein carbonylation analysis. Furthermore, in order to get information about the molecular mechanisms of cytotoxicity, a comparative proteomic investigation was performed[85].

the anti-proliferative activity of Rosmarinus officinalis and Salvia officinalis extracts against cancer cells was examined .The rosemary extract developed more pronounced antioxidant, cytotoxic and immunomodifying activities, probably due to the presence of betulinic acid and a higher concentration of carnosic acid in its phytochemical profile[86].

The antiproliferating activity of rosemary extract [RE] against human ovarian cancer cells was evaluated. This study showed that RE inhibited the proliferation of ovarian cancer cell lines by affecting the cell cycle at multiple phases. It induced apoptosis by modifying the expression of multiple genes regulating apoptosis, and holds potential as an adjunct to cancer chemotherapy [87].

## CONCLUSION

Rosmarinus officinalis was shown to possess lots of healing activity. Medicinal properties of its extract, essential oils, its stems and leaves should be further examined to be able to diagnose other useful and unknown properties of this valuable plant.

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