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A COMPREHENSIVE REVIEW ABOUT ANTICANCER AND ANTIMICROBIAL ACTIVITIES OF ROSEMARY OIL (*ROSMARINUS OFFICINALIS L*)

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Abstract: Nowadays, cancer is one of the most common diseases in all over the world. The concept that there is a close relationship between food and diseases like cancer is widely accepted. The scientists are now searching a natural drug in order to prevent or to cure this disease. Their attention is focused on bioactive compounds of plants that could have antitumorogenic activities. The following mini-review attempts to synthesize the importance of rosemary in cancer prevention, but also in food preservation industry thanks to its rich chemical composition on bioactive compounds that could also have antimicrobial activities.
Keywords: rosemary, cancer, bioactive compounds, carnosic acid, carnasol, antimicrobial.

Introduction

According to WHO (World Health Organization), in 2012, in many developed countries, 8.2 million people died because of cancer (Borrás-Linares *et al.*, 2015). The cancer treatment consist on a combination of chemotherapy and radiation/surgery which has negative influence on patients life and affects the memory function (Zuniga et al, 2017). Plants and herbs could be a source of compounds with potential anticancer activity that could be used in different stages but also to prevent carcinogenesis. Dietary constituents of rosemary like carnosic acid, carnosol and rosmanol could represent a new possibility to develop a natural drug that could fight against cancer.

Botanical description of *Rosmarinus officinalis L.*

Rosemary *(Rosmarinus officinalis L)* belongs to the class *Dicotyledon* order *Tubiflorae* family *Lamiaceae* and has been cultivated for thousands of years as a medicinal an aromatic plant according to (Luqman *et al.*, 2007) and (Devi and Premkumar, 2012). *Rosmarinus officinalis L*. is a perennial evergreen herb grown in Portugal, Algeria, France, Spain, Italy, Morocco and South India and it is use in medicine, perfumery, pharmaceutical products, cosmetic industries and it has also culinary uses (Devi et al, 2012). Rosemary it is one of the most popular plants in Morocco, having an annual production in essential oil of seventy tons and being widely used throughout the world (Fadil *et al.,* 2014).

The name *Rosmarinus* comes from Greek words *rhops myrinos* and means aromatic brush. *Rosmarinus* genus is a perennial bush with simple linear to lanceolate leaves downward curving, and whole, often with a rough surface, either hairless or tomentose. It has erect or procumbent hairy stems and spherical gland as shown in the Fig.1. The plants have 5-15 flowers and are characterized by a lax inflorescence in axillary or cymose verticillasters, as reported by (Hernández *et al.*, 2015).

Fig.1. Rosemary during the flowering stage (Source: (Hernández *et al.*, 2015))

Bioactive compounds and their role in cancer prevention

Rosemary is recognized as one of the natural spices with the highest antioxidant activity (Verma *et al.*, 2011). The bioactive compounds related with its antioxidant activity are carnosic acid, rosmanol, carnasol, methyl carnosate, rosmarinic and caffeic acids, but the highest content of antioxidants are present in carnosic acid and carnosol as reported Vázquez *et al*., 2013.

Rosemary extracts have a GRAS (Generally Recognized as Safe) status in the United States by the Food and Drug Administration (FDA) and it is listed by the European Food Safety Authority (EFSA), according to (Petiwala *et al*, 2015) and (Hernández *et al.*, 2015).

The rosemary leaves are used in foodstuffs thanks to the control of microbial infections and are also reported as being a strong antioxidant due to their chemical composition rich in rosmarinic acid, carnosol, carnosic acid and caffeic acid (Verma *et al.*, 2011). Carnosic acid (5,6-dihydroxy-1,1-dimethyl-7-propan-2-yl-2,3,4,9,10,10a-hexahydrophenanthrene-4a-carboxylic acid) is a natural benzenediol abietane diterpene and it is well known as an exhibitor against various human cancer cell lines according to Petiwala *et al.*, 2015. The principal anticancer molecular mechanisms of carnosic acid are represented in Figure 3. Carnosic acid, carnosol and rosmanol could inhibit tumor formation by different mechanisms like activation of apoptosis and autophagy, inhibition of signal transduction pathways and interruption of cell cycle arrest (Petiwala *et al*, 2015).

The leaves content in essential oil is about 1% to 2.5%. Due to the bioactive compounds like 1,8 cineole, camphor, borneol, bornyl acetate, α-pinene, rosemary oil has a complex taste.

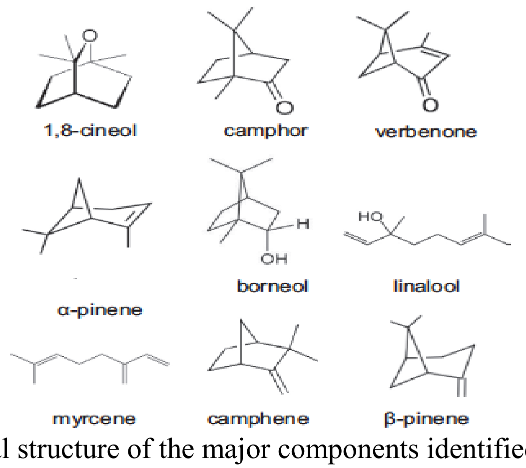

Fig.2. Chemical structure of the major components identified in rosemary essential oil. Source: (Hernández *et al.*, 2015)

The rosemary oil is a very strong antioxidant with tonic stimulant properties, being used as a pulmonary antiseptic, a choleretic and a colagoguic, also stomachic, antidiarrheal, antirheumatic properties (Fadil *et al.*, 2014). Also it was reported by (Lemos *et al.*, 2015) that rosemary oil has hepatoprotective, insecticide and antibacterial activities. The diterpenes like carnosic acid or carnosol, triterpenes, phenolic acids and flavonoids have been associated to biological activities like antioxidant and anticancer as reported by Fernández-Ochoa *et al*., 2017.

Sánchez-Camargo et al., 2017 reported that rosemary extract could have anticancer effects protecting against the main three stages of cancer development: initiation (chemopreventive activity), promotion (anti-proliferative activity) and progression (anti-invasive or anti-metastatic activity). The chemoproventive effect has been related to the antioxidant activity of rosemary extracts in particular with its capacity to scavenge free radicals in order to avoid the oxidative damage of lipid, proteins, and DNA (deoxyribonucleic acid).

The anti-proliferative activity of rosemary extract could be related to the capacity of carnoic acid to destabilize the mitochondrial membrane, which cause the release of proapoptotic proteins into the cytoplasm in order to activate other proteins which can promote programmed cell death.

The anti-proliferative activity of rosemary phenolic compounds in prostate, ovarian and colorectal cancer has been demonstrated by several studies. The antiproliferative/cytotoxic effects in colorectal cancer of these bioactive compounds reach the colon by means of the small intestine and bloodstream. Also, triterpenes and some diterpenes could have a positive influence in the large intestine due to their interactions with the gut microbiota and the direct effects with the colonocytes involved in cancer progression, having antitumor effect (Fernández-Ochoa *et al.*, 2017).

The anti-invasive or anti-metastatic activity of carnoic acid could be explained by the its capacity to reduce the phosphorylation of Akt, an activator of phosphatidylinositol 3-kinase (PI3K)/Akt signaling pathway, involved in the in the proliferation, growing and survival processes of cancer cells, according to (Sánchez-Camargo et al, 2017).

Also, rosemary extract has an important role in lung cancer by inhibiting the proliferation, blocking clonogenic survival and enhancing apoptosis of A549 lung cancer cells due to its polyphenols content, according to Moore *et al*., 2016.

Rosemary extract standardized to carnosic acid could have positive effects on promoting gastrointestinal health. In a study made on a nude mouse model, the researchers concluded that rosemary extract and carnosic acid decreased the colon cancer cell lines (Yan *et al.*, 2015)

Valdés *et al.*, 2015 reported that the mechanism of rosemary polyphenols is diverse and complex having influence also in the modulation of the transcriptome and metabolome, and are linked to glucose and lipid metabolism. They have inhibitory activity against lipase and reduce fasting plasma triacylglycerol and cholesterol levels protecting against steatosis.

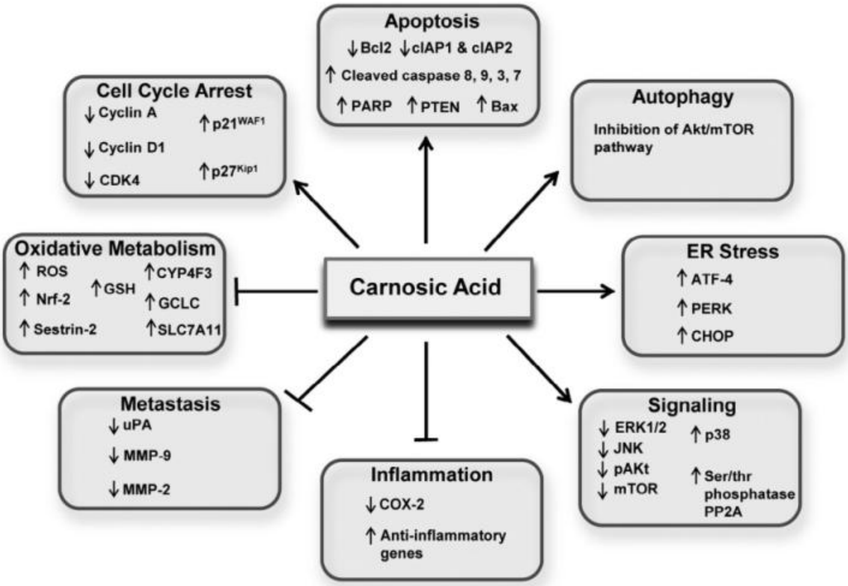

Fig.3. Anticancer molecular mechanisms of carnosic acid. Source: (Petiwala et al, 2015)

In the literature, there are several studies on the chemical composition of rosemary and have been reported three chemotypes: a 1,8-cineole chemotype, a camphor, borneol chemotype, a α-pinene and verbenone chemotype from different areas like France, Greece, Italy and Tunisia for the first chemotype, Spain for the second one, Corsica and Algeria for the third chemotype, as showed in the Figure 2.

There are a lot of factors that could influence the chemical composition of plant essential oil like environmental conditions, part and age of plant, the harvest period, storage terms (Verma *et al.*, 2011). For example, camphor was found as the major compound in essential oil (mainly in January/2013) and carnosic acid had the high amount in July/2013 (summer). The essential oil made from rosemary plant harvested in summer exhibited strong antibacterial activity against *Staphylococcus aureus*, thanks to the high amount of carnosic acid and camphor. To conclude this idea, the rosemary essential oil and the extracts collected in summer had better antioxidant and antimicrobial properties due to the high levels of camphor and carnosic acid (Lemos *et al.*, 2015).

In the technology area, electromagnetic fields emitted from mobile phone could have hazardous effects on the histology and histochemistry of parotid glands, and are also responsible for the oxidative stress effect. In a study made on rats by Ghoneim *et* al., 2016, was reported that rosemary due to its strong antioxidant activity could have a protective role against these harmful effects of electromagnetic fields.

Antimicrobial effects of rosemary oil

The bioactive compounds from the rosemary oil could have positive effect in *Mycibacterium smegmatis, Escherichis coli, Candida albicans* drug resistant mutants and in the control of gram-positive bacteria and fungi (Luqman *et al.*, 2007).

The rosemary essential oil could be used as a natural antimicrobial instead of synthetic preservatives and due to his bioactive compounds it may be used as a natural alternative for antibiotics. A minimum inhibitory concentration of 625, 1250, 312.5, 156.25 ppm rosemary essential oil could influence the growth of pathogenic bacteria like: *E. coli, S. typhimurium, S. aureus, L. monocytogenes* and *B. cereus* (Raeisi *et al.*, 2017).

The (*Rosmarinus officinalis L.)* essential oil can be used in order to improve the quality of poultry fillets by decreasing the lightness and increasing the redness, and it could be also used in combination with MAP (modified-atmosphere packaging) in order to reduce level of lipid oxidation and prolong the self-life (Kahraman *et al.*, 2015).

Also, the combination between rosemary oil, chitosan and vacuum packaging under refrigeration (2 °C), could influence the growth of microbial spoilage flora and improve the sensory quality of fresh stored turkey meat, according to (Vasilatos et al, 2013)

The rosemary essential oil could have multiple useful applications in foods preservation, infectious diseases in humans and plants, having antibacterial, antioxidant, antiproliferative activities according to (Fisher, 2009)

Mixed vegetal extracts are considered superior raw materials for functional foods and the researchers' attention is focused in developing of new products based on the mixed vegetal extracts. The mixture of spinach and rosemary leaves (50 wt.% of each plant) has 20% higher antioxidant activity than the antioxidant activity of the spinach and rosemary samples due to the synergic effects between β-carotene and lutein from spinach, and carnosic acid and carnosol from rosemary (Vázquez *et al.*, 2013).

Rosemary oil in combination with oregano oil could influence the shelf-life of cheese through the protective effect against lipid oxidation and fermented flavors (Olmedo *et al*, 2013).

The importance of rosemary extract is increasingly and it is used in food industry across the United States and Europe as a food preservative, according to (Yan *et al.*, 2015)

Nowak *et al.*, 2012 reported that rosemary oil in combination with modified atmosphere (80%O_2/20% CO_2) could be used in beef preservation with positive influence on microbial quality of meat and prolongation of shelf-life.

Rosemary oil could be used also in broiler dietary supplementation for improving broiler meat quality. Also, in the diet of quail (*Coturnix coturnix Pharaoh*), the rosemary oil had positive effects in live weight, live weight gain and carcass yields being considered as a potential natural growth promoter for quail, as reported by Hernández *et al*., 2015.

Rosemary oil (0.05% and 0.4%) was reported also in having effects on retarding the loss of thiols in pork meat during storage under modified atmosphere (MAP: 70% O2: 20% CO2: 10% N2). Thiols have been used as a marker of oxidative stability of the meat proteins for 12 days of storage. The results showed that rosemary oil have positive effects on prolongation of pork met shelf-life (Nieto *et al.*, 2013).

The rosemary extract could be also used in food industry in order to enhance stability of different type of oils like sunflower and soybean oils, as reported by (Chammem *et al.*, 2015). The addition of rosemary extract (0.08%) in a mixture of soybean and sunflower oils in equal proportions, reduce the peroxide value by 38% after 30 h of heating at 180°C.

Conclusions

To conclude, it can be said that rosemary oil could have positive effects on different types of cancer due to its chemical composition rich in bioactive compounds like carnosic acid, carnosol, rosmarinic acid and camphor. Also, rosemary oil could be successfully used as an aromatic plant in Mediterranean diet but also like a natural food preservative having antimicrobial effects and helping to prolong the shelf-life of products.

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