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Original Conrtribution

AROMATIC MEDICINAL PLANTS AND ESSENTIAL OILS, SUCH AS CHEMO-FUNGI-MODULATING PROTECTORS AND DIETARY AGENTS

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ABSTRACT
PURPOSE: Nowadays, herbal medicine offers many solutions to deal with respiratory, viral and, bacterial infections. More and more people are turning to natural antioxidants, so finding new drugs is a current goal of health and medical researchers. Medicinal plants traditional to different regions of the world (Lavandula angustifolia Mill., Mentha piperita Lin., Rosa damascena Mill., Azadirachta indica (neem oil)) contain a wide variety of bioactive compounds that have proven beneficial effects on human health. There is ample evidence that polyphenols, flavonoids, and vitamins counteract and neutralize genetic and environmental stressors, especially oxidative stress, which is closely related to the initiation of many diseases. Here we review the possible uses of the aromatic medicinal plants cited above.

Key words: aromatic plants, antioxidants, dietary agents, chemoprotection, radiomodulators

INTRODUCTION

The use of aromatic medicinal plants as preventive means for the treatment of various diseases is gaining more and more popularity. Today aromatic antioxidants are seen as potential agents for the prevention and therapy of various diseases; there is no side effect as in the case of synthetic agents (1). The most common causes of traditional plant remedies are for the treatment of chronic conditions and their perception as natural, safe and non-toxic (2). Aromatic medicinal plants after treatment are taken as teas, syrups, essential oils, powders, capsules, and tablets. Each tablet contains a dry or powdered form of raw herbs or dried extract. The plant extract is extracted by alcohol tinctures, hot water extract, long-lasting boiled extract, root potions, etc.

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In the past 25 years were increasingly being followed strategy, dietary plants to be used alone or in combinations in the form of natural antioxidant additives. Dietary plants containing natural compounds, groups of compounds, or essential oils with high stability and low volatility were used as food preservatives, which counteract the oxidative deterioration of food during storage and processing (3).

Herbs and aromatic medicinal plants as dietary agents

Natural dietary compounds (*curcumin, green tea, selenium*) on cellular and molecular pathways have shown options for cancer chemoprevention and after-cancer therapy (3, 4). Algae, seaweeds and fungi were also interesting sources as natural dietary agents with antioxidant power (4). Ascorbic acid (*Vit. C and E*) and tocopherols are the main antioxidants used as food additives. Vitamin C effectively absorbs the $^{\cdot}O_2^-$ radical and its derivatives and, through an antioxidant mechanism, promotes the conversion of quinones into phenolic forms by avoiding OD (4). Highly active against lipid-peroxidation vitamin E is converted to non-reactive tocopherol radicals and it ceases oxidative chain reactions (5).

Plant phenolic compounds (flavonoids, proanthocyanidins, stilbene, coumarins, benzoic acid, lignans) were widely used in dietary agents, because of the H atom abstraction of the phenolic groups. In cereal crops, phenolic acids (coumaric, gallic, vanilic, celulinic, synapic) are predominant. It has been reported that patients with low plasma levels of circulating antioxidants were responded easily to a rich phenolic diet (6). In the world literature, the attention has been focused on foods rich in herbal and plant antioxidants. They were useful for health and could be used in various diseases by providing a balanced combination of different antioxidants at suitable doses. Aromatic plant antioxidants dosing protects against oxidative disorders or completely neutralizes oxidative stress levels without disturbing normal ROS homeostasis (7). Bukovska *et al*. (8) reported that the inhibition of NF-kB in oils of thyme, cloves, oregano alone or in combinations, as dietary antioxidants crucial for the prevention of immune and inflammatory responses in models of colitis. Herbs and traditionally rich in antioxidants dietary plants, containing coumarin, quercetin, resveratrol, β-carotene, and lycopene regulate inflammatory processes in the cell, cell growth and differentiation (7, 9). In his studies Srikumar *et al*. (10) used dietary herbs and plant combinations containing *triphala* and demonstrate antibacterial and anti-inflammatory activity. The combination of herbs and nutrients maintains normal homeostasis in the body. Peterson *et. al*. (11) reported on the healing properties of the mixtures of three types of dried fruit (*Emblica officinalis, Terminalia bellerica and Terminalia chebula*). The combination included in the diet of patients for anti-mutagenic, anti-stress, hypoglycemic, anti-cancer, hepato-, radioprotective and chemoprophylactic effects. Few studies have reported the need to validate the use of various traditional herbs and nutritional supplements to provide therapeutical value for multiple pathologies (12).

Storage is the factor that directly affects the herbs and dietary plants, used as food. Studies have proven that the antioxidant content of foods changes on storage, the reason is the easy oxidation of polyphenols, flavonoids, carotenoids, and others. The change in organoleptic characteristics of foods is related to oxidation reactions and the formation of polymerized substances. Most of these changes were with harmful effects, because they lead to the loss of antioxidant substances in the food crops (13). The content of polyphenols antioxidants in apples and pears is not affected by the cold storage of fruits even an increase in inhibition of intestinal glucose absorption and support of the metabolic syndrome was observed (14). The presence of dietary fiber, vitamins A/C, folic acid, phenolic compounds, cinnamon acid derivatives, coumarins and flavonoids determines the current consumption of citrus as agents with potential antioxidant (15) dietary/ nutritional benefits. Some studies presented essential oils derived from culinary herbs such as *Rosmarinus officinalis*, *Lavandula angustifolia*, *Mentha piperita*, *Coriandrum sativum*, *Eucalyptus deglupta*, etc. as conventional dietary agents, preservatives processing of meat and fish. Also, new findings reported the consumption of *R. Damascena* as a functional food act effectively in the treatment of skin aging (16). The clustering of aromatic volatile compounds such as linalol, α-pinene, eugenol, carvacol, isothiocyanate, cinnamaldehyde, cinnamaldehyde, α-terpineol, describes the essential oils as food pathogen inhibitors, storage term enhancers, texture promoters, toxicity reducing agents (17). Therapeutic herbs and dietary plants, such as *R damascene, M. piperita*, *E. officinalis*, *Z. oficianale* etc., were used in Iranian medicine for different tonics with a strengthening effect on the liver to prevent the action of large doses of antibiotics or chronic alcohol consumption, with minimal adverse effects (18, 19). Patel (17) underlines that the fruits of rose plants (*rose hips*), rich in polyphenols, triterpenic acids, flavonoids, galactolipids, folates, vitamins, and minerals could be used as a dietary food.

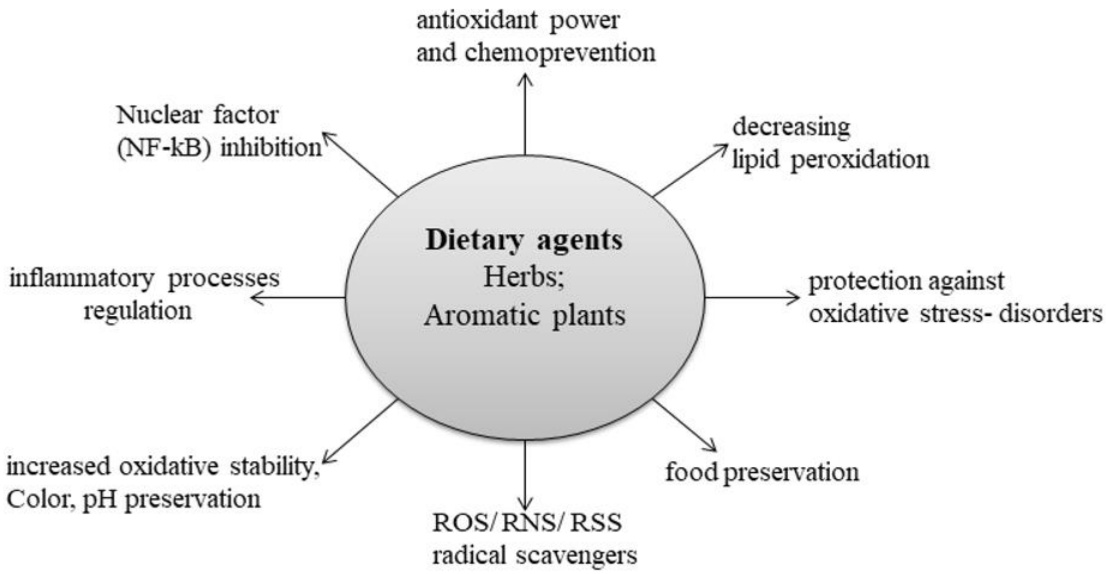

Figure 1. Schematic presentation of possible role of dietary agents in body homeostasis (Adapted from Saxena et al., 2014 (94)

Kumar *et al*., (20) draw attention to the effectiveness of herbs, spices, and plant extracts against lipid peroxidation, reducing the pH levels, colour, and smell in order to increase resistance to chicken, pork, beef, minced meat, sausages, and others. Mixtures of plant extracts increase the antioxidant potential and protect meat products due to the synergistic effects of various antioxidant components and factors (20). Kanat *et al*. (21) in parallel study confirm the combination of mint extract and chitosan neutralized superoxide and hydroxyl radicals and protects against oxidative raging, salami samples. Ganhão *et al*. (22) reported about increased oxidative stability, colour preservation, and texture after *Rosa* extracts treatment in cooked burgers in **Figure 1.**

Herbs and aromatic medicinal plants - antioxidant protective agents against oxidative disorders, radiation-modulating effect and chemoprevention

Since several studies, thousands of synthetic anti-cancer chemicals have been described as causing hepatic impairment, followed by acute hepatic symptoms. The ineffective drug metabolism led to liver transplantation cases or death (23, 24). Hepatocytes as primary metabolizing cells in the body carry out detoxification and elimination of xenobiotic and other medicals. Homeostatic dynamic equilibrium of the generation processes and ROS elimination and the prevention of oxidative disorders were also performed in the liver (25).

The efficacy of herbs and chemo-preventive plant antioxidants as therapeutic agents against drug-induced toxicity has been proven and widely used in Chinese and Indian traditional medicine. Saad *et al*. (26) reported the pharmacological effects of herbal drugs and plants, used alone or in combinations, which act on synergistic antioxidant mechanisms, thereby neutralized the side effects of cellular ROS and having potential as a radioprotectors and cancer therapeutic agents. Plant-derived bioactive compounds provide antioxidant protection against ROS-mediated damage on DNA repair, carcinogen metabolism, scavenging free radicals, inhibition of cellular toxins (27, 28) decreased angiogenesis, and radiation-induced toxicity (29). The mechanism of damage to cellular biomolecules induced by ionizing radiation includes direct and indirect action the latter is mediated via ROS formation. Ionizing radiation has been involved in the metabolic activation of carcinogens, changing intracellular physiology in terms of reductive status and oxidative modification of crucial biomolecules (e.g., DNA, lipid proteins) (30). Therefore, it is not surprising the use of herbal agents and plant extracts mitigates the radiation damage, and also promotes chemoprevention. This chapter draws attention to the antioxidant, chemo-preventive, radioprotective and cognate properties of herbs, and aromatic medicinal plants and their phytoconstituents.

Herbs and aromatic medicinal plants- against spores, mycotoxins and induced mycotoxicosis

Mycotoxins are chemically assorted compounds, secondary metabolites of structurally different groups. *Aspergillus flavus, Aspergillus ochraceus, Penicillium viridicatum and Fusarium moniliforme* spores/ mycotoxins are toxic to animals, humans and significantly reduce yields, because almost 25% of agricultural commodities were contaminated with them (31). The mycotoxins possessed carcinogenic, hepatotoxic, nephrotoxic, cytotoxic, mutagenic, and immunosuppressive effects in **Figure 2.**

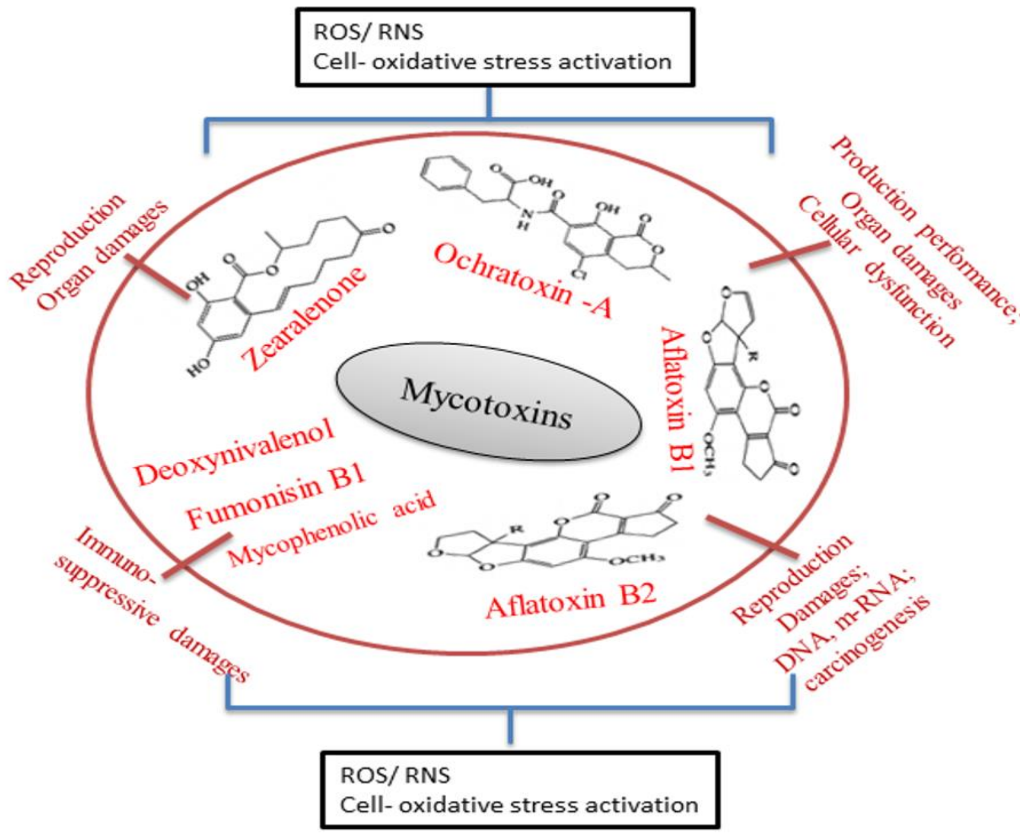

Figure 2. Types and structures of important mycotoxins, mechanism of action, and ROS-mediated damages

The toxicity and carcinogenic mechanisms of mycotoxins have been associated with induction of oxidative stress damages and to increase DNA and mitochondrial lesions, cell autophagy and apoptosis, protein synthesis inhibition, ROS generation, changes in the intracellular antioxidant enzymes (32). Herbs and spices grown in tropical and subtropical regions react with fungal agents (33, 34) and exhibit harmful activity. Macwan *et al*. note that use of herbs and spices loaded with mycotoxins results in serious diseases and risk of cancer (34-36). The ingredients contained in herbs, spices, and oils contribute to self-defence against infectious organisms.

This section discussed the beneficial properties of herbs, medicinal extracts, and oils as antioxidant- free radical scavengers and the ability to ameliorate/ modulate oxidative stress- the effect of induced mycotoxicosis in **Figure 3**.

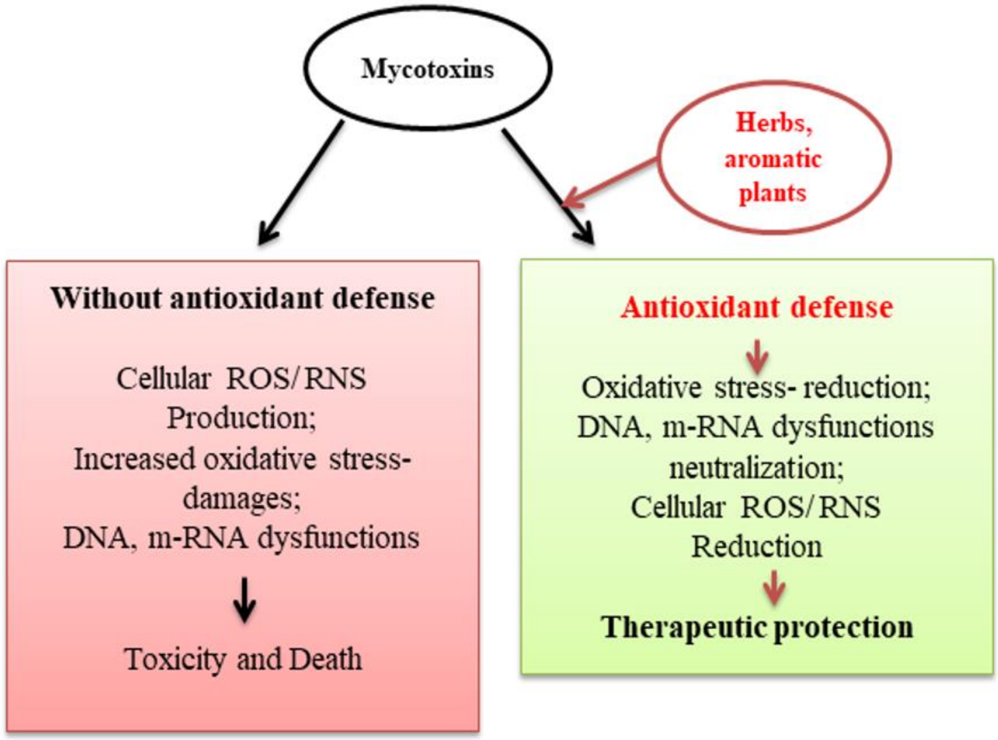

Figure 3. Schematic representation of mycotoxins by its toxic, and therapeutic design Adapted from Adhikari et al., 2017 (31)

Silymarin exhibits protective properties against hepato- and mycotoxicity, caused by ochratoxin, microcystin, and other toxins (36-38). Hepatoprotective treatment with milk thistle seeds ameliorating aflatoxin B1-induced toxicity increased the absorption of nutrients and decreased metabolic processes in the intestinal tract in the study conducted in broilers (36, 37). Silymarin inclusion as a food supplement inhibits the ileal populations of *Escherichia coli, Salmonella, Klebsiella* in aflatoxin-challenged chicks (36, 37). The *M. piperita* oil possessed inhibitory effects against fungi and aflatoxin B1 production and anti-fungal activity could due to menthol and menton (38-40). Recently it was reported that mint, garlic, oregano and tea oils are suitable nutritional preservatives against the production of toxins (40, 41). Oils and extracts of *R. officinalis L., O. basilicum L., E. globulus Labill., S. officinalis L., L. angustifolia Mill., Z. officinalis Rosc., M. piperita* and etc. tested by Císarová and co-workers, exhibited antibacterial activities against Aspergillus species B1-production (41). Oils of *C. longa, L. angustifolia and M. piperita* exhibited antifungal activity by inhibiting mycelial growth against *Fusarium moniliforme, Colletotrichum lindemuthianum and Pythium ultimum fungi* (34, 35). Powdered *C. longa* added as a food supplement reduced ochratoxin A-toxicity kidney amendments in boilers (42). In addition, chickens fed with the combination of *C. longa* and aflatoxin registered lower ALT, AST, uric acid, and delayed liver and kidney degeneration (42, 43). *Curcumin*, *C. longa* main active component, can serve against aflatoxicosis, modulating and transforming the immune system as reflected by interleukin-1β, growth factor-β, cytochrome P45,0 isoenzymes CYP1A, CYP3A, CYP2A, CYP2B, and CYP2C biotransformation (43,44).

Nerol and eugenol as general compounds of rose and lavender essential oils were effective against the carcinogenic aflatoxin B1 (300 ppm), directly disrupt the membrane in *Aspergillus types in vitro* and have promising use as a natural fungicide (45, 46). Administration of *T. cordifolia* ethanol extract decreases malondialdehyde levels, oxidative stress and inhibits the effect of aflatoxin-B1 in the liver and kidney tissues. Also, *T. cordifolia* extract provides oxidative-protective effects on plasma and spleen cells after experimental ochratoxicosis (47). Active alkaloid compounds of *T. cordifolia* extracts induced protective effects against aflatoxin-nephrotoxicity and prevent ROS generation (48).

***Lavandula angustifolia* Mill.**

Lavender oil (*L. angustifolia*, lavender, Lamiaceae family) covers approximately 39 flowering species that have a significant application in aromatherapy. 200 components belonging to terpenic and nonterpenic hydrocarbons, linyl acetate, alkanols, aldehydes, ketones, ethers, acids, lactones, phenols and esters are the ingredients determining the quality of lavender oil (49). An *in vitro* analysis, *L. angustifolia* oil recorded a complete elimination of the antiparasitic activity against the human protozoan pathogens Giardia duodenalis and Trichomonas vaginalis (50). The application of lavender oil, containing linalyl acetate and linalool, is an effective measure for relieving perinatal pain and episiotomy in women and for faster wound healing (51). The clinical study, including 96 females, with increased menstrual bleeding and symptoms of primary dysmenorrhea, proves the potential effects of lavender oil, after inhalation (52). Additionally, the bioavailability of inhaled lavender oil (2% oil, two drops/ethanol solution) was evaluated in 60 patients undergoing arterial bypass. Relatively decreased oxidative stress levels and normalization of vital signs were established (53). Increased linalool content in lavender oil probably leads to inhibition of serotonergic levels (SERT), which practically explains antidepressant effects and modulation of oxidative changes in spatial memory impairment in animals (54). As regards *in vivo* studies, Lopez and *et al*. clarify that the antidepressant activities of the *L. angustifolia* oil are partly due to NMDA receptor modulation and SERT inhibition. The free radical absorption by *L. angustifolia* oil protected SH-SY5Y cells from H_2O_2-induced neurotoxicity (55). Karamalakova *et al*. (48) investigated the radioprotective activity against UV and y-radiation of the oil prepared by hydrodistillation of *L. angustifolia* flowers by EPR spectroscopy. The irradiated samples recorded excellent DPPH radical-scavenging properties and their use as radioprotective antioxidants in the cosmetic and pharmaceutical industries was suggested. Tayarani-Najaran *et al*., (56) supposed, the possible apoptotic mechanism of action of *L. angustifolia* oil determined cytotoxic and apoptotic effects on malignant (HeLa and MCF-7) cell lines. As regards topological changes of DNA molecules, Horvathova *et al*., (57), published that *L. angustifolia* and *R. officinalis* extracts protect the plasmid DNA from alterations and modulated harmful effects of Fe^{2+}. Recently, was discussed the role of monoterpenoid alcohol linalol towards human colon cancer cells. Iwasaki *et al*., (58) describe ESR *in vitro* specific suppression overproduction of hydroxyl radicals from cancer-induced oxidative stress and simultaneously delayed lipid peroxidation following of linalol use. Moreover, monoterpenoid *in vivo* induced tumor-specific lipid peroxidation in SCID mice grafted with colon cancer cells without side effects (58) in other organs. Many studies (59) proved, linalol stimulates the secretion of IFN-γ, IL-2, 4, 6δR, 13, 21, 21R, TNF-α, and induce Th1 cell immune response in T-47D cells, has application in anti-cancer therapies. Last but not least, an *in vitro* study of the antitumor activities of *L. angustifolia* oil and its constituents (linalol and linalyl-acetate) were tested on human prostate cancer PC-3 and DU145 cell lines. The investigators demonstrated the anti-tumour and anti-proliferative effects of essential oil and the induction of apoptotic processes (60).

***Mentha piperita* Lin.**

The essential oils extracted from *M. piperita* (mint oil, Lamiaceae family) leaves and flowers contained menthol, menthone, eugenol, caffeic acid, limonene, menthyl acetate, menthofuran, 1,8 cineole, neomenthol, menthone, (*Z*)-caryophyllene, germacrene D and rosmarinic acid and α-tocopherol and other substances (29, 49, 61). Primary radical scavengers, identified in M. piperita oil are erythrocytrin, eugenol, menthol, menthone, luteolin-7-O-glucoside, caffeic and rosmarinic acid (61=128). In the conducted, in *vitro* study, the leaf oil of fresh *M. piperita* provides antimicrobial activity against clinical keratinophilic fungi isolated from patients with superficial fungi infections (49). To similar conclusions were reached by Samber *et al*. (62), whose investigations prove that the main compounds of *M. piperita* promote antifungal activity by reducing ergosterol levels, inhibiting PM-ATPase, and reduced intracellular acidification. Sun *et al.* (63) investigated *in vitro* antioxidant properties of *M. piperita oil* and cytotoxic activity against cancer cell lines (SPC-A1 cells of human lung carcinoma, SGC-7901 human cancer cells, human leukemia K562 cells, and human hepatocellular carcinoma BEL-7402 cells). The results summarized moderate antioxidant properties and cytotoxic sensitivity in the K562 and SGC-7901 cancer cell lines. Also, treatment with *M. piperita* extract provides bone-marrow protection and reduced chromosomal aberrations (29, 64) in animals exposed to γ-rays. *M. piperita* induces radioprotective activity in reproductive organs in mice and hemato-poietic damage is observed in mammals (29). Desam *et al*., (65) discussed that the containment of antioxidant components in the essential oil of *M. piperita* promotes antibacterial and antifungal activity against human pathogenic microorganisms. In vitro studies of Liu et al. (66) indicating polysaccharides (glucuronic acid, galacturonic acid, glucose, galactose and arabinose) as active compounds, derived from M. piperita inhibit the growth of A549 tumor cells and DNA topoisomerase I. New study (67), reported that *M. piperita* components exhibit anti-inflammatory activity, prevent cytotoxic effect on L1210 cancer cells and angiogenesis. Interpolate the *M. piperita*, as dietary agent to the food of old quails leads to a positive effect on levels of MDA, AOA, LDL and HDL, and blood parameters (68). Since, synergistic activity of *M. piperita* oil it can be used simultaneously with antibiotics such as amphotericin B, nystatin, fluconazole, ketoconazole, clotrimazole and itraconazole against clinically isolated Candida cases (69). Also, *M. piperita* hydroalcoholic extract (*containing epicatechin*), activate the antioxidant response in cells and contributes to increased SOD and glutathione peroxidase activity and modulates inflammatory responses, mediated in mouse peritoneal macrophages (70).

Rosa damascena Mill.

The largest producers of high quality essential oil of members of the family Rosa *(R. damascena; Family Rosaceae*; *Damask rose, oil-bearing rose)* are Bulgaria, Turkey, France and India. More than eighteen compounds have been isolated from P. damascena including geraniol, phenyl ethyl alcohol, citrenelol, neol, eugenol, camphorol, germaniol, nonadecane (71). Recent *in vitro* investigation, focused on the strong antioxidant properties of *R. damascena* leaves, extracts, leaven, syrup, jam, essential oil (72) and their use as important traditional products. The flavonoid structures isolated from *R. damascena* possessed radical- scavenging, antioxidant ability, protect the DNA from oxidative damage and display strong resistance to UV- radiation (73). In addition, studies (74) reported that a 50% ethanolic solution of *R. damascena* exhibits a protective effect against ultraviolet exposure and has an effect on MMP transcription by suppressing AP-1 activation and expression of TGF-β1 by regulating Smads in non-hair mice. Aleebrahim-Dehkordy *et al*. (75), demonstrated that *R. damascena* extracts contain phenolic components (carboxylic acid, myrcene, camphor and quercetin), perform the function of scavengers, by complex cellular mechanisms counteract angiogenic and metastatic growth. Meimandi and Yaghoobi, (76) discusses the ability of the water and ethanol extracts of *R. damascena* to reduce the viability and proliferation in stomach cancer, and also to induce processes of apoptosis. Khare and co-authors (77) investigated the *in vitro* and *in-vivo* immune status and activation against malaria pathogenesis of *R. damascena* acetate extract, contain rutin and glycic acid. The authors reported that the extract modulates pro-inflammatory mediators (IL6, TNF, IFN and NO), and at the same time restores the hepatocyte constitution. An experimental study demonstrated the combination of *R. damascena* and *L. angustifolia* essential oils, vit. C and trolox with L-dopa regulates cellular ROS/ RNS deactivation and reduced oxidative toxicity in mice (78). The same authors suggested that the herbal extracts isolated from *R. damascena* and *L. angustifolia* possessed antioxidant activity and reduce the oxidative degradation of biomacromolecules (78). Similar research describes the promising protective activity of *R. damascena* flavonoid extract on memory abnormalities and behavioral functions in Alzheimer's disease induced by amyloid β (A-β) in rats (79). Moreover, the treatment with *R. damascena*, *C. intybus* aqueous extracts and their mixture has nephroprotective properties, by reducing the serum urea levels, creatinine, urea nitrogen and serum albumin at gentamicin-induced damages (80). Mohammadpour *et al*. (81) presented that the *R. damascene* extract is antioxidantly active against brain oxidative disorders and by free-radical scavenging chain;

reactions prevent the depletion of scopolamine-induced memory deficits. Methanol extracts of *R. damascena* decreased glucose content after feeding by inhibition of enzyme secretion and therefore exhibit anti-diabetic activities (81, 82). Reduction in total cholesterol levels, triglycerides and low density lipoproteins were also reported. As regards *in vivo* studies (83), were reported antioxidant-mediated hepatoprotective ability of *R. damascena* extracts against acetaminophen- and tetrachloromethane - induced toxicity.

Azadirachta indica (A. Indica, Meliaceae, neem oil)

Azadirachta indica is a plant (extract or oil) antioxidant with protective properties, antioxidant action, and the ability to inhibit mycotoxins overproduction. The oil is extracted from ripe seeds, leaves, or fruits of Neem trees in India, characterized by more than >300 biologically active hytoconstituents such as: azadirachtin (C26 triterpene), 6-deacetyl-nimbin, azadiradion, nimbin, salanim, epoxyazadiradiol meliantriol (C30 triterpene), 3–Deacetylsalannin, salannol, etc. (84, 85). The antifungal, nematodes, and certain plant viruses' functions of neem oil are triterpenoidal and tetranortriterpenoid compound mixtures (83, 86). The chemical ingredients in *A. indica* extracts and oils potentially inhibit the Aflatoxin and Ochratoxin-A (OTA) production by Aspergillus parasiticus and inhibit the fungal agents' growth (87). *In vitro* studies have reported stable inhibition of polyketide mycotoxins: patulin, citrinin, sterigmacystin and OTA and oxidative changes regulation (87). The development of both the contagious species - Aspergillus and Rhizopus fungi was hindered and controlled with both alcoholic and water neem extracts (88). The increased *A. indica* antioxidant activity counteracts oxidative changes by free radical reduction. *A. indica* oil, at the molecular level, reduces or directly modulates cellular signaling, in combination with various pathogens (88). The *A. indica* hytoconstituents azadirachtin and nimbolide showed concentration-dependent antiradical scavenging activity and reductive potential in the following order: nimbolide>azadirachtin>ascorbate (88). Shareef and Akhtar, 2018, comment that azadirachtin and nimbolide administration inhibited the development of DMBA-induced HBP carcinomas through the prevention of procarcinogen activation of DNA oxidative damage and antioxidant and carcinogen detoxification enzymes non-regulations (88). In addition, nimbolides, derivatives of A. indica oil, were able to inhibit the pro-inflammatory transcription factor (NF) -κB, which is involved in the oncogenesis regulation (89). In vitro, nimbidin inhibited nitric oxide and prostaglandin E2 production in lipopolysaccharide-stimulated macrophages (90). The hepatoprotective role of *azadirachtin-A*, *A. indica* compound on CCl_4-induced, OTA- induced hepatotoxicity in animal models exhibited decreasements in PCC, AST, ALT, reduced hepatocellular necrosis (90, 91). Furthermore, different authors reported the *A. indica* oil use in food packaging and its effects on the properties of food packaging. Many reports comment that *A. indica* oil coating applications are favorable as the applications do not involve contact with the food and hence, the food is not exposed to the insect repellent agent (92).

The anticancer neem oil (93) effects were investigated on 7,12-dimethylbenz(a)anthracene (DMBA)-induced breast cancer in high-fat/sucrose-fed Wistar rats. The regular neem oil (3 mL/kg) consumption protected rats against DMBA-induced breast hyperplasia (80%), with an optimal effect on 4 times weekly, but activated histological liver abnormalities.

CONCLUSION

In modern urban life, people are exposed to elevated levels of microorganisms, food mutagens, toxins, environmental pollutants, carcinogens and various ionizing radiations. Over the last 20 years, there has been a strong body of evidence supporting the use of natural antioxidants as effective dietary phytochemical protectors against ROS/RNS. Based on the complex nature of herbs and aromatic herbs and the role of "redox signaling compounds", they have great potential not only to prevent disease and cancer, but also to improve recovery by regulating various types of cellular damage caused by radiation, ROS, and oxidative stress. A dosage of herbs and plant antioxidants protects against oxidative disorders or completely neutralized levels of oxidative stress. Various studies have provided information on the efficacy of herbs, chemo-preventive plant antioxidants, and microbial species as therapeutic agents against drug-induced toxicity and have been widely used in traditional medicine.

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