

Book Chapter

Rose Oil – Biological Effects and Application in Alternative and Conventional Medicine

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This Book Chapter presents an overview of the biological properties of rose oil obtained by the distillation of rose flower from different geographical regions of the world. The authors draw on information gathered from PubMed, Science Direct, and Google Scholar databases, as well as published data from their own research.

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Introduction

Until today, roses are one of the most important groups of ornamental plants, a sign of inspiration, purity, love, happiness, and beauty called the "Gift of Angeles", "The Queen of Flowers", and "Gol-E-Mohammadi".

In recent decades, there has been growing interest and basic research on essential oils as an alternative to conventional medicinal preparations. Antimicrobial and antioxidant activity as well as potential anticancer effects are the main target areas.

Presumably, the genus *Rosa*, to which the oil-bearing species belong, originates from the ancient evergreen lianas [5]. At present about 1,000 genotypes of roses are known, they are classified and grouped based on the botanical characteristics: hybrid teas, grand floras, polyanthus, floribundas, miniatures, climbing, shrub, and old roses, but only a few of them exhibit the marked fragrance which is preferred by perfumers [6,7].

Rose oil has a complex composition that includes more than 200 components from different classes of chemical compounds, and this provokes its multifaceted biological effect [8]. The recipes and practice of folk healers contain various rose extracts. The healing properties of the rose flower have been known for hundreds of years.

Placed on a scientific basis, the empirical knowledge from folk medicine is an important point for more and more in vitro and in vivo studies, including preclinical and clinical trials. They explore and explain the therapeutic efficacy of rose oils and extracts and their ingredients: antidepressant effects, psychological relaxation, improvement of sexual dysfunction, antioxidant, antimicrobial, antifungal, probiotic and antipyretic effects, smooth muscle relaxation, lipid-lowering content, antiulcerogenic effects, etc. [2,8,16-21]. Rose oils are

recommended not only for inhalation and topical application (in aromatherapy and dermatology) but also for oral administration at physiologically applicable doses. Rose oil has a complex composition that includes more than 200 components from different classes of chemical compounds, and this provokes its multifaceted biological effect.

Antimicrobial Effect

The first reports about the qualities of the essential oil, concrete, and rose water belong to Bulgarian scientists, who in the 1970s proved the bacteriostatic and bactericidal effect of *R. damascena* Mill products [22]. Modern research, using new methods, confirms and expands their spectrum of action against certain microorganisms.

Erdogan et al. (2017) analyzed the antimicrobial activity of essential oils from various medicinal and aromatic plants, including *R. damascena* and *Lavandula hybrida*. Pathogens *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* were used as test microorganisms. Antimicrobial activity was registered only against *S. aureus* [23]. Applied individually, the terpene alcohols geraniol and nerol showed potential activity against *E. coli*, and geraniol, citronellol, and nerol were more potent against *S. aureus* than as part of rose oil.

In a similar study, Ali et al. (2015) analyzed the antimicrobial activity of seven essential oils, including rose oil, in parallel with its main components - geraniol, citronellol, nerol, and eugenol [24]. A wide range of Gram - (+) and Gram - (-) microorganisms were used, such as *S. aureus*, *Enterococcus faecalis*, *E. coli*, *Proteus vulgaris*, *P. aeruginosa*, *Salmonella* sp., *Klebsiella pneumonia*, as well as the causative agent of fungal infections *Candida albicans*. Rose oil demonstrated strong antimicrobial activity against all test microorganisms. Geraniol, nerol, and eugenol showed clear activity against all strains, and in some combinations, it was even higher than that of the oil alone. On the other hand, citronellol has little or no activity against most microorganisms. The authors concluded that the antimicrobial properties are due to the complex synergistic and antagonistic

effect of the ingredients and the properties of the oil cannot be attributed to a particular component. The same is confirmed by other authors (Lisin et al., 1999) [25].

In another study, Ulusoy et al. (2009) [26] compared rose oil, rose absolute, and rose water in terms of their antimicrobial activity. The oil and absolute demonstrated strong activity against strains of *Esherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Staphylococcus aureus*, *Chromobacterium violaceum* and *Ervinia carotovora*, the latter being the most sensitive. Logically, hydrosol has the least impact. Pink absolute shows antibacterial activity against both Gram-positive and Gram-negative bacteria.

Of interest is the work of Gochev et al. (2008) who compared the composition and antimicrobial activity of rose oils from different geographical origins – Bulgaria, Turkey, Morocco, Iran, and China. Citronellol, geraniol, nerol, linalool, citronellyl acetate, geranyl acetate, and eugenol - substances in the composition of the oil - were used as references.

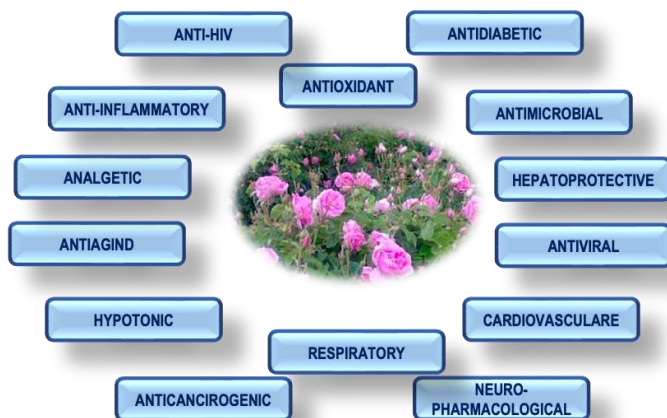


Figure 1: Pharmacological activities of rose essential oil.

The authors prove that Bulgarian rose oil has the strongest activity against all microorganisms, probably due to oxygen-containing acyclic monoterpenes, their acetate derivatives, and phenolic components.

At a later stage, the author's team focused on the stability of the composition and the antimicrobial qualities of the so-called "historical" rose oil [28]. An authentic sample of Bulgarian rose oil produced before 1944 showed a content of major components that generally fall within the requirements of the international standard ISO 9842. Applied to three species of Gram-positive and Gram-negative bacteria, as well as to two species of yeast, the old oil demonstrates minimal inhibitory and bactericidal concentrations that are not only equivalent but, in some cases, even better than those of oils of the modern varieties «Iskra», «Janina» and «Eleyna».

Propionibacterium acnes is a dangerous microorganism that causes tissue inflammation. The process can develop pathology affecting the cardiovascular system or even the brain [29]. Traditional medicine treatment with antibiotics or hormones has side effects or leads to resistance. Using a disc-diffusion method, Zu et al. (2010) tested ten pre-selected essential oils for antibacterial activity against the agent in question, in addition to performing an in vitro toxicological test against three human cancer cell lines [30]. The results showed that cinnamon, thyme and rose oils demonstrated the strongest inhibitory effect (respectively 40.0±1.2 mm; 33.5±1.5 mm 16.5±0.7 mm) with a minimum inhibitory concentration MIC of 0.016 % (v/v), 0.016 % (v/v) and 0.031 % (v/v). Rose and lavender together with thyme and clove show the fastest effect and destroy the bacteria within 5 min. The oils have a certain modeling cytotoxic effect.

An in vitro study proved the inhibitory effect on the growth of the bacterium *Helicobacter pylori*, the causative agent of peptic ulcer disease [31].

Another possible direction is the use of rose oil as an alternative to conventional chemical agents against plant pathogens. Basim

& Basim (2003) [32] published a study on the evaluation of rose oil against three strains of *Xanthomonas axonopodis* spp. vesicatoria – pathogens of tomato and pepper diseases. The next report [33] is about strong antimicrobial activity against *Erwinia amylovora* - the cause of the so-called "fire burn" in the family of Rosaceae. The bacterium can destroy an entire crop. The results obtained allow the authors to define rose oil as a strong natural bactericide that can be used in environmental problems.

In recent years, research has begun on the essential oil of the white rose (*Rosa alba* L.), its potency, and its spectrum of action. For the first time, Gochev et al. (2010) reported its potential against bacteria and yeast [34]. The most common causes of microbial contamination in cosmetic products were used as test organisms - *Staphylococcus aureus* ATCC 6538, *Staphylococcus epidermidis*, *Bacillus cereus* ATCC 11778, *Escherichia coli* ATCC 8739, *Pseudomonas aeruginosa*, *Pseudomonas fluorescens*, *Pseudomonas putida*, *Salmonella ebony*, *Citrobacter diversus*, *Candida albicans* 1, *Candida albicans* 2, and *Candida tropicalis*.

Research in this direction proves that rose oils and their ingredients have a double effect as a component of cosmetic and perfumery products – once as a fragrance, secondly as protectors and antimicrobial agents. Rose oil is a strong natural bactericide that can be used in environmental problems.

Antioxidant Activity

The identification of natural products and their constituents with potential antioxidant activity has been the focus of scientific research in recent decades. It is provoked by their ability to neutralize free radicals in the human body and extinguish their destructive effect on human cells. The antioxidant activity of rose oil has been the subject of several such studies.

Saleh et al. (2010) screened a large range of essential oils, including rose. DPPH and DPPH/TLC evaluation methods were used [35]. The authors found that 1.5 ml (at a concentration of 5 mg/ml) of Bulgarian rose oil could effectively neutralize 90% of

the DPPH radical in 2 ml of a 0.02 mM DPPH solution. In the DPPH/TLC isolated fractions with high antioxidant activity by GC/MS, the minor rose oil minor rose oil rosofuran was identified. According to the authors, this component may be related to the observed high antiradical activity.

In a similar study with several essential oils, Wei&Shibamoto (2007) used DPPH, A/CA (aldehyde/carboxylic acid) and MA/GC (malonaldehyde/gas chromatography) methods [36]. According to the A/CA test, rose oil at a concentration of 500 µg/ml had a 100% inhibitory effect over a period of 40 days, with the inhibitory effect changing significantly in the range 50 µg/ml (12%) to 100 µg/ml (100%). The DPPH test showed that 1 ml (200 µg/ml) of rose oil inhibited 70% in 1 ml of a solution of the radical with a concentration of 7.6×10^{-5} M. A better effect was reported only with jasmine oil. Based on the results of the MA/GC analysis of the oils, the authors propose the following descending order for the antioxidant activity of the tested essential oils: parsley seed (at a concentration of 500 µg/ml) > rose (100 µg/ml) > ylang-ylang (100 µg/ml) > devisil seed (500 µg/ml) > jasmine (500 µg/ml) > patchouli (100 µg/ml) > juniper fruit (500 µg/ml).

Taken together, the results of the described studies show that rose oil has one of the strongest antioxidant activities among a large set of oils analyzed by different criteria.

In subsequent work by Yassa et al. (2009) compared the antioxidant potential of rose oil and hydroalcoholic extract of flowers of *R. damascena* Mill. [37]. DPPH and lipid peroxidation (FTC test) methods were used. The results showed a similar effect in both products, much stronger than that of the antioxidant standards Vitamin E, BHT (butylhydroxy toluene) and purified kaempferol-3-rhamnose (a flavone glycoside contained in pink flowers). This suggests the successful application of rose oil and extracts in various end products. For example, rose petals or extracts would be applicable as cost-effective antioxidants in various food products, and expensive rose oil as an indispensable ingredient of the perfume composition and antioxidant in high perfumery and cosmetics.

Karamalakova et al. (2019) complete the studies and make the first report on the radiomodulatory properties of rose oil, testing it for stability by exposure to UV-VIS and γ -radiation at doses of 5, 10, 20 and 30 Gy. The intensities of the direct EPR signals in the untreated and treated samples demonstrate the probable formation of stable free radicals. The stable spectrum (two months after radiation exposure) and the excellent DPPH capacity of antioxidant and radioprotective ability indicate that *R. damascena* Mill. has potential as a radiomodulator and anticancer agent [38].

R. damascena Mill. oil manifests good antioxidant not only in chemical and biological model systems, but also in experimental models of oxidative stress in mice. In ex-vivo experiments with brain homogenates of mice treated with L-DOPA that causes increasing protein oxidation and LP, it was observed that the markers of oxidative stress are reduced upon pretreatment of the experimental animals with the antioxidants as vitamin C, and Trolox, and *R. damascena* Mill essential oil. The effect of the combination of L-DOPA with damask rose oil is very similar to that of Vitamin C and Trolox [93]. Nair et al. (2013) reported that the vapor of oil from *R. damascena* Mill. lowers the induced by chronic mild stress (CMS) LP in the rat cerebral cortex and restores concentrations of vitamin A, vitamin E, vitamin C, and b-carotene after depression. The vapor of *R. damascena* oil showed the same effect as Citronellol, geraniol, and nerol [40].

Anticarcinogenic Effect

Zu et al. [30] included rose oil in a study on the possible anticancer effect of multiple essential oils – cinnamon, thyme, chamomile, lavender, jasmine, grapefruit, lemon, ginger and peppermint. Methods were used to determine cytotoxicity against human prostate (PC-3), lung (A549) and breast (MCF-7) carcinomas. According to the obtained results, rose oil is in the fourth place in terms of growth inhibition power of PC -3 and A549 and in the third place in MCF -7.

Similar are the conclusions of Karamalakova et al. [38]. They studied antiradical and antioxidant properties of both before and

after UV and γ - irradiation of rose oil using electron donation potential estimation assay, DPPH, ABTS, Nitric oxide ion scavenging assay, and protection of lipid membranes against radiation damage. Samples after irradiation showed a significant reduction in the donor potential in comparison with non-irradiated oil, nevertheless in all studied concentrations ability of scavenging DPPH is higher than positive control of quercetin. Both γ -irradiated and non-irradiated oil samples demonstrate an increase in scavenging abilities towards ABTS and NO in a concentration-dependent manner [41,42].

Neuropharmacological Effect

Rose oil is one of the basics for aromatherapy, well known for its balancing effect in nervous disorders, states of anger or depression Konopacka-Brud [43,44].

Based on the traditions of folk medicine and the results of later scientific research by the doyens of the Bulgarian pharmacotherapeutic school - Prof. VI. Aleksiev and Prof. Nikolov, [44] made a large-scale study of the pharmacodynamics of Bulgarian rose oil in experimental and clinical conditions, looking for new possibilities and forms of therapeutic application. In this regard, he traces its influence on the peripheral and central nervous system, on non-vascular smooth muscles, on the cardiovascular system, on heart activity, some allergic reactions, on the activity of the brain, etc. Data concerning the regulatory effect of rose oil on heart rhythm are in accordance with the opinion expressed by the medieval authors Mathiolus and von Heller (17th century) to the effect that rose preparations “strengthen” the heart and eliminate its “fibrillation”. For the first time in the world, the total myorelaxing ability of rose oil on the smooth muscles was proven, explaining its antispasmodic effect. It has been proven its choleric power, its healing effect in cardiac disorders, the expansion of peripheral blood vessels, its ability to cause activation in the mesolimbic system of the brain, practically no toxicity, etc. Almost all subsequent research is based on this development [45].

Later, Boskabady et al. (2006) evaluated the effect of *R. damascena* oil on the respiratory system in rats. The authors analyzed the relaxing effect and the anticonvulsant effect on the tracheal smooth muscle, which in turn causes an antitussive effect comparable to that of a drug (theophylline). This also explains the anticonvulsant effect of the oil in epileptic seizures [46].

Kheirabadi et al. (2008) investigated the anticonvulsant activity of *R. damascena* oil in PTZ-induced seizures in experimental animals. The results show that it can weaken the latent period of the onset of convulsions, as well as suppress the strength of the convulsions. The effect depends on the dose [47].

Fukada et al. (2011) analyzed the influence of rose oil (*Rosa alba*) inhalations on chronically induced stress in humans and experimental rats [48]. The research is in three directions: (i) on the increased activity of the hypothalamus and the levels of plasma corticosterone in rats; (ii) on the destruction of the natural skin barrier in humans caused by chronic stress; (iii) on the increased concentration of cortisol in human saliva during chronic exposure to stress. The results presented provide evidence that in both humans and animals, rose oil inhalation has an inhibitory effect on stress-induced responses, possibly by dampening endocrine overactivity along the hypothalamic-pituitary-adrenal axis.

Naziroglu et al. (2012) evaluated the protective effect of rose oil in model-experimentally induced depression [49]. They used groups of experimental mice, one chronically stressed (CMS) and the other serving as a control. Both groups were given rose oil - orally (1.5 ml/kg) or by vapor (0.15 ml/kg) for a period of 28 days. At the end of the experiment, the authors analyzed samples from the brain's cerebral cortex for levels of lipid peroxidation. The results showed that the levels of lipid peroxidation in the untreated stressed animals were much higher than those that ingested rose oil. Furthermore, oil vapor treated groups had a lower level of peroxidation even than the controls. The researchers concluded that rose oil vapor treatment had a protective effect on oxidative stress in depression.

Sadraei et al. (2012) investigated the effect of rose oil on ileal contractions in experimental rats. The main terpene alcohols geraniol and citronellol were also tested. The results show that the inhibitory effect depends on the applied concentrations of the oil, and its main components geraniol and citronellol have an even more pronounced effect [50].

Umezu (2000) worked on the anti-conflict effect of essential oils of rose, ylang-ylang, chamomile, and orange, by applying commonly accepted tests. In contrast to the others, rose oil shows strong potential in this regard. Compared to the traditional drug diazepam, it has better performance because it is not affected by antagonists (flumazemil) [51].

Three years later, Umezu et al. (2002) focused on rose oil and identified by CG-MS analysis a total of 9 components – myrcene, benzyl alcohol, phenylethyl alcohol, citronellol, geraniol, citronellyl acetate, eugenol, geranyl acetate and eugenol. The authors used the same conflict tests when trying to explain the anti-conflict result with a particular oil constituent. Two of them – phenylethyl alcohol and citronellol – have such an indication. In addition, the two alcohols together showed a similar result to that of the oil in the tests, and on this basis the authors hypothesized that they were the cause of the effect [52].

In a subsequent study, Umezu (2012) presented the evaluation of the effect of 20 different essential oils (including rose) on the central nervous system (CNS) in experimental animals [53]. The findings confirm what was done by Neshev [45] about the ability of rose oil to activate centers of the central nervous system.

Unlike rose oil, rose water is a product with a wide practical application. It contains a small percentage of essential oil and cannot be compared in strength of effects with the concentrate. At the same time, its composition (or more precisely, the composition of the essential oil) is slightly different, and this determines differences in the effect. The main component is phenylethyl alcohol - a carrier of a euphoric or intoxicating, slightly narcotic effect on the psyche [44]. The soothing properties of rose water applied to skin or allergic reactions and

eye inflammations are due to it. In addition to the well-known antimicrobial properties discussed above, rose water can affect the nervous system and brain activity in nervous disorders such as chronic insomnia - the so-called insomnia [46]. Suffering can be a consequence of permanent stress, taking stimulants, hormonal changes, etc. life problems, mental disorders, or even genetic reasons. A demographic study in a clinical setting followed the effect of two types of rose hydrosol (with and without dilution) on female and male patients with chronic insomnia. Within a month, they took oral rose water according to a schedule, and after the third week, 25% of patients treated with the diluted type of water and 66.6% of patients treated with the concentrated type of rose water improved.

The study by Kose et al. (2012) described the protective effect of inhaled rose oil on formaldehyde-induced severe damage to the reproductive system in male rats [54]. Histological samples of the testes of the injured animals showed that in the rose oil-inhaled groups the tissue lesions were very small. In addition, their testosterone levels were higher compared to untreated specimens, but still lower than the control group of healthy animals. This proves the beneficial effect of the oil on the male reproductive system. Its beneficial influence on the female body has long been known.

Antiviral Activities

The antiviral activity of members of this family has not been well studied and information about their impact on viral replication and the mechanism by which it is produced is scarce. The research carried out by different teams in this area opens many perspectives for the study of different products obtained from different vegetative and propagating parts of these so precious plant species.

The effect of aqueous and methanol extracts of *R. damascena* Mill. on HIV infection in vitro was investigated. The activity of the crude extract is thought to be the result of the synergistic action of various compounds whose combination acts at different stages of replication of the virus [55,56].

Phytocomplexes that are extracted from different plant parts of roses are an endless source of molecules with therapeutic potential. Many of these secondary metabolites exhibit antiviral activity that can be expressed in impaired viral reproduction within the host cell at different stages of viral replication or inactivation of extracellular virions. Of the macro components contained in rose oil, monoterpene aldehydes and alcohols such as citral, citronellol, nerol, and eugenol have shown well expressed antiviral potential. *In vitro* antiviral activity of citral is manifested in the blocking of yellow fever virus replication [57]. Citral also inhibits infection with nonenveloped murine norovirus (MNV), the effect depends on the time of exposition and probably is due to nonspecific interaction with extracellular viral particles, which prevents its attachment to sensitive cells [58].

Acyclic terpenoids citronellol and eugenol are most active against the influenza virus after exposure for only 10 minutes. The main components of rose essential oil - nerol, citral, citronellal, citronellol, geraniol, eugenol showed antiviral activity against Herpes simplex virus type-1 (HSV-1) and parainfluenza virus type-3 (PI-3) [59]. Geraniol also shows low antiviral activity versus Coxsackievirus B1 (CVB1) replication with a selective index of 3.9 [60].

Nine compounds isolated from the methanol extract of *R. damascena* Mill. have shown promising anti-HIV activity, with a different mechanism of action on the development of viral progeny. Tetrahydroxyflavanone (kaempferol, 1) selectively inhibits viral protease, and two 3-substituted kaempferol derivatives as well as pentahydroxyflavone (quercetin, 2), inhibit HIV infection by preventing the binding of gp120 to CD4. Irreversible interaction with gp120 also produces 2-phenylethanol-O- (6-O-galloyl) -beta-D-glucopyranoside [61].

The increasing research of the Rosaceae family into the impact on replication of different kinds of viral families could be led to their natural use as antiviral agents. Something more, during the serious epidemic situation, such as Covid19, people have been faced with severe challenges both physical and emotional stress.

Rose essential oils with their valuable therapeutic properties - respiratory antiseptics, anti-inflammatories, mucolytics, antitussives, expectorants, decongestants, antioxidants, can act as symptomatic drugs and potentially help during a Covid 19 infection [62].

Rose Oils in the Treatment of Respiratory Tract Diseases

The antimicrobial potency of rose extracts against respiratory tract pathogens has been investigated from many years. The application technique is variable depending on the symptoms of the disease and the treated area. The commonly used method is inhalation, which significantly decreases oxyhemoglobin concentration and activity in the right prefrontal cortex and increases comfortable feeling conditions. Haze et al. (2002) found that inhalation of rose oil decreases relative sympathetic activity as measured by heart rate variability and low frequency amplitude of systolic blood pressure in healthy adult females [63]. It has been reported that rose essential oil also can be inhaled after sprinkling a drop or two of the oil onto a cloth or tissue. Inhaling essential oil molecules, or absorbing essential oil through the skin, transmits messages to the limbic system - a brain region responsible for controlling emotions and influencing the nervous system. Inhalation of rose oil showed protective effects against damages caused by exposure to formaldehyde in male reproductive system [64,65]. Rose oil also enhanced ileum contractions and gastrointestinal motility in rats [50].

Sadraei et al. reported that hydroalcoholic extract of *R. damascena* Mill. leaf (0.5, 0.75 and 0.75 $\mu\text{g/ml}$), induced contraction in the rat's trachea, aorta, and uterus smooth muscle. Smooth muscle relaxation requires a decreased intracellular calcium concentration and increased myosin phosphatase activity. *R. damascena* has potent relaxant effect on tracheal smooth muscle of guinea pigs that have been produced by β -adrenergic receptors stimulation, inhibition of histamine (H1) receptors or calcium channels [50].

Moreover, ethanolic extract of *R. damascena* has a relatively potent inotropic and chronotropic effect on isolated guinea pig heart that probably is mediated by β -adrenergic receptor stimulation [66]. Also, a potent relaxant effect for ethyl acetate fraction of *R. damascena* (but a relatively weak relaxant effect of aqueous and n-butanol fractions) on tracheal smooth muscles has been shown, which was comparable to the theophylline effect. A combination has been taken from flower bud (known as cyanidin-3-O- β -glucoside) inhibiting the angiotensin-converting enzyme [67]. In addition, *R. damascena* extract at microgram concentrations could show the stimulatory effect on ileum smooth muscles while at milligram concentrations, show an inhibitory effect.

Asthma is a disorder that is caused by chronic inflammation in the airway. One of the most major symptoms of asthma is chronic cough. The effectiveness of rose extracts has been accepted as a popular treatment in asthma [68]. It is accepted that there is a direct correlation between broncho dilating potency and cough inhibition [69]. It has been elucidated that flavonoids have a significant role on cyclooxygenase (COX)-1, (COX)-2, 5-lipoxygenase (5-LOX) and 12-LOX due to their anti-inflammatory effects. Bioflavonoids reduce serum leukotrienes and are therefore recommend in chronic asthma treatment.

Although the inhibition of proinflammatory genes expression suggest the major role of polyphenolic enriched ingredients as immunomodulators, the antioxidative effect of its flavonoids mainly found in alcoholic extracts, may also describe *R. damascena* Mill as a potent analgesic adjuvant in inflammatory states [70].

Other Effects

Rose oil has a lipotropic effect in liver dystrophy [71,72]. Its qualities are known as an epithelizing agent for skin burns, difficult-to-heal wounds or radionecrosis, combined with an analgesic effect [73,74]. Rose oil balances lipid metabolism and this explains its rejuvenating effect [73]. This finding of the cited authors is fully corroborated by subsequent clinical tests. It has

been shown that rose oil decreases the level of total cholesterol, serum triglycerides and lipoproteins with low and very low density, and increases the level of high-density lipoproteins which, as it is well known, exert a protective action regarding the development of atherosclerosis.

According to an anonymous source, taking a combination of Bulgarian rose oil and Bulgarian yogurt (*Lactobacillus*) guarantees an anti-allergic effect (<http://1232healthnews.blogspot.com/2011/09/rose-essential-oil-and-anti-allergic.html> .2013).

In conclusion, natural products have always played a pivotal role in new drug discovery. Due to their valuable therapeutic properties, the studied rose oil species are able to act as symptomatic drugs in the prophylaxis and treatment of many diseases. The described studies suggest the vast possibilities and powerful potential for the application of essential oil, concrete, absolute and rose water in pharmacology and medicine. A great challenge for future research in pharmacology and medical fields could be the study of roses from farms in preclinical and clinical trials.

References

1. Baser K, Altintas A, Kurkcuoglu M. Turkish rose: A review of the history, ethnobotany and modern uses of rose petals, rose oil, rose water and other rose products. *Herbal Gram*. 2012; 96: 40–53.
2. Mahboubi M. *Rosa damascena* as holy ancient herb with novel applications. *J. Tradit. Complement. Med*. 2016; 6: 10–16.
3. Labban L, Thallaj N. The medicinal and pharmacological properties of Damascene Rose (*Rosa damascena*): A review. *Int. J. Herb. Med*. 2020; 8: 33–37.
4. Akram M, Riaz M, Munir N, Akhter N, Zafar S, et al. Chemical constituents, experimental and clinical pharmacology of *Rosa damascena*: A literature review. *J. Pharm. Pharm*. 2020; 72: 161–174.

5. Nazarenko L, Minkov B, Mustyatse G, Murin A. Culture Oil-Bearing Rose. Kishinev: Pulisher Shtinitisa. 1983.
6. Antonelli A, Fabbri C, Giorgioni ME, Bazzocchi R. Characterization of 24 old (true) garden roses from their volatile compositions. *J. Agric. Food Chem.* 1997; 45: 4435–4439.
7. Gudin S. Rose: Genetics and breeding. *Plant. Breed. Rev.* 2000; 17: 159–190.
8. Gochev V, Dobрева A, Girova T, Stoyanova A. Antimicrobial activity of essential oil from *Rosa alba*. *Biotechnol. Biotechnol. Equip.* 2010; 24: 512–515.
9. Kovatcheva N, Zheljzakov VD, Astatkie T. Productivity, oil content, composition, and bioactivity of oil-bearing rose accessions. *HortScience.* 2011; 46: 710–714.
10. Chrubasik C, Roufogalis BD, Müller-Ladner U, Chrubasik S. A systematic review on the *Rosa canina* effect and efficacy profiles. *Phytother. Res. Int. J. Devot. Pharmacol. Toxicol. Eval. Natl. Prod. Deriv.* 2008; 22: 725–733.
11. Dossi CG, Cadagan C, San Martín M, Espinosa A, González-Mañán D, et al. Effects of rosa mosqueta oil supplementation in lipogenic markers associated with prevention of liver steatosis. *Food Funct.* 2017; 8: 832–841.
12. González-Mañán D, D'Espessailles A, Dossi CG, San Martín M, Mancilla RA, et al. Rosa mosqueta oil prevents oxidative stress and inflammation through the upregulation of PPAR- and NRF2 in C57BL/6J mice fed a high-fat diet. *J. Nutr.* 2017; 147: 579–588.
13. Mileva M, Krumova E, Miteva-Staleva J, Kostadinova N, Dobрева A, et al. Chemical compounds, in vitro of antioxidant and antifungal activities of some plant essential oils belonging to Rosaceae family. *Compt. Rend. Acad. Bulg. Sci.* 2014; 67: 1363–1368.
14. Mileva M, Kusovski VK, Krastev DS, Dobрева AM, Galabov AS. Chemical composition, in vitro antiradical and antimicrobial activities of Bulgarian *Rosa alba* L. essential oil against some oral pathogens. *Int. J. Curr. Microbiol. Appl. Sci.* 2014; 3: 11–20.
15. Christov G, Klimentova S. L'eau De Roses Dans Le Traitement De L'amphodontose Et De La Gingivite

- Rosewater in: The Treatment of Amphodontosis and Gingivitis. C R Acad Bulg Sci. 1964; 17: 1125-1128.
16. Erdogan Eliuz EA, Ayas D, Goksen G. In vitro phototoxicity and antimicrobial activity of volatile oil obtained from some aromatic plants. Journal of Essential Oil-Bearing Plants. 2017; 20: 758-768.
 17. Ali B, Al-Wabel NA, Shams S, Ahamad A, Khan SA et al. Essential oils used in aromatherapy: A systemic review. Asian Pacific Journal of Tropical Biomedicine. 2015; 5: 601-611.
 18. Lisin G, Safiyev S, Craker LE. Antimicrobial activity of some essential oils. Acta Horticulture. 1999; 501: 283-288.
 19. Ulusoy S, Boşgelmez-Tınaz G, Seçilmiş-Canbay H. Tocopherol, carotene, phenolic contents, and antibacterial properties of rose essential oil, hydrosol and absolute. Current microbiology. 2009; 59: 554-558.
 20. Gochev V, Wlcek K, Buchbauer G, Stoyanova A, Dobрева A, et al. Comparative evaluation of antimicrobial activity and composition of rose oils from various geographic origins, in particular Bulgarian rose oil. Nat. Prod. Commun. 2008; 3: 1934578X0800300706.
 21. Gochev V, Jirovetz L, Wlcek K, Buchbauer G, Schmidt E, et al. Chemical composition and antimicrobial activity of historical rose oil from Bulgaria. Journal of Essential Oil-Bearing Plants. 2009; 12: 1-6.
 22. Jappe UTA. Pathological mechanisms of acne with special emphasis on Propionibacterium acnes and related therapy. Acta dermato-venereologica. 2003; 83.
 23. Zu Y, Yu H, Liang L, Fu Y, Efferth T, et al. Activities of ten essential oils towards Propionibacterium acnes and PC-3, A-549 and MCF-7 cancer cells. Molecules. 2010; 15: 3200-3210.
 24. Boyanova L, Neshev G. Inhibitory effect of rose oil products on Helicobacter pylori growth in vitro: preliminary report. Journal of medical microbiology. 1999; 48: 705-706.
 25. Basim E, Basim H. Antibacterial activity of Rosa damascena essential oil. Fitoterapia. 2003; 74: 394-396.
 26. Basim H, Basim E, Jones JB, Minsavage GV, Dickstein ER. Bacterial spot of tomato and pepper caused by Xanthomonas

- axonopodis pv. vesicatoria in the western Mediterranean region of Turkey. *Plant Disease*. 2004; 88: 85-85.
27. Gochev V, Dobрева A, Girova T, Stoyanova A. Antimicrobial activity of essential oil from *Rosa alba*. *Biotechnol. Biotechnol. Equip.* 2010; 24: 512–515.
 28. Saleh MA, Clark S, Woodard B, Deolu-Sobogun SA. Antioxidant and free radical scavenging activities of essential oils. *Ethn. Dis.* 2010; 20: 78.
 29. Wei A, Shibamoto T. Antioxidant activities and volatile constituents of various essential oils. *J. Agric. Food Chem.* 2007; 55: 1737–1742.
 30. Yassa, Narguess, Fatemeh Masoomi SE, Rohani Rankouhi, Abbas Hadjiakhoondi. “Chemical Composition and Antioxidant Activity of the Extract and Essential oil of *Rosa damascena* from Iran, Population of Guilan.” *DARU*. 2009; 17: 175-180.
 31. Karamalakova YD, Nikolova GD, Kovacheva N, Zheleva AM, Gadjeva VG. Study of the radical-scavenging activities and radioprotective properties of Bulgarian essential rose oil from *Rosa Damascena* Mill. *Bulg. Chem. Commun.* 2019; 51: 101–107.
 32. Gochev V, Wlcek K, Buchbauer G, Stoyanova A, Dobрева A, et al. Comparative evaluation of antimicrobial activity and composition of rose oils from various geographic origins, in particular Bulgarian rose oil. *Nat. Prod. Commun.* 2008; 3: 1934578X0800300706.
 33. Nair MP, Mahajan S, Reynolds JL, Aalinkeel R, Nair H, et al. The flavonoid quercetin inhibits proinflammatory cytokine (tumor necrosis factor alpha) gene expression in normal peripheral blood mononuclear cells via modulation of the NF- system. *Clin. Vaccine Immunol.* 2006; 13: 319–328.
 34. Khalifa SA, Yosri N, El-Mallah MF, Ghonaim R, Guo Z, et al. Screening for natural and derived bio-active compounds in preclinical and clinical studies: One of the frontlines of fighting the coronaviruses pandemic. *Phytomedicine*. 2021; 85: 153311.
 35. Singh BB, Khorsan R, Vinjamury SP, Der-Martirosian C, Kizhakkeveettil A, et al. Herbal treatments of asthma: A systematic review. *J. Asthma*. 2007; 44: 685–698.

36. Konopačka-Brud I. Aromaterapia dla každého. Studio Astropsychologii. 2002.
37. Tisserand R, Balacs T. Essential Oil Safety: A Guide for Health Care Professionals. Amsterdam: Elsevier Health Sciences. 2013.
38. Neshev G. "Bulgarian rose oil-pharmacological and clinical studies." PhD diss, Medical University. 1990.
39. Boskabady MH, Shafei MN, Saberi Z, Amini S. Pharmacological effects of *Rosa damascena*. Iranian journal of basic medical sciences. 2011; 14: 295.
40. Kheirabadi M, Moghimi A, Rakhshande H, Rassouli MB. Evaluation of the anticonvulsant activities of *Rosa damascena* on the PTZ induced seizures in wistar rats. Journal of Biological Sciences. 2008; 8: 426-430.
41. Fukada M, Kano E, Miyoshi M, Komaki R, Watanabe T. Effect of "rose essential oil" inhalation on stress-induced skin-barrier disruption in rats and humans. Chemical senses. 2012; 37: 347-356.
42. Nazıroğlu M, Kozlu S, Yorgancıgil E, Uğuz AC, Karakuş K. Rose oil (from *Rosa damascena* Mill.) vapor attenuates depression-induced oxidative toxicity in rat brain. Journal of natural medicines. 2013; 67: 152-158.
43. Sadraei H, Shokoohinia Y, Sajjadi S, Ghadirian B. Antispasmodic effect of osthole and Prangos ferulacea extract on rat uterus smooth muscle motility. Research in Pharmaceutical Sciences. 2012; 7: 141-149.
44. Umezu T. Behavioral effects of plant-derived essential oils in the Geller type conflict test in mice. The Japanese Journal of Pharmacology. 2000; 83: 150-153.
45. Umezu T, Ito H, Nagano K, Yamakoshi M, Oouchi H, et al. Anticonflict effects of rose oil and identification of its active constituents. Life sciences. 2002; 72: 91-102.
46. Umezu T. Evaluation of the effects of plant-derived essential oils on central nervous system function using discrete shuttle-type conditioned avoidance response in mice. Phytotherapy Research. 2002; 26: 884-891.
47. Köse E, Sarsılmaz M, Taş U, Kavaklı A, Türk G, et al. Rose oil inhalation protects against formaldehyde-induced testicular damage in rats. Andrologia. 2012; 44: 342-348.

48. Mahmood N, Piacente S, Pizza C, Burke A, Khan AI, et al. The anti-HIV activity and mechanisms of action of pure compounds isolated from *Rosa damascena*. *Biochem. Biophys. Res. Commun.* 1996; 229: 73–79.
49. Boskabady MH, Shafei MN, Saberi Z, Amini S. Pharmacological effects of $\hat{\cdot}$. *Iran. J. Basic Med. Sci.* 2011; 14: 295.
50. Gilling DH, Kitajima M, Torrey JR, Bright KR. Mechanisms of antiviral action of plant antimicrobials against murine norovirus. *Appl. Environ. Microbiol.* 2014; 80: 4898–4910.
51. Vimalanathan S, Hudson J. Anti-influenza virus activity of essential oils and vapors. *Am. J. Essent. Oils Nat. Prod.* 2014; 2: 47–53.
52. Orhan IE, Özçelik B, Kartal M, Kan Y. Antimicrobial, and antiviral effects of essential oils from selected Umbelliferae and Labiatae plants and individual essential oil components. *Turk. J. Biol.* 2012; 36: 239–246.
53. Mileva M, Nikolova I, Nikolova N, Mukova L, Georgieva A, et al. Investigation of antioxidant and antiviral properties of geraniol. *Acta Microbiol. Bulg.* 2015; 31: 48–53.
54. Menezes IA, Barreto CM, Antonioli AR, Santos MR, de Sousa DP. Hypotensive activity of terpenes found in essential oils. *Z. Nat. C.* 2010; 65: 562–566.
55. Loey M, Smarandache F, M Khalifa NE. Within the lack of chest COVID-19 X-ray dataset: a novel detection model based on GAN and deep transfer learning. *Symmetry.* 2020; 12: 651.
56. Haze S, Sakai K, Gozu Y. Effects of fragrance inhalation on sympathetic activity in normal adults. *Jpn. J. Pharmacol.* 2002; 90: 247–253.
57. Köse E, Sarsılmaz M, Taş U, Kavaklı A, Türk G, et al. Rose oil inhalation protects against formaldehyde-induced testicular damage in rats. *Andrologia.* 2012; 44: 342–348.
58. Hongratanaworakit T. Relaxing effect of rose oil on humans. *Nat. Prod. Commun.* 2009; 4: 1934578X0900400226.
59. Rajbhandari M, Mentel R, Jha P, Chaudhary R, Bhattarai S, et al. Antiviral activity of some plants used in Nepalese traditional medicine. *Evid. Based Complement. Altern. Med.* 2009; 6: 328279.

60. Park JC, Kim SC, Choi MR, Song SH, Yoo EJ, et al. Anti-HIV protease activity from rosa family plant extracts and rosamultin from *Rosa rugosa*. *J. Med. Food*. 2005; 8: 107–109.
61. Mahmood N, Piacente S, Pizza C, Burke A, Khan AI, et al. The anti-HIV activity and mechanisms of action of pure compounds isolated from *Rosa damascena*. *Biochem. Biophys. Res. Commun.* 1996; 229: 73–79.
62. Boskabady MH, Shafei MN, Saberi Z, Amini S. Pharmacological effects of *Rosa damascena*. *Iran. J. Basic Med. Sci.* 2011; 14: 295.
63. Gómez LA, Stashenko E, Ocazonez RE. Comparative study on in vitro activities of citral, limonene and essential oils from *Lippia citriodora* and *L. alba* on yellow fever virus. *Nat. Prod. Commun.* 2013; 8: 1934578X1300800230.
64. Kirov M, Burkova T, Kapurdov V, Spavski M. Rose oil, lipotropic effect in modeled fatty dystrophy of the liver (morphological and enzymohistochemical study), *Medico Biologic Information*. 1988; 3: 18-22.
65. Mechkov G, Kirov M, Yankov B, Georgiev P, Marinova V, et al. Girosital, Hypolipidaemic effect in cholelithiasis and liver steatosis, *Medico Biologic Information*. 1988; 3: 26-29.
66. Kirov M, Vankov S. Rose, rose oil and "Girosital", *Medicina i fizkultura*. 1986.
67. Hajhashemi V, Ghannadi A, Hajiloo M. Analgesic and anti-inflammatory effects of *Rosa damascena* hydroalcoholic extract and its essential oil in animal models. *Iranian journal of pharmaceutical research: IJPR*. 2010; 9: 163.