

Rosa Damascena pharmacological effects and therapeutic use

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The Bulgarian Rosa Damascena, cultivated for over 300 years, is considered to be the best oil-bearing rose and is renowned worldwide. The Bulgarian Rose oil and Rose Water are distilled from the species Rosa Damascena Mill., subfamily - Rosoideae, family - Rosaceae. The cultivation of essential plants and especially of the oil-yielding Rosa Damascena in Bulgaria started around the end of the sixteenth century and beginning of the seventeenth century. The oil-yielding rose is very sensitive to different climatic and soil conditions in terms of production of high quality rose essential oil. In Bulgaria, the best area for growing roses is the Kazanlak area, called the Valley of Roses. Shaded by the slopes of two majestic mountain ranges, the Balkan Mountain and Sredna Gora, the Valley of Roses has the exclusively favorable geographical and climatic conditions for growing and harvesting the oil-yielding rose. The Valley of Roses is considered to have the best soil structure, air humidity, cloudiness and precipitation for obtaining the finest and most sought-after rose oil in the world. Bulgaria is known in the world as the land of roses.

There are several main products received from the Rosa Damascena. **Rose oil** is extracted from rose blossoms of Rosa Damascena through water distillation. Its fragrance is extremely potent. The Rose oil is extracted from the fresh flowers, picked before 8 am in the morning, by steam distillation and the yield is 0.02 -0.05 %. The heat used in the distillation process is carefully controlled, as the aroma can be damaged if the heat is too high. **Rose Concrete** is obtained from the fresh flowers of the Bulgarian oil-bearing rose (Rosa Damascena) through petroleum-ether extraction. **Absolute** is extracted from rose concrete. It is a red liquid mainly used in perfumery. **Natural rose water** is a by-product obtained during the distillation process of rose oil and contains 0.04 up to 0.05 per cent of pure rose oil.

Main chemical components of the rose oil distilled from Rosa Damascena Mill

The rose oil contains more than 275 macro and micro components. The main chemical components of rose oil are acyclic monoterpene alcohols, geraniol (up to 75%), citronellol (20%) and nerol (20%), and long-chain hydrocarbons like nonadecane or heneicosane (up to 10%). An important trace component of rose oil is β -damascenone: Despite its low concentration (0.01%), that C13-norisoprenoid has notable influence on the quality of the oil; together with the structurally related compounds β -damascone and β -ionone, it is enzymatically generated from carotenoids. Similarly, in both saffron and pandanus leaves, the dominant aroma molecules derive from enzymatic degradation of carotenoids.

Beta-Damascenone and another rose ketone, beta-Damascone, are two of the most important chemicals in the fragrance and flavoring industries. Citronellol and Damascenone are responsible for many of the rose oil's therapeutic properties. Characteristic of the fresh flower's scent is 2-phenyl ethanol, which is lost during steam distillation but accumulates in the rose water. Thus, rose oil and rose water do not equal each other exactly.

History of medicinal use of Rosa Damascena

Besides its well known role as a major ingredient of perfumery, rose oil has a history of medicinal use dating back at least five thousand years. The millennial history of the medicinal use of Rosa Damascena is described in detail by Kirov and Vankov (1). The use of the rose is wide and varied. The rose oil, along with other rose products, is a valuable medicinal agent. The beginning of its history should be traced to the cradle of human civilization. Hippocrates and his disciples (5th and 6th cent. B.C.) used rose products extensively in their curative practice in vapor baths, sitting water baths and suppositories.

Incense therapy with burning aromatic oils and resins was a characteristic feature of Hippocrates medicine. It was carried out with sweet-scented and repulsively smelling substances, and was used in the treatment of infectious and non-infectious diseases, and for curing the atmosphere of “miasmas”. This age-old practice which comes from the antiquity, and is linked to religious practice, has a sanitary and hygienic effect of its own. Only recently studies in the field of microbiology have shown that volatile oils, oleum rosae in particular, have bacteriostatic and bactericidal effect on a large number of Gram-positive and Gram-negative microorganisms.

In ancient Greek medicine the rose preparations were largely a privilege of the female sex. Rose preparations were applied mainly in cosmetics, gynecology and obstetrics. Rose ointment (pomade, cream) was extensively used for the removal of freckles. In case of alopecia frictions of the head with rose oil and incense were prescribed. Rose preparations were applied in the treatment of female sterility, uterine bleeding, dysmenorrhoea, leukorrhoea, aphthae of the genital organs, uterine ulcers, inflammation of the uterus, etc., and in obstetrics - for speeding up childbirth and post-delivery lochia cleansing.

Egyptian papyruses reveal that in ancient Egypt rose oil was considered a universal medicinal agent. Various rose products were essential constituents of the balms used for mummifying bodies.

Numerous and most variegated were the rose preparations applied by Avicenna. The rose honey (julanjubin) and sugar or honey sweetened rose water (julep) were used widely and were most characteristic of Arab medicine in general. Rose leaves, the juice of fresh rose leaves, rose syrup, attar of roses, and occasionally rose fruits, were likewise implemented. Julanjubin was recommended in febrile conditions and stomach pain, but it owed its fame primarily to its administration as an agent for treatment of pulmonary tuberculosis. This fame of julanjubin was preserved up to the first half of the twentieth century. Julep has a many-

sided use, being particularly indicated in febrility, gastric ulcer and gastrointestinal disorders for purging the gastrointestinal tract. On rose oil Avicenna wrote: “This oil augments the strength of brain and the quickness of wit”. Attar of roses was applied for headache, caused by a variety of factors: febrile conditions, sun and heat strokes, alcohol abuse, injuries and concussion of the brain, migraine, etc. For patients presenting open head wounds with skull and brain injuries Avicenna recommended warm rose oil. It was also applied to wounds with nerve exposure or lesion.

In the “Bruxelles Code IV 1024” emphasis was laid on the tonic action of rose preparations - “Rose water has the quality to invigorate and strengthen (the body)”. Dried rose powder inhalation was thought to strengthen the brain and heart, and to elevate the spirits. The analeptic effect of rose water is also mentioned - patients with heart diseases, susceptible to collapse, were advised to drink rose water. Rose juice was prescribed in erythema and skin burns. The cosmetic effect of rose water was particularly stressed - face washing with rose water was thought to improve the turgor and complexion of the skin.

Mathiolus recommended the juice of fresh roses as a mild agent for purging the bowels, blood purification, in jaundice, tachycardia, febrility, syncope, heat edemas and uterine hemorrhages; externally - in toothache, aphthae in the mouth and burns. Rose water was especially indicated in eye inflammations. The author pointed out that rose syrup strengthens the heart’s action, and copes with its “fibrillation”. Tabernemontanus also makes reference to the cardiotonic effect of rose preparations. Von Heller praised highly the rose as a tonicum - a remedy that restores enfeebled function and promotes the vigor of the heart and nerves.

The rose proves to be the favorite drug agent of folk healers. The oil of rose has traditionally been used in medicine. Today its application in treating various health problems is even larger and to a greater effect. Leaves, water and attar are equally utilized. A number of

therapeutic effects including hypnotic, antispasmodic, treatment of abdominal and chest pain and strengthening the heart have been described for the flowers of Rosa Damascena. It has a long history in its use in folk remedies in the area of skincare. It is suitable for all skin types, but it is especially valuable for dry, sensitive or aging skins. It has a tonic and astringent effect on the capillaries just below the skin surface, which makes it useful in diminishing the redness caused by enlarged capillaries. It is important to ensure that the product contains the genuine natural rose oil. Synthetic rose ingredients have no therapeutic value at all. Rose water is a less expensive way to provide skincare. It is a natural cosmetic product for cleaning and refreshing the skin. It is soothing to irritated skin and it is also a tonic and antiseptic.

There is an indication that rose essence may also positively influence digestion, bile secretion, womb disorders and circulation. In addition, a tea made with rose petals (150 ml of boiling water per 0.5 grams of rose petals) often soothes a mild sore throat. For emotional wellness, rose oil may also be used in a room diffuser.

Rose hips (the flowers which have swollen to seed) are an excellent source of vitamins A, B3, C, D and E. They also contain bioflavonoids, citric acid, flavonoids, fructose, malic acid, tannins and zinc. Taken in the form of tea they are good for infections, particularly bladder infections. It is an especially good source of vitamin C. A typical folk recipe for rose hip tea recommends to roughly chop up rose hips, cover with distilled or purified water, boil for 30 minutes (longer if desired), and strain through a fine strainer or cheesecloth, adding a bit of honey if desired. One can often find Rose hip tea in the local health food stores.

The Bulgarian pharmacotherapeutic theory and practice have their deep roots in the folk medicine. The founders of the pharmacotherapy in this country, prof. V. Alexiev and prof. P. Nikolov, have devoted considerable time and effort to investigate the experience of Bulgarian folk medicine and of the Bulgarian medicinal plants. V. Alexiev binds his name to the rose through the preparation rosalipchin, while P. Nikolov undertakes the first

experimental pharmacological study of rose preparations. In the pre-antibiotic era, V. Alexiev was successful in attaining remarkable results with rosaliipchin in the treatment of bronchial asthma, pulmonary abscesses and pulmonary tuberculosis.

The essence of rose need not only be used to treat ailments. Whether inhaled and enjoyed from a freshly cut bouquet of sumptuous blooms or splashed on as rose water after a shower or bath, it is simply a pleasure to be enjoyed by all.

Rose oil (attar of roses) is an indispensable ingredient in virtually all fine perfumes made by most famous producers like Christian Dior, Givenchy, Lancôme, Bulgari, Chanel. Modern cosmetics are unthinkable without rose oil. A gram of rose oil is as valuable as a gram of gold. It is a very expensive product which is of best quality and finest aroma when grown in particular areas. It is the Bulgarian-grown rose which is the most aromatic one. Every beginner in the fragrance industry knows that the top quality rose oil is produced in Bulgaria. Bulgarian rose oil named liquid gold is a glory and a pride of Bulgaria. The greatest experts in perfumery and cosmetics are unanimous in affirming that there is no modern and top-quality perfume without Bulgarian attar of roses, since it is unique in terms of quality. Its unparalleled aroma derives from the exclusively complex composition of more than 275 macro- and micro components and from their optimal proportion and combination.

Pharmacokinetic and toxicological data

The pharmacokinetic studies on rose oil show that after oral administration it accumulates in the liver. The accumulation process begins as early as the first hour to reach its maximum within 8 hrs of administration. Rose oil excretion occurs mainly by the kidneys (1). All available clinical studies show that rose oil is very well tolerated by the patients - no side effects have been reported and recorded. Toxicological studies characterize rose oil as a

substance with low toxicity. LD 50 for mice after oral administration amounts to 680 ± 80 mg/kg b.w.; for rats after intra peritoneal application of 437 ± 85 mg/kg, and per os for male rats 5525 mg/kg, and for female rats 2975 mg/kg. The assessment of rose oil for subacute toxicity shows that during per oral treatment of rats at the dose of 85 mg/kg over a 30-day period, it does not lead to intoxication phenomena. There are no toxic manifestations, neither in terms of the general state and behavior of animals, nor on behalf of the parenchymatous organs (2). Rose oil has no embryotoxic or teratogenic action and, therefore, it may be taken by pregnant women with no hazards to the fetus (3).

Pharmacological data

The earliest pharmacological studies in Bulgaria were conducted by prof. P. Nikolov, the founder of the Bulgarian Pharmacological School. The results were reflected in his classical treatise entitled “The Rose as a Medicine”, published in 1941. Later, during the 70-ies, academician A. Maleev continued the research into attar of roses and its pharmacology, toxicology, chemotherapeutic, pharmacokinetics and clinical effects. Contributions to the biological characterization of rose oil were made also by other Bulgarian scientists: N. Avramov, V. Todorov, G. Hristov, M. Kirov, M. Spasovsky, K. Rusinov, T. Tashev et al. (1).

Rosa Damascena is one of the most important *Rosa* species for the flavor and fragrance industries that has been traditionally used for centuries as a scent with relaxant and anxiolytic effects. *Rosa* leaves are used as choleric and laxative and several therapeutic effects such as hypnotic, antispasmodic and relaxant are utilized for the treatment of abdominal and chest pain. Inotropic effects on the heart have been described for the flowers of *Rosa Damascena*. Recent studies show that *Rosa Damascena* has anti-inflammatory, anti-HIV, antioxidant and antibacterial activities, hepatoprotective and antitussive effects. The toxicological studies have confirmed its safety.

Antimicrobial and anti-inflammatory effect

For centuries, the rose and rose products have been successfully used in the treatment of inflammatory diseases of the eyes, ears, throat, mouth, lungs, dysentery, erysipelas, infected wounds, eczema, herpes etc. The undisputed anti-inflammatory effect of the rose was scientifically explained in the past two decades. The credit for this goes to Bulgarian microbiologists who were successful in discovering the antimicrobial effect exerted by the rose and its products.

Rose concrete, in the form of 1 per cent Rosalin ointment, is implemented in dermatological practice for the treatment of un-healing wounds, resistant to other forms of treatment, varicose leg ulcers, decubital ulcers, radionecroses, radiodermatitis, all types of burns, etc. The favorable therapeutic effect of Rosalin in un-healing wounds results from a multimodal effect exerted on the disease process, namely: antiseptic, local anesthetic, anti-inflammatory and stimulation of regenerative processes in the damaged tissue. There is an ever increasing amount of data pointing to the fact that rose products enhance the regenerative capacity of tissues. Studies carried out by P. Nikolov, G. Hristov, A. Maleev, V. Gruncharov, V. Petkov and other Bulgarian and foreign researchers, have contributed greatly to the clarification of the antimicrobial properties of rose water and rose oil.

Rose water and rose oil have a marked antimicrobial effect on streptococci, staphylococci, diphtheria and coli group bacteria and bacillus anthracis. Microorganisms and bacterial strains resistant to the antibiotics used in routine clinical practice are also affected by the rose preparations. The effect of rose water and rose oil on Gram-positive microorganisms is bactericidal in nature, and on Gram-negative ones - bacteriostatic. Rose preparations have a number of advantages - they are very well tolerated by the body and the risk of allergic reactions is nil.

Rose absolute and essential oil contain high levels of phenolics and demonstrate strong antibacterial activity against *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Staphylococcus aureus*, *Chromobacterium violaceum* and *Erwinia carotovora* strains (5). Antimicrobial activity of *Rosa Damascena* against *Staphylococcus aureus* has been reported (6).

The products of *Rosa Damascena* are used in stomatology. Rose oil drip applied into the cavity of carious teeth, brings about pain relief lasting 3-4 hours. Rose water is used in periodontosis. The healing effect occurs very quickly: gingival bleeding and pain and concomitant inflammatory phenomena subside within 3-4 treatments; loose teeth get stabilized and the gums restore their normal turgor and color; the foul odor of the mouth disappears.

Rose water, rose concrete and rose oil are employed in the preparation of a paste for treatment of pulpitis, and for filling the canals of carious teeth. The paste has a high bactericidal activity. The microorganisms - streptococci, staphylococci and coli bacteria, are killed in the course of 5 min. The cavities of carious teeth treated with the paste are free of bacterial infection, and pain relief occurs after the first treatment session. Rose derived products are used in a mouthwash for gingivitis (7).

Study of the antimicrobial activity of a plant-derived extract (2 percent *Rosa Damascena* extract) with 5.25 percent sodium hypochlorite (NaOCl) and 2 percent chlorhexidine (CHX) on selected endodontic pathogens has been performed. It was established that all solutions were able to kill all test microorganisms after one minute (8).

Rose concrete has a favorable effect in vasomotor and other forms of rhinitis.

Eye diseases are the most frequent indication for the application of rose preparations. Rose water has been shown to be very valuable as an antiseptic for the treatment of eye infections and cataracts (4).

The essential oil of *Rosa Damascena* petals was evaluated for its antibacterial effects against three strains of *Xanthomonas axonopodis* spp. *vesicatoria*. The essential oil may be a potential control agent in the management of the disease caused by *X.a. vesicatoria* in tomato and pepper plants (9).

Water and methanol extracts of *Rosa Damascena* exhibited moderate anti-HIV (human immunodeficiency virus) activity. The anti-viral activities of 9 compounds isolated from the methanol extract were compared. The tetrahydroxyflavanone (kaempferol, 1) was effective in reducing the maturation of infectious progeny virus apparently due to selective inhibition of the viral protease. On the other hand, the pentahydroxyflavone (quercetin, 2) and two 3-substituted derivatives of kaempferol appeared to inhibit HIV-infection by preventing binding of gp120 to CD4. 2-Phenylethanol-O-(6-O-galloyl)-beta-D-glucopyranoside 8 interacted irreversibly with gp120 and neutralized virus infectivity. The differences in the modes of action of 1 and 8 can account for the apparent synergy of their anti-viral activities (10). To identify substances with anti-HIV activity from plant sources, 12 extracts of *Rosa* family plants were screened for their inhibitory effects against HIV-1 protease. Of the extracts tested, the strongest inhibitory effects were observed in the root of *Rosa rugosa* and the leaves of *Prunus sargentii*, at a concentration of 100 microg/mL. Rosamultin isolated from the root of *R. rugosa* inhibited HIV-1 protease by 53% at a concentration of 100 microM (11).

Rose hip has previously shown clinical efficacy in the treatment of osteoarthritis, and organic solvent extracts of rose hip have showed inhibition of cyclooxygenase-1 and -2. A petroleum ether extract of rose hip was fractionated by VLC on silica; on a C-18 column and by HPLC. Each step was COX-1/2 activity-guided. The bioassay-guided fractionation led to the isolation of linoleic acid. The COX-2/COX-1 ratio was 0.007 for linoleic acid and 0.2 for alpha-linolenic acid. Linoleic acid and alpha-linolenic acid contribute to the COX-1 and -2 inhibitory activity of rose hip (12).

Respiratory system

For the respiratory system Damask rose oil assists in cases of asthma, coughs and hay fever (13). The relaxant effects of ethanol extract and essential oils of *Rosa Damascena* on tracheal chains of guinea pigs were examined and compared with theophylline. The results showed a potent relaxant effect of *Rosa Damascena* on tracheal chains of guinea pigs that was comparable to that of theophylline (14).

Effects on the CNS

Damask rose oil soothes and harmonizes the mind and helps with depression, anger, grief, fear, nervous tension and stress. It addresses sexuality, self-nurturing, self esteem and dealing with emotional problems. Rose oil exerts a neurotropic effect. Introduced by subcutaneous and intraperitoneal route into frogs, mice and rats, it inhibits the CNS - decreases the motor activity, potentiates the narcotic effects of hexobarbital, alcohol and chloral hydrate; inhibits amphetamine stereotypy; averts the development of corazol-, strychnine- and electric-induced convulsions (1).

Electroencephalographic studies likewise point to CNS suppression and synchronization of the bioelectrical activity of the brain at cortical and subcortical level. An inhibition of the alpha-rhythm and desynchronization of the cortical bioelectric activity, an expression of activated reticular formation, are documented electroencephalographically. However, the results of investigations on healthy and mentally ill persons indicate that rose perfume stimulates CNS activity - the dreams become more frequent, more vivid and lasting.

To investigate the anxiolytic effects of prolonged rose odor exposure, mature gerbils were exposed to acute (24 h), chronic (2 week) rose odor, or a no odor condition. Anxiolytic effects were assessed using the elevated plus-maze and black white box. Rose odor profiles

were compared with diazepam (1 mg/kg intraperitoneally). In the black white box, rose oil had anxiolytic, spatiotemporal, and exploratory behavior effects. This anxiolytic profile strengthened after chronic exposure to rose odor as evidenced by increase in transitions between the compartments ($U=167$, $p<0.01$) and percentage of time moving around the arena ($U=154$, $p<0.001$). This profile was more representative of some serotonergic agents, rather than benzodiazepine type drugs (15).

Anxiolytic-like properties of rose oil observed using the elevated plus-maze (EPM) test is consistent with other behavioral and clinical studies (16). The effect of rose oil inhalation (1.0%, 2.5%, and 5.0% w/w) on the elevated plus-maze (EPM) test was investigated in adult male rats and compared with the effect of diazepam (DZP) (1.0 and 2.0 mg/kg) administered intraperitoneally 30 min before testing. Exposure to rose oil produced an anxiolytic-like effect similar to DZP (anxiolytic reference drug). At some concentrations, rose oil significantly increased the number of visits to and time spent in the open arms of the EPM.

The pharmacological actions of four different plant-derived essential oils (**rose**, ylang-ylang, and camomile, orange) in two types of conflict tests in mice were examined. In the Vogel conflict test, in which any drinking behavior of the mice was punished by an electric shock, the benzodiazepine agonist, diazepam increased the number of electric shocks the mice received. This number increased after administration of rose oil. Similarly, the response rate during the alarm period increased after administration of rose oil. In the Vogel conflict test, the anticonflict effect of diazepam was reversed by the benzodiazepine antagonist, flumazenil (Ro15-1788). However, the effect of rose oil in this test was not antagonized by flumazenil. This study showed that rose oil possesses anticonflict effects, and that the effects are not mediated by the benzodiazepine binding site of the GABA(A) receptor complex (17).

The investigation of the pharmacologically active constituents of rose oil, which possesses anti-conflict action was carried out. GC/MS analysis revealed that rose oil contains

9 substances that were identified as myrcene, benzyl alcohol, 2-phenethyl alcohol, citronellol, geraniol, citronellyl acetate, eugenol, geranyl acetate and methyl eugenol. The effects of each of these substances were examined by the Geller and Vogel conflict tests in mice. The authors founded that Myrcene, benzyl alcohol and citronellyl acetate did not produce any effects in these tests. Geranyl acetate and methyl eugenol produced no effect in the Geller conflict test. Geraniol and eugenol decreased the response rate during the safe period of the Geller conflict test, but did not affect the response rate during the alarm period. In contrast, 2-phenethyl alcohol and citronellol, like rose oil, produced an increasing effect on the response rate during the alarm period in the Geller conflict test. Both substances increased the number of electric shocks mice received in the Vogel conflict test in a manner similar to that of rose oil. Given that 2-phenethyl alcohol and citronellol produced the same anti-conflict effects in both tests as rose oil, the authors concluded that they are the pharmacologically active constituents of anti-anxiety-like effect of rose oil (18).

Rosa Damascena inhibits the reactivity of the hypothalamus and pituitary systems in rat. In traditional medicine hypnotic effect of Rose is also suggested. The hypnotic effect of ethanol, aqueous and chloroform extracts of *Rosa Damascena* was investigated in mice. The results showed that the ethanol and aqueous extracts in 500 and 1000 mg/kg doses significantly increased pentobarbital induced sleeping time which was comparable to diazepam (19).

The effect of *Rosa Damascena* Mill essential oil on the development of induced amygdala kindling seizures on male Wistar rats implanted with one tripolar and two monopolar electrodes in right basolateral amygdala and dura surface respectively was studied. The results suggest that *Rosa Damascena* essential oil significantly retarded the development of seizure stages and possessed the ability to counteract kindling acquisition. The flavonoids of *Rosa Damascena* may act via GABA(A) receptors as previous studies have proposed for

flavonoids of other medicinal plants. More detailed studies are recommended to define the effective component(s) of Rosa on different types of epilepsy (20).

Metabolic effects

The effect of a methanol extract of Rosa Damascena Mill. flowers was studied in normal and diabetic rats and compared to the alpha-glucosidase inhibitor acarbose. The inhibition mode of this extract was examined by measuring enzyme activity in different concentrations of substrate. The results showed that Rosa Damascena extract has an intensive inhibitory effect on alpha-glucosidase. Its inhibition was found to be noncompetitive. Oral administration of this plant extract (100 to 1000 mg/kg body wt) significantly decreased blood glucose after maltose loading in normal and diabetic rats in a dose-dependent manner. These results suggest that Rosa Damascena might exert an anti-diabetic effect by suppressing carbohydrate absorption from the intestine and can reduce the postprandial glucose level (21)

Gastrointestinal tract

Rose preparations are widely used in the treatment of digestive system diseases: cheilitis, stomatitis, fetor ex ore (halitosis), loss of appetite, gastritis, gastric ulcer, colitis, constipation, etc. In ulcerative colitis, rose oil enema and rose syrup given per os are being used. Rose oil application in the management of hemorrhoids and anal fissures is widespread. In liver diseases fresh rose juice is prescribed. There is an indication that rose essence may also positively influence digestion, bile secretion, and circulation. In addition, a tea made with rose petals often soothes a mild sore throat. The white rose blossom in the form of powder, or mixed with honey, is recommended in the treatment of habitual constipation. Pulvis laxantes compositus is used for treatment of enterobiosis.

Rose oil exerts a potent spasmolytic effect on the smooth muscles of the gastrointestinal tract. At a concentration of 100mcg/ml it causes a strong reduction of tonus and complete disappearance of the peristaltic movements in an isolated segment of rabbit small intestine. The spasmolytic effect of rose oil becomes manifest also with regard to spasms caused by a great number of spasmogens, such as acetylcholine, arecoline, cholinesterase inhibitors, serotonin, histamine and barium chloride. The spasmolytic effect of rose oil is attributed mainly to the direct myotropic action for the development of which, however, the cholinolytic, antihistamine and antiserotonine effects of rose oil also contribute (22).

Rose oil has a marked ulceroprotective effect regarding the gastric mucosa. Introduced per os into rats with experimentally histamine-induced ulcers, at a dose of 255 mg/kg, rose oil precludes the development of ulcers in 70 per cent of the test animals, whereas all of the controls present gastric ulcers. As it is well known, Arab physicians used extensively rose water and rose honey in the treatment of gastritis and stomach ulcer. The ulceroprotective effect of rose oil shows that rose preparations may prove helpful in the present day therapy of ulcers and, therefore, they should be employed in clinical practice (23).

In folk medicine rose oil has been applied in the treatment of liver and gall-bladder diseases. Experimental and clinical studies show that it exerts a strong choleric effect. In experiments, using rats with cannulated ductus choledochus, rose oil administered at a dose of 5 drops daily over a 12-day period, augments the total volume of bile secretion for 24 hours by 120 per cent, lipids - by 93.2 per cent, cholic acid - by 111.8 per cent and inorganic phosphorus - by 180.4 per cent. The reported data indicate that rose oil stimulates the excretion of both the liquid phase of bile, and its basic constituents by the liver cells. The latter effect of attar of roses has been demonstrated in humans using radioactive iodine-labeled Bengal rose. Under the effect of rose oil the radioactivity in the duodenum is

increased which in turn points to an enhanced secretion of hepatic and bladder bile into the duodenum (24).

The choleric effect of Bulgarian Rose oil is investigated after cannulating the main biliary duct. The total quantity of the bile secreted after administration of rose oil increased by 120% in comparison with the controls. Because of its good choleric effect Bulgarian rose oil may be recommended as a therapeutic agent in the diseases of liver, gallbladder and bile ducts (dyscholia, cholelithiasis and its complications, cholecystitis, cholangitis and biliary dyskinesias (25). In vivo and in vitro experiments, the cholinolytic action of rosanol which plays an essential role in the mechanism of gastrointestinal motility-inhibiting effect, was proved (26).

The Rose oil has been found to be a potent inhibitor of *Helicobacter pylori*. Boyanova, L. and Neshev, G. evaluated for the first time the effect of Bulgarian rose oil preparations on *H. pylori* growth *in vitro*. Both rose oil and geraniol showed considerable activity against *H. Pylori*. Rose oil and geraniol at concentrations of 2 mg/L inhibited the growth of 85.7% and 92% of the strains, respectively. The inhibitory properties of Bulgarian rose oil preparations may be related to their major component of aliphatic alcohols (27).

There is an ever increasing amount of data pointing to the fact that rose products enhance the regenerative capacity of tissues. Studies by M. Kirov et al. indicate that Girosital (a combination of rose oil, sunflower seed oil and Vitamin A) prevents steatosis and improves the regeneration of the hepatocytes in the liver of rats, treated with ethyl alcohol. Hence, it is reasonable to presume that Girosital, which combines the effects of attar of roses and vitamin A, may exert a favorable effect also in the event of chronic lesions of the liver parenchyma (28, 29, 30).

At present, there is some clinical evidence that rose oil is an efficient agent in the treatment of cholelithiasis and chronic inflammation of the bile ducts - pain is promptly

relieved, crisis episodes become less frequent and dyspeptic phenomena, hepatomegaly and subfebrile temperature subside. The therapeutic effect is produced by its spasmolytic, sedative, analgetic, anti-inflammatory and laxative pharmacodynamic action..

Antioxidative properties

Park et al. (31) evaluated the antioxidant activity of two different solvent fractions (butanol and hexane) obtained from white *Rosa Rugosa* flowers by employing various assays such as 2,2-diphenyl-1-picrylhydrazyl hydrate (DPPH), 2,2'-azino-bis(3-ethylbenzthiazoline-6-sulfonic acid) (ABTS) radical scavenging activity, and nitric oxide (NO) scavenging and inhibition activity in S-nitroso-N-acetylpenicillamine (SNAP) in the RAW264.7 model. In addition, more advanced antioxidant assays were conducted, including lipid peroxidation, hydroxyl radical-mediated oxidation, DNA fragmentation, apoptosis, and cell growth. The results revealed that the hexane fraction, which contained a significant amount of polyphenols and volatile components, had excellent antioxidant potency and could scavenge free radicals of DPPH and ABTS. Interestingly, the hexane fraction inhibited lipid peroxidation to almost the same degree as a chemical antioxidant. In the NO assay, the hexane fraction effectively scavenged free radicals at all dose ranges and is expected to inhibit NO production in mammalian cells. Based on the findings described in this study the authors concluded that the hexane fraction holds promise for use as a novel pharmaceutical antioxidant.

The effects of *Rosa Rugosa* (*Rosa Rugosa* Thunb) on lipid peroxidation, alanine transaminase (ALT), aspartate transaminase (AST), glutathione and protein oxidation levels in male Wistar rats treated with carbon tetrachloride (CCl₄) were investigated (32). The rats in the *Rosa Rugosa* group were found to have significantly lower liver peroxide, protein oxidation, glutathione levels and plasma ALT and AST activities compared with the rats in

the CCl₄ treated control group. These findings suggest that Rosa Rugosa possesses antioxidant activity.

Antioxidant activities of essential oil mixtures, thyme or clove leaf with cinnamon leaf, **rose**, or parsley seed, toward skin lipid, squalene oxidized by UV irradiation were investigated using the malonaldehyde/gas chromatography assay(33). At all concentrations (50, 100, or 500 mug/mL) tested, thyme oil mixed with 500 mug/mL clove oil showed over 90% inhibitory effect against malonaldehyde formation. Pro-oxidant effects were observed for some mixtures of thyme with cinnamon leaf or rose oils. The potent antioxidant effects resulting from a mixture of thyme and clove leaf oils may be due to the presence of thymol and eugenol.

Antioxidant potential of Rosa L. leaves methanolic extracts was evaluated in vitro using a spectrophotometric method based on measuring the radical scavenging effect on 2,2-di-phenyl-1-picrylhydrazyl (DPPH) radicals(34). The contents of ellagic acid, quercetin and kaempferol in the extracts from leaves of seventeen rose species were determined using SPE-RP-HPLC methods. Significant correlation between ellagic acid ($r(2) = 0.6131$), quercetin ($r(2) = 0.5158$), total phenolic content ($r(2) = 0.8485$) and antioxidant activity was observed. Basing on the studies conducted one may assume that the extracts of rose leaves are a rich source of natural antioxidants and could be used to prevent free-radical-induced deleterious effects.

Effects on the cardiovascular system

It has been established that Rosanol averts fatal disturbances of the cardiac rhythm induced by calcium dichloride and prevents the onset of severe changes on the electrocardiogram provoked by a high-frequency electric stimulation of the mesencephalic reticular formation and by an intravenous administration of high doses of norepinepharine

(36). The authors of this study made an attempt to explain this antiarrhythmic effect of rosanol by attributing it to stabilization of the membranous potential. Rosanol may be most helpful for poor circulation and heart problems, which would include heart palpitations, arrhythmia as well as high blood pressure.

Pharmacological studies along this line reveal some interesting effects of rose oil on the cardiovascular system of experimental animals. Injected i.v. into urethan-treated cats, it induces a short-lasting blood pressure fall. Rose oil in a dose of 30 mg/kg inhibits the hypertensive reaction of norepinephrine, and copes with the inotropic effect of isoproterenol on the myocardium; it prevents the contraction of the third eyelid in cats, produced by i.v. injection of epinephrine, cytoton and electrostimulation of the preganglionic fibers of the superior cervical sympathetic ganglion; in cats subjected to Feldberg's evisceration it reduces the hypertensive reaction, caused by the administration of acetylcholine in the upper mesenteric artery and n. splanchnicus electrostimulation. The presented data disclose a rich pharmacological effect of attar of roses, namely - its adrenergic blocking and ganglioplegic action.

Aromatherapy writers have stated that rose oil has a pronounced effect on the circulatory system, promoting circulation, cleansing the blood, relieving heart congestion, and toning the capillaries. One study validating this claim found that Girosital, a capsule containing 68 milligrams of Bulgarian rose oil, 30,000 IU vitamin A and 250 milligrams sunflower seed oil administered twice daily before meals for one hundred ten days had a marked hypolipidemic effect and reduced arterial hypertension. The remedy was tolerated well, with no side effects or contraindications for its use (35).

The antiarrhythmic activity of rose oil has great theoretical and practical implications. It is rather marked in the experimental arrhythmia model, produced by calcium bichloride. Rose oil has a life-saving effect when introduced i.v. at a dose of 30 mg/kg in the stage of

cardiac arrest of the animal - blood pressure nil and absence of electrical activity. Rose oil injection in the described condition leads to a slow restoration of ECG and blood pressure, which regain their normal values within 30 to 40 mm. An appreciable antiarrhythmic effect is exerted by the rose oil also in case of arrhythmia caused by norepinephrine and electrostimulation of the mesencephalic reticular formation (36).

These recent data concerning the regulatory effect of rose oil on the 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”.

Hypolipidemic effect

The lipotropic effect of rose oil was discovered by M. Kirov et al. (37, 38). It is thought that by regulating lipid metabolism in the liver, rose oil may affect the serum lipoprotein level and thereby, exert a favorable effect on the various types of hyperlipoproteinemia, considered as a risk factor in atherosclerosis and in the development of ischemic heart disease. This hypothesis 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. The presented experimental and clinical results reveal a new, unknown aspect of attar of rose pharmacodynamics. New prospects are opened for both prophylactic and therapeutic application of rose oil, particularly in the field of cardiovascular diseases and geriatrics.

Rose Oil Based Products

A number of medicinal products based on rose oil are created and applied successfully in the clinical practice in Bulgaria.

Rosaline

Rose concrete, in the form of 1% rosaline ointment, is implemented in dermatological practice for the treatment of un-healing wounds, resistant to other forms of treatment, varicose leg ulcers, decubital ulcers, radionecroses, radiodermatitis, all types of burns, etc. The favorable therapeutic effect of rosaline in un-healing wounds results from the many sided effect exerted on the disease process, namely: antiseptic, local anesthetic, anti-inflammatory action and stimulation of regenerative processes in the damaged tissue.

Girosital

Capsule containing 68 milligrams of Bulgarian rose oil, 30,000 IU vitamin A and 250 milligrams sunflower seed oil.

The lipotropic effect of Girosital were discovered by M. Kirov et al. (37, 38). Girosital affects the serum lipoprotein level and exerts a favorable effect on the various types of hyperlipoproteinemia, considered as a risk factor in atherosclerosis and in the development of ischemic heart disease. It has been shown that Girosital decreases the level of total cholesterol, triglycerides and lipoproteins with low and very low density, and increases the level of high density lipoproteins. The hypolipidemic effect of Girosital occurs promptly. After the third week, a considerable reduction of serum lipids and lipid fractions is recorded, with an ensuing weaker slower and gradual decrease. Girosital is an example of how a substance, used as an irreplaceable medicinal agent for many centuries and then forgotten, is reestablished, revealing unsuspected curative qualities, and regaining its due place in the

therapeutic practice. Girosital becomes invaluable in the prophylaxis and treatment of the aging processes in man.

Rosanol

Capsule, containing Rose oil 34.4 mg.

Indications: holelithiasis, chronic cholecystitis, dyskinesia of the biliary tract, post cholecistectomy, nephrolithiasis.

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