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Phytochemical composition and *in vitro* pharmacological activity of rose hip (*Rosa canina* L.)

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ABSTRACT

Rose hip (Rosa canina L.) Commonly known as the dog-rose, is a variable climbing wild rose species native to Europe, northwest Africa and western Asia. The aim of this study is to review its phytochemical composition and in vitro pharmacological activity. This review article was carried out by searching studies in PubMed, Medline, , Web of Science, and IranMedex databases up to 2016.totally, of 103 found articles,40 articles(42 in vitro and 5 animal studies) were included. The search terms were "Rose hip (Rosa canina L)","therapeutic", "pharmacological", Phytochemical .Various studies have shown that Rose hip (Rosa canina L.) Possess Antioxidant properties, Antibacterial and anti-cancer properties, Skin care properties, Antioxidant, anti-inflammatory and cytotoxic activity, Renal disturbances ,Anticancer properties, Anti-inflammatory properties, Hydro alcohol properties, melanogenesis properties, Pharmacological activity ,Anti-obese properties, Neutrophil respiratory burst, Chryptoxanthin properties, Immunomodulatory properties, Osteoarthritis properties, Antidiabetic properties, Hepatoprotective, Antidiarrheal properties. Rose hip (Rosa canina L.) is widely used for therapeutic and purposes that trigger its significant value. Various combinations and numerous medicinal properties of its extract, essential oils, its stems and leaves demand further and more studies about the other useful and unknown properties of this multipurpose plant.

Keywords: rose hip (Rosa canina L.), "therapeutic", "pharmacological", Phytochemical

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INTRODUCTION

It is proved that herbal medicine is effective in the treatment of many diseases[1-10].

Rosa canina, commonly known as the dog-rose, is a variable climbing wild rose species native to Europe, northwest Africa and western Asia. It is a deciduous shrub normally ranging in height from 1–5 m, though sometimes it can scramble higher into the crowns of taller trees. Its stems are covered with small, sharp, hooked prickles, which aid it in climbing. The leaves are pinnate, with 5-7 leaflets [11]. The flowers are usually pale pink, but can vary between a deep pink and white. They are 4–6 cm diameter with five petals, and mature into an oval 1.5–2 cm red-orange fruit, or hip [12].

The plant is high in certain antioxidants. The fruit is noted for its high vitamin C level and is used to make syrup, tea and marmalade. It has been grown or encouraged in the wild for the production of vitamin C, from its fruit [often as rose-hip syrup], especially during conditions of scarcity or during wartime. In the traditional Austrian medicine *Rosa canina* fruits have been used internally as tea for treatment of viral infections and disorders

of the kidneys and urinary tract. The hips are used as a flavoring in Cockta, a soft drink made in Slovenia. Forms of this plant are used as stocks for the grafting or budding of cultivated roses. The wild plant is used for stabilizing soil in land reclamation and specialized landscaping schemes. Numerous cultivars have been named, though few are common in cultivation. The cultivar *Rosa canina* 'Assisiensis' is the only dog rose without prickles [13-15].

Skin care

The effects of a rose hip powder made from seeds and shells on cell senescence, skin wrinkling, and aging was evaluated. Results suggest that intake of the standardized rose hip powder improves aging-induced skin conditions. The apparent stabilizing effects of the rose hip product on cell membranes of stored erythrocyte cells observed in this study may contribute to improve the cell longevity and obstructing skin aging [11].

The compounds present in rose hips exerting an inhibitory action against melanogenesis in B16 mouse melanoma cells were investigated by dividing an aqueous extract of rose hips [RE] into four fractions. The result suggest that proanthocyanidins from RE inhibited melanogenesis in mouse melanoma cells and guinea pig skin, and could be useful as a skin-whitening agent when taken orally [12].

Phytochemical characterization of secondary metabolites of black currant, dog rose and silver linden bud extracts was evaluated .The Tiliatomentosa extracts contained flavonols as principal components with the exception of a single commercial extract with hydroxycinnamic acids as the most abundant metabolites. Without applying accelerated ageing protocols, the stability over time of these liquid preparations was evaluated for up to 10 months and demonstrated negligible variations[13].

Antioxidant

The effect of dog rose (*Rosa canina* L.; RC), rich in polyphenols and ascorbic acid, on lipid and protein oxidation, colour stability and texture of frankfurters was investigated. Hexanal values were much higher throughout storage in NC compared to RC and PC frankfurters ($P<0.001$). The RC extracts protected against protein oxidation, but not as efficiently as PC ($P<0.05$). In the RC treated frankfurters, lower a* values were measured compared to PC due to the lack of sodium nitrite. In conclusion, dog rose can act as a natural antioxidant in frankfurters, but not as full replacer for sodium nitrite(14).

Canina fruit extracts were examined in a study. *R. canina* showed antioxidant activities at all concentrations with respect to the reducing power, hydrogen peroxide scavenging activity and superoxide anion radical scavenging ($O2(\circ:-)$) activity assays, whereas a negative correlation was observed with the metal ion chelating activity and free radical scavenging activity [1,1-diphenyl-2-picryl-hydrazil (DPPH) % inhibition] assays at higher concentrations with the phenolic content of *R. canina*. These results suggest that *R. canina* may act not only as an antioxidant, but also as a prooxidant with the effects depending on its concentrations [15].

Two new commercially available high linolenic oils, pressed at low temperature from rose hip seeds, were characterised for their composition, quality and DPPH radical scavenging activity. The oxidative stability of oils was assessed using differential scanning calorimetry (DSC). Phytosterols, tocopherols and carotenoids contents were up to 6485.4; 1124.7; and 107.7 mg/kg, respectively. Phenolic compounds determined for the first time in rose hip oil totalled up to 783.55 μg/kg, with a predominant presence of p-coumaric acid methyl ester. Antiradical activity of the oils reached up to 3.00 mM/kg TEAC. The acid, peroxide and p-anisidine values as well as iron and copper contents indicated good quality of the oils. Relatively high protection against oxidative stress in the oils seemed to be a result of their high antioxidant capacity and the level of unsaturation of fatty acids [16].

the amount of the main phytochemicals (vitamin C, total polyphenols, and total flavonoids) content and their antioxidant activity was evaluated. Eight Rose hip fruit species were compared taking into consideration the ascorbic acid, total polyphenols, total flavonoids contents and their antioxidant activity. Based on these results, two of the rosehip genotypes that were analysed could be of perspective for these species' amelioration, due to their content of phytochemicals mentioned above. These varieties are var. *transitoria f. ramosissima* (Bistrita-Nasaud, Agiesel) and var. *transitoria f. montivaga* (Bistrita-Nasaud, Salva) which can be used as a potential source of natural antioxidants [17].

Rose hip (*Rosa canina)* has been used as an herbal remedy against a wide range of ailments including inflammatory disorders. The anti-inflammatory and antioxidant properties of rose hips have been evaluated in vitro and active

constituents have been isolated. Rose hip contains antioxidant nutrients and an anti-inflammatory galactolipid. Rheumatoid arthritis (RA) is an inflammatory disease where activated cells release reactive oxygen substances. Thus it could be relevant to investigate if rose hip had an anti-inflammatory and/or antioxidant effect in this situation.

10.5 g Litozin in 28 days had neither effect on clinical symptoms or laboratory measurements in patients with RA or healthy controls. This is in contrast to previous intervention studies with rose hip powder that found a reduction in the concentration of CRP. The results of the present study indicate that a daily amount of approximately 10 g rose hip powder for one month has no anti-inflammatory and/or antioxidant effect [18].

Anticancer

the biosynthesis of zinc oxide (ZnO) NPs by both "conventional heating" (CH) and "microwave irradiation" (MI) methods has been reported. Stable and spherical ZnONPs were produced using zinc nitrate and flesh extract of Rosa canina fruit (rosehip) which was used as a precursor. The flesh extract acts as a reducing and capping agent for generation of ZnONPs. The structural, morphological and colloidal properties of the as-synthesized NPs have been confirmed by X-ray Diffraction (XRD), Scanning Electron Microscopy (SEM), Energy Dispersive X-ray (EDX), Fourier transform Infrared (FT-IR) and Dynamic Light Scattering (DLS). In comparison with the CH method, the MI method has some advantages such as significantly short reaction time (within 8min) owing to the high heating rate and thus the accelerated reaction rate. Both methods led to the synthesis of nearly identical NPs with respect to shape and size according to the results of DLS, XRD and SEM techniques. The possible mechanism for synthesis pathway has been proposed based on FT IR results, XRD patterns, potentiometric data and antioxidant activity. In addition, the antibacterial activity of as-prepared ZnONPs was investigated against several bacteria such as Listeria monocytogenes, Escherichia coli, Salmonella typhimurium. Moreover, the efficacy of ZnONPs to treat cancer cell lines were measured by means of cell viability test via MTT assay in which concentrations of 0.05 and 0.1mg/mL of ZnONPs induced a very low toxicity. Thus, the present investigation reveals that ZnONPs have the potential for various medical and industrial applications [19].

Antioxidant, anti-inflammatory and cytotoxic activity

Phenolic profile, vitamin C content, antioxidant, anti-inflammatory and cytotoxic activity of rose hips was compared. Purée of *R. canina* exerted cytotoxic activity only against the HeLa cell line among several others (HeLa, MCF7, HT-29 and MRC-5). The results support traditional use of rose hips and their fruit preserves as food with health and nutritional benefits [20].

Renal disturbances

The effects of *Rosa canina* L fruit extracts on histological damages, oxidative stress, and functional disturbances induced by bilateral renal ischemia and reperfusion was examined. The kidney tissues were collected and subjected to microscopic study for histological damages, while oxidative stress was measured by determining malondialdehyde and ferric reducing/antioxidant power levels. The findings of this study showed that *Rosa canina* fruit extract possesses protective effects against kidney function disturbances, oxidative stress, and histological damages [21].

Anticancer

The commercial development of plants as sources of antioxidants that can be used to enhance the properties of foods, for nutritional purposes and preservation as well as for prevention of oxidation-related diseases, is currently of major interest. Rosehip (*Rosa canina* L.) is a rich source of vitamin C and polyphenols. The results of this study confirm that vitamin C and flavonoids are responsible for the antioxidant activity of rosehip tea, while only polyphenols contribute to its antiproliferative activity(22).

Anti-inflammatory

In the present study the anti-inflammatory and the gastroprotective effects of a hydroalcoholic crude extract of Rosa canina fruits were tested in rat. Altogether, the present data demonstrate the anti-inflammatory property of Rosa canina suggesting its potential role as adjuvant therapeutic tool for the management of inflammatory-related diseases [23].

Hydro alcohol

This research evaluated the possible therapeutic potential of *Rosa canina* (RC) as a preventive agent in experimentally induced calcium oxalate (CaOx) nephrolithiasis with ethylene glycol (1% EG) in rats. In this

experiment, 50 Wistar rats were divided randomly into five groups (n = 10). These groups received tap drinking water (group I), 1% EG (group II), 250 mg/kg RC + 1% EG (group III), 500 mg/kg RC + 1% EG (group IV), or 2.5 g/kg potassium citrate + 1% EG (group V) for a period of 30 days. Blood and urine were collected for biochemical analysis, and the liver and kidneys were prepared for total lipid peroxides, calcium content and histological evaluation. The extract was analysed for total phenolics, flavonoids, ascorbic acid, citric acid and radical scavenger activity. The supplementation of the hydromethanol RC extract contributed to reducing the kidney and liver lipid peroxides to optimum levels in rats that had been treated with EG-induced CaOxlithiasis. The extract also decreased renal and urinary calcium contents, decreased the size and number of CaOx calculi in the kidneys, and significantly increased citrate excretion without changing the volume, pH, or urinary concentrations of oxalate in comparison with the control group. According to these results, RC can be useful as a preventive agent against the formation of CaOx kidney stones[24].

The effects of compounds isolated from a methanolic extract of rose hips on melanin biosynthesis in B16 mouse melanoma cells was investigated . Resul showed that quercetin was a particularly potent melanogenesis inhibitor. To reveal the mechanism for this inhibition, the effects on tyrosinase of B16 mouse melanoma were measured. Quercetin decreased the intracellular tyrosinase activity as well as the tyrosinase activity in a cell culture-free system. (25).

The genotoxic effects of cypermethrin and fenvalerate were examined with the micronucleus (MN) test. According to the results, cypermethrin and fenvalerate have genotoxic effects, the water and ethanol extracts of rosehip reduced the genotoxicity of the both insecticides(26).

Pharmacological activity

Powdered rose hip with and without fruits (Rosaepseudofructus cum/sine fructibus, Rosa canina L., Rosaceae) was compared with regard to their phytochemical profile and their in vitro anti-inflammatory and radical-scavenging properties. Result suggest that lipophilic constituents might play a more important role for the observed in vitro inhibitory activity on arachidonic acid metabolism. extracts derived from powdered rose hip without fruits were more effective in all assays carried out compared with extracts derived from powdered rose hip with fruits(27).

Anti-obesity

The 80% aqueous acetone extracts from the fruit (50 mg/kg/d) and seeds (12.5 and 25 mg/kg/d) of *Rosa canina* L., but not from the pericarps, were found to show substantial inhibitory effect on the gain of body weight and/or weight of visceral fat without affecting food intake in mice for 2 weeks after administration of the extracts. The results indicate the importance of both kaempferol 3-O-beta-D-glucopyranoside and p-coumaroyl moieties for anti-obese effects. Furthermore, a single oral administration of trans-tiliroside at a dose of 10 mg/kg increased the expression of PPAR-alpha mRNA of liver tissue in mice [28].

The main benefit of supercritical FE with CO2 is the solvent free oil while in the case of other extractions evaporation of the solvent is needed. Although the content of bioactive compounds in oils was different, all oils may be appropriate for medicinal use [29].

Neutrophil respiratory burst

Antioxidative properties of the polyphenolic contained in rose hips was evaluated. The results showed that the extract can inhibit ROS tested in acellular and cellular systems. The IC(50) obtained were 5.73 mg/L, 1.33 mg/L and 2.34 mg/L respectively for (O(2)(o-)), HOCl and H(2)O(2) in acellular experiments. For cellular experiments, the IC(50) were quite similar. Thus, the extract did not present an effect on PMN metabolism. Therefore, the antioxidative effects of Rosa canina are due not only to vitamin C but also to polyphenolics [30].

Chryptoxanthin

The carotenoid composition of fruits of *Rosa canina* (Rosaceae) was determined comparatively by thin-layer chromatography (TLC) and high-performance liquid chromatography (HPLC) in total extracts and in three different fractions derived from previous separation of the total fruit extract on alumina columns. The distribution of these compounds was reproducible by TLC and by HPLC. The I-III fractions eluted successively from alumina columns by increasing the polarity of the solvents were analysed also by TLC and HPLC. In all situations, carotenoids were better separated and identified by gradient HPLC systems than by isocratic HPLC or TLC [31].

Immunomodulatory
studies revealed that only oleanolic acid and ursolic acid, but not betulinic acid, could inhibit the lipopolysaccharide induced interleukin-6 release from Mono Mac 6 cells when tested separately. Combination of either oleanolic acid or ursolic acid with betulinic acid enhanced the immunomodulatory effect of the two triterpene acids [32].

Osteoarthritis
Although based on a sparse amount of data, the results of the present meta-analysis indicate that rosehip powder does reduce pain; accordingly it may be of interest as a nutraceutical, although its efficacy and safety need evaluation and independent replication in a future large-scale/long-term trial [33].

The impact of standardized rose-hip powder on mobility of the hip and knee joints, activities of daily living, quality of life, and pain in patients with osteoarthritis was assessed. Standardized rose-hip powder reduced symptoms of osteoarthritis, as 64.6% of patients reported at least some reduction of pain while receiving treatment. Standardized rose-hip powder may improve hip flexion and reduce pain in patients with osteoarthritis [34].

The efficacy ofa herbal remedy made from a subspecies of rose-hip (*Rosa canina*) on reducing symptoms of osteoarthritis and consumption of rescue medication in patients suffering from osteoarthritis was determined. The result suggest that the present herbal remedy can alleviate symptoms of osteoarthritis and reduce the consumption of 'rescue medication [35].

An identical pattern was observed when general wellbeing from the diary records was evaluated. When patients, on the basis of reduction in joint pain, were divided into responders and non-responders, the first 3 months of active treatment (group A) showed a response rate of 31/47 (66%) compared to that of placebo (group B) [36].

Antidiabetic
The in vitro mechanism of action of *R canina*in managing diabetes mellitus was evaluated. The results obtained from current study confirmed that *R canina*extract can act as a growth factor for pancreatic β-cell line providing a novel mechanism for the observed antidiabetic effect of this natural agent. Further preclinical studies are necessary to evaluate the perfect mechanism of action of *R canina*in diabetes mellitus [37].

Hepatoprotective
The hepatoprotective activity of hydro-ethanolic fruit extract of *Rosa canina* (R. canina) against carbon tetrachloride (CCl4)-induced hepatotoxicity in rats was investigated. finding indicated hepatoprotective effects of the hydro-alcoholic fruit extract of *R. canina* on CCl4-induced hepatic damage in rats and suggested that these effects may be produced through reducing oxidative stress (38).

The extraction parameters such as extraction time (30-90 min), temperature (30-50 °C) and solvent concentration (40-100% ethanol, v/v) was examined. All of the parameters (ethanol concentration, extraction time and extraction temperature) used in this research have the significant effect on the extraction efficiency of total phenolic content in rosehip extracts ($P < 0.05$). The solvent concentration was proved to be the most significant effective on the yields obtained by ultrasound-assisted extraction [39].

Antidiarrheal Activity
The effect of the leaf extract of *Rosa canina* L. against experimental diarrhea induced by castor oil in rodents was investigated. The presence of some of the phytochemicals in the leaf extract may be responsible for the observed effects, and also the basis for its use in traditional medicine as an antidiarrheal drug(40).

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