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Review article

Traditional and Recent Evidence on Five Phytopharmaceuticals from *Rosa damascena* Herrm.

Forough Afsari Sardari[1], Ghazaleh Mosleh[2], Amir Azadi[3], Abdolali Mohagheghzadeh[2,4], Parmis Badr[4,5*]

[1]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran.
[2]Department of Phytopharmaceuticals (Traditional Pharmacy), Shiraz University of Medical Sciences, Shiraz, Iran.
[3]Department of Pharmaceutics, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.
[4]Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.
[5]Phytopharmaceutical Technology and Traditional Medicine Incubator, Shiraz University of Medical Sciences, Shiraz, Iran.

Abstract

Damask rose or *Rosa damascena* Herrm. is one of the most widely-used medicinal herbs in Iranian Traditional Medicine (ITM). Because of different types of phytochemicals such as flavonoids, glycosides, terpenes, and anthocyanins, *R. damascena* flowers have a wide range of pharmacological effects. Five traditional *Rosa* phytopharmaceuticals are "Golangebin"/ "Golqand*"* (the mixture of petals in honey/sugar), "Jollab", rose oil, rose water, and rose syrup. In the current study, traditional information about these phytopharmaceuticals was extracted from three medieval manuscripts including "Al-Shamil fi al-Tibb" (13th century AD), "Qarabadin Salehi" (1766), and "Qarabadin Kabir" (1780). Articles on *R. damascena* petal were found by searching Pubmed, Scopus, and Google Scholar till June 2018. They were mainly related to effectiveness on CNS and GI systems. Numerous studies have been performed to evaluate the efficacy and safety of *R. damascena* extracts and essential oil, but little has been focused on these phytopharmaceuticals as complementary therapies for the mentioned effects. Comparing recent findings and traditional knowledge of these *R. damascena* phytopharmaceuticals shows a wide gap between these two viewpoints. Therefore, numerous opportunities are provided to evaluate traditional therapeutic notions about *R. damascena* phytopharmaceuticals leading to increase for their chances of application.

Keywords: *Rosa damascena*; Iranian Traditional Medicine; phytopharmaceutical

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Introduction

Damask rose or *Rosa*×*damascena* Herrm. (*R. damascena*), the well-known ornamental plant of Rosaceae family, is a hybrid derived from *Rosa gallica* and *Rosa moschata* [1]. Eastern Mediterranean region has been the origin for *R. damascena*, and Iran had traditionally a major role in preparation and export of its products. For instance, during 810-817 AD, the Faristan province of Iran was exporting 30000 bottles of rose water to Baghdad annually [2]. The images of rose flower on ancient gold woven cloths reflect the existence and importance of *R. damascena* in Iran [3]. The value of this economically important species is due to its fine fragrance, rose oil, rose water, and rose concrete [4].

Edible flowers of *R. damascena* are enormously applied in beverages or dishes of salads, soups, and desserts. For instance, they are the main ingredients of different types of "Zhourat*"*, a

*Corresponding author: badrp@sums.ac.ir

Middle Eastern herbal tea [5,6]. Because of different types of phytochemicals such as flavonoids, glycosides, terpenes, and anthocyanins, *R. damascena* flowers have a wide range of pharmacological effects. Also, various constituents like citronellol, nonadecane, geraniol, and henicosane have been reported in its essential oil, which has a dramatic medical effect, especially in aromatherapy [7,8]. Many studies have supported antimicrobial, anti-inflammatory and anti-oxidant activity of *R. damascena* [7].

This plant is one of the most widely-used medicinal herbs in Iranian Traditional Medicine (ITM). One earlier manuscript of ITM from 10th century, "Alabniyat an Haqayeq Aladviyeh" by Abou Mansour Ali Al-Heravi, has stated antipyretic, anti-obstructive, and cholagogue effects for *R. damascena* [9]. *Rosa* flowers, specifically the petals, were used in various traditional multi-component formulations like "Javarish" and "Majoun", however, they were the main component of traditional *Rosa* phytopharmaceuticals including "Golangebin"/ "Golqand", "Jollab", rose oil, rose water, and rose syrup [10]. These formulations which are prepared with simple pharmaceutical processes have potential of commercialization. Therefore, this study has been performed to find out traditional profile (ingredients, preparation method, temperament, usage, and dosage) of five *Rosa* phytopharmaceuticals, and the recent related animal and clinical studies.

Method

Traditional information of five phytopharmaceuticals from *R. damascena* was extracted from three medieval manuscripts including "Al-Shamil fi al-Tibb" (The comprehensive book on medicine) by Ibn al-Nafis (13th century AD), "Qarabadin Salehi" (1766) by Ghaeni Heravi, and "Qarabadin Kabir" (1780) by Aghili Shirazi. "Al-Shamil fi al-Tibb" has explained the effects and detailed mechanisms of actions for natural products, and Qarabadins are pharmacopoeias which have introduced mono- and multi-component medications, their ingredients and preparation methods, their effects, adverse effects, temperaments, and dosage. Then, articles on *R. damascena* petals and products were found by searching Pubmed, Scopus, and Google Scholar till June 2018. Traditionally, these five *Rosa* formulations were effective on central nervous system (CNS) and gastrointestinal (GI) disorders, fever, pain, and wound. Therefore, irrelevant articles to these effects were excluded. Recent findings were categorized based on clinical and animal studies.

Results and Discussion

Detailed traditional profiles of five Rose phytopharmaceuticals including "Golangebin"/"Golqand", "Jollab", rose oil, rose water, and rose syrup are summarized in table 1 and 2.

1. "Golangebin"/ "Golqand": a mixture of *R. damascena* petals with honey or sugar is called "Golangebin" or "Golqand", respectively. The proportion of rose petals to sugar in "Golqand" can be selected among 1:1, 1:2, or 1:4, but 1:2 was mentioned the most desirable one. Golangebin has been launched in the official market of herbal medicine, and is prescribed as a laxative, suitable for pregnant women and children over the age of two [11]. One of the most popular ethnic nutraceutical in Pakistan is "Golqand", which is applied as a tonic, cooling agent "Mobarred", and laxative, but it is prepared with *R. moschata* Herrm. or *R. indica* petals and sugar [12-14]. As an ayurvedic preparation, "Golqand" is traditionally used for fatigue, lethargy, muscular aches, biliousness itching, and heat-related conditions. It is used in milk shakes, cakes and pastries to improve the flavor [15].

2. "Jollab": Rose water, sugar, and saffron as a flavoring agent are ingredients of "Jollab". Its temperament is balanced i.e. hot and cold elements likewise wet and dry elements are the same in quantity (H^0 W^0), and this beverage has been traditionally suggested for colitis, gastralgia, and fever (table 2). Drinking 15 mL "Jollab" trice daily has significantly alleviated the severity and frequency of dyspepsia symptoms. Moreover, this dosage has improved depression scores in dyspeptic patients [16,17]. However, anti-depressant effect of "Jollab" may be attributed to saffron, one of its ingredients.

3. Rose oil: There are two traditional methods for preparation of rose oil. According to the most common method, fresh rose petals are macerated in sesame oil and kept under sunlight. After five days, they are removed, pressed, and substituted with fresh petals. Maceration step can be repeated up to seven times. Through the second method, fresh petals are ground and pressed to obtain rose extract, which is added to sesame oil.

Table 1. Traditional profile of *Rosa* Phytopharmaceuticals

Product	Temperament	Dosage	Ingredients	Preparation method
Golangebin	H^2D^2	25 g	Rose petals (1) + honey (1)	40 Days in sunlight, being stirred daily
Golqand	H^2W^0		Rose petals (1) + sugar (1 or 2 or 4)	3 Days in sunlight, being stirred daily
Jollab*	H^0W^0	nm	Rose water (3) + sugar (1) + saffron	Cooked with low heat until halved
Rose oil	nm**	< 40 g	Rose petals + sesame oil (enough to cover)	Up to 7 Times, rose petals are changed after decoloration.
Rose water	C^1W^0	100 g	Rose petals + water (enough to cover)	Distillation of rose petals
Rose syrup*	nm**	70 g	Rose petals (1) + rose water (12) + sugar (1)	Cooked with low heat until halved**,** then filtered

Temperaments have been introduced as H (hot), C (cold), D (dry), and W (wet); degrees have been presented with numbers in superscripts, for instance H^2D^2 means hot and dry in second degree; *different formulations of "Jollab*"* and rose syrup were found, but just one sample has been mentioned; ** not mentioned; dosage calculations: "Golangebin"/"Golqand" (5 "Misqal" × 5 = 25 g); rose oil (1 "Oqieh" × 37.5 = 37.5 g); rose water (20 "Misqal" × 5 = 100 g); rose syrup (1 to 2 "Oqieh" × 37.5 = 37.5 to 75 g)

Table 2. Effects of five *Rosa damascena* phytopharmaceuticals based on three traditional manuscripts. Disorders and effects were categorized to main groups of CNS and GI, and others that were limitedly related to heart, fever, pain, urinary tract, and wound.

Disorders or Effects		Golangebin	Jollab	Rose oil	Rose water	Rose syrup
CNS	Headache			◆	◆	◆
	Intoxication		◆		◆	
	Syncope				◆	◆
	Tonic	◆		◆	◆	
GI	Carminative	◆				
	Colitis	◆	◆			
	Cooling			◆	◆	◆
	Desiccant	◆				◆
	Digestive	◆				◆
	Dysentery			◆		
	Emesis				◆	
	Enteralgia			◆		
	Gastralgia		◆		◆	
	Gastritis			◆		◆
	Gripe	◆				
	Hepatalgia				◆	
	Laxative					◆
	Liver tonic	◆				◆
	Stomachic	◆		◆		◆
Other	Cardiotonic				◆	◆
	Fever	◆	◆			◆
	Pain			◆		
	Urinary retention	◆				
	Wound			◆		

This mixture is heated gently until evaporation of aqueous phase [18,19]. Rose oil has been marketed and prescribed for hemorrhoid. A soft gel formulation effective on gastritis and IBS symptoms has been also commercialized [11].

4. Rose water: This product from *R. damascena* contains 0.025-0.074% v/w of essential oil, with 2-phenylethanol, citronellol, geraniol, nerol, and linalool as the main components [20]. Rose water is widely used in topical formulations like rose water ointment that is beneficial for skin lesions such as acne or black heads [21,22]. A synergic effect of rose water with retinol has been reported leading to significant decrease of lesion count and acne grade [23]. As table 2 presents, rose water has been traditionally suggested for different types e.g. gastralgia, and hepatalgia. Among all five *R. damascena* phytopharmrceuticals, rose water is both a CNS tonic and a cardiotonic.

5. Rose syrup*:* This product can be prepared with either fresh petals (3 parts) or dry ones (1 part). The exact temperament of Rose syrup has not been mentioned in traditional manuscripts, however the cooling (refrigerant) and desiccant effect of this syrup along with its indication for fevers (table 2) may be some reasons for its coldness and dryness. It has mainly gastric effects. As a digestive and stomachic, rose syrup has been advised for gastritis. Clinical and animal studies relevant to traditional usages have been summarized in tables 3 and 4.

Table 3. Clinical trial studies relevant to traditionally-mentioned effects of *Rosa damascena*

	Clinical trials				
	Method	**Participants**	**Interventions**	**Outcomes**	**Ref**
1	Double-blind, placebo-controlled, cross-over	16 children (3-13 YO) with unequivocal seizure refractory to current antiepileptic drugs	RD EO 10% v/v in oil, 5 mg/kg/dose, 3 times daily, 4 weeks	Significant reduction of daily seizure frequency after oil consumption	[25]
2	Double-blind, randomized clinical trial, cross-over	40 patients (18-65 YO) with at least 2 migraine headache per month	RD petals 20% w/w in sesame oil, placebo: paraffin + 0.1% RD EO, 2 ml on forehead and temporal zones at onset of attacks, no massage	No significant difference between pain intensity (VAS) in 2 groups	[26]
3	Before- after pilot study	25 patients (18-55 YO) with at least three migraine attacks per month	1st phase: propranolol 20 mg (twice daily) for 45 days, 2nd phase: "Golangebin" (5mg morning, 10mg at night) plus propronolol	20% decrease in headache frequency compared to first phase, no significant change in intensity and duration of attacks	[27]
4	Controlled pre-test, post-test study	20 male futsal players	RD EO (3 drops aromatherapy, 8 hours, 4 nights), control group received nothing	No significant effects on sleep quality	[28]
5	Pre-test, post-test study	30 children (5-12 YO) with sleep disorder, not taking hypnotic drugs	RD EO 10%, aromatherapy 20 min every night	Effective on resistance to sleep and difficult waking, but no significant change in fatigue	[29]
6	Double-blind, placebo-controlled, randomized clinical trial	160 patients (18-65 YO) with functional dyspepsia	"Jollab" (15 mL, 3 times daily, after meal, 1 month), placebo: rose water in water (1:10)	Significant improvement in scores (beck depression inventory questionnaire)	[17]
7	Double-blind, placebo-controlled, randomized clinical trial	160 patients (18-65 YO) with functional dyspepsia	"Jollab" (15 mL, 3 times daily, after meal, 4 weeks), placebo: rose water in water (1:10)	Significant alleviation of severity and frequency of symptoms (SF- Leeds dyspepsia questionnaire)	[16]
8	Placebo-controlled, randomized clinical trial	120 women (18-35 YO) in 12-33 gestational weeks of pregnancy with low-back pain (VAS score ≥ 3)	RD oil (7 drops topically on 100 cm^2 painful part of body, 2 times daily, 4 weeks), placebo: almond oil, control: no intervention	Significant decrease in VAS score of treatment group, but significant increase in VAS score of control group	[30]
9	Placebo-controlled, randomized clinical trial	50 patients (18-65 YO) with second or third degree burn wound	RD EO 40% in water, 5 drops, 20 min aromatherapy for 2 days, placebo: water	Significant decrease in pain level after dressing in experimental group	[31]
10	Double-blind, placebo-controlled clinical trial	64 hospitalized children (3-6 YO) for surgery	RD EO, 2 drops aromatherapy after surgery, placebo: almond aroma	Significant time-associated decrease in post-operative acute pain intensity of RD group	[32]

EO: essential oil, ip: intraperitoneal; RD: *Rosa damascena*; YO: years old

"Golangebin"/ "Golqand", rose oil, and rose water are CNS tonics. Rose syrup and Rose water are suggested to raise consciousness after syncope. Moreover, "Jollab" and "rose water" are effective for loss of consciousness due to alcohol intoxication [10,18]. Since the main ingredient of "Jollab" is rose water, their similar effect is justifiable. *Rosa damascena* extract has shown a dose-dependent improvement of memory and spatial learning [33]. Both animal and clinical studies have proved anti-seizure effect of essential oil causing significant reduction of daily seizure frequency [25,34]. Anti-depressant property of *R. damascena* extract has been shown in animal studies [36,37]. Although topical usage of rose oil is traditionally suggested for headache, the concentration of 20% w/w has shown no significant difference with placebo in patients with migraine headache [26]. This can be due to its application without rubbing.

Golangebin and rose syrup are two digestive formulations which are also liver tonic. Traditional products of *R. damascena* improve the function of body organs. They act as stomachic, brain tonic, and cardiotonic. Recent animal studies have proved laxative effect of aqueous *R. damascena* extracts [40,41]. Rose syrup has been traditionally prescribed for this effect.

Topical application of rose oil is suggested for wound healing. *Rosa damascena* essential oil and extracts of rose petals like aqueous and ethanol extracts have shown broad-spectrum antimicrobial activity against Gram-positive,

Gram-negative bacteria and fungi [43]. Moreover, hydroalcoholic extract of *R. damascena* has shown strong free radical scavenging capacity and this herb has been introduced as a source of antioxidants [44,45]. Because antimicrobial activity and antioxidant property promote wound healing process, this effect can be justifiable for *R. damascena*. However, no clinical or animal study was found to confirm the wound-healing effect of rose oil.

Table 4. Animal studies relevant to traditionally-mentioned effects of *Rosa damascena*

	Animal studies			
	Assessment	**Method**	**Outcomes**	**Ref**
1	Spatial learning and memory improvement of RD extract in rats	6 groups (n=10): normal saline, 300 mg/kg RD extract, 600 mg/kg, 1200 mg/kg, control, sham, 1 month orally	Dose-dependent improvement of memory and spatial learning by RD extract using Morris water maze behavioral test	[33]
2	Anti-seizure effect of RD EO in rats	3 groups (n=8): 750mg/kg RD EO, 1000 mg/kg RD EO, normal saline & tween, ip injection, 30 before a daily kindling stimulation, once daily	Significantly larger number of stimulations required for 1st, 2nd, and 3rd stages of seizures in experimental groups, significantly shorter duration of 5th stage of seizure of fully-kindled rats in experimental groups	[34]
3	Potentiation of pentobarbital induced sleeping time in mice	10 groups (n=8): 100, 500, 1000 mg/kg ethanol extract of RD, 100, 500, 1000 mg/kg aqueous extract of RD, 500, 1000 mg/kg chloroformic extract of RD, saline, 3 mg/kg diazepam, ip	Relatively potent hypnotic effect for doses of 500 & 1000 mg/kg of ethanol and aqueous extracts of RD comparable to diazepam	[35]
4	Potentiation of pentobarbitone induced sleeping time in mice	4 groups (n=5): 250 mg/kg & 500 mg/kg RD extract, 1 mg/kg diazepam ip, 1% tween in water	Significant induction of sleep, increase duration of sleep, and significant decrease in locomotor activity (CNS- depressant activity of RD extract)	[36]
5	Anti-depressant effect of RD extract in mice	5 groups (n=6): 15 mg/kg, 60 mg/ kg, 90 mg/ kg RD aqueous extract, saline, imipramine (15 mg/kg), ip	Significant decrease of immobility & increase swimming time by 15 mg/kg & 90 mg/kg using forced swimming test & duration of immobility time	[37]
6	Analgesic and anti-inflammatory effect of RD extract & EO	8 groups (n=6): 250, 500, 1000 mg/kg hydroalcoholic extract of RD, 100, 200, 400 µL/kg of RD EO, 10 ml/kg isotonic saline 0.9 % , 10 mg/kg morphine, ip	Potent analgesic effect of hydroalcoholic extract of RD in acetic acid and formalin tests, anti-inflammatory activity in carrageenan model, no analgesic & anti-inflammatory effect by RD EO	[38]
7	Relaxant effects of RD on guinea pig tracheal chains	0.25, 0.5, 0.75, 1 g % ethanol extract of RD, 0.25, 0.5, 0.75, 1 vol % RD EO, 0.25, 0.5, 0.75, 1 mM theophylline anhydrous, saline 1 ml	Potent concentration-dependent relaxant effect of RD extract & EO comparable with theophylline on tracheal chain, significantly smaller relaxant effect of RD ethanol extract rather than RD EO	[39]
8	Laxative and prokinetic effects of RD in rats	(n=7) 1.5 g/kg aqueous extract of RD, 0.33 g/ml lactulose, 0.5 ml saline/ excreted feces were counted up to 32 h/ fecal samples were collected every 15 min up to 16 h to assess water content	Significant increase of feces number & its percentage of water by RD extract, but no effects on transit time of intestinal ingesta	[40]
9	Laxative effect of RD in dogs	Varying four doses (90-1440 mg/kg/day) aqueous RD extract, 300 mg/kg/day lactulose (n=4), 12 mL/kg distilled water, 10 days/ fecal water content was measured	Efficient dose-dependent laxative/ purgative effect of RD extract, tolerance to higher doses of RD no significant changes in fecal water content, symptoms of sedation and anorexia following 7th day by the highest RD dose	[41]
10	Effects of aqueous RD extract on histaminergic & muscarinic receptors of Guinea pig ileum & rabbit jejunum	(tests for rabbit jejunum) 0.16, 0.33, 0.50, 0.66, 0.83 mg/ml RD extract (alone & with 0.08 µg/mL atropine), 0.16, 0.33, 0.50, 0.66, µg/mL acetylcholine (alone & with 0.001 µg/mL atropine) (tests for pig ileum) 0.25, 0.66, 1 mg/mL RD extract (alone & with 1.6 µg/mL chlorpheniramine), 0.005, 0.5, 0.1 µg/mL histamine (alone & with chlorpheniramine), 0.66, 0.88, 1.3 mg/ml RD extract (alone & with 0.001 µg/mL atropine), 0.01, 0.03, 0.06, 0.1 µg/mL acetylcholine (alone & with 0.008 µg/mL atropine)	Significant increase in amplitude of contractions & significant decrease in contractile response ⇨ stimulatory effect of RD extract on cholinergic receptors Significant reduction of stimulatory effects on illeal contractions by aqueous RD extract after antagonizing the histaminergic receptors by chlorpheniramine ⇨ excitatory effect of RD extract on histaminergic receptors	[42]

EO: essential oil, ip: intraperitoneal; RD: *Rosa damascena*

The mixture of constituents in *R. damascena* essential oil could make it effective on GI disorders like gripe, flatus, gastritis and colitis, so this herb has been introduced as carminative, digestive, and stomachic. Containing flavonoids and antioxidants, the products like rose oil and rose syrup are useful for headaches.

Conclusion

Five phytopharmaceuticals from *R. damascena* with a long history in ITM are "Golangebin"/ "Golqand", "Jollab", rose oil, rose water, and rose syrup, mainly effective on CNS and GI systems. Although much work has been focused on different fractions of *R. damascena*, clinical knowledge about these products are scarce. Seemingly, some of their old indications have been forgotten. To revive traditional therapeutic notions about *R. damascena* phytopharmaceuticals, it is suggested that their effects be evaluated clinically, which leads to opportunities for commercialization.

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Author contributions

Forough Afsari Sardari and Ghazaleh Mosleh participated in designing the work, reviewing recent and traditional literature, and drafting the manuscript. Amir Azadi and Abdolali Mohagheghzadeh contributed in conception of the work and revised the manuscript critically. Parmis Badr designed the work and contributed in drafting.

Declaration of interest

The authors declare that there is no conflict of interest. The authors alone are responsible for the content of the paper.

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Abbreviations

ITM: Iranian Traditional Medicine; CNS: central nervous system; GI: gastrointestinal; EO: essential oil; ip: intraperitoneal