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Article Info	Abstract
Article type:	Introduction: Increasing antibiotic resistance in microorganisms and the advantages that natural
Original Article	compounds have over synthetic chemicals led to more investigation of plant resources. Rosa damascena is
	one of the valuable species of the Rosaceae family that has different therapeutic effects. This review studies
	the antimicrobial effects of R. damascene and its derivation in the prevention and treatment of infectious
Article History:	disease and bibliometric analysis at the family level.
Received: 03 March 2023	Methods: Data collection was done from Scopus and Web of Science databases; after choosing the database
Received in revised form:	that published the most data, the information was analyzed by VOS viewer and Bibliometrix-package.
21 April 2023	Results: The results of most research show the antimicrobial effect of this plant against human pathogens.
Accepted: 28 April 2023	The bibliometric results of 412 searched documents also revealed that most of the published documents
Published online: 31	belong to the countries of China, Iran and Turkey. The process of publishing documents over the years has
December 2023	generally increased and the keyword "Rosaceae" has been used more than others.
	Conclusion: In this review article, scientific documents related to the role of <i>R. damascene</i> and its derivation
	showed this plant have potential in the prevention and treatment of infectious diseases such as dental caries
Keywords:	and periodontal diseases.
Rosaceae, Antimicrobial,	
Infection Control,	

Bibliometric Analysis

Rosa damascena belongs to the family of Rosaceae, mostly cultivated as an ornamental plant. R. damascena is known as a medicinal herb [1]. The name of R. damascena species comes from Damascus, Syria; where there is originally a wild plant. However, it is now cultivated in different regions of the world, such as Turkey, Bulgaria, Iran, India, Morocco,

France, China, Italy, Libya, Russia and Ukraine [2, 3]. In Iran, R. damascena known as Gole Mohammadi (Figure1) is cultivated especially in Kashan for producing rosewater and essential oil [4]. R. damascena is a plant that is used in traditional medicine for various purposes. In Iranian traditional medicine, using of R. damascena had been proposed, because of its presumptive prevention and

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therapeutic effects such as chest pain, relief, strengthening of the heart, treatment of menstrual bleeding and digestive disorders, reduction of inflammation [4], depression and nervous tension [5].

Scientific research has recently shown that this plant has various therapeutic effects. For example, it is reported that *R*. damascena has the effect of analgesic, anti-inflammatory, antioxidant [6], antitussive, anti-depressant [5], anti-diabetic effect [7] and anti-aging properties [8]. Various studies reported the cytotoxic effects of R. damascena methanolic extract and rose oils against cancer cell lines [9]. Another important effect of this plant is its antimicrobial effects, which have been shown in various studies. R. damascena has the potential for control, prevention and treatment of infectious diseases. Recently seen increasing interest in the use of plants because they do not develop antibiotic resistance same as the synthetic antibiotics [10]. These studies showed the antimicrobial effect of this plant against bacteria [11], fungi [12], and viruses [13]. This review is focused on scientific documents about the application potential of R. damascena as a valuable therapeutic strategy for the prevention and treatment of infectious diseases.

R. damascena and its therapeutic potentialities

The Rosaceae family is consisting of 100 genera and 3,000 species. R. damascena is one of the most important species in the Rosaceae family with high-value products which included fruit, nut, ornamental, herb, and woody plants. This plant has many different uses as an ornamental plant, perfume, pharmaceutical and cosmetic industries [14]. R. damascena has an aromatic, light pink flower that appears in spring [15]. This plant has an upright shrub with a height of 12 meters [2]. The chemical composition of R. damascena is including terpenes, glycosides, flavonoids, anthocyanins, carboxylic acid, myrcene, vitamin C, kaempferol and quercetin and etcetera. The major products of R. damascena are rose water, rose oil, dried flowers, and hips [4]. Rose water has traditionally been used for several skin problems [10], abdominal pain as an antispasmodic, eye washing as an antiseptic agent, mouth disinfection and chest congestions [16, 17]. Rose water is mainly applied in cosmetics creams and facial cleansers [2].



Figure 1: Gole Mohammadi (Rosa damascene).

Rose oil is a volatile combination that is obtained from the distillation of the flowers of *Rosa damascene* [4]. The essential oil is used in perfumery. Rose oil had been used in aromatherapy for the treatment of cardiac diseases Avicenna [1]. It is believed that it can have a positive effect on depression and nervous stress control [17]. For the treatment of some allergies, headaches, and migraine vapor therapy of rose oil can be useful [4].

Antimicrobial activity of *R. damascena* and its derivatives

Infectious diseases are one of the most important health problems and cause about 20% of death in the world [18]. Increasing resistance to common antibiotics due to irregular use of them has threatened public health. Identification and use of new antibacterial compounds especially natural materials can overcome this important threat [19].

A number of surveys have indicated that *R. damascena* has antimicrobial activity on a wide range of bacteria, including gram-negative and gram-positive species and antifungal associated with skin and mucosal infection, dental caries, and periodontal diseases. For example:

Antibacterial activity of *R. damascena* flower extracts was determined against 15 species of bacteria: *Aeromonas hydrophila*, *Bacillus cereus*, *Enterobacter aerogenes*, *Enterococcus feacalis*, *Escherichia coli*, *E. coli* O157:H7, *Klebsiella pneumoniae*, *Mycobacterium smegmatis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas fluorescens*, *Salmonella enteritidis*, *Salmonella typhimurium*, *Staphylococcus aureus* and *Yersinia enterocolitica*. and showed were effective against all the bacteria except *E. coli* O157:H7 [20].

It was reported that extracts of *R. damascena* (rose oil, aqueous extract, concrete, ethanol extract, chloroform fraction, ethyl acetate fraction, butanol fraction, residue fraction) have antifungal and antibacterial activity against *Bacillus subtilis, S. aureus, Streptococcus pyogenes, Mycobacterium phlei, P. aeruginosa, E. coli, Klebsiella pneumoniae, Salmonella typhimurium, Shigella flexneri, Proteus vulgaris, Acinetobacter baumannii, Aspergillus niger, Penicillium chrysogenum, Saccharomyces cerevisiae [3].*

Tofighi et al. showed *R. damascena* extract has antibacterial activities against *B. cereus*, *S. aureus*, *and S. epidermidis* as gram-positive bacteria and *P. aeruginosa* as gram-negative bacteria [10].

Another study evaluated the antimicrobial activity of alcoholic and aqueous extracts of *R. damascena* against *S. aureus*, *S. aureus*, *P. aeruginosa*, *E. coli*, *Streptococcus pneumoniae*, *Acinetobacter calcaoceuticus*, *Salmonella enteritidis* and showed methanol and water extracts inhibited the growth of these bacteria [21].

It was reported that rose absolute and essential oil has strong antibacterial activity against *E. coli, P. aeruginosa, B. subtilis, S. aureus, Chromobacterium violaceum,* and *Erwinia carotovora* strains [22] and evaluated the antimicrobial activity of rose petal and pollen extracts of *R. damascena* with the six solvents (water, ethyl alcohol, isoamyl alcohol, acetone) against *B. subtilis, E. coli, Candida albicans, Micrococcus leutus, P.aeroginosa* and showed that ethyl alcohol and acetonic extracts had antimicrobial activity on most of the tested microorganisms, ethyl alcohol extracts of rose petals had highest antibacterial activity against *P. Aeruginosa* [23].

El-Shouny et al (2016) studied the antibacterial activity of methanol and acetone *R. damascena* and *Terminalia chebula* against 22 bacterial isolates including *Bacillus clausii*, *S. aureus*, *Enterobacter cloacae*, *E. coli*, *Salmonella typhi*, *Shigella dysenteriae* and showed these extracts have widely effect of inhibition against the tested isolates and acetone extracts have the more antibacterial activity than the methanol extracts [24].

Furthermore, reported rose water to reduce inflammation by evaluating its anti-bacterial effect on infections of cause skin and mucosal including *C. albicans* and methicillinresistant *S. aureus* (MRSA) [25].

Li et al showed that a new isoflavone derivative isolated from *R. damascena* had an antibacterial activity with MIC_{90} value of 46±4 mg/L for methicillin-resistant *S. aureus* (MRSA) strain [26].

Zu et al tested 10 essential oils for their antibacterial activities against *Propionibacterium acnes*, rose essential oils were one of the best for antibacterial activities with inhibition diameters of 16.5 +/- 0.7 mm, and minimal inhibitory concentrations of 0.031% (v/v) [27].

Gavam et al. studied essential oil of *R. damascena* effects against gram-negative and gram-positive bacteria and fungi and showed depend on the origin of the plant have an antimicrobial effect against *S. aureus*, *Streptococcus pyogenes*, *P. aeruginosa*, *C. albicans* and *Aspergillus brasiliensis* [28].

R. damascena and dental caries

Dental caries is a chronic disease that is prevalent around the world and people are always susceptible to this infectious disease [29]. World Health Organization (WHO) reports show dental caries is a generally important health problem that affects about 60–90% of schoolchildren and most adults [30]. Although there are many prophylactic methods, dental caries is one disease persistent in humans [31]. The tooth can be destroyed, if proper care is not provided [32]. The microbiome of the human oral cavity is composed of various bacteria, fungi, and viruses [31]. Microbial pathogens in oral, especially cariogenic bacteria such as *Streptococcus mutans*, are mostly a factor in the occurrence of dental caries [33]. Biofilm formation by oral bacteria that are causative resistant to the antimicrobial drug can cause the development of dental caries [34].

Oral major diseases, such as dental caries, gingivitis, periodontitis, and oral malodor, are caused by oral biofilm [35].

Several studies showed *R. damascena* has an inhibitory effect on cariogenic bacteria:

Tsai et al investigated methanolic extracts from 12 herbs on *S. mutans, Streptococcus sanguinis* and *Streptococcus sobrinus* and reported *R. damascena* could inhibit the growth of these bacteria at MIC > 8 mg/mL [36].

Aliasghari et al reported that ethanol extract of R. damascena has bacteriostatic or bactericidal and anti-

adhesion effects on the cariogenic streptococci such as *S. mutans, S. sobrinus, Streptococcus salivarius* and *Streptococcus sanguis.* They showed this extract reduces biofilm formation by>93%, > 74%, >84% and >79% by *S. mutans, S. sobrinus, S. salivarius,* and *S. sanguis,* respectively [37].

In vitro study assessed the effect of rose water on the most common cariogenic bacteria including; *S. mutans* and *S. sobrinus* and showed rose water decreased the adhesion of these bacteria by 80 and 57%, respectively [38].

Effect of *R. damascena* and its derivatives on periodontal diseases

Periodontal diseases are prevalent that can affect up to 90% of worldwide people. Periodontitis is an important cause of tooth loss in adults [39].

Periodontal diseases are belonging to the genera Porphyromonas gingivalis, Actinobacillus, Prevotella and Fusobacterium [40]. In vitro study has suggested R. damascena extract has antimicrobial activity against endodontic pathogens containing, E. faecalis, Actinomyces naeslundii, P. gingivalis, Fusobacterium nucleatum, and C. albicans [6].

The clinical study has shown that mouthwash containing *R. damascena* extract was effective in the treatment of recurrent aphthous stomatitis on pain, size, and the number of ulcers [41].

Materials and Methods Bibliometric analysis

A quantitative search was conducted on July 2, 2022, using the term (TITLE-ABS-KEY ("antimicrobial*" OR "antibacterial*" OR "anti-microbial*" OR "anti-bacterial*" OR "antiinfective*" OR "microbial sensitivity" OR "antiinfective*" OR "antifungal*" OR "bactericidal*" OR "fungicidal*" OR "virucidal*" OR "antivirus*" OR "antiviral*" OR "anti-infectious") AND TITLE-ABS-KEY ("*Rosa damascene*" OR "Damask Rose" OR "*Rosa X Damascena*" OR "*Rosaceae*")) in the Scopus database (http://Scopus.com) which resulted in the identification of 412 documents. This term was searched on the Web of Science (https://www.webofscience.com/) at the same time, and 256 documents were displayed, so in the continuation of bibliometric reviews, the documents published in the Scopus database, which include a larger number, were used. Due to the limited number of documents with the term "*Rosa damascene*", the family name "*Rosaceae*" was also used in the search term. In the following, the searched documents were bibliometrically examined using VOSviewer v 1.6.16 (http://www.vosviewer.com/) [42] and R Package Bibliometrix (http://www.bibliometrix.org/) [43].

Results and Discussion

The results of the analysis indicated that most of the documents are articles (333 items) and reviews (68 items), while conference papers are 5 items and book chapters are only 4 items. The most documents are in the fields of pharmacology, toxicology and pharmaceutics (21.3%), biochemistry, genetics and molecular biology (18.7%), agricultural and biological sciences (17.7%) and medicine (15.7%). Other main information about the documents published in the Scopus database is shown in Table 1.

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MAIN INFORMATION ABOUT DATA		DOCUMENT TYPES		DOCUMENT CONTENTS		AUTHORS		AUTHORS COLLABORATION	
				Keywords				Single-authored	
Timespan	1971:2022	Article	333	Plus (ID)	6249	Authors	1926	documents	17
Sources				Author's					
(Journals,		Book		Keywords		Author		Documents per	
Books, etc)	235	chapter	4	(DE)	1266	Appearances	2172	Author	0.214
						Authors of single-			
		Conference				authored		Authors per	
Documents	412	paper	5			documents	16	Document	4.67
Average years						Authors of			
from						multi-authored		Co-Authors per	
publication	8.57	Editorial	1			documents	1910	Documents	5.27
Average									
citations per								Collaboration	
documents	28.5	Letter	1					Index	4.84
Average									
citations per									
year per doc	2.651	Review	68						
References	21788								

Table 1: Main information about the documents published in Scopus.

As shown in figure 2, the process of producing and publishing documents related to this issue has had ups and downs. But in 2020, this trend has increased more rapidly. The countries of China, Iran, Turkey and India have the highest number of documents published in Scopus with 234, 214, 133 and 112 documents, respectively. Figure 3 shows the affiliation of organizations with at least 5 published documents and the corresponding author's country. Organizations such as Tehran University of Medical Sciences, Shahid Beheshti University of Medical Sciences, Mashhad University of Medical Sciences and Shahrekord University of Medical Sciences belong to Iran. However, inter-country (MCP) collaboration between countries in China and Germany is more than in Iran. Also, Japan has generally intra-country (SCP) collaboration.





Figure 2: Publication process of scientific documents by year.





Figure 3: *A*) Affiliation and *B*) corresponding author's country. Inter-country (MCP) and intra-country (SCP) collaboration.

The results of keyword co-occurrence analysis using VOSviewer are shown in figure 4. Based on the minimum occurrence of 5 of each keyword, 568 keywords were selected and categorized into 5 clusters shown with blue, red, green, yellow and purple colors. Based on this graph, it seems that keywords such as hypertension, liver protection, influenza, stomach pain, phytochemicals and green chemistry have been used more in the last several years. Also, the growth trend of some top keywords by year is shown in Figure 5.



Figure 4: Keyword analysis using VOSviewer. A) Classification of keywords into 5 clusters shown with green, blue, red, yellow and purple colors. B) Keywords graph in terms of time.

In Table 2, the top 20 documents based on total citations per year are listed. Among these documents, there are articles on the subject of pharmacological effects and especially the phenolic compounds of *R. damascene*. However, most of the attention seems to be focused on other members of this family. Anyway, probably the climatic conditions required for the growth and breeding of *R. damascene* can be effective in the research process.

 Table 2: Most global cited documents.

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	Paper	Total	TC*	Normalized	Ref
		Citations	per Year	ТС	
1	1 Berry phenolics: antimicrobial properties and mechanisms of action against severe human pathogens		21.6471	4.5352	[44]
2	Effect of quince seed mucilage edible films incorporated with	163	18.1111	4.7941	[45]
	oregano or thyme essential oil on shelf life extension of refrigerated				
	rainbow trout fillets				
3			17.8182	4.6047	[46]
	chemistry, metabolism and bioavailability, and health benefits				
4	Pharmacological effects of Rosa damascena	205	17.0833	4.2051	(4)
5	Berry phenolics selectively inhibit the growth of intestinal	307	17.0556	1.4994	[47]
	pathogen				
6			16.1111	4.2647	[48]
	mucilage films containing thyme essential oil				
7	Honeybee-collected pollen from five Portuguese Natural	189	15.75	3.8769	[49]
	Parks: Palynological origin, phenolic content, antioxidant				
	properties and antimicrobial activity				
8	Aronia plants: a review of traditional use, biological activities,	201	15.4615	3.0687	[50]
	and perspectives for modern medicine				
9	Antimicrobial activity of Tunisian quince (Cydonia oblonga	245	15.3125	5.8764	[51]
	Miller) pulp and peel polyphenolic extracts				
10	Ethnopharmacological survey of medicinal plants in Maden	181	15.0833	3.7128	[52]
	(Elazig-Turkey)				
11	Potentilla—A review of its phytochemical and pharmacological	194	13.8571	3.5466	[53]
12	Activities of ten essential oils towards Propionibacterium acnes	176	13.5385	2.687	(27)
	and PC-3, A-549 and MCF-7 cancer cells				
13	Extracts and molecules from medicinal plants against herpes	239	13.2778	1.1673	[54]
	simplex viruses				
14			12	4.0244	[55]
	extracts of berries, leaves, and branches of berry plants				
15	Engineered nanomaterials inhibit Podosphaera pannosa	47	11.75	4.7832	[56]
	infection on rose leaves by regulating phytohormones				
16	Ellagic acid derivatives from Rubus ulmifolius inhibit	129	11.7273	3.0306	[57]
	<i>Staphylococcus aureus</i> biofilm formation and improve response to				
	antibiotics				
17	An overview on ethnobotanico-pharmacological studies	22	11	9.9478	[58]
	carried out in Morocco, from 1991 to 2015: Systematic review (part				
	1)				
18	Ethnobotanical study of medicinal plants by population of	83	10.375	4.4674	[59]
	valley of Juruena region, legal Amazon, Mato Grosso, Brazil				
19	Physicochemical characterization, antioxidant activity, and	31	10.3333	4.6368	[60]
	phenolic compounds of hawthorn (Crataegus spp.) fruits species				
	for potential use in food applications				
20	Phenolic compounds, antiradical activity and antioxidant	101	10.1	5.0605	[61]
	capacity of oil-bearing rose (Rosa damascena Mill.) extracts				

* TC: Total Citations.

The analysis of connections between top authors, top keywords and top sources in this study is graphically displayed in Figure 6. Based on this figure, the top keyword *Rosaceae* is displayed more in sources such as phytochemistry and the journal of ethnopharmacology.

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Conclusion

Today, the issue of antibiotic resistance has become a global challenge. The need to discover and identify new compounds with antimicrobial properties to eliminate drug-resistant pathogens has received more attention than in the past [62].

The use of natural compounds with antimicrobial properties, for example, plants has an advantage over marine resources due to the ease of harvesting. Soil areas in the world have a wide variety of plants due to the variety of climate conditions. In Iran, *R. damascena* has a special place in traditional medicine. The research results show that the antimicrobial effects of *R. damascena* are widespread. This plant has an antimicrobial effect on a wide range of bacteria and fungi associated with skin and mucosal infection, dental caries and periodontal diseases. *R. damascena* as a medicinal plant is capable of inhibiting and treating oral infectious diseases. The application of *R. damascena* and its products can decrease the use of chemical antimicrobial agents.

Since the climatic conditions of Iran are suitable for the growth and cultivation of *R. damascene*, this is probably the reason why most of the research has been carried out in this

country. However, the growing conditions of this plant are likely to be available in other countries and regions with similar climate conditions in Iran. Nohynek et al. (2006) article's rank first with the highest TC per year. In this document, the antimicrobial effect and the mechanism of action of the phenolic compound from one of the members of the *Rosaceae* family have been investigated [63]. For this reason, it is possible to study the antimicrobial mechanism of other members of this family, especially *R. damascene*, in the future.

Generally, further studies must be done to complete the knowledge gap in the antimicrobial activity of R. damascena. 1) Investigation of the antimicrobial effect of R. damascena on a wider spectrum of microorganisms that cause infectious diseases such as respiratory, urinary and digestive system infections, etc.; 2) Investigations on mechanisms of antimicrobial actions of R. damascena on microorganisms; 3) Determining which R. damascena product has the most antimicrobial effect; 4) Preparation of different pharmaceutical formulations from R. damascena and assessment their antimicrobial activity. These studies can support the application of this plant as an antimicrobial agent for infection control and healing.







Figure 6: Three fields plot. Middle field: top keywords, left field: top authors and right field: top sources.

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Conflicts of interest

No potential competing interest was reported by the authors.

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