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Review Article

Chemical Composition and Biological Activities of *Rhus coriaria* L.: A Systematic Review

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ABSTRACT

Rhus coriaria L. (Sumac) is native to the Mediterranean Basin and is a useful plant for food and medical purposes. To the best of our knowledge, there is no comprehensive review of the chemical composition and biological activities of R. coriaria. The present review was conducted by systematically searching online databases including PubMed, Scopus, Web of Science, and EMBASE from the beginning of 2003 to September 2022. The inclusion criteria included articles published in English and evaluating the physical activity and chemical composition of sumac. Articles were searched by two independent researchers. The quality assessment of the articles was done based on a quality assessment checklist. A total of 30 studies were included, most of which were related to the countries of Turkey and Iran. The results of this systematic review showed that most of the studies were interventional and focused on the properties of the R. coriaria fruit instead of its leaves. Chemical compositions mentioned in the articles for R. coriaria included: proximate, mineral, fatty acid, vitamins, amino acids, and organic acids. The most biological activity of R. coriaria was related to antimicrobial (11 studies), antioxidant (7 studies), neuroprotective, and anticancer effects. antimicrobial, antioxidant, anticancer, and antidiabetic properties of this plant, make it a good candidate for pharmaceutical and food industries as well as human health-related purposes.

Keywords: Rhus coriaria L., Chemical composition, Antimicrobial, Antioxidant, Anticancer, Antidiabetic

INTRODUCTION

Tanner's sumac (*Rhus coriaria* or Sicilian sumac), is a small, ornamental, medicinal, and aromatic shrub and a member of the Anacardiaceae family. The Anacardiaceae family includes at least 250 members including species of flowering plants, and sumac is the name of a genus (Rhus) of this family. Nonagricultural herbal sumac is native to temperate and tropical regions around the world, especially in Mediterranean countries, North Africa, Southern Europe, Afghanistan, and Iran. The leaves stems, flowers, and fruits of this plant are effective in reducing inflammation, digestive, respiratory, joint, cancer, and diabetes due to their antimicrobial and antioxidant properties [1-3].

Different types of sumac include *R. coriaria* or Tanner's sumac (native to Mediterranean Basin, southern Europe, and western Asia), *R. copallina*or Winged or shining sumac (native to Eastern North America), *R. glabra*Smooth sumac (native to Western North America), *R. retinorrhoea* (native to Southern Saudi Arabia), *R. semialata* or *R. chinensis* or Chinese sumac (native to Asia), *R. succedanea* Japanese wax tree (native to Asia), *R. typhina* Staghorn sumac (native to Eastern North America), *R. undulate*Kuni bush (native to South Africa), and *R. verniciflua* Japanese sumac (native to Asia). This plant has biologically active compounds such as hydrolysable tannins, organic acids, flavonoids, and anthocyanins. Flavones include: myricitin, quercetin, isoquercitrin, kaempferol, and fiber[3-5].

Due to having a lot of tannins (which is a type of polyphenol), *R. coriaria* affects digestive system cells and reduces diarrhea. Polyphenolic, flavonoid compounds, and fatty acids of this plant are effective in rheumatic diseases, gout, and diabetes treatment [6-9]. The existing antioxidant compounds affect blood health by reducing inflammation and removing blood waste products such as urea [10-12]. Quercetin present in sumac, with its antioxidant and anti-coagulant properties, plays a role in reducing cardiovascular inflammation as well as decreasing blood pressure and cholesterol levels [7, 13]. Flavonoid compounds are effective in reducing stomach bleeding and blood concentration, as well as reducing pneumonia complications in respiratory diseases. Phenolic, flavonoid, and flavonol compounds of *R. coriaria* are known for microbial population reduction [8, 14-16]. Some studies showed that the fruit, leaves, and stem (Figure 1) of *R. coriaria* have high antioxidant properties due to their high phenolic content [16-19].

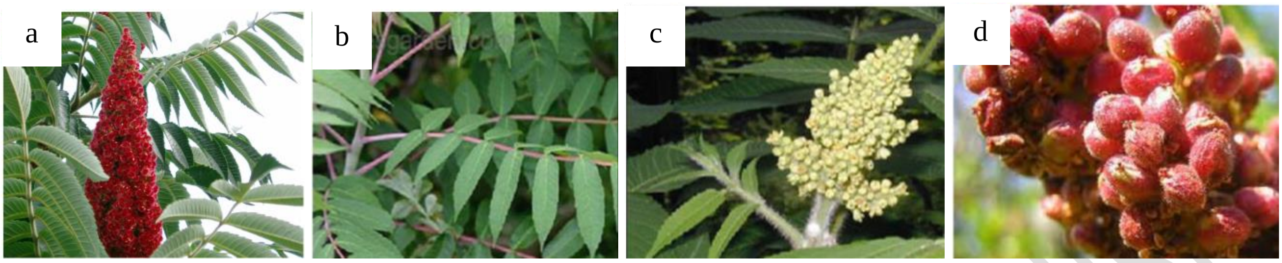

Fig. 1 Different parts of *R. coriaria*: (a) shrub; *R. coriaria* is a shrub with highly cold hardy properties, and flowers from early July to August. Its height can range from 3 m (9 ft 10 in) to 10 m (30 ft 33.3 in), (b) leaves; the spiral shape of the leaves in trifoliate or simple format distinguishes this plant from others. (c) flowers; the flowers of the plant are five-petalled and usually in three colors, white, green, and red, in the form of small and dense clusters (5 to 30 cm long). (d) fruits; There is also a permanent hairy brown calyx with a length of 3.5-4.0 cm and a width of 2-2.5 cm, which protects the flowers of the plant after being picked from the field, the bunches of the plant are dried and then usually ground to obtain the main spice. On the other hand, the brown and resistant seeds of the plant have a pungent smell and are 0.3-0.5 cm long and 0.2-0.3 cm wide in terms of diameter [20].

Few studies are focused on the biological activities and chemical composition of all types of *R. coriaria* extract [21]. To the best of our knowledge, there is no systematic and comprehensive review of the biological activities, chemical composition, and unique properties of *R. coriaria*. The aim of this review is to summarize the biological activities and chemical composition of *R. coriaria* extract for many years up until October 5, 2022.

METHODS

The present systematic review was conducted by systematically searching online databases including PubMed, Scopus, Web of Science, and EMBASE from database inception until September 2022.

Data Sources and Research Strategy

A systematic search was performed in scientific databases without using any filters. In addition, we included Iranian databases, SID and Iran Medex, and Google Scholar in our research. Mesh keywords were used for manual searching. For sumac, the Mesh keyword was "rhus". Mesh keyword was not found for biological activity and chemical composition. Table 1 shows the summary of our research strategy.

Inclusion and Exclusion Criteria

Endnote software was used for all searched documents. Irrelevant articles were identified and removed. Inclusion criteria included English language, articles with clinical trial design, and experimental, intervention containing the characteristics of chemical decomposition and biological activity of sumac. Exclusion criteria included all review articles, conference articles, and all gray texts including newspapers, student theses, unpublished research, and government publications.

Data Extraction and Quality Assessment

Extracting the characteristics of the studies was done by two researchers in the field of food science and the extracted variables included the name of the first author, the year of the study, the type of study, the part of sumac used (flowers, fruits, roots, stems, leaves), the type of use (food-medicinal), the type of chemical composition and biological activity, and study location (where the research was done).

In this review study, due to the inclusion of studies with different designs, different tools were used to evaluate the quality of the studies. To evaluate the quality of articles, the Jadad scale and checklists available by the Critical Appraisal Skills Program (CASP) were used. Regarding the Jadad scale, 5 factors of randomization, blinding, non-participation of participants, randomization method, method of assigning people to study groups, and blinding method were examined. The flow chart of the article selection process is shown in Figure 2. It is worth mentioning that no meta-analysis was performed in this study.

Table 1 Search strategy in PubMed and ISI

Some online databases	Search strategy	Number of related article
PubMed	("rhus"[MeSH Terms] OR "rhus*"[Title/Abstract] OR "sumac*"[Title/Abstract]) AND ("chemical composit*"[Title/Abstract] OR "biological activit*"[Title/Abstract])	42
Web of Science (ISI)	(((TS=(Rhous)) OR TI=(Rhous) OR TS=(Sumac*) OR TI=(Sumac*)) AND (TI=(chemical composit*) OR TI=(chemical composit*) OR TS=(biological activit*) OR TI=(biological activit*)))	123
Scopus	("rhus"[MeSH Terms] OR "rhus*"[Title/Abstract] OR "sumac*"[Title/Abstract]) AND ("chemical composit*"[Title/Abstract] OR "biological activit*"[Title/Abstract]) OR (biological activit*)	150

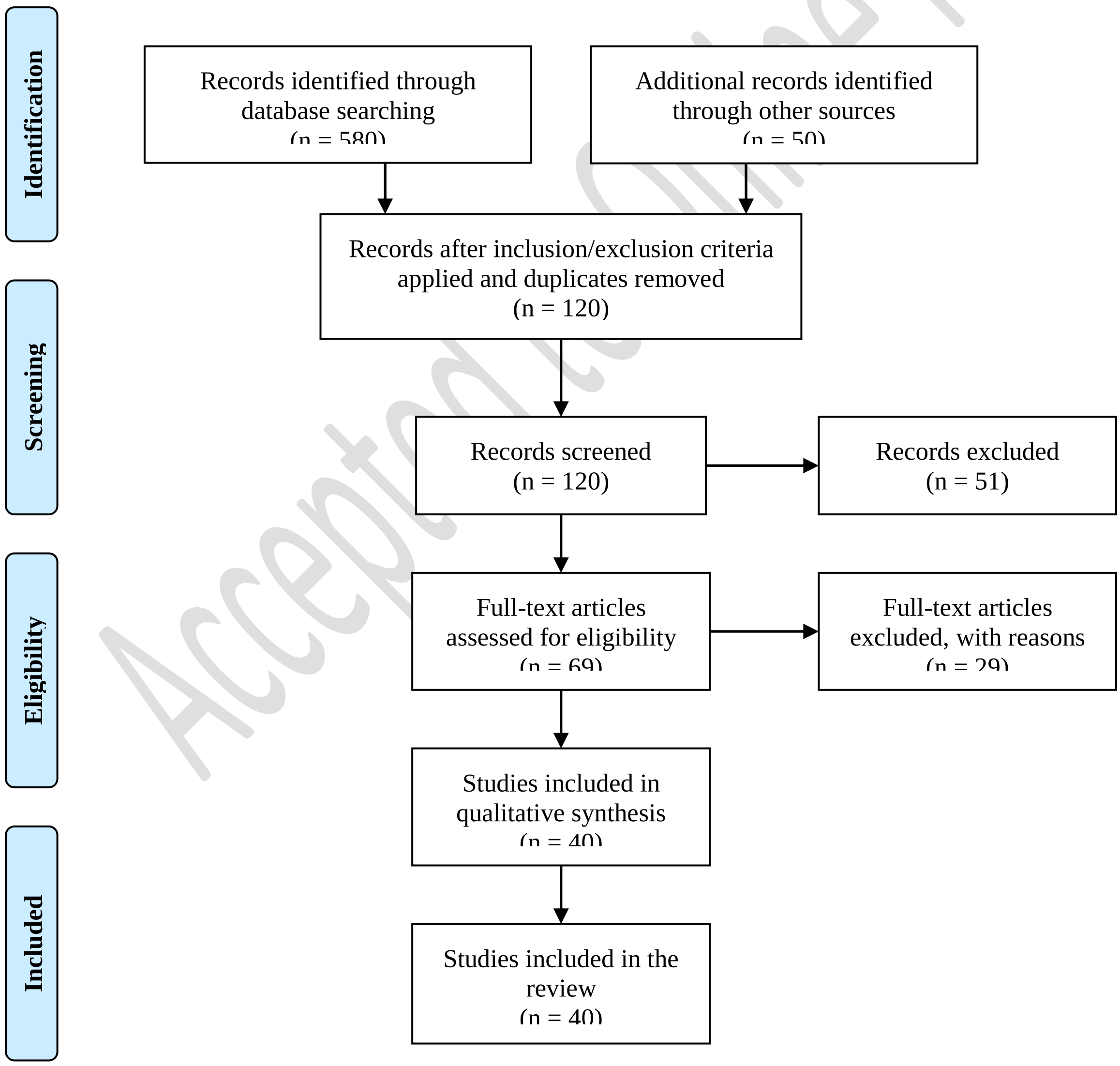

Fig. 2 PRISMA 2009 Flow Diagram

RESULTS

Study Selection

A total of 315 articles were found in the initial research in scientific databases. Out of 315 articles, 42 were related to PubMed database, 150 were related to Scopus, and 123 were related to Web of Science. After reviewing the titles and abstracts, 112 articles with repetitive titles or irrelevant themes were discarded. Finally, 30 articles were included in the study for systematic review.

Study Characteristics

Table 2 shows an overview of biological activity reported in the eligible studies and their important characteristics.

The final studies retrieved for full analysis were mostly from Turkey (8 studies), whereas others were conducted in Iran (4 studies), Pakistan (2 studies), Egypt (1 study), Italy (1 study), Jordan (1 study), Palestine (1 study, and Slovakia (1 study). All studies were conducted in interventional design settings. Most of the studies (15 studies) were interventional and focused more on the properties of the sumac fruit than its leaves.

The predomionant biological activities studied were as follows: antimicrobial (11 studies); antioxidant (7 studies), neuroprotective (two studies), anticancer (1 study), antidiabetic (1 study), and antifungal (1 study). Two ways of administering research instruments were reported in the other studies (Table 2).

R. coriaria chemical compositions mentioned in the articles include proximates, minerals, fatty acids, vitamins, amino acids, and organic acids (Table 3). Based on the average of the compounds, *R. coriaria* contained more than water-soluble extracts. The most abundant mineral was potassium. Oleic fatty acid was the most abundant fatty acid in extracts with an average of 38 grams. The most abundant vitamin was B6 with an average of 68.8 grams, and the most abundant amino acid was glutamic acid with an average of 2.49 grams. Quercetin was the most abundant flavonoid compound, and gallic acid was the most abundant phenolic compound.

Table 2 Biological activity (BA) mentioned in articles for sumac and summary of article characteristics. Anti-oxidative (AO), Antimicrobial (AM), Anti-fungal (AF), Anti-cancer (AC), Hypoglycaemic (H), Neuroprotective (Np)

First Author, Year. (REF)	Type of BA	Sumac part	Type of study	Location	Main results
[22]	AM	Seed	Interventional	Palestine	*Rhus coriaria* showed additive action against pathogens.
[23]	AM	Fruits	Interventional	Pakistan	Sumac extract showed a considerable antimicrobial effect
[24]	//	//	//	Turkey	The use of sumac extract can be beneficial for poultry processors and consumers
[25]	//	//	//	Jordan	Among 15 plants, *R. coriaria* had the best antimicrobial effect
[26]	//	//	//	Pakistan,	Sumac extract had a good antimicrobial effect on pathogenic bacteria
[27]	//	//	//	Turkey	The crude extract of *R. coriaria* had considerable antimicrobial properties
[28]	//	//	//	Iran	Sumac had promising inhibitory effects on food-borne bacteria and can be used as a natural food preservative
[29]	//	//	//	Iran	The fruit of *R. coriaria* can be used as a new source of natural antimicrobial and antioxidant agents for food and pharmaceutical industries
[30]	//	//	Experimental	Italy	Appropriate antimicrobial activity against multidrug-resistant (MDR) microorganisms was observed
[31]	AO	Fruits	Interventional	Turkey	High concentrations can increase the antioxidant effect of sumac extracts

[32]	//	//	//	Turkey	Sumac extract has a significant effect on quality of fermented sausage during ripening period, so it can be easily used to increase the quality of sausages
[33]	//	//	//	Turkey	The crude extract of *R. coriaria* had good antioxidant properties by removing superoxide radicals and xanthine oxidase
[34]	//	//	//	Iran	Despite antioxidant activities in sumac fruit extract, the fruit may be useful as a raw material for the production of natural antioxidants
[35]	//	Leaves	Interventional	Turkey	Sumac extract is promising as a source of natural antioxidants
[36]	//	Whole plant	//	Turkey	Sumac extract had a positive effect on reducing free radicals and antioxidant capacity
[37]	H	Fruits	//		Sumac ethyl acetate extract may be useful for the treatment and prevention of hyperglycemia, diabetes and obesity
[38]	AC	//	Experimental	Slovakia	Sumac showed significant oncostatic activities in rodent models of breast cancer, which was confirmed by *in vivo* and *in vitro* mechanistic studies
[39]	AM, AO, NP	//	Interventional	Turkey	Aqueous and methanolic extracts had good activity in cholinesterase inhibition and nervous system protection, together with antioxidant and antimicrobial propeties
[40]	AF	Leaves	//	Egypt	Phenolic and flavonoid compounds of *Rhus coriaria* are recommended as targets for new drugs formulation against fungal infections with minimal side effects
[41]	NP	Leaves	//	Iran	*R. coriaria* extract can be useful in reducing damage to the optic nerve and treating optic neuropathy

Table 3 Chemical composition of *Rhus coriaria* in previous studies

First Author, Year	Chemical composition		Mean ± SD Value
[42]	Proximate composition (%)	Moisture	11.35±1.07
		Protein	2.55±1.84
[43]		Fat	7.58±2.43
[44]		Fiber	20.56±3.57
[30]		Water-soluble extract	61.13±2.49
[45]		Ash	2.91±1.02
[46]	Minerals (mg/kg)	K	7354.24±28.46
		Na	98.04±0.15
[44]		Mg	413.17±72.12
		Ca	3142.15±88.50
[30]		Fe	168.49±2.13
		Cu	44.33±5.12
[43]		Zn	55.13±1.66
		Mn	10.57±3.39
		P	312.75±0.73
		Al	125.54±2.41
[47]	Fatty Acids (g/100 g)	Myristic	0.37±0.06
		Palmitic	29.11±0.63
		Palmitoleic	0.69±0.21
[30]			

		Stearic	2.99±0.42
[43]		Oleic	38.81±3.45
		Linoleic	30.44±0.83
		TUFA	68.33±7.54
		TSFA	31.62±4.10
[48]	Vitamins (mg/kg)	B1	29.65±1.17
		B2	24.69±1.34
		B6	68.89±1.42
[43]		B12	11.22±0.49
		PP	17.90±0.55
		Biotin	4.32±0.23
		C	39.17±1.41
[49]	Amino Acids (mg/g protein)	Leucine	1.24±0.18
		Isoleucine	0.62±0.07
		Lysine	0.96±0.03
		Phenylalanine	0.73±0.09
		Threonine	0.74±0.05
		Methionine	0.19±0.03
		Valine	0.79±0.07
		Tryptophan	0.58±0.09
[43]		Arginine	1.15±0.16
		Histidine	0.62±0.03
[44]		Cysteine	0.19±0.05
		Aspartic acid	1.74±0.32
		Glutamic acid	2.49±0.16
		Serine	0.92±0.15
		Glycine	0.58±0.09
		Alanine	0.97±0.28
		Tyrosine	0.55±0.39
		Proline	2.11±0.29
[43]	Organic acids (mg/kg)	Malic acid	1568.04±0.05
		Citric acid	56.93±0.35
		Tartaric acid	2.15±0.13
		Fumaric acid	3.40±0.46
[30]	Flavonoids (mg/g)	Quercetin	23.13 ± 0.02
		Quercetin 2′O-gallate	5.30 ± 0.02
[38]		Myricetin	2.71 ± 0.02
		Kaempferolo	3.34 ± 0.01
[30]	Phenols (mg/g)	Pentagalloyl-hexoside	128.09 ± 0.01
		Methyl digallate	110.96 ± 0.01
[38]		Gallic acid	142.549 ± 0.02

DISCUSSION

R. coriaria is used as a well-known endemic spice in Iran which can be found in many regions. The benefits of this plant for treating diseases have been proven in various studies. To the best of our knowledge, our review is the first systematic study evaluating the classification of *R. coriaria* chemical composition and biological activities of those compounds. According to the results, the predominant biological activity of *R. coriaria* is related to antimicrobial and antioxidant effects.

Regarding *R. coriaria* antimicrobial effects, the study of Fazeli *et al*. (2007) showed that plant extracts with concentrations between 0.5 and 1% had the best activity against gram-positive bacteria, while higher concentrations between 1 and 2% had a better effect against gram-negative bacteria than Shirazi thyme. *Salmonella* sp. showed high resistance against high concentrations of *R. coriaria*extract [27]. Based on the results of the study conducted by Mahdavi *et al*. (2018), *R. coriaria* fruit extracts had high antimicrobial and antioxidant properties. In addition, antioxidant and free radical scavenging activities were investigated. Antioxidant properties of sumac ethanolic extracts were noticeable at all studied concentrations (Mahdavi *et al*., 2018). According to Fazeli *et al*. (2007), the dominant ingredients in sumac essential oils are malt (39.7%), butanedioic acid, and diethyl ester (22.01%). Gulmez *et al*. (2006) studied the influence of *R. coriaria* extracts on psychrotrophs, mesophiles, and Enterobacteriaceae and found that treating the mentioned bacteria with *R. coriaria* extracts was almost as effective as using disinfectants. Also, because sumac extracts have a positive effect on the color of food products, they can be effective in poultry processing and food health [24]. Nimri *et al*. (1999) showed that the application of sumac extracts generated considerable diameters of bacterial growth inhibition zones. Based on their findings, out of 15 investigated plants, only three plants, *Punica granatum* L., *Quercus infectoria*, and *Rhus coriaria* L., had a wide range of antibacterial activity [25]. Lo Vecchio *et al*. (2022) showed that polyphenolic extracts of *Rhus coriaria* had antimicrobial activity. For the food industry, *R. coriaria* has antimicrobial and inhibitory effects on food-borne bacteria. As shown repeatedly by many studies, this plant can be considered a natural food preservative [27]. According to Özcan (2003b), *R. coriaria* extracts have a significant effect on quality indicators of fermented sausage during the ripening period; therefore, they can be easily used to increase the quality of sausage [31].

In this systematic review, different antioxidant effects of *R. coriaria* were reviewed and collected from different studies. In [47], twelve fruits of Iranian sumac (*R. coriaria* L.) were investigated and results showed that the oil content varied from 5.15 to 16.70% among the studied populations. Oleic acid (32.3-47.41%), palmitic acid (18.90-36.29%), and linoleic acid (10.31-35.39%) were the predominant fatty acids in oil samples. Among the population, the sumac of the Paveh region had the highest antioxidant traits. Such changes allow the use of elite populations containing a high proportion of unsaturated fatty acids and antioxidant compounds in the food industry [47]. Other findings showed that methanolic extracts of *R. coriaria* act as a non-competitive inhibitor of xanthine oxidase and superoxide radical inhibitor. Crude extracts of *R. coriaria* have interesting antioxidant properties with the capacity to remove superoxide radicals or via non-competitive inhibition of xanthine oxidase [32]. However, Özcan *et al*. (2003a) stated that after 28 days of storage, the antioxidant effects of *R. coriaria* extracts decreased. The antioxidant activity of extracts may be due to polyphenolic compound reduction. Their results showed that high concentrations can increase the antioxidant effect of *R. coriaria* extracts [35].

In the present study, based on the results of many studies, we conclude that fiber is the second most abundant compound in *R. coriaria* after water-soluble extract. The most abundant mineral compound in *R. coriaria* extractis potassium, and oleic acid is the most abundant fatty acid in the extract. Vitamin B6 and glutamic acid are the most abundant vitamins and amino acids, respectively. The most abundant flavonoids are quercetin and phenolic compounds of gallic acid. A study on the chemical characteristics of Iranian *R. coriaria* populations showed that different species of Iranian sumac differ in terms of chemical compositions. Acid contents of flavonoid compounds were positively correlated with tannins and flavonoids in different species. Flavonoid content was positively correlated with pH and tannin content. In addition, antioxidant capacity was positively correlated with flavonoid and tannin contents [34]. Furthermore, another study showed that Chinese *R. coriaria* has a higher percentage of total unsaturated fatty acids than Syrian *R. coriaria*, and oleic and linoleic acids were dominant. The amount of potassium and calcium in the fruits of Syrian *R. coriaria* is higher than that of Chinese *R. coriaria*. However, both Syrian and Chinese *R. coriaria* fruits have significant amounts of magnesium, phosphorus, sodium, and iron and therefore can be appropriate sources of food or additives. Syrian *R. coriaria* has more vitamins than Chinese *R. coriaria*, while the latter has higher amounts of essential and non-essential amino acids than the former. Syrian *R. coriaria* has a higher concentration of organic acids than Chinese *R. coriaria* [43].

Ethyl acetate of *R. coriaria* extract has also been effective in reducing blood sugar and regulating it. Antioxidant compounds play an important role in reducing inflammation by reducing cell damage [37]. According to some studies, in addition to antioxidant compounds, beneficial fatty acids in *R. coriaria* extract can be effective in reducing cholesterol. The presence of unsaturated fatty acids in nutrition plays an effective role in reducing blood lipids [50, 51]. It is also worth considering that consumption of *R. coriaria* extract can reduce the rates of atherosclerosis and stroke.

R. coriaria extracts have a positive effect on free radicals reduction and antioxidant capacity [36, 52]. One of the most important factors affecting carcinogenesis in its initial stage are free radicals which are toxic to cellular components and cause DNA damage through mutation. Kubatka *et al*. (2020) focused on the anticancer effects of *R. coriaria* extracts using mice as a model animal and breast cancer cell lines. Results showed that in mice suffering from cancer, high doses of *R. coriaria* extracts significantly reduced tumor volume, mitotic activity, and tumor incidence compared to the control group. Carcinoma severity showed a strong dose-dependent reduction of 66% and 73% compared to the control groups. In mice recovered from cancer, a significant increase in cancer inhibitory protein expression such as caspase 3, Bax, and Bcl-2 was observed. Also, in a studied cell line, a significant decrease in expression of oncogenic miR210 and an increase in tumor suppressor miR145 were observed. All findings demonstrated the anti-cancer effects of *R. coriaria* [38]. Based on the results of another study conducted by [53] in Mexico, *R. coriaria* decoction lowered the survival of cancer cells. The decoction contained flavonoids, fatty acids, and phenolic acids. The most abundant compounds in *R. coriaria* decoction were quercetin and myristin derivatives (glycosides), methyl gallate, epigallocatechin-3-cinnamate, β-PGG, fistin, and margaric acid, which may be related to the anticancer properties of RHTR [53]. Naz *et al*. (2020) also focused on the anti-cancer effects of *R. coriaria.* [41] stated that *R. coriaria* extracts can also affect diseases related to the nervous system, including ischemic optic neuropathy, by reducing oxidative stress and inflammation. Findings showed that extracts of *R. coriaria* can be useful in reducing damage to the optic nerve and for treating optic neuropathy [41]. According to Gezici (2019), aqueous and methanolic extracts had a significant antioxidant capacity and they concluded that the medicinal use of *R. coriaria* helps to reduce nervous system disorders [39].
Due to many limitations in *R. coriaria* L. systematic studies, most of the manuscripts were published in non-valid journals, and some studies were related to the comparison of several plants. In this review, we only selected manuscripts based on the inclusion criteria of the articles (see Methods) to remove these limitations.

CONCLUSIONS

*R. coriaria*extracts have various positive biological effects and are effective in reducing oxidants and carcinogenesis and inhibiting bacterial pathogens in different ways. Beneficial fatty acids in *R. coriaria* extracts can be effective in reducing LDL (low-density lipoprotein) cholesterol, also known as bad cholesterol, and in reducing inflammation in the body and may act as a potential neuroprotective, which can be beneficial for treatments of neurological diseases. Despite the presence of polyphenolic and flavonoid compounds, the consumption of *R. coriaria* extracts has a potential protective effect in reducing carcinogenesis, reducing inflammation, and reducing nerve damage. Taken together, *R. coriaria* extracts contain anti-microbial and anti-diabetic antioxidant compounds and therefore can be used as a supplement in health, as pharmaceuticals, and for the treatment of cancer patients, and can help the food industry.

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Author Contributions

Conception and design: Fatemeh Azizi Soleiman and Zahra Pilevar; acquisition, analysis, and interpretation of data: Vahid Ranaei, Hedayat Hosseini, and Mansoureh Taghizadeh; statistical analysis: Zahra Pilevar, Fatemeh Azizi Soleiman and Vahid Ranaei; drafting of the manuscript: Zahra Pilevar and Mansoureh Taghizadeh; writing—review and editing: Nasim Maghboli Balasjin; supervision: Hedayat Hosseini
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Competing Interests

None declared.

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