

SAMBUCUS EBULUS - FROM TRADITIONAL MEDICINE TO RECENT STUDIES

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ABSTRACT

Sambucus ebulus L. (Dwarf elder) is an herbaceous plant well-known in traditional medicine of Bulgaria and other countries from Central Europe to the Middle East. It is used for treatment of inflammation-related gastrointestinal disorders, influenza, kidney and lung diseases, and rheumatoid arthritis as well as of wounds, snake and insect bites. Recent research of Dwarf elder shows a high content of total polyphenols, anthocyanin, quercetin and vitamin C, which may be related to its antioxidant activity. Compounds with antiinflammatory and antinociceptive action such as chlorogenic and ursolic acids in the herb have been established, too. Some studies reveal anticancer properties of the herb, and plant ebulins are considered as the main compounds with anticancer properties. Fruit extracts modulate the gene expression of antioxidant enzymes in a preadipocyte cell culture model. Data available indicate that Dwarf elder is a good source of phytotherapeutic means to treat pathological conditions related to inflammation and oxidative stress.

Key words: *Sambucus ebulus*, traditional medicine, polyphenols, antioxidant effect, anti-inflammatory effect, antimicrobial effect

INTRODUCTION

Sambucus ebulus L. (SE) (Dwarf elder) is an herbaceous plant well-known in traditional medicine of Balkans and Anatolia for its healing effects in many disorders. It has been used for a long time for treatment of inflammation-related gastrointestinal disorders, influenza, kidney and lung diseases, and rheumatoid arthritis as well as of

wounds, snake and insect bites. Traditional medicine provides more data about elderberry fruit usage as immune stimulator, for treatment of respiratory and gastrointestinal diseases, dropsy, and even as an anticancer agent (16,22,31,39). Recent research reveals the phytochemical composition and many biological activities of SE in different study models. This review aims at summarizing the traditional use of this plant as a remedy and phytotherapeutic source useful in inflammation-related disorders.

Botanical characteristics

SE is an herbaceous species of genus *Sambucus* (elder or elderberry). *Sambucus* is a genus of flowering plants in *Adoxaceae* family formerly placed into *Caprifoliaceae* one, however, reclassified due to genetic evidence (7). It contains between 5 and 30 species of famous perennial herbaceous plants, deciduous shrubs, or small trees (26). In Bulgaria, there are three species such as SE (Dwarf elder), *S. nigra* (Black elder) and *S. racemosa* (European red

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elder). SE is a perennial plant with long, creeping and branched rhizome. It grows to 1-2 m in height, with erect, usually unbranched stems growing in large groups. Leaves are opposite, pinnate, 15-30 cm long, with 5-9 leaflets with a foetid smell. The stems terminate in a corymb of 10-15 cm in diameter with numerous white, occasionally pink flowers. The fruit is a small glossy, dark blue to violet black berry of 5-6 mm in diameter, juicy, with three pits. It is flowering from May to August and fruits ripen from August to September (3,26).

Distribution

Dwarf elder also known as Dane weed, Danesblood, Danewort or European dwarf elder and Walewort is a species native to Southern and Central Europe and South-West Asia (43). Habitats include places near cities, roads, railways, through the bushes, near forests, rivers and as a weed in fields up to 1900 m of altitude (3).

Usage in traditional medicine

Traditional Bulgarian medicine uses the berries (*Fructus ebuli*) and rhizomes (*Radix ebuli*) but less commonly the flowers (*Flores ebuli*) (26). Traditional medicinal usage of different parts of the herb is

Table 1. SE applications in traditional medicine

References	Used plant parts	Form of application/preparation	Actions/Treatment
Dimkov (14)	F	¹ jam	tbc, hemorrhoids
Kültür (27)	F	¹ decoction, ¹ fresh	hemorrhoids, gastric pain
El Beyrouthy <i>et al.</i> (20)	F	² fresh, ² decoction bath	rheumatoid arthritis
Nikolov (30)	F	¹ syrup	appetite stimulating, toning, hematopoietic
Dimkov (14)	Fl	¹ decoction	diuretic, diaphoretic
Kültür (27)	Fl	¹ decoction	cough
El Beyrouthy <i>et al.</i> (20)	Fl	¹ decoction	gout, rheumatoid arthritis
Dimkov (14)	L	¹ tea	influenza
Kültür (27); El Beyrouthy <i>et al.</i> (20)	L	² decoction, ² fresh	rheumatoid arthritis, insect bites
Kültür (27)	Ls	² decoction	snake bites
Kültür (27)	Ap	² poultice, ² fresh	wounds, rheumatoid arthritis, snake bites,
Kültür (27)	Ap	¹ decoction	gastric pain
El Beyrouthy <i>et al.</i> (20)	Ap	² decoction bath	rheumatoid arthritis
Dimkov (14)	R	¹ decoction	kidney diseases
Kültür (27)	R	² poultice, ² decoction bath	rheumatoid arthritis, analgesic
Saric-Kundalic <i>et al.</i> (36)	Wp	² fresh	snake bites, insect bites
Ahtardzhiev (2)	Wp	² poultice, ² decoction bath	rheumatoid arthritis, neuralgia, catarrh

Legend: F, fruits; Fl, flowers; Ap, aerial parts; L, leaves; Ls, leafy stems; R, roots; Wp, whole plant; ¹oral administration, ²external application

summarized in Table 1. It is a poorly studied species known for its healing effects in inflammation-related gastrointestinal diseases (14,27). Berries are said to have diuretic, antiseptic, tonic and purgative activity. Only ripe berries, which do not contain any toxic glycoside sambunigrin, may be used (3). The dried roots are a source for preparation of one of the best remedies for dropsy (14).

Phytochemical composition

Phytochemical composition differs in the different parts and extracts of the plant. Flowers, fruits and roots contain different groups of compounds. The most specific ones are briefly presented in Table 2. The content of flavanoids, anthocyanins, vitamin C, steroids, tannins, glycosides, cardiac glycosides, caffeic acid derivatives, chlorogenic acid, volatile substances, ursolic acid and phenols has been previously reported (17,19,33,37,39-41,44) (Table 3). The plant contains type 1 and type 2 ribosome inactivating proteins (RIPs) and lectins as well (Table 3).

compounds to quench free radicals (23,41). The report about SE fruit aqueous extract modulating antioxidant genes expression presents other possible mechanism of its AOA (42). This effect is most likely mediated by polyphenol compounds in the extract (28,29).

Antiinflammatory activity

Nitric oxide (NO) is also implicated in inflammation and other pathology, therefore, the very powerful radical scavenging activity of SE fruit extract may predict for and explain its antiinflammatory activity (19). Different SE extracts produce significant inhibition of inflicted edema and wound healing activity in animal models (15,16,44). A similar effect of root extract with additional antinociceptive activity is reported, too (1). One of the first studies of SE effects on cell culture model demonstrates that the extracts from leaves and flowers are effective in suppression of IL1 α , IL1 β , and TNF α biosynthesis (45). The plant exhibits its

Table 2. Phytochemical composition of different SE parts

References	Plant parts	Phytochemical composition
Pieri <i>et al.</i> (32); Staneva <i>et al.</i> (39)	Fl	essential oils, sugars, cyanogenic glycosides
Pribela <i>et al.</i> (33); Staneva <i>et al.</i> (39)	F	anthocyanins, sugars, valerianic acid, malic acid, tartaric acid, tannins, pectin, resins, vitamin C
Staneva <i>et al.</i> (39)	R	tannins, saponins

Legend: F, fruits; Fl, flowers; R, roots

SE biological activities

The biological activities of SE vary in different extracts depending on their phytochemical content. Recent scientific achievements in this field are summarized in Table 4. These extracts exert high antioxidant, antiinflammatory, antiarthritic, antinociceptive and antimicrobial activities (1,15-19,23,37,40-42,44,45). Latest investigations suggest a possible anticancer activity, too (4,5,10,38).

Antioxidant activity

Many studies report in vitro antioxidant activity (AOA) of SE extracts (17-19,23,41). Some of them establish a strong correlation with total polyphenol and anthocyanin content indicating the role of these

antiinflammatory activity by inhibition of TNF α -induced gene expression of vascular cell adhesion molecule 1 (VCAM-1), too (37). VCAM-1 is associated with a variety of chronic inflammatory disorders, making it a target for therapeutic intervention (6). This latest study supports traditional use of plant extracts and preparations rich in ursolic acid for the treatment of chronic inflammatory processes.

Anticancer properties

Immunotoxic conjugates composed by SE RIP ebulin 1 as a toxic moiety or mucin-binding lectin SELld (dimeric D-galactose and mucin-binding lectin) are effective inhibitors of protein synthesis and/or cell viability in many types of cancer cell lines

Table 3. Phytochemical composition of different SE extracts

References	Extract (plant part)	Phytochemical composition	Method
Yesilada (44)	(Ap) MeOH ext	chlorogenic acid	¹ H, ¹³ C, 2D-NMR
Pribela <i>et al.</i> (33)	(F) pentane-diethyl etheric ext	eugenol (26,8%), valeric acid (16,1%), methyl salicylate, hexane-ol, 2-hexen-1-ol, pentadecan-oic acid, 2-hexenal. citronellal (3,7-dimethyl-6-octen-1-ol), methyl palmitate, 7-methyleicosane and methyl linoleate (1-10%)	Gas chrm.
Ebrahimzadeh <i>et al.</i> (17)	(F) AQ and MeOH ext	polyphenols and flavonoids	colorimetric (Folin Ciocalteu and AlCl ₃)
Ebrahimzadeh <i>et al.</i> (19)	(F) aqueous	polyphenols and flavonoids	colorimetric (Folin Ciocalteu and AlCl ₃)
Tasinov <i>et al.</i> (41)	(F) AQ and MeOH ext	polyphenols and anthocyanins	colorimetric method (Folin-Ciocalteu, pH-differential)
Suntar <i>et al.</i> (40)	(L) MeOH ext	quercetin 3-O-glucoside	HPLC, NMR
Schwaiger <i>et al.</i> (37)	(L) diethyl ether fr	ursolic acid	NMR, HSCCC
Pieri <i>et al.</i> (32)	(L) NA	10 and 7-O-acetylpatrinoside-aglycone-11-O-[4''-O-acetyl-alpha-L-rhamnopyranosyl-(1->2)-beta-D-ribohexo-3-ulopyranoside], 10-O-acetylpatrinoside-aglycone-11-O-[alpha-L-rhamnopyranosyl-(1->2)-beta-D-ribohexo-3-ulopyranoside], patrinoside-aglycone-11-O-[4''-O-acetyl-alpha-L-rhamnopyranosyl-(1->2)-beta-D-ribohexo-3-ulopyranoside], 10-O-acetylpatrinoside-aglycone-11-O-[4''-O-acetyl-alpha-L-rhamnopyranosyl-(1->2)-beta-D-ribohexo-3-ulopyranoside], and patrinoside-aglycone-11-O-2'-deoxy-beta-D-glucopyranoside	1D- and 2D-NMR spctr., mass spctr., and chemical degradation
De Benito <i>et al.</i> (13)	(L)	Type 1 RIPs: Ebulitins α , β and γ	chrm.
Girbes <i>et al.</i> (21)	(L)	Heterodimeric type 2 RIPs: Ebulin I	affinity chrm.
Citores <i>et al.</i> (9)	(F)	Ebulin f	NA
Citores <i>et al.</i> (8)	(R)	Ebulins r1 and r2	NA
Iglesias <i>et al.</i> (24)	(R)	Tetrameric type 2 RIPs: SEA	mass spctr.
Citores <i>et al.</i> (11)	(L)	Monomeric lectins: SELIm	mass spctr.
Citores <i>et al.</i> (8)	(R)	SEA II	NA
Rojo <i>et al.</i> (35)	(L)	Homodimeric lectins: SELId	NA
Citores <i>et al.</i> (9)	(F)	SELfd	NA

Legend: F, fruits; Ap, aerial parts; L, leaves; R, roots; AQ, aqueous; MeOH, methanol; ext, extract; fr, fraction; spctr., spectroscopy; chrm., chromatography; NMR, nuclear magnetic resonance; HPLC, high-performance liquid chromatography; HSCCC, high-speed counter-current chromatography; NA, not available; SEA, *Sambucus ebulus* sialic acid-binding four-chain lectin; SELIm, *Sambucus ebulus* monomeric d-galactose binding lectin; SEA II, *Sambucus ebulus* monomeric N-Ac-galactosamine-binding lectin; SELId, *Sambucus ebulus* dimeric d-galactose and mucin-binding lectin; SELfd, *Sambucus ebulus* homodimeric D-galactose-binding lectin.

(4,5,10). Ethyl acetate SE extracts possess a lower IC50 in cancer cell lines in comparison with the normal cell lines (38).

Antimicrobial activity

Staphylococcus aureus (*S. aureus*) is one of the most common *Staphylococcus* species causing infections (12,25). Ethanol extract from SE leaves demonstrates a significant inhibition of δ -hemolysin production in a methicillin-resistant *S. aureus* isolate, thus proving a strong antimicrobial activity (34). Extracts from herbaceous parts exert anti-*Helicobacter pylori* activity (46). This study confirms the traditional use of such extracts as a remedy for treatment of gastric disturbances associated with inflammation, including peptic ulcers (14,29).

CONCLUSION

The high AOA, along with the proven antiinflammatory properties of SE imply the usage of the plant in various pathological conditions involving oxidative stress and inflammation. Studies revealing the possibilities for the application of SE derivatives in cancer therapy should continue, as scientific data indicate the plant's potential to reduce effectively cancer cell lines viability via protein synthesis inhibition.

In Bulgaria and in the other Balkan countries, there is a common use of traditional medicine along with a consumption of tea, syrups, and jams in everyday life. This suggests a need for further research in order to clarify the effects and mechanisms of SE influence on human health.

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