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Review Article

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A Review on *Chenopodium botrys* L.: traditional uses, chemical composition and biological activities

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Abstract

Chenopodium botrys L. is native to Europe and Asia and adventive in much of North America. The plant has been used traditionally for medicinal purposes; generally, these therapeutic uses and health benefits of *C. botrys* are largely based on folklore rather than on scientific substantiation, making it a good candidate to gather documentations, including the phytochemical content, *in vitro* experiments, animal models and human studies available in the scientific studies. The herb contains flavonoids, alkaloids and several terpenoids. *C. botrys* of different origins yielded 0.08-2% essential oil. Pharmacological reports support medicinal potential of *C. botrys* for developing new drugs. Different isomers of ascaridole were identified in *C. botrys* oil from different origins. In some reports, these compounds were major constituents of the essential oil. Ascaridole has various properties including anthelmintic, antifungal, sedative and pain-relieving. Ascaridole also showed activity against different tumor cell lines *in vitro*. These data suggest that *C. botrys* may be an interesting novel candidate plant for cancer treatment, but many studies are needed to confirm this possibility.

Keywords: *Chenopodium botrys* L., traditional uses, chemical composition, biological activity

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Introduction

According to the WHO, about three-quarters of the world population relies upon traditional remedies (mainly herbs) for the health care of its people. In fact, plants are the oldest friends of mankind. They not only provided food and shelter but also served the humanity to cure different ailments (1). The WHO is encouraging, promoting and facilitating the effective countries for herbal health programs. The potential of higher plants as a source of new drugs is still largely unexplored (2). The family Chenopodiaceae is a large family comprising about 102 genera and 1400 species (1).

The genus *Chenopodium* (Family-Chenopodiaceae) includes varieties of weedy herbs (more than 200 species) native to much of Europe, Asia, India, China and both North and South America (3). In Ayurveda *Chenopodium* L. is well-known for its applications in the treatment of various ailments like pectoral complaints, cough, abdominal pain, pulmonary obstruction and in nervous affections (4). The genus *Chenopodium* comprises 5 species, which have been widely distributed in Iran (5). *Chenopodium botrys* L. has been found in Azerbaijan,

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Hamedan, Khorasan, Mazandaran, Sistan & Bluchestan and Tehran provinces of Iran (6). This plant is an annual or biennial herb (7) and has various uses in traditional medicine (6). Since there is not a review article on *C. botrys*, so we decided to summarize the studies on this plant. *Ambrosia mexicana* hort is a scientific (Latin) synonym for this plant (Fig. 1) (8); the other synonyms are *Dysphania botrys* (L.) Mosyakin & Clemants, *Ambrina botrys* (L.) Moq.; *Ambrina botrys* Moq.; *Atriplex botrys* (L.) Crantz; *Botrydium botrys* (L.) Small; *Neobotrydium botrys* (L.) Moldenke; *Roubieva botrys* (L.) Fuss; *Roubieva botrys* Fuss; *Teloxys botrys* (L.) W.A.Weber; *Vulvaria botrys* (L.) Bubani; *Vulvaria botrys* Bubani (7). *Dysphania* was formerly included in the genus *Chenopodium* (9).

Figure1 *Chenopodium botrys*

English names for this plant are Ambrosia, sticky goosefoot, feather geranium, Jerusalem oak, Jerusalem oak goosefoot, turnpike goosefoot (8). *C. botrys* is a sticky, strongly aromatic annual with an incense-like odour and characteristically lobed, oak-like leaves (10) and with taproots (11). The young leaves of *C. botrys* look like miniature versions of those of the oak (12). The stems are usually heavily branched, erect to ascending, covered with stalked glandular hairs and attain a height of 15-60 cm. Minute, green flowers are clustered in numerous, short, axillary cymes forming large, terminal, pyramidal panicles, often reddening in the fruiting stage. The seeds are almost round, 0.5-0.75 mm in diameter, black and shiny. These plants grow in cultivated fields, on ruderal sites in towns and villages and on disturbed soil patches in steppes and semi-deserts, preferring loose, sandy soil (10). *C. botrys* is sometimes cultivated as a garden plant, particularly for its intensely fragrant foliage, and for its arching stems and flowers, valued in dried flower arrangements (8). *C. botrys* can grow in some heavy metal contaminated soils and is a high accumulator plant species for Cu and moderately accumulator plant species for Fe, Mn, and Zn (13). *C. botrys* accumulated Cu and Mn in its root and shoot (14).

This review summarizes some of the main reports on the traditional uses, chemical composition and biological activities of *Chenopodium botrys* from the data in the literatures.

Traditional uses

Plant extract given in catarrh and asthma, also used as anthelmintic. Leaves analgesic, anthelmintic, for headache, colds, influenza (7). In Iranian herbal medicine, *C. botrys* is used as expectorant, anticonvulsant and tonic

and for treatment of asthma (6). In France and Southern Europe, *C. botrys* (feather Geranium) is used in catarrh and humoral asthma and said to be a good substitute for *C. ambrosioides* (4). In Serbian traditional medicine, dried aerial parts are used for preparing infusions or liquid extracts as remedies with diuretic, antispasmodic, carminative and antidiarrhoic properties; sometimes as a spice (15). In Skardu valley of Pakistan, whole plant infusion is used orally for treatment of stomachache, liver complaints and headache; it is also known as laxative and diuretic (16). Young leaves and branches of *C. botrys* are used for healing of wounds in Kohistan valley, Khyber Pukhtunkhwa, Pakistan (17). In India, *C. botrys* is known as stimulant, diuretic, carminative, antispasmodic, emmenagogue, pectoral; it is also used in asthma, catarrh; diseases of the stomach and liver (18). In Lahul, a province of the Punjab of India, *C. botrys* is used as a popular flavoring for a soup of meat, cheese and barley (10, 19). In Ladakh, India, *C. botrys* is considered to be anthelmintic, diuretic and laxative (10). In Jaunsar-Bawar hills, Uttar Pradesh of India, leaf juice dropped into the nostrils of cattle to expel leeches (20). In Lahaul-Spiti region of Indian western Himalaya, vegetable prepared from tender shoots and leaves of *C. botrys* is found effective to cure severe headache (21). Seeds are considered toxic (18). An ethnomedicinal survey reports that in the Kashmir Himalays a decoction of the seeds is ingested in cases of tapeworm infestation, especially in children (10). This plant is a vermifuge, for example, the prescription from Alabama: for worms, one teaspoonful of the seed or the stalk tea mixed with syrup, three times a day. There is, too, a remedy, using the inner bark of this plant, boiled and mixed with molasses to make a candy. It also seems to have been used in some way for tuberculosis (12). Dioscorides said that *botrys* (old World *Chenopodium*) was mainly used to place in clothing because its odor repelled clothes moth (22). In Germany still in the 19th cent. frequently cultivated against moths and as a medicinal plant (23). In Spain, *C. botrys*, known as *té de Valladolid* (Valladolid tea), has been used to treat coughs and probably for digestive disorders; it is also antihelminthic (24). Fernald *et al*. recommend that *C. botrys* not be consumed as a potherb (8). This plant contains pharmacologically active principles. It is suggested that its consumption be avoided, or at least highly limited (8). Traditional uses of *C. botrys* in different countries are summarized in Table 1.

Chemical composition

The herb contains flavonoids, alkaloids and several terpenoids. *C. botrys* of different origins yielded 0.08-2% essential oil. According to several studies, the essential oil varied in amount and composition (10, 18, 25-28). Bicyclic sesquiterpenoids were found in *C. botrys* (1). The characteristic odour of the plant is due to monoterpenes and sesquiterpenes (10). The headspace of *C. botrys* was analyzed; monoterpenes (camphor, *δ*-3-carene, fenchone, linalool, menthone, nerol, *β*-pinene, pulegone, terpineol-4 and thujone) and sesquiterpenes (*β*-elemene, elemol and *β*-eudesmol) were found to be responsible for the aromatic, herbaceous, earthy, dull, heavy and pine-like odor of slimy anserine (29). Early studies on the essential oil refer to ascaridole as a compound (10, 30). Ascaridole is a bicyclic monoterpene that has an unusual bridging peroxide functional group (3). Indian oil is reported to be devoid of ascaridole, the anthelmintic principle (18). Studies on benzene and hexane extracts of Spanish plant samples led to the isolation of numerous elemane, eudesmane and guaiane type sesquiterpenes; chenopodic acid, a terpenoid, was also identified as a constituent of the essential

Table 1 Traditional uses of *Chenopodium botrys* in different countries

Origin	Parts used/Formulation	Applications	Ref.
Iran	*flowering aerial Parts* -*	expectorant anticonvulsant, tonic and in asthma	6
France and Southern Europe	-	catarrh and humoral asthma	4
Serbia	dried aerial parts, infusions or liquid extracts	as remedies with diuretic, antispasmodic, carminative and antidiarrhoic properties, sometimes as a spice	15
Pakistan, Skardu valley	whole plant, oral infusion	treatment of stomachache, liver complaints and headache, as laxative and diuretic	16
Pakistan, Kohistan valley, Khyber Pukhtunkhwa	young leaves and branches	healing of wounds	17
India	-	stimulant, diuretic, carminative, antispasmodic, emmenagogue, pectoral, in asthma, catarrh, diseases of the stomach and liver	18
India, Lahul	-	a popular flavoring for a soup of meat, cheese and barley	10,19
India, Ladakh	-	anthelmintic, diuretic and laxative	10
India, Jaunsar-Bawar hills, Uttar Pradesh	leaf juice, drop into the nostrils of cattle	to expel leeches	20
India, Lahaul-Spiti region	vegetable prepared from tender shoots and leaves	to cure severe headache	21
India, Kashmir Himalays	decoction of the seeds	tapeworm infestation	10
USA, Alabama	seed or the stalk tea mixed with syrup -	vermifuge in some way for tuberculosis	12
Germany	-	against moths and as a medicinal plant	23
Spain	-	antihelminthic, to treat coughs and probably for digestive disorders	24

*-: It has not been explained.

oil (10, 31, 32). *C. botrys* growing in Saudi Arabia was rich in essential oil (2% v/w); the sesquiterpenes *α*- and *β*-eudesmol were found to be the major compounds (26). Both sesquiterpenes, *α*- and *β*-eudesmol, also occur in the essential oil of Egyptian origin (10). The major components of *C. botrys* oil from North America include *α*- and *β*-chenopodiol (36%), eudesma-3,11-dien-6*α*-ol (9.4%), botrydiol (9.0%), elemol (6.5%), elemol acetate (5.5%), *γ*-eudesmol (5.4%), and *α*- and *β*-eudesmol (3.7%); guaia-3,9-dien-11-ol, a new sesquiterpene alcohol, accounted for 7.4% of the oil (33). The main components of *C. botrys* oil from two different localities of Iran (east of Tehran, Khojir Park and Khalkhal, province of Ardebil) were juniper camphor (16.5% and 25.7%), elemol (14.3% and 13.4%) and *α*-cadinol (8.2% and 11.6%), respectively (27). Essential oil from aerial parts of *C. botrys* collected from Khoy county, West Azerbaijan province of Iran was obtained by two methods, hydro-distillation and solvent extraction using *n*-hexane. In the first oil, the major constituents were *α*-eudesmol (15.2%), *epi*-*α*-muurolol (11.1%) and cubenol (10.2%); in the second oil, *α*-chenopodiol acetate (35.0%) and eudesma-3,11-dien-6-*α*-ol (18.9%) were identified as the main compounds (34). The main components of the essential oil of *C. botrys* collected from the suburb of Sari (Mazandaran province, North of Iran) were *γ*-terpineol (52.8%), *p*-cymene (19.0%) and *iso*-ascaridole (7.0%) (28). The oil of *C. botrys* from Greece comprised mainly

sesquiterpenes with elemol acetate (16.3%), elemol (14.1%), botrydiol (11.1%), *α*-chenopodiol (9.5%), *β*-eudesmol (7.0%) and selina-3.11-dien-6*α*-ol (6.1%) being the major components (35). Ascaridole (7.5% and 40%) was reported in essential oils of *C. botrys* collected from Spain and Slovakia, respectively (3). *α*-Terpinene (21.4%), *p*-cymene (15.2%), *E*-caryophyllene (6.5%) and limonene (6.1%) were identified as major compounds in the essential oil of *C. botrys* from the East Mediterranean; in addition, *β*-myrcene was also found in *C. botrys* oil (3). 2,3-dehydro-4-oxo-*β*-Ionone (22.4%), (+)-7-*epi*-amiteol (11.5%) were found as the major components of the oil of *C. botrys* collected from suburb of Kashan, Iran (36). 2-(4*α*.8-dimethyl-1.2.3.4.4*α*.5.6.7-octahydro-naphthalen-2-yl)-prop-2-en-l-ol was identified as the main compound in the essential oil of sticky goosefoot, *C. botrys*, growing in Turkey (37). Reported major compounds of *C. botrys* oil from different origins are outlined in Table 2.

Studies on the flavonoid content of the plant led to the isolation of flavonols; chrysoeriol, quercetin, quercetin-3-O-*β*-D-glucopyranoside and quercetin-3-O-*β*-(D-glucopyranosyl-6-*β*-D-glucopyranoside); flavones: hispidulin, salvigenin, 5-methylsalvigenin, 7-methyleupatulin, sinensetin and jaceosidin (10, 38-41). The plant contains alkaloids e.g. betaine has been isolated (42, 43). Betaine is found in all parts of the plant (18). Some species of chenopods had previously been investigated for the presence of phytoecdysteroids; these compounds are plant steroidal analogues of invertebrate steroid hormones (ecdysteroids). Phytoecdysteroids were not found in seeds of *C. botrys* (44).

Biological activities

Antimicrobial, Giardicidal and Nematicidal activities

The essential oil (0.43%w/w) isolated from aerial parts of *C. botrys* collected from locus typicus near the town of Vlasotince (Southern Serbia) exhibited significant

Table 2. Major essential oil components (>%5) of *Chenopodium botrys* from different origins

Compounds	Origin	Ref.
ascaridole	Kazakstan	10,30
α- and *β*-eudesmol	Saudi Arabia	26
α- and *β*-eudesmol	Egypt	10
α- and *β*-chenopodiol, eudesma-3,11-dien-6*α*-ol, botrydiol, elemol, elemol acetate, *γ*-eudesmol, guaia-3,9-dien-11-ol	North America	33
juniper camphor, elemol, *α*-cadinol	Iran, east of Tehran, Khojir Park	27
juniper camphor, elemol, *α*-cadinol	Iran, Ardebil province, Khalkhal	27
α-eudesmol, epi-*α*-muurolol, cubenol (by hydro-distillation method) *α*-chenopodiol acetate, eudesma-3, 11-dien-6-α-ol (by solvent extraction method using *n*-hexane)	Iran, West Azerbaijan province, Khoy county	34
γ-terpineol, *p*-cymene, *iso*-ascaridole	Iran, Mazandaran province, suburb of Sari	28
elemol acetat, elemol, botrydiol, *α*-chenopodiol, *β*-eudesmol, selina-3.11-dien-6*α*-ol	Greece	35
ascaridole	Spain	3
ascaridole	Slovakia	3
α-terpinene, *p*-cymene, *E*-caryophyllene, limonene	East Mediterranean area	3
2,3-dehydro-4-oxo-*β*-Ionone, (+)-7-*epi*-amiteol	Iran, suburb of Kashan	36
2-(4*α*.8-dimethyl-1.2.3.4.4*α*.5.6.7-octahydro-naphthalen-2-yl)-prop-2-en-l-ol	Turkey	37

bactericidal and fungicidal activity against selected strains of microorganisms, *viz. Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa, Aspergillus niger, Candida albicans, Sarcina lutea, Klebsiella pneumoniae, Salmonella enteridis* and *Shigella flexneri* (15). The oil of *C. botrys* growing in Saudi Arabia showed the antimicrobial activity (26). The results of antimicrobial activity of the essential oil from aerial parts of *C. botrys* growing in Greece were also reported (35). *C. botrys* oil exhibited significant antibacterial activity against *Salmonella aureus* and *Bacillus cereus*; the residual water solution showed a good activity against *Salmonella heidelberg* and *Bacillus cereus* (1, 45). The essential oil of *C. botrys* collected from suburb of Kashan (Iran) showed strong antimicrobial activity against *Staphylococcus saprophyticus* followed by *Klebsiella pneumoniae, Bacillus cereus, Staphylococcus epidermidis, Streptococcus mutans, Listeria monocytogenes* and *Salmonella typhimurium*; the oil had slight effect on *Candida albicans* and showed inhibitory effect on *Aspergillus* species and *Bacillus subtilis* (36). The essential oil obtained from *C. botrys* showed a strong activity against the tested dermatophytes, e.g., *Trichophyton mentagrophytes, Epidermophyton floccosum* and *Microsporum canis*; the oil possessed bactericidal but not bacteriostatic effects (1). The aqueous extracts of *C. botrys* collected from Guba region of Azerbaijan showed the high fungistatic activity (46).

Both alcoholic and aqueous extracts of *C. botrys* collected from suburb of Birjand (Iran) have *in-vitro* giardicidal effect on *Giardia lamblia* cysts. The highest giardicidal effect of alcoholic and aqueous extracts of *C. botrys* at 37°C, in 20 mg/ml and 5 hour after experiment were 100% and 66.1% respectively. Giardicidal effect of both extracts of *C. botrys* significantly increased by rising the concentration, time and temperature ($P < 0.0001$). The ethanol extracts of this plant have more giardicidal effect (47). Ayazpour et al. reported that the leaf extract of *C. botrys* was effective on citrus nematode control in Fars province, Iran (48).

Anti-inflammatory and allergenic activities

The aerial parts of *C. botrys* have anti-inflammatory activity (49, 50). Amjad studied pollen extracts allergenicity of *C. album* and *C. botrys* collected from area of Tehran, Karaj city and around Kandovan (Iran). Pollens were extracted using phosphate-buffered saline, pH 7.4. Male guinea pigs were sensitized and treated with *C. album* and *C. botrys* pollen extracts and skin prick tests were performed on guinea pigs and quantified on the basis of wheal diameter. During the skin prick test, the allergenic sensitivity was observed for *C. album* pollen grains, with an average wheal diameter of about 4 cm and for *C. botrys* pollen grains, with an average wheal diameter of about 2.5 cm. The presence of blood eosinophilia, an increase in neutrophilia number with the presence of the other factors which have been reported as allergic indicators proved the allergenicity of *C. album* and *C. botrys* pollen grains. Moreover, the observations suggest that *C. album* pollen grains are more allergenic than *C. botrys* pollens (51).

Effects on cardiovascular and respiratory system

Alkaloids extracted of *C. botrys* by Et_2O-H_2SO_4, when applied in doses of 0.005-0.01 g/kg caused temporal excitation of respiration and increase of the arterial pressure by 10-40 mm Hg. Tartrates from the petroleum ether extract had an analogous

effect in doses of 0.002-0.03 g/kg. On the other hand tartrates from the $CHCl_3$ extract caused a marked decrease in the arterial pressure and respiration, when applied in doses of 0.001-0.009 g/kg. Doses of 0.01-0.015 g/kg led to a complete loss of the pressure and caused a block in respiration (1).

Mitochondrial-mediated toxicity

Approximately 50% of the drugs with FDA Black Box Warnings for hepatoxicity and cardiovacular toxicity are known to interfere with mitochondrial function. Nagle et al. evaluated extracts from more than 350 species of plants and other organisms used in traditional Chinese, Indian, African, and Western herbal medicine for their ability to disrupt mitochondrial function. Several species, including *C. botrys*, possess compounds that have been demonstrated to interfere with mitochondrial function (52).

Conclusion

This article briefly reviews the traditional uses, chemical composition and biological activities of *Chenopodium botrys* that is a rich source of organic compounds and varying structural patterns. Pharmacological reports support medicinal potential of *C. botrys* for developing new drugs. Different isomers of ascaridole were identified in *C. botrys* oil from different origins (10, 28, 30). In some reports, these compounds were major constituents of the essential oil (3, 10, 28, 30). Ascaridole apparently undergoes partial thermal isomerization to isoascaridole (53). Ascaridole has anthelmintic properties (18). Ascaridole has been documented with sedative and pain-relieving properties as well as antifungal effects. Ascaridole was found to be a potent inhibitor *in vitro* development of *Plasmodium falciparum*, *Trypanosoma cruzi*, and *Leishmania amazonensis* (3, 54). Ascaridole also showed activity against different tumor cell lines *in vitro* (CCRF-CEM, HL60, MDA-MB-231) (3). Ascaridole was cited as having carcinogenic activity by Van Duuren. However, ascaridole, extracted from wormseed oil, exhibited cytotoxic activity towards two human leukemia cell lines (HL60 and CCRF-CEM), one human breast cancer cell line (MDA-MB-231) and their multidrug-resistant counterparts MDR1, MRP1 and BCRP. Ascaridole was cytotoxic to human cell lines for colon cancer and leukemia, and inhibited connective tissue cancer in mice at 10 or 20 mg/kg, with little damage to normal tissue. It is generally regarded as highly toxic, and is more toxic to humans than rodents. It may be anticarcinogenic (53). These data suggest that *C. botrys* may be an interesting novel candidate plant for cancer treatment, but many studies are needed to confirm this possibility.

Conflict of interest statement

The authors declared no potential conflict of interest with respect to the authorship, and/or publication of this study.

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