An Updated Phyto-pharmacological Review on Medicinal Plant of Saudi Arabia-*Dodonaea viscoa* Linn

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Abstract

Dodonaea viscosa (Family sapindaceae) is an evergreen medicinal plant with woody perennial shrub widely distributed throughout the tropics. In Saudi Arabia, it is found in Hijaz region, Eastern region and Southern part. Various plant parts such as stem, leaves, seeds, roots, bark and aerial parts are used in traditional system of medicine. The leaves of this plant has been used to treat various ailments like sore throat, wounds, fever, piles, malaria, angina, cold, arthritis, sinusitis, flu and boils. It is also used as dressing for skin diseases of the head and face. In addition to this, leaves extract has been reported to have antibacterial activity against *Staphylococcus aureus*, *Micrococcus luteus, Escherichia coli* and *Pseudomonas aeruginosa*. Other pharmacological activity viz antinociceptive, antiulcer, wound healing, antioxidant, anti-inflammatory, neurological, antidiabetic, anti-diarrheal, antihyperlipidemic and hepatoprotective activity has also been reported.

The present review is an effort to provide a detailed updated survey of the literature on scientific researches of pharmacognostical characteristic, chemical constituents, and pharmacological activity of this Saudi medicinal plant.

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Introduction

Dodonaea viscosa Linn. (Fig 1) is a shrub or small tree, 2-4 m high, with angular, viscid branches belonging to family Sapindaceae. Leaves are linear oblanceolate, often glossy, subsessile with long-tapering base and obtusely apiculate apex. Flowers are small yellowish, in terminal panicles or racemes. The centre of origin of *Dodonaea viscosa* is believed to be Australia, but it occurs throughout the tropics and subtropics, widely distributed in all over the world (Rajamanickam *et al.*, 2010). In Saudi Arabia, it is found in Hijaz, southern, eastern and eastern Najd region (Mighaid, 1978).

The genus *Dodonaea* comprises about 60 species, which are almost all restricted to Australia, suggesting Australia is an evolutionary centre of dispersal. In Australia, *Dodonaea viscosa* is described as having seven subspecies, which are largely geographically distinct. In tropical Africa, two varieties of *Dodonaea viscosa* are distinguished: the coastal var. *viscosa*, which has usually bisexual, whitish flowers, a strongly 2-lobed scar of fallen sepals beneath the fruit and not or only slightly compressed seeds, and the mainly inland var. *angustifolia* (L.f.) Benth., which has usually shorter and narrower leaves, usually unisexual, greenish-yellow flowers, a more or less annular scar of fallen sepals beneath the fruit and more compressed seeds.

Geographical Indication

Dodonaea viscosa has a pantropical distribution occurring in temperate regions of Australia, Africa, Mexico, New Zealand, India, Samoa, Guam, Northern Mariana Islands, Virgin Islands, Puerto Rico, Florida, Arizona, South America and Hawaii (West *et al.*, 1984).

Morphology

Fig. 1. *Dodonaea Viscosa.*

Plant description

Dodonaea viscosa is a dioecious or monoecious multi stemmed shrub or single-stemmed small tree up to 7 m tall; bark blackish, of variable roughness, thin and exfoliating in long thin strips; twigs blackish or reddish-brown, glandular, developing vertical fissures; uppermost part of young branches greenish and prominently angled; Leaves alternate, simple; stipules absent; petiole very short, up to 2.5 mm long or absent; blade oblanceolate or broadly to narrowly elliptical, (1–)4–13 cm × (0.5–)1.5–4 cm, narrowly cuneate at base, obtuse but minutely apiculate at apex; margins entire, both surfaces glabrous but glandular and coated (especially when young) with viscid glandular exudates; midrib on both sides and 15– 20(–30) often indistinct pairs of lateral veins.

Inflorescence

Inflorescence a loose thyroid panicle at the end of twigs; Flowers bisexual or unisexual, whitish to greenish-yellow; pedicel 8–15 mm long; sepals 3–4, free, 2– 2.5 mm long; petals absent; stamens 7(–9), filaments very short, anthers oblong, up to 3 mm long in male flowers, up to 2 mm long in bisexual flowers and reduced to staminodes or completely lacking in female flowers; ovary superior, oblong in outline, flattened, 2–3-celled, strongly rudimentary in male flowers, style 2–3-lobed.

Fruit

It contains 2– 3-winged papery capsule, 15–23 mm × 18– 25 mm, white or straw-coloured to brown or purplish, dehiscent by splitting along 2–3 central septa, each cell 2-seeded.

Seed

Seeds is subglobulose, more or less compressed, 3 mm in diameter, black; Seedling with epigeal germination; hypocotyls 8–16 mm long; cotyledons lanceolate, acute; epicotyls 0.5–1.5 cm long.

Phytochemistry

Recent phytochemical studies have confirmed that *Dodonaea viscosa* contains all the major secondary plant metabolites like alkaloids, flavonoids, saponins, tannins, carbohydrate, steroids and gum mucilage.

A number of chemical constituents have been isolated from *Dodonaea viscosa.* However most of these were conducted on outside species of Saudi Arabia.

The major investigation of flavonoids was conducted by Sachdev and Kulshreshtha, who isolated a number of compounds. Ghilbert has reviewed the chemical

constituents of *Dodonaea viscosa* and found 23 flavones from seeds, bark, flowers and leaves of *D.viscosa*, characterized by oxygenation at C-3 and, in 50% of cases, methoxylation at C-6 (Rani *et al.*, 2009).

Siddiqui's review makes reference to eighteen flavonoids including glycosides of quercetin (rutin) and isorhamnetin (Siddiqui, 1998). Mata and co workers isolated sakuranetin from Mexican *D.viscosa* in 1991 (Mata *et al.*, 1991). Getie et al isolated relatively large concentrations of quercetin, kaempferol and isorhamnetin in *D.viscosa* crude leaf extract (Getie *et al.*, 2000).

Important compounds isolated from *D viscosa* were listed in Table 1.

Medicinal Uses

It possesses many medicinal properties and has been used by native peoples from all regions where it is found. Its leaves can be used to combat rheumatism, skin infections, fevers, swellings, aches, and "gastrointestinal disorders" including diarrhea, and can be used as a antispasmodic agent (Rojas *et al.*, 1996). The Australian aborigines used the leaves and roots as a painkiller to soothe toothaches and headaches (Cribb *et al.*, 1981). The flowers are used as a "home-brew" substitute to bestow a bitter flavor, and also used as a tonic. A red dye is extracted from the fruit, and the capsules are also commonly used in leis. In India the seeds are used as fish poison (Wagner *et al.*, 1987). The wood is extremely hard and has been used for tools, spears and weapons. In India it is an important source of fuelwood (Jain *et al.*, 1999).

Pharmacological Activity

Antibacterial activity

The crude ethanolic extract and *n*-hexane, dichloromethane, ethyl acetate, *n*-butanol and aqueous fractions of *Dodonaea viscosa* were analyzed for antibacterial potential against four Gram positive bacteria: *Bacillus subtilis, Bacillus cereus, Micrococcus luteus, Staphylococcus aureus,* and three Gram negative bacteria: *Escherichia coli, Salmonella typhi, Pseudomonas aeruginosa*. Preliminary screening showed inhibition against two gram positive (*Staphylococcus aureus*, *Micrococcus luteus*) and two gram negative *(Escherichia coli* and *Pseudomonas aeruginosa)*. The MIC of each fraction was determined through a 96-well micro-titer plate method (Khurram *et al.*, 2009).

In another study, antibacterial activity of dichloromethane and acetone fractions obtained by serial extraction from the leaf powder of *Dodonaea viscosa* was

determined using a serial dilution microplate technique. The minimum inhibitory concentration (MIC) of isolated compounds against *Staphylococcus aureus, Enterococcus faecalis, Escherichia coli* and *Pseudomonas aeruginosa* was found to be varied from 16 µg/ml to more than 250 µg/ml (Teffo *et al.*, 2010). The methanolic extract of *Dodonaea viscosa* showed activity against multiresistant Gram-positive bacteria (Mothana *et al.*, 2010).

The antibacterial activity of newly isolated compounds from dichloromethane and acetone fractions of leaf powder of *Dodonaea viscosa* was evaluated and found positive for different organism. The minimum inhibitory concentration (MIC) of isolated compounds against *Staphylococcus aureus, Enterococcus faecalis, Escherichia coli and Pseudomonas aeruginosa* varied from 16 µg/ml to 250 µg/ ml (Teffo *et al.*, 2010).

Antifungal activity

Antifungal activity of solvent extracts of leaves and shoots of *Dodonaea viscosa* have been determined against fungi *Aspergillus niger*, *Aspergillus flavus, Paecilomyces varioti, Microsporum gypseum, and Trichophyton rubrum* causing skin diseases. All crude extracts were found to be effective against tested fungi. However among different extracts (Ethanol, methanol, ethylacetate, chloroform and aqueous extracts), chloroform has strong inhibition activity against fungi as compared to others (Pirzada *et al.*, 2010).

Antinociceptive activity

The leaf extracts of *Dodonaea viscose* was evaluated for anti-nociceptive activity on chemical and thermal induced pain. Various experimental pain models (Hot plate, Tail flick and writhing induced by glacial acetic acid) were used for assessing antinociceptive activity of *D. viscosa*. All the leaf extracts of *D. viscosa* showed antinociceptive activity in both rats and mice. All tested extracts showed significant antinociceptive activity. The ethyl acetate extract exhibited the best activity. The antinociceptive efficacy of the extracts may be attributed due to the presence of flavonoids, sterols and saponins (Joshi *et al.*, 2006).

Table 1 Flavonoids of *Dodonaea Viscosa*

Parent moiety	Chemical name	Reference
Viscosol	3'-(γ,γ-dimethyl alllyl)-5,7-dihydroxy-3,6,4'-trimethoxy flavone	(Sachdev *et al.*, 1986)
Aliarin	5,7,4'-trihydroxy-3'- (3-hydroxy methyl butanol) 3,6-dimethoxy flavone, 5,7-dihydroxy-3'- (3 hydroxymethyl butanol), 3,6,4'-trimethoxy flavone, 5,4'-dihydroxy-3'-(3-hydroxymethylbutanol)3,5,6,4'-tetramethoxyflavone	(Sachdev *et al.*, 1983)
Pinocembrin	5,7-dihydroxy-3'- (3- hydroxymethyl butyl)-3,6,4'-trimethoxy flavone	
	5,7- dihydroxy flavanone	
Penduletin	5,4-Dihydroxy-3,6,7-tri methoxyflavone	
Santin	5,7-dihydroxy - 3,6,4'3' Tetra methoxy flavone	(Sachdev *et al.*, 1983); (Harborne *et al.*, 1999)
Pectolinarigenin	5, 7 -Dihydroxy-6, 4'-Dimethoxy flavone	(Wollenweber, 1993)
Cirsimaritin	5, 4'-Dihydroxy-6,7-dimethoxy flavone	
Rhamnocitrin	3,5,7,4'-Tetrahydroxy-7- Methoxy flavone	
Kumatakenin	3,5,7,4'-Tetrahydroxy-3,7-dimethoxy flavone	
Ermanin	3,5,7,4'-Tetrahydroxyl-3,4'-dimethoxy flavone	
Isokaempferide	3,5,7,4'-Tetrahydroxyl-3'-methoxy flavone, 3,5,7,4'-Tetrahydrox yl-7,4'-dimethoxy flavone, 3,5,7,4'-tetrahydroxyl-3,7,4'-trimethoxy flavone	
Kaempferol	5-Hydroxy-3,7,4'-trimethoxy flavone	(Harborne *et al.*, 1999)
	6 Hydroxy-3,6,7 trimethoxy flavone	(Wollenweber *et al.*, 2007)
	5,7,4'Trihydroxy-3-methoxyflavone	
Sakuranetin	(S)-5,4'-dihydroxy-7-methoxyflavone	(Mata *et al.*, 1991)
Acacetin	5 hydroxy -7,4'- Dimethoxy flavone	(Abdel-Mogib *et al.*, 2001)
Narigenin	5,7,4 -trihydroxy -7 –methyoxy flavanone	(Wollenweber *et al.*, 2007)
	5,7,4 -trihydroxy -7,4' –dimethyoxy flavanone	
Genkwanin	5,7,4'-Trihydroxy-7- Methoxy flavone	

Antiulcer activity

Various fractions of *D.viscosa* was tested for antiulcer activity in various experimental gastric ulcer models. Among the tested extracts, ethyl acetate fractions exhibited higher ulcerative lesion index, increased serum calcium level and decreased alkaline phosphatase activity in all experimental models. The antiulcer activity of the extracts may be attributed to cytoprotective and healing activity of flavonoids present in plants (Veerapur *et al.*, 2004).

Wound healing activity

Ethanolic extract of dried leaves showed potent wound healing activity in excised and incised wound model in rats. In excision model, 10% extract treated wounds were found to have faster rate of wound contraction and epithelization. Suspension and ointment of ethanol extract produced a significant response in wound models like breaking strength of skin, granuloma and wound contraction and also found to overcome the anti-healing properties of dexamethasone (Habbu *et al.*, 2007).

Antioxidant activity

Antioxidant potential of four newly isolated compounds [3, 5, 7-trihydroxy-4'-methoxyflavone (1); 5, 7, 4'-trihydroxy-3, 6-dimethoxyflavone (2); 5, 7-dihydroxy-3, 6, 4'- trimethoxyflavone (3); 5-hydroxy -3, 7, 4'-trimethoxyflavone (4) and 3,4',5,7-tetrahydroxy flavones (5)] from fractionation of dichloromethane and acetone fractions obtained by serial extraction from the leaf powder of *Dodonaea viscosa* was evaluated using a DPPH spectrophotometric assay. Compounds 1 and 5 demonstrated significant antioxidant activity (EC50=75.49±1.76 µM and 35.06±0.85 respectively) that was comparable with standard ascorbic acid (EC50=13.55±0.28 µM) (Teffo *et al.*, 2010).

Anti-inflammatory activity

Antiinflammatory activity of an isolated molecule, hautriwaic acid (Diterpene) from *D. viscosa* leaves was evaluated. It exhibited good anti-inflammatory activity in 12-*O*-tetradecanoylphorbol 13-acetate (TPA) induced mice ear edema models at doses of 0.25, 0.5 and 1.0 mg/ear (60.2, 70.2 and 87.1% inhibition, respectively); additionally *Dodonaea viscose* dichloro-methane extract also showed 97.8% anti-inflammatory effect at dose of 3 mg/kg (Salinas-Sanchez *et al.*, 2012).

Neurological (Analgesic, depressant and anti-convulsant) activity

Ethanolic extract of the seeds of *Dodonaea viscosa* showed significant CNS depressant activity at the dose level of 30 mg/kg, when compared with morphine

sulphate, diazepam and phenytoin as standard drugs. Significant analgesic and anticonvulsant activities were also observed at the same dose. *In vivo* analgesic activity was demonstrated in the mouse acetic acid-induced writing test and hot plate method. Water extract of the plant significantly inhibited the writhes induced by 2% acetic acid. It shows antipyretic activity in the rat (LP-induced rectal temperature increase) at a concentration of 100.0mg/kg. Preliminary photochemical screening, showed the presence of alkaloids, saponins and carbohydrates which may responsible for the activity of the extract (Anilreddy, 2009).

Antidiabetic activity

Antidiabetic activity of water extract and the polar fraction of ethanol extract of *Dodonaea viscosa* was investigated in type 2 diabetes induced by a standardized high fat diet (HFD) and low dose streptozotocin (STZ) (25 mg/kg) in rats. It was evaluated by change in biochemical parameters. Results suggested that water extract and the polar fraction of ethanol extract inhibits HFD + STZ-induced insulin resistance, reduced blood glucose, serum insulin, lipid abnormalities and oxidative stress. The effects may be due to interaction with multiple targets operating in diabetes mellitus (Veerapur *et al.*, 2010).

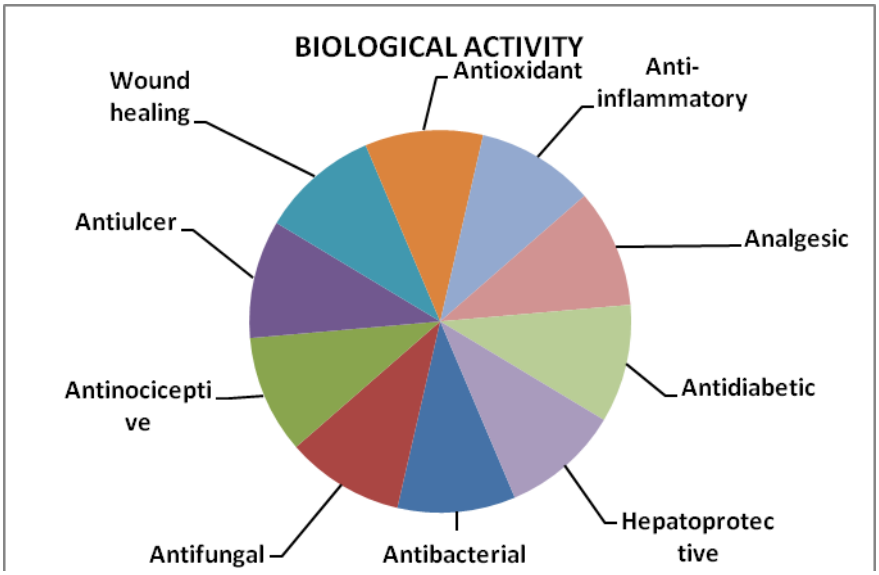
In another study, the ethyl acetate methanolic extract of *Dodonaea viscosa* leaves were evaluated for ant-diabetic efficacy after oral administration of extracts at different doses (200 and 400mg/kg bw) to normal as well as STZ induced diabetic rats. Various biochemical (glucose tolerance, fasting glucose level, glycogen level, total cholesterol) and enzymatic (MDA, GSH, GOT and GPT) parameters were assessed. These results indicated that *Dodonaea viscosa* methanolic extract possess antidiabetic effect in experimental diabetic rats. Methanolic extracts produced significant effect in normal rats after 6h of administration. It showed improvement at both doses (Meenu *et al.*, 2011).

Anti-diarrheal activity

The anti-diarrheal activity of the alcohol and aqueous extracts of the roots of *Dodonaea viscosa* was investigated by castor oil induced diarrhoea in mice. The parameters of this study were number of diarrheal episodes and mean weight of stool of mice. The percentage protection in extract treated animals showing diarrhea was compared with castor oil treated and loperamide treated animals. The results revealed that the alcohol and aqueous extracts significantly reduced diarrhea in mice with reduction in weight of stools (Rajamanickam *et al.*, 2010).

Anti-hyperlipidemic and Hepatoprotective activity

The antihyperlipidaemic and hepatoprotective activity of *Dodonaea viscosa* leaves extracts in the alloxan-induced diabetic rabbits was carried out. Serum levels of triglycerides, total cholesterol, LDL-cholesterol, HDL-cholesterol, ALT, and AST were estimated by using commercially available kits. The oral administration of aqueous:methanol (70:30) extract of the *Dodonaea viscosa* leaves significantly decreased the raised parameters (triglyceride, total cholesterol and LDL cholesterol) to normal values. But the extract has significantly increased HDL cholesterol, ALT and AST levels. In the groups recieving aqueous:methanol (70:30) extract**,** the average serum level of total cholesterol was 60.00±1.30 mg/dL, LDL cholesterol was 92.80±2.29 mg/dL, HDL-cholesterol was 31.80±1.0 mg/dL and triglyceride was 15.40±0.75 mg/dL while the average serum levels of ALT and AST were 45.60±3.08 and 27.20±1.36 IU/dL, respectively. It confirmed that aqueous:methanolic (70:30) extract of *Dodonaea viscosa* leaves exerts antihyperlipidaemic and hepatoprotective effects in the alloxan-induced diabetic rabbits (Ahmad *et al.*, 2012).



Future trends

In recent years ethno medicinal studies received much attention on natural resources to light the numerous medicines, especially of plant origin which needs evaluation on modern scientific lines such as phytochemical analysis, pharmacological and clinical

trials. The reported phytochemical and pharmacological studies on *Dodonaea viscosa* support its traditional uses and may prove to be useful for clinical evaluation and development of drugs.

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