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A review on Dodonaea viscosa: A potential medicinal plant

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Abstract: The chemical analysis of *Dodonaea viscos*a (Sapindaceae), revealed that the plant contained alkaloids, flavonoids, fixed oil and fat, steroids, phenolics, saponins, tannins, gums, mucillages, carbohydrates, reducing sugar, glycosides and trace elements. The pharmacological studies showed that *Dodonaea viscos*a possessed antidiabetic, antimicrobial, insecticidal, antioxidant, cytotoxic, antifertility, wound, anti-inflammatory, analgesic, anti-ulcer, antispasmodic, anti-diarrheal and detoxification effects. This review highlights the chemical constituents and pharmacological effects of *Dodonaea viscos*a.

Keywords: *chemical, constituents, pharmacology, Dodonaea viscosa*

Plant profile:

I. INTRODUCTION:

In the last few decades there has been an exponential growth in the field of herbal medicine. It is getting popularized in developing and developed countries owing to its natural origin and lesser side effects. On the other hand, two thirds of the new chemicals identified yearly were extracted from higher plants. 75% of the world's population used plants for therapy and prevention. In the US, where chemical synthesis dominates the pharmaceutical industry, 25% of the pharmaceuticals are based on plant-derived chemicals [1].Plants are a valuable source of a wide range of secondary metabolites, which are used for therapeutic purposes [2-50]. The chemical analysis of *Dodonaea viscos*a (Sapindaceae), revealed that the plant contained alkaloids, flavonoids, fixed oil and fat, steroids, phenolics, saponins, tannins, gums, mucillages, carbohydrates, reducing sugar, glycosides and trace elements. The pharmacological studies showed that *Dodonaea viscos*a possessed antidiabetic, antimicrobial, insecticidal, antioxidant, cytotoxic, antifertility, wound, anti-inflammatory, analgesic, anti-ulcer, antispasmodic, anti-diarrheal and detoxification effects. This review will shed some light on the chemical constituents and pharmacological effects of *Dodonaea viscos*a.

Synonyms:

Dodonaea arabica Hochst. & Steud., *Dodonaea arborea* Herter, *Dodonaea aspleniifolia* var. arborescens Hook.f., *Dodonaea bialata* Kunth, *Dodonaea candolleana* Blume, *Dodonaea candolleana* var. minor Blume, *Dodonaea cuneata* var. rigida Benth., *Dodonaea dioica* Roxb. ex DC., *Dodonaea ehrenbergii* Schltdl., *Dodonaea eriocarpa* Sm., *Dodonaea eriocarpa* f. acuminata O. Deg. & Sherff, *Dodonaea eriocarpa* var. amphioxea O. Deg. & Sherff, *Dodonaea eriocarpa* var. confertior Sherff, *Dodonaea eriocarpa* var. costulata O. Deg., I. Deg. & Sherff, *Dodonaea eriocarpa* f. decipiens Sherff, *Dodonaea eriocarpa* var. degeneri Sherff, *Dodonaea eriocarpa* f. degeneri Sherff, *Dodonaea eriocarpa* var. forbesii Sherff, *Dodonaea eriocarpa* f. galapagensis Sherff, *Dodonaea eriocarpa* var. glabrescens Sherff, *Dodonaea eriocarpa* var. hillebrandii Sherff, *Dodonaea eriocarpa* var. hosakana Sherff, *Dodonaea eriocarpa* var. lanaiensis Sherff, *Dodonaea eriocarpa* var. molokaiensis O.Deg. & Sherff, *Dodonaea eriocarpa* var. oblonga Sherff, *Dodonaea eriocarpa* var. obtusior Sherff, *Dodonaea eriocarpa* f. obtusior Sherff, *Dodonaea eriocarpa* f. obtusiorgalapagensis Sherff, *Dodonaea eriocarpa* var. pallida O.Deg. & Sherff, *Dodonaea eriocarpa* f. pallida O. Deg. & Sherff, *Dodonaea eriocarpa* var. sherffii O. Deg. & I. Deg., *Dodonaea eriocarpa* var. skottsbergii Sherff, *Dodonaea eriocarpa* var. vaccinioides Sherff, *Dodonaea eriocarpa* var. varians O.Deg. & Sherff, *Dodonaea eriocarpa* var. waimeana Sherff, *Dodonaea fauriei* H. Lév., *Dodonaea forsteri* Montrouz., *Dodonaea illita* F.Muell. ex Regel, *Dodonaea jamaicensis* DC., *Dodonaea kohautiana* Schltdl., *Dodonaea latifolia* Salisb., *Dodonaea linearifolia* Turcz., *Dodonaea lucida* Moench, *Dodonaea microcarya* Small, *Dodonaea ovata* Dum. Cours., *Dodonaea pallida* Miq., *Dodonaea pauca* Herrera, *Dodonaea paulinia* Herrera, *Dodonaea pentandra* Griff., *Dodonaea repanda* Thonn., *Dodonaea sandwicensis* Sherff, *Dodonaea sandwicensis* var. latifolia O. Deg. & Sherff, *Dodonaea sandwicensis* var. simulans Sherff, *Dodonaea spatulata* Sm., *Dodonaea thunbergiana* Radlk., *Dodonaea thunbergiana* var. linearis Sond., *Dodonaea viscosa* var. arborescens (Hook.f.) Sherff, *Dodonaea viscosa* f. arborescens (Hook. f.) Sherff, *Dodonaea viscosa* var. aspleniifolia (Rudge) Hook. f., *Dodonaea viscosa* var. candolleana (Blume) Backer, *Dodonaea viscosa* f. ehrenbergii (Schltdl.) Sherff, *Dodonaea viscosa* f. elaeagnoides (Rudolphi ex Ledeb. & Adlerstam) Briziсky, *Dodonaea viscosa* f. eriocarpoidea Sherff, *Dodonaea viscosa* var. galapagensis (Sherff) D. M. Porter, *Dodonaea viscosa* f. hispidula Sherff, *Dodonaea viscosa* f. lilacina Kuntze, *Dodonaea viscosa* f. minor (Blume) Backer, *Dodonaea viscosa* var. minor Sherff, *Dodonaea viscosa* var. obovata C. L.Hitchc.,

Dodonaea viscosa f. repanda Radlk., *Dodonaea viscosa* var. spatulata (Sm.) Benth., *Dodonaea viscosa* f. spatulata (Sm.) Sherff, *Dodonaea viscosa* subsp. spatulata J. G. West, *Dodonaea viscosa* var. stokesiana F. Br., *Dodonaea viscosa* f. viridula Kuntze, *Dodonaea viscosa* var. viscose and *Ptelea viscosa* L[51].

Taxonomic classification:

Kingdom: Plantae, **Subkingdom**: Viridiplantae, **Infrakingdom**: Streptophyta, **Superdivision**: Embryophyta, **Division**: Tracheophyta, **Subdivision**: Spermatophytina, **Class**: Magnoliopsida, **Superorder**: Rosanae, **Order**: Sapindales, **Family**: Sapindaceae, **Genus**: *Dodonaea*, **Specie**: *Dodonaea viscos*a [52].

Common names:

Afrikaans: Gansies, Kankerbos; **Arabic**: Dodonia, Daidon, Dodanaia, Shath**; Australian:** broad leaf hopbush, candlewood, giant hopbush, narrow leaf hopbush, sticky hopbush, native hop bush, soapwood, switchsorrel, wedge leaf hopbush, and native hop; **Brazil:** faxina-vermelha, vassourão-vermelho, vassoura-do-campo, vassoura-vermelha; **English**: broadleaf hopbush, Florida hopbush, giant hopbush, hopshrub, sticky hopbush; **Pakistan**: Sanatha [53-54].

Distribution:

The center of origin of *Dodonaea viscosa* is believed to be Australia, but it occurs throughout the tropics and subtropics**.** The plant is distributed in **Africa** (Kenya; Tanzania; Uganda, Ethiopia, Somalia, Sudan, Angola, Malawi, Mozambique, Zambia, Zimbabwe, Botswana, South Africa, Ghana, Nigeria, Senegal, Togo, Cameroon, Zaire, Madagascar, Mauritius, Reunion, Seychelles); **Asia (**Saudi Arabia, China, Japan, Afghanistan, Iran, Iraq, India, Pakistan, Sri Lanka, Myanmar, Thailand, Vietnam, Indonesia, Malaysia, Philippines); **Australasia** (Australasia, New Zealand); **Northern America** (Mexico, United States); **Southern America** (Brazil, Bahamas, Bermuda, Cuba, Dominican Republic, Grenada, Guadeloupe, Haiti, Jamaica, Martinique, Puerto Rico,Trinidad and Tobago, Suriname, Venezuela, Argentina, Chile, Uruguay, Bolivia, Colombia, Ecuador, Peru) [53].

Description:

Large shrubs or small trees up to 5 m tall. Leaves: simple, alternate, spiral, clustered at twig ends; petiole ca. 0.2 cm long, stout, swollen at base, planoconvex in cross section; lamina 2.5-6.5 x 0.5-1.2 cm, narrow elliptic to oblanceolate, apex acuminate to acute with apiculate tip, base decurrent, margin entire and revolute, shining above, glabrous, viscid; midrib raised above; secondary nerves ca. 16 pairs, nearly parallel; tertiary nerves closely reticulate. Flowers : Inflorescence panicled cymes, up to 7 cm long, terminal or axillary; flowers small, polygamous; pedicel up to 0.5 cm long. Fruit and seed : Capsule, membranous, compressed, with 3 wings; seeds 1-2, black [55-56].

Traditional used:

Traditionally, *Dodonaea viscos*a was used in the treatment of rheumatism, skin infections, diarrhoeas, stomacheches, pains of hepatic or splenic origin, uterine colic and other disorders involving smooth muscles, antipruritic in skin rashes, dermatitis, hemorrhoids and sore throat. The infusion of leaves were used to treat rheumatism, gout, hemorrhoids, fractures and snake bites [57-60].

II. PHYSICOCHEMICAL CHARACTERISTICS AND CHEMICAL CONSTITUENTS:

Physicochemical characteristics:

Ash values of *Dodonaea viscosa* leaf: total ash: 2.09%, acid insoluble ash 0.25%, water soluble ash 1.45% and sulphated ash 5.47%. Extractive values of *Dodonaea viscosa* leaf: petroleum ether (60-80^{o}) 1.38%, chloroform 1.28%, ethyl acetate 2.67%, butanol 0.89% and ethyl alcohol 9.6% [61].

Chemical constituents:

The preliminary phytochemical screening revealed that *Dodonaea viscos*a contained alkaloids, flavonoids, fixed oil and fat, steroids, phenolics, saponins, tannins, gums, mucillages, carbohydrates, reducing sugar and glycosides [56, 61-66]. *Dodonaea viscosa* seeds contained water soluble polysaccharide comprised of D-glucose and D-mannose in 5:2 molar ratio. The analysis of the component monosaccharides indicated α- linkages in D-glucopyranose and β- linkages in D-mannopyranose units [67].

The plant contained many flavonoids, aliarin (5,7,4'-trihydroxy-3'-(3hydroxymethylbutanol) 3,6-dimethoxy flavone), pinocembrin (5,7-dihydroxy flavanone), penduletin,(5,4'–Dihydroxy-3,6,7-trimethoxy flavone); viscosol (3'-(ϒ,ϒ-dimethyalllyl)-5,7-dihydroxy-3,6,4'-trimethoxy flavone); sakuranetin ((S)-5,4'-dihydroxy-7-

methoxyflavone); isokaempferide (3,5,7,4'-tetrahydroxyl-3'-methoxy flavone). Ten new isoprenylated flavonol derivatives, dodoviscins A-J; 5,7-dihydroxy-3'-(4"-acetoxy-3"-methylbutyl)-3,6,4'-trimethoxy flavones; C-alkylated flavonoids 5,7-dihydroxy-3'-(3-hydroxymethylbutyl)-3,6,4'-trimethoxyflavone, 5,7,4'-trihydroxy-3'-(3-hyroxy methyl butyl)-3,6-dimethoxyflavone; 5,7-dihydroxy-3'-(2-hydroxy-3-methyl-3-butenyl)-3,6,4'-trimethoxyflavone(4),5,7,4'-trihydroxy-3,6-dimethoxy-3'-isoprenyl-flavone; 5,7-Dihydroxy-3,6-dimethoxy-2-(4-methoxyphenyl)-4H-chromen-4-one; Kaempferol methyl ethers, 3, 5, 7-trihydroxy-4'-methoxyflavone ; 5, 7, 4'-trihydroxy-3, 6-dimethoxyflavone ; 5, 7-dihydroxy-3, 6, 4'- trimethoxyflavone (santin); 5-hydroxy -3, 7, 4'-trimethoxyflavone; 3,4',5,7-tetrahydroxy flavones (kaempferol); 5,7,4'-trihydroxy-3',5'-di(3-methylbut-2-enyl)-3,6-dimethoxyflavone and 5,7,4'-trihydroxy-3'-(4-hydroxy-3-methylbutyl)-5'-(3-methylbut-2-enyl)-3,6-Dimethoxyflavone; acacetin-7-Me ethers the flavonol-3- methyl ethers 4',5,7-trihydroxy-3,6-dimethoxyflavone, penduletin; 3, 6, 4'-trimethoxy-5,7-dioxyflavone; kaempferol 3,7-di-methyl ether and kaempferol-3,4',7- trimethyl ether were isolated from the aerial parts. Isorhamnetin and quercetin were isolated from the root bark of *D viscos*a. Catechin or chromene groups, chalcones with trimethoxyphenyl group and tannin with 4-O-β-D-xylopyranoside were isolated from the leaves of *Dodonaea viscosa* var. angustifolia [68-83].

Two new antiproliferative oleanane-type triterpenoid saponins, dodoneasides A and B (I and II) were isolated from the ethanol extract of the roots of the *Dodonaea viscosa*. 3β, 15α,21β,22α,28-pentahydroxy-16α-angeloyloxy-Δ 12-oleanene, a triterpenoidal sapogenin was isolated from seeds ethanolic extract77. Doviscogenin (3β, 15α, 21β, 22α,18-pentahydroxy-16α-angeloyloxy-Δ 12-oleanene were isolated from *Dodonaea viscosa* flowers. Stigmasterol, 21,22-diangeloyl barringtogenol C, 21,22-diangeloyl-R1-barringenol, 21-angeloyl-R1-barringenol, and cleomiscosin were obtained from the stem of *Dodonaea viscosa*. Genins R1-barrigenol and jegosapogenol and 2 novel prosapogenins, R1- barrigenol 21,22-diangelate and jegosapogenol 21-(2,3-dihydroxy- 2-methylbutyroyl) 22-angelate were isolated from the the stem bark of *Dodonaea viscosa* [84-89].

Dodonaea viscosa flowers yielded pentanol, β-pinene, myrcene, limonene, p-cymene, citronellal, linalool, linalyl acetate, ϒ-terpineol, geraniol, α-spinasterol, 4-hydroxy-3,5-diprenylbenzaldehyde, β-sitosterol, stearic acid, syringic acid, fraxetin, cleomiscosin A, cleomiscosin C, and β -sitosterol β -D-glucoside [90-91].

Dodonaea viscosa contained many minerals and trace elements: Aluminum 6.93-7.44, Calcium 11683.98-12054.90, Copper 6.48-9.69, Iron 83.85-120.08, Magnesium 2711.53-2965.67, Manganese 11.42-14.25, Phosphorous, 167.37-224.11, Sulphur 213.66-222.31 and Zinc 55.30-59.45 mg/Kg [92].

III. PHARMACOLOGICAL EFFECTS:

Antidiabetic effect:

Dodonaea viscosa leaves extracts (A-M) were evaluated in normal and alloxan-diabetic rabbits. Blood glucose levels were determined after oral administration of 250 and 500 mg/kg of *Dodonaea viscosa* leaves extracts. These doses of the leaves significantly reduced blood glucose in normal and in alloxan-diabetic rabbits. It was also found that blood glucose levels of rabbits treated with aqueous: methanolic extract of *Dodonaea viscosa* leaves 500 mg/kg body weight, was decreased significantly at 2, 4 and 6 h. Oral glucose tolerance test was carried out in rabbits treated orally with aqueous: methanolic extract (500 mg/kg). Blood glucose of aqueous: methanolic extract treated rabbits was significantly decreased after oral glucose load. In addition, simultaneous administration of aqueous: methanolic extract and human insulin (3 units/kg body weight) reduced more potently the blood glucose levels of treated diabetic rabbits than those treated with the aqueous: methanolic extract only. Furthermore, oral administration of aqueous: methanolic extract of *Dodonaea viscosa* (250 and 500 mg/kg) continuously for 30 days produced significant reduction of blood glucose levels in diabetic rabbits compared with controls [54].

The methanolic extract of leaves of *Dodonaea viscosa* was evaluated for antidiabetic activity. The antidiabetic activity was studied using the glucose uptake by isolated rat hemi-diaphragm *in vitro* model. The value of glucose uptake by rat hemi-diaphragm for *Dodonaea viscosa* was 13.80 ± 0.1697 compared to control (5.34 ± 0.12) and insulin 15.45 ± 0.12 mg/g/min [93].

The ethyl acetate extract (DEA) and methanolic extract (DME) of *Dodonaea viscosa* leaves were administered orally at different doses (200 and 400mg/kg bw) to normal as well as STZ-diabetic rats. DME produced significant hypoglycemic effect in normal rats after 6h of administration. After acute treatment, DME 400mg/kg produced marked fall (30.87%) after 6h of administration. Both DME 200mg/kg and 400mg/kg showed improvement in glucose tolerance. Treatment of diabetic rats for 28 days with DME reduced the fasting glucose level by 43.81% than their pretreatment level. It brought about fall in level of total cholesterol by 36% and 38.89% and HbA1c by 29.44% and 35.6%. The increase in glycogen level was found to be 68.97% after treatment with DME 400mg/kg bw. It also normalized the elevated level of MDA in diabetic rats. DME 200mg/kg and 400mg/kg brought about the decreased level of GSH to near normal. The level of SGOT, SGPT were also found to be decreased which was comparable to the standard [59]. The different extracts of the *Dodonaea viscosa* were tested for anti-diabetic activity by glucose tolerance test in normal and alloxan induced diabetic rats. Aqueous ethanol and butanol extracts had shown significant protection and lowered the blood glucose levels to normal limit in glucose tolerance test. In alloxan induced diabetic rats, the maximum reduction in blood glucose was observed

after 3h at a dose of 250 mg/kg of bw. The percentage of glucose reduction by aqueous ethanol and butanol extracts were 30 and 48% respectively [94]. Methanol and chloroform extract of *Dodonaea viscosa* were administered to alloxan induced diabetic albino rats. Blood glucose, triglycerides, cholesterol, protein, urea, creatinine, SGPT, SGOT were checked. Histological changes in pancreas and liver of the animal were also examined. Extract treated groups showed reduction in blood glucose level to normal limit. Increased levels of all other biochemical parameters like SGPT, SGOT, triglycerides, cholesterol, protein, creatinine and urea with alloxan treatment have been significantly reduced by extracts. Histological changes associated with alloxan induction was also attenuated by extracts [95].

Antimicrobial effects:

The growth inhibitory activity of *Dodonaea viscosa* var. angustifolia (DVA) leaves extract was investigated against *Streptococcus mutans* and its biofilm. The results revealed that the reduction of the growt of *Streptococcus mutans* was concentration and exposure time dependent. The crude extract killed 48% of *S. mutans* at a lowest concentration of 0.1 mg/ml and 100% at 25 mg/ml after 6 h. Biofilm formation was reduced by 95, 97 and 99% after 6, 24 and 30 h of exposure to the sub-inhibitory concentration of crude extract respectively. At high concentration the crude extract was bactericidal to *Streptococcus mutans* but sub-inhibitory concentration significantly reduced the planktonic cells and biofilm formation [68].

The minimum inhibitory concentration and the time taken by *Dodonaea viscosa* var. angustifolia (PLE), chlorhexidine gluconate (CHX) and triclosan (TRN) to kill *Candida albicans* was investigated *in vitro*. 41 strains of *Candida albicans* were used, 20 from HIV-positive patients, 20 from HIV-negative subjects and one *Candida albicans* ATCC 90028. The MICs of an acetone extract of PLE, CHX and TRN were measured using a microtitre double dilution technique, and the time taken to kill 99.5% of the strains was determined. The MICs of PLE, CHX and TRN were 6.25–25, 0.008–0.16 and 0.0022–0.009 mg/ml, respectively. PLE killed all the test strains within 30 s and CHX 40% of the isolates from HIV-positive patients and 20% of strains from HIV-negative subjects in 1 min. During the same time TRN killed 55% and 35% of isolates from HIV-positive and HIV-negative patients [96]. The n-hexane, dichloromethane, ethyl acetate, n-butanol and aqueous fractions of *Dodonaea viscosa* were analyzed for antimicrobial potential against four Gram positive bacteria [*Bacillus subtilis* (MRL M 1), *Bacillus cereus* (MRL M 52), *Micrococcus luteus* (ATCC 10240), *Staphylococcus aureus* (ATCC 6538)], three Gram negative [bacteria: *Escherichia coli* (ATCC 25922), *Salmonella typhi* (Cl. I. 140), *Pseudomonas aeruginosa* (ATCC 9721)] and the yeast *Candida albicans* (Cl. I. 4043). Extracts possessed antibacterial activity against *S. aureus*, *M. luteus*, *B. subtilis*, *E. coli*, *P. aeruginosa* and *C. albicans*. However, 15, 16-epoxy-cis-cleroda-3, 13(16),14-trien-18-oic acid-18,6-olide, a clerodanefuranolactone isolated from n-hexane fraction of *Dodonaea viscosa's* crude ethanolic extract showed antibacterial effects against Gram positive and Gram negative bacteria, its MIC's against *S. aureus* (NCIMB 6571) and *E. coli* (NCIMB 8797) were 64 μg/ml and 128 μg/ml respectively. The MBC's against these organisms were 128 μg/ml and 256 μg/ml, respectively [97].

The antibacterial activity of crude and step gradient solvent of methanol and chloroform of whole *Dodonaea viscosa* was studied using agar well diffusion technique against six bacterial human pathogens (*S. typhi*, *S. flexneri E. coli*, *V. cholerae*, *M. tuberculosis*, *P. fluorescens*). The growths of *S. flexneri and V. cholerae* were inhibited by the crude and step gradient extracts of *Dodonaea viscosa*. The maximum inhibition zone was obtained with the using of methanol 80% and chloroform 20% against the tested pathogens [64].

Methanol and n-hexane extracts of the leaves of *Dodonaea viscosa* were screened for antibacterial activities, against different Gram positive and Gram negative bacterial strains. The results showed that n-hexane extract of plant was inactive against *Pseudomonas aeruginosa* while methanolic extract of the plant was active against all the tested organisms [98].

The anti-biofilm activities of leaves of *Dodonaea viscosa* in successive different concentration were tested against *E. coli*. The leaves extracts of *Dodonaea viscosa* showed broad spectrum antibiofilm activity [99].

The antibacterial effect of methanolic and hot aqueous extracts of *Dodonaea viscosa* was studied against *Staphylococcus aureus* ATCC 6538, *Bacillus subtilis* ATCC 6059, *Micrococcus flavus* SBUG 16, *Escherichia coli* ATCC 11229, *Pseudomonas aeruginosa* ATCC 27853, *Candida maltosa* SBUG, multiresistant *Staphylococcus epidermidis*, multiresistant *Staphylococcus haemolyticus* and North German multiresistant *Staphylococcus aureus*. *Dodonaea viscosa* methanolic extract showed antibacterial activity against all tested bacteria with MIC 10-15 mm, except *Escherichia coli*, *Pseudomonas aeruginosa* and *Candida maltosa* SBUG, while hot aqueous possessed activity against *Staphylococcus aureus*, *Bacillus subtilis*, *Micrococcus flavus* and multiresistant *Staphylococcus epidermidis* only, with MIC 7.3-16mm[100].

The antimicrobial activity of *Dodonaea viscosa* leaf, stem and root using aqueous, methanol and chloroform solvents was studied using disc diffusion method. *Vibrio cholerae* was controlled by all parts of *Dodonaea viscosa* extracted by all the three types of solvent. Maximum zone of inhibition was recorded by the methanol extract of stem against *Vibrio cholerae*. Similarly, *Bacillus subtilis* was controlled by all the extracts except that of methanol extract of root. The root extract of the weed showed no efficacy against the *Escherichia*

coli and *Proteus mirabilis*. Among the extracts studied for antifungal efficacy of different parts of the plant, maximum efficacy was recorded for the methanol extract. Other solvents like aqueous and chloroform extract showed poor zone of inhibition or no effects. The methanol extract of leaf of the plant showed maximum activity against *Curvularia lunata* and *Fusarium oxysporum*. The methanol extract of root of the plant showed maximum activity against *Aspergillus flavus*. While, the methanolic extract of stem of the plant showed maximum activity against *Penicillium citrinum*. However no significant activity was recorded against *Aspergillus niger* by all extracts studied [101].

The inhibitory effects of the aerial plant part (leaves and bark) extracts of *Dodonaea viscosa* before and during flowering were evaluated against some pathogenic bacteria isolated from human and plants (*Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Streptococcus agalactiae*, *E. carotovora and A. tumefaciens*), and against *Candida albicans* using ethanol and diethyl ether solvents (0, 2.5, 5, 10, 20, 30, 40 or 50 mg/ml). The results showed that ethanolic extracts of the bark and leaves, and diethyl ether extracts of the leaves demonstrated potent inhibitory effect against the tested microorganisms. Ethanolic extracts of the bark was superior to leaf extracts in the its inhibitory effects on the growth of *C. albicans*. No significant differences between concentrations of 30, 40 or 50 mg/ml were recorded [102]. Anti- *salmonella* activity of aqueous and ethanol extracts of *Dodonaea viscosa* was studied using well and disc diffusion assay. The highest inhibition zone was (22 mm) for well diffusion and (15mm) for disc diffusion assay were recorded. The results revealed that ethanol extract possessed more antibacterial effect than aqueous extract, the percentage of bacterial isolates affected by ethanol extract was (71.19%) comparing with aqueous extract (28.81%) by using disc diffusion assay, while the percentage of bacterial isolates affected by ethanol extract was (88.13%) comparing with aqueous extract (52.54%) by using well diffusion assay [103]. 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* and *Staphylococcus aureus*), and three Gram negative bacteria (*Escherichia coli, Salmonella typhi* and *Pseudomonas aeruginosa*). The results revealed that the crud extract possessed antibacterial activity against *Staphylococcus aureus, Micrococcus luteus, Bacillus subtilis, Escherichia coli* and *Pseudomonas aeruginosa* with zones of inhibition of 11-13.3mm. The results also showed that ethyl acetate fraction was active against five out of seven tested organisms, followed by the *n*-butanol fraction which inhibited four organisms and the *n*-hexane fraction which inhibited two organisms [104].Chloroform, ethanol and methanol crude extracts of stem bark and leaves of *Dodonaea viscosa* were investigated for their antibacterial and antifungal potential against two Gram positive bacteria (*Bacillus subtilis*, *Staphylococcus aureus*), one Gram negative bacterium (*Escherichia coli*) and two yeast strains (*Candida albicans*, *Sccharomyces cervisiae*). Ethanol and methanol extracts were found to be active against the tested Gram positive and Gram negative bacteria. Extracts showed no effect against *Candida albicans* and *Sccharomyces cervisiae*. All the tested microorganisms were resistant to chloroform extracts. However, Gram positive bacteria were more sensitive to the extracts of *Dodonaea viscosa* than Gram negative bacterium [105].

Antifungal activity of solvent extracts of leaves and shoot of *Dodonaea viscosa* was studied 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 the tested fungi. However chloroform has strong inhibitory activity against fungi as compared to ethanol, methanol, ethylacetate and aqueous extracts. The maximum inhibitory activity of the ethanol extract was observed against *P.variety, T. rubrum* and *M. gypseum* 81.82%, 80% and 73.34% respectively, while, it possessed moderate inhibitory activity against *A.flavus* 65.72% and minimum inhibitory activity against *A.niger* 62.5%. The maximum inhibitory activity of the ethyl acetate extract was observed against *T. rubrum, M. gypseum* and *P. varioti* 80%, 73.34 and 63.64% respectively, while it possessed moderate inhibitory activity against *A. flavus* 57.15 and minimum inhibitory activity against *A.niger* 50%. The maximum inhibory activity of the chloroform extract was recorded against *P.varioti T. rubrum* and *M. gypseum* 90.91%, 80% and 73.34% respectively, while it exerted moderate inhibitory activity against *A.flavus* 71.41% and minimum inhibitory activity against *A.niger* 50%. The maximum inhibitory activity of the methanol extract was observed against *P.varioti* and *T.rubrum* 81.82 and 80%, while, it possessed moderate inhibitory activity against *A.niger* and *A.flavus* 62.5% and 57.15% respectively and minimum inhibitory activity against *M.gypseum* 53.34%. The maximum inhibitory activity of the aqueous extract was observed against *P.varioti*, *T.rubrum* and *A.niger* 81.82%, 80% and 75%, while, it exerted moderate inhibitory activity against *M.gypseum* 60% and minimum inhibitory activity against *A. flavus* 57.15% [92].

The fractions derived from hydroalcoholic extract of *Dodonaea viscosa* leaves was evaluated against *Candida albicans* (Cl. I.4043). With the exception of aqueous fraction, all the fractions exhibited anticandidal activities (zone of inhibition $\geq$ 10 mm). The MIC of n-hexane fraction was 62.5 µg/ml [106].

The *in vitro* antiviral activity of different extracts from *Dodonaea viscosa* leaves was studied against coxackievirus B3 (CVB3) and rotavirus SA-11 (RV SA-11) infections. *Dodonaea viscosa* exhibited ttherapeutic index (TI) ranging from 0.3 to 25 with reduction in virus titer ranging from 0.25 to 5 log10 TCID 50/0.1 ml for CVB3, whereas TI ranging from 0.4 to 29.2 with reduction in virus titre ranging from 0.25 to 5.25 log10 TCID50

for RV SA-11**.** Crude extract provided the potent inhibition of CVB3 and RV SA-11, replication by binding to a viral capsid of CVB3 and viral receptor of RV SA-11 preventing viruses entry into host cells for both viruses [107].Petroleum ether, chloroform and methanol 80% extracts of *Dodonaea viscosa* aerial parts were tested for their anti-HIV-1 activity using the syncytia formation assay. Petroleum ether extract of *Dodonaea viscosa* was the most active as an anti-HIV-1 agent while other extracts were less effective. The authors concluded that the antiviral effects could be attributed to *β*-sitosterol and stigmasterol identified in the petroleum ether extract of *Dodonaea viscosa* [108].

Insecticidal effects:

Insecticidal activity of the ethanolic extracts of the leaves of *Dodonaea viscosa* was studied by using four insect models (*Epilachna paenulata, Spodoptera littoralis, Myzus persicae*, and *Rhopalosiphum padi*), which were pests of crops of economic importance. Bioguided fractionation and supercritical fluid extraction led to the isolation of active insecticidal compounds. Lupeol, stigmasterol, stigmast-7-en-3-ol, and a labdane diterpene were isolated and showed differential insecticidal activity against the insects [109]. The larvicidal activity of *Dodonaea viscosa* leaf, stem and root, using aqueous, methanol and chloroform solvents, was studied against *Artemia salina* larvae. *Artemia salina* cysts were incubated in saline water and the eggs were hatched in 24 hours. The hatched nauplii (larvae) were then used (48h growth) for larvicidal activity assay. One gram of dried extract was dissolved in 10ml of saline water (master dilution). Four different concentrations (0.5, 1, 1.5 and 2) were prepared from the master dilution. Ten nauplii were transferred to each test sample and incubated in room temperature for 24h. After 24 hours the susceptibility of the nauplii were observed. Among different parts of *Dodonaea viscosa*, the leaf extract alone showed significant level of lethality. The aqueous extract of leaf showed 100 % lethality against the larvae at the concentration of 1 %. Aqueous extract of root extract of the plant showed 100 % lethality of larvae at the concentration of 1.5% and only the methanol extract of stem at the concentration of 2 % showed 100 % lethality of larvae [101].

Antioxidant effect:

Dodonaea viscosa exhibited a high effective free radical scavenging at 50 µg/ml (50.72%) and the free radical scavenging activity was concentration dependently, increased reaching 92.45% at 1000 µg/ml. The water extract was only weak antioxidant. Water extract free radical scavenging reached 31.80% at the highest concentration 1000 µg/ml [100].

100, 200 and 300 µl of *Dodonaea viscosa* extract showed that a maximum scavenging activity was offered by 300 µl of *Dodonaea viscosa* extract with inhibition of 82.09 ± 0.15%, followed by 200 µl with inhibition of 81.02 ± 0.11%, and 100 µl with inhibition of 79.91 ± 0.16%[62].

Cytotoxic effect:

Cytotoxic activities of *Dodonaea viscosa* extracts were examined on breast carcinoma cell line (MCF7). The results showed that the 80% ethanolic extract of *Dodonaea viscosa* possessed strong cytotoxic activity, with IC_{50} of 19.4 µg/ml, compared with the standard drug (cisplatin), which showed IC_{50} of 5.48 µg/ml [62].

Antifertility effect:

The methanolic extract of the leaves of *Dodonaea viscosa* was investigated for its anti-fertility activity in female rats. It was found that the extract reduced significantly ($P< 0.01$) the number of liters when administered through oral route. It also produced anti- fertility effect in a dose dependent manner and the contraceptive effect was continued for a definite period of time. Furthermore, the extract significantly showed anti-implantation and early abortifacient activity [63]. *Dodonaea viscosa* leaf extracts showed antifertility activity in male rats. It decreased sperm count and reproductive organ weights with the appearance of necrotic changes in the seminiferous tubules of testis. Total protein and glycogen levels were reduced in treated rats compared to the control group. The glycogen depletion in the testis and liver under *Dodonaea viscosa* leaf extracts treatment, was the probable mechanism of the toxic manifestations on male reproductive system [110].

Wound healing effect:

The effect of ethanol extract and flavonoid rich fraction of *Dodonaea viscosa* was investigated on a simplified *in vitro* wound healing study. Cultured Keratinocytes were exposed to ethanol extract and flavonoid rich fraction at different concentrations for 48 hours. The resultant cellular proliferation was determined after 48 hours by MTT assay and calculated relatively to control. Flavonoid rich fraction of the *Dodonaea viscosa* induced a significant cell proliferation after 48 hours exposure, when compared to the control group. The flavonoids rich fraction of the *Dodonaea viscosa* has better efficiency in inducing cell proliferation than ethanol extract [111]. Ethanolic extract of dried leaves showed wound healing activity in excised and incised wound in rats. 10% extract treated excision wound were found to have faster rate of contraction and epithelization. Ethanol extract

suspension and ointment induced significant wound response (breaking strength of skin, granuloma and wound contraction) and overcome the anti-healing properties of dexamethasone [112].

Anti-inflammatory and analgesic effects:

The hydroalcoholic extract of the leaves of *Dodonaea viscosa*, given by oral route at dose of 300 mg/kg, significantly inhibited the paw edema induced by carrageenin injection [113].

Hautriwaic acid (HA), a diterpene extracted from *Dodonaea viscosa* leaves, exhibited good anti-inflammatory activity in 12-*O*-tetradecanoylphorbol 13-acetate (TPA) mice ear edema models when applicated at doses of 0.25, 0.5 and 1.0 mg/ear (60.2, 70.2 and 87.1% inhibition, respectively); additionally *Dodonaea viscosa* dichloro-methane extract (DvDE) displays a 97.8% anti-inflammatory effect at 3 mg/kg. Multiple applications of DvDE at doses of 100 mg/kg on TPA mice ear edema inhibited the edema-associated inflammation by 71.8%, while HA at doses of 15 mg/kg, reduced edema to 64% compared with indomethacin 40% [114].

Viscosine was isolated from *Dodonaea viscosa*, showed significant lipoxygenase inhibitory activity (IC_{50}: value 39 ± 0.17), the enzyme responsible for the metabolism of the fatty acids and their metabolites eliciting inflammatory responses in the body. Molecular interactions of viscosine with catalytic triad (His523, His518, Ile875) inside active site of lipoxygenase via hydrogen bonding, seemed to be the major effect involved in its significant lipoxygenase inhibitory activity [115].

Various leaf extracts of *Dodonaea viscosa* were evaluated for antinociceptive activity on various experimental pain models (glacial acetic acid induced writhing, hot plate and tail flick and). All extracts of *Dodonaea viscosa* leaves showed antinociceptive activity in rats and mice. Ethyl acetate extract possessed the highest activity [116].

Anti-ulcer effect:

The gastroprotective effect of *Dodonaea viscosa* was studied in two different models (ethanol and indomethacin induced gastric ulcer) in wistar rats. Gastric protection was evaluated by measuring the ulcer index, gastric glutathione assay, alkaline phosphate assay and histopathological studies. Water and ethanol extract (500 mg/kg body weight) showed moderate activity compared to hexane extract. Hexane extract of *Dodonaea viscosa* dose dependently inhibited ethanol induced gastric lesions, causing 90% protection at 500 mg/kg, 81% protection at 250 mg/kg, and 70% protection at 125 mg/kg, and it also, dose dependently inhibited indomethacin induced gastric lesions, causing 92% protection at 500 mg/kg, 77% protection at 250 mg/kg, and 52% protection at 125 mg/kg. The various degrees of inhibition were statistically significant ($p \leq 0.05$). Hexane extract of *Dodonaea viscosa* (500 mg/kg) also decreased the amount of total acid in gastric juice [117].

Antispasmodic effect:

Bioassay-directed fractionation of the chloroform-methanol (1:1) extract of *Dodonaea viscosa* resulted in isolation of four active spasmolytic principles: sakuranetin , 6-hydroxykaempferyl 3,7-dimethyl ether, hautrivaic acid, and ent-15, 16-epoxy-9 alpha H-labda-13(16)14-diene-3 beta, 8 alpha-diol. All the isolated compounds elicited a concentration-dependent inhibition of the spontaneous and electrically-induced contractions of guinea-pig ileum. Sakuranetin and the ent-labdane inhibited ileum contractions evoked by acetylcholine, histamine, and barium chloride [57].

Anti-diarrheal effect:

The anti-diarrheal activity of the alcohol and aqueous extracts of the roots of *Dodonaea viscosa* was investigated by castor oil induced diarrhea in mice. The number of diarrheal episodes and mean weight of stool of mice were determined. The results revealed that the alcohol and aqueous extracts significantly reduced diarrhea in mice with reduction in weight of stools [60].

Detoxification effect:

The protective effect of crude leaves of *Dodonaea viscosa* was studied on lead acetate induced synthesis of glycoproteins and sialic acid in liver and plasma. Enhanced synthesis of glycoproteins (protein - bound hexose and protein - bound hexosamine) and sialic acid levels were found in liver and plasma of the lead acetate poisoned rats. Administration of crude leaves of *Dodonaea viscosa* (100 mg/100 g bw orally) effectively suppressed the synthesis of glycoproteins and sialic acid in liver and thereby controlling the concentration in plasma. The authors concluded that *Dodonaea viscosa* exerted its membrane protection effect by inhibiting the synthesis of glycoproteins and sialic acid induced by lead acetate [118].

Toxicity:

Acute toxicity study of *Dodonaea viscosa* was carried out in rats. Higher dose, 1250 mg/kg did not manifest any toxicological signs in rats [117]. The hydroalcoholic extract did not show any sign of toxicity and mortality in mice up to 5000 mg/kg orally. The animals were followed with continuous observation for initial 4 hours and then for 14 days [113]. The potential dermatotoxicity of 80% methanol extract of the leaves of *Dodonaea viscosa* was studied in rabbit. The skin irritation test revealed negligibly irritation. The sensitization tests carried in mice by the mouse ear swelling test exhibited no sensitization in the dose range of 12 – 30 mg/ml. The repeated dermal toxicity tests on rats did not show any sign of toxicity [119].

IV. CONCLUSION:

The review discussed the chemical constituents, pharmacological effects and therapeutic importance of *Dodonaea viscosa* as promising herbal drug because of its safety and effectiveness.

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