

A REVIEW ON DODONAEA VISCOSA: PHYTOPHARMACOLOGICAL APPROACH

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Abstract

Dodonaea viscosa (Sapindaceae) is an evergreen shrub or small tree, contains various secondary metabolites such as alkaloids, flavonoids, terpenoids, carbohydrates, saponins, glycosides, fixed oils and fats, gums and mucilage. The pharmacological studies showed that the plant possessed various activities like anti-diabetic, anti-cancer, anti-oxidant, anti-inflammatory, anti-fertility, anti-ulcer, anti-microbial, anti-diarrheal and toxicity effects. This current review highlights phytochemical constituents and pharmacological activities of *Dodonaea viscosa*.

Key words: *Dodonaea viscosa*, phytochemicals, pharmacological effects, hautriwaic acid, anti-inflammation

Introduction

Over the past few decades, herbal medicinal products are tremendously used as a balanced and moderate approach to healing as home remedies. It is mainly due to efficacy, safety, acceptability in society and lesser side effects. It is estimated that about 80% of world's population depends on herbal medicines as the primary source of healthcare (Mukherjee, 2002). In the developing countries like US, about 25% of pharmaceuticals are based on the plant derived secondary metabolites (Orhan, 2012). *Dodonaea viscosa* commonly known as Hop bush or Hop seed plant is an evergreen shrub or small tree belongs to the family Sapindaceae. The biochemical evaluation of the plant reveals the presence of certain secondary metabolites such as alkaloids, steroids, carbohydrates, flavonoids, triterpenoids, fixed oil and fats, tannin and phenolic compounds (Mahadevan *et al.*, 1998). It is used in the treatment of headaches and back-pains by tribes (Muthuvan) of Kerala region. High temperature water decoction of leaves is utilized to cure swellings and pains (Ramkumar and Periyasamy, 2019).

Plant Description

Dodonaea viscosa is an evergreen shrub or small tree up to 4-5m tall. The upper surface of leaf is dark green and lower are pale green with length of 3.8-10cm. The leaves are simple, alter-

nate, lanceolate or obovate. Both the ends of the leaves are acute, entire margins and narrowed to distinct petiole showing pinnately parallel venation. The leaves also have a resinous coating (Sama *et al.*, 2008). The young branchlets are angular to subterete and scurfy puberulous. The inflorescence is paniced cyme up to 7cm long which are terminally or axillary positioned. The flowers are small, polygamous with 3-4 oblong sepals, linear anthers and superior ovary. The pedicel has a length of 0.5cm long. The fruit are 2-3 winged papery capsule, white or straw coloured to brown or purplish membrane with 1-2 black seeds. The flowering and fruiting occur in the month of January- May (Manjulatha, 2012, Ali Esmail, 2017).

Taxonomic Classification/Hierarchy

Domain: Eukaryota

Kingdom: Plantae

Subkingdom: Viridiplantae

Infrakingdom: Streptophyta

Division: Tracheophyta

Sub division: Spermatophyta

Class: Magnoliopsida

Order: Sapindales

Family: Sapindaceae

Genus: *Dodonaea*

Species: *Dodonaea viscosa* (L.) Jacq

(classification details from ITIS)

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Common names in India

Malayalam: Vrali, Unnataruvi, Aattotta;

Tamil: Virali; Telugu: Bandaru, Pullena;

Kannada: Bandaru, Bandarike, Hangarika, Hengarulu; **Hindi:** Sanatta, Sinatha, Vilayti-

mehdi; **Marathi:** Lutchmi; **Oriya:** Mohra;

Sanskrit: Aliar, Rasna, Sanatta; **Manipuri:** Bilaiti mehendi.

I. Distribution

By origin *Dodonaea viscosais* native to Australia but it is widely distributed throughout the tropics and subtropics region. In India, the plant is widely distributed in Andaman and Nicobar Island, Assam, Bihar, Maharashtra, Kerala, Gujarat, Meghalaya, Punjab and Tamil Nadu. In Kerala region, the plant found to be in Kottayam, Kollam, Thiruvananthapuram, Idukki, Malappuram, Kozhikode and Wayanad and in the localities such as Alampetty, Vellimala, Munnar, Vattavada and Varkala.

II. Phytochemical constituents

The preliminary phytochemical analysis of *Dodonaea viscosa* found the presence of major secondary metabolites like alkaloids, carbohydrates, glucosides, flavonoids, steroids, terpenoids, tannins, saponins, fixed oils, fats, gums and mucilage (Jawahar *et al.*, 2004, Kumar *et al.*, 2013). The phytochemical profiling on aerial parts of *Dodonaea viscosa* led to the isolation of new compounds along with known compounds. The isolated new compounds were found to be *ent*-labdane and *p*- coumaric acid ester of 1-L-*myo*-inositol. In addition, many known compounds were also isolated are hautriwaic acid, dodonoside B, dodonic acid, kaempferol, sakuranetin, dehydrohautriwaic acid, hautriwaic lactone, alizarin, penduletin, 3,5,7-trihydroxy-4'- methoxy flavone, isorhamnetin-3-rhamnosylgalactoside, donoside A and 5 - hydroxy-3,6,7,4'- tetra methoxy flavone (Riaz *et al.*, 2012). Evaluation of flavones composition in *Dodonaea viscosa* found the presence of one flavanone (pinocembrin) and eight flavanones (santin, kaempferol, 3-*o*-methyl ether, kaempferol 7-*o*-methyl ether, quercetin 3'-*o*-methyl ether, quercetin, 5,7,4'-trihydroxy-3,6-

dimethoxy flavone, 5,7-dihydroxy 3,6,3'4'- tetra methoxy flavone and isorhamnetin-3-*o*-robinobioside (Nagwa *et al.*, 2012).

Gas chromatographic and mass spectroscopic analysis in *Dodonaea viscosa* leaf extract revealed the presence of various new secondary metabolites with known compounds. 3,7,11,15-Tetramethyl-2-Hexadecen-1-ol, 2,3-Dihydro-3,5-Dihydroxy-6-Methyl, 4H-pyran-4-one, 9, 12, 15-Octadecatrienoic Acid, N-Hexadecenoic Acid, Methyl ester, 9,12-Octadecadienoic Acids, phytol isomer, 2-Hexadecanoic-1-ol, 1,2-Benzene-dicarboxylic and N-Hexadecenoic Acid were identified in methanolic leaf extract of *Dodonaea viscosa* (Saranya and Divyabharaathi, 2019). A phytochemical study on *Dodonaea viscosa* leaf extract revealed the presence of a new compound 3,5,7-trihydroxy-6,4' dimethoxy -3'-isoprenyl-flavone along with three known compounds (Mashhad *et al.*, 2018).

III. Pharmacological effects

Anti-Diabetic Activity

The effect of Polar fraction of ethanolic extract (DVE-4) and aqueous extract (DVW) of *Dodonaea viscosa* on type 2 diabetic rats were investigated in vitro. High fat diet (HFD) and low dose streptozotocin (STZ) is used as an ideal model for type 2 diabetics. Different doses of the extracts were allowed to intake once daily for about two weeks to HFD+STZ diabetic rats. Both extracts reduced blood glucose, serum insulin, lipid profiles, homeostatic model dose dependently and improve glucose tolerance and HDL-c levels (Veerapur *et al.*, 2010a). The effect of action of water extract (DVW) and polar fraction of ethanol extract (DVE-4) of *Dodonaea viscosa* in high fructose diet induced insulin resistant by feeding fructose (66%) and coconut oil (1.1%) mixed with normal pellet diet for six weeks in male Wistar rats. At the end, it was observed that DVW and DVE-4 extracts significantly reduced blood glucose, serum insulin, HOMA, lipid profiles and improves glucose tolerance and HDL-c levels (Veerapur *et al.*, 2010b). Antidiabetic activity were tested in aqueous ethanol and butanol extracts of

Dodonaea viscosa by glucose tolerance test in normal rats and alloxan induced diabetic rats. In glucose tolerance test, the extracts shown significant protection and lowered the blood glucose level to normal state. It was observed that the maximum reduction in blood glucose after 3 hours at a dosage of the 250mg/kg by aqueous ethanol and butanol extract were 30 and 48% respectively in alloxan induced diabetic rats. Both the extracts show significant anti-diabetic activity (Muthukumaran *et al.*, 2011).

Evaluation of anti-diabetic activity of water (DVW) and polar fraction of ethanol extract (DVE-4) of *Dodonaea viscosa* in streptozotocin - induced diabetic rats in a single dose one day study showed dose dependent reduction in glucose level.

The maximum effect of DVW and DVE-4 were 42.16% and 72.9% respectively at 6-hour post drug treatment. But in a multidose fifteen-day study, lower doses of DVW (400mg/kg) and DVE-4(200mg/kg) exhibited higher percentage reduction in glucose levels compared to glibenclamide (Veerapur *et al.*, 2010). Anti-diabetic effect of powdered leaves of chloroform, methanol, aqueous and aqueous methanolic (A-M) extract of *Dodonaea viscosa* was evaluated in normal and alloxan-diabetic rabbits. The oral administration of 250 and 500mg/kg of *Dodonaea viscosa* leaves significantly reduced blood glucose in normal and alloxan-diabetic rabbits. At 5 mg/kg of glibenclamide (control drug) reduce the blood glucose level only in normal rats. It was also observed that blood glucose level reduced in aqueous methanolic (500mg/kg) extract of *Dodonaea viscosa* leaves at 2,4 and 6 hours. Evaluation of oral glucose tolerance test in rabbits treated orally with A-M extract and glibenclamide significantly reduced blood glucose. It was also founded that simultaneous intake of A-M extract and exogenous human insulin reduce blood glucose level of treated diabetic rabbits than treated with A-M extract only. In addition, oral intake of A-M extract continuously for 30 days significantly reduces blood glucose level and increased plasma

insulin level in diabetic rabbits (Muhammed *et al.*, 2011).

Antimicrobial Activity

Using different polar and non-polar solvents such as petroleum ether, methanol acetone, acetonitrile and water were used for the extraction of active compounds from *Dodonaea viscosa* leaves to obtain distinct morphological silver nanoparticles with different physical, chemical, anti-bacterial and cytotoxic properties. The XRD, HR-SEM and HR-TEM revealed different nano size (15,18,12,20 nm) of the nanoparticles. As a result, it was observed that the anti-bacterial activity shows a significant zone of 20,16,13,18 nm of inhibition against *Streptococcus pyogenes* for a AgNPs synthesized by extract of methanol, acetone, acetonitrile and water respectively (Anandan *et al.*, 2019).

Antibacterial activity was studied by copper zero-valent iron (ZVI) and silver nanoparticles by using *Dodonaea viscosa* leaf extract. Biosynthesised nanoparticles were characterised by UV-VIS spectroscopy, x-ray diffraction, atomic force microscopy and high-resolution transmission electron microscopy which show average size of 29, 27 and 16 nm for Eu, ZVI and Ag nanoparticles respectively. The synthesized nanoparticles were tested against Gram-negative and Gram-positive human pathogens such as *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas fluorescens*, *Staphylococcus aureus* and *Bacillus subtilis* and show good anti-microbial activity (Kiruba Daniel *et al.*, 2013).

Four Gram positive bacteria such as *Bacillus subtilis*, *B.cereus*, *Micrococcus luteus*, *Staphylococcus aureus* and three-gram negative bacteria such as *Escherichia coli*, *Salmonella typhi*, *Pseudomonas aeruginosa* were subjected against antibacterial activity by bioautography using various extracts like ethanol, n-hexane, dichloromethane, ethyl acetate, n-butanol and water. Some of the bacteria show zone of inhibition itself in preliminary screening while others shown only after subjected to contact autobiography. All bacteria except *B.cereus* display antibacterial activity. *B. subtilis* show prominent

zone of inhibition for n-hexane, ethyl acetate and n-butanol extracts. The minimum inhibitory concentration of extracts shows a range between 5-20.0mg/ml (Muhammad *et al.*, 2009).

Fractions of dichloromethane and acetone from *Dodonaea viscosa* Jacq.var. *angustifolia* leaves powder were used for isolate four kaempferol methyl ethers which are subjected to carried out its antibacterial activities. It was determined by using serial dilution microplate technique. The isolated kaempferol show MIC range from 16mg/ml-250mg/ml against *Staphylococcus aureus*, *Enterococcus faecalis*, *Escherichia coli* and *Pseudomonas aeruginosa* (Teffo *et al.*, 2010).

Antimicrobial activity of *Dodonaea viscosa* were carried by conducting antibacterial and antifungal assay using different extracts (ethanol, n-hexane, chloroform, ethyl acetate and aqueous) in leaf and flower. Antibacterial assay was determined by using disc diffusion method against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumonia* and *Pseudomonas aeruginosa*. The ethanolic extract of leaf displayed high activity against *P. aeruginosa* and *S. aureus*. The n-hexane and chloroform extracts of root and n-hexane, chloroform and ethanolic extract of flower show high potential against *B. subtilis* while chloroform and ethanolic extracts of flower show antibacterial activity against *K. pneumonia*. In addition, antifungal activity was carried out by agar disc diffusion protocol against *Aspergillus fumigatus*, *Mucor* sp, *A. niger*, *A. flavus* and *Fusarium solani*. Almost all parts of the plant show significant antifungal activity within range of 7-12 mm (Marya *et al.*, 2022).

Antibacterial activities against human pathogens by using crude extract of ethanol, acetone, diethyl ether, ethyl acetate and benzene were investigated. The activity was determined by diffusion method developed by Kirby Bauer. About 10 strains of bacteria used are *E. coli*, *Salmonella typhi*, *S. marcescens*, *S. epidermidis*, *S. aureus*, *S. agalactiae*, *S. pyogenes*, *S. dysgalactiae*, *B. cereus*. By comparing other extract, a

maximum zone of inhibition 11nm was obtained in ethanolic extract at a dosage of 150mg against *S. typhi*, *B. cereus*, *E. coli* and *S. Agalactiae* (Thamil Priya *et al.*, 2021).

Biosynthesis of silver nanoparticles from aqueous extract of *Dodonaea viscosa* is characterised by UV-VIS spectroscopy, FTIR, SEM, EDX, XRD. Antibacterial activity was tested by using 2 strains of Gram-positive bacteria named *Bacillus subtilis* and *Enterococcus faecalis* and 2 strains of Gram-negative bacteria named *Proteus vulgaris*, *Klebsiella pneumonia*. The bacteria *K. pneumonia* shows highest zone of inhibition (19mm). It was followed by *E. faecalis* (18mm), *P. vulgaris* (10mm) and *B. Subtilis* (9mm) (Balashanmugam and Kalaichelvan, 2014).

Methanolic and hot water extracts of *Dodonaea viscosa* were tested for their anti-bacterial activity against gram-positive, gram-negative bacteria, yeast sp and three multi resistant strains using agar diffusion method. Methanolic extract shows highest antimicrobial activity (10%) against *Micrococcus flavus* (Ramzi *et al.*, 2010).

The crude methanolic extract of *Dodonaea viscosa* var. *angustifolia* leaves were tested for anti-bacterial against *Streptococcus mutans*. The extract was characterized by GC-MS. The extract shows an inhibition of 48% against *S. mutans* at lower concentration of 0.1mg/ml and 100% at 25mg/ml (highest concentration) (Roxanne *et al.*, 2012).

Antiviral activity of different extracts from leaves of *Dodonaea viscosa* were investigated invitro. The crude extracts methanol, chloroform, ethyl acetate, butanol and aqueous were used against Coxsackie virus B3 (CVB3) and rotavirus SA-11 (RV SA-11). The cytotoxic effect of the extracts was determined by MTT reduction colorimetric assay. The plant exhibits therapeutic index (TI) 0.3-25 with reduction in virus titre ranging from 0.25-5log₁₀ TC1D₅₀ / 0.1ml for CVB3 and TI of RV SA-11 shows 0.4-29.2 with reduction in virus titre ranging from 0.25-5.25log₁₀ TC1D₅₀ (Mohamed *et al.*, 2015).

Anti-viral activity of seven new clerodane diterpenoids were isolated from *Dodonaea viscosa* were investigated invitro against herpes Simplex virus type 1(HSV-1). The result revealed all the seven diterpenoids show significant anti-viral activity (Lai bin *et al.*, 2016).

Anti-cancer effect

The leaves of *Dodonaea viscosa* were subjected to in vitro anti-cancer activities against three malignant growth cell lines and mitigating impact in RAW 264.7 macrophages. The hydro alcoholic extract was used for the assessment of the cell lines (HCT 116, MCF-7 and Hela cell). The extract shows a potent cytotoxicity towards HCT 116, MCF-7 and Hela with IC-50 value of $60.43 \pm 0.76 \mu\text{g/ml}$, $75.26 \pm 0.45 \mu\text{g/ml}$ and $72.12 \pm 0.87 \mu\text{g/ml}$ respectively. In addition, the extract treatment in macrophages significantly reduced NO level at the concentration of 5,10 and $20 \mu\text{g/ml}$ (Ramkumar *et al.*, 2021).

The different fractions of *Dodonaea viscosa* leaves of ethanolic extract are n-hexane, chloroform, ethyl acetate, n-butanol and aqueous were subjected to the cytotoxic effect on colon cancer cell line (HT-29). It was determined by the sulforhodamine B(SRB) test. As the end of the result, it was observed that the ethanolic extract exhibit as the major inhibitory effect in colon cancer cell with IC 50 value $10.52 \pm 2.5 \mu\text{g/ml}$ (Oscar *et al.*, 2020).

Methanol, acetone, acetonitrile and water were used as the leaf extract of *Dodonaea viscosa* for the biosynthesis of gold nano particles with varied morphologies. The characterization is carried out by XRD, EDX, SEM and TEM. The synthesized gold nanoparticles (AuNPs) show a IC₅₀ values of 4, 60, 8 and $100 \mu\text{g/ml}$ of methanol, acetone, acetonitrile and water respectively. The AuNPs exhibit cytotoxicity effect by inhibiting the growth of A549 NSCLC cells strongly (Anandan and Gurumalles Prabu, 2018).

The leaves of *Dodonaea viscosa* are investigated for their anti-cancerous study against human breast cancer cell line (MCF-7) using methano-

lic and chloroform extract. The cytotoxicity determined by MTT assay and trypan blue assay revealed that the leaf extracts of the *D. viscosa* has potent anti-cancerous activity with IC₅₀ value 8.571 and viable cells counted as 352 out of 391 (Karthikeyan and Akilan, 2021).

The cytotoxic effect of *Dodonaea viscosa* using different extracts (methanol, n-hexane, chloroform and n-butanol) is reported. The evaluation of anti-cancerous activity was performed by MTT assay against breast (MDA-MB-231), lung (A549) and liver (HepG2) cancer cell line showed an IC₅₀ value 24.6, 50 and $52.6 \mu\text{g/ml}$ respectively. In additionally, among all fractions, chloroform has potent cytotoxic effects (Omer *et al.*, 2022).

Antioxidant Effect

Antioxidant effect of different extracts (methanol, n-hexane, chloroform and n-butanol) from *Dodonaea viscosa* was evaluated by using DPPH assay and ABTS assay. Chloroform fraction has the highest antioxidant effect on both DPPH and ABTS with IC₅₀ value $172.72 \mu\text{g/ml}$ and $257.7 \mu\text{g/ml}$ respectively (Omer *et al.*, 2022).

The methanolic and chloroform extracts from leaves of *Dodonaea viscosa* were determined by DPPH assay at different concentration of extracts ranges from $10 \mu\text{l}$ - $100 \mu\text{l}$. High antioxidant activity was observed at $100 \mu\text{l}$ of chloroform extract with 66.53% scavenging activity. It was concluded that the chloroform extract from leaves of *Dodonaea viscosa* have potent antioxidant activity (Karthikeyan and Akilan, 2021).

Evaluation of antioxidant activity of *Dodonaea viscosa* in streptozotocin induced diabetic rats were shown potent antioxidant activity of *D. viscosa*. DPPH, hydroxyl radical, ABTS assay and lipid peroxidation assay were carried out in water (DVW) and ethanolic (DVE-4) extracts. In DPPH assay, the DVW and DVE-4 has an IC₅₀ levels of 49.09 and $27.13 \mu\text{g/ml}$ respectively. IC₅₀ value of DVW and DVE-4 in ABTS found to be 18.11 and $20.12 \mu\text{g/ml}$ respectively

while that of hydroxyl radical has 279.95 and 279.27 $\mu\text{g/ml}$ respectively. Finally, lipid peroxidation shows IC_{50} value 68.02 $\mu\text{g/ml}$ for DVW and 54.53 $\mu\text{g/ml}$ for DVE-4. The study revealed a potent antioxidant activity for both extracts (Veerapur *et al.*, 2010).

The antioxidant potential of different fractions such as methanol, chloroform, ethyl acetate and n-butanol from *Dodonaea viscosa* were investigated. The four methods used for the determination of antioxidant activity are DPPH, total antioxidant activity, FRAP and Ferric thiocyanate assay along with determination of total phenolic content. At a concentration of 60 $\mu\text{g/ml}$ in DPPH, ethyl acetate fraction exhibits highest inhibition (81.14 \pm 1.38%) and IC_{50} level found to be 33.95 \pm 0.58 $\mu\text{g/ml}$ while that off in FRAP has 380.53 \pm 0.58 $\mu\text{g/ml}$. But in total antioxidant activity, chloroform fraction exhibits highest potential (1.078 \pm 0.59) (Riaz *et al.*, 2012).

The four Kaempferol methyl ethers isolated from leaf extracts of *Dodonaea viscosa*. Var. angustifolia were subjected to its antioxidant activity. DPPH assay are used for the evaluation of antioxidant activity using extracts of hexane, dichloromethane, acetone and methanol. Out of four derivative, compound one has strong antioxidant activity with EC_{50} value of 75.49 \pm 1.76 μm (Teffo *et al.*, 2010).

The wound healing effect of chloroform and methanolic extracts of *Dodonaea viscosa* were investigated in in-vivo animal models namely, excision wound and incision wound model. In excision model, both extracts increased the speed of epithelization in less number of days (methanol-12 days, chloroform-14 days). In incision model, tensile strength of methanolic extract was double than chloroform extract (Naira *et al.*, 2021).

Anti-Inflammatory effects

In vivo study on anti-inflammatory activity of *Dodonaea viscosa* were investigated on Wister albino rats. Methanolic extracts are fractioned into Petroleum ether, chloroform, ethyl acetate

and n-butanol fraction for qualitative and anti-inflammatory screening by carrageenin induced paw edema model. The experiment was carried out at a concentration of 200mg/kg in all extract/fractions at regular time duration. The methanolic and chloroform extract has significant anti-inflammatory activity of 50 and 46% respectively (Mahadevan *et al.*, 1998).

Anti-inflammatory activity of Nebrodenside A isolated from *Dodonaea viscosa* was determined by Carrageenin-induced paw edema model. Molecular docking method used as a computational approach to predict the ability of anti-inflammatory compound (Kashif *et al.*, 2019).

Carrageenin induced paw edema determines the anti-inflammatory effect of hydro alcoholic extract of *Dodonaea viscosa* leaves. At a concentration of 300mg/kg the extract significantly inhibited the edema (Khalil *et al.*, 2006).

Hautriwaic Acid (HA) isolated from the leaves of *Dodonaea viscosa* were subjected for its anti-inflammatory activity. An in vivo application of HA to TPA mice ear at doses of 0.25, 0.5 and 1.0mg/car exhibit 60.2, 70.2 & 87.1% inhibition respectively. In addition, a 3mg/kg of dichloromethane extract (DvDE) show a percentage of 97.8% anti-inflammatory effect while multiple application of DvDE exhibit 71-8% at dosage of 100mg/kg on TPA edema model (David *et al.*, 2012).

Anti-inflammatory Study on whole plant of *Dodonaea viscosa* were investigated on the hydro alcohol and n-hexane extracts in vivo. It was studied by Carrageenin induced paw edema model. Indomethacin used as the standard drug. At a concentration of 100 and 200 mg/kg, hydro alcohol extract displays a promising inhibition of paw edema with 34.34 and 56.01% respectively (Ramkumar and Periyasamy, 2019).

Anti-diarrheal effects

Alcohol and aqueous extracts of roots of *Dodonaea viscosa* were investigated for its anti-diarrheal activity by castor oil induced diarrhoea in mice. The two parameters used for the test are

number of diarrheal episodes and mean weight of stool. Both the extracts display significant anti-diarrheal activity by reduction in weight of stools (Rajamanickam *et al.*, 2010).

In vivo castor oil- induced diarrhoea model was used to determine anti-diarrheal activity of 80% methanolic extract from *Dodonaea viscosa* leaves. Different concentration (100, 200 and 400mg/kg) of the extract were used for the evaluation of anti-diarrheal activity. The result showed a drastic inhibition in frequency of defecation of wet feces compared to control group (Jemal, 2019).

Anti-fertility effects

The methanolic extract of *Dodonaea viscosa* leaves were investigated for their anti-fertility in female rats by measuring early abortifacient activity and anti-implantation activity. The extract displays an anti-implantation activity of 68.42%. The total anti-fertility activity of the plant extract was 96.05% and hence showed the plant has effective anti-fertility activity (Ramya *et al.*, 2011).

Anti-fertility effects of methanolic extract of *Dodonaea viscosa* were reported in both male and female albino mice. For albino males, concentration of 200 and 400mg/kg for 21 days were administered orally while for females, 400mg/kg were given for 17 days. As a result, significant decrease in sperm count, degeneration in most seminiferous tubules and formation of nuclear pyknosis were observed. But there is no contragestive effects on treated females. Therefore, the plant is recommended for the control of house mice (Sohail *et al.*, 2017).

Reproductive toxicity of *Dodonaea viscosa* were investigated in vivo experimental animal model (zebrafish). The methanolic and fractions of hexane, chloroform and butanol were used for the study. The embryo short term toxicity test revealed that the extract is toxic for the development and survival of embryos. Even small amount of extracts are toxic to the embryo. It is found that the hexane fraction is most toxic with

LD₅₀ value 0.589± 0.30µg/ml (Khan *et al.*, 2021).

Anti-ulcer effect

Dodonaea viscosa extracts (water, ethanol and hexane) were used for the evaluation of gastro-protective and acute toxicity effect in various experimental models. Gastric protection study was performed in ethanol and indomethacin induced gastric ulcer by measuring ulcer index, gastric glutathione assay, alkaline phosphate assay and histopathological study in Wistar rats. Compared to hexane extract, water and ethanol showed moderate activity. The result showed that the hexane extract reduces gastric lesions dose dependently (Arun and Asha, 2008).

The various extracts (chloroform, ethanol and water) from *Dodonaea viscosa* roots were subjected to conduct anti-ulcer activity in rats by pylorus ligation experiment. At a dosage of 100mg/kg and 200mg/kg, the extracts significantly inhibited gastric lesions, volume and total acidity. It is found that the chloroform and ethanolic extracts has strong anti-ulcer activity (Rajamanickam *et al.*, 2009).

The ethanolic extract of *Dodonaea viscosa* leaves against in vivo aspirin induced gastric ulcer were conducted for its potential anti-ulcer activity. At a concentration of 500mg/body weight, the extract reduces ulcer index, volume, free and total acidities. In additionally, the extract enhanced the level of reduced glutathione and reduced MDA level (Sathya and Prasanna, 2012).

Anti-ulcerogenic activity of various extracts of *Dodonaea viscosa* leaves were conducted in gastric ulcer models. Aspirin plus pylorus-ligation, indomethacin-induced ulcer and ethanol-induced ulcer are the three assays used to evaluate anti-ulcer activity by using extracts of petroleum ether, ethyl acetate, ethanol, benzene, chloroform and chloroform water. The extract of ethyl acetate displays high ulcerative lesion index, increased serum calcium level and decreased alkaline phosphatase activity compared

to other extracts (Veerapur *et al.*, 2004).

Toxicity effects

At a concentration of 5000mg/kg p.o of hydroalcoholic extract of *Dodonaea viscosa* leaves did not show any sign of toxicity (Khalil *et al.*, 2006).

Evaluation of dermatotoxicity were determined in 80% methanolic extract of leaves of *Dodonaea viscosa* in animal models (rabbits and mouse). In rabbit, skin irritation test causes a slight irritation and display a primary irritation index (PII) value 0.45. The skin sensitization test on mouse ear found to be also a slight irritant while the acute and dermal toxicity test show no toxicity (Kefale *et al.*, 2010).

IV. Conclusion

The review discussed phytochemical profiling and pharmacological effects of *Dodonaea viscosa* as promising medicinal plant for human healthcare.

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