IJRAR.ORG E-ISSN: 2348-1269, P-ISSN: 2349-5138

INTERNATIONAL JOURNAL OF RESEARCH AND ANALYTICAL REVIEWS (IJRAR) | IJRAR.ORG

An International Open Access, Peer-reviewed, Refereed Journal

Albizia lebbeck (L.) Benth – An untapped source of medicinal wisdom

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Abstract

Medicinal plants have been the main source of drugs for the curing of the ailments of humans throughout their evolution. With the development and advancement of chemistry several drug molecules were synthetically prepared and used as medicines. Initially plant derived secondary metabolites proved to the template over which the synthetic chemistry worked to substitute functional groups that potentiated the activity of the drug. Several studies are available on a variety of plants and still dramatic molecules are yet to be identified from them. Albizia lebbeck is one such plant on which several studies are available and is one of the important medicinal tree described in Ayurveda. This paper is reviewing the important chemical ingredients, its morphological features and pharmacological activities reported.

Key words: Albizia lebbeck, Ayurveda, Pharmacological activity

Introduction

Medicinal plants had immense importance in human lives as they provided for all their basic amenities like food, medicine, shelter, clothing and other articles of day-to-day use. Health being considered the most important factor contributing to human existence, medicinal plants have been exploited to the maximum to free human lives from the crutches of diseases. Though several medicines have been derived from medicinal plants, there are many plants and compounds derived from them yet to be tapped for their medicinal potential. This article aims at reviewing the pharmacological activities reported on *Albizia lebbeck*.

Distribution and Habitat

Albizia lebbeck (L.) Benth. Is a deciduous tree belonging to the family Mimosaceae; growing to a height of 12 – 21 m, with a pale exfoliating bark giving the tree a rough appearance, while the young shoots of the plant are glabrous (Ali S and E Nasir, 1973; Zia-Ul-Haq et.al., 2013; Sharma G.K amd Nishtha Dubey, 2015)). This plant

is also cultivated in many parts of the world and has been naturalized in countries as far as Southeast Asia, Australia, Western Asia, North Africa, West Africa, Caribbean, Central America, Northern South America and eastern South America (Adams and Charles Dennis, 1972; Grisebach, 1864; Hutchinson et.al., 1958; Little and Elbert, 1983; Williams et.al., 1951). There are about 150 related species of Albizia distributed throughout subtropical regions of Asia and Africa. In India, this tree is widely distributed throughout and the neighboring eastern regions of Pakistan, Sri Lanka and Burma (Kumar et.al., 2007).

Description

Bark

Bark is covered with longitudinal and transverse fissures on its outer surface with greyish tone with flaky appearance and slightly reddish on its inner surface. Fresh specimens shows a whitish inner surface with numerous fine longitudinal striations (Yadav et.al., 2011).

Heartwood

Heartwood on cut surface shows dark brown coloration due to the deposition of tannin with differing shades of darker and lighter browns. The surface was hard to touch with rough, slightly fibrous and coarse in touch. Fracture showed splintery characteristic with an astringent taste and a characteristic resinous odour (Yadav et.al., 2011).

Leaf

Leaves are compound with bipinnate arrangement with 3-11 pairs of oblong, elliptic-oblong leaflets that are bright green on adaxial surface. The base of the leaves is asymmetrical, glabrous and usually fold up during dusk. Mature leaves show a ashy green or dull glaucous green colour. Young leaflets show nyctinastic movements (Verma et.al., 2013; Lowry et.al., 1994).

Flower

Flowers are borne on inflorescences which are mainly seen in globular clusters or axillary clusters of around 15-40 white fragrant flowers. Peduncles are around 100 mm long with a 1.5 – 5 mm long pedicel, clayx lobes are 3.5 – 5 mm long and puberulous. Corolla elements are inconspicuous and are 5 – 11 mm long, ending in triangular lobes which are five in number and covered with soft downy hairs at the apex. Stamens are free with numerous filaments which are 15 – 30 mm long and fused at the base and with a white to cream colour, tipped with pale green turning dark well as they mature (Lowry et.al., 1994).

Pods

Pods are light yellowish-brown in colour when mature, glabrous, flat, leathery and indehiscent growing up to a length of 12 – 35 cm and 3 – 6 cm wide, rolling along the sutures and contains from 3 – 12 seeds per pod. Mature pods remain on the tree till they detach from the tree (Yadav et.al., 2011).

Seed

Seeds are round with a creamy-brownish tinge (Bobby et.al., 2012).

Table 1. Phyto-constituents of *Albizia lebbeck*

Plant Part	Extract	Phyto-constituents
Root	n-hexane and chloroform fractions of methanolic extract	• Lupeol • Stigmasterol • 4-hydroxy-3-methoxycinnamic acid • Trans-p-coumaric acid • Echinocystic acid • Stigmast-4,20 (21), 23-trien-3-one (Lebbeksterone) • Tricosanyloctadec-9-en-1-oate • Pentacosanyloctadec-9-3n-1-oate (Sesaltani et.al., 2011, Ahmed et.al., Alam et.al., 2012)
Bark	Ethanolic and petroleum ether extract	• D-catechin • Leucocyanidin • Mekacacidin • Leucoanthrocyanidin • Lebbecacidin • Friedelin • β-sitosterol • Acacic acid lactone 3-*O*-beta-D-xylopyranosyl-(1 leads to 2)-alpha-L-arabinopyranosyl-(1 leads to 6)-beta-D-glucopyranoside • 3-*O*-beta-D-xylopyranosyl-(1 leads to 2)-alpha-L-arabinopyranosyl-(1 leads to 6)-*O*-[beta-D-glucopyranosyl (1 leads to 2)-beta-D-glucopyranoside • Anthraquinone glycosides (Prajapati et.al., 2003; chulet et.al., 2010; Verma SC et.al., 2013; Chaddha V et.al., 2011)
Heartwood	Methanol extract	• Melanoxetin • d-pinitol • okanin

		• leucopelangonidin • melacacidin (7,8,3',4'-tetrahedroxyflavan-3,4-diol) • lebbecacidin (Yadav et.al., 2011)
Leaf	Ethanolic extract	Flavone,3', 5-dihydroxy-4', 7-dimethoxyflavone N-benzoyl-L-phenylalaninol Friedelan-3-one g-sitosterol Hexaglycosylated saponins Quercetin Albigenic Albigenin Kaempferolquercetin Albizziahexoside (Chulet R, 2010; Sasmal et.al., 2013; Bobby et.al., 2012)
Flower	Methanol and chloroform extracts	Lupeol α amyrin β amyrin Benzyl acetate Benzyl benzoate Crocetin Taxerol Cycloartemol Campestrol Sitisterol Lebbekanin Crocetin lebbekannin-D,F, G & H (Prajapati et.al., 2003; Bobby et.al., 2012)
Seed		Protein Minerals – Calcium, Phosphorous, Iron, Niacin Ascorbic acid Amino acids – Arginine, Histidine, Leucine, Isoleucine, Lysine, Methionine, Phenyl alanine, Threonine, Tyrosine, Valine Echynocystic acid Sitosterol

		N-demethyl budmunchiamines *Albizia lebbeck* a-amylase inhibitor (AL-a AI) Fatty acids – palmitic, stearic, oleic, linoleic, linolenic, arachidic, cis-11-eicosenoic, behenic, pentadecanoic and myristic acids (Prajapati et.al., 2003; Bobby et.al., 2012; Chaddha V et.al., 2011; Saha et.al., 2009; Kachole et.al., 2013)

Mousallamy et.al., (A M el-Mousallamy, 1998) reported two new tri-O-glycoside falvonols namely Kaempferol and quercetin 3-O-alpha-rhamnopyranosyl (1→6)-beta-glucopyranosyl (1→6)-beta-galactopyranosides from the leaves of *Albizia lebbeck* by conventional methods of analysis followed by confirmation using ESI-MS, 1H and 13C-NMR spectral analysis. Al-Massarani et.al., 2017 studied the total extract from *Albizia lebbeck* flowers for bioactivity by assessing their hepatoprotective activity against the standard drug Silymarin and was found to exert significant hepatoprotective activity at higher doses. Fractionation of the extract by liquid-liquid partition and reexamination showed highest hepatoprotective was exhibited by the n-butanol fraction followed by n-hexane fractions. Chloroform fraction showed highest activity in serum lipid parameters. They further purified the compounds in these fractions using chromatography and found two new compounds, one belonging to the acyclic farnesyl sesquiterpene glycoside group 1-O-[6-O-*α*-l-arabinopyranosyl- *β*-d-glucopyranoside] -(2E,6E-)-farnesol and the other, a squalene derivative namely 2,3-dihydroxy-2,3-dihydrosqualene. They also identified eight more compounds from the flowers of *Albizia lebbeck* namely benzyl 1-O-*β*-d-glucopyranoside, benzyl 6-O-*α*-l-arabinopyranosyl *β*-d-glucopyranoside, linalyl *β*-d-glucopyranoside, linalyl 6-O-*α*-l-arabinopyranosyl-*β*-d-glucopyranoside, (2*E*)-3,7-dimethylocta-2,6-dienoate-6-O-*α*-l arabinopyranosyl-*β*-d-glucopyranoside, *n*-hexyl-*α*-l arabinopyranosyl-(1 → 6)-*β*-d-glucopyranoside (creoside), *n*-octyl *α*-l-arabinopyranosyl-(1 → 6)-*β*-d-glucopyranoside (rhodiooctanoside) and ethyl fructofuranoside (Al-Massarani; 2017).

Medicinal uses

Traditional medical systems used *Albizia lebbeck* in the treatment of asthma, inflammation, infertility, diarrhea, infection, dysentery, leprosy, paralysis, helminthic infection, cardiac diseases and as an anti-tubercular agent. The drug has also found use in allergic rhinitis, as an astringent, eye disorders, as a psychoactive drug, flu, lung diseases, cough, gingivitis and abdominal tumors. They are used externally for the treatment of ring worm and wounds for washing purpose, in gonorrhea, leucorrhoea and other genital diseases and ulcers (Chulet et.al., 2010; Hassan et.al., 2007; Sasmal et.al., 2013).

Bark of *Albizia lebbeck* are having the properties of astringent, bitter, acrid and sweet tastes, giving a feeling of mild thermo generation. It also has properties like expectorant, aphrodisiac, ophthalmic, depurative, restorative, tonic, bronchitis, leprosy, paralysis, helminthes, infections, antidiarrheal activity, dental infections, tooth ache and diseases of the gum, eczema, pruritus, worm infestation, alexiteric, blood diseases, leukoderma, itching, skin diseases, excessive perspiration, piles, deafness, boils, scabies, syphilis and weakness. It is widely used for

bathing purpose and for tanning of leather (Chulet et.al., 2010; Prajapati et.al., 2003; Davidson et.al., 2009; Zia-Ul-Haq, 2013). Root is used in hemicrania (Pathak et.al., 2010).

Leaves are used in tuberculosis, conjunctivitis, trauma to eyes, as an antiseptic, antimicrobial, anti-protozoal, anti-dysenteric, anti-ovulatory, anti-fertility and anti-cancer agent (Bobby et.al., 2012). Flowers of *Albizia lebbeck* are used in cough, bronchitis, tropical pulmonary eosinophilia, asthma, inflammation, scrofula, skin diseases, leprosy, leukoderma, chronic catarrh, seminal weakness, ophthalmopathy, poisoning, spermatorrhoea and snakebite (Zia-Ul-Haq, 2013; Sasmal et.al., 2013; Prajapati et.al., 2003; Pathak et.al., 2010; Chaddha V et.al., 2011). Pods of the plant is used as an antiprotozoal, hypoglycemic and as an anticancer agent (Zia-Ul-Haq, 2013; Chulet et.al., 2010). Seeds are having astringent and aphrodisiac properties and are used in diarrhea, as a brain tonic and in the treatment of gonorrhea. Seed oil is used as a topical application in leukoderma and scrofulous swellings ((Zia-Ul-Haq, 2013; Uma et.al., 2009).

Research activities in *Albizia lebbeck*

Albizia lebbeck whole plant is widely used for medicinal purposes in different parts of the world. Many related species of Albizia are utilized owing to their morphological similarity. Traditional medical practitioners do not make difference in the species of Albizia, and neither do they are concerned about their phytochemical profile bringing about those pharmacological properties. In Ayurveda, this drug is considered to be the best antidote against both inanimate, animate, concocted and delayed poisoning (Deepak et.al., 2018). Leaves of *Albizia lebbeck* are widely used for their property of vision enhancement, especially in night blindness, and other related ophthalmic diseases (Hussain et.al., 2008; Pathak et.al., 2009). Traditional and folklore medicine has also made of this drug for respiratory diseases like cold and cough (Pratibha N et.al., 2004; Saha et.al., 2009). Different parts of the plant have also gained wide use as a veterinary medicine and the leaf of the tree is used as a fodder for the domestic animals like cattle. They also found wide use in agricultural practices as mulch and manure owing to its high nitrogen content (Uddin et.al., 2009).

Antioxidant property

Zia-Ul-Haq et.al., studied the in vitro total antioxidant property of the pods, leaves, root and stem of *Albizia lebbeck* and found that the plant parts exhibited statistically significant activity in Trolox equivalent antioxidant capacity (TEAC), ferric reducing antioxidant power (FRAP) and total radical-trapping antioxidant parameter (TRAP). Stem extracts showed highest activity in FRAP, TEAC and TRAP assays than the root and pods. The IC50 value for TEAC, FRAP and TRAP were 981.3, 514.2 and 98.2 umol/g respectively for the stem extract. (Zia-Ul-Haq et.al., 2013). Abriham et.al., reported 70% methanolic extract of leaves, flowers and bark of *A. lebbeck* to be having a significant dose dependent DPPH (1,1-diphenyl-2-picryl hydrazyl) radical scavenging activity when tried at 50, 100, 200 and 400 ug/ml doses. The IC50 value value was found to be 156 ug/ml (Abriham et.al, 2015). Ali et.al., also reported DPPH radical scavenging activity of *A. lebbeck* of petroleum ether, ethyl acetate and methanol extracts at 20, 40, 60, 80 and 100 ug/ml concentrations. The study also evaluated the hydroxyl free radical scavenging activity also of the *A. lebbeck* petroleum ether, ethyl acetate and methanol extracts and the IC50 values were obtained as 70.9, 64.7 and 68.9 ug/ml respectively (Ali et.al., 2018). Imran

et.al., studied the total phenolic content of various species of Albizzia and other medicinal trees in Pakistan and found that *A. lebbeck* showed highest amount of phenolic compound content of 388.5 mg/g. Among the five species of plants tested for antioxidant activity, *A. lebbeck* bark showed the highest antioxidant activity than others in TEAC, FRAP and TRAP assyas with an IC50 values of 502.6, 2561.5 and 43.66 respectively (Imram et.al., 2014). Aqueous extract of the leaves of *A. lebbeck* showed reduction in TBARS and conjugated diene levels in alloxan induced diabetic rats treated with the plant extract. GSH, SOD, CAT, GPX and GST activities showed significant elevation on treating with *A. lebbeck* extract (Resmi et.al., 2006). A study on the antioxidant potential of the seed cake and seed oil of *A. lebbeck* was performed by DPPH radical scavenging assay along with the determination of the total phenolics, flavonoids and tocopherol contents. The amount of phenol, flavonoids and tocopherol was found to be present in higher concentration in seed cake than the oil. But the IC50 value of DPPH radical scavenging assay was found to be more for the seed oil than the seed cake (0.067 mg/ml). The seed oil showed a reduction amounting to 79% on the DPPH radical scavenging assay. Umar H et.al., (2019) studied the activity of zinc oxide nanoparticles (ZnO NPs) synthesized using *A. lebbeck* stem bark extract showed significant cytotoxicity against MDA-MB 231 and MCF-7 human breast cancer cell lines along with significant antioxidant property against hydrogen peroxide (H2O2) free radical scavenging assay. ZNO NPs at 0.1, 0.05 and 0.01 M concentrations produced dose dependent antioxidant property with an IC50 values of 48.5, 48.7 and 60.2 ug/ml respectively (Umar H et.al., 2019). Joshi et.al., 2013 studied the wound healing potential of the ethanolic extract of the roots of *A. lebbeck* in incision and excision wound models in rats. They found that the extract at 500 mg.kg dose significantly produced wound healing property. The investigators also studied the antioxidant property of the extract and found that it significantly elevated the levels of superoxide dismutase. Glutathione levels were found reduced in this study. Lipid peroxidation levels were significantly reduced along with nitric oxide levels (Joshi et.al., 2013). Ahmed et.al., 2014b, studied the hypoglycemic effect of the methanolic extract of *A. lebbeck* in rats fed orally at 100, 200, 300 and 400 mg/kg b. w doses induced with diabetes by administering Streptozotocin administered intraperitoneally at 60 mg/kg dose. The study even though noted only a momentary decrease in the serum fasting blood glucose levels as compared to the diabetic rats, there was a very significant lowering in the lipid profile. The study also demonstrated a significant activity in antioxidant enzymes also. Reduced glutathione, glutathione peroxidase, catalase and superoxide dismutase levels were significantly elevated on treating with the extract. Levels of lipid peroxidation were reduced on administering the extract in liver and kidney tissues (Ahmed et.al., 2014b).

Anti-inflammatory activity

Bark of *A. lebbeck* was extracted with petroleum ether, chloroform and 95% ethanol and were screened for anti-inflammatory activity in rats with Carrageenan induced rat paw edema, Dextran induced rat paw edema, cotton pellet induced granuloma and Freund's complete adjuvant induced arthritis models. The study showed significant anti-inflammatory activity exhibited by the petroleum ether and ethanol extracts at a dose of 400 mg/Kg showed the maximum anti-inflammatory activity. In carrageenan induced paw edema pet. Ether extract showed 48.6 % while ethanol extract produced 59.6% reduction. In dextran induced paw edema, pet ether showed 45.9 % and ethanol extract showed 52.9 % inhibition. In cotton pellet granuloma model pet ether showed 34.6% and ethanol

extract showed 53.57% activity. In Freund's adjuvant model, pet ether extract showed 64.9 % and ethanol extract showed 68.57% inhibition (Babu et.al., 2009). Ethyl acetate extract of *A. lebbeck* at 100, 200 and 400 mg/Kg also exhibited significant anti-inflammatory activity against acute inflammatory model induced by carrageenan induced paw edema with 62.2 % inhibition while histamine produced 43.19%, dextran induced paw edema was inhibited by 42.3% and serotonin produced 68.84% activity. Sub-acute inflammatory model with formaldehyde-induced hind paw edema model showed 31.5% inhibition and cotton pellet induced granuloma had 13.48% inhibition. The extract was found to be non-ulcerogenic and produced no signs of any toxicity at a dose level of 5000 mg/Kg per orally in rat and mice (Suman et.al., 2019). Aqueous and ethanolic extracts of *A. lebbeck* leaves at doses of 50, 100 and 200 mg/Kg doses on oral administration reduced carrageenan induced paw edema in rats with a percentage protection of 22.3, 30.85, 39.36 and 22.53, 32.98, 42.55 percentage respectively. Cotton-plug induced granuloma model had a protection of 19.07, 27.57, 38.55 and 23.93, 32.23, 42.33 % respectively (Meshram et.al., 2016). In another study, the anti-inflammatory activity of the aqueous extract of leaves of *A. lebbeck* was performed by assessing protein denaturation, membrane stabilization and hypotonicity induced hemolysis assays. The maximum inhibition of protein denaturation was found to be 78.1% with an IC_{50} value of 330 ug/ml. The maximum membrane stabilization was found to be 74.1% with an IC_{50} value of 440 ug/ml. the percentage of protection in hypotonicity induced hemolysis was found to be 69.34% with an IC_{50} of 400 ug/ml. all these activities were produced by a dose of 500 ug/ml of the extracts (Kamala et.al., 2020). Avoseh et.al., (2021) reported the anti-inflammatory activity of the volatile oils extracted from the two species of Albizia; *A. lebbeck* and A. zygia. Essential oils isolated from *A. lebbeck*; (E)-α-ionone and 3-Octanone significantly inhibited carrageenan-induced inflammation probably by inhibiting pro-inflammatory pain biomarkers like histamine, serotonin, bradykinin and interleukins induced by the inflammation. Other essential oils isolated from *A. lebbeck* were 2-pentylfuran, (E)-methyl iseugenol and 2-methyl tetradecane (Avoseh et.al., 2021). Yadav et.al., 2010 demonstrated the anti-inflammatory activity of an Ayurvedic formulation containing *A. lebbeck*, Shirishavaleha. The formulation made according to the standard recommendation in Ayurvedic formulary was prepared using the bark as well as the heartwood and compared for their anti-inflammatory activity. Carrageenan induced paw edema model was used in albino rats. Phenylbutazone was used as the standard drug and the results of the study showed that the formulation prepared from heartwood at a dose of 1.8 g/kg b. w for 5 days administration produced only weak anti0inflammatory activity while the formulation prepared with the bark showed a significant anti-inflammatory activity after 6 hours of administration (Yadav SS. et.al., 2010).

Antimicrobial activity

Umar H et.al., (2019) studied the activity of zinc oxide nanoparticles (ZnO NPs) synthesized using *A. lebbeck* stem bark extract showed significant cytotoxicity, antioxidant property and antimicrobial property ZNO NPs at 0.1, 0.05 and 0.01 M concentrations produced dose dependent cytotoxicity on the cancer cell lines, produced antioxidant property against hydrogen peroxide free radical scavenging assay and antimicrobial activity against several gram-positive and gram-negative microbes. The gram-positive organisms selected for the study were Bacillus cereus (ATCC 7064) and Staphylococcus aureus (6538 P) and the gram-negative organisms selected were Escherichia coli (O157:H7). Klebsiella pneumoniae (ATCC 27738) and Salmonella typhi (B-4420).

Salmonella typhi showed an equivalent zone of inhibition as that of Ciprofloxacin standard (10 ug) (Umar H et.al., 2019). Lam et.al., 2011 investigated on an isolated protein of 5.5 kDa from the seeds of *Albizia lebbeck* which exhibited strong haemolytic activity in rabbit erythrocytes and anti-tumour activity against MCF-7 breast cancer cells and HepG2 hepatoma cells. They also demonstrated anti-fungal activity against *Rhizoctonia solani* species by inhibiting mycelial growth with an IC_{50} of 39 μM. the protein however, failed to show any anti-fungal activity against *Fusarium oxysporum*, *Helminthosporum maydis*, *Valsa mali* and *Mycosphaerella arachidicola*. The isolated protein named Lebbeckalysin also showed significant activity against *Escherichia coli* with an IC_{50} value of 0.52 μM (Lam et.al., 2011). Joshi A et.al., 2013, studied the wound healing property of the ethanolic extract of *A. lebbeck*. They found that administering the extract at a dose of 500 mg/kg significantly inhibited *E. coli* growth on incision and excision wound model on rats (Joshi et,al., 2013). Gharpure et.al., 2019, studied the antibacterial effect of silver nanoparticles synthesized using the white flower extract of *A. lebbeck* agiant Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa and Bacillus subtilis cultured on Mueller Hinton agar, nutrient agar and Luria Bertani agar by well diffusion methods. The extract didn't show any significant antibacterial activity at either lower or higher concentrations. The result shows that there is a potential to use the silver nanoparticles derived from *A. lebbeck* could be utilized for drug delivery as they do not show any decrease in the viability of the cells treated with silver nanoparticles (Gharpure et.al., 2019).

Hematotoxicity

Albactam, a b-lactam derivative isolated from *A. lebbeck* showed anti-platelet aggregation activity against adenosine diphosphate and arachidonic acid induced platelet aggregation assay in guinea pigs in a dose dependent manner (El Gamal et.al., 2015). Lam et.al., 2011, isolated a monomeric 5.5-kDa protein which produced hemolysis in rabbit erythrocytes from *Albizia lebbeck* seeds. The isolation was done using ion-exchange chromatography on Q-Sepharose and SP-Sepharose, hydrophobic interaction chromatography on Phenyl-Sepharose and gel filtration on Superdex 75. The protein adsorbed well on to Phenyl-Sepharose and its hemolytic activity was preserved throughout a wide range of pH from 0 – 14 and at a temperature range of 0 – 100^0C. The authors also reported that the hemolytic activity was preserved in the presence of a wide range of metal ions and carbohydrates (Lam et.al., 2011).

Hepatoprotective activity

The methanolic, ethanolic and acetone extracts of seed and leaves extract of *A. lebbeck* were studied for their in vitro hepatoprotective activity on human liver hepatocellular carcinoma (HepG2) cell line with paracetamol as the liver damage inducing agent. Paracetamol treated HepG2 cells showed maximum cell viability (131.6 %) on *A. lebbeck* seed extract treatment. The standard drug silymarin showed a cell viability of 156.6 % (Kumar A et.al, 2016). Chloroform, ethyl acetate and n-butanol extracts of the *A. lebbeck* leaves were investigated for its hepatoprotective and antioxidant properties. The chloroform and ethyl acetate fractions showed significant hepatoprotective activities against CCl4 induced hepatotoxicity. The elevated plasma amino-transferases and alkaline phosphatase levels were brought down by the extracts in comparison with silymarin (Sokkar et.al., 2016). In another study the total extract of the flowers of *A. lebbeck* was examined for their hepatoprotective activity

against the standard drug silymarin. Serum AST, ALT and bilirubin levels were reduced by the plant extract at a higher dose by the n-butanol and n-hexane fractions (Al-Massarani et.al., 2017). Hydro-alcoholic extract of *A. lebbeck* was tried for its hepatoprotective activity in wistar albino rats with CCL4 induced hepatotoxicity. The extracts were given per-orally and the doses of 200 and 400 mg/Kg showed significant hepatoprotection by reducing the elevated hepatic enzymes in comparison to the standard drug silymarin.

Anti-cancer property

Desai TH (2019) studied the anticancer activity of *A. lebbeck* saponin rich fraction in various in vitro models. Albiziasaponins (A-E) and oleanane triterpene were initially studied in silico for their anti-cancerous properties and were then tested in vitro in MCF-7 human breast cancer cells and was found to inhibit angiogenicity, prevented chromosomal aberrations – hypodiploid, hyperdiploid, ring, premature separation, Dicentric fragments, Acentric fragments, chromatid break and chromosomal gap. They also increased the Caspases-3 and Caspases-8 levels indicating that they induced apoptosis. IC50 value of saponin rich fraction was found to be 1 ug/ml in MCF-7 cells (Desai TH et,al., 2019). Kavitha et.al. (2021), studied the antitumor activity of the ethanolic extract of pods of *A. lebbeck* on Ehrlich ascites carcinoma (EAC) in Swiss albino mice and its in vitro cytotoxicity effect on HeLa and A549 cell lines. The extract was tried in two doses of 200 and 400 mg/Kg body weight against 5-fluorouracil as the standard drug. The extracts showed dose dependent cytotoxicity against EAC and reduced the body weight, tumor volume, viable cell count, tumor weight and increased the lifespan of the animals. The extract also showed cytotoxicity against HeLa and A459 cells comparable to that produced by Cisplatin (Kavitha et.al., 2021). Umar H et.al., (2019) studied the activity of zinc oxide nanoparticles (ZnO NPs) synthesized using *A. lebbeck* stem bark extract showed significant cytotoxicity against MDA-MB 231 and MCF-7 human breast cancer cell lines assessed using the trypan blue dye exclusion assay and MTT assay. ZNO NPs at 0.1, 0.05 and 0.01 M concentrations produced dose dependent cytotoxicity on the cancer cell lines (Umar H et.al., 2019). Malaikolundhan H et.al., (2020) demonstrated the gold nanoparticles (AuNPs) formulated using *A. lebbeck* aqueous leaf extracts (AL-AuNPs) exhibited cytotoxicity against cancer cells. Colon cancer cells were inhibited by AL-AuNPs with an IC50 concentration of 48 ug/ml and exhibited significant apoptosis capability and escalated ROS generation, decreased $\delta\psi m$, apoptotic morphological changes by AO/EtBr and altering pro and anti-apoptotic protein expressions in HCT-116 colon cancer cells (Malaikolundhan H et.al., 2020). Note et.al., (2019) isolated a new acacic acid – type saponin from the bark extract if *A. lebbeck* namely lebbeckoside C. They demonstrated the cytotoxicity of this compound against human glioblastoma cell line U-87 MG and TG1 stem-like glioma cells isolated from a patient tumour and exhibited IC50 value of 1.69 and 1.44 uM respectively. (Note et.al., 2019). Lam et.al., 2011, studied the anti-tumour activity of a monomeric protein of 5.5 kDa isolated from the seeds of *Albizia lebbeck* using ion-exchange chromatography. They noticed that the isolated protein was haemolytic to isolated rabbit erythrocytes and it preserved its haemolytic property to a wide range of pH, temperature, presence of metallic ions and carbohydrates. The protein decreased murine splenocyte viability and inhibited the proliferation of MCF-7 breast cancer cells with an IC_{50} of 0.21 and 0.97 μM and inhibited HepG2 hepatoma cells with an IC_{50} of 1.37 μM respectively (Lam et.al, 2011).

Anti-hyperglycemic activity

Patel et.al., (2015) reported the anti-hyperglycemic activity of the methanolic extract of *A. lebbeck* bark in female Sprague-Dawley rats induced with streptozotocin induced diabetes mellitus model. Methanolic extract of *A. lebbeck* significantly reduced the serum glucose, creatinine, urea, cholesterol, triglycerides, low-density lipoprotein cholesterol and very low-density lipoprotein levels and increased high-density lipoprotein levels against the standard metformin. The doses of extracts at 200, 350 and 620 mg/Kg showed significant activity when compared to the standard drug (Patel PA et.al., 2015). Ahmed et.al., 2014, isolated flavonoids from the stem bark extract of *A. lebbeck* and conducted in-vitro anti-diabetic studies. Flavonoids, 5-deoxyflavone (Geraldone), luteolin and isookanin were isolated from the ethanolic and methanolic extracts of *A. lebbeck* stem bark. All these flavonoids exhibited significant a- glucosidase and a-amylase enzyme inhibition as comparable to the reduction in plasma glucose levels. Further confirmation of the anti-diabetic property was done by in-silico docking of the compounds with these enzymes and determining the biding affinities. The study showed a corroborative result in both in-vitro and in-silico studies. (Ahmed et.al., 2014a). In another study Ahmed et.al., 2014b studied the antidiabetic activity of the methanol extract of *A. lebbeck* on streptozotocin induced diabetic rats. The extracts at a concentration of 100, 200, 300 and 400 mg/kg b.w showed a momentary decrease in the fasting blood glucose levels in comparison to the streptozotocin treated group. The study also showed a significant reduction in the lipid profile and a significant elevation in the antioxidant enzyme levels also (Ahmed et.al., 2014).

Anti-dyslipidaemic activity

Methanolic extract of *A. lebbeck* significantly reduced the serum glucose, creatinine, urea, cholesterol, triglycerides, low-density lipoprotein cholesterol and very low-density lipoprotein levels and increased high-density lipoprotein levels against the standard metformin. The doses of extracts at 200, 350 and 620 mg/Kg showed significant activity when compared to the standard drug. This study proved the cardioprotective activity of *A. lebbeck* (Patel PA et.al., 2015). Ahmed et.al., 2014b, studied the lipid lowering activity of the methanolic extract of *A. lebbeck* in Streptozotocin induced diabetic rats. The study showed a significant lipid lowering activity of the extract in total cholesterol, triglycerides. Low density lipoprotein-cholesterol and very-low -density lipoprotein cholesterol levels. The study also demonstrated an increased levels of HDL cholesterol as well. The study was conducted in the doses of 100, 200, 300 and 400 mg/kg b.w doses of the extract (Ahmed et.al., 2014b).

Neurodegenerative diseases

Uzma Saleem et.al., (2019) studied the system pharmacology of *A. lebbeck* on haloperidol-induced catalepsy experimental model of Parkinson's disease (PD) in wistar albino rats. The study explained the mechanism of action of *A. lebbeck* in PD. The study found that *A. lebbeck* improved the motor functions and endurance as evident from the significant changes in behavioural studies and strengthening the antioxidant defence and reversal of the micro-architectural damages produced on neuronal tissue as evidenced in histological studies. System pharmacology investigation led to the identification of 25 compounds which acted synergistically interacting with the targets. Kaempferol, phytosterol and okanina were found to be more significant compounds that formed prominent target nodes of TDP1 and MAPT (Saleem U et.al., 2019). Saleem U et.al., (2019) investigated the potential of *A. lebbeck* seed hydro-methanolic extract in Alzheimer's disease (AD). The study was performed on

Wistar albino rats after inducing AD with the help of aluminium chloride (AlCl3). 100, 200 and 300 mg/Kg dose levels were fixed for the study against the standard drug selected to be galantamine at a dose of 0.5 mg/Kg. behavioural functions were assessed using Y-maze, T- maze, Morris water maze, hole board, and open field behaviour test. Biochemical, histological and computational assessments were also performed. The extracts showed significant improvement of memory and cognitive impairments. Antioxidant levels and histological parameters positively correlated with the therapeutic benefits of the hydro-methanolic extracts. Cholinergic deficits were corrected by the extracts probably by inhibiting the hyperactive acetylcholinesterase. Computational docking studies also showed a positive correlation with that of the study findings (Saleem U et.al., 2019).

Antitoxic property

Amog et.al., (2016) studied the activity of the various extracts of seeds of *A. lebbeck* against Echis carinatus venom (ECV)-induced local toxicity. Various extracts taken ranging from the most non-polar to the polar were screened for their phytochemical constituents and among them the methanolic extract of *A. lebbeck* showed the most promising inhibitory activity against ECV proteases, the major enzyme-toxin responsible for local-toxicity. Further evaluation of the hyaluronidases and phospholipase A2 were also performed in in vivo models in mice for the characteristic local-toxicity of haemorrhage and myotoxicity. *A. lebbeck* methanolic extract are rich source of phenolics and flavonoids and exhibited strong inhibition of ECV protease (IC50 = 36.32 ug), hyaluronidase (IC50 = 91.95 ug). The methanolic extract also neutralized ECV induced haemorrhage (ED50 = 37.5 ug) and lactate dehydrogenase (ED50 = 31.44 ug) (Among PU et.al., 2016).

Anti-allergic and Immunomodulatory activity

Ventakesh et.al., (2010) investigated on the anti-allergic activity of standardized ethanolic extract of *A. lebbeck* with respect of catechin as a biomarker. The extraction of the plant yielded 14.72 % of catechin. The extract was administered to mice at a dose of 50 to 300 mg/Kg and catechin was administered 50 mg/Kg. mice were evaluated for mast cell stabilization and estimation of histamine in plasma. Graded doses of *A. lebbeck* extract showcased strong mast cell stabilization potential with an IC_{50} value of 85 ug/ml. The histamine inhibitory activity of catechin from *A. lebbeck* is thought to be due to the modulation of histamine release and cytokine expression of antigen – IgE activated mast cells (Venkatesh et.al., 2010). Nurul IM et.al., (2011) investigated the anti-allergic property of *A. lebbeck* bark extract. They studied the effect of the extract on H1R and HDC gene expression on rat models induced with toluene-2,4-diisocyanate (TDI) sensitization and on HeLa cells expressing H1R. administration of the extract suppressed TDI induced H1R and HDC mRNA expression and [(3)H] mepyramine binding, HDC activity and histamine content in the nasal mucosa. The extract also suppressed TDI-induced up-regulation of IL-4, IL-5 and IL-13 mRNA. In HeLa cells, the extract down-regulated phorbol-12-myristate-13-acetate and histamine-induced up-regulation of H1R mRNA (Nurul IM et.al., 2011). Barua et.al., 2000, studied the immunomodulatory activity of the hot aqueous extract and its butanolic fraction of *A. lebbeck* fed orally at a dose of 6.25, 12.5 and 25 mg/kg orally once a week to mice pre-treated with sheep red blood cells. The extract treated mice developed high serum levels of antibody than the vehicle treated which was comparable with that of the standard drug muramyl dipeptide. Delayed hypersensitivity reactions were suppressed on treating with the extract and the microphage migration index also remained unaltered (Barua et.al., 2000). Shashidhara et.al., 2008,

demonstrated the mast cell stabilization activity of the leaf extract of *A. lebbeck*. Successive chloroform, methanol and water extracts of bark and leaves of *A. lebbeck* showed significant mast cell stabilizing activity against compound 48/80 and the result was comparable to that of disodium chromoglycate (shashidhara et.al., 2008). Tripathi et.al., 1979, investigated the decoction of *A. lebbeck* bark's activity on guinea pigs. Antigen induced challenge was done and the *A. lebbeck* treated animals showed significant activity while disodium cromoglycate treated group did not showed any action. Treatment with *A. lebbeck* inhibited Dale-Schultz reaction in sensitized albino rats and it significantly inhibited antibody synthesis in the animals as evidenced in antigen-antibody precipitation by the micro agar gel diffusion technique. Marked reduction in secretion of macrophage migration inhibition factor was also noted. *A. lebbeck* significantly inhibited the phyto-haemagglutinin induced blastogenic response of human lymphocytes by titrated thymidine incorporation in DNA. The anti-anaphylactic activity of *A. lebbeck* is due to cromoglycate like action on the mast cells (Tripathi et.al., 1979).

Cosmeceutical activity

Tasneem et.al., (2021) evaluated the cosmeceutical activity of an emulgel containing 3% *A. lebbeck* bark extract. The gel was evaluated for this physical parameterslike liquefaction, color, phase separation, centrifugation and pH changes. In vivo evaluation of the emulgel was carried out in 13 female volunteers for their effects on melanin, erythema, moisture content, sebum content and elasticity of skin on regular usage. The study was found to produce statistically significant favourable changes in these parameters (Thasneem et.al., 2021).

Anti-malarial activity

Kalia S et.al., (2015) evaluated the anti-malarial activity of ethanolic extract of *A. lebbeck*. The extract was evaluated for its in vitro anti-malarial activity against chloroquine (CQ) sensitive and (MRC2) and chloroquine resistant (RKL9) strains of Plasmodium falciparum. Cytotoxicity of the extract was also evaluated on HeLa cells. In vivo study was conducted on BALB/c mice to determine the median lethal dose of the extract. The study also evaluated the schizonticidal and preventive activity of the extract against Plasmodium berghei followed by the curative activity of the extracts. The ethanolic extract of *A. lebbeck* exhibited an IC50 value of 8.2 ug/ml against MRC2 and 5.1 ug/ml against RKL9 strians of Plasmodium falciparum. CC50 value of the extract on HeLa cells were well above 1000 ug/ml. Selectivity indices (SI) of > 121.9 and >196.07 against MRC2 and RKL9 strains of P. falciparum was observed. LD50 of the extract in BALB/c mice was found to be > 5 g/Kg. the extract exhibited chemo-suppression with significant schizonticidal activity at 1000 mg/Kg with ED50 value > 100 mg/Kg. significant curative and repository activities were also exhibited bat 750 mg/Kg concentration of the extract on day 7 (Kalia S et.al., 2015). Al-Musayeib et.al., 2012 studied the antiprotozoal activity of selected medicinal plants. Methanolic extract of several plants including *A. lebbeck* were tested for in vitro activity against erythrocytic schizonts of Plasmiodium falciparum, intracellular amastigotes of Leishmania infantum and Trypanosoma cruzi and trypomastigotes of T. brucei. *A. lebbeck* methanolic extract showed significant activity against amastigotes of T. cruzi (Al-Musayeib et.al., 2012).

Anti-fertility activity

Gupta et.al., (2005) investigated the anti-fertility activity of *A. lebbeck* bark derived sapnonins on male rats at a dose of 50 mg/Lg/b.w per day for 60days. The study showed significant decrease in weight of the testes, epididymides, seminal vesicle and ventral prostrate. Round spermatid production was reduced to 73.04% and preleptotene spermatocytes and spermatogonia were reduced 65.07 and 47.48 % respectively. On histopathology, the cross-sectional surface area and number of mature Leydig cells were decreased by 57.47 and 54.52 % respectively. Sperm motility, sperm density was significantly reduced. The outcome of the study shows that *A. lebbeck* saponins reduced fertility in male rats by 100 %. The study however, does not produced any statistically significant changes in RBC, WBC counts, haemoglobin, haematocrit and blood glucose, cholesterol, protein, triglyceride and phospholipid levels. Saponins from *A. lebbeck* also significantly reduced protein, glycogen, cholesterol contents of testes and fructose content in seminal vesicle and protein contents in epididymides. Histoarchitecture showed vacuolations at primary spermatocyte stage, reduced seminiferous tubular diameter and increased inter-tubular space (Gupta et.al., 2005; Gupta et.al., 2006).

Larvicidal activity

Govindarajan et.al., 2015 studied the toxicity of the leaf and seed extracts of *Albizia lebbeck* in hexane, benzene, chloroform, ethyl acetate and methanol against three important disease vector species; *Culex quinquefasciatus*, *Aedes aegypti* and *Anopheles stephensi*. The methanolic extract of the leaves and seeds showed 100% Ovicidal activity after 48 hours of exposure. All the other extracts also showed ovicidal activity at a moderate level. The adulticidal activity was exhibited to a moderate level only by the leaf and seed extracts of *Albizia lebbeck* after 24 hours of exposure. The highest adulticidal activity was shown by the methanol extract of the leaves against Anopheles stephensi with an LC50 and LC90 values of 65.12 and 117.70 ppm respectively. Compared to seeds leaves exhibited more adulticidal activity against the three species. Authors claimed that these results supported that Albzia lebbeck as an eco-friendly alternative for vector control against *Culex quinquefasciatus*, *Aedes aegypti* and *Anopheles stephensi* species. Salles et.al., 2014, investigated the ovicidal activity of *A. lebbeck* against *Haemonchus contortus*. Low molecular weight fractions of *A. lebbeck* showed significant ovicidal activity. They also exhibited hemolysin activity and serine protease inhibitory activity (Salles et.al., 2014).

Analgesic activity

Aqueous and ethanolic extracts of *Albizia lebbeck* leaves were studied by Meshram et.al., 2015, for their analgesic activity in Wistar rats using Eddy's hot plate and tail flick methods. Animals pretreated with naloxone, bicuculline or methysergide were administered orally with the aqueous and ethanolic extracts of the drug. There was significant elevation in the mean basal reaction time in hot plate apparatus method and a similar elevation in latency time in tail flick method was noted by the investigators. They have also found out that there was a significant reduction in the analgesic activity in rats pre-treated with bicuculline and methysergide. The investigators concluded that the aqueous and ethanolic extracts of *Albizia lebbeck* exhibited significant central analgesic activity and that the action was produced through the GABAergic and serotonergic pathways and the flavonoids and saponins present in the leaves of the plants may be responsible for this activity (Meshram GG et.al., 2015).

Wound healing activity

Joshi et.al., 2013, studied the ethanolic extract of *A. lebbeck* for its wound healing activity using incision and excision wound models in rats. The extract significantly increased wound breaking strength showing a ceiling effect at 500 mg/kg dose. The dose of 500 mg/kg showed the optimum wound contraction on day 18 and complete wound contraction on day 22. A significant increase in dry tissue weight, total protein, hydroxyproline, hexosamine, hexuronic acid, superoxide dismutase levels were noted. Glutathione levels were reduced along with levels of lipid peroxidation and nitric oxide levels. The extract also showed significant inhibition of E. coli growth. Histopathology revealed normal epithelialization and fibrosis evidenced by increased collagen density (Joshi A et.al., 2013). Une et.al., 2001, demonstrated the saponin rich n-butanolic fraction from the dried leaves of *A. lebbeck* in albino mice. The extracts at 0, 10, 25 and 50 mg/kg were evaluated for transfer latency and anxiolytic property was assessed by the duration of occupancy in closed arms. Significant improvement was noted against their respective control animals. 25 mg/kg dose exhibited the maximum anxiolytic activity. The baclofen induced hypothermia and passivity was inhibited at this dose (Une et.al., 2001).

Learning, memory and anxiolytic activity

Chintawar et.al., 2002, demonstrated the activity of the saponin rich n-butanolic fraction of dried leaves of *A. lebbeck* on learning and memory in albino mice using shock avoiding paradigm and the elevated plus maze. Considerable improvement in the retention ability of the normal and amnesic mice was noted against their respective controls. In the study the neurotransmitter levels were also assessed to corroborate the findings. In this study, the dopamine and gamma-aminobutyric acid (GABA) levels were decreased while, the serotonin (5-HT) levels were increased. The study established the involvement of monoamine neurotransmitters in the nootropic action and established the role of butanol extract of *A. lebbeck* has nootropic activity (Chintawar et.al., 2002).

Anticonvulsant activity

Kasture et.al., 2000, studied the anticonvulsive activity of the ethanolic extract of the flowers of *A. lebbeck*. The methanolic fraction of chloroform soluble part of the ethanolic extract of *A. lebbeck* leaves showed anticonvulsant activity in mice induced by electric shock, electrical kindling and pentylenetetrazole-induced convulsions. There was also a significant protection against lithium-pilocarpine induced and electrical kindling, but the extracts failed to protect the mice from strychnine induced convulsions. The fractions antagonized D-amphetamine and potentiated pentobarbitone-induced sleep and raised the levels of GABA and serotonin in the central nervous system (Kasture et.al., 2019).

Anti-diarrhoeal activity

Besra et.al., 2002, studied the antidiarrhoeal activity of the seed extract of *A. lebbeck* by castor-oil induced diarrhoea, upper gastrointestinal transit and fluid secretion. Aqueous methanolic extract of *A. lebbeck* seeds at 2.5 to 5 mg.kg i.p possessed significant anti-diarrhoeal activity. The extract seems to potentiate the anti-diarrhoeal

activity of loperamide and naloxone. The study confirmed the role of opioid system in the reversal of anti-diarrhoeal activity and the role of the seed extract of *A. lebbeck* in activating this system (Besra et.al., 2002).

Conclusion

With the vast array of pharmacological activities, *A. lebbeck* proves to be one of the most commonly used ethnobotanical plant source in traditional as well as folklore systems of medicine. The wide distribution of the plant was instrumental in the wide use of this plant. Extensive works as to be conducted in this plant to come out with pharmaceutical preparations that can alleviate human sufferings. The scattered knowledge on the use of *A. lebbeck* in the folklore and tribal populations are yet to be tapped and brought to the main stream medical systems.

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