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BIOACTIVE CHEMICAL CONSTITUENTS OF *BLEPHARIS* AND *LEPIDAGATHIS* (ACANTHACEAE) - A REVIEW

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Keywords:

Acanthaceae, Blepharis, Lepidagahtis, Flavonoids, *Triterpenic Saponins*

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ABSTRACT: The herbal drugs derived from plant sources are used in traditional pharmacopeia and also act as precursor in lab to synthesize medicines at large scale. *Acanthaceae* is a large family comprising of various medicinally valuable species. In traditional use, the leaves of this family are commonly recognized to alleviate the poisonous bites of reptiles and insects and whole plants for the treatment of external wounds and ulcers. The pharmacological effects evaluated from various species of this family are antibacterial, antifungal, antipyretic, hepatoprotective, anti-inflammatory, cytotoxic, antioxidant, anti-platelet aggression and insecticidal activities. The phytochemicals reported from this family are mainly flavonoids, alkaloids, lignans, benzonoids, fatty acids, terpenoids, tannins and a few triterpenoid saponins. In the present study two genera namely *Blepharis* and *Lepidagathis* of the family *Acanthaceae* were selected with the focus on their traditional use, chemical constituents, and pharmacological activities. Various pharmacological experiments have verified their practice in traditional use and species of both the genera emerged as good source of herbal medicines. However, uncharacterized crude extract was employed in most of the studies with few exceptions. These species need to be explored for isolation of more compounds with their pre-clinical and clinical studies to establish as potential drugs. The review will help the researchers.

INTRODUCTION: Plants are potential source of phytonutrients and phytochemicals used as therapeutic aids across the globe. The herbal plants have been used as raw base in all the Unani, Chinese, Ayurveda, Siddha pharmacopeias [1] and provided a valuable lead in establishing the life saving drug formulation to modern medicines. However, to the large available data of medicinal plants only 15% got phytochemical exploration [2]. In the developing world with increasing poverty and population, health care is the major concern and herbs have proven as inexpensive, reliable and accessible source of therapeutic significance [3].

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Many drugs available in market are associated with serious side effects, toxicity, resistant to pathogenic microorganisms and even have restriction of use in some countries [4]. Whereas the herbs have long history of their use in traditional medicines and latter as clinical candidate to treat serious diseases one might expect a little side effects [5]. Acanthaceae species have been practiced as herbal medicines for centuries for the treatment of various diseases. The species have been investigated for extraction and isolation of chemical compounds responsible for various traditional uses.

In the present study two genera, namely *Blepharis* and *Lepidagathis* of the family *Acanthaceae* were selected with the focus on their traditional use, chemical constituents and pharmacological activities. The species of both the genera emerged as good source of traditional medicines. The objective of the study was to evaluate whether traditional claims of species have been validated in

pre-clinical and clinical studies and whether any structure activity relationship studies have been carried out. The database was extracted from Google scholar, PubMed, Scopus-Elsevier, AGRICOLA and Shodhganga.

Family *Acanthaceae*: *Acanthaceae* comprises of 346 genera and 4300 species most of which have been herbs, shrubs and vines. The plants of this family are cosmopolitan and distributed in the old and new world. Mainly present in Africa, Central America, Malaysia, Indonesia, with few species extending to South Europe, Japan, Southern cost of New Holland and Southern to the Cape of Good Hopes [6]. In India, *Acanthaceae* genera are peculiar to the Southern parts, Indian Archipelago and Malayan Penisula but have spreaded from Sultej to Silhet and lower ranges of Himalayas [7].

Traditional uses of Family *Acanthaceae*: In traditional medicines the species *Andrographis paniculata* is used for the treatment of diarrhea, leprosy, malaria, flu, sinusitis, tuberculosis, rabies, respiratory infections, syphilis and HIV/ AIDS [8]. The whole plants of mangrove (*Avicennia*) are used in treatment of tumor, ulcer, snakebites, rheumatism, asthma and diabetes [9]. The parts of whole plant of *Staurogyne merguensis* are used in abstetrics, gynocoligical disorder and infertility [10]. The most common species of *Acanthus* namely *A. montanus, A. ilicifolius,* and *A. ebracteatus* are mainly used for diseases of respiratory, nervous and reproductive system, gastrointestinal and urinary tract, and skin illness [11]. *Athatoda vasica* a shrub is commonly used in traditional practice in Asia and Europe. The whole plant is prescribed for the treatment of respiratory tract infection, bronchodilator and antiallergic activities, antitussive activities. The leaves of this plant are the main gradient of commercially used Kada used in India, France, Sweden *etc* [12].

Rhinacanthus nasutus has been used by local people for treatment of tinea versicolor, ringworm, eczema, herpes, influenza, and to relief from prickly heat, scruff and dedruff [13]. Various parts of *Phlogacanthus thyrsiflorus* has been used as components in several folk medicines to treat fever, antidote to pox, skin diseases like sore, scabies, jaundice, liver and spleen diseases, indigestion, acidity, gastritis, pharyngitis, chronic leucorrhoea, cough and cold, chronic bronchitis, asthma and rheumatism [14]. In upper Assam leaves of *P. thyrsiflorus* are used against helminthiasis, allergy, gout, rheumatism and fever [15]. All parts of *Justicia athatoda* the official herb in Indian Pharmacopoeia is used in various ailments. The leaves are used for treatment of snakebites, expectorant, antispasmodic, malarial fever, nausea, and anthelmintic agent [16]. Many species of Acanthaceae have been placed in different pharmacopeia for the treatment of various diseases like – *Rungia linifolia*-ulcers, *Ruellia prostrata*-fever, asthma, hair fall, cold, *Barleria priontis*- toothache, urinary irritation, antiseptic, gingival wounds, *Diptera canthus* prostate- hypoglycaemic, anticancer, ear-diseases, *Rhinacanthus nasutus-leucoderma*, hepatoprotective, antipyretic, snakebite, *Thunbergia fragrans*-snake bite, rheumatism and cough [17].

Infusion of two or three species is also used for various ailments. Ash leaves of *Justicia betonica*, *Acathus pubescens* and *Justicia flava* has been used for cough, ulcers and flu. The leaves of the species *Acanthus eminens, Aystasias chimperi*, *Dyschoristethum bergiiflora*, *Thunbergiaalata*, *Dyschoris teradican*s and *Lepidagathis scariosa* are infused to treat cough, skin diseases, wounds, eye infections, anti-diarrhea, edema, pneumonia [18]. *Andrographis paniculata, Hygrophila spinosa*, *Barleria prionitis* and *Adhatoda vasica* are used traditionally as antiviral, antipyretic, antiasthmatic and in respiratory diseases [19].

Genus *Blepharis*: Blepharis genus has characteristic features adopted as diagnostic tools in taxonomical studies. The general floral patterns of *Blepharis* species are colorful petals, bracteoles, pistils of flowers, stamens and fruits are distinct [20]. *Blepharis* is recognized as Afro-Asian genus has wide ecological distribution extended to Southern parts of Middle East, Central Asia, Southern Africa, Southern China, and India including one species in Indonesia [21].

Traditional uses of *Blepharis* species: *Blepharis* is a large genus comprising of 126 species. For the purpose of traditional use, all parts of plant have been used while the use of leaves was predominant followed by seeds, whole plant, roots, young shoot and plant ash. The species are widely used to cure

different ailments. *Blepharis ciliaris* is distributed in Egypt, Oman, Pakistan, Jordan, Sudan and Iran. The leaves and whole plant are used for the treatment of Inflammation, wounds, sores, cough, cold, estringent, diuretic, and lungs diseases [22]. The root charcoal 'Kohl-el-agouz' is used to improve vision [23]. *B. edulis* – distributed from Soudi Arabia, Egypt, Iran, Pakistan, and India [24]. Popularly known as Shikhi in Ayurveda, whole plant is used for the treatment of asthma, cough, fever, inflammation of throat. Seeds possess diuretic, aphrodisiac, expectorant effects. Leaves "Utingana" have milk increasing effects in milching animals [21]. *B. linariifolia* is distributed in Mali, Somalia and Sudan [25].

The whole plant is used to treat malaria, measles, infections, fever, kidney disorder, and dental problems [26]. *B. maderaspatensis* is distributed mainly in China and India [27]. Locally called as "Murivu porunthi" in Tamil is used by tribal people of India for the treatment of wounds, ulcers, throat inflammation, liver and spleen disorder. Decoction of whole plant is used to relieve abdominal gas problems and paste of leaves is used for bone fracture and heart pain [28]. *B. scindica* mainly present in India and Pakistan [29]. Seeds are used as tonic and to increase milk production of cattle, earache, eye disease, roots for urinary discharge and dysmenorrheal [30].

Chemical Constituents Isolated from *Blepharis* species: Various extraction and isolation methods including GC-MS have been employed to obtain chemical compounds from Blepharis. The aerial parts of the plant were mainly employed for the purpose of extraction. The compounds identified from the genus *Blepharis* are 10 flavonoids from the species *B. ciliaris*, *B. scindica* and *B. linarifolia*. 9 phenolic acid derivatives from *B. ciliaris*, *B. linarifolia* and *B. edulis.* 5 alkaloids from B. *edulis* and *B. scindica,* 8 steroids, tritrpenoids and fatty acids from *B. ciliaris*, *B. scindica*. Major flavonoids were Apigenin, Naringenin, Genistein and their glycosides, Rutin, Blephariside A & B. Polyphenolic acid derivatives have been Vanillic acid, Verbaciside, Cis-Verbaciside, Isoverbaciside and leucoverbaciside. Steroids and Terpenoids- Stigmasterol, Sitosterol and their glycosides, oleanolic acid and fatty acids have been reported.

B. ciliaris [31, 21]- Apigenin, Apigenin 7-O-glucoside, Apigenin-7-O-(6″-E-p-coumaroyl)- β-D-glucopyranoside, Apigenin7-(3"-acetyl-6"-E-p-coumaroyl)-glucopyranoside, Naringenin-7-O-(3″-acetyl-6″-E-p-coumaroyl) -β-$_D$-glucopyranoside, Naringenin-7-O-(6″-E-p- coumaroyl)-β-D-Blephariside A, Blephariside B, Genistein-7-O-(6″-O-E-caffeoyl)-β-D glucopyrano side, Protocatechuic acid, Methyl vanillate, Methyl veratrate, Verbascoside, β-Sitosterol-3-O-β-D-glucopyranose, Stigmasterol, Stigmaste rol-3-O-β-D-glucopyranose, Stigmasterol tetracosanoate.

B. edulis [32, 33]- Verbascoside, Cis-verbascoside, Isoverbascoside, Leucosceptoside A, Blepharin, Blepharigenin, 2-Benzoxazolone. The phytochemicals analysed through UHPLC/Q-TOF-MS-MS were Apigenin-7-O-glucoside, Diosmetin 7-O-rutinoside, Baicalein-7-O-guluronide, Diosmetin, Acacetin 7-O-neohespridoside, Biochanin A-7-O-glucoside, Isorhamnetin-3-O-rutinoside, Kaempferol-3- O –glucouronoid, Eriodictyol-7-O-glucoside, Kaempferol-3,7-O-bis-α-L-rahmnoside, Quercetin-4'- O –glucoside, Eriodictyol-7-O-neohespridoside, Pelargonidin-3,5-O- di-glucoside, Cyanidine-3- O –glucoside, Malvidin-3-O-glucoside, Cyanidine-3-O-rutinoside and Chalcone- Okanin-4'-O-glucoside, Naringenin chalcone.

B. linariifolia [26]- Apigenin, Naringenin-7-O-(6″-E-p-coumaroyl)-β-D-glucopyranoside, Vanillic acid, Verbascoside.

B. scindica [34, 35]- Apigenin, Apigenin-7-O-(6″-E-p-coumaroyl)- β-D-glucopyranoside, Naringenin-7-O-(6″-E-p- coumaroyl)-β-$_D$-glucopyranoside, Blepharin, Allantoin, Betaine hydrochloride, Oleanolic acid, β-Sitosterol, 9-Hydroxydodecanoic acid.

B. maderaspatensis [36, 37]- Rutin, Allantoin, Blepharin. Through GC-MS the chemical constituents identified are 9- Eicosyne, Sqalene, Phytol, 3,4-Dihhdro-3,5,8-trimethyl-3-(4,8,12trimethyltridecyl)-(2H)-benzopy- ran-6-acetate, 3,7,11,15 Trimethyl-2- hexadecen-1-ol and Cholestan-3-ol, 2 methylene,(3á,5à). The leaf extract showed Caffeic acid, Rutin, Quercetin, and Ferulic acid.

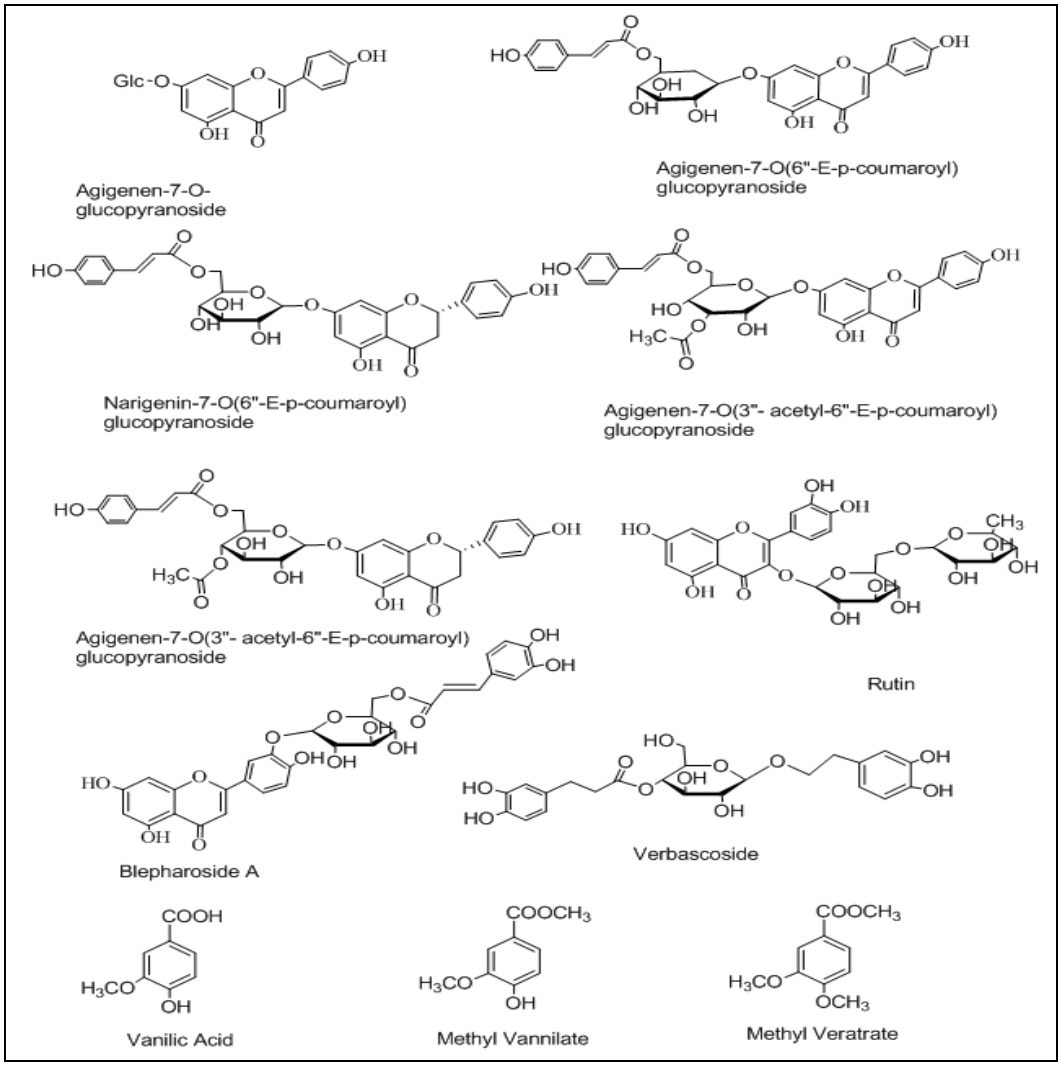

FIG. 1: STRUCTURES OF FLAVONOIDS FROM *BLEPHARIS* SPECIES

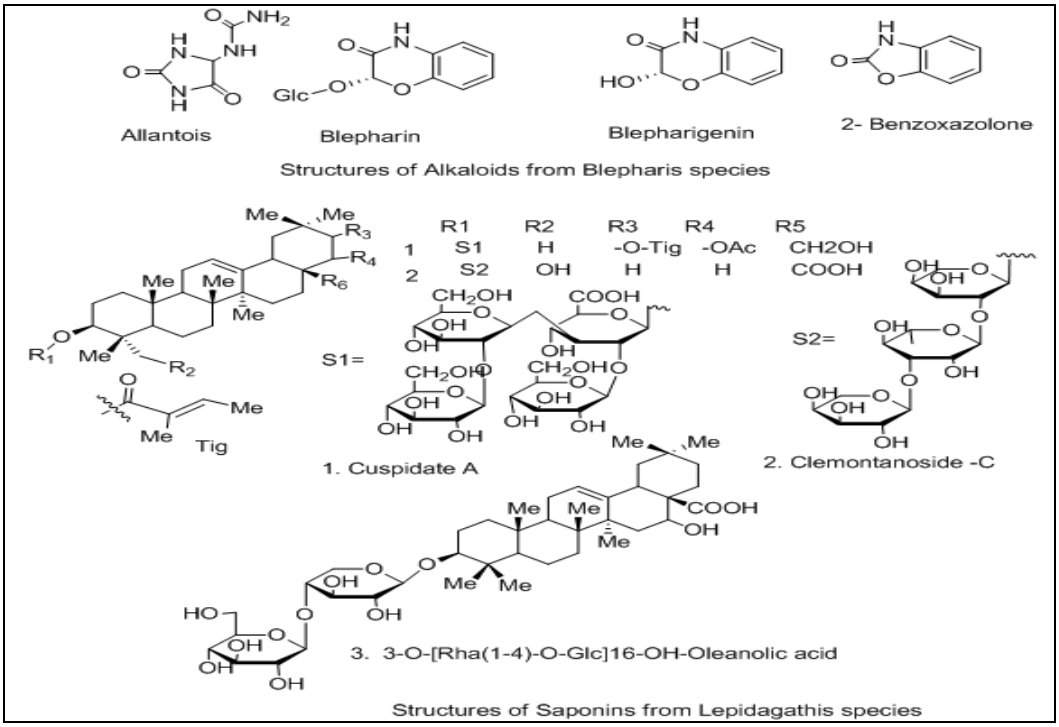

FIG. 2: STRUCTURES OF ALKALOIDS AND SAPONINS FROM *BLEPHARIS* AND *LEPIDAGATHIS* SPECIES.

Activities from *Blepharis* species: The traditional use and different phytochemicals isolated from Blepharis invited the attention to investigate these species for pharmacological activities responsible for their traditional claims. Several activities have been reported on various pharmacological methodologies. In vitro antioxidant activity was evaluated from *B. edulis, B. maderas patensis, B. molluginifolia* and *B. linariifolia* in DPPH assay Table 1. Different extracts exhibited strong antioxidant activity suggested to be attributed to the phenolic and flavonoids compounds as recorded in phytochemical screening tests of these species. Many species showed high antimicrobial potency with IC_{50} value comparable to the standard. The species *B. edulis, B. repens, B. maderaspatensis* have expressed mortality against bacterial and fungal strains such as *Staphylococcus aureus, Enterococcus faecalis, Staphylococcus epidermidis, Enterococcus faecium, Streptococcusagalactiae, Bacillus cereus, Bacillus subtilis, Streptococcus pyogenes, Staphylococcus saprophyticus, Klebsiella pneumoniae, Escherichia coli, Salmonella typhimurium, Shigella dysenteraie, Proteus vulgaris, Streptococcus sanjuis, Streptococcuss alivarius, Enterobacter aerogenes, Pseudomonas aeruginosa,* and fungi *Candida albicans, Aspergillusf lavus, Aspergillus niger, Aspergillus parasiticus*. The cytotoxic activity from butanol extract of *B. edulis* was highest against MCF-7, HCT-116 and HepG2 cell lines using neutral red uptake assay **Table 1**. The cytotoxic concentration (CC50) ranged between 4.19 ± 0.51 µg/mL and 25.24 ± 2.3 µg/mL which is an acceptable level of plant extracts. The UHPLC/Q-TOF-MS-MS analysis revealed the presence of baicalein-7-O-glucuronide and malvidin-3-O-glucoside as major compounds 33. The anti-inflammatory activity was evaluated from *B. ciliaris* and *B. maderaspatensis*. The ethanol and chloroform extracts of both the species were compatible anti-inflammatory agents compared to their standard counterparts in carragean induced rat paw edema and tail clip pharmacological method. Enzyme inhibitory activity was recorded from *B. linariifolia* for isolated compounds namely Verbascoside, Vanillic acid, Apigenin, and 6”-O-p-Coumaroylprunin. Out of these apigenin and 6”-O-p-coumaroylprunin were more potent for all inhibitory activities. The apigenin was specifically more effective against α-Glucosidase and 6”-O-p-coumaroylprunin against lipase. The compounds were flavonoids and such activities have been recorded from other studies as well [26].

TABLE 1: PHARMACOLOGICAL ACTIVITIES FROM *BLEPHARI*S SPECIES

Activity	Species	Extract	Tested Dose	Bioactive Dose	Positive control	Animals	Experimental Model
Antioxidant	*B. edulis*[32]	PE, DE, EtOH, MeOH, AQ	1 mg/ml	IC_{50} (µg/ml) 635, 81 ,98, 104 195	Ascorbic acid	*In-vitro*	DPPH assay
	B. maderas patensis[38]	EtOAc	1 mg/ml	IC_{50} (µg/ml) 39.33±0.58	Rutin	*In-vitro*	DPPH assay
	B. molluginifolia[38]	EtOH	1 mg/ml	IC_{50} (µg/ml) 49.67±0.58	Rutin	*In-vitro*	DPPH assay
	B. linariifolia[26]	Verbascoside	25 µl	IC_{50} (µM) 22.03±0.04	Trolox	*In-vitro*	DPPH assay
Cytotoxic activity	*B. edulis*[33]	BuOH	1 mg/ml	IC_{50} (µg/ml) MCF-7 – 9.12± 0.92, HCT-116 6.79±0.65,Hep G_2-4.19±0.51	Doxorubicin	Human Cancer cell lines	Sulforho damine B (SRB) assay
Antimicrobial activity	*B. edulis*[39]	1AQt 2MeOH 3MeOH-Water 4EtOH-water	02-100 mg/ml	MIC (mg/ml) 1 42.2 2 19.6 3 15.9 4 20.7	-	Bacterial & fungal strains	Micro broth dilution assay
Antimicrobial activity	*B. repens*[40]	AQ AC MeOH		Zone of Inhibition(mm) St Lf Rt 6-11 6-12 6-10 10-12 8-15 6-11	-	Bacterial & fungal strains	Disc diffusion Method

				12-14 9-18 9-11			
Antibacterial activity	*B. maderas patensis*[41]	EA Ac	50 µL	Zone of Inhibition (mm) 20.21 18.67	Ciprofloxin Fluconazole	Bacterial strains	Agar Well & Disc diffusion Method
Antifungal activity	*B. maderas patensis*[41]	EA Ac	50 µL	Zone of Inhibition (mm) 20.21 11.83	Ciprofloxin Fluconazole	Fungal strains	Agar Well & Disc diffusion Method
Anti-inflammatory	*B. maderas patensis*[42]	EtOH	75 mg/kg	75 mg/kg 84.5%, 90min	Xylene, Histamine	Whister rats	MW and tail clip method
Anti-inflammatory	*B. ciliaris* [21]	$CHCl_3$	400 mg/kg	0.1ml of 1% Sol. 59.98	Indometharin	Albino rat	Carragean induced rat paw edema.
Anti-hyperglycaemic	*B. ciliaris* [21]	EtOAc	400 mg/kg	0.1ml of 1% Sol. 109.97	Glidazide	Albino rat	-
Enzyme inhibitory	*B. linariifolia* [26]	1.Apigenin 2. 6"-O-P-Coumaroylprunim	10 µL	α- Glucosidase 1. 34.73±1.78 2. 46.30±2.92 Control Acarbose	Lipase 12.46±2.04 2.25 ±0.17 Cetilistat	Tryosinase 23.14±1.83 136.12 ±0.51 Arbutin	-

Genus Lepidagathis: The genus *Lepidagathis* (*Acanthaceae*) is represented by more than 110 species distributed throughout the tropical and subtropical areas of Africa and Asia. *Lepidagathis* has nearly 30 species in India [43]. *Lepidagathis* has sinapomorphic feature of cytoliths on vegetative organs aclade within *Acanthoidea*e subfamily and have *Barlerieae* lineage of quincuncial aestivation of the corolla [44].

Traditional uses of *Lepidagathis* species: Though the *Lepidagathis* genus is less explored for scientific experimentations regarding biological activities still plants of this genus have been customarily used in traditional medicines to treat fever, headache, polyuria, dysentery, skin infections, jungle fever and calculi in the urinary tract [45]. *L. keralensis* is endemic to Kerala found on lateritic rocks near seashores. In tradition the plant is used by the paniya tribes for treating bronchial asthma in children [46].

The spines of *L. keralensis* with rice are used to treat malabsorption, malnutrition, and digestive disorders. Decoction of the whole plant is recommended for kidney stone and albumin in urine. The plant is also used as a blood purifier and increases blood. Whole plant decoction with cumin seeds is given for chest pain [47]. *L. cristata* is spreaded in eastern and central parts of India including Karnatic, Deccan and Konkan. Dried plant material with honey is administered to treat asthma and powder mixed with coconut oil is used for skin infection. The plant of *L.cristata* mixed with honey is administered as regular dose for twenty days to treat asthma. The powder of plant mixed with coconut oil is used by local people for skin infections in Kurnool and Andhra Pradesh. The ash of entire plant is boiled with coconut oil and the infusion is applied externally on chronic wounds of pet animals twice a day up to 6-8 days [48], dried shoot ash used for skin infections and paste of whole plant is used for itching infections.

The mixture of roots pastes of *L. cristata*, karanj oil and seed powder of *Abrus precatorius* is applied to treat leucoderma. The roots of L. cristata are also used as antidysenteric and to reduce heat in the stomach. The fumigation of herbs is inhaled to treat epilepsy. In Chhattisgarh, leaf extract is used for malarial fever and to clean the cattle in rainy season. The extract in boiled water is also used for skin itchy affection, burns and wounds. The leaf juice with copper sulphate is given during snake bite for gaining consciousness [49].

L. hyline also known as "Curved Lepidagathis" is a wild herb from the *Acanthaceae* family that has various therapeutic potentials including antimicrobial and antidiabetic activities. This plant has been reported in various subtropical locations across the world, particularly in the Indian subcontinent. In Bangladesh, it is mostly found in hill tract regions which have a long history of use in the treatment of coughs and cardiovascular disorders [50]. *L. cuspidata* commonly known as spiny shrub (adulsa) is found in tropical Himalayas between the altitudes of 300-700m including

Westerrn Ghats. In traditional herbal medicines of whole plant is used for the treatment of painful inflammation of fingers, boils and blisters, tonic in fever and itchy infections [51]. The roots are used to procure abortion during the first three months of pregnancy.

Chemical Constituents Isolated from Lepidagathis species: *L. cristata* [52]- 6-hydroxyLuteolin, 6-hydroxyLuteolin-7-apioside a tryptophan derived alkaloid Cristatin A, Oleic acid, 3-(octadecyloxy) propyl ester, Heptadecane, 9-hexyl, Ethyliso-allocholate, Heptadecane, 9-hexylOctade cane, 3-ethyl-5-(2-ethylbutyl). *L. hyaline* Nees [53]- 3-β-O-[(-α-L-rhamnopyranosyl (1→4) - O-β-D-glucopyranosyl] 16 – α - hydro-xy-olean-12-en(13)-28-oic acid. *L. scariosa* [54]-1-Methyl-1-caprolactone,1-Tetra decanol, 1-Nonanol, Isopropylmyristate, Isopropyl, Tetradecanoate,5-(Hydroxy methyl)-2-(1-methyl-2-imidazolyl)-1H-benzimidaole, Hexadecanoic acid, Ethyl ester, 2-Hexadecen-1-ol, 3, 7, 11, 15-tetramethyl[R-[R*,R*-(E)]], Octa decanoic acid, Methy2-(4,8-Diacetoxy-3-bromo-6-methoxy-9,10-dioxo-9, 10-dihydro anthrax quinon-2-ylmethyl)-4-(2-methyl[1,3]dioxolane-2-yl)-3 - oxobutanoate, Lucenin, Quassin, Dimethoxyglycerol Docosyl Ether.

L. fasciculate [55]- δ-Cadinene, γ-Curcumene, Sandaracopimarinal, Germacrene D-4-ol, Cembrene, β-Calacorene, Arcurcumene, trans-4,10-epoxy-Amorphane, Abietatriene, and α Cubebene. The oil sesquiterpene hydrocarbons, oxygenated sesquiterpenes, diterpene hydrocarbons, oxygenated diterpenes. *L. keralensis* [56]- Cyclopentane, Decanoic acid methyl ester, Benzene, n-Hexadecanoic acid (palmitic acid) 10-Undecynoic acid, methyl ester, Benzene, (ethenyloxy)-, 2-Methoxy-4-Vinylphenol and n-Hexadecanoic acid, Cyclopentaneundecanoic acid, 1, 6-Octadiene, 3, 7-dimethyl, 10-Undecyn-1-ol, 3-Hydroxy-4-methoxybenzoic acid, 3-Hydroxy-4-methoxy benzoic acid, 2-Methoxy-4-vinylphenol, vanillic acid and 2-Piperidinone, N-[4-bromo-n-butyl], n-Hexadecanoic acid, Vanillic acid, (E)-4-(3-Hydroxyprop-1-en-1-yl)-2-methoxy phenol and 1,6-Octadiene,3,7-dimethyl. *L. cuspidata* [57]- 16,28-dihydroxy 22-acetyl-21-tigloylolean-12-ene-3-O-β-D-glucopyranosyl-(1→2)-β-D-glucopyrano syl-(1→3)-[β-D-glucopyranosyl - (1→2)] – β – D – glucopyranosi duronic acid (Cuspidate A), 3-O-α-L-arabinopyranosyl-(1→3)-α-L-rhamnopyrano syl-(1→2)-α-L-arabinopyranoside hederagenin (Clemontanoside C).

TABLE 2: PHARMACOLOGICAL ACTIVITIES OF LEPIDAGATHIS SPECIES

Activity	Species	Extract	Dose tested	Bioactive dose	Positive control	Animals	Experimental Model
Anti-oxidant	*L. prostrate* [58]	Butanol Ethyl Acetate	IC_{50} (µg/ ml) BuOH- 25.12± 0.52 EtOAc- 64.26± 2.02	ABTS DPPH 20.81± 1.13 68.41± 6.15	Ascorbic acid	*In-vitro*	ABTS, DPPH, Assay
	L. hyaline [59]	Methanol	500 µg/mL	IC_{50} 125.16 µg/ ml	Ascorbic acid	-	DPPH Assay
	L. keralensis [56]	Methanol	200-600 µg/mL	IC_{50} 122.46 µg/ml	Ascorbic acid	-	DPPH Assay
	L.cuspidata [60]	Ethanol	100 mg/Kg	IC_{50} 91.01 µg/ml	Trolox	-	DPPH Assay
	L. pungens [61]	Ethanol	10-100 µg/ ml	IC_{50} 49.23 µg/ml IC_{50} 31.19 µg/ml	Ascorbic acid Rutin	*In-vitro*	DPPPH Assay NO Assay
Anti-Inflammatory	*L. hyaline* [62]	Methanol	1000 µg/mL	IC_{50}55.01± 3.22	Diclofane	Human RBC	Hypotonic-Induced HBC Hemolysis
	L.criststa [48]	Methanol	200- 400 mg/kg	($p<0.05$), ($p<0.01$) ($p<0.001$)	-	Wister Rats	Carrageenan induced paw edema Method
Cytotoxic activity	*L. spinosa* [63]	Methanol	5.62-35.53GAE/g	I_{AC} 28.95 MCF_7 41.44 $HEPG_2$ 39.73		Cancer cell lines	MTT assay

				HeLa 64.63			
Cytotoxic activity	*L. hyaline* [62]	Methanol	1000 µg/mL	LC_{50} 135.35 µg/mL	-	-	Brine Shrimp Assay
Antitumor	*L. pungens* [64]	Ethanol	200, 400 mg/Kg	IC_{50} 25.77± 0.36 IC_{50} 30.85± 0.35	Flurouracil	Swiss albino mice	EAC Induced Tumor Method
Anti-cancer	*L. pungens* [65]	Ethanol	1000 µg/mL	IC_{50} 185 µg/ml	-	-	Short –Term Trypan Blue Exclusion Method
Anti-diabetic	*L.criststa* [48]	Ethanol	100-400 mg/Kg	400 mg/ Kg	Glibenclamide	Wister Rats	Alloxan induced diabetic Method
Anti-urolithiotic	*L. prostrate* [58]	Pet Ether	-	IC_{50} 336.23±30.76	Cystone	-	-
Antiemetic activity	*L. cristata* [66]	Ethanol	50, 100, 200 mg/Kg	53± 3.75, 35± 1.59, 18± 1.22	Metaclopramide	Male Chicks	-
Anti depressant	*L. hyaline* [67]	Methanol	400 mg/Kg	IC_{50} 83.33± 6.39 ($P < 0.01$)	Fluoxetine	-	-
Anti-arithritic	*L. hyaline* [62]	Methanol	31.25 to 1000 µg/mL	21.71± 3.52 to 71.97± 2.71	Diclofane	-	-
Insecticidal	*L. alopecuroides* [68]	Aq. Pet Ether Methanol	0.025-0.055 µg/mL	0.055 µg/mL 88.88± 16.32% 86.60± 9.34%	-	Termites	
Antifungal	*L. cristata* [69]	Oleic acid	100-800mg/ml	MIC 4.50-10.50 mg/ml	Bavistine	Fungal Stains	Petri Dish Suspension
Antifungal	*L.cuspidata* [57]	Cuspidate A Clemontanoside C	10 mg/ml	10 mg/ml (7-11 mm)	Mancozeb	Fungal strains	Disc Diffusion Method
Thrombolytic	*L. hyline* [62]	Methanol	10 mg/ml	33.98%	Streptokinase	Albino mice	Clot Lysis lethality Bioassay
Anxiolytic	*L. hyaline* [62]	Methanol	400 mg/kg	78.77± 4.42% ($P < 0.05$)	Diazapam	Albino mice	Elevated Plus Maze Test
Analgesic	*L. cristata* [62]	Methanol	200-400 mg/kg	50% ($p<0.01$) & 55% ($p<0.001$)	-	Wister Rats	Hot plate and Tail Immersion Method
Wound Healing Activity	*L. cristata* [65]	Ethanolic	10 mg/kg	$p<0.01$	Nitrofurazone	Wister Rats	
Antipyretic	*L. cristata* [62]	Pet. Ether	100-200 mg/kg	$p<0.01$	Paracetamol	Wister Rats	

Pharmacological activities of *Lepidagathis* Species: Antimicrobial, Immune suppressive, larvicidal, anti-inflammatory, analgesic and haemostatic agents [58, 62]. Phytochemicals present in plants such as flavonoids, phenolic, alkaloids and tannins possess antioxidant property. Various species *of Lepidagathis* are rich in such chemicals and are recorded as potential antioxidant [58-61]. The free radical scavenging action of the extract/ fraction is evaluated by ABTS and DPPH free radical decolorizing Assay. The DPPH is for lipophilic and ABTS for hydrophilic and lipophilic radicals. The ABTS free radical is generated by reaction of ABTS with Potassium persulfate to give blue-green $ABTS^{+}$ chromophore. The ability of extract/ fraction to decolorize the chromophore has been measured as percentage scavenging potency. The scavenging effect of various extracts of *L. prostrata* was BuOH > Et OAc > MeOH > Pet. Ether > AQ (Table-). The IC_{50} (µg/ ml) of BuOH-extract was 25.12± 0.52, 20.81± 1.13 and EtOAc-extract was 68.41± 6.15, 64.26± 2.02 for ABTS and DPPH respectively (Table-). The methanolic extracts of *L. hyline* and *L. keralensis* showed antioxidant potential with IC_{50} value of 125.16, 122.46 µg/ ml using ascorbic acid as positive control in DPPH Assay. The ethanol extracts of *L. cuspidata* and *L. pungens* were also potential antioxidant in comparison to standard trolox, ascorbic acid and rutin in DPPH and NO Assay.

The brine shrimp lethality and MTT assay are commonly used to evaluate cytotoxic potential of extract/ fraction. At low concentration of LC_{50} 135.35 µg/ ml at with a quick response indicates that the plant extract of L. hyline is quite potent to give cytotoxic activity. The I_{AC} 28.95 for methanol extract of L. spinosa in different cancer cell lines indicates as potential cytotoxic effect. The antitumor and anticancer effects from ethanol extract of *L. pungens* with IC_{50} 25.77± 0.36 and IC_{50} 185 µg/ml respectively have been recorded.

The activity was tested for two doses 200 and 400 mg/kg. The activity was dose dependant for tumor and other haemological measures like RBC, WBC counts. The extract also exhibited potent anticancer activity recorded by short-term cytotoxicity trypan blue exclusion methods with IC_{50} value 185 µg/ml. From *L. cuspidata* the isolated saponins cuspidate A, Clemontanoside C were potential antifungal compounds against the fungal strains-*Aspergillus flavus*, *Rhizopus stolonifer*, *Penicillum nodatum* and *Aspergillus fumigates* comparable to the synthetic counterpart Mancozeb [57]. Oleic acid isolated from *L. cristata* was also strong antifungal agent. The methanol extract of L. hyaline expressed various pharmacological effect such as anti-inflammatory, antidepressant, antiarithritis, thrombolytic and anxiolytic. The ethanol/methanol extracts of *L. cristata* possessed anti-diabetic, antiemetic, wound healing and anti-inflammatory activities [62].

CONCLUSION: All parts of plants of *Acanthaceae* have been reported for traditional use, but leaves part are used the most. Fresh leaves of the species *Aystasias chimperi*, *Dyschoris teradicans*, *Acanthus eminens*, *Dyschoristethum bergiiflora*, *Lepidagathis scariosa* and *Thunbergia alata* have been infused to treat cough, skin diseases, wounds, eye infections, anti-diarrhea, edema, pneumonia. The pharmacological activities investigated from the species of *Acanthceae* are antibacterial, antifungal, cytotoxic, anti-inflammatory, antipyretic, antiviral, antioxidant, hepatoprotective, insecticidal and anti- platelet aggregation activities. Various chemical compounds to the class of flavonoids, phenolic acids, alkaloids, saponins, oils, acids, esters, alcohols, aldehydes and their glycosides are characterized through different isolation and analysis methods. The two genera *Blephris* and *Lepidagathis* were selected to study the traditional use, chemical constituents and pharmacological effects. The survey revealed that compounds isolated from the genus *Blepharis* were Flavonoids - Apigenin, Naringenin, Genistein and their glycosides, Rutin, Blephariside A & B. Polyphenolic acid Deriveatives, Vanillic acid, Verbaciside, Cis-Verbaciside, Isoverbaciside and leucoverbaciside. Alkalois- Blepharin, Allantoin, Betain hydrochloride, Blepharigenin, Steroids and Terpenoids- Stigmasterol, Sitosterol and their glycosides. Whereas, from the genus *Lepidagathis* triterpenic saponins- Cuspidate A and Clemontanoside C, 3-β-O-[(-α-L-rhamnopyranosyl (1→4) – O – β – D - glucopyranosyl] 16 – α - hydroxy-olean-12-en(13)-28-oic acid, Alkaloids- a tryptophan derived oleic acid, 3-(octadecyloxy) propyl ester Cristatin A, oils, alcohols, esters, fatty acids have been isolated. The pharmacological activities reported from these genera were mainly antioxidant, cytotoxic, antimicrobial, anti-inflammatory, antidiabetic and insecticidal. The data revealed that the uncharacterized crude extract was used to evaluate these pharmacological effects with the exception of *L. cuspidata* where isolated pure compounds Cuspidate A and Clemontanoside C to evaluate antifungal potential [57]. The traditional use of the species of *Acanthaceae* pointed the strong evidence of pharmacological importance, but no systematic work has been carried out to validate their biological effects. The flavonoids and alkaloids are most potent compounds of these species responsible for these effects. The research remains possible for their bioactive principle. In lieu, of these observations it is suggested that research is needed to investigate more species for scientific validation. To isolate bioactive crude extract and to establish mode of action of *Acanthceae* species.

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