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REVIEW ARTICLE

Blumea lacera (Burm.f.) DC: A review on ethnobotany, phytochemistry, ancient medicinal and pharmacological uses

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Abstract

Blumea lacera (Burm. f.) DC., a member of the Asteraceae family, is an annual herbaceous plant with a rich array of phytochemicals that hold immense therapeutic promise. Commonly known as Karanda jangli muli (in Hindi) and kukkuradru (in Sanskrit), this herb is cultivated for its applications in food, essential oil extraction and various ethnomedical purposes. It thrives in diverse regions, including the Indian plains, the northwest Himalayas, China, Tropical Africa, the Malay Islands, Australia, Ceylon and Malaya. *B. lacera* boasts a multitude of valuable phytochemical components, including α-amyrin, ß-sitosterol, acetates, hentriacontane, stigmasterol, lupeol and lupeol acetate. These phytochemicals exhibit a wide range of pharmacological properties such as antipyretic, anti-inflammatory, anthelmintic, diuretic, antidiarrheal, antimicrobial, cytotoxic, astringent, hepatoprote-ctive, sedative, anxiolytic, anti-viral, analgesic, hypothermic, anti-bacterial, anti-atherothrombotic, anti-leukemic and tranquilizing effects. Additionally, the phytochemicals derived from *B. lacera* align with various Ayurvedic attributes, encompassing dravya (substance), rasa (taste), guna (qualities), veerya (potency), vipaka (post-digestion outcome), karma (pharmacological actions) and prabha (therapeutics). Despite the plant's extensive bioactive chemical profile and therapeutic significance, scientific studies on *B. lacera* remain surprisingly scarce. In light of its numerous applications, this review aims to elucidate the diversity of phytochemicals, ethnomedicinal uses and therapeutic potentials of *B. lacera*.

Keywords

Blumea lacera; folk medicine; pharmacology; ethnomedicinal; phytochemical; Ayurvedic

Introduction

Blumea lacera (Burm. f.) DC. is an annual member of the Asteraceae family (Table 1). The plant typically grows to a height ranging from 40 to 90 cm and features obovate leaves with a camphor-like fragrance (1). Its bright yellow flowers are clustered in cymes at the plant's axils and have sharp points. Fruiting usually occurs between December and March (2). *Blumea lacera* thrives in regions across tropical Africa, Malaya, Australia, China and India

(3). With a long history of use in traditional medicine, this plant is employed for various purposes, including as a diuretic, remedy for blood dysentery, treatment for piles and gout, and to facilitate the expulsion of the placenta after childbirth (4). Ethnomedicinal and ethnobotanical knowledge about *B. lacera* has been passed down through generations, making it an integral part of traditional medicine in various regions. In addition to its culinary applications, local communities have utilized this herb for various health-related purposes. Moreover, the plant's pharmacological potential has garnered scientific interest, with studies revealing the presence of several terpenoids, fatty acids and other bioactive molecules (5). These sesquiterpenoids exhibit potential medicinal properties, including anticancer, antimicrobial and antioxidant effects (6-8).

The essential oils extracted from *B. lacera* leaves have been found to contain various bioactive molecules, including flavonoids and terpenes (9). Reports suggest that the plant's methanolic leaf extract (PMLE) possesses diverse properties such as antifungal, bactericidal, cytotoxic, febrifuge, antiviral, antileukemic and antidiarrheal activities (10).

Table 1. Systematic classification of *Blumea lacera* (Burm.f.) DC.

Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Asterales
Family	Asteraceae
Genus	*Blumea*
Species	*Blumea lacera* (Burm.f.) DC.
Infra Species	*Blumea lacera lacera*

Given the rich ethnomedicinal knowledge, the vast array of therapeutic possibilities and the phytochemical diversity of *B. lacera*, this article provides an expanded and detailed overview of the existing research outcomes . By delving into its traditional uses, phytochemical composition, and pharmacological potential, this article reveals various facets of this valuable herb and emphasizes the importance of further scientific investigations to support and expand its applications in modern medicine.

Materials and Methods

The review is based on an extensive literature search conducted using specialized databases such as Web of Science, Scopus, PubMed, Google Scholar and a general search using the Google search engine. The search involved keywords like *B. lacera*, ethnomedicinal uses, traditional medicinal uses, bioactive compounds, phytochemical compositions, pharmacological potential, therapeutic applications and various combinations of these terms. These carefully selected keywords aimed to encompass the diverse aspects of the plant's ethnomedicinal importance and potential therapeutic applications. The search criteria included papers published up to July 30, 2023. Prioritizing accessibility and comprehension, the focus was on research reported in English, and only peer-reviewed journal articles were considered to ensure relevance, accuracy and reliability.

Furthermore, preference was given to studies providing detailed information on the ethnomedicinal uses, therapeutic properties and phytochemical constituents of *B. lacera*. The review encompassed investigations into the bioactive compounds of the plant and their pharmacological activities. Exclusion criteria were applied to filter out publications with insufficient data, lacking in-depth analysis or primarily discussing other plants, ensuring alignment with the focus of this review. Articles not available in full text or written in languages other than English were also omitted from the final selection. The literature search utilized a combination of relevant keywords to comprehensively explore *B. lacera*.

Morphology

This plant is characterized by its strong odor, gregarious viscid annual herb; stem densely glandular, pubescent, leaves sessile, sharply serrate, lower leaves lyrate or lobed, 5-12 cm long, 2-6 cm wide, heads yellow in short axial cyme, involucral bracts silky hairy, receptacle glabrous, pappus white, stigma hairy. Inner florets are hermaphrodite and only a handful are fertile; involucres are ovoid or campanulate and bracts are numerous, seriate, narrow, sharp, soft or herbaceous, with the outer being smaller and the receptacle flat and naked. Calyx limb bristly. Female floret petals connate in filiform corollas, which are shorter than their styles and have a minutely 2-3 toothed apex; stamens syngenecious; anther sagittate at the base, with small, slender tails. Cypsela small, subterete or angled. Small fruits typically appear in December-March (11, 12). Flowering and fruiting time is mostly December to May. The plant is very abundant and listed under the least concern (LC) IUCN list.

Common Names

Blumea lacera, owing to its widespread distribution and traditional usage, is known by several local names in different regions. These local names reflect the plant's cultural significance and highlight its diverse applications in various traditional medicine systems. The abundance of local names for *B. lacera* underscores its status as a versatile and cherished medicinal herb in different cultural contexts. Throughout history, local communities have relied on this valuable plant to address various health concerns, making it an integral part of their indigenous healing practices. Different vernacular names of *B. lacera* known throughout the country are listed in Table 2.

Ethnomedicinal uses

Blumea lacera, a herb rich in ethnomedicinal significance, holds a venerable position in folk medicine across diverse cultures and regions. With its roots deeply entrenched in Ayurveda, this plant has garnered renown for its versatile medicinal properties, encompassing a wide range of

Table 2. Common names of *Blumea lacera*

Vernacular Names	Language	Reference
Kukurbanda	Hindi	
Kukrondha	Hindi	
Kukranda	Hindi	
Thaevuppula	Tamil	(13)
Korupoganu	Telegu	
Pokasunga	Odia	
Kukurandru	Sanskrit	
Shealmutra	Bengali	
Barakukshima	Bengali	
Kukursunga	Bengali	(14)
Shealmoti	Bengali	
Healmutra	Bengali-Noakhali	
Lettuce-leaf Blumea	English	(15)
Kukurhuta	Assamese	(15)
Kukkura-Chedi	Malayalam	(16)
Rakila	Malayalam	

attributes such as astringency, acridity, thermogenic, errhine, anti-inflammatory, styptic, ophthalmic, digestive, anthelmintic, liver tonic, expectorant, febrifuge, anti-pyretic, diuretic, deobstruent and analeptic (10). Among its applications is the use of fresh leaf juice, often administered to youngsters, as a remedy for threadworm problems. Embracing a broader spectrum of healing, *B. lacera* leaves find usage in various regions to treat cuts, wounds, and boils, accentuating the plant's significance in the management of injuries (17-19). Beyond these applications, its therapeutic versatility extends to the treatment of edema, piles, weakness, cholera and microbiological diseases in certain regions (20). It is also utilized for the topical management of anal fissures and piles (21). The multifaceted medicinal uses of *B. lacera* have established it as an indispensable component of traditional healing practices across various communities and ethnic groups (Fig. 1). Table 3 illustrates the various ethnomedicinal uses of *B. lacera*.

Usage in traditional system of medicine

Blumea lacera is a fragrant and therapeutic plant widely used in Ayurvedic medical systems (37). *B. lacera* is employed to treat various disorders in several medical systems, including Ayurveda, Homoeopathy, Unani, Siddha and Allopathy (1). This plant has been given numer-

Fig. 1. Ethnomedicinal uses of *Blumea lacera.*

Table 3. Ethnomedicinal use of *Blumea lacera* as reported from tribes and localites of different regions

Region of usage	Tribes/people	Plant part used	Mode of application	Ethnomedicinal uses	Reference
Uttar Pradesh, India	People of the region	Leaf	Juice	Used to remove threadworms	(22)
Gadchiroli, Maharashtra	Madia-Gond	Leaf	Extract (topical application) and oral consumption	Used to cure anal fissures and piles	(21)
Morang, Nepal	Bantar	Leaf	Extract	Treatment of Cuts	(17)
Baghraidih (Dumka) of Santhal Pargana and Chutupalu Ghati, Jharkhand, India	Santhal, Paharia (Sauria Paharia, Mal Paharia and Kumar Bhag), Oraon, Munda, Kol, Kharwar, Ho, Asur, Baiga	Leaf	Extract	Treatment of cuts and boils	(18)
Gorakhpur, Uttar Pradesh, India	Local people	Leaf	Extract	Used to treat bruises on toes, cuts and boils	(19)
Dindori, Nashik, Maharashtra, India	Bhil, Kankanas, Malis	Leaf	Juice/paste	Used to check bleeding from wounds	(23)
Nashik, Maharashtra	Bhils, Katkaris, Kunabi-Kokana, Thakur, Warli and Mahadeo Koli	Leaf		Used for treatment of mouse disease	(24)
Sewa Valley, Jammu, and Kashmir, India	Local people	Leaf	Juice	Used as antipyretic, febrifuge, diuretic and anthelmintic.	(25)
Barak Valley, Assam	Dimasa, Jaintea, Kuki, Rongmai Naga, Hmar	Leaf		Used to treat stomach disorder	(26)
Sabroom and Santirbazar subdivision of South Tripura district	Mog and Reang	Leaf	Warmed leaf	Applied in Rheumatic pains	(27)
Rajshahi, Bangladesh	Local tribal people	Leaf	Juice	Used as anthelmintic, febrifuge, astringent and diuretic; mixed with black pepper. It is used for the treatment of piles.	(28)
Dhemaji, Assam	Mishing	Leaf	Infusion	Used to treat dental problems	(29)
Hoshangabad, Madhya Pradesh, India	Gond, Kurku	Leaf	Juice	Used for the treatment of fever, earache, and elimination of worms in children	(30)
Hathazari, Chittagong, Bangladesh	Local people	Leaf	Paste	Applied to stop hemorrhage	(31)
Noakhali, Bangladesh	Local people	Leaf, Root		Treatment of weakness, edema, piles, cholera, diuretic, microbial infections	(20)
Nashik, Maharashtra	Bhils, Katkaris, Kunabi-Kokana, Thakur, Warli and Mahadeo Koli	Roots		Used for treatment of piles and cholera	(24)
Sewa Valley, Jammu, and Kashmir, India	Local people	Roots		Used in the treatment of cholera	(25)
Rajshahi, Bangladesh	Local tribal people	Root	Mixed with black pepper	Used to treat cholera	(28)
Jhapa, Nepal	Meche	Root	Paste	Applied around the swollen region to prevent infection.	(32)
Bara, Nepal	Tharu	Root	Ointments	Used in the treatment of wounds	(33)
Bagerhat, Bangladesh	Recommended by local healers (Kaviraj)	Root		Used as diuretic, edema, gastrointestinal and respiratory disorders and also as insect repellant	(34)
Chandpur, Bangladesh	Local people	Whole plant	Decoction made in boiled water	Used to treat diseases of skin and purify blood	(35)
Khashi and Garo Region, Meghalaya	Khashi, Garo and Jayantia tribes	Whole plant		Expectorant for the treatment of cold	(36)

ous names in traditional literature, including Ayurvedic Kukundara, Kukkuradru, Tamrachuda, Mriducchada and

Kukrondaa (38). According to Bhaavaprakaasha, the herb can treat fever, respiratory infections and vitiated blood. The root is claimed to cure oral illness if maintained in the mouth (39). It has traditionally been used internally and externally as a styptic and anti-inflammatory medication (38). In the Ayurvedic system of medicine, the plant is used to treat vata and kapha, fever, thirst, edema, worms, leprosy and menorrhagia (40). Additionally, it has been utilized traditionally in Indian medicine to treat a variety of illnesses as a diuretic, deobstruant, bitter, astringent, acrid, thermogenic, errhine, anti-inflammatory, styptic, ophthalmic, digestive, anthelmintic, liver tonic and stimulant (11).

Phytochemical compositions

The primary application of phytochemical research is to ensure the quality control of traditional medicines derived from bioactive substances obtained from medicinal plants. Investigating the chemical components and studying the pharmacological activities of *B. lacera* for its therapeutic purposes, which could be highly beneficial in medicine as a new emerging drug, is therefore of considerable significance (41, 42). India, Bangladesh, Sri Lanka and Nepal are home to the perennial, branching Rabi weed known as *B. lacera* ; this 1-2 m long herb belongs to the Asteraceae family. Different parts of the plant comprise valuable therapeutic constituents, with leaves of the plant being well-known for their unique healing potential worldwide (1). Numerous beneficial substances, including phenol, flavones, monoterpene, triterpenes, stigmasterol, cineol, campesterol, lupeol, artemisinin etc. are present in the essential oils extracted from the leaves (9, 43, 44).

A study revealed that (Z)-Lachnophyllum ester, discovered in *B. lacera*, possesses diverse biological properties, including cytotoxic effects against human cancer cells as well as antifungal and antibacterial capabilities (43). The seeds of the plant exhibited antibacterial activity (45) and Linalool was reported to have larvicidal activity with a lethal concentration 50 (LC_{50}) value of 46.86 mg/L (46). The crucial phytochemical constituents identified from the herb include camphor, (Z)-lachnophyllum ester, (Z)-lach-nophyllic acid, nerolidol, gernacrene, monoterpene glycosides, flavonoids, β-farnesene, dihydroxy-trimethoxy flavone, diacetylglucopyranoside, β-caryophyllene, campesterol, α-humulene, amyrin, amyrin acetate, lupeol acetate, hentriacontane, hentriacontanol, β-sitosterol, cineol and others as listed in Table 4. Fig. 2 represents the molecular structures of selected compounds present in *B. lacera*.

Pharmacological activity

Blumea lacera (Burm.f.) DC. is renowned for its significant therapeutic properties in multiple well-established systems of medicine. The World Health Organization (WHO) acknowledges medicinal plants as excellent sources for deriving various new herbal drugs. To comprehensively understand the potential of herbal medicine, it is crucial to focus on the scholarly investigation of medicinal

Table 4. Phytochemical compositions reported from different parts of *Blumea lacera*

Plant Parts	Group of compound	Trivial name of the compound	Mode of Isolation/Detection	Reference
		Linalool	HPLC/GC-MS	(46)
		Germacrene D	HPLC/GC-MS	(43, 46)
		Borneol	HPLC/GC-MS	
		γ-terpinene	HPLC/GC-MS	(46)
		Allo-ocimene	HPLC/GC-MS	
		Sabinene	Silica gel chromatography	(43)
		Viridiflorene	HPLC/GC-MS	(46)
		1,8-Cineole	Silica gel chromatography	(43)
Stem and Leaves	Terpenes	(E)-β-Ocimene	Silica gel chromatography	
		Caryophyllene oxide	HPLC/GC-MS	(47)
		(E)-Caryophyllene	HPLC/GC-MS Silica gel chromatography	(43, 47)
		α-trans-bergamotene	Silica gel chromatography	
		(E)-β-Farnesene	Silica gel chromatography	(43)
		Bicyclogermacrene	Silica gel chromatography	
		a-humulene	GC and GC-MS	(47)
		Phytol	H-NMR spectroscopic	(10)
		Neophytadiene	GC-MS	(48)
Stem and Leaves		Protocatechuic Acid	Column chromatography	(44)
	Phenolics	p-vinylguaiacol	H-NMR spectroscopic	(10)
Stem, Roots and Leaves		Cuminol	GC-MS analysis	(49)
		Eugenol	Silica gel chromatography	(43)

Stem and leaves	Sterols	β-sitosterol	Column chromatography	(44)
		Campesterol	Column chromatography	
	Hydrocarbon	Hentriacontane	GC-MS	(2)
Leaves	Ethers	Thymoquinol dimethyl ether	GLC and GC-MS	(50)
Stem	Esters	EMERY-2216	GC-MS	(51)
		Lachnophyllum ester	Silica gel chromatography	(43)
leaves	Fatty acid	Linolenic acid	1H NMR spectroscopic	(10)
		Oleic acid	1H NMR spectroscopic	
		Lachnophyllic acid	Silica gel chromatography	(43)
Steam and leaves	Steroidal glycoalkaloid	(SGA) 1	C18 SPE and HPLC	(52)

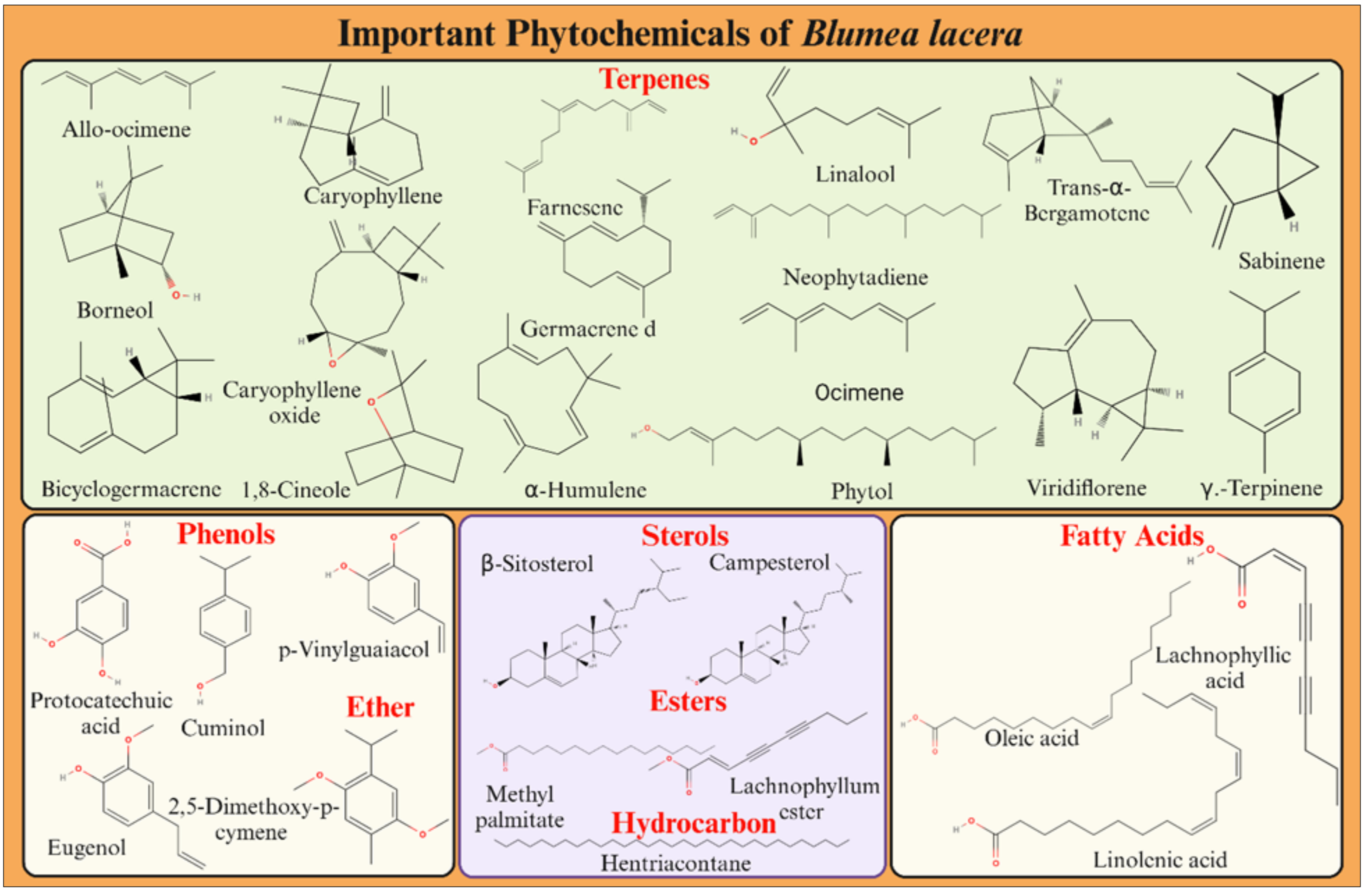

Fig. 2. Selected phytoconstituents present in *Blumea lacera*.

plants deeply rooted in history and culture. Consequently, identifying the possible uses of herbal medicine relies on the study of these medicinal plants (53). *B. lacera* possesses numerous medicinal properties, making it highly versatile in traditional applications. It is recognized for its antispasmodic, antipyretic, antioxidant, anti-diarrheal, hepatic stimulant, expectorant, diuretic, astrin-gent and stimulant qualities. Furthermore, it has been utilized in treating bronchitis, fevers and skin irritations (54). The essential oil extracted from the leaves has been found to exhibit analgesic, hypothermic and sedative characteristics (49). Moreover, several experimental studies have illuminated various medicinal chara-cteristics of *B. lacera.*

Anti-diarrheal Activity

Diarrhea refers to the frequent expulsion of loose or watery stools lacking defined form or consistency (55). *B. lacera* is known to contain various phytoconsti-tuents, including flavonoids, tannins, cardiac glycosides and alka-loids. These constituents have been suggested to poten-tially contribute to the antidiarrheal effect of *B. lacera* in animal models (11, 56). The efficacy of the methanolic leaf extract of *B. lacera* was investigated using castor oil-induced diarrhea in Swiss albino mice. In a dose-dependent experiment, the 400 mg/kg concentration of the extract reduced mice's defecation by 40.275%, a rate close to that of the typical medication Loperamide, which has a 62.068% inhibition rate (57). Further investiga-tion assessed the anti-diarrheal attributes of the entire botanical specimen of *B. lacera*, including its root struc-ture. Following the extraction process using methanol, the resulting extract was subjected to fractionation utilizing pet-ether, chloroform and ethyl acetate. The ethanolic fraction exhibited significant inhibition of diarrhea by 57.96% and 63.36% at doses of 200 mg/kg and 400 mg/kg respectively, comparable to the reference medicine Loperamide, which showed 74.01% inhibition at 2 mg/kg (10). The aerial portion of *B. lacera* was extracted using ethanol as the solvent and afterward evaluated for its potential antidiarrheal effects on Swiss albino mice induced with castor oil. The extract, when given at doses of 250 mg/kg and 500 mg/kg, along with the standard treatment at a dose of 3 mg/kg, demonstrated significant inhibition of defecation. The decreases were 34.1%, 48.2% and 83.5% respectively (2).

Table 5. Antimicrobial activity of various parts of *Blumea lacera*

S.No.	Plant part taken	Name of extract/ pure compound isolated	Bacteria inhibited	Important findings of the experiment	Reference
1	Dried leaves	Ethyl acetate extract	*E. coli, S. aureus, K. pneumonia, P. aeruginosa, P. acnes, S. typhi*	Highest inhibition zone of 12 mm against *P. aeruginosa*	(58)
2	Leaves	Methanolic leaf extract	*S. typhi*	Inhibition zone of 20 mm against *S. typhi*	(59)
3	Entire plant	Petroleum ether extract	*S. aureus, E. coli*	Antibacterial efficacy observed against *S.aureus* and *E. coli*	(60)
4	Leaves	Petroleum ether, dichloromethane, ethanol extracts	*Bacillus pumilus*	Inhibition zone diameters between 13 and 15 mm against *B. pumilus* species	
5	Leaves	Petroleum ether, methanol, ethanol extracts	*Candida albicans, P. aeruginosa, S. aureus*	Inhibition zone sizes ranging from 13 to 15 mm against *C. albicans*, *P. aeruginosa* and *S. aureus*	(61)
6	Roots	Dichloromethane, ethyl acetate, ethanol, methanol extracts	*Bacillus subtilis, S. aureus, B. pumilus, C. albicans, E. coli*	Inhibitory zones between 11 and 15 mm against *B. subtilis*, *S. aureus*, *B. pumilus*, *C. albicans* and *E. coli* species	
7	Aerial Parts	Ethyl acetate extract	*Bacillus cereus*	Efficacious against *B. cereus* regardless of habitat choice	(4)

Antimicrobial Activity

In the ongoing battle against bacterial resistance, the search for new antimicrobial medications persists. Studies have evaluated the antibacterial qualities of various *Blumea* extracts, including ethyl acetate, methanol, petroleum ether, dichloromethane, 95% ethanol and water. The antibacterial activity of the ethyl acetate extract obtained from dried *B. lacera* leaves was observed against 6 bacterial strains: *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Propionibacterium acnes* and *Salmonella typhi*. Particularly, *P. aeruginosa* showed the highest inhibition zone of 12 mm (58).

The methanol extract of leaves effectively inhibited the gram-negative bacteria *S. typhi*, demonstrating a 20 mm inhibition zone (59). Additionally, petroleum ether extracts from the whole plant of *B. lacera* exhibited antibacterial efficacy against *S. aureus* and *E. coli* (60). Extracts from various parts of *B. lacera*, including pet-ether, dichloromethane, ethyl acetate, 95% ethanol, methanol and aqueous extracts, demonstrated antibacterial activity against different bacterial species (61). Moreover, it was observed that the ethyl acetate fraction derived from *B. lacera* had dose-dependent efficacy against the gram-positive bacterium *Bacillus cereus* (4). The antimicrobial activity of different solvent extracts from various plant parts of *B. lacera* is represented in Table 5.

Antifungal activity

Death and disease among humans, agricultural breakdowns, and changes in forest ecosystem dynamics are consequences of fungal diseases. Despite numerous antifungal agents in healthcare, the growing resistance of fungi to these drugs demands the discovery and development of new safe and non-toxic compounds.In one study, the efficacy of various solvent extracts derived from *B. lacera* leaf and root against 5 distinct fungal strains (*Aspergillus flavus*, *Aspergillus niger*, *Alternaria sp*., *Penicillium sp*. and *Fusarium sp*.) was evaluated. The findings indicate that the aqueous extract exhibited noteworthy inhibitory effects, while the methanol and acetone extracts did not demonstrate any inhibitory effects against these fungal strains (62).

Anti-inflammatory Activity

Inflammation can result from tissue injury, cell death, or cancer (63). In the conducted experiment, it was shown that the administration of a 500 mg/kg dose of an ethanolic extract derived from the aerial portions of *B. lacera* resulted in a reduction of xylene-induced mouse ear edema by 41%. In comparison, the positive control, ibuprofen, exhibited a 65.6% reduction in ear edema at a dose of 100 mg kg-1.A study evaluated the *in vitro* anti-inflammatory efficacy of the ethyl acetate fraction and biofabricated herbal silver nanoparticles derived from *B. lacera*. This was achieved by measuring their ability to inhibit protein (albumin) denaturation and antiproteinase activity. Protein denaturation refers to the disruption of the structural and functional integrity of a protein due to various physical, chemical or biological factors. Therefore, the denaturation of tissue proteins can be utilized as a biomarker of inflammation. The herbal silver nanoparticles exhibited the greatest potential in inhibiting albumin denaturation, as indicated by their half maximal inhibitory concentration (IC_{50}) value of 63.29 µg/mL. The IC_{50} value for the ethyl acetate fraction was subsequently determined to be 93.65 g/mL, indicating a slightly reduced potential. The standard medicine aspirin exhibited a prevention rate of 50.56 µg/mL. Inflammatory responses encompass a diverse array of agents, including proteinases. Therefore, the inhibition of these proteinases has the potential to contribute to the protection of tissue injury. Aspirin, ethyl acetate fraction, and herbal silver nanoparticles were each found to have IC_{50} values of 46.61 g/mL, 96.41 g/mL and 69.69 g/mL for their antiproteinase activity respectively (64). The plant contains substances such as β-sitosterol, cineol, lupeol, hentriacontane, artemisinin, protocatechuic acid and β-caryophyllene, which may be responsible for its anti-inflammatory effects (2).

Anti-diabetic Activity

Diabetes mellitus results from a lack of insulin secretion, tissue insulin sensitivity loss or abnormalities in pancreatic cells (65). A study was conducted utilizing an oral glucose tolerance test to examine the hypoglycemic effects of the methanolic extract derived from dried leaves of *B. lacera*. Glibenclamide was utilized as the reference medication and 4 test groups received 50-400 mg/kg leaf extract orally. The study found that the administration of leaf extract to hypoglycemic mice, which were given a glucose load, led to a substantial reduction in blood glucose levels. This reduction was statistically significant ($P<0.0001$) and exhibited a dose-dependent relationship (66). In another study, the anti-diabetic effect of *B. lacera* methanolic extract was tested in alloxan-induced (150 mg/kg) diabetic rats following oral administration at dosages of 125, 250, 500, 750 and 1000 mg/kg. The results showed that 14 days of oral treatment of methanolic extract (500 mg/kg) to alloxan-induced diabetic rats returned blood glucose levels to normal (67). In an independent investigation, methanol extracts and aqueous extracts of *B. lacera* DC. were administered to streptozotocin-induced hyperglycemic rats at dosages of 200 and 400 mg/kg body weight. Blood glucose levels were found to be significantly reduced ($p< 0.05$) after administration of *B. lacera* methanol extract of aerial part at 200 mg/kg and 400 mg/kg body weight. The initial values of blood glucose were 289.983 ±9.83 and 289.983 ±2.71 respectively. These values have since dropped to 201.887 ±8.87 and 105.005 ±2.05 respectively. The corresponding decreases in blood glucose percentages were 30.40±1.79% and 63.78±0.59%. Additionally, it resulted in a reduction of glycated hemoglobin (HbA1c) to levels comparable to those observed in individuals without diabetes and the restoration of lipid and biochemical levels. Furthermore, it exhibited the ability to rejuvenate pancreatic beta cells, enhancing insulin production (68). A recent investigation was conducted to examine the possible anti-diabetic effects of micropropagated plants of *B. lacera* in a mammalian (mouse) model of type 2 diabetes. The aim was to further the understanding of the molecular mechanisms behind its therapeutic action. The aqueous extract effectively mitigated hyperglycemia, halted the progression of weight loss and ameliorated dyslipidemia in murine subjects. Furthermore, it was seen that the intervention resulted in a decrease in liver injury as well as a reduction in several toxicity indicators that were examined such as serum glutamate-pyruvate transaminase, serum glutamic oxaloacetic transaminase and serum anti-inflammatory marker C-reactive protein. The study on intramolecular interactions revealed that the inherent polyphenolic constituents of the plant exhibited a greater inhibitory effect on α-amylase, α-glucosidase and lipase compared to the standard (69).

Antioxidant Activity

Chronic illnesses can be induced by free radicals or reactive oxygen species (ROS). Antioxidants possess the ability to stabilize or render inactive free radicals prior to their infliction of harm onto biological cells. The present work involved the evaluation of the free radical scavenging activity of various fractions obtained from *B. lacera*. These fractions, namely petroleum ether soluble, chloroform soluble, ethyl acetate soluble and aqueous soluble, were subjected to analysis using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging assay. Findings of the study revealed that different extracts of *B. lacera* exhibited dose-dependent free radical scavenging activity compared to the standard. The petroleum ether extract demonstrated notable scavenging activity (92.96%) at a concentration of 200 g/mL in comparison to the typical butylated hydroxytoluene (BHT) (96.48%) (10).

In a similar study, *B. lacera* methanolic extract substantially neutralized DPPH free radicals at concentrations ranging from 1000 to 5000 g/mL (58). In a separate study, the free radical scavenging activity of methanolic and ethanolic extracts of *B. lacera* leaves was investigated using a DPPH scavenging assay. The results indicated that The IC_{50} for methanolic extracts was 3-4 mg/mL, whereas the IC_{50} for ethanolic extracts was 25-30 mg/mL for fresh samples and 15-20 mg/mL for dry ethanolic extract. In addition, the ferric reducing assay (FRAP) was also performed and the results indicated that methanolic extracts demonstrated more reducing ability than ethanolic extracts. The extracts also conferred protection against lipid peroxidation, with the methanolic extract of fresh conferring maximum protection of 60.04%, followed by the methanolic extract of dried specimens at 51.25% (70).

Additional research has documented similar findings, wherein the methanolic extract derived from *B. lacera* leaves demonstrated an IC_{50} value of 29.03 µg/mL. This value was lower than that of the control substance, ascorbic acid, which exhibited an IC50 value of 33.64 µg/mL (71). Another study was conducted to assess the antioxidant activity of leaf and root extracts of *B. lacera* using a DPPH scavenging test. The IC_{50} values for the ethanol extract of the leaf and root were determined to be 37.04 and 11.42 µg/mL respectively. Similarly, the IC_{50} values for the aqueous extract of the leaf and root were found to be 33.49 and 30.07 µg/mL respectively (61).

In a recent investigation, researchers noticed that Long Evan rats treated with CCl_4 displayed an increased concentration of malondialdehyde in both liver homogenate and serum samples. In contrast, the administration of *B. lacera* leaf extract and its liposomal formulation to groups of rats resulted in a significant reduction in the elevated concentration of malondialdehyde (MDA). In addition, when comparing the treatment group administered with the *B. lacera* leaf extract solution to the group of rats treated with the liposomal formulation of *B. lacera* leaf extract, it was seen that the latter exhibited a more significant reduction in MDA levels. Furthermore, the administration of leaf extracts of *B. lacera* and its liposomal nanoformulations resulted in a decrease in the levels of advanced protein oxidation products that were enhanced in animals treated with CCl_4. Comparable trends were also noted in the concentrations of nitric oxide in plasma and liver homogenates. The administration of *B. lacera* extracts resulted in the restoration of antioxidant enzyme levels (namely SOD, GSH and CAT) that had been raised in rats treated with CCl_4 (72).

Anticancer Activity

The anticancer properties of *B. lacera* have been explored in multiple studies. A study conducted in Taiwan demonstrated the *in vitro* anti-leukemic effect of the plant. The findings demonstrated a wide-ranging antileukemic effect and the suppression of K562 cell proliferation (73).

In one study, Bioactivity-guided fractionation of the methanol extract of *B. lacera* led to the isolation of compound (25R)-3β-{O-β-D-glucopyranosyl-(1→4)-O-α-L-rhamnopyranosyl-(1→4)-[O-α-L-rhamnopyranosyl-(1→2)]-α-L-rhamnopyranosyl}-22αN-spirosol-5-ene, a steroidal glycoalkaloid. The compound proved to be the most cytotoxic against various human cancer cell lines, with an IC_{50} against MCF-7 cells of 2.62 µM. When compared to other cytotoxic steroidal glycoalkaloid analogs, it had the highest apoptotic potential (32% AV+/PI-) on MCF-7 cells and a small but considerable cell cycle-arresting effect (52).

In a similar study, a noble diterpenoid glycoside, 6E,10E,14Z-(3S)-17-hydroxy geranyl linalool-17-O-β-d-glucopyranosyl-(1→2)-[α-l-rhamnopyranosyl-(1 → 6)]-β-d-glucopyranoside along with the known diterpenoid glycoside and 2 known flavonoid glycosides were isolated from the methanolic extract of *B. lacera* leaves. The novel diterpenoid glycoside demonstrated high cytotoxic action against MCF-7 breast cancer cells, with the lowest IC_{50} value (8.3 M). The drug demonstrated substantial apoptotic action against MCF-7 cells (45.5% AV+/PI-) after 24 hours but displayed no cell cycle arrest (52). In a separate investigation, it was discovered that the extracts derived from *B. lacera* exhibited significant toxicity towards various human cancer cell lines, including gastric adenocarcinoma cells (AGS, ATCC: CRL-1739), colorectal adenocarcinoma cells (HT-29, ATCC: HTB-38) and breast ductal carcinoma cells (MDA-MB-435S, ATCC: HTB-129) (74).

In another study, the anticancer potential of methanolic extract of both dried and fresh materials of *B. lacera* was tested against B16F10 murine melanoma cell lines. The findings of the investigation revealed that the maximum inhibition in colony formation (47.82±4.27%) was brought about by the dried specimen at a dose of 100 mg/mL within 24 h of treatment. In addition, the wound scratch assay revealed that the fresh specimen conferred 100% inhibition within 24 h of treatment at a dose of 100 µg/mL (70).

In a recent study, it was found that the methanolic extracts of the leaves of *B. lacera* were toxic to Ehrlich's Ascites Carcinoma. Experiments on tumor-bearing mice revealed that treatment with the extract at a dose of 25 and 50mg/kg increased the survival of Ehrlich's Ascites Carcinoma-bearing mice (35.67 % and 75.53% respectively). In addition, there was a decrease in weight gain in the mouse treated with the methanol extract on the 15th day after inoculation with Ehrlich's Ascites Carcinoma cells (71).

In a recent study, researchers discovered that silver nanoparticles were successfully generated utilizing leaf extracts of *B. lacera*. These nanoparticles had significant anticancer properties against human lung carcinoma cell A549, with a low inhibitory concentration of approximately 20 µg/mL (37).

Anthelmintic Activity

The aqueous and alcoholic extracts of *B. lacera*, as well as a combination of both, exhibited dose-dependent anthelmintic efficacy against *Pheretima posthuma* and *Ascaris lumbricoides*. In comparison to piperazine citrate, used as a reference, both extracts demonstrated good anthelmintic action, particularly at a concentration of 100%. However, it is noteworthy that the concentration of the extract required to achieve equivalent potency with the standard was exceptionally high. Furthermore, the combination of extracts showed greater efficacy than either extract when administered independently (75).

Hepatoprotective activity

One study investigated the hepatoprotective efficacy of an ethanolic extract derived from *B. lacera* in rats with ethanol-induced hepatotoxicity. The findings of the study revealed a significant reduction ($P < 0.001$) in the levels of serum glutamic oxaloacetic transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), alkaline phosphatase (ALP), total bilirubin and direct bilirubin in the group treated with *B. lacera* extract at doses of 200 mg/kg and 400 mg/kg, compared to the group treated with ethanol. The mice treated with *B. lacera* extract exhibited minimal liver damage, as evidenced by the preservation of hepatic cell structures and architectural integrity (76).

In a recent study, the hepatoprotective activities of leaf extracts from *B. lacera* and their liposomal formulation were examined in Long Evan rats that had been inflicted with liver injury using CCl_4. The administration of a liposomal formulation of *B. lacera* leaf extract resulted in a greater improvement in liver wet weight in Long Evan rats compared to rat groups treated with a *B. lacera* solution. The wet weight of the spleen in the disease group exhibited a significant increase compared to that of the control group. However, following the administration of *B. lacera* leaf extract suspension and its liposomal formulation, there was a notable reduction in the spleen's wet weight.

Biochemical liver function investigations demonstrated that the introduction of carbon tetrachloride (CCl_4) resulted in a substantial increase in the levels of plasma biomarkers such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) compared to the control group of rats ($p < 0.05$). In comparison to the illness group exposed to carbon tetrachloride (CCl_4), the rat groups that received *B. lacera* leaf extract suspension, as well as its liposomal preparation, exhibited a significant reduction in the high amounts of biomarkers in the plasma serum.

The control groups exhibited typical morphological characteristics of liver tissue. Histopathological changes, including inflammatory cells infiltrating the liver tissue, hepatocyte ballooning towards the portal tract and extensive cellular necrosis, were observed in the liver samples of the group exposed to CCl_4 and stained with hematoxylin and eosin. The hepatotoxicity caused by CCl_4 was ameliorated with the administration of *B. lacera* leaf extract (25 mg/kg) and its liposomal formulation (72).

Anxiolytic and Antidepressant Activity

A study was conducted to explore the anxiolytic impact of *B. lacera*. The experiment involved administering a methanolic extract of *B. lacera* to Swiss albino mice at a dosage range of 200-400 mg/kg orally. The researchers employed the elevated plus maze (EPM), light-dark box (LDB) and holeboard (HBT) tests to evaluate the anxiolytic effects. In contrast, the forced swimming (FST) and tail suspension tests (TST) were utilized to evaluate the antidepressant effects. The reference standards used in the study were diazepam, administered intraperitoneally at a dose of 1 mg/kg and fluoxetine HCl, administered orally at a dose of 20 mg/kg. The results of the EPM and LDB tests demonstrated an increase in the duration of time spent in the open arms and light boxes respectively. Additionally, the HBT yielded a higher frequency of head dipping behavior, indicative of anxiolytic effects. The results of the TST and FST revealed a significant reduction in immobility duration, suggesting the efficacy of the antidepressant effects (49).

Antiulcer activity

The antiulcer activity of the methanolic extract of *B. lacera* was investigated in the ethanol-induced Long-Evan rat model system. The results indicated that the administration of *B. lacera* extract at concentrations of 250 mg and 500 mg/kg resulted in a significant decrease in stomach length and weight compared to the control group. Furthermore, the administration of the extract exhibited a substantial increase in stomach mucus levels, which were found to be dose-dependent. In addition, the volume of gastric juice was significantly reduced upon treatment with the plant extract. The pH of the gastric juice exhibited a simultaneous increase following the administration of the plant extract. Finally, the plant extract conferred protection to ulcers in a dose-dependent fashion with a minimum ulcer index of 11.42 ± 2.02 at a dose of 500 mg/kg, which corresponded to 60.24 ± 4.96% protection (49).

In a separate investigation, the efficacy of the ethanolic extract of *B. lacera* was evaluated concerning Indomethacin, Ethanol (1 mL/200 gm) and stomach ulcers generated by 6 h of Pylorus ligation in Wistar rats. The findings of the study revealed that the administration of *B. lacera* extracts at doses of 200 mg and 400 mg/kg of body weight exhibited a reduction in ulcer indices that was directly proportional to the dosage. This effect was observed across all 3 types of ulcers. Similar trends were observed in % protection in all 3 ulcer cases. Moreover, the extracts at both doses reduced the volume of gastric secretion, increased the gastric pH and decreased the free acidity in a dose-dependent manner (76).

In another study, it was found that the treatment of methanolic extract of *B. lacera* in mice subjected to ethanol-induced gastric ulcer resulted in the attenuation of ulcers. In addition, the integrity of gastric mucosa was also protected through the prevention of mucosal ulceration. Moreover, the total carbohydrate content of the gastric juice, which was markedly reduced upon treatment with ethanol, was normalized by the intervention of the plant extract. Moreover, the protein and pepsin content in the gastric juice were reduced upon treatment with the extract, which was initially increased upon treatment with ethanol (49).

Antipyretic effect

The human body's multifaceted reaction to infectious or aseptic stimuli is fever, characterized by a spike in prostaglandin E2 (PGE2) in the brain, leading to an increase in core body temperature. While a high temperature can aid in a patient's nonspecific immunological response, it can also cause discomfort. Antipyretics exert their effects through the inhibition of cyclooxygenase, thereby reducing the production of prostaglandin E2 (PGE2) and subsequently suppressing fever (77). Natural COX-2 inhibitors exhibit less selectivity but present a lower incidence of adverse effects. Conversely, synthetic antipyretic medications demonstrate high selectivity in inhibiting COX-2 but are associated with deleterious effects on several organs, including the glomeruli, cortex of the brain, hepatic cells and cardiac muscles (78).

In an experiment, the administration of a 500 mg/kg dose of crude methanol extract derived from *B. lacera* leaves to pyrexia-induced Swiss albino mice significantly reduced elevated body temperature to 96.06 ± 0.11 °F after a 3 h treatment period (54). In an independent experiment involving male Wistar rats, the administration of the methanolic leaf extract of *B. lacera* at doses of 200 and 400 mg/kg showed noteworthy antipyretic efficacy ($P<0.05$ for the 200 mg/kg dose and $P<0.01$ for the 400 mg/kg dose) at 1, 3 and 6 h post-administration in a pyrexia model induced by Brewer's yeast (79). The administration of a whole plant extract of *B. lacera* using 3 different solvents (methanol, ethanol and chloroform) resulted in a notable reduction in baseline body temperature in Swiss albino mice with induced pyrexia. This effect was observed at doses of 200 mg/kg and 400 mg/kg 2 h after administration (80).

Toxicity reports

There is a lack of reliable scientific information regarding the safety and toxicological profile of many commercially available formulations of natural products. It is important to have solid scientific data on the toxicity and safe administration levels of natural remedies (81). The Brine Shrimp Cytotoxicity Test (BSCT) is a valuable method for evaluating the diverse bioactivities of a broad spectrum of chemical substances and has been effectively employed for screening and fractionating physiologically active plant extracts.

In a study, three fractions of aerial components of *B. lacera*, namely n-hexane, methanol and ethyl acetate, exhibited a concentration-dependent increase in the % of death observed in Brine Shrimp nauplii. The LC_{50} values for mortality in the 3 fractions were reported and these values were higher than those achieved with vincristine sulfate, indicating a cytotoxic impact (82).

The methanol extract derived from the leaves of *B. lacera* also exhibited cytotoxic activity. The crude extract showed a moderate level of cytotoxic activity with an LD_{50} value and the comparison with the gallic acid standard demonstrated the relative cytotoxicity (71).

In another investigation on the cytotoxicity and lethality bioassay test of *B. lacera* extracts on brine shrimp, a comparison was made with the standard vincristine sulfate and the pet-ether soluble fraction exhibited notable cytotoxicity (10).

A separate study evaluated the acute cytotoxic property of *B. lacera* extract on Swiss albino mice. The study reported the administration of different concentrations of *B. lacera* extract and monitored mouse mortality. The LD_{50} value could not be calculated due to low mortality and no unusual behavior or toxicity was detected in the mice (2).

A study conducted in Bangladesh highlighted the high toxicity of the *B. lacera* plant, leading to significant injury in cattle. However, toxicological testing indicated a modest degree of toxicity, prompting the recommendation to avoid using the unrefined extract for pharmacological applications and instead use isolated bioactive compounds (83).

Conclusion and Future Perspective

Blumea lacera (Burm.f.) DCholds significant ethnobotanical importance and is widely utilized in traditional healing systems. The plant contains bioactive secondary metabolites, including alkaloids, steroids, terpenoids, cardiac glycosides, tannins and phenolic chemicals. These metabolites exhibit astringent, acrid, thermogenic, anti-diarrheal, antimicrobial, anxiolytic, anti-inflammatory, styptic, ophthalmic, digestive and anti-thrombotic properties. While some plant metabolites may be poisonous, there is a substantial opportunity for selecting, isolating, testing and validating their medicinal benefits. This exploration may lead to the discovery of novel therapeutic chemicals; however, plant metabolites should be used cautiously, only after extensive isolation and thorough pharmacological and toxicological studies. In conclusion, *B. lacera* has the potential to be a valuable source of phytochemical constituents for the pharmaceutical industry. Nevertheless, rigorous screening tests are essential to develop more useful formulations and establish the plant's comprehensive phytochemical profile.

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Authors contributions

Conceptualization, planning, structuring and original drafting- DS and SB. Literature search and sectional contribution- DS; SB; AM; P; SD; SC; MC. Artwork, chemical structure - P; AKM; DS. Reference management- DS; RB. Internal quality management, review and editing- DS; SB; AKM; AM; RB. Overall supervision, guidance and quality evaluation- DS and AKM.

Compliance with ethical standards

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