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The Pharma Innovation

ISSN (E): 2277-7695
ISSN (P): 2349-8242
NAAS Rating: 5.23
TPI 2023; 12(11): 2021-2030

www.thepharmajournal.com
Received: 18-08-2023
Accepted: 22-09-2023

Anurag Pandey
Research Scholar, Department of Pharmaceutical Science, Sam Higginbottom University of Agriculture, Technology and Sciences, Prayagraj, Uttar Pradesh, India

Rajani Srivastava
Department of Pharmaceutical Science, Sam Higginbottom University of Agriculture, Technology and Sciences, Prayagraj, Uttar Pradesh, India

Corresponding Author:
Anurag Pandey
Research Scholar, Department of Pharmaceutical Science, Sam Higginbottom University of Agriculture, Technology and Sciences, Prayagraj, Uttar Pradesh, India

A review on traditionally used medicinal plants of genus *Leea* and its phytochemicals

Anurag Pandey and Rajani Srivastava

Abstract
The research aimed to evaluate the phytochemicals and traditional uses of the medicinal plants of the genus *Leea* of the Vitaceae family. The main objectives of the research were an ethnobotanical survey and use of traditional knowledge for pharmacological significance of the genus leea; and a phytochemical analysis of the genus leea. These days a large number of medicinal plants are used as traditional medicine in the treatment of various diseases by the tribal community. Relevant information on all possible aspects was extracted using various databases such as Web of Science, Scopus, PubMed, Google Scholar, Science Direct, Research Gate, etc. Vitaceae family contains around 700 species, assigned to 13-15 genera. *Leea* species consist of 70 species that are used for various medical purposes across the globe. *Leea* species (*Leea indica, Leea macrophylla, Leea asiatica, Leea aequata, Leea rubra,* Leea *Leea philippinensis, Leea thorelii, and Leea guineensis*) are an important ethnobotanical plant species in the Valmiki Tiger Reserve, is used through the traditional knowledge of the people living in West Champaran district, which has immense potential in treating and curing various diseases such as asthma, snake-bite, constipation, cough and cold, parasitic intestinal worms, blood coagulation, bone fracture, diabetes, hepatic disorder, osteoarthritis, hair fall, wounds, and other oxidative stress-related disorders. Phytoconstituents such as steroids, tannins, flavonoids, glycosides, phenolic compounds, diterpenes, triterpenes, saponins, alkaloids and many other constituents are present in *Leea* species. Therefore, the traditional uses and presence of phytochemicals are related to the pharmacological activity of other species of the Vitaceae family.

Keywords: Leea genus, medicinal plants, phytochemicals, traditional knowledge, traditional use

Introduction
For millennia, mankind has relied heavily on plants for food and relief from disease. Natural products have always contributed extensively to the development of modern medicine, and continue to play an important role in drug discovery [1]. Recently, phytotherapies represent an approximately $14 billion/year industry, approximately 5% of the current $280 billion/year market. Here, it is pertinent to mention that significant regional differences exist between developed and developing countries, where herbal products represent 25 and 80% of medicines, respectively [2]. Chemical diversity and biodiversity are two sides of the same coin where plant products provide a vast reservoir of chemical diversity which in turn can provide a range of lead structures. Interestingly, most therapeutically active molecules are plant secondary metabolites, which are able to interact with a diverse range of proteins, DNA, and similar macromolecules, and thus exhibit important biological functions that can be used to obtain biomolecules of therapeutic importance [3]. Several *Leea* species (Family- Vitaceae; former family is Leeaceae) are found to possess many beneficial effects in the field of traditional medicine [4]. Especially, different species of *Leea* contain bioactive compounds active against diabetes, inflammation, blood clot, and oxidative stress, such as flavonoids, alkaloids, glycosides, and terpenoids [5]. Leea (Vitaceae- the grape family) has over 900 species, ranking it as the 14th largest genus of the eudicots class. Species of this genus are found mostly in tropical, subtropical and evergreen forest regions of Asia. *Leea* genus presents a great morphological diversity and is widely distributed in moist deciduous and evergreen forests [6]. A large number of phytochemicals have been reported from plants belonging to the genus *Leea* [7]. *Leea* species contains phytochemicals like alkaloids, flavonoids, glycosides, phenols, terpenoids, steroids, volatile oils, proteins, quinine derivatives, tannins, saponins, etc. which are active against jaundice, hyperglycemia, coagulation and liver disorders [8]. Their Latin name, *Leea*, was named in memory of Scottish nurseryman James Lee for his many plant discoveries.

Leea is found in the Vitaceae family, based on morphological and anatomical differences between the two families. Based on morphology, Leea species differences have carpel number, ovule number per locale, and presence and absence of a floral disc and staminoidal tube [9, 10]. Based on transeverse sections, Leea species differences have the leaf margin, the shape of stem, midrib, petiole, and druses in the leaf and stem of both species, and raphides in the lamina [11]. Eighty percent of the world's population relies on traditional medicines and plant extracts and the active constituents are used to meet people's primary healthcare needs [12]. Bioactive phytochemicals of the species of the genus *Leea* such as *L. thorelii*, *L. indica*, *L. asiatica*, *L. macrophylla*, and *L. guineense* contain flavonoids: (+)-catechin, (-)-epicatechin, (-)-epiafzelechin, juglanin, afzelin, astragalin, mearnsetin 3-*O*-rhamnopyranoside, myricitrin, quercitrin; triterpenoids: Oleanolic acid, maslinic acid, ursolic acid, corosolic acid; coumarin; essential oils; hydrocarbons, and have been determined from the various extracts of *Leea* species. Although several *Leea* species have been evaluated from both biological and phytochemical perspectives [13]. The phytochemicals of the extract of *Leea indica* (Burm. F.) Merr. Leaves and *Leea asiatica* (L.) Ridsdale was elucidated using TLC, HPTLC methods, and 31 compounds and 24 compounds of different classes were identified using spectroscopic [13, 14]. Traditional and ethnic medicinal literature has shown that this plant is very effective and safe for medicinal use [15].

Traditional Use

Our country, India is recognized throughout the world as a rich source of ethnomedicinal and non-ethnomedicinal plants. The northern region of India is very rich in plant biodiversity as well as ethnic diversity. The medicinal plants of *Leea* genus are being used for many traditional and ethnic purposes of humans. *Leea* genus is traditionally used in the treatment of cancer, inflammation, snake bites, cough and cold, blood coagulation, bone fracture, osteoarthritis, diabetes, dysentery, jaundice body-ache, coagulation, and sexual disability. The leaves are used in tetanus, tonsillitis, snake bites, arthritis, pain, sore, rheumatism, nephrolithiasis, and blood coagulation. *Leea asiatica is* an important medicinal plant species of West Champaran district, Bihar *viz*. Bagaha, Bettiah, and Narkatiaganj are used by traditional medicine practitioners and tribal communities for the treatment of coagulation, jaundice, hyperglycemia, and liver disorder. The leaves are used as animal fodder. By sticking its roots and applying it on mouth wounds, the wounds get cured. Fresh stems were used to make baskets [6, 16]. *Leea macrophylla* is traditionally used for urinary problem by the local tribal communities of West Champaran district of Bihar. The leaves are used to treat gastric tumors, goiter, lipoma, and tetanus. Other tribal communities Tharu in this landscape are Oraon, Hohra, Munda, and Bhuiya use the leaf as vegetables.

The powder of raw leaves and roots is traditionally used in the treatment of wounds, cancer, urolithiasis, wounds, goiter, gastric tumors, tetanus, guinea worm and ringworm, and urinary disorders [17]. The powdered root of *Leea indica* is used to treat of diabetes, pain, diarrhea, dysentery, muscle spasms bone fracture, sore, fever, heart, and skin diseases. A decoction of the leaves is consumed by women during pregnancy and childbirth control, and body pain. Fresh flowers of *Leea indica* were reported to have antifungal and antibacterial activity. Roasted leaves are digestive, and useful in vertigo [15, 18]. Other than this, dried leaves are consumed as a tea drink considered effective against cancer [35]. *Leea guineense* and *Leea macrophylla* was used to treat cancer disease [8]. The leaves of *Leea guineense* are used against cancer. The roots of *Leea thorelii* are mainly used as a tonic [19]. *Leea aequeta* is known as tetanus plant. *Leea aequeta* is used in itching, and dyspraxia. Its leaves and twigs are used as an antiseptic to treat wounds [20]. Previous research has shown that the stems, seeds, and roots of *Leea aequeta* have antibacterial activity. *Leea aequeta* is used to treat wounds, and skin diseases [19]. *Leea rubra* is a useful indoor plant. It may have medicinal properties [21]. The leaves of *Leea rubra* are used as antipyretic, antitumor, antibacterial, and diaphoretic agents. It is used to treat rheumatism, arthritis, and stomach ache etc [22]. Leea *Leea philippinensis* are often used as ornamental plants because they help to attract pollinators, and birds to gardens [23]. There is little data available regarding its biological use. However, other species of the genus have been used traditionally to treat a number of diseases [24]. The whole plant poultice of Leea philippinensis is Merr. is active against bacteria [25]. The medicinal plants of genus *Leea* shown in Figure 1.

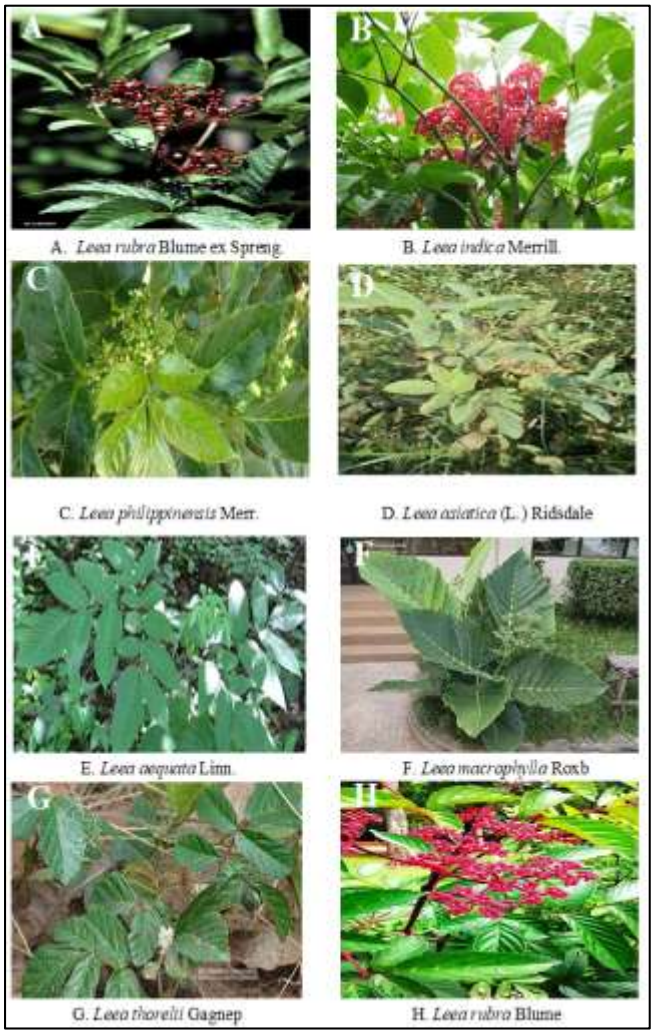

Fig 1: Medicinal Plants of the genus *Leea*

The traditional uses of the *Leea* species available in regions of New Guinea, Africa to Asia, northeastern Australia, and islands of the Pacifc (Fiji, Solomon Islands, Caroline Islands) is shown in Table 1.

Table 1: Traditional uses of the *Leea* species

Plant	Common Name	Plant Parts	Uses	Region	Reference
Leea asiatica	Kumali, Basant jari, Nagashya, Nanli	Leaf	Hepatic disorder, Earthworms infection, wound, eye diseases, bone fracture, diabetes and gastrointestinal disorders, hair fall, osteoarthritis, and oxidative stress-related disorders	North-Eastern India and in western parts of peccan peninsula	[25, 13, 27]
		Root tuber	Snake-bite, Guinea worms	India	[28, 29, 30]
		Root	Icteric hepatitis	China	[38]
Leea macrophylla	Hathikana, Gajakarni	Leaf	Gastric tumor, cancer, goiter, lipoma, tetanus, urinary disturbances	North-Eastern India	[31]
		Leaf	Tetanus, tonsillitis	Bangladesh	[7]
		Whole plant	Urolithiasis	Asia, Europe, America and Middle East	[32]
		Root	Guinea worm infection, pain, sore, blood effusion	Bangladesh	[32]
		Root	Guinea worm	Myanmar	[19]
		Root tubers	Wounds, sores, ringworm and guinea worm	India	[30]
Leea indica	Chhatri, Karkani, Kukurjihvaa, Bandicoot berry	Leaf	Cancer, Genital herpes, vertigo, diabetes, anxiety	India	[32, 33, 34]
		Stem	Malaria	India	[7]
		Root	Dysentery, diarrhea, muscle spasm cardiac and skin diseases	India	[30, 34]
		Leaf and root	Diabetes, cardiac diseases, fever, headache, sprain, dizziness, soreness, eczema, leprosy, body pain, bone fracture, muscle spasm, dysentery, and diarrhea	India, Malaysia	[33]
Leea guineense	West Indian Holly, Hawaiian Holly, Agyaben	Leaf	Toothache, rheumatism, skin ulcer, vertigo, anxiety, convulsion, and paralysis	West African sub-region	[35]
		Root and seed	Constipation	India, Ghana	[35]
		Leaf	Enlarged spleen in children	Southern Nigeria	[7]
		Leaf	Pelvic inflammation, tumor	Cameroon	[36]
		Leaf and Stem	Diarrhea, urinary tract infection, anaemia, kidney failuire, candidiasis	Nigeria	[29]
		Leaf	Cancer	Guinea	[19]
Leea thorelii	Katang bai tia	Root	Tonic	Thailand	[19, 38]
		Leaf	Fever, Inflammation	Thailand	[39]
Leea aequata	Kaakajanghaa, Sulomaasha, Surapadi	Aerial parts	Wounds and skin diseases	Myanmar	[19]
		Stem and root	Astringent, anthelmintic, indigestion, jaundice, chronic fever and malaria	India, Indonesia	[30, 42]
		Root, tuber and stem	Mucilaginous, astringent	India	[30]
		Leaf and twig	Antiseptic	India, Indonesia	[30, 42]
		Leaf	Diarrhea, cancer, tuberculosis	Bangladesh, India	[30, 40, 41]
		Leaf	Wounds and tetanus	Indonesia	[42]
Leea rubra	Red tree shrub, Red Leea	Leaf	Stomach ache, rheumatism, arthritis, fever, tumor, wound	Bangladesh	[22, 43]
		Stem and Root	Intestinal diseases	Thailand	[44]
		Root	Antipyretic and diaphoretic	India, Myanmar	[45]
		Fruit	Dysentery	India, Myanmar	[45]
Leea philippinensis	Kaliyantan, Kalitantan-ilanan	Leaf	Oxidative cell damage diseases	Philippines	[24]
		Whole Plant	Antibacterial	Philippines	[25]

Phytochemicals

Medicinal plants have long been used to treat fatal diseases like diabetes, cancer, liver disorders, and heart diseases due to the presence of bioactive phytochemical components. Phyto or herbal therapy has less severe side effects than traditional synthetic drugs, and can be used as an alternative source of treatment. Phytochemicals of herbal medicine are very important because they can be used as primary data for the prediction of biological effects, safety information, and clarification of medicinal use. The phytochemical review of the *Leea* species was carried out and contain flavonoids, glycosides, phenols, terpenoids, steroids, volatile oils, alkaloids, proteins, quinine derivatives, tannins, saponins, etc. in Figure 2. An overview of the detailed phytochemical literature review of the *Leea* genus is shown in Table 2.

Table 2: A list of phytochemicals isolated from the medicinal plants of the *Leea* genus

Phytochemical	Isolated/ Identified Compounds	Description	Reference
Alkaloid	Alkaloids	The presence of alkaloids in non-polar (Ethyl acetate, Chloroform, and Hexane) solvent extract of *Leea guineensis* leaves.	[46]
	Alkaloids	The identification of alkaloids in the aqueous extract of *Leea giuneensis* fresh leaves.	[49]
	Alkaloids	The identification of alkaloids in the ethanol extract of *Leea indica* fresh leaves.	[51]
	Alkaloids	The identification of alkaloids in petroleum ether, ethyl acetate, chloroform, methanol, ethanol, and aqueous extracts of leaves and stems of *Leea asiatica*.	[16]
	Alkaloids	The presence of alkaloids in hexane, chloroform, acetone, methanol, and ethanol extract of *Leea guineensis* leaves.	[37]
	Alkaloids	The identification of alkaloids from ethyl acetate, butanol, and aqueous fraction of ethanol extract of *Leea macrophylla* root tubers.	[53]
Steroid	Steroids	The identification of steroids in ethanol extract of *Leea indica* fresh leaves.	[51]
	Steroids	The identification of steroids from hexane, ethyl acetate, chloroform, butanol and aqueous fraction of ethanol extract of *Leea macrophylla* root tubers.	[53]
	Stigmasterol	The solation of stigmasterol from ethanol extract of *Leea macrophylla* roots.	[54]
	Steroids	The presence of steroids in alcoholic extracts of *Leea macrophylla* leaves.	[31]
	Steroids	The presence of steroids in methanol extract of *Leea indica* and *Leea macrophylla* leaves.	[48]
Cardiac Glycoside	Cardiac glycosides	The identification of glycosides from hexane, acetone, methanol, and ethanol extract of *Leea guineensis* leaves.	[37]
	Cardiac glycosides	The identification of cardiac glycosides from ethanol extract of *Leea indica* leaves.	[18]
	Cardiac glycosides	The identification of cardiac glycosides in petroleum ether, ethyl acetate, chloroform, ethanol, methanol, and aqueous extracts of *Leea asiatica* fresh leaves and stems.	[16]
	Cardiac glycosides	The presence of cardiac glycosides in hot methanol extract of *Leea macrophylla* root.	[47]
Terpenoid	Oleanolic acid, Ursolic acid, Maslinic acid, Corosolic acid, Chebuloside II, Hederagenin-3-*O*-arabinopyranoside, Oleanolic acid 3-*O*-glucopyranosyl -(1→2)-arabinopyranoside	The identification of triterpenoids from methanol extract of *Leea asiatica* aerial parts.	[13]
	Triterpenes	The isolation of triterpenes from methanol extract of whole plant of *Leea asiatica.*	[50]
	Oleanolic acid & derivatives	The identification of compounds from ethanol extract of *Leea macrophylla*nroot.	[54]
	Terpenoids	The identification of terpenoids from ethanol extract of *Leea indica* leaves.	[18]
Flavonoid	Flavonoids	The identification of flavonoids in petroleum ether, ethyl acetate, chloroform, methanol, ethanol, and aqueous extracts of fresh leaves and stems of *Leea asiatica*.	[16]
	Flavonoids	The presence of flavonoids from ethanol extract of *Leea indica* leaves.	[51]
	Flavonoids	The identification of flavonoids from acetone, hexane, methanol, and ethanol extract of *Leea guineensis* leaves.	[37]
	(+)-Catechin, (-) - Epicatechin,(-)-Epiafzelechin, Juglanin, Mearnsetin 3-*O*-rhamno pyranoside, Myricitrin, Quercitrin, Afzelin, Astragalin	The identification of flavonoids from methanol extract of aerial parts of *Leea asiatica.*	[13]
	Quercitrin, Quercetin, Quercetin-3'-sulphate-3- *O*- α-L-rhamnopyranoside, Quercetin-3,3'-disulphate, Quercetin-3,3',4'-trisulphate, Kaempferol, Quercetin, Mearnsitrin, Quercitrin	The isolation of flavonoids from butanol extract of leaves of *Leea guineense*.	[52]
	Flavonoids	The presence of flavonoids in chloroform, butanol, ethyl acetate, and aqueous fraction of ethanol extract of *Leea macrophylla* root tubers.	[53]
	Mearnsitrin	The isolation of flavonoid from the ethyl acetate extract of *Leea rubra* leaves.	[43]
	(-)-Epicatechin, 4"-*O*-methyl -(-)-epicatechin gallate, (-)-epicatechin gallate	The isolation of flavonoids from the ethyl acetate extract *Leea thorelii* roots.	[39]
	Quercetin 3-*O*- α -L-rhamnopyranoside, myricetin 3-*O*-α -L-rhamnopyranoside	The isolation of two flavonol glycosides from the methanolic extract of the leaves of *Leea thorelii.*	[39]
	Flavonoids	The identification of flavonoids from the acetone extracts of the leaf of *Leea Philippinensis.*	[24]
Tannin	Tannins	The identification of tannins in ethanol extract of *Leea indica* leaves.	[51]

	Tannins	The identification of tannins from hexane, chloroform, methanol and ethanol extract of *Leea guineensis* leaves.	[37]
	Tannins	The identification of tannins in the butanol, and aqueous fraction of ethanol extract of *Leea macrophylla* root tubers.	[53]
	Tannins	The presence of tannin in hot methanol extract of *Leea macrophylla* root.	[47]
	Tannins	The presence of tannin in methanol extract of *Leea indica* leaves.	[48]
Glycoside	Glycosides	The identification of glycosides from methanol extract of whole plant of *Leea asiatica*.	[50]
	Astragalin, Isorhamnetin	The isolation of flavonoid glycosides from the ethanol extract of *Leea aequata* leaf.	[19]
	3-O-β-D-glucopyranoside, Isoquercitrin, Mauritianin 7-O-methylmearnsitrin and roseoside A	The characterization of two glycosides from the methanol extract of the leaves of *Leea aequata*.	[41]
	Glycosides	The presence of glycosides from ethanol extract of *Leea indica* leaves.	[51]
	Glycosides	The presence of glycosides from ethyl acetate, butanol, and aqueous fraction of ethanol extract of *Leea macrophylla* root tubers.	[53]
	Glycosides	The presence of glycosides from ethyl acetate, and methanol extract of seeds of *Leea macrophylla*.	[55]
	Mollic acid α-L-arabino-side, Mollic acid β-D- xyloside	The isolation of glycosides from ethyl acetate fraction of *Leea indica* leaves.	[33]
Phenolic Compound	4-hydroxyphenol-[6-*O*-(4"-hydroxy-3",5"-dimethoxy benzoate)]-β-D-glucopyranoside, Breynioside A	The identification of phenolic glucosides from methanol extract of *Leea asiatica* aerial parts.	[13]
	9'-*O*-acetylisolariciresinol, (+)-Lariciresinol, (+)-Syringaresinol, Urolignoside	The isolation of five lignans from the ethanol extract of *Leea aequata* aerial parts.	[19]
	Gallic acid, Ethyl gallate	The isolation of phenolic compounds from butanol extract of leaves of *Leea guineense*.	[52]
	Phenolics	The identification of phenolic compounds from butanol and aqueous fraction of ethanol extract of *Leea macrophylla* root tubers.	[53]
	Phenolics	The identification of phenolic compounds from ethyl acetate and methanol extract of *Leea macrophylla* seeds.	[55]
	Phenolics	The identification of phenolic compounds from the acetone extracts of the leaf of *Leea philippinensis.*	[24]
Saponin	Saponins	The identification of saponins in aqueous extract of *Leea guineensis* leaves.	[49]
	Saponins	The identification of saponins in hexane, acetone and ethanol extract of *Leea guineensis* leaves.	[37]
	Saponins	The identification of saponins in the ethanol extract of *Leea macrophylla* root tubers.	[53]
	Saponins	The identification of saponins from ethanol extract of *Leea indica* leaves.	[18]
	Saponins	The identification of saponins in n-hexane and chloroform extract of *Leea macrophylla* seeds.	[55]
Sugar	Reducing Sugars	The identification of reducing sugars from aqueous extract of *Leea guineensis* leaves.	[49]
	Sugars	The identification of sugars from ethanol extract of *Leea macrophylla* root tubers.	[53]
	Reducing sugars	The presence of reducing sugar in ethanol extract of *Leea macrophylla* leaves	[58]
	Reducing sugars	The presence of reducing sugar in methanol extract of the leaf of *Leea indica* and *Leea macrophylla*.	[48]
Carbohydrate	Carbohydrates	The identification of carbohydrates from ethanol extract of *Leea indica* leaves.	[18]
	Carbohydrates	The identification of carbohydrates in ethyl acetate and methanol extract of *Leea macrophylla* seeds.	[7]
	Carbohydrates	The presence of carbohydrates in alcohol extracts of *Leea macrophylla* leaves.	[31]
Essential Oil	di-*n*-butyl phthalate, Butyl-Isooctyl phthalate, 2-ethylhexyl phthalate	The identification of essential oils from 1-butanol fraction of methanol extract of *Leea indica* leaves.	[56]
	di-*n*-butylphthalate, di-isobutylphthalate, Butylisohexylphthalate, *n*-butylisobutylphthalate	The isolation of essential oils from diethyl ether extract of *Leea indica* flowers.	[57]
Protein	Proteins	The identification of proteins in butanol and aqueous fraction of ethanol extract of *Leea macrophylla* root tubers.	[53]
	Proteins	The identification of proteins in ethyl acetate and methanol extract of *Leea macrophylla* seeds.	[55]
Others	Amino Acids, Mucilage's	The identification of these compounds from aqueous fraction of ethanol extract of *Leea macrophylla* root tubers.	[53]
	Gum & mucilage	The identification of these compounds in aqueous extracts of leaves and stems of *Leea asiatica.*	[16]

	Gums	The presence of gums in methanol extract of leaves of *Leea indica* and *Leea macrophylla*.	[48]
	Leeaoside	The isolation of a new megastigmane diglycoside from the methanol extract of the leaves of *Leea thorelii*.	[39]
	Waxes, chlorophyll and fatty acids	The identification of lipohilic compounds from the hexane extracts of the leaf of *Leea philippinensis.*	[24]

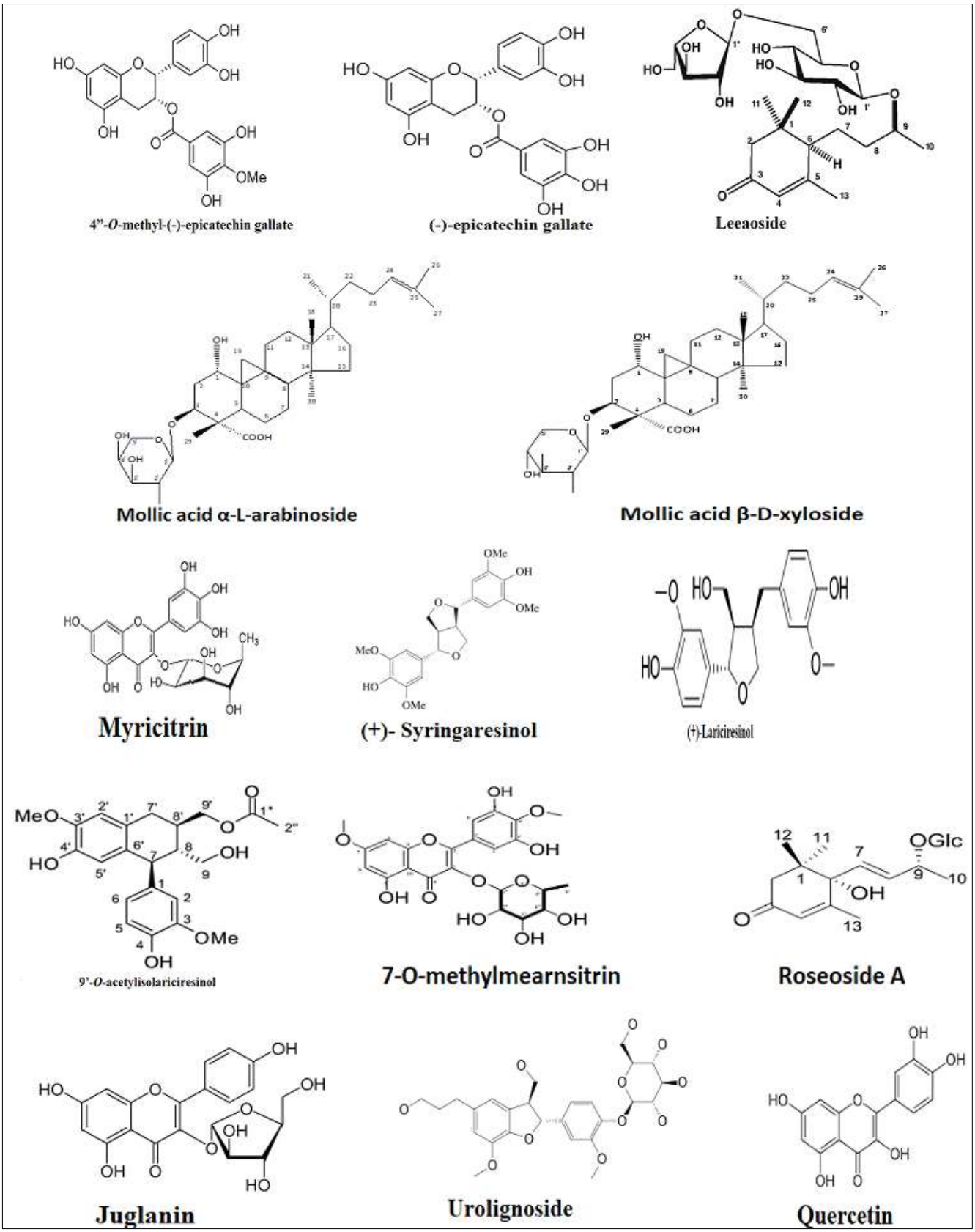

Fig 2: Phytochemicals isolated from the medicinal plants of the *Leea* genus

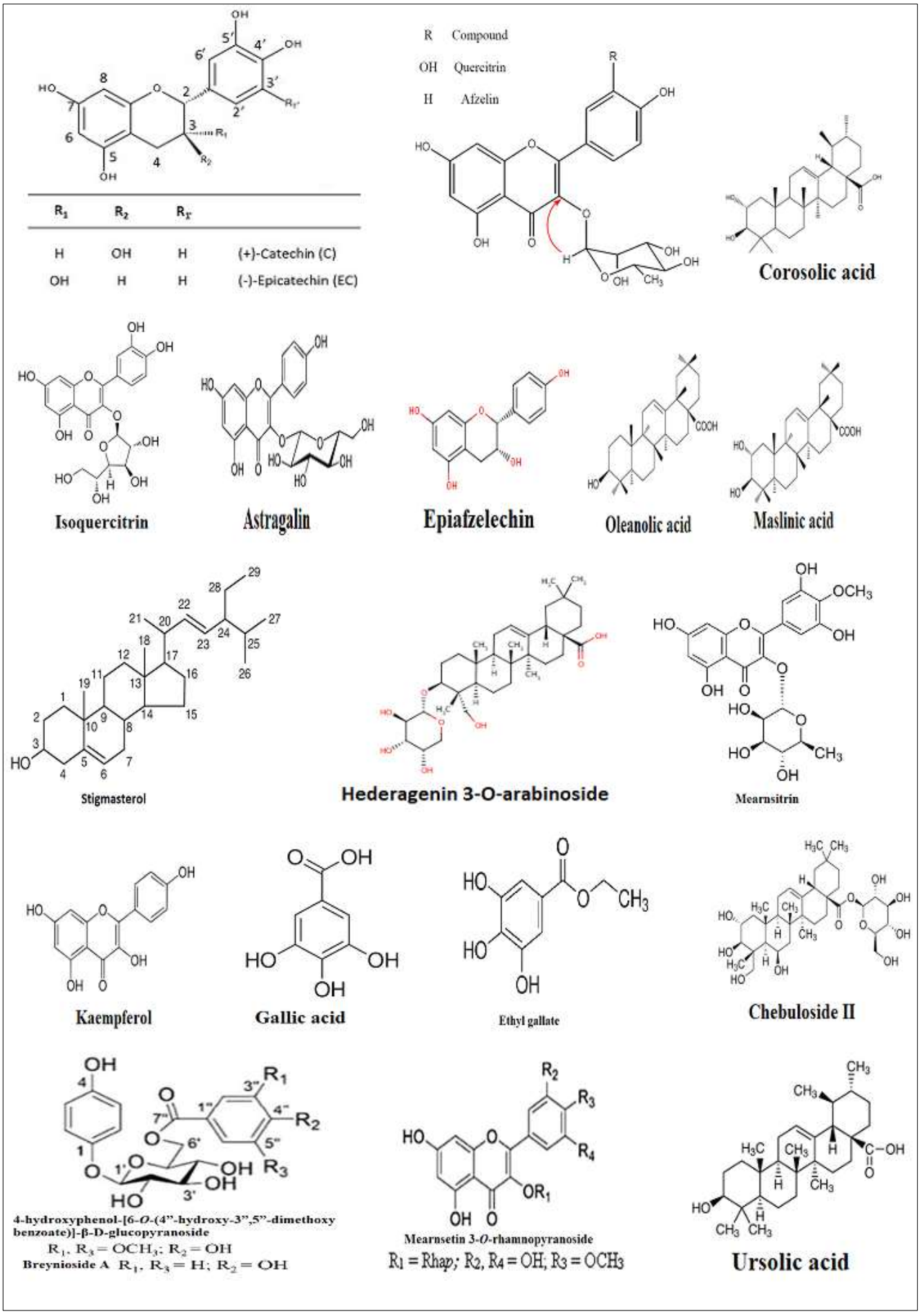

Fig 2: *Continued*

Conclusion

The genus *Leea* has about 70 species distributed in the world's tropical, subtropical, and evergreen forest regions. Of the 36 species, 11 species are distributed in different states in India, as reported in the database of the Botanical Survey of India. Of the 11 species, the genus *Leea* is represented by 3 species in the state of Telangana., i.e., *Leea asiatica* L. Ridsdale, *Leea indica* Burm.f. Merr. and *Leea macrophylla* Roxb. ex Hornem. In-depth study of the genus *Leea* and an extensive literature survey has clearly revealed that the plant serves as an essential source of many therapeutically efficient phytoconstituents and many other components that are responsible for different pharmacological activities. Previous studies on the genus *Leea*, and the traditional use of the species as medicinal plants, *Leea asiatica*, *Leea indica* and *Leea macrophylla* are the most important species, whose stems, leaves, roots, and whole plants possess different pharmacological activities as they are an abundance of flavonoids, triterpenoids, tannins, and phenolic compounds. So, the presence of such naturally occurring compounds indicates the plant's ability to act against diseases like cancer, dibetes and cardiac diseases. Therefore, there is a wide scope for further research to establish *Leea* plants as an important source of new drugs in drug discovery.

Acknowledgements

The authors are deeply grateful to the Department of Pharmacognosy, FHS, SIHAS, SHUTS, Prayagraj for providing the facility to conduct the study. The author also heartily thanks Dean and HOD SIHAS of SHUTS.

Funding Support

The authors declare that they have no funding support for this study.

Conflict of Interest

The authors declare that there are no conflict of interests regarding the publication of this paper.

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