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Review Article

An Insight into the Elusive Healer Plant "*Luffa echinata* Roxb."

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ABSTRACT

Recent years have seen a global rise in the use of herbal medicine. Many naturally occurring bioactive substances, especially those derived from plants, have been studied as potential cures for various diseases. *Luffa echinata* Roxb., a mysterious medicinal plant from the Cucurbitaceae family, has recently gained recognition as one of the most important medicinal herbs among them. Many phytochemicals found in this plant have been found to have therapeutic potential, including xanthones, alkaloids, phytosterols, flavonoids/isoflavonoids, chalcone, glycosides, terpenoids, saponins, carbohydrates, proteins, reducing sugars, fatty acids, tannins, and phenolic compounds. Other potent phytoconstituents of this plant include saponins, hentriacontane, gypsogenin, sapogenin, cucurbitacin (A, B, C, D, E, K, S, and I), β-sitosterol, echinatol (A and B), oleanolic acid, isoquercetin, quercimeritrin, and sitosterol glycoside. Cucurbitacin, a prominent class of triterpenoids found in *L. echinata*, has been proven effective in numerous reports. Recent research has shown that cucurbitacins can decapitate or inhibit the proliferation of cancer cells. *Luffa echinacea's* fruit and leaves have long been used as purgatives and to cure liver disease, hemorrhoids, jaundice, migraines, emesis, and other conditions by Indian and Chinese physicians. Ulcers and sores have also been expelled using them. During the field study, it was found that the tribal community (Tharus) of Khatima utilized extremely bitter, squeezed fruit stuff given to sufferers of dog bites in the morning on an empty stomach, and more than 500 people have been adequately treated thus far. The therapeutic potential and phytoconstituents of *Luffa echinata* have been clarified by pharmacological and phytochemical studies; further study is required to investigate these phytoconstituents and their structures.

Keywords: Cucurbitaceae, Cucurbitacin, Ethnobotanical, *Luffa echinata* Roxb., Pharmacobotanical, Pharmacological Testimony, Phytomolecules..

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INTRODUCTION

Plants are an essential component of life on Earth, supplying us with oxygen, food, fuel, medicine, and much more. Plants also aid in temperature regulation, offer shelter and food for insects and other creatures, and act as a natural flood control system. To enhance agricultural production and sustainability, find novel medicines, prepare for and minimise the worst consequences of climate change, and get a deeper knowledge of life as a whole, a deep understanding of plants is required.[1] Plants are split into smaller categories based on common characteristics. Because plants are so intricate, it might be difficult to recognise them. Experts found it simple to recognise familiar plants; sometimes, especially in medicine, we need to identify prejudiced or toxic plants, which botanists can do quickly; however, he must find a way to interpret the many different species when there are millions of different plant species with similar parts (roots, stems, leaves, etc.). Plant recognition systems must be designed in order to save time and money.[2] Knowledge regarding the usage of medicinal plants is passed down from generation to generation in the form of local folklore in families, tribes, and civilizations all over the world. There has been a surge in the usage of health products derived from plants in both developed and developing nations in recent years, resulting in an exponential expansion of herbal goods worldwide. In the field of herbal research, there has been an increased trend.[3]

Ayurveda is based on Indian medicinal herbs. Treatment of disease and preservation of health using herbal medicine is the traditional and widely used type of healthcare practised by all civilizations throughout history. The fibrous sponge-like texture of the fruits of the genus *Luffa* is widely recognised. *Luffa* is a genus that includes over eight species, three of which are native to India (*Luffa acutangula, Luffa echinata* and *Luffa aegyptiaca*). *Luffa echinata* grows abundantly in Pakistan, India, Bangladesh, and Northern Tropical Africa, having bifid bristly or silky

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tendrils with a very bitter flavour. Gujarat, Bihar, Rajasthan, and Madhya Pradesh are the most common locations in India. *Luffa echinata* Roxb., is a member of the Cucurbitaceae family, which comprises over 130 genera and 800 species of medicinal plants.[4,5] *L. echinata* is the only species having highly bristled fruits, thus the popular name *Bristly Luffa*. Fruits have a harsh flavour and are highly fibrous. The dried fruit of *L. echinata* is used in the ancient Ayurvedic system to treat chronic bronchitis, dropsy, nephritis, intestinal and biliary colic, fever, and jaundice, among other ailments. Hepatoprotective, digestive stimulant, diuretic, purgative, anti-inflammatory, antipyretic, and cough expectorant are some of the other uses. Various life-threatening disorders such as enlargement of the liver and spleen, leprosy, diabetes, nephritis, rheumatism, cirrhosis, dropsy, anthelmintic, stomachache, snake bite, dog bite, fever, diarrhoea, and haemorrhoid condition can all be treated with this plant. Several researchers have found bioactivity such as antioxidant, analgesic, anti-inflammatory, antidepressant, anxiolytic, antiepileptic, hepatoprotective, antibacterial, antifungal, antiulcer, and anticancer.[5-8] As a result, the goal of this studies was to offer a comprehensive summary of current information about the *Bristly Luffa*'s (*L. echinata*) ethnomedicinal, phytochemical, and pharmacological manifestations.

TAXONOMIC POSITION, SYNONYMS, AND VERNACULAR NAMES

Luffa is a genus of tropical and subtropical vines in the cucumber family (Cucurbitaceae). Furthermore, all *Luffa* species were monoecious and unisexual, with the exception of *Luffa hermaphrodita*, which possessed bisexual blooms. William Roxburgh originally described it as *Luffa echinata* in Hortus Bengalensis, or a catalog of the Plants growing in the righteous East India Company's Botanical Garden at Calcutta (India), published in 1814. *Luffa echinata* is a climbing plant with bifid bristly or silky tendrils and a very bitter flavour. [Table 1] illustrates the taxonomic status of *L. echinata* along with synonyms, while [Table 2] depicts the vernacular names.[5,9,10]

Table 1: Taxonomical classification and synonyms of *L. echinata*.

Kingdom	Plantae
Subkingdom	Viridiplantae
Infrakingdom	Streptophyta
Superdivision	Embryophyta
Division	Tracheophyta
Subdivision	Spermatophytina
Class	Magnoliopsida
Superorder	Rosanae
Order	Cucurbitales
Family	Cucurbitaceae
Genus	Luffa
Species	*Luffa echinata* Roxb.

ECOLOGY IMPACTS AND GEOGRAPHICAL ALLOCATION

In India, immature fruits of harvested *Luffa* species are frequently consumed as a summer vegetable. In agricultural *Luffa* species from different growing regions of the country, there is a lot of morphological variation. The distribution of *L. echinata* was formerly thought to be limited to Bengal, Gujarat, Bihar, Orissa, and Andhra Pradesh. Later distributional data suggest that it migrated from Gujrat to Maharashtra's neighbouring cities of Mumbai and Pune. Mauritania to Somalia, Bangladesh, Cameroon, Chad, Ethiopia, Mali, Mauritania, Niger, Nigeria, Pakistan, Sudan, and the Indian Subcontinent are all home to this species.[11-14] Harvesting for medicine and trade has become indiscriminate. The native habitat of *Luffa echinata* is dwindling. Additionally, this plant is extremely difficult to cultivate owing to low seed viability, low seed germination rate, low vegetative propagation rate, overexploitation, and habitat loss, all of which contribute to the species' decline from its natural environment. Only 1% of the world's population is available. This species has been designated as endangered by the International Union for Conservation of Nature (IUCN). This species is mostly found in Raipur, Chhattisgarh. Chhattisgarh has a population decrease rate of 50-80%.[15]

PHARMACOBOTANICAL AND PHARMACOGNOSTICAL DESCRIPTION

Luffa echinata is an annual herbaceous climber medicinal herb [Figure 1]. The smooth or somewhat hairy grooved stem axis. There are two components to the fluffy hairy or naked tendrils. A petiole and a leaf blade contain the alternating leaves. The petiole is up to 12 centimetres long and delicately hairy. Because of its extensive applicability for the possibility of harnessing, converting, and recycling discarded seeds for diverse reasons such as industrial and residential applications, *L. echinata* is becoming an essential crop species. The utilisation of *L. echinata* as a source of vegetable protein in animal and human nutrition has a lot of promise.[16,17]

The plant has bristly or silky tendrils and is a light climber [Figure 2]. Slender stem portions are yellowish-brown to blackish brown in colour, longitudinally wrinkled, glabrous, and measure 1.5-1.7 cm in length and 5-8 mm in diameter. The stems are odourless, have a harsh flavour, and have a brief fracture. Single-layered epidermis, seven layers of collenchyma under five ridges but only one to two layers of parenchyma in the remainder of the area beneath the epidermis, and a continuous broad wavy layer of pericycle made up of three to eight layers of fibre in mature stem. There are five bi-collateral open vascular bundles in the pith, one

Synonyms	*Luffa bendaul* Roxb. *Luffa bindaal* Roxb. *Luffa bondel* Buch. -Ham. *Luffa bondel* Buch. -Ham. ex Steud. *Luffa echinata* var. *longistyla* (Müll.Stuttg.) C.B.Clarke *Luffa longistyla* Edgew. *Luffa longistyla* Müll.Stuttg. *Momordica echinocarpa* Fenzl *Momordica echinocarpa* Fenzl ex Hook.fil. *Momordica erinocarpa* Fenzl *Momordica erinocarpa* Fenzl ex Naudin
Allied species	*Luffa graveolens* Roxb.

Table 2: Vernacular names of *L. echinata*.

Sanskrit	Jimuta
Hindi	Bindaal, Ghagarbel, Kakora
Urdu	Bindaal
English	Bitter luffa, Bristly luffa, Rag gourd, Sponge gourd, Vegetable-sponge, Courge torchon
Bengali	Deyatada
Telugu	Panibira, Paanibira
Kannada	Daivadaali
Marathi	Devadali, Devadangari, Kukadvel, Kunjalata
Tamil	Pey-p-pirkku
Gujarati	Kukadvel
Tibetan	Dji mu ta ka

Figure 1: An annual herbaceous climber herb "*Luffa echinata* Roxb."

Figure 2: The slender stem parts of *L. echinata* and its bristly or silky tendrils.

below each ridge, and four medullary vascular bundles in the pith, each facing furrows.[18]

The leaves of *Luffa echinata* were sparingly hairy on both sides, shallowly five angled, reniform-suborbicular, and sparsely puberulent [Figure 3]. The leaves are kidney-shaped, spherical, and have five lobes that are shallow or deep. The leaf stalk is thick, bristly, and up to 12 cm long, with a rounded or rarely pointed tip, bristly on both sides, a minutely serrated border, and a bristly tip.[5,8] A single layer of cuticle was found in the leaf. Underneath the cuticle was the epidermis layer. Trichomes were rosette-shaped, elongated, thin-walled, and flattened at the base. The vascular bundles are surrounded by parenchyma under the epidermis. Additionally, the reported quantitative microscopical examination of plant leaves included the following measurements: stomatal number for the upper epidermis and lower epidermis are 35.6 and 62.2, respectively; stomatal index for the upper epidermis and lower epidermis are 9.6 and 13.5; vein islet number (14.4); vein-let termination number (13.2); and palisade ratio was 4.1.[19]

Flowers are white and stalked [Figure 4], with a diameter of 2.5 cm. Male flowers appear in a raceme with 5-12 blooms and a length of up to 15 cm. The hairy sepal tube is roughly 5.6 mm long. The petals are oval, 1.0-1.2 cm long, blunt, and hairy at the base, while the sepals are lance shaped. Female flowers are solitary, axillary, and bracteate; bracts are oblong with 5 conspicuous nectarines; and the pedicel is 3-3.5 cm long and striate. The teeth of the calyx are thin and linear, 8-9 mm long, hairy, and persistent. Corolla white, 2.5 cm wide; lobes 1 x 1.5 cm, sparsely hairy inside and along border, densely hairy at base but not as much as male flower; Stylar column around 3 mm long, stylar arms clearly grooved; ovary spherical, thickly bristely with bulbous base; There are five types of staminodia. Furthermore, the unisexual flowers have a five-fold envelope and a double flower envelope. The hairy calyx tube measures around 0.56 inches in length. The calyx lobes are lanceolate in shape and have a pointed tip. The five white petals are unattached, and the corolla is around

Figure 3: *Luffa echinata* leaves include sporadic hairs.

Figure 4: Flower of *Luffa echinata*.

Figure 5: *Luffa echinata* mature fruit, both ripe and unripe.

Figure 6: *Luffa echinata's* seeds and dried seed coat.

2.5 cm in diameter. The petals are egg-shaped and hairy at the base, measuring 1 to 1.2 centimetres in length with a blunt top end. The floral tube is connected to the three stamens, which have grown together and are 0.3 to 0.9 centimetres long. The dust bags are made up of one or more sections. The ovary below is formed like an egg. Three bilobed scars appear at the end of the stylus.[6,18]

Fruit has its own personality in *Luffa* [Figure 5]. At maturity, the fruit of all *Luffa* species was dry and fibrous, and it dehisced by stopple. *Luffa echinata* produces ashy, oblong, ovoid fruits that are 2-5 cm long and thickly coated with 4-7 mm long bristles. The fruits are ash grey when fully mature. Each fruit carries a number of seeds. Seeds are oblong to oval, 4-5 mm long, 3-5 mm wide, and 2 mm thick, compressed, dull blackish brown, and covered with thin membrane while young; membrane shrinks as it dries, turning black and giving the seed a verrucose appearance [Figure 6].[20] Bitter compounds in *Luffa echinata* seeds and oil meal may be harmful to animals. Only two effective uses of *Luffa* products have been documented as of 2014: *Luffa* seeds for rabbits and oil meal for African catfish (*Clarias gariepinus*). It was previously considered that feeding *Luffa* oil meal to cattle was not a healthy approach. Horses, cattle, sheep, and goats may eat the leaves.[21] According to the reported seed sample analysis, it includes two mineral elements (potassium and calcium), six essential elements (chromium, manganese, iron, nickel, copper, and zinc), one perilous element (lead), and five non-essential elements (titanium, bromine, rubidium, strontium, and zirconium).[17,22] Furthermore, the documented histological research claimed that the fruit's upper layer is made up of many trichomes (unicellular pointed trichomes) that point outwards in the shape of spines. Parenchyma cells were located underneath the top layer. A dark-coloured testa layer was identified, consisting of a single layer of cells enclosing the endosperm. Endosperm is wide, white, and centred. Mesocarp was displayed next to it. Centrally, phloem fibres were visible.[19] Interestingly, the mature sponge of the *Luffa echinata* fruit is an effective natural matrix for immobilising micro-organisms and has proven to be effective in the biosorption of heavy metals from wastewater. The plants have a taproot, and their branches thicken as food and water are stored. Epidermis, cortex, endodermis, and vascular bundles are commonly seen in *L. echinata* roots.[23] [Table 3 and Table 4] reflect the specifics of the reported physicochemical parameters and organoleptic characteristics of *L. echinata*.[19,24]

INDIGENOUS SYSTEMS OF REMEDIES WITH ETHNOBOTANICAL INSIGHTS

The advantages of the plant in terms of economics, ecology, and medicine are widely recognised. The ethanomedicinal effects of the Ayurvedic herb *Luffa echinata* are well-known.[25] The whole plant is used to cure a variety of ailments. *L. echinata's* Ayurvedic strengths include rasa, guna, ruksha, virya, vipaka, and karma. In the Vedic literature, the applications include jwara (fever), kasa (cough), shwasa (dyspnea), hikka (hiccups), arochaka (anorexia), pandu (anemia), rajayakshma (chronic respiratory disorder), arsha (haemorrhoids), shopha (inflammation), kshaya (depletion of body tissues), krumi (worm infestation), gulma (tumors of the abdomen), prameha (obesity, prediabetes, diabetes mellitus, and metabolic syndrome), shoola (abdominal colic pain), akhuvisha (rat bite, rhodent bite), visha (toxic conditions, poisoning), kamala (jaundice, liver diseases), bhuta (psychiatric disorders) and suryavarta (migraine).[6,26] Its uses in Folk medicine are well established, such as in the Konkan, where a few grains of the bitter fibrous contents of the fruit were given in infusion in cholera after each stool, in putrid fever the infusion was also applied to the whole body, and in jaundice it was applied to the head and also given internally, and the infusion also has a reputation as a colic remedy. The fruit is assumed to be a remarkable remedy for 'Dropsy' in North India, as well as having a purgative effect.[23,25,27] According to Unani medicine, the fruit has a bitter flavour and heals chronic bronchitis and lung complaints. The anthers of the flower are given orally in Ayurveda to assist delivery. The mature seeds and fruit are cathartic and emetic in nature. Women use *Luffa* to restore missing feminine cycle, while nursing mothers use it to enhance milk supply, according to Ayurveda.[26,28] To eliminate dead skin and stimulate the skin, the entire *Luffa* "sponge" is sometimes rubbed on the skin. *Luffa* charcoal, which is managed to make by burning *Luffa* fibres in a closed container, is used directly to the skin to treat shingles in the face and eye area, and powdered *Luffa* is now used in cosmetics to decrease swelling and cleanse the skin.[8,29] The fruit is bitter, powerful cathartic, anthelmintic, antipyretic, stomachic, and treats boils, piles, jaundice, chronic sinusitis, epilepsy, and kaphaja shiroroga, according to Ayurveda.[9] When taken in modest doses, it can help with indigestion, hepatic disorders, jaundice, piles, and so on; when taken in high doses, it can help with ascitis, anaemia, poisoning, worm infestation, and so on. It acts as a purgative and emetic by causing projectile vomiting and a significant volume of loose droppings.[30,31] In the Garhwal hills tribes of northern Uttar Pradesh, India, fruits are also used as snuff.[32] People with cardiac disorders should avoid taking *Luffa echinata* or its formulations, according to a recent investigation, because it provokes emesis and sometimes purgation, which can bring auxiliary pressure on the cardiac muscles. *L. echinata* should also be avoided by children, the elderly, and expectant mothers. Table 5 highlights the home remedies and ethanomedicinal benefits of *Luffa echinata.*[6,33-36]

During the survey, it was observed that the Tribal community (Tharus) of Khatima utilised a soaked sponge of fruits of *Luffa echinata* adequately squeezed in a glass of water. Then this highly bitter, squeezed fruit material is given to victims of dog bites in the morning with an empty stomach, and more than 500 people have been treated successfully till now. However, it still has not grabbed considerable attention. I hope it will provide a novel idea for further research on the phytochemical aspects of these plants, which might lead us towards developing new medicines for the welfare of human beings.[37]

DIETARY AND NUTRITIONAL CONSIDERATIONS

The *Luffa* fruit contains a wide range of antioxidants, minerals/trace elements, vitamins, nutrients, and fats. The nutritional potential of the *Luffa* fruit is evidenced in [Table 6] based on its biochemical profile.[38] The dosage of dry *Luffa* fruit recommended by the conventional medical system ranges from 1-3 g per day. According to a literature review, *Luffa echinata* has a lethal dosage for mice of 21.5 mg/kg body weight.[39] The seeds of *Luffa echinata* are a rich source of nutrients such as proteins and oils that might be used directly or indirectly to alleviate malnutrition in underdeveloped nations by including them into various food and feed fortification formulas. This valuable crop may be used to make edible oil, food, and fodder, or it can be used to make industrial oil/biodiesel from non-edible seed varieties. The protein-rich seed might be investigated further for use in the fortification of food items to increase their value.[17]

PHARMACOLOGICAL TESTIMONY

Luffa echinata has been shown to help inhabitants with diverse of maladies. Hypoglycaemic, anti-cancer, ulcer-protective, anti-microbial, hepatoprotective, thrombolytic, anti-inflammatory, antiarthritic, analgesic, antipyretic, antihypertensive, anthelmintic, diuretic and laxative, cytotoxic, antioxidant, and anti-hyperlipidemic activity have all been reported from extracts of *Luffa echinata* and its parts.[4,40]

This plant's active ingredients include saponins, hentriacontane, gypsogenin, sapogenin cucurbitacin-B and E, β-sitosterol, echinatol-A and B, oleanolic acid, elaterin glycoside, chrysoeriol-7-glucoside, and sitosterol glycosides, among others.[39,41] These active ingredients are known to affect the human body in a wide range of pathological ways. Although there haven't been many reports of *Luffa echinata*-related human toxicity in the past, there have been a few instances of other cucurbit-related human toxicity. Additionally, documented five cases of colocynth toxicity-related bloody diarrhoea[42] and reported hematemesis from consuming bitter gourd juice.[43] Consequently, it stated that a significant number of 15 cases of gastrointestinal bleeding and hypotension caused by consumption of bitter bottle gourd juice had been reported. This plant is also listed in the US-listing FDA's of toxic plants.[44]

Cucurbitacin, a complex chemical found in varying amounts in *Luffa echinata*, gives the plant its distinctive aroma, bitter flavour, and protection against pests and animals. The cytotoxic effects of cucurbitacin B and C result in the G_2 cell cycle arrest and death of cancerous cells *via* a reactive oxygen species dependent mechanism [Figure 7].[45] They also block the JAK/STAT and STAT3 pathways. Many types of cancer, including pancreatic, melanoma, breast, and colon cancer [Figure 8],[46] have been tested with them. Additionally, the antioxidant, anti-inflammatory, and cardiovascular properties of cucumbertin are present. Some cucurbitacin's anti-inflammatory properties are associated with the suppression of the cyclooxygenase enzyme.[47] Similarly, through the cell cycle arrest and induction of apoptosis in human bladder T24 cancer cells *in-vitro*, cucurbitacin also reduced the percentage of viable T24 cells [Figure 9]. Cucurbitacin E-induced G2/M phase arrest was connected to STAT3 phosphorylation inhibition, STAT3 promotion of p53 and p21, and CDK1 and cyclin B decrease. The death of T24 cells caused by cucurbitacin E was followed by an increase in Fas/CD95, a decrease in the amount of $\Delta\Psi m$, the release of cytochrome-*c* from mitochondria, and enhanced activation of caspase-8, caspase-9, and caspase-3.[48] Similarly, the leaves and flowers contain the flavonoid chrysoeriol, which has strong antioxidant, anti-inflammatory, anti-thrombogenic, anti-atherogenic, and anti-cancer activities. Numerous studies have been conducted on the use of flavonoids and their synthetic counterparts in the treatment of various malignancies. By blocking oxygen radical-forming enzymes, enzymes involved in DNA synthesis, enzymes that imitate ATP, or protein kinases involved in proliferative signal transmission, they prevent the promotion stage of carcinogenesis. By blocking DNA topoisomerase II, p53 downregulation, or by producing mitochondrial toxicity, they may stop the growth of tumours by forcing tumour cells to apoptosis. Excess flavonoids can result in hemolysis, liver failure, contact dermatitis, and other conditions. Flavonoids' toxicity is a topic of ongoing research.[49]

The global incidence of viral comorbidities caused by SARS-CoV and MERS, which are members of the coronavirus family, have increased during the past two decades. As a consequence, the most recent findings suggested that the natural chemical cucurbitacin has the potential to be a therapeutic medication against COVID-19, especially in light of the extremely positive outcomes obtained with cucurbitacin. Utilizing various pertinent tools and simulated screening techniques, cucurbitacin analogues were tested for activity against the SARS-CoV-2 main protease protein, angiotensin-converting enzyme 2 binding receptor, non-structural protein 12 RNA-dependent RNA polymerase, NSP13 helicase, and Janus kinase 2/signal transducer and activator of transcription 3 pathway. Only the cucurbitacin G 2-glucoside and cucurbitacin H with the lowest global energy were found to bind all essential proteins effectively. Future studies on SARS-CoV-2 preventative measures and treatments may use the study's encouraging results as a jumping off point.[50]

Table 3: Physicochemical parameters of *Luffa echinata*.

Parameter	Aerial parts (%w/w)	Fruit part (%w/w)
Total Ash Values	23.66	8.33
Acid Insoluble Ash Values	8.1	6.66
Water Soluble Ash Values	21.33	4.1
Moisture content	12.1	11.70
Water Soluble Extractive Values	13.6	15.20
Alcohol Soluble Extractive Values	7.20	8.10
Foreign matter	1.10	0.50

Reported analgesic effects of the seeds after being macerated in cold methanol for 72 hr. Eddy's hot plate method and tail immersion were used to measure activity in Swiss albino mice. Significant activity was noted at increasing concentrations, and the highest response was noted at 180 min after the dosages of 50, 150, and 200 mg/kg body weight were delivered orally. Additionally, paw volume significantly decreased (by 60.57%) at the documented dose level due to the extract's anti-inflammatory activity as compared to the reference drug, diclofenac sodium. Treatment with the extract resulted in a considerable, dose-dependent reduction of paw oedema, suggesting the possibility of using it to treat inflammation and pain naturally by acting as an antioxidant.[51] Consequently, fruit extract has considerable anti-arthritic efficacy against adjuvant-induced arthritis, supporting its use as a treatment for the ailment. At a dose of 250 mg/kg/p.o., Freund's adjuvant induced arthritis rats in both the developing and developed stages showed normalisation of haematological and biochemical abnormalities.[52]

The documented evidence backed up the traditional medical applications of *Luffa echinata* for treating stomach ulcers. The ethanolic extract of the aerial parts of the plant has dose-dependently decreased gastric content, total acidity, ulcer index, and elevated pH of gastric fluid.[53] Recent research further suggests that the methanolic fruit extract had bronchodilatory, anti-inflammatory, and mast cell stabilising effects. In asthmatic animals, leucocytosis and the condition known as anaphylactic hypersensitivity were also reduced by the methanolic extract of the fruit.[54]

The traditional usage of the plant for treating and managing diabetes mellitus has been supported by recent research using a 200 mg/kg dose of hydroalcoholic extract of *Bristly luffa* fruit. Researchers investigated the beneficial effects of the fruit extract in regulating hyperglycemia. The extract improved renal and hepatic functions and decreased glycated hemoglobin levels in both acute and chronic models, demonstrating its anti-hyperglycaemic efficacy.[55] Subsequently, fifteen members of the Cucurbitaceae family were examined by Shukla *et al.*, (2019) for the presence of

Table 4: Organoleptic characters of *Luffa echinata*.

Plant parts	Parameters	Perception
Flowers	Colour	White
	Odour	Slightly aromatic
	Taste	Bitter
Fruits	Colour	Greenish yellow
	Odour	Disagreeable
	Taste	Bitter dull
Seeds	Colour	Blackish brown
	Odour	Characteristic aroma
	Taste	Bitter
Stem	Colour	Yellowish-brown to brownish black
	Odour	Disagreeable
	Taste	Bitter
Aerial part without fruit and flower	Colour	Greenish yellow
	Odour	Slightly disagreeable
	Taste	Slightly bitter

anti-diabetic activities. The *Luffa echinata* fruit fraction preserved in chloroform performed better than the other eight fractions of the four plants that the researchers claimed demonstrated potential activity. The glucose absorption experiment showed that this active fraction, which underwent bioactivity-guided column fractionation, was the most potent. The 0.59 μg/mL EC_{50} value identified a strong anti-diabetic compound. Further study into the anti-diabetic characteristics of the *L. echinata* fruit would be intriguing since it could develop a novel plant-based compound for the treatment of Type II diabetes.[56]

The liver plays a crucial function in the metabolism, secretion, storage, and detoxification of both endogenous and foreign chemicals. Free radicals and oxidative stress increase the severity of liver damage, which the antioxidant mechanism can mitigate. Plant extracts are the best source of these antioxidants that promote hepatoprotective activity.[57] The various *Luffa echinata* fruit extracts were examined for their ability to protect albino rats' livers from carbon tetrachloride-induced damage. The petroleum ether, acetone, and methanolic extracts demonstrated significant hepatoprotective efficacy comparable to that of silymarin. The serum levels of SGOT, SGPT, ALKP, TP, and TA were all considerably reduced when exposed to carbon tetrachloride. All crude extracts decreased SGOT, SGPT, and ALKP; acetone, methanol, and petroleum extract were, respectively, the most effective.[41] Similar to this, several researchers have tried to assess the potential impact of an acetone extract of the root of the *L. echinata* on the induced hepatotoxicity in albino rats. Biochemical markers such as total bilirubin, direct bilirubin, aspartate aminotransferase, alanine aminotransferase, and complete protein in serum were used to determine the level of

Table 5: The home remedies and ethanomedicinal benefits of *Luffa echinata*.

Fruit and seed	Cold infusion of seeds or fruits causes moderate purgation and vomiting, as well as copious nasal discharge. This recipe can also be used to treat jaundice and headaches.
Fruits	After soaking for 5-10 min in a glass of water, a mature sponge of fruit is pressed completely. On an empty stomach, the extracted material is given to the dog bite victim in the morning. Furthermore, in situations of dog bite, a fine powder of ripe *L. echinata* fruits, *Aegle marmelos* leaves, and *Piper betle* leaves is given once a week for three weeks. Fruit decoction has also been used as a toxin-removal enema.
Seeds	The seeds' fine powder can help with gaseous tumors and alcoholic liver disorders.
Leaf	Fresh leaf juice is used to purify the blood, whilst decoction is used to cure rheumatism topically.
Roots	Root powder taken orally once a day in the morning aids in the management of haemorrhoids, whilst root paste brined in mustard oil and applied topically to the body surface aids in the treatment of leprosy.
Whole plant	The decoction or hot infusion of dried *L. echinata* plants is used to expunge wounds and sores, while daily 20-30 ml dosage of hot infusion of the plant (dried) is given to adults with abdominal worms. If the drug is used for 5-6 days, it has a profound effect.

contribution. A histopathology investigation was also reported to assess the impact of root extract on the liver's tissues. The outcomes demonstrated the considerable hepatoprotective action of acetone extract.[58] *L. echinata*'s effect on liver damage has been scientifically examined and documented concurrently. Researchers found that albino rats' experimentally caused liver damage was better prevented by ether extract.[59] According to practitioners of the traditional medicine system, this plant's fruits are effective in treating jaundice. Thus, *Luffa echinata* fruits' impact on experimental jaundice in rats was documented by S.K. Bapat and Vimal Chandra in 1968. Chlorpromazine given intraperitoneally to albino rats of either sex caused jaundice, and various doses of the fruit extract were fed to sick rats through a stomach tube. The aqueous extract dramatically reduced total and conjugated bilirubin levels in rats, resulting in this distinctive effect.[60] Although the natural course of viral hepatitis is very variable, it has been demonstrated and documented that a single dosage of *L. echinata* significantly impacts liver function within 2 to 7 days. Six male patients between the ages of 20 and 24 participated in the trials. Clinical and analytical standards were used to determine the diagnosis of viral hepatitis. The dry fruits

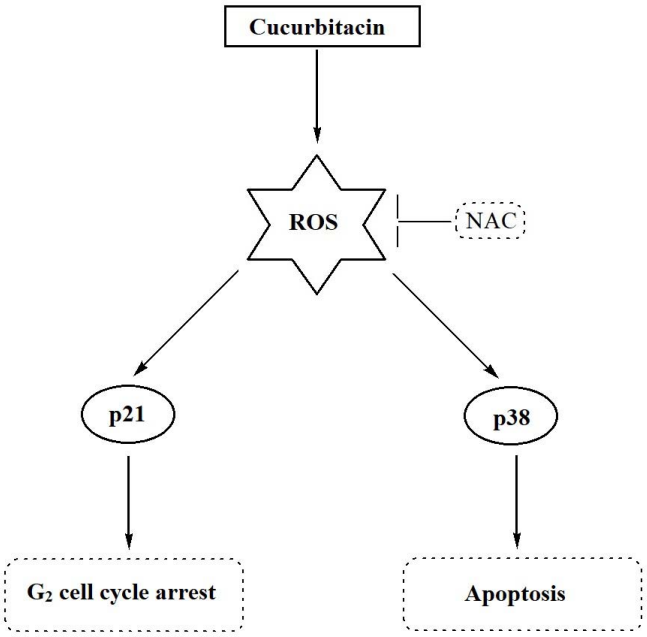

Figure 7: Cucurbitacin's effects are illustrated schematically. The stress-activated protein kinases (p21 and p38) signaling pathways are triggered by cucurbitacin's inhibition of ROS, which leads to the induction of apoptosis and the arrest of the G2/M cell cycle, accordingly.

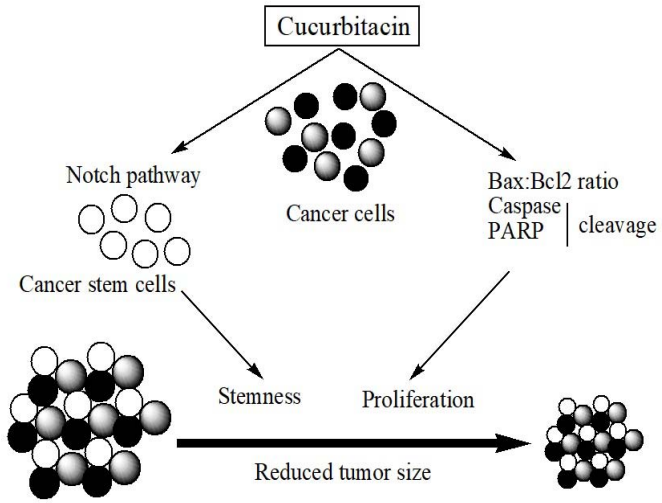

Figure 8: According to a schematic, cucumbertin prevents colon cancer tumour growth.

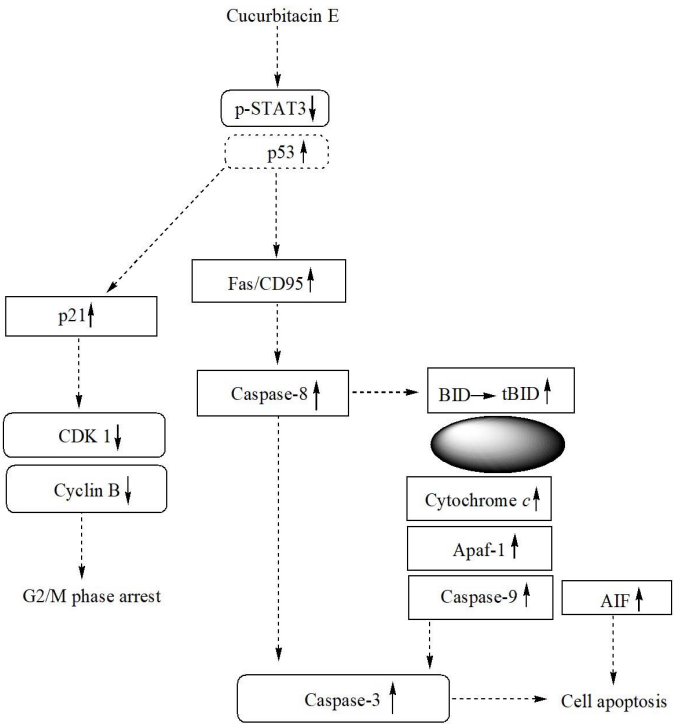

Figure 9: The putative signaling pathways for cucurbitacin E-induced G2/M phase arrest through STAT3/p53/p21 signaling and apoptosis via Fas/CD95 and mitochondria-dependent pathways in human bladder cancer T24 cells.

of *L. echinata* were soaked, squeezed, and then three to five drops were delivered once into each nostril of the patient. Freshly soaked fruits were used for each patient in place of the used fruits, which were discarded. Blood counts, urinalysis for the presence of bile salts and bile pigments, as well as serum tests for bilirubin, transaminases, and alkaline phosphatase, were all monitored. The nasal fluids' bilirubin content was examined in order to challenge the widespread idea that yellow nasal secretions exist. Clinical symptoms, especially anorexia and malaise, experienced a significant improvement along with the biochemical response. Hepatomegaly and icterus were reduced more gradually. After the drops were placed in the nose, a profuse rhinorrhea began after an hour or so and continued for 18 to 20 hr. Two patients complained of earache, ear burning, and epigastric discomfort as minor symptoms. Total bilirubin levels in the nasal secretions ranged from 1.62 to 5.5 mg%. The observations do not support a straightforward explanation of the alleviation of jaundice by increased nasal bilirubin excretion, and the levels were not higher than the serum levels. The active ingredients may pass through the nasal mucosa and affect the liver.[61]

It has been claimed that Bindaal has CNS depressive, anxiolytic, and anti-epileptic properties. Many responses have been observed in experimental animals given methanolic fruit extract.[62] Similarly, Chaturvedi *et al.* (2013), demonstrated the antiepileptic activity of fruit extract exposed to phytochemical screening, acute toxicity investigations, and antiepileptic activity by maximal-electroshock (MES) and pentylenetetrazol (PTZ) caused convulsions in Swiss albino mice. Mice in the acute toxicity investigation did not exhibit any toxicological symptoms. The results indicate that *Luffa echinata* methanolic fruit extract may exert its anticonvulsant effects through non-specific pathways because it both decreased the length of seizures brought on by maximum electroshock and postponed the onset of seizures brought on by pentylenetetrazol.[63]

One of the underutilised medicinal plants, *Luffa echinata* is employed in many Ayurvedic formulations and is a significant source of bioactive metabolites. According to the verified survey, the fruit and leaves can be exploited as a potent bioresource for natural antioxidants, anti-diabetic, and anticancer drugs. The antioxidant capacity of the leaf and fruit extracts was

Table 6: Nutritional potential of *L. echinata* fruits.

Parameters	Fruit
Total protein (g)	1.17
Total fat (g)	0.61
Carbohydrate (g)	25.53
Total sugars (mg%)	9.2
Dietary fibres (g%)	5.2
Vitamin A (µg)	463
Vitamin E (mg)	0.43
Vitamin K (µg)	3
Vitamin B_1 (mg)	0.082
Vitamin B_2 (mg)	0.075
Vitamin B_3 (mg)	0.463
Vitamin B_5 (mg)	0.892
Vitamin B_6 (mg)	0.176
Vitamin B_9 (µg)	21
Vitamin C (mg)	10.1
Sodium (mg)	37
Potassium (mg)	806
Calcium (mg)	16
Manganese(mg)	0.397
Copper (mg)	0.151
Iron (mg)	0.64
Zinc (mg)	0.3
Magnesium(mg)	36
Selenium (µg)	0.4
Phosphorous (mg)	55
Palmitic acid(g)	0.034
Oleic acid(g)	0.112
Stearic acid (g)	0.014
Linoleic acid(g)	0.263
Food energy value (kcal/cup) 1 cup (178 g)	100

reported and assessed by assessing DPPH, ABTS, FRAP, PMA, and MC activities. The methanolic extract of the leaf and fruit depicted the most promising DPPH radical scavenging activity of all the extracts studied. Additionally, leaf and fruit extracts demonstrated promising anti-acetylcholine esterase and anti-diabetic (α-amylase, α-glucosidase inhibitory) properties. The proliferation of the cancer cell lines MCF-7 and HT-29 was successfully inhibited by a methanolic extract of fruit.[64] Similarly, hydroalcoholic (50%)[65] and hydromethanolic (80%)[66] extract of dried fruit was also asserted to have a high content of total flavonoid and total phenolic compounds and possess better antioxidant activity in ORAC, TEAC, and DPPH free radical scavenging activity assay as well as in lipid peroxidation and possessed hydroxyl radical scavenging activity.

The search for antimicrobial activities of *Luffa echinata* found that the fruit extract (dichloromethane: methanol; 1:1) at 500 µg/mL dose level totally inhibited *Bordetella bronchiseptica, Streptococcus faecalis*, and only partially inhibited *Staphylococcus aureus* when used in agar dilution streak methods. In contrast, a dose of 1000 µg/mL totally inhibited *Bacillus subtilis, Staphylococcus aureus*, and *Micrococcus luteus*. It did not effect on *Aspergillus niger, Candida albicans, Bacillus cereus, Staphylococcus epidermidis, Escherichia coli, Klebsiella pneumonia, Bacillus pumilus,* or *Saccharomyces cerevisiae.*[67]

It is becoming better acknowledged that medicinal plants and their phytocompounds are effective adjunct therapies for cancer. Recent research portrayed that the methanolic extract of *Luffa echinata* fruits inhibits the proliferation of human colon cancer cells (HT-29) by triggering G2/S arrest and promoting apoptotic cell death in a dose- and time-dependent manner. Additionally, the extract stimulates the production of reactive oxygen species (ROS) and mitochondrial membrane potential (MMP) loss while controlling the Bax and Bcl-2 genes. According to these literature surveys, the *Luffa echinata* fruit induces the apoptosis of colon cancer cells, which has anticancer effects.[68] The methanolic extract of fruits similarly exerts its anti-proliferative effects on the human colon cancer SW480 cell line by causing apoptotic cell death, as was mentioned before. The intracellular metabolic system was also stimulated by treatments using different extract concentrations, which resulted in the dose-dependent release of *Lactate dehydrogenase* (LDH). *Luffa echinata* fruit extract damaged DNA, induced apoptosis, and produced more reactive oxygen species in AW480 cells. These findings revealed that the usage of fruit extracts resulted in the mitochondrial apoptosis pathway, which is responsible for cell death, by upregulating the p53 protein, which controlled the expression of proteins that promote apoptosis.[69]

EXPLORATION OF BIOACTIVE COMPOUNDS AND PHYTOMOLECULES

Numerous Researchers have discovered this plant's possible therapeutic constituents to include various biochemicals such as alkaloids [Figure 10], phytosterols [Figure 11], flavonoids/ isoflavonoids [Figure 12], chalcone, glycosides, terpenoids [Figure 13], saponins, carbohydrates, proteins, reducing sugars, fatty acids, tannins, phenolic compounds and xanthones [Figure 14]. The active constituents of the plant also include saponins, hentriacontane, gypsogenin, sapogenin, cucurbitacin (A, B, C, D, E, K, S and I), β-sitosterol, echinatol (A and B), oleanolic acid, isoquercetin, quercimeritrin and sitosterol glycosides.[39] The aerial parts of *Luffa echinata* showed the presence of alkaloids, glycosides, carbohydrates, proteins, and flavonoids; but the roots exhibited sterols, triterpenes,

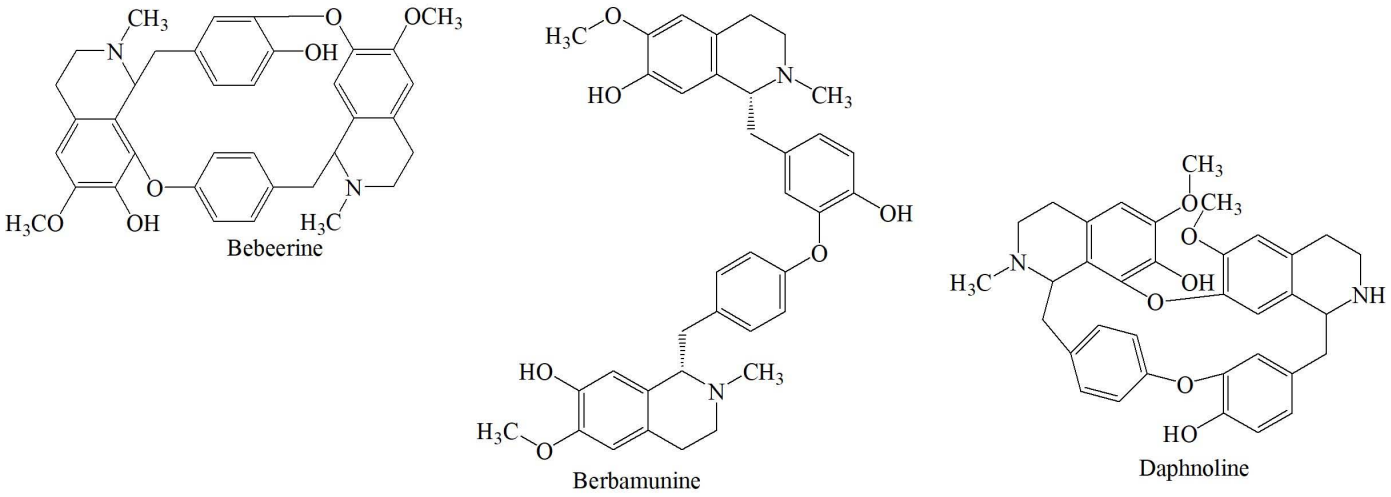

Figure 10: Alkaloids purportedly isolated from *Luffa echinata*.

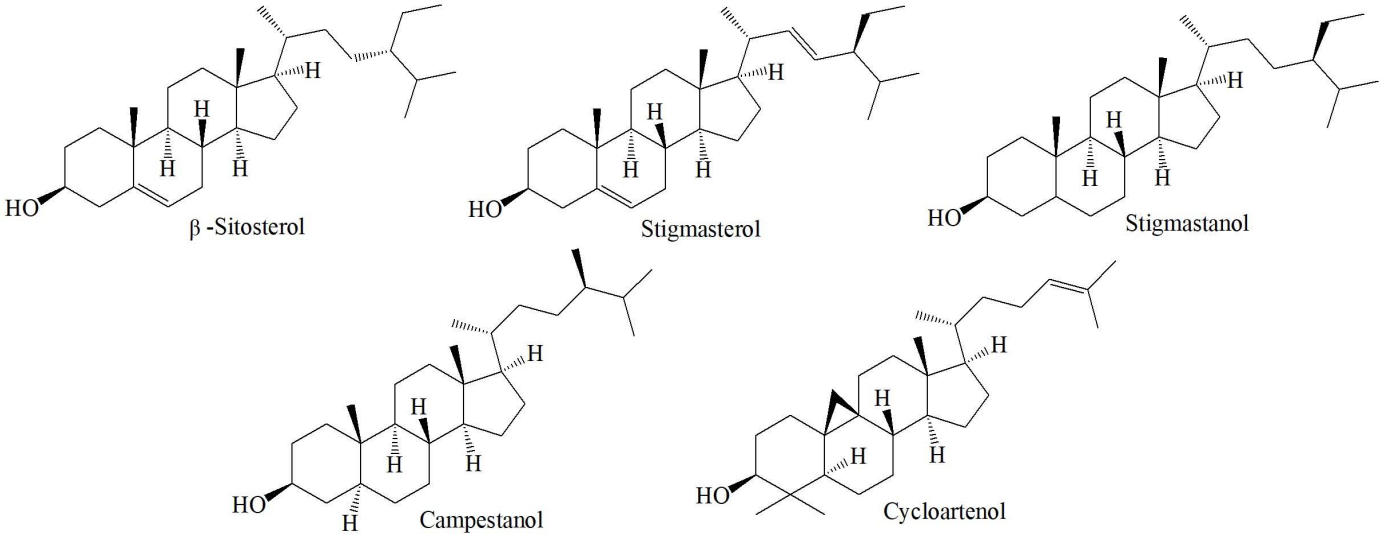

Figure 11: List of isolated phytosterols documented from *Luffa echinata*.

reducing sugars, glycosides, flavones, and tannin; whereas the fruit includes chrysoeriol and its glycosides as the primary flavonoids; however, the seed contain triterpene alcohols, echinatin, sapogenin, and cucurbitacin.[70] Cucurbitacins are chemically characterized by tetracyclic cucurbitane (triterpene hydrocarbon) nucleus skeleton 19-(10→9β)-abeo-5α-lanostane base, varied by the positional substitution of an oxygen atom [Figure 15].[71] The hydrocarbon, hentriacontane, saponin and the sapogenin known as gypsogenin are all present in the oil of the fruits of *Luffa echinata*.[72] Additionally, analysis of fruit extract using High-performance liquid chromatography in conjunction with Electrospray Ionization-Quadrupole-Time of Flight-Mass Spectrometry (LC-ESI-QTOF-MS/MS) revealed a variety of compounds belonging to terpenoids, phenolics, alkaloids, and fatty acids, all of which were disclosed concurrently [Table 7]. As compared to leaves, fruits had the highest content of cucurbitacin B, followed by cucurbitacin I and cucurbitacin E, as evidenced by reversed-phase high-performance liquid chromatography analysis. Gallic acid, catechin, vanillic acid, chlorogenic acid, and coumaric acid were also detected in fruit and leaf extracts after RP-HPLC analysis, with the highest concentrations observed in the fruits.[64] 2-O-β-d-glucopyranosyl cucurbitacin B, 2-O-β-d-glucopyranosyl cucurbitacin Sand Datiscacin, a novel cytotoxic α-cucurbitacin 20-acetate have been isolated from the fruits of *Luffa echinata*.[73] Additionally, the fruit also contains rare flavonoid, chrysoeriol occurs along with its 7-glucoside and 7-apioglucoside and other flavones like apigenin (apigenin 7-*O*-glucoside and apigenin 7,4'-diglucoside) and luteolin along with the graveobiosides-B, bitter elaterin-2-glucoside (Cucurbitacin E), isocucurbitacin-B, β-sitosterol glucoside[74] and a bitter gelatinous substance luffein[75] Subsequently, two new lanostane type triterpenes like lanost 6(7),23(24)-dien e-3,11,22trione-20,25-diacetoxy-2-β-16-α-diol and lanost 1(2),6(7),23(24)-triene-3,11,22-trione-20,25-diacetoxy-

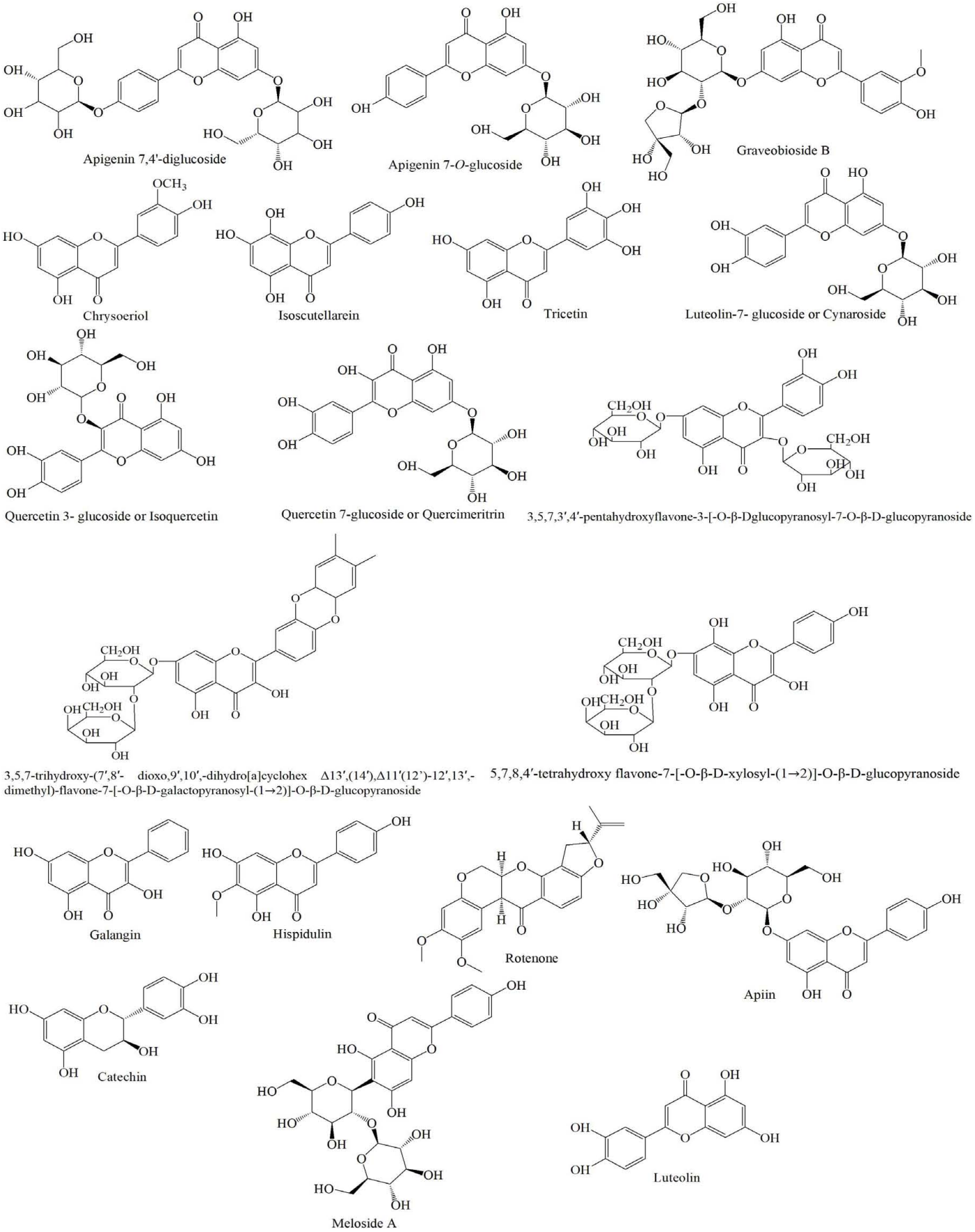

Figure 12: List of *Luffa echinata* isoflavonoids and flavonoids that have been identified and reported previously.

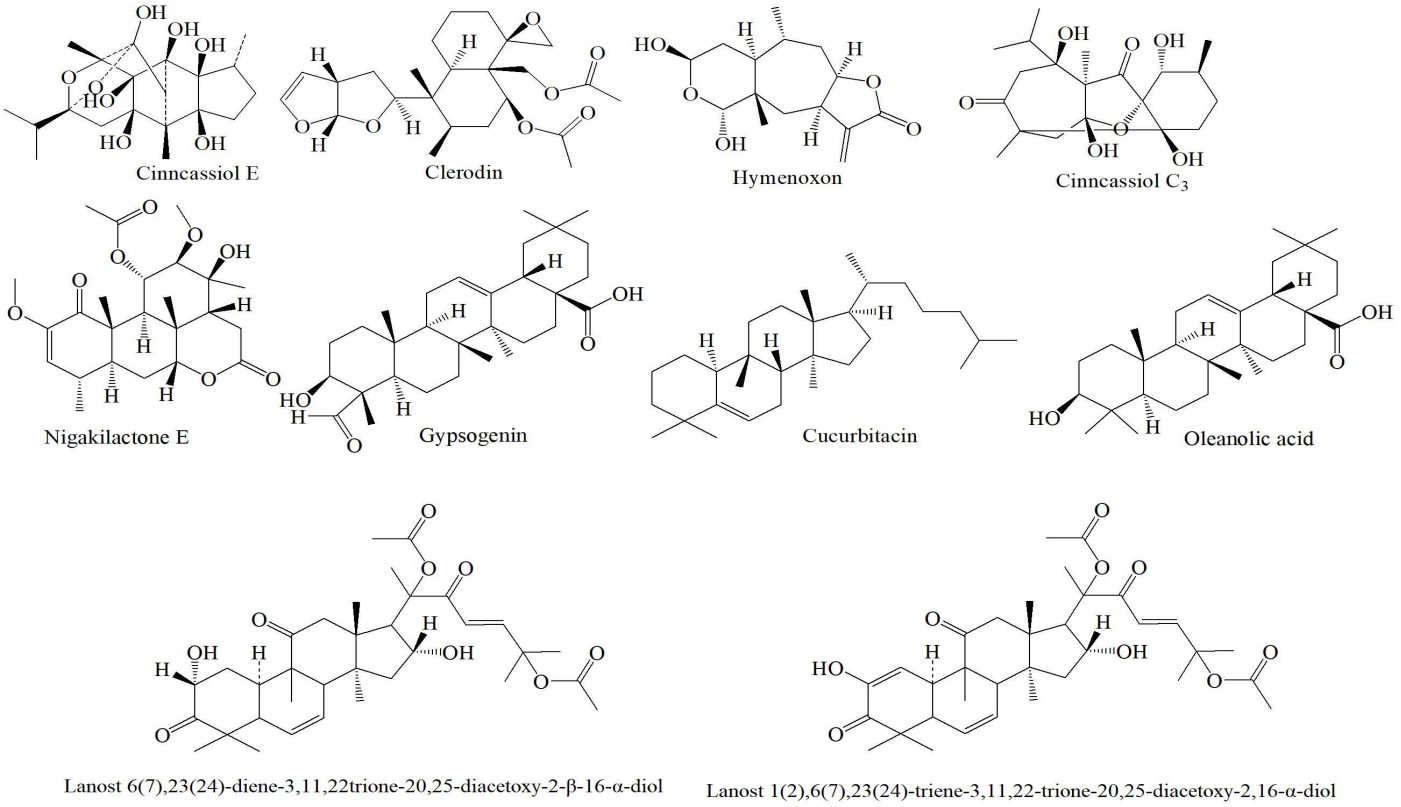

Figure 13: List of isolated terpenoids from *Luffa echinata*.

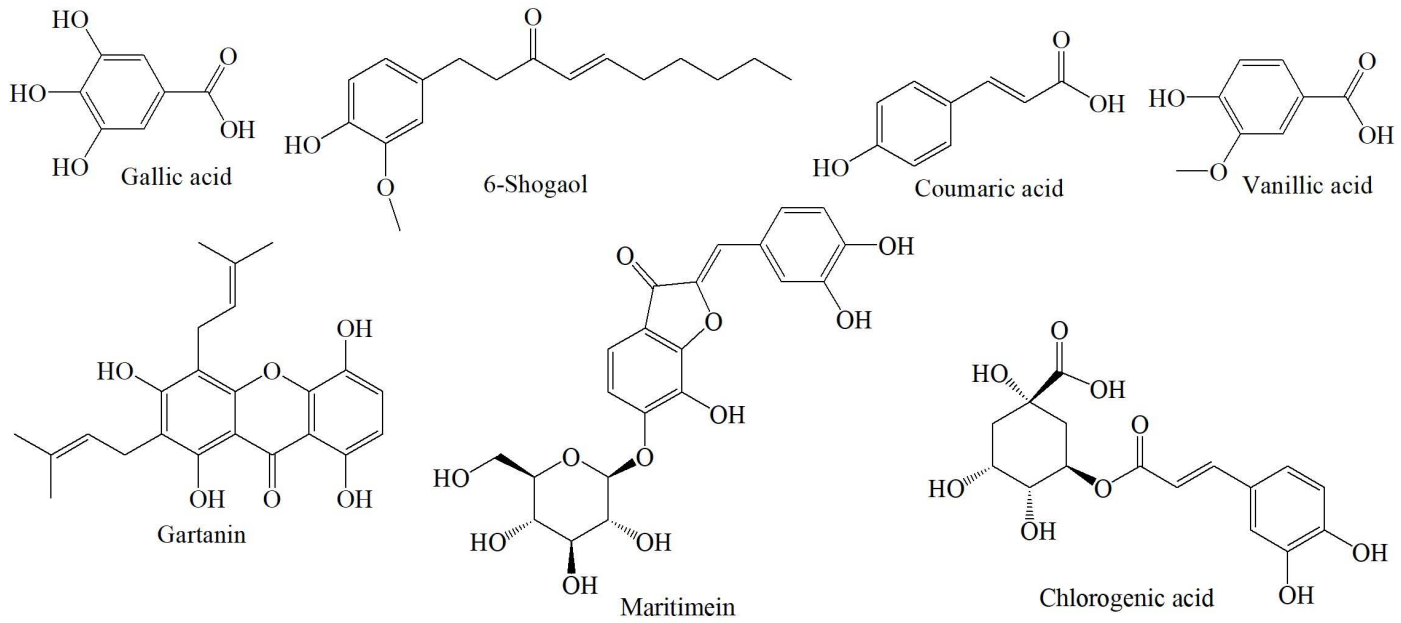

Figure 14: Reported of xanthones and phenolic compounds from *Luffa echinata*.

2,16-α-diol were isolated and reported from active acetone fruit extract which have potent hepatoprotective activity.[76] In addition, bioactive polar extracts of fruits also contain three new flavone glycosides like, 3,5,7,3′,4′-pentahydroxyflavone-3-[-O-β-D-glucopyranosyl-7-O-β-D-glucopyranoside; 3,5,7-trihydroxy-(7′8′-dioxo,9′,10′-dihydro-[a]cyclohex$\Delta^{13'(14')}$, $\Delta^{11'(12')}$-12′13′-dimethyl)-flavone-7-[-O-β-D-galactopyranosyl-(1→2)]-O-β-D-glucopyranosideand5,7,8,4'tetrahydroxyflavones-7-[-O-β-D-xylosyl-(1→2)]-O-β-D-glucopyranoside. These three isolated reported compounds are new analogues of tricetin,

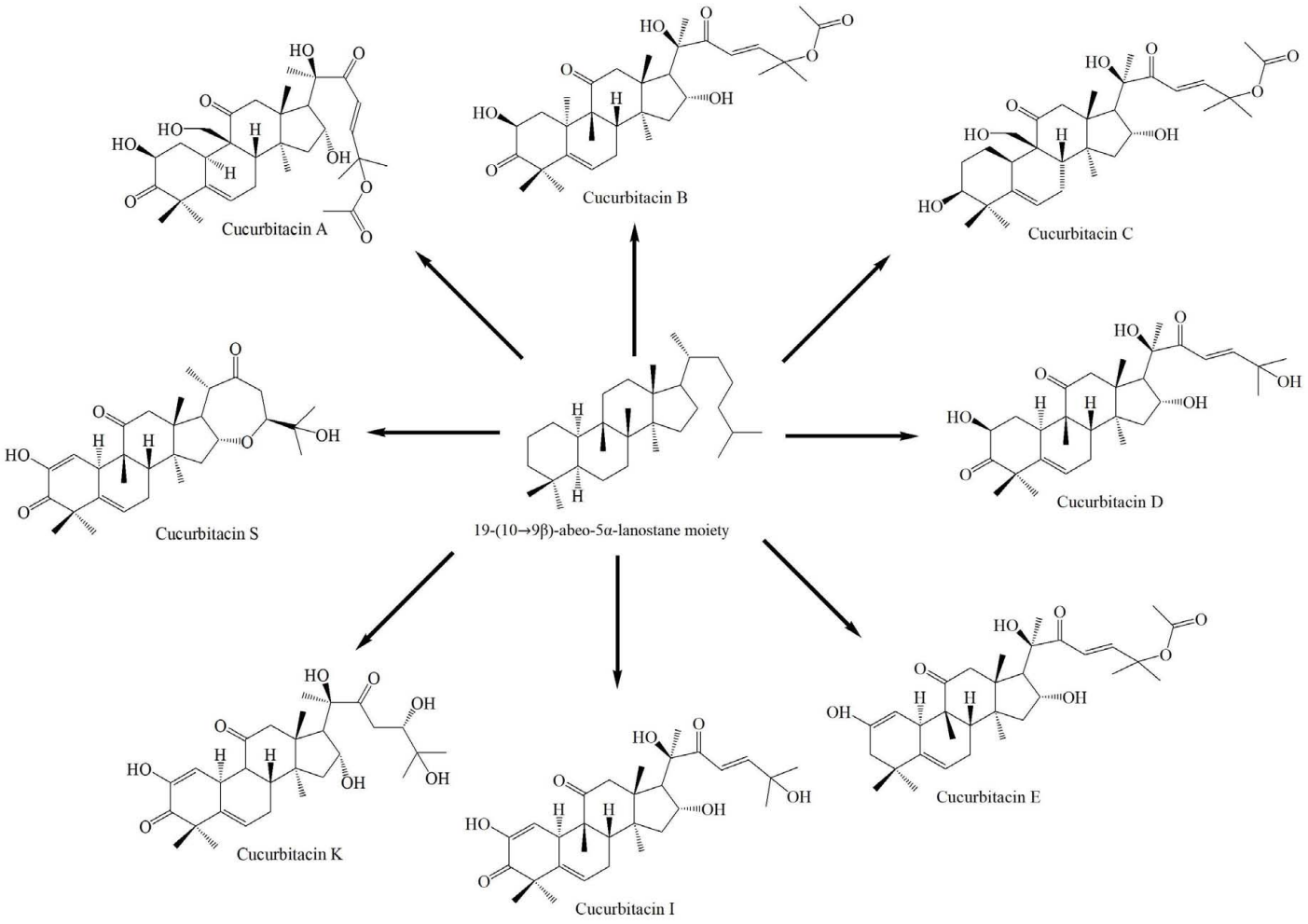

Figure 15: Cucurbitacins, which were found in *Luffa echinata*, are chemically distinguished by the tetracyclic cucurbitane (triterpene hydrocarbon) nucleus skeleton 19-(10→9β)-abeo-5α-lanostane.

Table 7: LCMS-ESI-Q-TOF-MS detected reported phytoconstituents from *L. echinata* fruit extract.

Category	Name of the compounds
Alkaloids	Berbamunine, Bebeerine, Daphnoline
Flavonoids/ isoflavonoids	Galangin, Hispidulin, Rotenone, Apiin, Meloside A.
Triterpenoids	Cinncassiol E, Clerodin, Hymenoxon, Cinncassiol C_3, Nigakilactone E
Phenols/ Xanthones	6-Shogaol, Gartanin, Maritimetin (yellow pigment).
Fatty acid	Methyl N-(a-methylbutyryl) glycine, Dimethyl adipate, Traumatic Acid, Chaulmoogric acid, Di(2-ethylhexyl) adipate, Palmitic acid, Petroselinic acid, 2-Isopropylmalic acid, 3-Hydroxyisoheptanoic acid, Traumatic Acid, Sebacic acid,9S,12S,13S-trihydroxy-10E-octadecenoic acid, 9,10-hydroxyoctadec-12(Z)-enoate.

quercetin and isoscutellarein.[77] Schilling and Heiser (1981) identified flavonoids in leaves and flowers, finding that luteolin 7-glucoside (Cynaroside) was detected in the leaves while chrysoeriol-7-glucoside and luteolin-7-glucoside were observed in the flowers.[78]

PERSPECTIVE AND EMERGING EXPECTATIONS

Luffa echinata, one of the underutilised medicinal plants, is used in many Ayurvedic formulations and is a substantial source of bioactive metabolites. The validated survey claims that the fruit and leaves can be a powerful bioresource for natural antioxidants,

anti-diabetic, and anticancer medications. Extensive research have revealed that this plant may contain a wide range of phytochemicals that have medicinal potential, including alkaloids, phytosterols, flavonoids/isoflavonoids, chalcone, glycosides, terpenoids, saponins, carbohydrates, proteins, reducing sugars, fatty acids, tannins, and phenolic compounds as well as xanthones. Additional active plant phytoconstituents include saponins, hentriacontane, gypsogenin, sapogenin, cucurbitacin (A, B, C, D, E, K, S, and I), β-sitosterol, echinatol (A and B), oleanolic acid, isoquercetin, quercimeritrin, and sitosterol glycosides. Numerous reports have unambiguously demonstrated that Cucurbitacin, a significant class of triterpenoids present in *Luffa echinata*, is compelling. Review of their biological activity over many years has likely demonstrated the importance of natural bioproducts in drug detection at this point. According to numerous research models, Cucurbitacin and its derivatives are the main chemical entity responsible for the therapeutic impact. However, more research is needed to ascertain the specific activity of the bioactive substances found in *Luffa echinata*. Numerous research teams have thoroughly examined the medicinal effects of Cucurbitacin. Depending on the target cells, Cucurbitacin is thought to exert powerful biological effects such as cytotoxicity, anti-tumor properties, hepatoprotective properties, anti-inflammatory properties, antibacterial properties, cardiovascular outcomes, and anti-diabetic benefits on both humans and animals. Since ancient times, Indian and Chinese physicians have employed the fruit and leaves of *Luffa echinata* to treat liver disease, haemorrhoids, jaundice, migraines, emesis, and purgatives. They have also been used to expel ulcers and wounds. Recent studies have demonstrated that cucurbitacins can decapitate or slow the growth of cancer cells. To establish bench-to-bedside translation, however, it is essential to comprehend the physiopathological nature of numerous diseases linked to research on malignant neoplasms and how nanomaterials interact with biological systems at various levels (i.e., systemic, organ, tissue, and cell). It is crucial to fully understand the processes by which cucurbitacin works in diverse disease-related contexts. The efficacy of *Luffa echinata* has not yet been proven in toxicology and clinical trials. Even though the phytochemical data on roots, stems, and leaves also lacks scientific backing, this review's conclusion indicates a tonne of room for additional study of the neglected medicinal plant *L. echinata*. In-depth, longer-term experiments that contrast *Luffa echinata* with the current conventional drugs are needed to determine whether it is a functional complementary medicine for treating the illnesses above. The methods from these studies, which should be standardized, could be applied to future meta-analysis research.

EXPLORATORY CONCLUSION

Around the world, the use of herbal treatments has grown in recent years. Numerous natural substances, including those derived from plants, have been investigated as potential cures for various diseases. *Luffa echinata* Roxb., a mystery healing plant belonging to the Cucurbitaceae family, has recently become one of the most significant medicinal herbs. It is commonly utilised therapeutically in the Orient and is becoming more well-known everywhere. Following Prisma's recommendations, the literature was sourced from databases including Scopus, PubMed, Google Scholar, and Science Direct, and it was subsequently evaluated using a quality grading approach. This review mainly concentrated on pharmacological and phytochemical investigations that have clarified the therapeutic potential and phytoconstituents of *L. echinata*; more research is necessary to identify those phytoconstituents and their structures.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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ABBREVIATIONS

L. echinata: *Luffa echinata*; **IUCN:** International Union for Conservation of Nature; **cm:** Centimetre; **mm:** Millimetre; **g:** Gram; **mg/kg:** Milligram/kilogram; **FDA:** Food and Drug Administration; **JAK/STAT:** Janus Kinase/Signal Transducers and Activators of Transcription; **STAT3:** Signal Transducer and Activator of Transcription 3; **CDK1:** Cyclin-Dependent Kinase 1; **DNA:** Deoxyribonucleic acid; **ATP:** Adenosine Triphosphate; **SARS-CoV:** Severe Acute Respiratory Syndrome Coronavirus 2; **MERS:** Middle East Respiratory Syndrome; **COVID-19:** Coronavirus disease; **RNA:** Ribonucleic acid; **NSP13:** Non-structural protein 13; **mg/kg/p.o.:** Milligram/kilogram/by mouth; **pH:** Potential of Hydrogen; ***et al.*:** and others; **µg/mL:** Micrograms per millilitre; **EC_{50}:** Half maximal effective concentration; **SGOT:** Serum glutamic-oxaloacetic transaminase; **SGPT:** Serum glutamic pyruvic transaminase; **ALKP:** Alkaline phosphatise; **TP:** Total protein; **TA:** Total albumin; **hr:** Hours; **CNS:** Central nervous system; **MES:** Maximal-electroshock; **PTZ:** pentylenetetrazol; **DPPH:** 2,2-diphenyl-1-picryl-hydrazyl-hydrate; **ABTS:** 2,2'-azi no-bis(3-ethylbenzothiazoline-6-sulfonic acid); **FRAP:** Ferric reducing ability of plasma; **PMA:** Para-methoxyamphetamine; **MC:** Methylene Chloride; **ORAC:** Oxygen radical absorbance capacity; **TEAC:** Tetraethylammonium Chloride; **ROS:** Reactive oxygen species; **MMP:** Mitochondrial membrane potential;

Bax: BCL-2 associated x protein; **Bcl-2:** B-cell lymphoma 2; **LDH:** Lactate dehydrogenase; **LC-ESI-QTOF-MS/MS:** Liquid chromatography-electrospray ionization-quadrupole time-of-flight-mass spectrometry; **HPLC:** High Performance Liquid Chromatography.

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