

A Systematic Review of the Genus *Lactuca*

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Abstract— The genus *Lactuca* belonging to Asteraceae family is considered as the largest group of flowering plants. It is widely distributed in temperate and warm area, most widely in Northern Hemisphere and it includes nearly 150 species. A large number of *Lactuca* L. species have been farmed for their commercial as well as therapeutic use since ancient times. Several phytochemicals found in the *Lactuca* species are vital for treating a variety of illnesses in traditional medicine, such as pain, inflammation, lack of appetite, indigestion, urinary tract infections and pneumonia. The species exhibits a broad range of pharmacological properties, including antimicrobial, anti-cancer and antioxidant properties. It is also utilized in the management of neurological diseases. Due to its pain-relieving properties, lactucarium, a white, milky substance isolated from wild lettuce (*Lactuca virosa*), is sometimes referred to as "Opium lettuce" and has effects comparable to those of opium. The species is suggested as a natural remedy for a number of illnesses, including cancer, menstrual cramps, respiratory issues, arthritic problems, sleeplessness, poor circulation, and infections of the bladder. The purpose of this present review is to provide a thorough knowledge on taxonomical classification, geographical distribution, plant phytochemistry, traditional uses and pharmacological activities of genus *Lactuca*. The papers published in journals indexed in Science Direct, PubMed, and Google Scholar were reviewed to gather the information of various species of *Lactuca*.

Keywords— *Lactuca*; Asteraceae; Distribution; Pharmacological activities.

I. INTRODUCTION

Family Asteraceae is considered as the biggest family of flowering plants or angiosperms, consisting of about 1,600 genera and 24,000 species of trees, herbs and shrubs¹. This family of plant species can be found in nearly every type of habitat and has a global distribution. In addition to the arctic and alpine regions, these are widespread in temperate and tropical climates. Certain plants are aquatic or marsh plants, xerophytes, and epiphytes in addition to mesophytes. Rarely are there trees; instead, majority of the plants are either annual or perennial herbs, with a small number of shrubs and woody climbers^{2,3}. Cultivated lettuce (*Lactuca sativa*) is an economically important species of genus *Lactuca*, while important genitors for lettuce are *Lactuca serriola*, *Lactuca saligna* and *Lactuca virosa* are closely related species⁴.

Taxonomy

The term "*Lactus*", is a latin word which means milk, or the Greek word "Lac," are the sources of both the common name "Lettuce" and the generic name "*Lactuca*," which refer to the plant's milky sap. The species of the genus *Lactuca* was known by its common (vernacular) name, "Lettuce". Egypt was the first civilization to cultivate lettuce in order to get oil from its seeds.⁸ Around 150 species make up the genus *Lactuca*, which is mostly found in the Africa, Europe, North and Central America, Asia and Indonesia and other warm, temperate regions. With a few exceptions, most species are xerophytes that have evolved to thrive in arid climates. These plants are native to the rain forests of Central Africa^{2,5-7}. *Lactuca* species vary ecologically and can be found in a variety of habitats. *L. virosa*, *L. saligna* and *L. serriola* are some of the common European species, often favour and

ruderal environments that are disturbed². The species commonly referred to as "salad lettuce" in gardens is *Lactuca sativa*. Perhaps the closest relative of *L. Sativa* is *L. serriola* L., also referred to as "prickly lettuce" or "wild lettuce." however, *L. virosa* is a kind that is closely linked to *L. serriola*⁸. Various species of *lactuca* are given in Figure 1 and Table 1 shows the taxonomical classification of genus *Lactuca*.

Lactuca serriola (Prickly lettuce):

L. serriola is an annual to biennial therophyte. It grows preferably on carbonate-rich, fertile soil. The plant has naturalized in North America, Southern Africa, and South America and Australasia, is thought to be native to West Africa, East, and North (Mediterranean), as well as Europe and South Asia. Open habitats such as quarries, agricultural fields, ruins and scree and are home to this pioneer plant. It spreads throughout surfaces of disturbed soil and have become a common weed in suburban regions and growing cities. Due to its strong potential for invasiveness, especially its ability to establish at high elevations, *L. serriola* is a weedy species that is spreading throughout Europe along transportation routes such as highways and railroad tracks⁹⁻¹². Prickly lettuce is popularly known by different names and different languages which are as follows: Bazrul Khas (Arabic) Kahu, Kahukebeej (Hindi) Wild Lettuce (English), Salad Beej (Bengali) Prickly Lettuce, Kavuvitula (Telugu), Thridox (Greek), Guado, Sallattu Virai (Tamil), Kahu (Punjabi), Lattuga (Italian). In Persian and Urdu, the drug is commonly called as TukhmeKahu¹³. The whole plant of *L. serriola* is rich in milky sap. This milky sap pours freely from any incisions on the entire plant. Air contact causes this to solidify and dry out¹⁴.



Fig. 1. Various species of *Lactuca*

TABLE 1: Taxonomical classification of genus *Lactuca*

	<i>Lactuca serriola</i>	<i>Lactuca virosa</i>	<i>Lactuca sativa</i>	<i>Lactuca indica</i>
Kingdom	Plantae	Plantae	Plantae	Plantae
Clade	Tracheophytes	Tracheophytes	Tracheophytes	Tracheophytes
Clade	Angiosperms	Angiosperms	Angiosperms	Angiosperms
Clade	Eudicots	Eudicots	Eudicots	Eudicots
Clade	Asterids	Asterids	Asterids	Asterids
Order	Asterales	Asterales	Asterales	Asterales
Family	Asteraceae	Asteraceae	Asteraceae	Asteraceae
Genus	<i>Lactuca</i>	<i>Lactuca</i>	<i>Lactuca</i>	<i>Lactuca</i>
Species	<i>L. serriola</i>	<i>L. virosa</i>	<i>L. sativa</i>	<i>L. indica</i>

Lactuca virosa

L. virosa, belonging to family Asteraceae, also known as *Lactuca silvestris* Lam., is distributed in West Asia, North Africa, and Southwest Europe. It is also found in America. It thrives on rocky soil, either alone or in groups, on hills and plains up to 100Mm above sea level, and as a ruderal plant. *L. virosa* is a periodic herb with dense, branching roots that are fusiform. It generates a rosette of base leaves in the first year of vegetation, and an erect stem with branches in the upper section grows in the second year. It produces yellow, ligulate blooms that are arranged in unattached, pyramidal panicles, elongated. The flowering season starts from June to August. The leaves are blue-green in color, with tiny sagittate veins on top side and an egg-shaped or oblong-oval form at the base (15–20 cm long). White latex is produced by the stem, leaves, and roots; this latex darkens in the open air¹⁵. When smashed, the plant releases a white, milky material called lactucarium. This substance, when dried, mimics opium, a substance used to relieve pain that is opium poppies' immature seedpods. Opium and lactucarium may have comparable effects; however lactucarium has less negative consequences.

Wild lettuce has a long history of use, dating back to 1815, when it was studied for its potential as a whooping cough remedy and as a pain reliever. Products made from wild

lettuce are now widely accessible and include extracts from the leaves, milky fluid and seeds of plant. Those liquids, pills, powders, and oils are sold to cure a variety of ailments, such as joint pain, anxiety, insomnia, and breathing problems¹⁶. Lactucin, a sesquiterpinoid lactone, has been reported to be present in lactucarium at a concentration of about 0.2%. A mannitol, lactucerol (taraxasterol), caoutchoucand volatile oil are present in the mixture. Taraxasterol's acetyl derivative is lactucerin, which is also present in latex¹⁷⁻²⁰.

Lactuca sativa

L. sativa is considered as one of the most important group of green leafy vegetables. It belongs to the Asteraceae family²¹, which is believed to be the biggest family of plants, with between 23,000 and 30,000 species²². Its thought that domesticated lettuce originated in the Mediterranean region. A good source of almost all vitamins, lettuce also has a lot of minerals, such as calcium, phosphorus, iodine, iron, copper, and arsenic. Lettuce is well-known for its high vitamin C content, which helps to prevent infections and fight anaemia. The phytochemicals found in *L. sativa* are mostly classified as secondary metabolites, which are which are produced either in response to various environmental stimuli or during a plant's regular growth²³.

Lactuca indica

L. indica L., commonly referred to as Indian lettuce, is a laciferous plant in the Asteraceae family. It is extensively dispersed throughout Asia, particularly in Malaysia, Indonesia, China, Japan, India, and the Republic of Korea. This plant's leaves have been used for a very long time to wrap meat or rice and to make salads, soups, and fermented meals, known as "Kimchi" in Korea²⁴. The Roots, flowers, stems, seeds and leaves have been traditionally used as Chinese medicines for many years ago²⁵.

Phytochemical screening of *Lactuca* species:

Earlier phytochemical screening of *Lactuca* species had indicated the presence of bioactive compounds such as triterpenoids, saponins, sesquiterpene lactones, phenols, lignans, coumarins, phytosterols and numerous other miscellaneous metabolites. The plants remarkable therapeutic potential in the treatment of numerous ailments is directly attributable to the combination of these phytochemicals.

The phytochemical screening of *L. serriola* indicated the presence of secondary metabolites like sesquiterpene esters, lactucone, phenolic contents, lactucin, vitamins, iron, beta-carotene, lactucic acids, oxalic acid, lactucopicrin and alkaloids²⁶.

The plant *L. virosa* contains N-methyl- β -phenethylamine, coumarins and flavonoids and have anti-oxidant properties. These plants also have steroids, alkaloids, phenols, terpenes, volatile oils etc.

Methanolic extracts of the stems and leaves of various species of *L. sativa* were found to contain different types of secondary metabolites, including mucilage, saponins, steroids, flavonoids, carbohydrates and coumarins²⁷⁻³⁴. *L. indica* consists of secondary metabolites including alkaloids, phenolic compounds, sesquiterpene lactones, flavonoids, triterpenes, quinic acid derivatives³⁵⁻⁴⁰.

Traditional uses:

A large number of *Lactuca* L. species have been grown for their commercial and therapeutic benefits since ancient times. The sap's ingredient, "lactucarium," has antispasmodic, hypnotic, narcotic, digestive, sedative, anodyne and diuretic effects in medicine. Lactucarium functions similarly to a weak form of opium; however it does not have the same gastrointestinal side effects or addictive qualities. It is administered internally to treat rheumatic pain, whooping cough, dry cough, sleeplessness, anxiety, neuroses, and hyperactivity in children. Lactucarium concentrations are lowest in immature plants and reach their maximum when the plant flowers. Cutting off the plant heads and collecting the juice into china jars many times a day is how it is professionally gathered¹⁴.

L. virosa is used for whooping cough, asthma, urinary tract issues, cough, muscular or joint pains, difficulty falling asleep (insomnia), restlessness and excitability in children, men's swollen genitals (priapism), painful menstrual periods, women's excessive sex drive (nymphomania), poor circulation and in cough preparations as an opium substitute. The seed oil is a replacement for wheat germ oil and is used to treat "hardening of the arteries" (atherosclerosis). To eradicate

bacteria, some people apply the latex of wild lettuce directly onto their skin. Inhaling wild lettuce can provide a recreational "high" or hallucinogenic effect in some people¹⁹⁻²⁰.

Lettuce (*Lactuca sativa*) is well-known for its high vitamin C content, which helps to prevent infections and fight anaemia. The phytochemicals found in *L. sativa* are mostly classified as secondary metabolites, which are produced either in response to various environmental stimuli or during a plant's regular growth. Traditionally, the plants could be used to treat a vast range of conditions like pain, inflammation, bronchitis, urinary tract infections, and stomach issues including indigestion and appetite loss, and stomach problems like indigestion²³. *L. indica* has been traditionally used as tonic to treat diabetes, fever, gastro intestinal disorders and cough. This plant also has immune-enhancing activities, cytotoxicity, anti-inflammatory, antibacterial, antioxidant, antidiabetic, α -glucosidase-inhibiting, and antidiarrheal activities⁴¹.

Biological activities

Purgative effect

The isolated rabbit jejunum preparations were pre-treated with (0.1 μ M), of atropine before extract of *L. serriola* was developed. This led to the dominance of the relaxant action and the reduction of the contractile effect. As a muscarinic antagonist, atropine can block the effects of acetylcholine that activates M3 receptors to cause contractile activity in the gut^{42,43}. It has also been shown that acetylcholine regulates the peristaltic movements of the gut⁴⁴. The traditional use of *L. serriola* in constipation may have its roots in the methanol extract's reported contractile effect, which is comparable to that of cholinergic.

Respiratory disorders

Traditionally, *L. serriola* has been used to treat a variety of respiratory conditions, such as bronchitis, asthma, coughing, and congestion of the airways. The plant's crude extract was examined for potential bronchodilator activity by subjecting isolated rabbit tracheal preparations to sustained contractions generated by carbachol (1 μ M) and K⁺ (80 mM). The extract demonstrated a relaxant effect on both types of induced contractions; however, contractions caused by CCh (carbachol) were found to be eased at a concentration significantly lower than contractions induced by K⁺ (80 mM), in a way akin to that of dicyclomine. Furthermore, CCh is a cholinergic agonist that works by activating muscarinic receptors to contract smooth muscle⁴⁵. Therefore, it was discovered that the Ca⁺⁺ channel blocking and muscarinic antagonist was responsible for the relaxation of airway muscles following the injection of the methanol extract⁴⁶. Blockade of the Ca⁺⁺ channel may potentially mediate the bronchodilator action. It's interesting to note that muscarinic antagonists are now utilized to treat and relieve asthma and related conditions⁴⁷.

Anti-Epileptogenic effect

Mice treated with *L. serriola* extracts were significantly protected against convulsive activity caused by picrotoxin. It's thought that *L. serriola* increased GABAergic neurotransmission, which lessened the convulsions caused by picrotoxin. Furthermore, the increased protection provided by

n-hexane and chloroform extracts totally reduced the convulsive activity in the mice treated with them. This specific protection may result from these solvents' active anti-convulsant ingredients being easier to extract⁴⁸.

Anxiolytic effect

In elevated plus maze, each extract of *L. serriola* increased the amount of time spent in the light zone significantly when compared to control, hence supporting that *L. Serriola* possess anti-anxiety activity⁴⁹.

CNS depressant activity

In the investigation, the anxiolytic, CNS depressing, and anticonvulsant properties of several *L. serriola* dried seed extracts were examined. The quick method to ascertain the mental and animals' anxiety-related reactions is hole-board test⁵⁰. According to research, in animal models, fewer head dips serve as a sign of CNS depressive activity⁵¹. In various research investigations, there was a reduction in head dips when compared to control group, indicating the CNS depressive effect of *L. serriola*.

Hepatoprotective activity

In comparison to the control group, the paracetamol treatment increased the levels of TG, LDL, and cholesterol while lowering the levels of HDL. Administration of methanolic extract of *L. serriola* raised the HDL levels and there is a reduction in the raised levels of TC, TG, and LDL. According to reports, paracetamol degrades hepatic cells, which slows down the metabolism of fats⁵². The triglyceride level reduction attributed to the extract of *L. serriola* may be the result of its protection against the harmful effects of paracetamol.

Anticoagulant activity

The anticoagulant properties of *L. sativa* due to its antioxidant enrichment. For the purpose of determining the coagulant impact, the mean clotting times of the positive control (aspirin) (54 s) and negative control (10% DMSO) (122 s), respectively, were utilized as the lowest and upper grades. With a clotting time of 110 s, the MC leaf extract demonstrated the highest level of activity. Although, the seed extracts showed shorter clotting time than that of the negative control, showing their coagulant nature and potential application in the treatment of diseases such as hemophilia⁵³.

Anti-inflammatory activity

L. sativa have shown anti-inflammatory activity. Different extracts of *L. Sativa* controlled the biphasic inflammatory response produced by carrageenan. The release of histamine and serotonin is responsible for the first phase of inflammation, which lasts for 1-2 hours, while the peak volume of the hind paw determines the last phase, which lasts for 3-4 hours⁵⁴. Leaf extracts demonstrated the highest percentage of inflammation inhibition. When compared, the activity of exudates of cell suspension was greater than that of the extract of seed and about identical to that of a leaf extract. Conversely, the outcomes showed that MC extracts were less effective than aqueous extracts in decreasing inflammation. According to findings, an oral administration of *L. sativa* inhibited the first edema from the first hour and all the stages of inflammation, which occurs due to inactivation of various inflammatory mediators. Phenols, triterpenoids and saponins

are various secondary metabolites of *L. Sativa*, of which, anti-inflammatory response was produced by triterpenoids⁵⁵.

Anti-diabetic Activity

The ethanolic extract, N-hexane fraction and ethyl acetate fractionation of leaves of *L. indica* have anti-diabetic effects. The chemical composition of the extracts, which includes flavonoids, tannins, saponins, glycosides, and triterpenoids/steroids, supports these findings. It is believed that flavonoids, which can improve blood glucose solubility and prevent kidney glucose reabsorption, are the source of the hypoglycemic process by making blood glucose easier to excrete in urine⁵⁶⁻⁵⁸. Accordingly, there is a possibility revealing flavonoid group present in *L. indica* leaves could lower blood glucose levels.

Sedative effect

Pentobarbital-induced sleeping model is used to investigate the sedative effects of ethanolic extracts of leaves and seeds of various types of *L. sativa*. Seed extract of *L. Sativa* had showed a strong sedative effect which is mainly due to lactucopicrin⁵⁹. Other studies showed that lactucin and lactucopicrin exhibited sleeping effects, but 11 β , 13-dihydrolactucin showed no effect at doses 15 mg/kg and 30 mg/kg. Hence, lactucopicrin and lactucin are the main active constituents which are responsible for the sedative activity which is proved through spontaneous locomotor activity tests⁶⁰.

II. CONCLUSION

The current study concluded the taxonomy, phytochemical constituent, traditional uses and pharmacological potentials of *Lactuca* genus. Numerous different types of phytochemical constituents were reported. It was discovered that a number of species had good medicinal potential and feasibly utilized as instinctive cure, often most of them are eaten as veggies. The study brought to light the truth that several genus populations had inadequate chemical investigation. It would be helpful for other studies to pinpoint the precise phytochemical constituents found in these species in this regard. Furthermore, the bioactivity of a number of isolated compounds has not yet been thoroughly studied; it would be fascinating to learn more about their precise mechanism of action and bioactivity potential.

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