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# Kuth (*Saussurea lappa* L.): A review of its traditional uses, phytochemistry and pharmacological potentials

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**Abstract**

*Saussurea lappa* is an ever green perennial herb belonging to the family Asteraceae. It has been cultivated in many parts of the world and used for thousands of years for traditional medicine and essential oil applications. Mostly, it contains, terpenoids and other related biological active components e.g., phenols, flavonoids and acids. The extent of each of these chemical constituent varies depending on the types of species or cultivars as well as environmental conditions such as soil type, weather, irrigation, pruning, and other horticulture practices. *S. lappa* has found important applications from traditional to pharmaceutical products. It is the source of many biologically active agents and further active component are also finding applications. Due to extra harvesting for the demand of drug components, it is at the verge of extinction. Further research on optimizing yield, preservation and production of potent active components is required.

**Keywords:** *Saussurea lappa*, terpenoid, Costunolide, essential oil, anticancer

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## 1. Botany

### *1.1. Introduction*

Kuth *(Saussurea lappa*) is an herb belonging to the family *Asteraceae*. Since the ancient time, oil from the roots of plant has found uses in traditional medicine and perfumes. The genus *Saussurea* contains a range of about 300 species native to regions of Asia, Europe, and North America. The uncertainty in the exact number of species within genus is largely attributed to the great variability among constituent species. Variability is prevalent in morphology, growth habit, flower colour, leaves, roots, and chemical composition. It has different names in different languages. In English, it is called Costus. In Sanskrit, it is called Kushta. In Arabic/Persian, it is termed Kuy or Kur. In Hindi, it is called Kostum. In Tamil, it is known as Potchuk. In Punjabi, it is called Kot/Kust. While, its Urdu name is Minal [1-3]. The essential oil content of aromatic plants varies considerably between species, relating growing conditions and region where it is found [4-6]. More than thirty compounds have been recognized from essential oil composition of kuth plant. Generally, chemical composition of essential oils is found by GCMS analysis [7-9]. The majority of essential oil is concentrated in roots while other parts also contain small amount of volatile oil [10-11]. *S. lappa* has a huge demand in pharmaceutical industry, but in the past decades, it has become more popular over the globe as endangered species. Being a threatened species, it was enlisted in Appendix I of CITES. Trade of *S. lappa* is factually not allowed under Foreign Trade Development Act-1992. It is first listed in Appendix II of CITES on 1.7.1975 as *S. lappa* and afterward up listed to Appendix I in 1985. Therefore, the species is considered as Critically Endangered [12].

### *1.3. Demography/Location*

*Saussurea lappa* is local to frosty, cool and temperate areas of North America, Himalayas, Central Asia, Europe and certain Asian Countries (Pakistan, China, and India). It grows best in moist sloppy areas of northern Himalayas at an altitude of 2438-3962 meters above the sea level. In Pakistan, it is wild in Azad Kashmir, and Kaghan [13].

### *1.4. Botany, Morphology, Ecology*

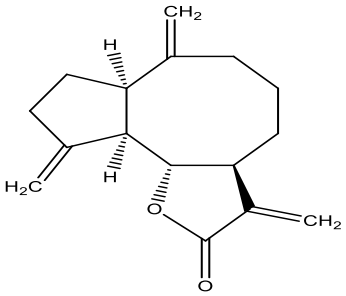
*Saussurea lappa* is a straight, pubescent, stout, and perennial plant, with 1 to 2m long robust stem. Leaves are membranous, irregularly toothed, and auricled at the base. Basal leaves are 0.5 to 1.25m in length with long petiole,

while, upper leaves are sub-sessile and small, having two tiny lobes at the bottom. Flowers; sessile, purplish blue to black, tough, curved, present in form of clusters of 2-5 flowers in leaf axils. Corolla: 0.02 m long, black, tubular. Anther tails fimbriate. Pappus: fluffy, brown. Roots: 0.4m long, robust, grey or brown [14].

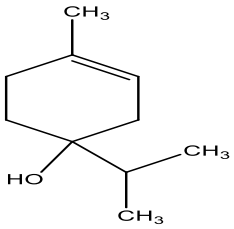
*Saussurea lappa* requires mild-cold and arctic environment for growth. Cultivation is usually through seeds. Optimum temperature for seed germination is 20° C [15] [16]. Plants are adaptable to very harsh climates and grow at extremely high altitudes. They require winter rest period of 8 – 9 months and flourish best in humus rich and well-drained loamy soil.

**2. Chemistry**

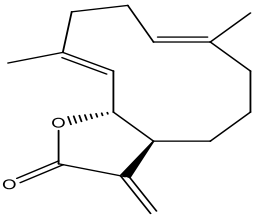
*Saussurea lappa* has explicit aromatic odour because of the existence of essential or volatile oil which is largely confined in roots. This scented volatile oil from root is chiefly comprises of hydrocarbons, oxides, alcohols, aldehydes, ketones, esters and acids [17]. In a recent investigation, 39 constituents have been recognized from *Saussurea lappa* roots essential oil. The principal constituents were dehydrocostus lactone (44-47%), 8-cedren-13-ol (3-5%), costunolide (6-9%), and α-curcumene (3-5%), β-costol (12-14%), δ-elemene (11-13%), α-costol (2-4%), α-ionone (1-3%), α-selinene (3-5%), 4-terpinol (2-4%), and elemol (1-3%). However, trace amounts of (+)-selina-4, 11-diene, 2-β-pinene, (+)-γ-costal, (-)-(E)-trans-bergamota-2,12-dien14-al, (-)-caryophyllene, and 12-methoxy-dihydro-dehydro costus lactone were also reported [18-19]. Amounts of above mentioned volatile constituents vary greatly between different cultivars due to variable climatic conditions including temperature, irradiation, and humidity. Moreover, genetic background of plant also affects the chemistry of volatile constituents. Roots also contain alkaloid saussurin (0.05%), a bitter resin (4-6%) and tannins. Plant contains small amounts of various essential vitamins such as vitamin A, vitamin B1, vitamin B2, vitamin B12, and vitamin C. Figure 1 shows structures of some important chemicals found in *Saussurea lappa*. Mineral analysis suggest that following minerals are present (the quantities in brackets are parts per million): Ca (17602), Mg (2486), Fe (1221), Mn (148), Zn (115), Pb (90), Sr (87), Cu (35), Ni (12) and Cr (04) [20]. *Saussurea lappa* is generally considered safe when used as directed under the supervision of an expert. When smoked, however, it causes narcotic effects. It should be consumed in pure form as impure costus contains a contaminant called aristocholic acid, which damages the kidneys and causes cancer. Individuals who are allergic to plants and herbs of *Asteraceae* family should not consume costus [21].




**Dehydrocostus lactone**




**4-terpenol**




**Costunolide**

**Fig.1. Structures of some important chemicals found in *Saussurea lappa***

**3. Postharvest technology**

Post-harvest treatments affect the quality of medicinal herbs to a greater extent. Usually, the collectors pay less attention to maintain quality of products during harvesting and storage. It is observed that mycotoxin producing fungus frequently attacks the stored herbal materials. Herbal drugs containing mycotoxins, beyond the standard value pre-determined by the WHO (World Health Organization) for human use, would be rejected in the international market. Therefore, encouragement for the sustainable management of herbs is necessary to enhance the cultivation, harvesting, collection, and storage practices.

**4. Processing**

Kuth like other plants is consumed in a variety of ways and for various purposes. In addition to fresh leaves, other processed forms of kuth include dry, freezed, powdered roots with or without extracted essential oils. Shelf life of whole shrub or chopped roots can be extended by freezing with or without additives e.g. salts or other oils.

**5. Value addition**

Kuth roots can be combined with other substances such as water, milk, mustard oil, jaggery, Vacha (Acorus calamus) roots and honey. Root powder; mixed with water is used to treat cough and cold, cooked in mustard oil is used to cure Stomachache, mixed with jiggery to cure scanty urination, mixed with ghee/ butter to treat skin rashes and mixed with honey to cure epilepsy.

**6. Uses**

Many herbs and spices contribute appreciably to health despite the minute amount of consumption, as they are full of nutrients such as antioxidant and minerals. Even though the reported work suggests the safety and efficiency of *S. lappa*, the worth of the evidence is inadequate; bioactive components, physiological pathways, bioavailability, and pharmacokinetics are not available in sufficient detail. The extracts of *S. lappa* are reported to possess curative potential. Variety of biological applications reported by the scientists opened the doors for the use of plant in pharmaceuticals. Whole plant extracts have remarkable action against fever, inflammations, microbial infections, and convulsions. Moreover, the elaborative studies can lead to development of the safe activities of *S. lappa* for remedial use in modern medicine and will offer better insight of its pathway of action.

***6.1. General uses***

*S. lappa* has been used in a wide variety of indigenous medicinal systems all over the globe to cure a number of diseases [22-23]. In the southern regions of Punjab, Kashmir, and Himalaya, the root stalks and whole roots are used to cure rheumatism, skin infections, dysentery, toothache, and bronchial asthma. In Ayurvedic medicine systems, the roots of *S. lappa* are used as skin toner; and to treat vomiting, leucoderma, scabies, epilepsy, itching, blood diseases, and hysteria. In Unani medicinal system, plant extracts are used as aphrodisiac, tonic, carminative, to stimulate CNS, ant-helminthic, and to cure the disorders of liver, blood, and kidney. Plant is also used in the treatment of paralysis, old fever, ophthalmic disorders, and deaf. Roots arre rich in alkaloids and volatile oils and are used as insecticides. Powdered roots are sprayed over crops to kill insects. Ariel parts of plant are used as fodder and fuel. Dried leaf are smoked like tobacco [24]. The fragrant oil obtained from *S. lappa* is very valuable in perfumery. Its odour slightly resembles with the oil of orris. It is also blended with other oriental perfumes in a lasting manner [25].

**7. Pharmacological uses**

***7.1. Anti-cancer activity***

A phytoconstituent (Costunolide) obtained from the roots of *S. lappa* was investigated for its anticancer activity in human cancer cells (HL-60). Using apoptosis analysis, assessment of mitochondrial membrane potential, and measurement of ROS (reactive oxygen's), costunolide was proved to be a potential anticancer agent [26]. Chemopreventive effect of *S. lappa* extract (hexane) was studied in human cancer cell lines (DU145). Dehydrocostus lactone (isolated from extract) showed strong anticancer effect and inhibited the growth of cancer cells by inducing apoptosis. Another compound Cynaropicrin (isolated from *S. lappa* roots), was investigated for its Immuno-modulatory action. Cynaropicrin showed inhibitory effects against growth of Eol-1, Jurkat T, and U-937 cell lines, in a dose dependent behaviour. $IC_{50}$ values were 10.90, 2.36, and 3.11µmol/l, respectively [27]. Alcoholic extract of *S. lappa* induced apoptosis in a time and dose dependent way, as it inhibited the growth of gastric cancer cell lines in 48 hours at a dose level of 80 µg/ml [28].

***7.2. Anti-inflammatory activity and Anticonvulsant activity***

In a study, the anticonvulsant effects of *S. lappa* root extracts were assessed in mice, using picrotoxin based convulsions, pentylenetetrazole, and maximal electroshock assays. Petroleum extracts showed potent anticonvulsant activity at concentrations of 0.1 and 0.3g/kg. *S. lappa* extract (methanolic) was assessed for its anti-inflammatory activity. It showed inhibitory effect (50%) against neutrophil chemotactic factor induced by cytokine [29]. Anti-inflammatory action of *S. lappa* ethanol extract was investigated in mice and rats using carrageenan based edema and peritonitis animal assays. Maximum anti-inflammatory effect was shown at concentration level of 0.05-0.2g/kg [30]. Anti-inflammatory action of costunolide (isolated from roots of *S. lappa*) was investigated using electrophoretic mobility shift model. Costunolide delayed the interleukin-1b's messenger RNA and protein expressions. It also masked the activity of transcription factor AP-1 [31]. Anti-inflammatory effect of dehydrocostus lactone was evaluated against osteoblast's oxidative damage. Significant increase in the number of osteoblasts was shown at dose level of 0.4-2 µg/ml; moreover, calcium deposition and levels of alkaline phosphatase and collagen were also improved [32].

***7.3. Hepatoprotective activity***

Dehydrocostus lactone and constunolide (obtained from *S. lappa* extracts) had slight effect against cells viability. But they showed inhibitory potential against Hep3B (human hepatoma) cells and HBsAg (surface antigen of Hepatitis B) at doses of 1.0 µmol/l and 2.0µmol/l, respectively.

***7.4. Anti-ulcer and cholagogic activity***

*S. lappa* acetone extract and costunolide inhibited the development of gastric ulcer in mice [39]. Antiulcer potential of *S. lappa* herbal formulation (UL-409) was examined using male pigs and wistar rats. Drug (0.6g/kg) was administrated orally. Potent inhibitory effect was shown against aspirin and alcohol induced gastric ulcer, duodenal ulcers, and cold-restraint stress induced ulcer models [33]

***7.5. Imuno-modulatory activity***

Costunolide and dehydrocostus lactone act as inhibitors of killing activity of cytotoxic T lymphocytes (CTL). Through preventing the increase in tyrosine phosphorylation, constunolide inhibited the killing activity of CTL in response to the crosslinking of T cell receptors as inhibitors of the killing function of CTL and the induction of intercellular adhesion molecule-1, dehydrocostus lactone from S. lappa and other guaianolides were examined for their structure activity relationship [34]. It was confirmed that the guaianolides moiety exhibited considerable inhibitory effects towards the induction of intercellular adhesion molecule-1 and killing function of CTL [35].

### *7.6. Anti-hepatotoxic activity*

Anti-hepatotoxic potential of *S. lappa* root extracts (methanol and aqueous) was investigated against hepatic damage induced by D-galactosamine and lipopolysaccharide, in mice. Pre-treatment of animals, with *S. lappa* extracts, resulted in elevation in levels of creatinine plasma, aspartate aminotransferase, and alanine transaminase. While, limited progression of hepatic damage was observed in post-treatment. Results proved the anti-hepatic potential of root extracts [36].

### *7.7. Antidiarrheal activity*

Antidiarrheal potential of methanolic extract of roots of *S. lappa* was exmined using Wistar rats. Significant inhibition of diarrhoea was shown at dose levels of 0.1, 0.3, and 0.5g/kg. Loperamide (standard drug) showed diarrheal inhibition at dose of 0.05g/kg [37].

### *7.8. Hypolipedemic activity*

Oral administration of *S. lappa* aqueous extract at dose level of 2mg/kg exhibited potential Hypolipedemic effect in rabbits. Serum cholesterol and triglyceride levels were significantly reduced.

### *7.9. Resistance to pathogenic microorganisms*

Herbal formulations *S. lappa* are used clinically to treat gastric ulcers, skin infections, diarrhoea, gastritis, and various oral cavity disorders, as it provides resistance against infection causing microbes. *Helicobacter pylori* (a pathogenic bacteria) causes disorders of digestive tract (dyspepsia, gastric cancer, and gastritis), endocrine, and autoimmune [38]. Antimicrobial potential of various *S. lappa* extracts was examined against five strains of *Helicobacter pylori*, and maximum inhibitory effect was shown by petroleum extract at concentration of 40µg/ml [39]. Anti-bacterial activity of ethanol extract of *S. lappa* was investigated against *Streptococcus mutans*. Results showed significant ($P<0.05$) inhibitory effect on growth and adherence of *Streptococcus mutans* [40]. In an investigation, a flavonoids fraction containing compounds KSR1, KSR2, KSR3, and KSR4 was isolated by fractionation of ethanol extract of *S. lappa* roots. Microdilution technique was used to assess the antifungal effect of *S. lappa* roots against nine strains of fungus i.e. *Aspergillus niger*, *Alternaria*, Cladosporium cladosporioides, *Aspergillus versicolor*, *Penicillium funiculosum, Aspergillus flavus, Penicilium ochrochloron, Trichoderma viride, and Aspergillus ochraceus*. Maximum inhibitory effect was shown by KSR1, while minimum inhibitory effect was shown by KSR3 [41].

### *7.10. Anti-parasitic activity*

Anti-parasitic potential of *S. lappa* was examined against *Clonorchis sinensis, Trypanosoma cruzi*, and various nematodal infections. Oral administration of plant decoction was effective in rabbits infected by *Clonorchis sinensis* [42]. Activity of *S. lappa* was assessed in infected children on the basis of %age decrease in faecal eggs. No adverse effect was shown by tested doses of *S. lappa* [43].

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