



**PHYTOCHEMICAL AND PHARMACOLOGICAL STUDY OF SAUSSUREA LAPPA  
CLARKE: A REVIEW**

**Gajendra P. Choudhary\***

Division of Pharmacognosy, School of Pharmacy, Devi Ahilya University, Indore, 452001, India.

**\*Correspondence for Author: Gajendra P. Choudhary**

Division of Pharmacognosy, School of Pharmacy, Devi Ahilya University, Indore, 452001, India.

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**ABSTRACT**

India is one of the richest floristic regions of the world and has been a source of plants and their products since antiquity and man uses them in different ways according to his needs, particularly as food or as medicine. *Saussurea lappa* Clarke. (Compositae) commonly known as Qust-e-shireen is a long, erect herb found mostly in Northern mountainous regions of Pakistan and India. In the present study, a review has been done on *Saussurea lappa*, Clarke. extensively for treating a variety of ailments in various system of indigenous medicine. The present review concluded that *Saussurea lappa* has various pharmacological activities such as hepatoprotective activity, antibacterial, anti-inflammatory activity and many more.

**KEYWORDS:** *Saussurea lappa*, Costunolide, Dihydrocostunolide, Anti epileptic activity, Anti-inflammatory activity, Antiulcerogenic activity, Cytotoxic Activity, Hepatoprotective Activity.

**1. INTRODUCTION**

*Saussurea lappa* has been used as medicines for thousands of years.<sup>[1]</sup> Plants have also been used as medicines for thousands of years all over the world. WHO estimates indicate that 80% of the population, mostly in developing countries still relies on plant-based medicines for primary care WHO 1978. Medicinal plants contain numerous biologically active compounds which are helpful in improving the life and treatment of disease. Compounds such as carbohydrates, proteins, enzymes, fats, oils, terpenoids, flavonoids, sterols simple phenolic compounds are responsible for various pharmacological activities of plants.<sup>[2,3]</sup>

Use of medicinal plant to cure specific ailments has been invoked from ancient times. This Medico lore is passed over from generation to generation traditionally all over the world. Nature has bestowed mankind with several plants which contains natural substances which cure diseases and promote health. Such medicinal plants are also rich sources to develop secondary metabolites which are also potential in curing different ailments. In the past decades, there is increased attention and interest in use of herbal medicines globally.<sup>[4]</sup>

*Saussurea lappa* Clarke. (Family: Compositae) commonly known as Qust-e-shireen is a long, erect herb found mostly in Northern mountainous regions of Pakistan and India.<sup>[5]</sup> Traditionally it has been used for the treatment of large number of diseases such as asthma, cough, throat infections, tuberculosis, leprosy, malaria, convulsions, fever, helminthic infestations and as

antispasmodic.<sup>[6, 7]</sup> It is 1-2 m tall, with a thick fibrous stem. Leaves are radical with long lobately winged stalks. Root are stout, carrot like, 60 cm long, possessing a characteristic penetrating odour. Flowers are dark purple or black in colour.<sup>[8, 9, 10]</sup> It is distributed between 2500- 3000 mtsl in the Himalaya, and native to the Himalayan region. Its natural populations are reported from the higher elevations of Jammu and Kashmir and Himachal Pradesh and now cultivated in Kashmir, Himachal Pradesh and in some part of Uttarakhand.<sup>[11]</sup>

**Scientific Classification**

- Kingdom: Plantae
- Sub-group: Phanerogamae
- Division: Angiosperms
- Class: Dicotyledon
- Sub-Class: Gamopetalae
- Order: Asterales
- Family: Asteraceae ( Compositae)
- Tribe: Cynareae
- Genus: *Saussurea*
- Species: *lappa*.<sup>[12]</sup>

**Synonyms**

Common names include saw-wort and snow lotus. Hindi: Kuth; Urdu: Minal, Qust, English: Costus; Chinese: Mu Xiang; Tamil: Kostum; Sanskrit: Amayam, Puskara; Gujrati: Upleta; German: Practige kostwurz ; French: Costus elegant; Marathi; Kustha ; Kannad: Chungal kustha ; Malyalam: Kottam ; Bengali: Kudo<sup>[12]</sup>

## 2. PHYTOCONSTITUENTS

Mainly plant contains phytoconstituents as resins, alkaloids, steroids and flavonoids.<sup>[13]</sup> Costunolide is one

of the major bioactive constituent of *Saussurea lappa* root.<sup>[14,15]</sup>

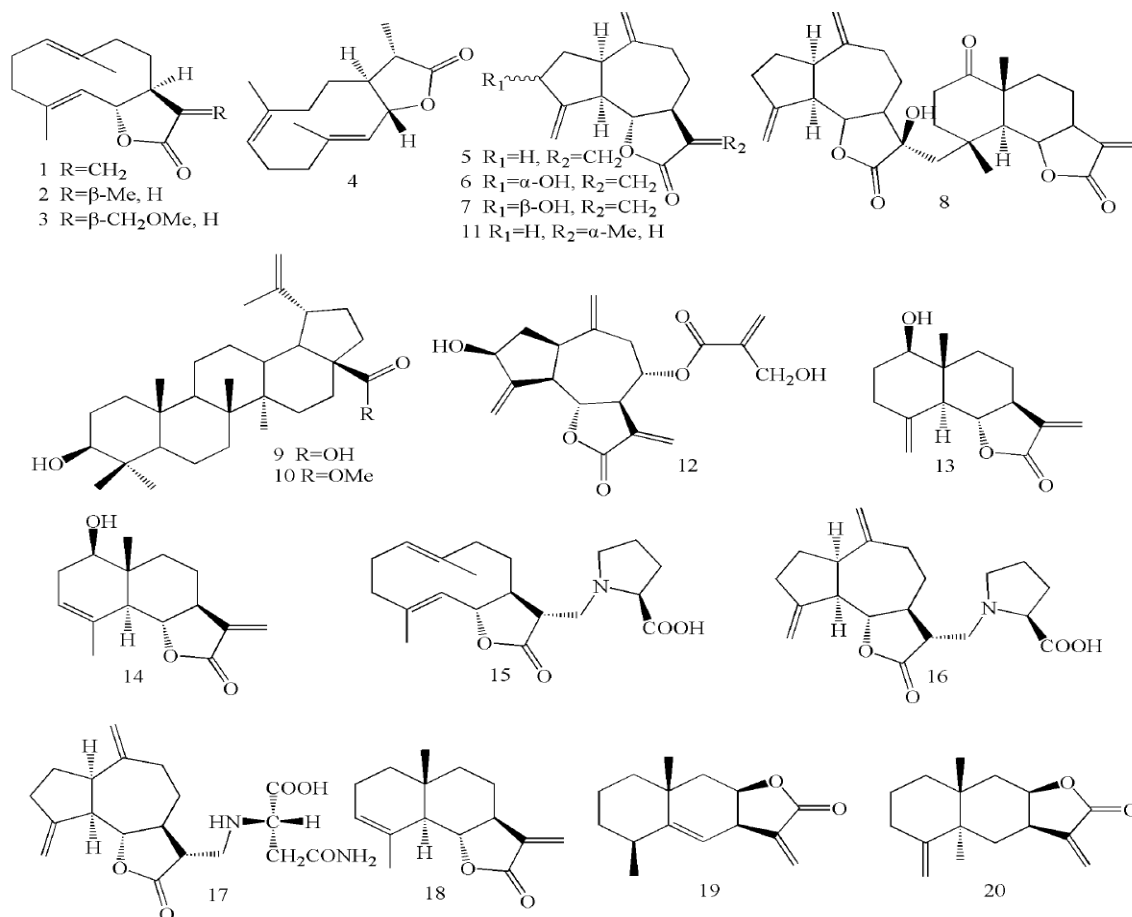


Figure :1 Structure of various phytoconstituents of *Saussurea lappa*

Costunolide (1), dihydrocostunolide (2) 12-methoxydihydrocostunolide (3), dihydrocostus lactone (4), dehydrocostus lactone (5), α-hydroxydehydrocostus lactone (6), β-hydroxydehydrocostus lactone (7), lappadilactone (8), betulinic acid (9), betulinic acid methyl ester (10), mokko lactone (11), cynaropicrin (12), reynosin (13), santamarine (14), saussureamines A–C (15–17), α-cyclocostunolide (18), alantolactone (19), isoalantolactone (20), isodihydrocostunolide (21), β-cyclocostunolide (22), 1β-hydroxy arbusculin A (23), 14 arbusculin B (24), 15 saussureal (25), and so on. Other compounds *S. lappa* has three anthraquinone compounds, namely, aloemodin-8-O-β-d-glucopyranoside (26), rhein-8-O-β-d-glucopyranoside (27), and chrysophanol (28)<sup>[16,17]</sup>

## 3. PHARMACOLOGICAL STUDY

### Antiulcerogenic activity

Ethyl acetate extract of *Saussurea lappa* roots was found to be effective in different model of gastric and duodenal ulceration in rats. The extract was induced at two doses 200 and 400 mg/kg body weight, 30 min prior to ulcer induction. Gastric ulceration was caused by oral administration of ethanol and aspirin where as pyloric

and duodenal ulcer was induced by cysteamine HCl. Ranitide at dose of 50 mg/kg a standard drug and the result revealed that at the *Saussurea lappa* showed maximum inhibitory effect on the gastric acid, free acid and total acid by 53.53%, 52.55% and 30.30%, respectively at the dose of 400 mg. Thus it can be concluded that *Saussurea lappa* possess significant antiulcer property which could be due to cytoprotective action of drug strengthening of gastric or duodenal mucosa with enhancement of mucosal defense.<sup>[18]</sup>

### Cytotoxic Activity

A study revealed that treatment with *Saussurea lappa* dramatically reduces cell viabilities in dose and time dependent manner as compared to *Taraxacum mongolicum*. also flow cytometry analysis and Annexin V staining assay also showed that *Saussurea lappa* induces apoptotic cell death of human gastric cell line and Expression analyses via Reverse transcription polymerase chain reaction (RT-PCR) and Western blots revealed that *Saussurea lappa* increased expression of the p53 and its downstream effector p21Waf1, and that the both increased expression of apoptosis related Bax and cleavage of active caspase-3 protein.<sup>[19]</sup>

Cytotoxicity studies of the chloroformic extract of *Saussurea lappa* was carried out on three cancer cell lines - HT-29 (Colon cancer), A549 (Lung cancer) and MDA-MB (Breast Cancer). Cytotoxic activity on breast cancer cell lines (MDA-MB) was nearly comparable to that of the standard compound, doxorubicin. However, it was not significant on the other two cell lines (HT-29 and A549) studied.<sup>[20]</sup>

This study demonstrate that costunolide extracted from *Saussurea laapa* suppresses tumor growth and metastases of MDA-MB-231 highly metastatic human breast cancer cells via inhibiting TNF $\alpha$ -induced NF- $\kappa$ B activation. Costunolide inhibited MDA-MB-231 tumor growth and metastases without affecting body weights in the in vivo mouse orthotopic tumor growth assays. In addition, costunolide inhibited in vitro TNF $\alpha$ -induced invasion and migration of MDA-MB-231 cells thus it is concluded that *Saussurea laapa* and its derivative costunolide suppress breast cancer growth and metastases by inhibiting TNF $\alpha$ -induced NF- $\kappa$ B activation, suggesting that costunolide as well as *Saussurea lappa* Clarke may be promising anticancer drugs, especially for metastatic breast cancer.<sup>[21]</sup>

Another study on review showed that the Antitumor capacity of costunolide is due to inhibition of proliferation, invasion and metastasis, as well as induction of apoptosis, indicating that costunolide has the potential to become an effective, systemic antitumor remedy.<sup>[22]</sup> Treatment with *Saussurea lappa* extract onto KB cells reduced cell viability significantly with an IC<sub>50</sub> value of 300 $\mu$ g/ml. Thus it can be concluded that suggested that *Saussurea lappa* extract inhibited cell proliferation through the apoptosis pathway in KB human oral cancer cells.<sup>[23]</sup>

#### Antiinflammatory activity

*In vitro* Anti-inflammatory activity was evaluated by monitoring the TNF- $\alpha$  levels and Nitric Oxide (NO) levels in mouse macrophage cells. RAW-264.2 mouse macrophage cells were cultured in T25 flasks in Dulbeccos Modified Eagles Medium (DMEM) without phenol red and 10% heat inactivated serum at 37°C temperature and 5% CO<sub>2</sub> with 90% relative humidity. After 85% confluence, cells were trypsinized with trypsin Ethylene diamine tetraacetic acid, (EDTA) solution and plated in 12 well plate at a density of 1 x 10<sup>5</sup> cells to each well and incubated at 37°C for 24h. and the result indicated that The test compound exhibited significant effect on TNF- $\alpha$  levels. Thus it can be concluded that the percent inhibition of TNF alpha by the test compound is 33.76%. Whereas, Rolipram showed an inhibition of 38.3%.<sup>[20]</sup> In other study it was seen that the sesquiterpene lactone fraction of *Saussurea lappa* roots were evaluated for their effect on the transudative, exudative and proliferative phases of inflammation using the cotton pellet granuloma assay in rats and the result revealed that fraction (25–100 mg/kg, p.o.) showed significant dose-dependent inhibition of the increase in

wet weight of the cotton pellet at 3 h (transudative phase). Thus it can be concluded anti-inflammatory activity of the sesquiterpene lactone fraction of *Saussurea lappa* may, in part, be due to stabilization of lysosomal membranes and an antiproliferative effect.<sup>[24]</sup>

#### Anti epileptic activity

The alcoholic extract of root of *Saussurea lappa* was reported to shows significant anti epileptic activity maximal electroshock seizure (MES) induced convulsions and Pentylene tetrazole-induced seizures PTZ-induced convulsions at the doses of 50, 100 and 200 mg/kg p.<sup>[25, 26]</sup>

#### Antibacterial Activity

The aqueous and methanol extracts of 12 plants including *Saussurea laapa* each belonging to different families were evaluated for antibacterial activity against medically important bacteria viz. *B. cereus* (ATCC11778), *S. epidermidis* (ATCC12228), *E. aerogenes* (ATCC13048), *P. vulgaris* (NCTC 8313), *S. typhimurium* (ATCC 23564). The in vitro antibacterial activity was performed by agar disc diffusion and agar well diffusion method. The result revealed that aqueous extracts were inactive but methanol extracts showed some degree of antibacterial activity against the tested bacterial strains.<sup>[27]</sup>

#### Hepatoprotective Activity

The aqueous-methanolic extract of *Saussurea lappa* Clarke root (Sl.Cr) was investigated against D-galactosamine (D-GalN) and lipopolysaccharide (LPS)-induced hepatitis in mice. Co-administration of D-GalN (700 mg/kg) and LPS (1 microg/kg) significantly raised the plasma transaminase levels (ALT/AST) as compared to the control group (p < 0.05). Pretreatment of mice with different doses of Sl.Cr (150, 300 and 600 mg/kg) significantly prevented the D-GalN and LPS-induced rise in plasma levels of ALT and AST in a dose-dependent manner (p < 0.05). Post-treatment with Sl.Cr (600 mg/kg) significantly restricted the progression of hepatic damage induced by D-GalN and LPS (p < 0.05). The improvement in plasma enzyme levels was further verified by histopathology of the liver, which showed improved architecture, absence of parenchyma congestion, decreased cellular swelling and apoptotic cells in treatment groups as compared to the toxin group of animals. These data indicate that the Sl.Cr exhibits hepatoprotective effect in mice and this study rationalize the traditional use of this plant in liver disorders.<sup>[28]</sup>

#### Immunomodulatory Acitivity

The immunomodulatory effect of hydroalcoholic *Saussurea lappa* root extract was observed at the dose of 100 mg/kg and 200 mg/kg and found that at 250mg/kg did not show significant effect on humoral immunity and number of antibody producing cells of spleen, reflecting *Saussurea lappa* has no effect on such responses on short term treatment. Higher dose of *Saussurea lappa* extract has shown potentiation of immunomodulatory activity in

both humoral as well as cellular arms of the immune system.<sup>[29]</sup>

A study conducted on Costunolide and dehydrocostus lactone which were isolated from an extract of *Saussurea lappa* reported that Costunolide inhibited the killing activity of CTL through preventing the increase in tyrosine phosphorylation in response to the crosslinking of T cell receptors.<sup>[30,31]</sup>

#### Cardiovascular diseases

The present study was designed to investigate the cardioprotective effect of aqueous extract of root of *Saussurea lappa* against isoproterenol induced myocardial injury. Myocardial injury in rat was induced by the administration of isoproterenol at a dose of 85 mg/kg, i.p., The rats were pretreated with the aqueous extract of *Saussurea lappa* in three different doses (100, 200 and 300 mg/kg, p.o.) through the oral route. Thus, we observed that AESL at 200 mg/kg only significantly reduced the oxidative stress and lower (100 mg) or higher (300 mg) doses do not offer significant protection against oxidative stress. The mechanism of such protection by the chronic oral administration of AESL may be due to myocardial adaptation, oxidative stress is mediated through reduction in the TBARS level.<sup>[32]</sup>

The cardiac activity of *Saussurea lappa* roots was evaluated in isolated perfused rabbit heart by the Langendorff's technique. Heart rate, contractility and coronary flow were determined in the presence of different concentrations of methanolic extract of *Saussurea lappa*, digoxin and diltiazem. It is concluded therefore, that the cardiostimulant effects of methanolic extract of *Saussurea lappa*, Linn. roots might be due to the presence of flavonoids, sesquiterpene lactones, calcium channel blocker and cholinergic constituents.<sup>[33]</sup>

#### Anticonvulsant

Anticonvulsant activity various extract such as petroleum ether extract, alcoholic extract and water extract of *Saussurea lappa* was evaluated against pentylenetetrazole and picrotoxin-induced convulsions, and maximal electroshock (MES) test in mice and it was found that Petroleum ether extract of *S. lappa* roots have potent anticonvulsant activity against pentylenetetrazole and picrotoxin-induced convulsions in mice, by elevating the seizure threshold through GABAergic the mechanism.<sup>[34]</sup>

#### Angiogenesis Activity

An experiment reported that Costunolide (CT), a sesquiterpene lactone constituent isolated from *Saussurea lappa* exhibit an antiangiogenic effect by inhibiting the endothelial cell proliferation which is induced by vascular endothelial growth factor (VEGF). Durg in-vitro method of chemotaxis which was induced by VEGF of human umbilical vein endothelial cells (HUVECs) was significantly inhibited at IC<sub>50</sub> of 3.4 μM. When the same compound was tested for

angiogenesis for in-vivo method by mouse corneal micro pocket assay the neo vascularisation of mouse corneal induced by VEGF was significantly inhibited at a dose of 100 mg/kg/day, which demonstrated its angiogenesis effect.<sup>[35,36]</sup>

#### Antidiarrheol Activity

The Methanolic extract of *Saussurea lappa* significantly protected the rats against diarrhea evoked by castor oil in dose dependent manner. β-Castol and δ-elemene were found as major components in the extracted essential as major components in the extracted essential oil.<sup>[37]</sup>

#### Antihyperlipidemic Activity

The study projected that ethanolic extract of *Saussurea lappa* reduces the triglycerides level as well as it significantly increased the HDL-C level in both serum and as well as in tissue.<sup>[38]</sup>

#### Antimycobacterial activity

The in vitro antimycobacterial activity of *Saussurea lappa* was investigated where whole oil and its fractions and pure active compounds were determined by fluorometric Alamar Blue microassay (FMABA) and the result revealed that costunolide and dehydrocostuslactone are mainly responsible for antimycobacterial activity against *Mycobacterium tuberculosis* H37Rv with MICs of 6.25 and 12.5 mg/L, respectively. Antimycobacterial activity was found to be better for the mixture than for pure compounds thus Both lactones presented synergistic activity, i.e. analysis of relative fluorescence units presented an X/Y value <0.5 at a concentration of 1/8 MIC of each compound in the combination.<sup>[39]</sup>

#### 4. CONCLUSION

The use of herbal medicines is wide spread among the patients in treating varieties of diseases. Present review is a compilation of the research work carried out on various parts of *Saussurea lappa*. It reveals that this plant has great scope for future research as it has some very interesting phytochemicals moreover, isolation and purification of pure compounds should be carried out. The review on *Saussurea lappa* clarke highlights the importance of its different pharmacological activities.

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