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Review Article

QUST (*SAUSSUREA LAPPA* CLARKE.) - A POTENT HERB OF UNANI MEDICINE: A REVIEW

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ABSTRACT

Humanity has been solely dependent on plant materials for treating day to day ailments since time immemorial and endures till date. Many herbal drugs are extensively being validated to explore its use. One such potent herb *Saussurea lappa* belongs to Compositae family which is traditionally identified as an effective plant known for its therapeutic uses in different indigenous systems of medicine. It is generally known as Qust and used in Unani System of medicine for *Muqavvi Dimagh* (neuroprotective), *Dafe Tassannuz* (anti-convulsant), *Dafe Sartan* (anti-cancer), *Dafe Qarha* (anti-ulcer), *Dafe Wajaul Mafasil* (anti-arthritic), *Muqavvi Kabid* (hepatoprotective), *Mane Vairusi* (anti-viral) properties etc. Chemical constituents derived from this plant such as costunolide, Isodihydrocostunolide, cynaropicrin etc. were proven to be bio-active and prospective source for developing innovative molecules. Several of its actions are validated and proved through *in-vitro and in-vivo* studies which necessitate a meta-analysis to explore new vistas. This review is an effort to explore the different phytoconstituents and the pharmacological activities of *Saussurea lappa*.

Keywords: Qust, *Saussurea lappa*, Unani Medicine, Drug Review

INTRODUCTION

Humanity has been solely dependent on plant materials for treating day to day ailments since time immemorial and endures till date. Many herbal drugs are extensively being validated to explore its use. One such potent herb *Saussurea lappa* is traditionally identified as an effective plant known for its therapeutic uses in different indigenous systems of medicine. It is generally known as Qust and used in Unani System of medicine for a variety of disorders viz; *Muqavvi Dimagh* (neuroprotective), *Dafe Tassannuj* (anti-convulsant), *Dafe Sartan* (anti-cancer), *Dafe Qarha* (anti-ulcer), *Dafe Wajaul Mafasil* (anti-arthritic), *Muqavvi Kabid* (hepatoprotective), *Mane Vairusi* (anti-viral) properties etc.

Saussurea lappa belongs to the family Asteraceae (Compositae) which is commonly known as Sunflower family. It is the largest family of dicotyledons, comprising 950 genera and 20,000 species, out of which 697 species occur in India. They are worldwide in distribution and abundance in the tropics, cold arctic or alpine regions. [**1]**It is an erect robust perennial herb 1- 2 cm. tall, apparently, at altitude of 25,500-3,000 meter, and also cultivated in Kashmir and neighbouring Himalayan regions for its roots used in medicine. Root stout, often up to 60 cm. long, possessing a characteristic penetrating odour; stem stout, fibrous; radicals leaves with long lobately winged stalk, up to 1m. long; flower heads stalk less, very hard, rounded, 3-5 cm. in diam., flowers dark blue-purple or almost black, in axillary and terminal clusters; achene 3 mm. Long, curved, compressed. [**2]**Kuth, which is also commonly known as Costus in trade has however no connection with the botanical genus Costus. It is found growing wild only in Jammu and Kashmir in the Kishenganga valley and the higher elevations of the Chenab valley, although it may occur sporadically in non-commercial quantities in adjoining tracts in Kashmir and elsewhere. The plant has become almost extinct in many places by uncontrolled exploitation. Since the supply of plants growing wild was not sufficient to meet the market requirement, commercial cultivation of Kuth was taken up during the second and third decades of this century in its natural growing areas in Kashmir, Lahul in Himachal Pradesh and Garhwal in Uttar Pradesh. It has been successfully cultivated in semi-natural conditions in the forest areas in Kashmir and Garhwal. **[3,4,5]**

TAXONOMICAL CLASSIFICATION [6]

KingdomPlantae

UnrankedAngiosperm

UnrankedEudicot

UnrankedAsterids

OrderAsterales

Family Asterceae

GenusSaussurea

VERNACULAR NAMES: [7,8,9,10,11]

Arabic Qust

Persian Qust

Assamese Kud, kur

BengaliKudo, Pachak, Kur, Kut

English Costus root

GujaratiUpaleta, Kath, Kur

Hindi Kot, Kur, Kut, Kust, Pachak

Kannada Changal, Koshtha

Kashmiri Kuth, Chob-i-Kud, Post khai

Malayalam Kottam, Sepuddy

Marathi Upleta, Kushtha

Oriya Kudha

Punjabi Kuth

Sanskrit Kushta, Kashmirja, Utpalam

Tamil Goshtam, Kostam, Kottam

TeleguChangala, Kustam

Urdu Qust

BOTANICAL DESCRIPTION

A tall robust perennial herb, Stem erect, 1.2 meter height, Simple leaves membranous, irregularly toothed; basal ones very large, 0.6-1.2 meter long, triangular, with a long lobately winged stalk, endolobe often 30cm. Diameter. Stem leaves smaller, stalked or stalkless, hard, rounded, 2.5-3.8 cm. Diameter, 2.5 forming axillary and terminal clusters. Bracts surrounding the heads many, ovate-

lancelate, long pointed, rigid, bent back, hairless. Corolla 2 cm. long, tubular, dark blue purple or almost black, Stamens free, anther tails fringed. Pappus hair 1.7cm. long, brown, all feathery. Fruit (achene) up to 8mm. Long, compressed, curved, tip narrowed, with 1 rib on each face, top contracted, cupped. The root is hot bitter, sweetish, pungent; fattening, aphrodisiac, alterative; improve the complexion; cures leucoderma, erysipelas, itching, ring worm, "tridosha", disease of blood, bronchitis, vomiting, scabies, "vata", used in epilepsy, headache, hysteria.

The roots are two kinds: sweet and bitter; alexipharmic, carminative, tonic, analgesic antihelminthic. **[12]**

Macroscopic

Drug greyish to dull brown, thick stout, susiform to cylindrical, 7-15 cm. Long, 1.0-5.5 cm broad, thicker roots with collapsed centre, occasionally ridged, wringles longitudinal and anastomosd.; rotlests rarely present; cut surface shows two regions, outer periderm ring thin, inner porous woody portion lighter in colour showing fine radial striations and often the central portion collapsed; fracture, short, horny; odour, strong, characteristically aromatic, taste, slightly bitter.**[11]**

Microscopic:

Transverse section of thin root shows thin periderm, followed by a broad zone of phloem still a broader zone of xylem traversed by wide medullary rays; cork. 3-5 layered wide, secondary cortical cells polygonal, mostly elongated, secondary phloem consists of mostly storage parenchyma, small groups of sieve tubes and companion cells and often phloem fibres, bast fibres thick-walled, lignified, up to 350 m in length, with many simple pits associated 75 with fibre, tracheids and parenchyma; wood fibres smaller than bast fibres; with wider lumen and obtusely tapering ends, medullary rays mutiseriate and wider in phloem region; resin canals found throughout as large cavities; some roots possess a central cylinder of sclerenchyma while others have parenchymatous centre with scattered xylem elements; in older roots, wood parenchyma collapses and takes a spongy appearance in the centre of root; inulin present in storage parenchyma.**[11]**

Powder:

Deep brown or rusty; under microscope irregular bits of yellow, brown or orange-red fragments of resins and oils associated with thin-walled parenchymatous cells, broken bits of xylem vessels with scalariform, reticulate thickening and horizontal end walls. **[11]**

CHEMICAL CONSTITUENTS

The roots contain odorous principles composed of two liquid resins, an alkaloid, a solid resin, salt of valeric acid, an astringet principal and ash which contain manganese. The oil of root was found to have the following approximate composition:- Camphene 0.04%, phellandren 0.4%, terpen alcohol0.2%, a-costen6.0%, aplotaxene 20.0%, costol 7.0%, di-hydrocostus lactone 15.0%costus lactone 10.0% , costic acid 14.0%. Active principal of the root are (a) an essential oil of a strong aromatic penetrating and fragrance odour 1.5%. (b) aglucoside and (c) an alkaloid Saussurine 0.05%. Kuth roots contain resinoids (6%), and essential oil (1.5%), alkaloid (0.05%) inulin (18%), saussurea lactone (20-25%), a fixed oil and minor constituents like tannin and sugars.**[9,10]**.[5]Eleven compounds were isolated and identified as: 5,7-dihydroxy-2-methylchromone, p hydroxybenzaldehyde, 3,5-dimethoxy-4-hydroxy-benzaldehyde, 3,5-dimethoxy-4-hydroxy-acetophenone,ethyl 2-pyrrolidinone-5(s)-carboxylate, 5-hydroxymethyl-furaldehyde, palmitic acid, succinic acid, glucose, daucosterol, beta-sitosterol.**[13]**

MIZAJ (Temperament): **[14,15,16,17,18]**

Dry3^0, Hot3^0

BADAL (Substitutes): Aqarqrha, Wajtarqi

MUSLEH (Correctives): Aneesoon and Bazrulbanj

MURAKKABAT (Compound Formulations):

Jawarish Jalinoos, Triyaq-e-Samaniya, Dawa-ul-Misk Motadil Jawharwali, Roghan Qust Jawarish Bladur, Dawa-ul-Kurkum kabir, Majoon-e-Boolis, Amroosiya, Majoone-Dabeedul Ward, Majoon-e-Juntiyana, Majoon-e-Khidr, Tiryaq-e-Samania, Zimad-e-Khanazeer, Sabadaritoos and Anqaruya-e-Kabir.**[11,19,20,21,22,23]**

AF'AL (Pharmacological Actions):

Muqawwi-e-Asab (Neuroprotective) , Mudirr-e-Baul (Diuretic), Mudirr-e-Haiz (Emmenagogue), Muqawwi-e-Meda (Stomachic), Jali (Detergent), Mohallil-e-Waram (Anti-inflammatory), Muqawwi-e-Bah (Aphrodisiac), Dafa-e-Humma ruba (Quartidian fever), Qatil-e-janeen (foeticide), Mujaffif (Desiccant), Munaffis-e-Balgham (Expectorant), Musakkin-e-Alam (Analgesic), Kasir-e-Riyah (Carminative), Qatil-e-Deedan-e-Ama (Anthelmentic). **[4,24,25,26,27]**

ISTEMAL (Therapeutic Uses):

Falij (Paralysis), Laqwa (Palsy), Rasha (Tremors), Istirkha (Muscular Dystrophy) Wajaul Mafasil (Arthritis), Niqras (Gout), Waram-e-Tehal (Splenomegaly), Deedan-e-ama (Wormicide), Ehtebas-e-Tams (Amenorrhoea), Daf-e-Taffun (Anti-septic), Damma (Asthama), Suda (Headache), Zoef Wa Naqahat (Asthenia).**[3,14,11,25,27]**

PHARMACOLOGICAL STUDIES

S. lappa has been screened for various pharmacological activities and been proved for activities such as angiogenesis effect, anti-arthritic, anti-convulsant, anti-cancer, anti-inflammatory, anti-ulcer, anti-viral and hepatoprotective activities using different and suitable in-vitro and in-vivo models. The various pharmacological activities of the *S. lappa* extracts and its isolated phytoconstituents has been summarised here.

Anti-cancer activity

It was reported that *Saussurea lappa* showed strong anticancer activity against malignant, leukaemia and lymphoma. It is due to main chemical constituents *viz*; sesquiterpenes, costunolide, dehydrocostuslactone, Cynaropicrin.**[28]** Another study also reported that water extract of *Saussurea lappa* inhibits the growth & spread of intestinal cancer due to Costunolide. Mokkolactone is an alkaloid isolated from *Saussurea lappa* which induces apoptosis in leukaemic cells.**[29]**Shikokiols isolated from *Saussurea lappa* reveal anticancer activity due to inhibits growth & spread of cancers by arresting cancer cell division in G2 phase of cell cycle and inducing apoptosis and against various cancers of the ovary, lung, colon and central nervous system.**[30]**

Anti-hepatotoxic activity

Water and methanolic extracts of *S. lappa* root was found for hepatotoxic activity against D-galactosamine (D-GalN) and lipopolysaccharide (LPS)-induced hepatitis in mice. Pre-treatment

of mice with different doses of *S. lappa*, led to rise in creatinine plasma levels in a dose dependent manner and AST, ALT level as well whereas, post-treatment led to the restricted progression of the hepatic damage which was induced by D-Gal and LPS. By the studies it is revealed that the root extract works against hepatotoxic activity**.[31]**

Antiviral activity

Crude root extract of S. lappa showed antiviral activity. It probably due to two active components, costunolide and dehydrocostus lactone, were identified which show the strong suppressive effect on the expression of the hepatitis B surface antigen (HBsAg) in human hepatoma Hep3B cells, but have little effect on the viability of the cells. Both costunolide and dehydrocostus lactone suppress the HBsAg production by Hep3B cells in a dose-dependent manner with IC50s of 1.0 and 2.0 micro M, respectively. The suppressive effect of costunolide and dehydrocostus lactone on HBsAg and hepatitis B e antigen (HBeAg), a marker for hepatitis B viral genome replication in human liver cells, was also observed in another human hepatoma cell line HepA2 which was derived from HepG2 cells by transfecting a tandemly repeat hepatitis B virus (HBV) DNA. Similarly, the mRNA of HBsAg in HepA2 cells was also suppressed by these two compounds. It suggests that costunolide and dehydrocostus lactone may have potential to develop as specific anti-HBV drugs in the future.**[32]**

Antibacterial Activity

Evaluation of anti-resistant activity of Saussurea lappa (Auklandia) root against some human pathogens. Dose dependent antibacterial activity of the ethanolic extract of S. lappa root against human bacteria isolates through the agar diffusion method (zone of inhibition in mm). The extracts showed significant inhibitory activity against clinical isolates of methicillin resistant Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumonia, Extended Spectrum Beta-Lactemase, Acinetobacterbaumannii. The minimum inhibitory concentration values obtained using the agar dilution test ranged from 2.0 µg/µL-12.0 µg/µL. However, the water extract showed no activity at all against tested bacteria. **[33]**

Anti-inflammatory activity

Ethanolic extract of S. lappa at a dose range of 50–200 mg/kg, p.o. was studied for the acute and chronic inflammation induced in both mice and rats. The extract showed considerable values for anti-inflammatory activity through carrageenan-induced paw edema and peritonitis animal models which showed the anti-inflammatory activity in a dose dependent manner. **[35]**

Antioxidant activity

The antioxidant activity of the plant has been studied using its ability to scavenge DPPH, nitric oxide, superoxide radicals along with its ability to inhibit lipid peroxidation and glutathione assay (GSH) oxidation. The 1 mg ml–1 extract had antioxidant activity with a 85.2 % reduction of DPPH and a 72.7% decrease in lipid peroxidation. It shows maximum inhibition of superoxide radical of 66.0%, and 58.4% inhibition of nitric oxide formation. The concentration of chlorogenic acid was 0.027% in the extract of S. costus. Thus, the therapeutic activity of the plant may be due to its antioxidant activity, probably as a result of the presence of chlorogenic acid. **[35]**

Anti-microbial activity

The root extract of *S. lappa* was investigated for antimicrobial activity using disc diffusion technique and appeared to have antibacterial activity against some specific bacteria (*Escherichia coli, Pseudomonas aeroginosa, Neisseria gonorrhea*, *Klebsiella pneumonia and Enterobacter aerogenes*) with a minimal inhibitory concentration (MIC) ranged from 250-400 µg/ml. **[37]**

Standard and clinically isolated microorganism strains were used for antimicrobial assays. Bacteria were first grown in LB (Luria-Bertani) broth to an OD600 nm of 0.8. A 10mlaliquot of the bacteria was then taken and added to 8 ml of fresh LB broth with 0.7% agar and poured over a 90 mm Petri dish containing 25 ml of 1.5% agar in LB broth. After the top agar hardened, a 20 ml aliquot of the test sample filtered on a 0.22 mm Millipore filter was dropped onto the surface of the top agar and completely dried before being incubated overnight at 37oC. If the sample examined had antimicrobial activity, a clear zone would be formed on the surface of the top agar representing inhibition of bacterial growth. Minimal inhibitory concentration (MIC) was determined in liquid LB medium by incubating the bacteria in LB broth with variable amounts of the sample tested. **[37]**

Angiogenesis effect

Costunolide (CT), a sesquiterpene lactone constituent isolated from Saussurea lappa exerted an antiangiogenic effect. Costunolide inhibited the endothelial cell proliferation which is induced by vascular endothelial growth factor (VEGF). The in-vitro method of chemotaxis induced by VEGF of human umbilical vein endothelial cells (HUVECs) was significantly inhibited at IC50 of 3.4 µM. When the compound was tested for angiogenesis in in-vivo method by mouse corneal micro pocket assay the neo vascularisation of mouse corneal induced by VEGF had significantly inhibited at a dose of 100 mg/kg/day, which demonstrated its angiogenesis effect. Its inhibition on VEGFR KDR/Flk-1 was also proved through signalling pathway. **[38]**

Anti-ulcer activity

Herbal formulation, UL-409 consisting of six herbal ingredients in which SL is also one of the major ingredients was tested for its antiulcer activity in Wistar rats of either sex and in male guinea pigs. 600 mg/kg dose of the drug was given orally and it significantly showed effect in cold-resistant induced ulcerations, gastric ulceration induced by alcohol and aspirin, cysteamine and histamine induced duodenal ulcer models.**[39]**

Another study the antiulcer activity of ethyl acetate extract of the Saussurea lappa root using different models of gastric and duodenal ulceration in rats. Gastric ulcers were induced by oral administration of ethanol, aspirin and by pyloric ligation and duodenal ulcers were induced by oral administration of cysteamine HCl. The extract was administered at a dose of 200 and 400 mg/kg orally 30 min prior to ulcer induction. Ranitidine (50 mg/kg) was used as a reference standard. The antiulcer activity was accessed by determining and comparing the ulcer index in the test group with that of the standard drug treated group. Gastric volume, total acid and free acid were estimated in the pylorus-ligated rats. Saussurea lappa root (400mg/kg) showed maximum inhibition of gastric acid, free acid and total acid to 53.54%, 52.55% and 30.30%, respectively. The ulcer index in the Saussurea lappa root treated animals was found to be significantly less in all the models compared to standard drug treated cases. The antiulcer activity of Saussurea lappa root was, however, less than that of ranitidine. The results suggest that Saussurea lappa root possesses significant antiulcer property which could be due to cytoprotective action of the drug or strengthening of gastric and duodenal mucosa with the enhancement of mucosal defences.**[40]**

Anti-convulsant activity

S. lappa root extracts prepared from different solvents such as petroleum, ether, water were evaluated for the anticonvulsant activity by pentylenetetrazole, picrotoxin-induced convulsions and maximal electroshock tests performed in mice by which it is proved the petroleum extract of SL roots at a dose of 100 and 300 mg/kg i.p. showed potent anticonvulsant activity. Another study reported it shows significant anti epileptic activity MES induced convulsions and PTZ-induced convulsions at the doses of 50, 100 and 200 mg/kg p.o.**[41]**

Cytotoxicity Study

Short term cytotoxicity studies were done on DLA cells by Trypan blue exclusion method. Cells were aspirated from the peritoneal cavity of tumour bearing mice and washed in PBS twice and counted using a haemocytometer. 1 million cells were taken for cell cytotoxicity studies. Different concentrations of the compound were added to the cells and then made up to 1 ml with PBS. Cells were incubated for 3hours at 37^0C. After incubation, the cell death was evaluated using Trypan Blue exclusion method. To the cell suspension, 3 drops of Trypan Blue (0.5 % in PBS) were added and the cells were loaded immediately on to a haemocytometer. The number of Dead cells was counted and the percentage of dead cells was calculated. Viable cells exclude the dye while non-viable cells take up the dye and appear blue in colour.**[37]**

Gastro-protective effect

Saussureamines A, B, C, (15, 16, 17) Costunolide (1) and dehydrocostus lactone (2) isolated from the methanolic extract of S. lappa showed the gastro protective effect on acidified ethanol induced gastric mucosal lesions in rats in a dose dependent manner (5 and 10 mg/kg). An inhibitory effect was also shown prominently by saussureamine at on gastric mucosal lesions induced by water immersion stress in mice, which showed the gastro protective effect. **[42]**

Larvicidal Activity:

The aim of this research was to determine the larvicidal activity of the essential oil derived from roots of *Saussurea lappa* (Compositae) and the isolated constituents against the larvae of the Culicidae mosquito *Aedesalbopictus*. Essential oil of *S. lappa* roots were obtained by hydrodistillation and analyzed by gas chromatography (GC) and GC-mass spectrometry (MS). A total of 39 components of the essential oil of *S. lappa* roots were identified. The essential oil has higher content of (79.80%) of sesquiterpenoids than monoterpenoids (13.25%). The principal compounds in *S. lappa* essential oil were dehydrocostus lactone (46.75%), costunolide (9.26%), 8-cedren-13-ol (5.06%), and α-curcumene

(4.33%). Based on bioactivity-directed fractionation, dehydrocostus lactone and costunolide were isolated from *S. lappa* essential oil. Dehydrocostus lactone and costunolide exhibited strong larvicidal activity against *A. albopictus* with LC_{50} values of 2.34 and 3.26 µg/ml, respectively, while the essential oil had an LC_{50} value of 12.41µg/ml. The result indicated that the essential oil of *S. lappa* and the two isolated constituents have potential for use in control of *A. albopictus* larvae and could be useful in search of newer, safer and more effective natural compounds as larvicides.**[43]**

CONCLUSION

From the above deliberation it is evident that Qust (*Saussurea lappa)* is a potent Unani herb used therapeutically since antiquity by the Unani scholars in various ailments which is now validated by ethno botanist, phytochemist, pharmacologist etc. through above cited in vitro and in vivo studies.

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