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## Therapeutic potential of Qust (*Saussurea lappa*) in the management of musculoskeletal diseases: A comprehensive review

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### Abstract

This review aims to synthesize the ethnobotanical, phytochemical, pharmacological, and clinical evidence supporting the therapeutic application of *Saussurea lappa* Clarke (Qust), a cornerstone herb in Unani medicine, for managing musculoskeletal disorders (MSDs) like osteoarthritis, rheumatoid arthritis, gout, and sciatica. Through a systematic survey of classical Unani texts and modern scientific literature, we collated data on its traditional uses, bioactive constituents, and relevant experimental studies. The findings reveal that Qust is extensively documented in Unani classics for treating *Waja'ul Mafasil* (arthritis) and related conditions due to its anti-inflammatory (*Muhallil-e-Waram*) and analgesic (*Musakkin-e-Alam*) properties, and is a key component in formulations like *Zimad-e-Khanazeer*.

Phytochemical studies identify sesquiterpene lactones costunolide, dehydrocostus lactone, and cynaropicrin as the primary bioactive constituents. Modern pharmacological research validates these traditional claims, demonstrating that Qust and its isolates exert potent effects by inhibiting key inflammatory mediators (TNF- $\alpha$ , IL-6, NF- $\kappa$ B, COX-2), suppressing angiogenesis, exhibiting significant antioxidant activity, and modulating both humoral and cell-mediated immunity. In conclusion, there is a compelling concordance between traditional knowledge and contemporary scientific evidence, positioning *Saussurea lappa* as a highly promising, multifunctional phytotherapeutic agent for musculoskeletal health. However, it warrants further investigation through rigorous, large-scale randomized controlled trials to standardize extracts, determine optimal dosages, and fully elucidate its molecular mechanisms and long-term safety profile in humans.

**Keywords:** *Saussurea lappa*, Unani medicine, sesquiterpene lactones, costunolide, musculoskeletal disorders, gout, anti-inflammatory

### Introduction

Musculoskeletal diseases (MSDs) represent a diverse group of conditions that impair the function of joints, bones, muscles, and connective tissues, leading to chronic pain, physical disability, and diminished quality of life for millions globally [1]. The pathological hallmarks often include persistent inflammation, oxidative stress-induced tissue damage, and dysregulated immune responses, as seen in rheumatoid arthritis (RA) and gout, or progressive cartilage degradation in osteoarthritis (OA) [2]. The mainstay of conventional pharmacotherapy Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), corticosteroids, and disease-modifying antirheumatic drugs (DMARDs) while effective, is frequently associated with significant adverse effects, including gastrointestinal ulceration, cardiovascular risks, hepatorenal toxicity, and immunosuppression [3]. This clinical dilemma has accelerated the search for safer, multi-targeted alternatives derived from natural products.

The Unani system of medicine, a holistic healing science with Greco-Arabic roots, offers a profound understanding of medicinal plants for managing chronic ailments like musculoskeletal diseases. Within its extensive pharmacopeia, Qust (*Saussurea lappa* Clarke, Family: Asteraceae) is revered as a potent and versatile drug. Classical Unani scholars, including *Ibn Sina* (Avicenna) in his seminal work *Al-Qanoon fi al-Tibb*, have meticulously described its properties and applications [4]. With a temperament (*Mizaj*) classified as Hot and Dry in the second degree, its pharmacological actions (*Afal*) are particularly suited for conditions involving cold and phlegmatic pathologies, which often manifest as stiffness, swelling, and pain in the joints [5, 6].

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The therapeutic claims of traditional medicine systems require validation through the lens of modern science. Recent decades have seen a surge in phytochemical and pharmacological research on *Saussurea lappa*, isolating its active principles and elucidating its mechanisms of action. The discovery of bioactive sesquiterpene lactones has provided a molecular basis for its celebrated effects [7, 8]. This comprehensive review, therefore, aims to bridge the gap between traditional wisdom and scientific evidence by providing a detailed analysis of the potential of *Saussurea lappa* in the management of musculoskeletal diseases, drawing upon its rich ethnomedical history and the latest pharmacological findings.

## Botanical and Ethnobotanical Profile

### 1.1 Taxonomic Classification [9, 10]

Rank	Classification
Kingdom	Plantae
Subkingdom	Tracheobionta-Vascular plants
Superdivision	Spermatophyta-Seed plants
Division	Magnoliophyta-Flowering plants
Class	Magnoliopsida-Dicotyledons
Subclass	Asteridae
Order	Asterales
Family	Asteraceae (Compositae)
Genus	<i>Saussurea</i> DC.
Species	<i>Saussurea lappa</i> C.B. Clarke

### 1.2 Botanical Description [11, 12]

*Saussurea lappa* is an erect, robust perennial herb growing 1-2 meters in height. The plant features:

- **Roots:** Stout, often up to 60 cm long, possessing a characteristic penetrating odour; greyish to dull brown, thick, fusiform to cylindrical
- **Stem:** Stout, fibrous, erect
- **Leaves:** Radical leaves with long lobately winged stalk, up to 1 m long, triangular; stem leaves smaller, stalked or stalkless
- **Flowers:** Dark blue-purple or almost black, in axillary and terminal clusters; flower heads stalkless, very hard, rounded, 3-5 cm in diameter
- **Fruits:** Achene 3 mm long, curved, compressed



Fig 1: *Saussurea lappa* plant

**1.3 Ethnobotanical Significance:** Qust has been used for centuries in various traditional medicine systems across different cultures [13, 14]. The ethnobotanical uses include:



Fig 2: Dried roots of *Saussurea lappa* used medicinally

### 1.4 Unani Description of Qust [15-17]

Parameter	Description
Unani Name	Qust
Botanical Name	<i>Saussurea lappa</i> C.B. Clarke
Family	Asteraceae (Compositae)
Mizaj (Temperament)	Hot 2°, Dry 2°
Zauq (Taste)	Bitter, slightly sweetish, pungent
Boo (Smell)	Strong, characteristically aromatic
Parts Used	Dried roots
Afal (Actions)	<i>Muhallil-e-Waram</i> (Anti-inflammatory), <i>Musakkin-e-Alam</i> (Analgesic), <i>Muqawwi-e-Asab</i> (Neurotonic), <i>Kasir-e-Riyah</i> (Carminative)
Musleh (Corrective)	Anisoon ( <i>Pimpinella anisum</i> ), Gul-e-Qand
Badal (Substitute)	Aqarqarha ( <i>Anacyclus pyrethrum</i> ), Daroonj ( <i>Doronicum hookeri</i> )
Migdare Khurak (Dose)	2-5 grams

### In Unani Medicine

- Treatment of inflammatory joint conditions (*Waja'ul Mafasil*).
- Management of gout (*Niqras*) and sciatica (*Irq-un-Nasa*).
- As a neurotonic for paralysis (*Falij*) and facial palsy (*Laqwa*).
- For respiratory conditions like asthma and chronic bronchitis.
- As a digestive tonic and carminative

### Regional traditional uses

- In Kashmir, used for stomach ailments and as a general tonic.
- In Punjab, employed for skin diseases and as an anti-helminthic.
- Various tribal communities use it for fever, cough, and skin disorder.

### 2. Phytochemical Constituents: The basis of bioactivity

The therapeutic potency of Qust is attributed to its complex phytochemical profile, primarily concentrated in the root and its essential oil [7, 9, 16, 18].

## 2.1 Major Chemical Composition

### Essential Oil (1.5-2%)

- Dehydrocostus lactone (46.75%)
- Costunolide (9.26%)
- 8-Cedren-13-ol (5.06%)
- A-Curcumene (4.33%)
- Camphene, phellandrene, costol, dihydrocostus lactone

### Sesquiterpene Lactones (Primary Actives)

- Costunolide (C<sub>15</sub>H<sub>20</sub>O<sub>2</sub>)
- Dehydrocostus lactone
- Cynaropicrin
- Isodihydrocostunolide

### Alkaloids

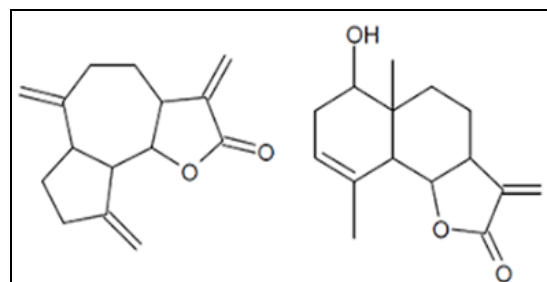
Saussurine (0.05%)

### Other Constituents

Resinoids (6%)

- Inulin (18-19%)
- Fixed oil
- $\beta$ -sitosterol, stigmasterol, daucesterol
- Tannins and sugars
- Salts of valeric acid

## 2.2 Chemical Structures of Key Constituents



**Fig 3:** Molecular structures of major sesquiterpene lactones in Qust

**Table 1:** Major bioactive constituents of *Saussurea lappa* and their relevance to Musculoskeletal Diseases (MSDs)

Constituent Class	Specific Compounds	Potential Role in MSDs
Sesquiterpene Lactones	Costunolide, Dehydrocostus Lactone, Cynaropicrin	Anti-inflammatory, Analgesic, Anti-angiogenic, Immunomodulatory
Essential Oil Components	Dehydrocostus Lactone, Costunolide, $\alpha$ -Curcumene	Anti-inflammatory, Analgesic (via topical application/absorption)
Alkaloids	Saussurine	Neurotonic, potential role in neuropathic pain (Sciatica)
Sterols	$\beta$ -Sitosterol, Stigmasterol	Anti-inflammatory (similar to mechanisms of other plant sterols)
Polysaccharides	Inulin	Prebiotic, potential indirect immunomodulation

## 3. Pharmacological evidence for efficacy in musculoskeletal diseases

### 3.1 Anti-inflammatory and Anti-arthritis Activities

*In vivo* evidence, A seminal study by Gokhale *et al.* demonstrated that an ethanolic extract of *S. lappa* root, at oral doses of 50-200 mg/kg, produced significant dose-dependent inhibition of both acute inflammation (carrageenan-induced paw edema) and chronic inflammation (cotton pellet-induced granuloma) in rodent models [19]. This validates the *Muhallil-e-Waram* action.

### Mechanistic Insights (Cellular and Molecular)

- **Cynaropicrin:** Cho *et al.* reported that cynaropicrin potently inhibits nitric oxide (NO) production, prostaglandin E<sub>2</sub> (PGE<sub>2</sub>), and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) in lipopolysaccharide (LPS)-activated macrophages by suppressing the expression of inducible NO synthase (iNOS) and cyclooxygenase-2 (COX-2) [20]. This dual inhibition of key inflammatory pathways is crucial in managing arthritis.
- **NF- $\kappa$ B Pathway Suppression:** Matsuda *et al.* showed that sesquiterpene conjugates from Qust inhibit inducible NO synthase (iNOS) and heat shock protein in LPS-activated macrophages by suppressing the activation of Nuclear Factor-kappa B (NF- $\kappa$ B), a master regulator of inflammation [21].
- **Anti-angiogenesis:** Angiogenesis is a key process in the progression of RA and pannus formation. Jeong *et al.* found that costunolide inhibits VEGF-induced proliferation and chemotaxis of human umbilical vein endothelial cells (HUVECs) and suppresses

angiogenesis in a mouse corneal model by targeting the VEGFR KDR/Flk-1 signaling pathway [22].

### 3.2 Analgesic Activity

The Musakkin-e-Alam property is supported by anticonvulsant studies, which often correlate with central nervous system-mediated analgesia. The petroleum ether extract of Qust roots (100 and 300 mg/kg) showed potent activity against pentylenetetrazole and picrorotoxin-induced convulsions in mice, suggesting a modulatory effect on the GABAergic system, which is also implicated in pain perception [23].

### 3.3 Immunomodulatory Activity

Rheumatoid arthritis is an autoimmune condition. Pandey *et al.* demonstrated that a hydroalcoholic extract of *S. lappa* modulated both humoral and cell-mediated immune responses in mice. It increased the phagocytic index, antibody-secreting cells, and prevented myelosuppression induced by immunosuppressive drugs, indicating a broad-spectrum immunomodulatory effect that could be beneficial in balancing the dysregulated immune response in RA [24].

### 3.4 Antioxidant Activity

Oxidative stress plays a significant role in the pathogenesis of OA and RA. Pandey *et al.* evaluated the free radical scavenging potential of *S. lappa* and found that 1 mg/ml of the extract caused an 85.2% reduction of the DPPH radical and a 72.7% decrease in lipid peroxidation [25]. This potent antioxidant activity helps protect joint tissues from oxidative damage and complements its anti-inflammatory effects.



**Table 2:** Summary of key pharmacological studies on *Saussurea lappa* relevant to musculoskeletal diseases

Activity	Model Used	Extract/Compound	Key Findings	Reference
Anti-inflammatory	Carrageenan-induced paw edema in rats	Ethanol extract (50-200 mg/kg, P.O.)	Significant, dose-dependent inhibition of edema.	[18]
Anti-inflammatory (Mechanism)	LPS-activated macrophages	Cynaropicrin	Inhibited NO, PGE2, TNF- $\alpha$ ; suppressed iNOS & COX-2 expression.	[19]
Anti-angiogenesis	HUVECs & mouse corneal model	Costunolide	Inhibited VEGF-induced proliferation & angiogenesis; blocked VEGFR signaling.	[21]
Immunomodulatory	Swiss albino mice	Hydroalcoholic extract	Increased phagocytic index, antibody-secreting cells; prevented drug-induced myelosuppression.	[23]
Antioxidant	<i>In vitro</i> assays	Methanolic extract	85.2% DPPH scavenging; 72.7% inhibition of lipid peroxidation.	[24]
Anticonvulsant/Analgesic	PTZ-induced convulsions in mice	Petroleum ether extract (100, 300 mg/kg)	Showed potent anticonvulsant activity, suggesting CNS modulation.	[22]

#### 4. Traditional formulations and safety profile

##### 4.1. Compound Formulations (*Murakkabat*)

Qust is rarely used alone in Unani practice. It is a key ingredient in numerous compound formulations, demonstrating its integral role [4, 13, 26].

- **Zimad-e-Khanazeer:** A topical paste for abscesses and inflammatory swellings
- **Majoon-e-Dabeed-ul-Ward:** A confection used for joint pains and strengthening the body
- **Jawarish Jalinoos:** A digestive tonic that also strengthens the nerves and joints
- **Roghan Qust:** A medicated oil for massage in paralysis, tremors, and joint pains
- *Triyaq-e-Samaniya, Dawu-ul-Misk Motadil Jawharwali, Jawarish Bladur*

##### 4.2 Safety and Correctives (*Musleh*)

Due to its hot and dry temperament, Unani scholars caution that Qust may cause irritation, especially in individuals with a hot constitution. To mitigate this, correctives (*Musleh*) like Anisoon (*Pimpinella anisum*) and *Gul-e-Qand* (candied rose petals) are often co-prescribed [4, 14]. Its substitutes (Badal) include Aqarqarha (*Anacyclus pyrethrum*) and Daroonj (*Doronicum hookeri*) [15].

##### Reported adverse effects

- Irritation and discomfort in abdomen at high doses (10-20 cc extract).
- Drowsiness and headache at higher doses.
- Irritation in urethra during excretion of essential oil.
- Allergic dermatitis upon topical use [27, 28].

#### 5. Conclusion

The extensive body of evidence presented in this review firmly establishes *Saussurea lappa* (Qust) as a therapeutically significant herb for musculoskeletal disorders. Its revered status in Unani medicine for conditions like *Waja'ul Mafasil* and *Niqras* is not merely anecdotal but is robustly supported by modern phytochemical and pharmacological sciences. The synergy between its multiple bioactive constituents, particularly costunolide and dehydrocostus lactone, enables a multi-targeted approach simultaneously quenching inflammation, alleviating pain, modulating immune dysfunction, and protecting tissues from oxidative damage.

The convergence of traditional knowledge and empirical data makes a strong case for integrating Qust into contemporary management strategies for MSDs, either as a

standalone therapy or, more traditionally, as a vital component of polyherbal formulations. However, to fully translate this potential into evidence-based practice, future research must focus on:

- Conducting rigorous, large-scale, randomized, double-blind, placebo-controlled clinical trials with standardized extracts.
- Isolating and studying the synergistic effects of its various phytoconstituents.
- Developing sustainable cultivation practices to conserve this endangered species.
- Exploring novel drug delivery systems to enhance bioavailability and efficacy.

In conclusion, *Saussurea lappa* stands as a prime example of how ancient medical wisdom, when interrogated with modern scientific rigor, can yield safe and effective solutions for pressing global health challenges like musculoskeletal diseases.

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