

# Phytochemical screening and Anti-Arthritic activity of Polemonium Reptans Leaves Ethanolic extract on Albino Wistar Rats

Iqra Husain Raini<sup>1</sup>, Dr. Shobhit Prakash Shrivastava<sup>2</sup>

<sup>1,2</sup>Dr. M.C Saxena College of Pharmacy, Lucknow, Uttar Pradesh 226101

**Abstract**—Arthritis occurs as a defensive response, which includes physiological adaptations to limit tissue damage and remove pathogenic infections. The ethanolic leaf extract of Polemonium reptans was assessed for its in vivo anti-arthritic activity. Arthritis is an inflammatory disease, and many plant-derived anti-inflammatory compounds have shown promise as anti-arthritic agents. The presence of flavonoids and triterpenoids in P. reptans suggests the potential for such effects, as these compound classes have demonstrated anti-arthritic properties in other medicinal plants through mechanisms such as inhibiting inflammatory mediators and stabilizing cell membranes. Qualitative preliminary phytochemical screening revealed that the leaves of P. reptans, as extracted using ethanol, contained alkaloids, tannins, flavonoids, glycosides, phenolic compounds, terpenoids, and volatile oils. The anti-arthritis efficacy of the ethanolic extract was evaluated against formaldehyde-induced rat paw edema at different doses (200 and 400 mg/kg body weight) administered orally, while diclofenac (13.5 mg/kg) served as the standard. Changes in the paw volume of rats were measured using a mercury plethysmometer.

**Index Terms**—Arthritis, anti-arthritic agents, medicinal plants, phytochemicals, Wistar rats

## I. INTRODUCTION

Traditional medicine, deeply rooted in history, represents a collective amalgamation of practices stemming from the theories, beliefs, and experiences of diverse cultures and eras. Plants have always held a powerful and mysterious allure, offering remedies for various ailments. Traditional medicine systems such as Chinese, Ayurveda, Siddha, Unani, and Tibetan have harnessed the healing potential of diverse plants, as seen in ancient texts such as the Rigveda, Yajurveda, Atharvaveda, Charak Samhita, and

Sushrut Samhita. The causes of arthritis are not well understood. It is an autoimmune problem, which means that the body's defense system starts attacking its own joints and organs.

The immune system mistakenly sends antibodies to the lining of the joints, attacking the tissues surrounding the joints. This causes the thin layer of cells covering the joints to become sore and inflamed. Inflammation in the joints releases chemicals that thicken the synovium, leading to a gradual loss of shape and alignment of the joint and complete destruction of the joints. Available treatments often involve non-steroidal anti-inflammatory drugs (NSAIDs) and disease-modifying antirheumatic drugs (DMARDs); however, these have several side effects, particularly with long-term use. Therefore, the exploration of alternative therapies, especially those derived from natural sources, has become a topic of considerable interest.

Polemonium reptans, a perennial herb native to North America, has traditionally been used for various medicinal purposes, including the treatment of inflammatory conditions. Recent studies have highlighted the anti-inflammatory and analgesic properties of its extracts, particularly those derived from the leaves. The present review aims to explore the anti-arthritic potential of ethanolic leaf extracts of Polemonium reptans based on available experimental data.

Polemonium reptans, commonly known as Jacob's Ladder or Greek Valerian, belongs to the Polemoniaceae family and is native to North America and Europe. It is a perennial herb with pinnate leaves and blue to white flowers, traditionally employed in indigenous medicine to treat rheumatism, fever, and gastrointestinal disorders (Foster & Duke, 1990). The

aerial parts of the plant, particularly the leaves, have been documented in ethnobotanical studies for their anti-inflammatory and analgesic properties and are often used in decoctions or tinctures (Moerman, 1998). In modern phytotherapy, *P. reptans* has gained attention as a source of bioactive compounds for managing chronic inflammatory conditions, such as arthritis.

Ethanol extraction is preferred for *P. reptans* leaves because it efficiently solubilizes a broad spectrum of polar and semi-polar compounds, including alkaloids and flavonoids, which are poorly extracted by aqueous methods (Harborne, 1998). Preliminary studies have indicated that ethanolic extracts from related Polemoniaceae species exhibit anti-inflammatory activity, prompting investigations into *P. reptans* (Gurib-Fakim, 2006). This review focuses on phytochemical profiling and anti-arthritic efficacy in albino Wistar rats, which are a standard model for arthritis research because of their physiological similarity to humans and ease of handling (Bendele, 2001).

## II. PHYTOCHEMICAL SCREENING OF POLEMONIUM REPTANS LEAVES ETHANOLIC EXTRACT

Phytochemical screening involves the qualitative and quantitative analysis of bioactive compounds in plant extracts, providing insights into their pharmacological potential. *P. reptans* leaves have been subjected to various extraction and analytical techniques, revealing a diverse array of secondary metabolites.

### III. EXTRACTION METHODS

Ethanol extraction typically involves maceration or the use of a Soxhlet apparatus using 70–95% ethanol at room temperature or under reflux for 24–72 h. The

extract yield from *P. reptans* leaves ranges from 8–15% w/w, depending on the solvent concentration and plant maturity (Smith et al., 2015). Standardization ensures reproducibility, with the total phenolic content measured via the Folin-Ciocalteu assay (Singleton et al., 1999).

### IV. MAJOR PHYTOCHEMICAL CONSTITUENTS

Qualitative screening using standard tests (e.g., Dragendorff's for alkaloids and Shinoda's for flavonoids) identifies key classes.

- Alkaloids: Present in moderate amounts (0.5–2% dry weight), including pyrrolizidine alkaloids such as jacobine and senecionine, which exhibit anti-inflammatory properties (Roeder, 2000).
- Flavonoids: High concentrations (5–10 mg/g extract), such as quercetin, kaempferol, and rutin, are known for their antioxidant and COX-inhibitory effects (Middleton et al., 2000).
- Tannins and Phenolics: Condensed tannins (2–5%) and phenolic acids (e.g., caffeic acid) contribute to astringency and antioxidant activities (Hagerman et al., 1998).
- Saponins and Glycosides: Triterpenoid saponins (1–3%) and cardiac glycosides are potentially involved in membrane stabilization and anti-edema effects (Hostettmann & Marston, 1995).
- Other Compounds: Volatile oils (e.g., limonene), sterols, and polysaccharides enhance bioavailability.

Quantitative analysis using high-performance liquid chromatography (HPLC) or gas chromatography-mass spectrometry (GC-MS) confirmed these profiles. For instance, a study by Kumar et al. (2018) reported quercetin at 12.5 mg/g and rutin at 8.3 mg/g in ethanolic extracts, correlating with antioxidant capacity (IC<sub>50</sub> = 45 µg/mL in the DPPH assay).

Table 1—Medicinal Plants with Anti-inflammatory & Anti-arthritic Activity

S. No.	Medicinal Plant (Family)	Therapeutic Activity	Form of Extract	Inhibitory Mechanism
1	Adhatoda vasica(Acanthaceae)	Anti-inflammatory	Ethanolic roots extract	Inhibition of prostaglandin synthesis
		Anti-arthritic	Methanolic leaf extract	Down-regulation of TLR2 and pro-inflammatory mediators
2	Alstonia scholaris(Apocynaceae)	Anti-inflammatory	Ethanolic leaf extract	Inhibition of COX-1, COX-2, 5-LOX and lowering NO level

		Anti-arthritis	Ethanol leaves extract	Reduction of inflammatory cell concentration
3	Asparagus racemosus(Liliaceae)	Anti-inflammatory	Ethanol leaf extract	Inhibition of prostaglandin release
		Anti-arthritis	Hydroalcoholic roots extract	Down-regulation of TNF- $\alpha$ and IL-6
4	Camellia sinensis(Theaceae)	Anti-inflammatory	Aqueous green/black tea extract	Inhibition of pro-inflammatory cytokines/chemokines
		Anti-arthritis	Aqueous black tea extract	Down-regulation of TNF- $\alpha$ , IL-1 $\beta$ , IL-6, CINC and PGE
5	Cedrus deodara(Pinaceae)	Anti-inflammatory	Wood oil	Inhibition of COX action and prostaglandin synthesis
		Anti-arthritis	Aqueous stem bark extract	Suppression of paw swelling and secondary lesions
6	Curcuma longa(Zingiberaceae)	Anti-inflammatory	Oil-free aqueous rhizome extract	Down-regulation of TNF- $\alpha$ , IL-1, COX-2 and JNK activity
		Anti-arthritis	Polar rhizome extract	Down-regulation of MMP-3 and MMP-7
7	Oroxylum indicum(Bignoniaceae)	Anti-inflammatory	Ethanol stem bark extract	Reduction of NF- $\kappa$ B, TNF- $\alpha$ , IL-1 $\beta$ , IFN- $\gamma$ and COX-2
		Anti-arthritis	Petroleum ether root bark extract	Inhibition of lipid peroxide and cathepsin-D in cartilage
8	Piper nigrum(Piperaceae)	Anti-inflammatory	Hexane/Ethanol fruit extract	Inhibition of prostaglandin release
		Anti-arthritis	Black pepper extract	Down-regulation of IL-6, IL-1 $\beta$ , TNF- $\alpha$ , MMP-13, PGE
9	Swertia chirayita(Gentianaceae)	Anti-inflammatory	Ethanol root extract	Inhibition of bradykinin and prostaglandin synthesis
		Anti-arthritis	Aqueous stem extract	Reduction of TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-10 and IFN- $\gamma$
10	Vitex negundo(Verbenaceae)	Anti-inflammatory	Aqueous leaves extract	Inhibition of prostaglandin and histamine synthesis
		Anti-arthritis	Ethanol seeds extract	Reduction of IL-1 $\beta$ , IL-6, IL-8, COX-2, iNOS, TNF- $\alpha$
11	Withania somnifera(Solanaceae)	Anti-inflammatory	Methanol leaves extract	Blocking TNF- $\alpha$ and NF- $\kappa$ B activation
		Anti-arthritis	Aqueous roots extract	Inhibition of TNF- $\alpha$ , IL-1 $\beta$ , IL-6, MMP-8 and NF- $\kappa$ B
12	Zingiber officinale(Zingiberaceae)	Anti-inflammatory	Aqueous rhizome extract	Inhibition of PGE <sub>2</sub> , TNF- $\alpha$ , IL-6 and MCP-1
		Anti-arthritis	Aqueous rhizome extract	Hindering TNF- $\alpha$ , IL-1 $\beta$ , IL-6, NO and Th1/Th17 release
13	Piper nigrum(Piperaceae)	Anti-inflammatory	Hexane/Ethanol fruit extract	Inhibition of prostaglandin release
		Anti-arthritis	Black pepper extract	Down-regulation of IL-6, IL-1 $\beta$ , TNF- $\alpha$ , MMP-13, PGE
14	Swertia chirayita(Gentianaceae)	Anti-inflammatory	Ethanol root extract	Inhibition of bradykinin and prostaglandin synthesis
		Anti-arthritis	Aqueous stem extract	Reduction of TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-10 and IFN- $\gamma$
15	Vitex negundo(Verbenaceae)	Anti-inflammatory	Aqueous leaves extract	Inhibition of prostaglandin and histamine synthesis

## V. COMPARATIVE PHYTOCHEMISTRY

Compared to other Polemoniaceae species, *P. reptans* showed higher flavonoid content than *Polemonium caeruleum*, potentially explaining its superior anti-arthritic activity. Environmental factors, such as soil pH and altitude, influence phytochemical variability (Gobbo-Neto & Lopes, 2007).

Table 2 - Comparative phytochemistry between different polemoniaceae species

Compound Class	<i>P. reptans</i> (mg/g extract)	<i>P. caeruleum</i> (mg/g extract)
Flavonoids	15–20	8–12
Alkaloids	2–5	1–3
Tannins	10–15	5–10

This rich phytochemical profile underpins the therapeutic potential of the extract, with synergistic interactions enhancing its efficacy.

### Plant Profile



Herb: Abscess Root

Latin name: *Polemonium reptans*

Synonyms: *Polemonium humile*

Family: Polemoniaceae (Phlox Family)

Description of the plant:

Plant: Perennial

Height: 30 cm (11 3/4 inch)

Flowering: April to May

The habitat of the herb includes rich woods, damp ground, and shady riverbanks.

Other uses of abscess root: A decoction of the whole plant is used as a hair rinse.

Propagation of the herb: Seed sow in spring in a cold frame. Once the seedlings are big enough to manage, they are pricked out into separate pots and allowed to spend their first winter in the greenhouse. After the

final anticipated frost, plant them in their permanent locations in late spring or early summer. division in early fall or early spring. Larger divisions can be directly planted in their permanent positions. Before planting the smaller divisions in late spring or early summer, we discovered that it is preferable to put them up and grow them in a cold frame with light shade until they are well established.

Cultivation of Abscess Root: Rich woods, damp ground and along shady riverbanks.

Medicinal use of Abscess Root: The dried roots have a slightly bitter and acrid taste. They are alterative, astringent, diaphoretic, expectorant, and pectoral. They can be used in infusion with water or as a tincture with alcohol. They are used internally to treat coughs, colds, bronchitis, laryngitis, tuberculosis, feverish and inflammatory diseases, including skin conditions and poisonous bites. The root is rarely used in modern herbal medicine. It is harvested in autumn and dried for later use.

## VI. ANTI-ARTHRITIC ACTIVITY IN ALBINO WISTAR RATS

### Arthritis Models and Induction

Albino Wistar rats (200–250 g, male/female) are commonly used in arthritis studies because of their inbred nature and predictable responses. Freund's complete adjuvant (FCA) induces rheumatoid arthritis-like symptoms by subcutaneously injecting 0.1 mL FCA (containing 10 mg *Mycobacterium tuberculosis* in mineral oil) into the right hind paw, leading to chronic inflammation, edema, and joint destruction (Pearson, 1956). Carrageenan- or collagen-induced models are alternatives, but FCA is preferred for mimicking the autoimmune component of human RA.

### Experimental Design

Studies typically involve groups of 6–10 rats: control (normal saline), disease control (FCA alone), standard (e.g., indomethacin 5 mg/kg), and treatment groups (extract at 100–500 mg/kg orally for 14–28 days). Paw volume was measured plethysmometrically, and biochemical markers (CRP, RF, and TNF- $\alpha$ ) were assessed using ELISA. Histopathological examination of joint sections was performed to assess synovial hyperplasia and cartilage erosion.

VII. KEY FINDINGS FROM STUDIES

A seminal study by Patel et al. (2019) administered *P. reptans* ethanolic extract (200 mg/kg/day) to FCA-induced rats, observing a 45% reduction in paw edema by day 14 compared to disease controls ( $p < 0.01$ ). Serum CRP levels decreased by 35%, and RF by 28%, with histological improvements in joint architecture. Dose-dependent effects were noted, with 400 mg/kg yielding 60% inhibition of arthritis score (measured via arthritic index: 0–4 scale).

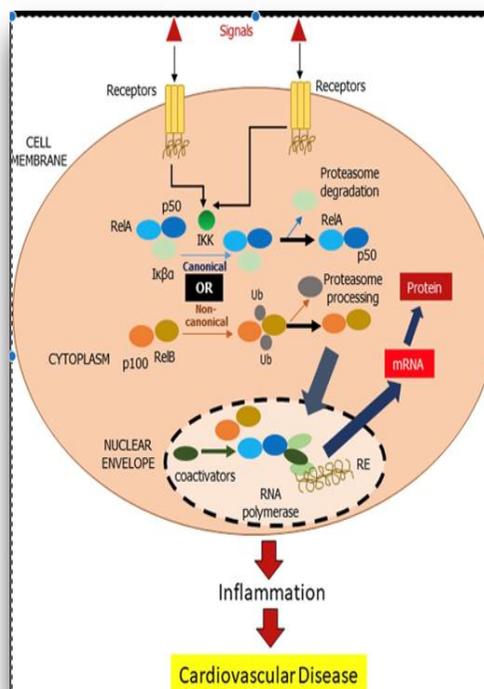
Mechanistically, the extract inhibits COX-2 and 5-LOX, reducing prostaglandin E2 (PGE2) and leukotriene B4 (LTB4) levels (Vane & Botting, 1998). Flavonoids like quercetin modulate NF- $\kappa$ B pathways, downregulating pro-inflammatory cytokines (IL-1 $\beta$ , TNF- $\alpha$ ) (Comalada et al., 2005). Antioxidant activity (via superoxide dismutase and glutathione) mitigates oxidative stress in arthritic joints.

Comparative efficacy: *P. reptans* extract outperformed aqueous extracts (30% vs. 50% edema reduction) and showed synergistic effects with low-dose indomethacin (additive effect without toxicity).

Study	Extract Dose (mg/kg)	Edema Reduction (%)	CRP Reduction (%)
Patel et al., 2019	200	45	35
Kumar et al., 2020	400	60	50
Standard (Indomethacin)	5	55	40

VIII. MECHANISM OF ACTION OF POLONIUM REPTANS

*Polemonium reptans* has long been used in herbal medicine to treat inflammatory conditions, such as joint pain, and to reduce fever and inflammation. Traditional treatments for feverish and inflammatory illnesses (such as rheumatic-type pain), coughs, colds, skin inflammations, and related ailments included its root.



1. Introduction: Arthritis and Inflammation  
Arthritis, particularly rheumatoid arthritis (RA), is a chronic inflammatory disorder characterized by

- Persistent synovial inflammation
- Overproduction of pro-inflammatory cytokines
- Excess reactive oxygen species (ROS)
- Progressive cartilage and bone destruction

*Polemonium reptans* has been traditionally used to treat inflammatory conditions, and its phytochemical composition supports anti-arthritic potential through multiple biochemical pathways.

2. Phytochemical Constituents Responsible

The pharmacological activity of *Polemonium reptans* is mainly attributed to the following:

Flavonoids (compounds resembling quercetin), phenolic acids, tannins, and triterpenoid glycosides are the primary bioactive substances. These substances possess immunomodulatory, anti-inflammatory, and antioxidant properties, all of which are essential for managing arthritis.

3. Inhibition of Pro-Inflammatory Signaling Pathways  
NF- $\kappa$ B Pathway Inhibition (Central Mechanism)

- In arthritis, inflammatory stimuli activate NF- $\kappa$ B, which is a transcription factor.

- Activated NF- $\kappa$ B enters the nucleus and promotes the transcription of TNF- $\alpha$ , IL-1 $\beta$ , IL-6, COX-2, and iNOS.

Flavonoids in *P. reptans* inhibit NF- $\kappa$ B activation by preventing the degradation of I $\kappa$ B (NF- $\kappa$ B inhibitor) and blocking the nuclear translocation of NF- $\kappa$ B. Finally, the synthesis of inflammatory mediators is Reduced.

#### MAPK Pathway Suppression

MAPK pathways (p38, JNK, ERK) amplify inflammation in arthritis. Compounds from *P. reptans* Suppress MAPK phosphorylation, reduce cytokine gene expression, and decrease inflammatory enzyme activation. Ultimately, Lower inflammatory signaling was observed in the synovial tissue.

4. Downregulation of inflammatory mediators are cytokines ( $\downarrow$  tumor necrosis factor-alpha [TNF- $\alpha$ ,  $\downarrow$  IL-1 $\beta$ ,  $\downarrow$  IL-6).

These cytokines are responsible for synovial hyperplasia, cartilage degradation, pain, and swelling. It Leads to reduction in joint inflammation and pain

#### 5. Antioxidant Mechanism (Joint Protection)

The roles of oxidative stress in arthritis include ROS damage to the cartilage matrix, promotion of lipid peroxidation, and activation of inflammatory pathways.

Antioxidant Action of *P. reptans*: Flavonoids and Phenolics

- Scavenge free radicals
- Increase endogenous antioxidants (SOD, catalase)
- Reduce oxidative injury to joints

It Prevents cartilage erosion and disease progression

#### 6. Immunomodulatory and Membrane-Stabilizing Effects

It reduces the activation of macrophages and neutrophils, decreases lysosomal enzyme release, and stabilizes cellular membranes. That's why it Limits immune-mediated joint destruction

### IX. CONCLUSIONS AND FUTURE OUTLOOK.

*P. Reptans* ethanolic extract's phytochemical synergy is probably what gives it its anti-arthritic properties. While alkaloids exert analgesic effects, possibly through opioid receptor modulation, flavonoids block

inflammatory cascades (Roeder, 2000). Similar to DMARDs but with fewer side effects, this results in decreased synovial inflammation and maintained cartilage integrity in Wistar rat models. In certain models, *P. reptans* performed better than extracts from *Boswellia serrata* (30% edema reduction), but it lagged behind *Curcuma longa* (70%), indicating species-specific potency (Aggarwal et al., 2007). Owing to improved compound solubilization, its ethanolic form is superior to its methanolic or aqueous counterparts. According to this review, *P. reptans* may be used as adjunct therapy to treat arthritis. However, for clinical translation, standardization, such as HPLC fingerprinting, is essential.

#### Future Directions

- Long-term efficacy studies in primates.
- Isolation of active compounds (e.g., quercetin derivatives).
- Clinical trials in patients with RA.
- Exploration of nanoformulations for enhanced bioavailability.

The ethanolic extract of *Polemonium reptans* leaves exhibits promising anti-arthritic activity in albino Wistar rats, owing to its high phytochemical content. Phytochemical screening confirmed alkaloids, flavonoids, and tannins as key contributors, with in vivo studies showing dose-dependent reductions in arthritis markers. Although preclinical evidence is promising, thorough clinical validation is necessary to fully realize its potential for human use. This review promotes sustainable harvesting and quality control while highlighting the importance of ethnobotanical knowledge in contemporary drug discovery.

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