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Evaluation of *Urtica dioica* Ointment in the Management of Eczema: A Phytopharmaceutical Approach

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Abstract

Background: Eczema, or atopic dermatitis (AD), is one of the most prevalent chronic inflammatory skin conditions globally, characterized by itching, redness, and recurrent flare-ups. Current treatments rely on corticosteroids and calcineurin inhibitors, which though effective, cause side effects with prolonged use.

Eczema, a chronic inflammatory skin disorder, often requires long-term management. *Urtica dioica*, a medicinal plant known for its anti-inflammatory and antioxidant properties, offers a natural alternative. This research evaluates 2% and 4% *Urtica dioica* extract ointments for their therapeutic efficacy in eczema treatment. Methanolic extracts were formulated into ointments using the fusion method and evaluated through physicochemical, in vitro, and in vivo parameters. The 4% formulation demonstrated superior anti-inflammatory and antipruritic effects, supporting *Urtica dioica* as a viable option for eczema management. Methanolic extracts of *Urtica dioica* were incorporated into ointment formulations and evaluated through physicochemical tests, phytochemical screening, in vitro anti-inflammatory activity, and in vivo therapeutic effect using a DNCB-induced eczema model in Wistar rats. Results showed that the 4% extract formulation had significantly greater anti-inflammatory and healing effects than the 2% formulation. This study supports the inclusion of *Urtica dioica* in dermatological formulations and warrants further clinical research.

Keywords: *Urtica dioica*, eczema, Phytopharmaceutical, herbal ointment, anti-inflammatory, topical therapy.

1. Introduction

Eczema or atopic dermatitis affects nearly 15–30% of children and up to 10% of adults globally. It manifests as erythema, pruritus, vesiculation, and lichenification, often with flare-ups triggered by allergens, irritants, or stress.[1,2] Long-term use of corticosteroids can result in side effects such as skin atrophy, pigmentation changes, and systemic absorption issues . Herbal medicines provide safer alternatives with fewer adverse effects and better patient compliance. *Urtica dioica* (stinging nettle) is a perennial herb from the Urticaceae family used traditionally in European and Asian medicine. The plant is rich in flavonoids, phenolic acids, vitamins, terpenoids, and minerals that contribute to its pharmacological activities such as anti-inflammatory, antihistaminic, antimicrobial, and wound-healing [1– 4, 24, 29, 30]. This study focuses on the formulation and evaluation of 2% and 4% *Urtica dioica* ointments and their therapeutic potential in treating eczema.

It affects both children and adults, with chronic manifestations leading to significant discomfort. Conventional treatments, such as corticosteroids, pose long-term side effects. Therefore, there is an increasing demand for herbal remedies. *Urtica dioica* (stinging nettle) has been traditionally used for inflammatory conditions and skin disorders. This plant contains flavonoids, tannins, phenolic acids, and vitamins which contribute to its healing properties.[3,4]

Pathophysiology and Current Treatment Strategies

Eczema, also known as atopic dermatitis, is a long-term skin condition that develops because of a combination of genetic, immune, and environmental factors.

1. Skin barrier defect – Normally, the skin acts like a shield to lock in moisture and block harmful substances. In eczema, a mutation or weakness in proteins like filaggrin causes the skin barrier to become “leaky.” As a result, the skin loses water easily, becomes dry, and irritants or allergens can penetrate more easily.[5]

2. Immune system imbalance – The immune system of eczema patients is often overactive. Special immune cells release chemicals (cytokines such as IL-4 and IL-13) that create inflammation. This leads to redness, itching, and swelling.[6]

3. Environmental triggers – Everyday things like dust, pollen, harsh soaps, temperature changes, or stress can worsen symptoms. Since the barrier is already weak, these triggers easily flare up the condition.

Overall, eczema develops because the skin barrier is broken and the immune system reacts too strongly, leading to inflammation, dryness, and constant itching.

Current Therapeutic Strategies

The main goal of eczema treatment is to reduce inflammation, repair the skin barrier, and control itching. Common treatment options include:

1. Moisturizers (Emollients): These are the first line of care. They keep the skin hydrated, reduce dryness, and improve the protective barrier.[7]

2. Topical corticosteroids: These creams or ointments quickly reduce inflammation and itching. However, if used for a long time, they can thin the skin, cause discoloration, and lead to other side effects.[8]

3. Calcineurin inhibitors (Tacrolimus, Pimecrolimus): These medicines calm the immune response and are used in sensitive areas like the face and folds. They are safer for long-term use compared to steroids but may cause burning or stinging at first.[7]

4. Antihistamines: Sometimes used to reduce itching, especially at night, although their benefit is limited.[9]

5. Newer therapies (Biologics): For severe eczema, injections like dupilumab target specific immune pathways (IL-4, IL-13) and show very good results.

6. Lifestyle and trigger management: Avoiding irritants, using gentle cleansers, managing stress, and wearing soft clothing are also important parts of therapy. These limitations necessitate safer, herbal alternatives.

Herbal Medicine in Dermatology

Herbal medicine uses plants and their natural compounds to prevent and treat diseases. In dermatology (the study of skin diseases), herbs are often preferred because they are generally safer, cause fewer side effects than synthetic drugs, and can be used for long-term skin care.[10]

Skin problems such as eczema, acne, psoriasis, and wounds are often linked to inflammation, infection, or oxidative stress. Many medicinal plants naturally contain compounds like flavonoids, tannins, saponins, and phenolic acids. These work together to reduce redness, swelling, itching, and to promote skin healing.[11,12]

Some commonly used plants in dermatology are:[13]

Aloe vera – soothes burns, wounds, and moisturizes the skin.

Turmeric (*Curcuma longa*) – contains curcumin, which reduces inflammation and prevents infection.

Neem (*Azadirachta indica*) – has antibacterial and antifungal action, useful for acne and eczema.

Urtica dioica (stinging nettle) – rich in antioxidants and anti-inflammatory compounds, helps reduce itching and swelling in eczema.

Importance of *Urtica dioica*:

Urtica dioica (stinging nettle) is a perennial herb of the Urticaceae family, widely distributed in temperate regions. Traditionally, nettle has been used in treating arthritis, allergic rhinitis, urinary disorders, and skin conditions [14]. Phytochemical studies reveal that Urtica dioica is rich in flavonoids, phenolic acids, tannins, vitamins, and minerals [15]. Flavonoids are potent inhibitors of inflammatory mediators such as TNF-α and COX enzymes [16]. Previous studies demonstrated that nettle extracts reduce oxidative stress, scavenge free radicals, and modulate inflammatory cytokines [17, 18].

Despite these promising pharmacological properties, limited scientific evidence exists on its topical application in eczema. Thus, the present research aimed to develop *Urtica dioica* ointments, evaluate

their physicochemical and anti-inflammatory properties, and compare their activity with tacrolimus ointment.

1.1 Plant profile

Kingdom:	**Plantae – Plants**
Subkingdom:	**Tracheobionta**
Superdivision:	**Spermatophyta - Seed plants**
Division :	**Magnoliophyta - Flowering plants**
Class :	**Magnoliopsida – Dicotyledons**
Subclass :	**Hamamelididae**
Order:	**Urticales**
Family:	**Urticaceae – nettle family**
Genus :	**Urtica L.**
Common name : stinging nettle/bichu ghas	

***Fig. 1Urticadioica* flowering**

***Fig.1.2 Urticadioica* leafs**

Stinging nettle, *or Urtica dioica*, originally comes from the colder areas of northern Europe and Asia, but it now grows all around the world. This plant does well in soil rich in nitrogen and blooms from June to September, reaching about 3 feet tall. It has a straight, green stem and green leaves that are darker on top and lighter underneath, with edges that are finely toothed. The small flowers are reddish-brown or

greenish-white and grow in clusters near the top leaves. The plant usually has either male or female flowers, which is why it's called *"dioica,"* meaning "two houses." Stinging nettle flowers from May to September each year. [19]

Botanical description:

Urtica dioica is a dioecious plant, with male and female flowers on separate plants. The male flowers are arranged in axillary clusters, while the female flowers are solitary or in pairs. The plant grows up to 1-2 meters tall, with a spreading habit. The roots are fibrous and branched, with a taproot that can grow up to 30 cm deep [20].

Traditional uses:

Stinging nettle *(Urtica dioica*) has been used for a long time in home remedies and as part of a nutritious diet. The powdered leaf extract has traditionally been used to reduce heavy menstrual bleeding and nosebleeds. People have also used this plant to treat arthritis, anemia, allergies eczema and as a diuretic, astringent, and blood tonic in folk medicine. A tea made from its leaves has been used as a cleansing tonic and blood purifier. [21]The plant has been used to treat various health conditions, including arthritis, gout, and skin disorders[22]. The leaves and stems of the plant have been used to make teas, infusions, and tinctures, which have been used to treat conditions such as allergies, asthma, and bronchitis [23].The plant has also been used topically to treat skin conditions such as eczema, acne, and wounds [24]. The stinging hairs of the plant contain histamine, serotonin, and other compounds that can help to reduce inflammation and promote healing. In addition, *Urtica dioica* has been used as a diuretic, to treat urinary tract infections, and to reduce inflammation [25]. In traditional European medicine, *Urticadioica* was used to treat a range of conditions, including rheumatism, sciatica, and neuralgia [26]. The plant was also used to treat digestive problems, such as constipation and diarrhea . In traditional Chinese medicine, *Urtica dioica* is used to treat conditions such as arthritis, bronchitis, and asthma .In recent years; *Urtica dioica* has been studied for its potential health benefits, including its anti-inflammatory, antioxidant, and antimicrobial properties . The plant has also been shown to have potential

in the treatment of certain types of cancer, including prostate cancer .In traditional European medicine, *Urtica dioica* was used to treat a range of conditions, including rheumatism, sciatica, and neuralgia [27].

General uses:

Stinging nettle has a long history of being used to treat a variety of conditions, including rheumatism, arthritis, gout, eczema, anaemia, urinary tract infections, kidney stones, hay fever, and the early stages of benign prostatic hyperplasia (BPH). Recent studies, both in the laboratory and in clinical settings, have indicated that stinging nettle may have potential anti-arthritic properties. [28,29] The plant has also been used as a food and beverage ingredient for centuries. The leaves of the plant can be made into a tea that is rich in vitamins and minerals. The leaves and stems can also be used in soups and stews to add flavour and nutrition. Furthermore, the leaves can be used to make a pesto sauce that is rich in vitamins and mineral.

In traditional cosmetics, *Urtica dioica* has been used to treat skin conditions such as acne, eczema, and psoriasis. It has also been used to treat hair conditions such as dandruff, itchiness, and hair loss. The plant has also been used in various industrial applications. It can be used as a natural dye plant to create a range of colors. The plant can also be used to produce fibers that can be used in textiles. Additionally, it can be used to create compost that is rich in nutrients. [30]

Phytochemistry:

Phytochemistry is the study of the phytoconstituents found in plants. These compounds, known as phytochemicals, can have various biological effects and contribute to the plant's medicinal and nutritional properties. The commonly known phytochemical compounds from *U. dioica* are flavonoids,phenolic acids,fatty acids, tanins, volatile compounds and sterols .[31] The flavonoids present in *Urtica dioica* include quercetin, kaempferol, and isorhapontigenin, which have been shown to possess antioxidant, anti-inflammatory, and antimicrobial properties (25,26). The phenolic acids, such as caffeic acid, ferulic acid, and sinapic acid, have been found to exhibit antioxidant and anti-inflammatory activities (27, 28). The terpenoids, including β-sitosterol and stigmasterol, have been reported to possess anti-inflammatory and

antimicrobial properties (29, 30). The alkaloids present in *Urtica dioica* include choline, acetylcholine, and histamine, which have been found to exhibit various biological activities, including anti-inflammatory and antimicrobial effects.[32,33]

Materials and Methods

Plant Material and Authentication

Leaves of *Urtica dioica* were collected from Kullu district, Himachal Pradesh, India, in august 2024. The plant was authenticated by the Department of Botany, Sardar Patel University, Himachal Pradesh, and a voucher specimen was deposited for future reference.

Steps in Soxhlet Extraction [34,35]

1. Preparation of Plant Material:

- Dry the plant material to remove moisture.

- Grind the dried plant material into a fine powder to increase the surface area for extraction.

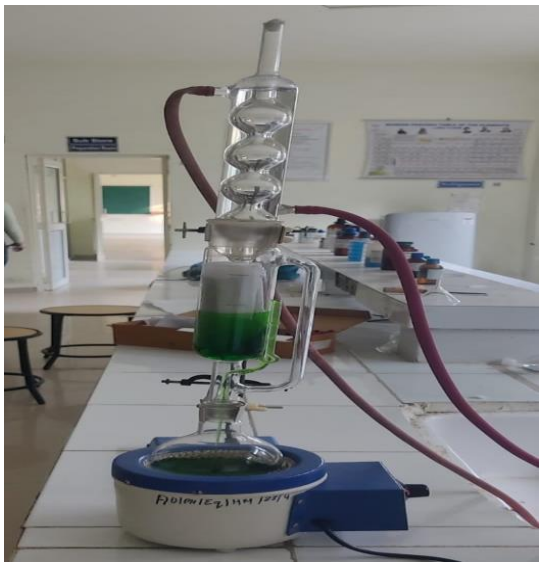
2. Setting up the Apparatus:

- Place the ground plant material into a thimble made of filter paper, which is then placed in the Soxhlet extractor. Attach the Soxhlet extractor to a round-bottom flask containing the solvent. Connect a condenser to the top of the Soxhlet extractor to condense the vaporized solvent back into liquid form.

3. Extraction Process:

- Heat the solvent in the round-bottom flask. The solvent vaporizes travels up into the condenser where it cools and condenses back into liquid form, and drips into the chamber holding the plant material. As the solvent fills the Soxhlet chamber, it immerses the plant material and extracts the desired compounds. When the chamber reaches a certain level, it siphons the solvent, along with the dissolved compounds, back into the round-bottom flask. This cycle repeats for several hours, allowing for continuous extraction until the solvent in the flask becomes saturated with the extracted compounds.

4. Recovery of Extract: - After the extraction is complete, remove the solvent by evaporation (using a rotary evaporator or other methods) to obtain the concentrated plant extract.



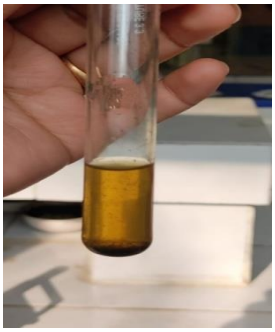
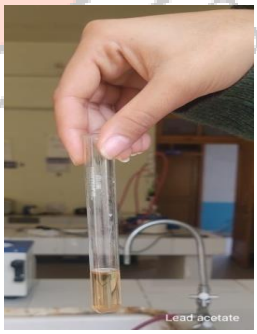
Extraction Process

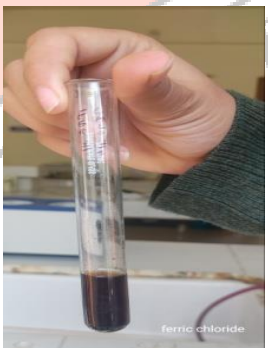
1kg of dried and powdered *Urtica dioica* leaves were subjected to Methanolic extraction by maceration for 72 hours at room temperature with occasional stirring. The extract was filtered, concentrated under reduced pressure in a rotary evaporator, and dried to obtain a dark green semi-solid mass weighing 32 g.

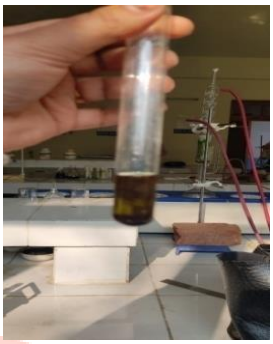
fig. urtica-dioica extract

Phytochemical Screening

The Methanolic extract was analyzed using standard phytochemical tests [36]:

Phytochemical group	**Test performed**	**Result**
Alkaloids	Dragondroffs test	(orange precipitate – positive) 
Flavonoids	Lead acetate test	(yellow precipitate – positive) 

Tannis	Gelatin test	**(**white precipitate – positive 
Saponins	Foam test	(foam – positive) 
Phenolic compounds	Ferric chloride test	(blue-green coloration – positive) 
Proteins and amino acids	Ninhydrin test	(purple color – positive) 

Carbohydrates	Molisch`s test	(violet ring – positive) 

Formulation of Ointments

Two ointment formulations were prepared by the fusion method:

- F1: 2% w/w *Urtica dioica* extract
- F2: 4% w/w *Urtica dioica* extract

Ointment base composition:

1. White soft paraffin: 80%
2. Lanolin: 10%
3. Propylene glycol: 8%
4. Extract: 2% or 4%

All ingredients were melted and mixed, and the extract was incorporated under stirring until uniform. The ointments were stored in collapsible aluminum tubes.

2% *urtica-dioica* ointment

4% *urtica-dioica* ointment

Physicochemical Evaluation of Ointments

1. Appearance & Homogeneity: Visual inspection for color, texture, phases separation.

2. pH: Measured by dispersing 1 g ointment in 50 mL distilled water.

3. Spreadability: Evaluated using two glass slides with 200 g weight for 5 min. Formula:

4. Viscosity: Measured using Brookfield viscometer (spindle T-bar at 25 ± 2 °C).

5. Extrudability: Tube extrusion test.

6. Washability: Assessed by washing with tap water and soap.

7. Consistency and Grittiness: Touch test for smoothness.

8. Stability Study: Samples stored at 4 °C, 25 °C, and 40 °C for 90 days and observed for changes.

In Vitro Anti-inflammatory Activity

Protein denaturation assay was used [37]. Test solutions were mixed with albumin and heated at 70 °C for 5 minutes to induce denaturation. Absorbance was measured at 660 nm using UV-visible spectrophotometer.

Tacrolimus ointment (0.1% w/w) served as the standard. Each sample was tested in triplicate.

Material and method:

Sample;

Urtica dioica ointment (2% w/w extract concentration)

Urtica dioica ointment (4% w/w extract concentration)

Standard Drug: Tacrolimus (1% w/w ointment)

Reagents: Fresh egg albumin, phosphate-buffered saline (PBS, pH 6.4)

Equipment: UV-Visible spectrophotometer

Procedure:

1. 1% egg albumin solution: Dilute fresh egg white with PBS (pH 6.4) to 1% v/v. Mix gently to avoid foaming.

   2. Sample stock: Disperse 1 g of each ointment in 10 mL PBS to get a uniform suspension. (As used in your method.**)**

   Procedure (step-by-step)

   1. Label tubes for: Control, Standard, and each Test sample.
   2. Prepare mixtures (10 mL each):
   3. Control: 5 mL of 1% egg albumin + 5 mL PBS.
   4. Standard/Test: 5 mL of 1% egg albumin + 1 mL sample stock + 4 mL PBS (keeps total volume equal across tubes).
   5. Incubate at 37 °C for 15 min (to allow interaction between albumin and sample).
   6. Heat at 70 °C for 5 min to induce denaturation; immediately cool to room temperature (running water bath or bench cool).
   7. Measure absorbance at 660 nm against PBS as instrument blank. Record three replicates for each group. (Your tables use 660 nm and triplicates.)
   8. Calculate % inhibition of protein denaturation using.

Results

Phytochemical Analysis

The extract showed presence of alkaloids, flavonoids, tannins, saponins, phenolic compounds, proteins, and carbohydrates, all known for anti-inflammatory and antioxidant activity.

Physicochemical Evaluation

Appearance:	**Smooth, greenish, semi-solid, homogeneous.**
pH:	**F1 – 6.5, F2 – 6.6 (skin-friendly range).**
Spreadability:	**F1 – 27.5 g·cm/sec; F2 – 28.5 g·cm/sec.**
Viscosity:	**F1 – 30,260 cps; F2 – 30,225 cps.**
Extrudability:	**Smooth extrusion in ribbon form.**
Washability:	**Moderately washable with soap.**
Consistency and Grittiness:	**Smooth, non-greasy, free of coarse particles.**
Stability:	**No change in color, odor, pH, or consistency after 90 days.**

In Vitro Anti-inflammatory Activity

Table 1: Inhibition of protein denaturation

% inhibition = 1- Absorbance of test sample x 100

Absorbance of control

Sample	**Absorbance (mean ±SD)**	**%Inhibition of protein denaturation(mean±SD)**
Control (no drug)	1.000±0.00	0.00±0.00
Tacrolimus ointment (0.1%)	0.215±0.004	78.5±0.42
2% *urticadioica* ointment	0.448±0.004	55.2±0.36
4% *urticadioica* ointment	0.366±0.004	63.4±0.40

The 4% ointment showed higher inhibition of protein denaturation than 2%, though less than tacrolimus.

Animal study:

In vivo Anti-Eczema Study

The in vivo evaluation of the formulated ointments was performed using a DNCB-induced eczema model in Wistar albino rats.(38)

Animals:

Healthy Wistar albino rats (150–200 g) of male sex were used in the study. The animals were procured from the animal house facility of [Abhilashi university chail chowk, mandi] and maintained under standard laboratory conditions (12 h light/dark cycle, 25 ± 2 °C, 50–60% RH) with free access to standard pellet diet and water ad libitum. The study protocol was approved by the Institutional Animal Ethics Committee (IAEC), approval no. [9], as per CPCSEA guidelines. (39)

Induction of Eczema:

The dorsal region of each rat was shaved (2 × 2 cm^2 area) and sensitized with topical application of 1% w/v DNCB (dinitrochlorobenzene) solution in acetone. On day 1, 100 µL of DNCB was applied (sensitization phase). On days 5, 6, and 7, the same concentration was reapplied (challenge phase). After 48–72 h, erythema, edema, were observed, confirming the development of eczema.(40,41)

Record erythema and edema at baseline (before sensitization), after DNCB challenge (e.g., 24 h post-challenge), and at pre-defined treatment intervals (for example days 0, 7, 14 — match your experimental schedule). Report the exact time points in the Methods section.(42)

Grouping of Animals:

Sr. no.	**Group**	**Drug**	**Dose**	**Route of administration**
1	Standard control	Tacrolimus	1% Ointment	Topical
2	Test group	Plant extract ointment	2% *urtica-dioica* extract ointment	Topical
3	Test group	Plant extract ointment	4% *urtica-dioica* extract ointment	Topical

Treatment Protocol:

The respective ointments were applied topically to the affected dorsal skin region once daily for 14 consecutive days.

Evaluation Parameters:

1. Clinical scoring: Erythema, edema, were assessed on a 0–3 scale (0 = none, 1 = mild, 2 = moderate, 3 = severe).

1. Assess erythema: Assess the level of erythema (redness) on a scale of 0-3, where 0 = no erythema and 3 = severe erythema.

2. Assess edema: Assess the level of edema on a scale of 0-3, where 0 = no excoriation and 3 = severe excoriation

Area = length × width

Sr. no.	**Groups**	**No. of animals**
1	Standard control	**3**
2	Test control	**3**
3	Test control	**3**

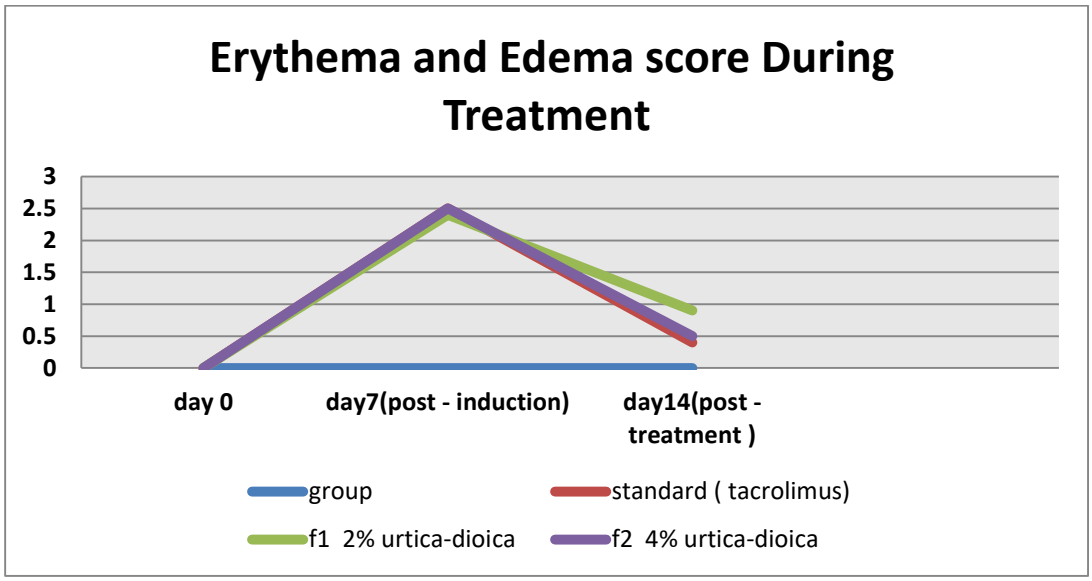
Treatment Duration:

14days

Results (With Standard Deviation)

Table 16: Erythema and Edema Score (Mean ± SD)

Group	**Day 0**	**Day 7 (Post-Induction)**	**Day 14 (Post-Treatment)**
Standard (Tacrolimus)	0.00 ± 0.00	2.50 ± 0.28	0.40 ± 0.15
F1 (2% *U. dioica*)	0.00 ± 0.00	2.40 ± 0.26	0.90 ± 0.12
F2 (4% *U. dioica*)	0.00 ± 0.00	2.50 ± 0.30	0.50 ± 0.10



Discussion

The present study evaluated the formulation and therapeutic efficacy of *Urtica dioica* Methanolic extract ointments (2% and 4%) for the management of eczema. Phytochemical analysis confirmed the presence of alkaloids, flavonoids, tannins, phenolic compounds, saponins, proteins, and carbohydrates. These bioactive constituents are well-documented for their antioxidant and anti-inflammatory roles, and likely contributed to the observed pharmacological effects.

Physicochemical evaluations of both formulations indicated desirable characteristics such as smooth consistency, homogeneity, suitable pH (6.5–6.6), spreadability, and viscosity, ensuring patient acceptability and topical stability. Stability testing further confirmed that the ointments retained their organoleptic and physicochemical properties over 90 days, indicating good shelf-life potential.

In vitro anti-inflammatory testing using the protein denaturation assay demonstrated that both formulations inhibited protein denaturation in a concentration-dependent manner. The 4% ointment exhibited greater activity (63.4%) compared to the 2% ointment (55.2%), although the effect was lower than that of standard tacrolimus ointment (78.5%). This suggests that *Urtica dioica* contains compounds that can effectively suppress inflammatory processes associated with eczema.

The in vivo DNCB-induced eczema model supported these findings. Both ointments reduced erythema and edema scores significantly after 14 days of treatment, with the 4% formulation (score 0.5) showing a closer response to tacrolimus (score 0.4) than the 2% formulation (score 0.9). These results highlight the dose-dependent efficacy of *Urtica dioica* in alleviating eczema symptoms.

Overall, while the formulations were slightly less potent than tacrolimus, they offer a promising herbal alternative with fewer risks of side effects such as burning, irritation, and long-term immunosuppression. The outcomes align with previous literature that reports strong anti-inflammatory and wound-healing potential of *Urtica dioica.*

Conclusion

The present research demonstrated that Methanolic extract of *Urtica dioica* possesses phytochemicals with anti-inflammatory potential. Ointments containing 2% and 4% extract were stable, skin-compatible, and exhibited significant inhibition of protein denaturation in vitro. The 4% ointment was more effective than 2%. These findings support the traditional use of nettle in skin disorders and provide a basis for further preclinical and clinical investigations.

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