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# Formulation and Evaluation of Polyherbal Anti-Inflammatory Gel Containing Pyrus Pashia (Kainth) Fruit Extract

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**Abstract:** *Inflammation represents a vital protective response to tissue injury; however, uncontrolled or chronic inflammatory cascades can cause substantial pain, edema, and tissue damage.*
*Conventional treatment with oral nonsteroidal anti-inflammatory drugs (NSAIDs) is severely restricted by systemic complications, including gastrointestinal ulceration, hepatotoxicity, and renal stress. To overcome these limitations, the present study developed and evaluated a topical polyherbal hydrogel incorporating the bioflavonoid-rich fruit extract of Pyrus pashia Buch.-Ham. ex D. Don (commonly known as Kainth). Air-dried fruit powder was extracted using a 70% v/v hydroethanolic solvent system via cold maceration and continuous hot extraction (Soxhlet), achieving an extraction yield of 12.4% w/w. Phytochemical screening confirmed substantial concentrations of phenolics, flavonoids, condensed tannins, and saponins. Three distinct hydrogel formulations (F1, F2, and F3) were compounded utilizing varying concentrations of Carbopol 940 (1.0%, 1.5%, and 2.0% w/w), plasticized with propylene glycol and neutralized to physiological neutrality with triethanolamine.*
*The prepared formulations were characterized for organoleptic properties, skin-compatible pH, dynamic viscosity, spreadability, extrudability, and in-vitro anti-inflammatory activity. All formulations exhibited homogeneous appearance, absence of phase separation, and physiologically tolerable pH values ranging between 6.4 ± 0.12 and 6.8 ± 0.11. Formulation F2 (1.5% w/w Carbopol 940) demonstrated an optimal rheological balance, displaying a viscosity of 5,800 ± 210 cps, superior spreadability (5.5 ± 0.18 cm), and excellent extrudability. In the egg albumin protein denaturation assay, formulation F2 demonstrated a maximum inhibition of 78.4% ± 1.5%, which was significantly higher than F1 (62.1%) and F3 (71.5%), while closely approaching the standard reference diclofenac sodium gel (85.2% ± 1.2%). These findings confirm that formulation F2 provides an effective, skin-compatible topical delivery system capable of sustained local anti-inflammatory action..*

**Keywords:** *Pyrus pashia*, Kainth, polyherbal gel, topical drug delivery, anti-inflammatory activity, Carbopol 940, protein denaturation.

## I. INTRODUCTION

Inflammation is a fundamental protective vascular and cellular response elicited by living tissues against noxious stimuli, including mechanical trauma, microbial invasion, or cellular damage [1].

The acute inflammatory phase is classically defined by cardinal clinical signs: rubor (redness), calor (heat), tumor (swelling), dolor (pain), and functio laesa (loss of function). At the microvascular level, the process entails immediate local vasodilation, elevated capillary permeability, plasma extravasation, and the chemotactic recruitment of inflammatory leukocytes—principally neutrophils and macrophages—to the afflicted anatomical site. Although acute

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inflammation functions as an essential mechanism for clearing necrotic debris and initiating tissue regeneration, unchecked or prolonged inflammation triggers chronic tissue destruction and progressive inflammatory disorders.

Oral administration of synthetic nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids represents the conventional pharmacological strategy for managing inflammatory symptoms [2]. However, prolonged systemic exposure to these agents is linked to significant clinical liabilities, including gastrointestinal mucosal ulceration, hemorrhage, cardiovascular complications, and renal insufficiency [3]. Oral therapy is also constrained by extensive hepatic first-pass metabolism, which diminishes active drug bioavailability before it reaches peripheral inflammatory foci. Consequently, there is an urgent clinical imperative to formulate localized topical delivery platforms that deliver high active concentrations directly to target tissues while averting systemic adverse reactions.

The integration of botanical bioactive agents into pharmaceutical formulation science represents a rapidly expanding paradigm aimed at discovering safer, multi-targeted therapeutics [4].

Botanical secondary metabolites, most notably polyphenols, flavonoids, tannins, and terpenoids, possess broad pharmacological activities that modulate multiple enzymatic cascades of inflammation, including cyclooxygenase (COX-2) and lipoxygenase (LOX) pathways, as well as oxidative stress cascades [11, 12]. Plant extracts offer notable clinical advantages over single synthetic molecules due to the synergistic bioactivity among co-existing phytochemicals, paired with a lower propensity for producing long-term systemic toxicities.

Pyrus pashia Buch.-Ham. ex D. Don, commonly known as wild Himalayan pear or Kainth, is a deciduous tree belonging to the family Rosaceae, widely distributed across the temperate and subtropical Himalayan ranges at altitudes between 700 and 2700 meters [5, 6]. In traditional ethnomedicinal systems across Northern India and Nepal, fruit decoctions and leaf poultices of Pyrus pashia have long been utilized topically to treat joint pain, muscular swellings, skin eruptions, and local inflammatory disorders [7, 8]. Phytochemical investigations confirm that the fruits contain high concentrations of bioactive flavonoids (such as quercetin, rutin, and kaempferol derivatives), condensed tannins, and polyphenolic acids that exert powerful membrane-stabilizing and free-radical scavenging activities [10].

Topical hydrogels have gained prominence as ideal carrier vehicles for plant bioactives [13, 14]. Hydrogels consist of three-dimensional polymeric networks capable of holding substantial volumes of aqueous solvent while preserving structural consistency and yield stress [15]. Unlike greasy ointments or thin lotions, aqueous gels exhibit favorable spreadability, pleasant cooling sensation, non-greasy aesthetic appeal, and prolonged dermal retention. By cross-linking polymers such as Carbopol 940 with neutralizing agents, a vehicle is established that facilitates steady percutaneous permeation of botanical constituents through the stratum corneum.

Formulating Pyrus pashia fruit extract into a standardized topical hydrogel therefore presents a scientifically grounded, non-invasive alternative for the local management of inflammatory conditions.

## II. BOTANICAL PROFILE OF PYRUS PASHIA

### 2.1 Taxonomy and Botanical Description

Pyrus pashia Buch.-Ham. ex D. Don, commonly designated as wild Himalayan pear or Kainth, is a small to medium-sized deciduous tree belonging to the family Rosaceae [5]. Taxonomically, the plant is classified under the Kingdom Plantae, Division Magnoliophyta, Class Magnoliopsida, Order Rosales, Family Rosaceae, Genus Pyrus, and Species P. pashia [6]. Morphologically, the species possesses ovate to lanceolate, finely serrated foliage and produces small white or pinkish-white blossoms arranged in corymbose clusters during the spring season. The fruits are small, globose or pyriform pomes measuring roughly 1.5 to 2.5 cm in diameter. During early development, the fruit is firm, astringent, and greenish-brown, which gradually matures into a dark brown or blackish pome characterized by pale surface spots.

### 2.2 Geographical Distribution and Vernacular Names

Pyrus pashia is widely distributed across the temperate and subtropical belts of the Himalayas, spanning Northern India, Nepal, Bhutan, Myanmar, Pakistan, and Southwestern China [7, 9].

The tree establishes itself readily in well-drained soils, open woodland slopes, and hillside terrains at altitudes ranging between 700 and 2700 meters above sea level [5]. Regionally, the plant is recognized by diverse vernacular names,

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including Kainth or Kaith in Hindi and Punjabi, Wild Himalayan Pear in English, Passi in Nepalese, and Mahalup across local Himalayan dialects.

### 2.3 Traditional and Ethnomedicinal Uses

In traditional Himalayan medicine and Ayurvedic practices, various parts of Pyrus pashia have extensive documentation for managing gastrointestinal, thermal, and inflammatory disorders [6, 8]. The ripe fruits are conventionally consumed to manage gastrointestinal complications, including diarrhea, dysentery, and indigestion [7]. Furthermore, leaf decoctions and fruit extracts are traditionally applied topically to soothe joint pain, localized swelling, muscular soreness, and inflammatory skin conditions, relying on the astringent and soothing characteristics of the botanical tissue [10].

## III. PHYTOCHEMICAL CONSTITUENTS

Phytochemical characterization of Pyrus pashia fruit extract reveals an abundant profile of bioactive secondary metabolites responsible for its therapeutic properties. The dominant classes of compounds identified include polyphenols, flavonoids (specifically quercetin, rutin, and kaempferol derivatives), condensed tannins, and proanthocyanidins, alongside organic acids and saponin glycosides. These secondary metabolites confer potent free-radical scavenging, antioxidant, and lysosomal membrane-stabilizing activities, which suppress the generation of pro-inflammatory mediators and support their application in topical anti-inflammatory formulations.

Preliminary qualitative phytochemical screening of the crude hydroethanolic fruit extract systematically confirmed the presence of these key chemical classes:

- Flavonoids: Confirmed by the Shinoda test, where treatment with magnesium ribbon and concentrated hydrochloric acid yielded a characteristic pinkish-scarlet coloration, as well as a positive reaction with lead acetate reagent.
- Phenolic Compounds: Verified through the ferric chloride test, where addition of neutral 5% ferric chloride solution to the extract produced an intense deep blue-black coloration.
- Tannins: Identified via the gelatin test, wherein the addition of a 1% gelatin solution containing sodium chloride produced a distinct white precipitate.
- Saponins: Evidenced by the persistent froth test, where vigorous manual agitation of an aqueous extract dilution generated a stable honeycomb foam layer that persisted for more than 15 minutes.
- Glycosides and Steroids: Confirmed through positive qualitative responses in Fehling's test and the Salkowski reaction, respectively.

## IV. REVIEW OF RELEVANT LITERATURE

### 4.1 Pharmacological and Ethnobotanical Investigations on Pyrus pashia

Pyrus pashia Buch.-Ham. ex D. Don has attracted sustained scientific interest owing to its established prominence in indigenous Ayurvedic and Himalayan traditional health practices. Ethnobotanical documentation across the Western and Central Himalayas identifies the fruit, bark, and leaves of this deciduous Rosaceae species as effective natural remedies for chronic inflammatory afflictions, localized swelling, musculoskeletal aches, and oxidative stress-induced cellular damage.

Contemporary pharmacological investigations have systematically validated these folkloric assertions. Modern extraction and analytical profiling confirm that the fruits contain high concentrations of bioactive secondary metabolites, predominantly polyphenolic acids, flavonols, condensed tannins, catechins, and triterpenoids. Quantitative screenings indicate that the hydroethanolic crude extracts possess marked free-radical scavenging capacity against DPPH (2,2-diphenyl-1-picrylhydrazyl), ABTS, and superoxide radicals, correlating directly with total phenolic and flavonoid content. Furthermore, preliminary bioassays demonstrate that these phytoconstituents directly attenuate the release of key inflammatory mediators, including nitric oxide (NO) and prostaglandins, in lipopolysaccharide-stimulated cellular models, while preserving cellular viability.

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### 4.2 Polymeric Hydrogel Matrices and Controlled Topical Delivery

A review of contemporary formulation literature underscores the critical role played by polymeric excipients in translating crude plant extracts into therapeutically viable topical vehicles. While conventional topical formulations—such as greasy hydrocarbon ointments and water-in-oil creams—frequently exhibit poor patient acceptability, phase separation, and skin occlusiveness, synthetic cross-linked hydrogels have emerged as superior carrier matrices.

Among synthetic polymers, Carbopol 940 (a cross-linked polyacrylic acid polymer) has been extensively benchmarked against semi-synthetic cellulose derivatives such as hydroxypropyl methylcellulose (HPMC), carboxymethyl cellulose (CMC), and sodium alginate. Comparative rheological and biopharmaceutical evaluations demonstrate that Carbopol 940 creates a robust three-dimensional, cross-linked network upon alkaline neutralization. This structural network confers high yield stress, notable shear-thinning (pseudoplastic) flow behavior, clear optical transparency, and superior adherence to epidermal surfaces, thereby prolonging the retention time of active botanical phytoconstituents at the localized site of application.

## V. PROPOSED ANTI-INFLAMMATORY RATIONALE AND MOLECULAR MECHANISMS

### 5.1 Membrane Stabilization and Lysosomal Integrity

During acute and chronic inflammatory responses, mechanical trauma, endotoxins, or reactive chemical species destabilize the lipid bilayer membranes of circulating neutrophils, macrophages, and intracellular lysosomes. Rupture of lysosomal membranes precipitates the uncontrolled release of potent hydrolytic enzymes, acid proteases, and bactericidal peptides into extracellular interstitial spaces, resulting in extensive tissue catabolism, connective tissue degradation, and persistent edema.

The polyphenols, flavonoids (principally quercetin, rutin, and kaempferol derivatives), and condensed tannins identified in Pyrus pashia fruit extract interact electrostatically and hydrokinetically with membrane-bound proteins and polar heads of phospholipids. By intercalating into the phospholipid bilayer, these bioflavonoids decrease membrane fluidity, inhibit hypotonically induced erythrocyte lysis, and prevent the degranulation of lysosomes. This stabilizes biological membranes against extracellular shear and osmotic lysis, directly mitigating tissue damage.

### 5.2 Suppression of Pro-Inflammatory Enzymes and Eicosanoid Cascades

The cellular inflammatory cascade is driven by the enzymatic cleavage of membrane phospholipids by phospholipase A2 to liberate free arachidonic acid, which subsequently metabolizes down two primary pathways: the cyclooxygenase (COX-1 and COX-2) pathway and the 5-lipoxygenase (5-LOX) pathway. COX-2 enzymatic activity catalyzes the biosynthesis of pro-inflammatory prostaglandins (notably PGE2) and thromboxanes, which trigger intense microvascular dilation, increased microvascular permeability, and sensory pain fiber sensitization. Concurrently, the 5-LOX pathway synthesizes leukotrienes (such as LTB4), which serve as potent chemotactic agents for leukocyte migration and tissue edema.

Bioflavonoids derived from Pyrus pashia act as dual-pathway modulators. Through competitive active-site occupancy and hydrogen-bonding interactions with key catalytic residues, these phytochemicals downregulate COX-2 and 5-LOX activity. The simultaneous attenuation of prostaglandin and leukotriene biosynthesis reduces local vascular permeability, prevents extravasation of plasma fluids into interstitial spaces, and suppresses nociceptive signal transduction.

### 5.3 Free Radical Scavenging and Attenuation of Oxidative Stress

Inflammatory loci are characterized by the rapid infiltration of activated polymorphonuclear leukocytes, which undergo a respiratory burst that generates reactive oxygen and nitrogen species (ROS/RNS), including superoxide anions, hydrogen peroxide, and peroxynitrite.

Excessive ROS accumulation overwhelms endogenous antioxidant defenses, inducing lipid peroxidation of cellular membranes, oxidative DNA damage, and the activation of redox-sensitive transcription factors such as nuclear factor-kappa B (NF-κB).

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Pyrus pashia fruit polyphenols act as primary chain-breaking antioxidants. Possessing multiple phenolic hydroxyl moieties arranged across conjugated aromatic ring frameworks, these compounds readily donate hydrogen atoms and single electrons to neutralize free radicals into chemically inert products. By halting the self-propagating cascade of lipid peroxidation, the extract reduces ROS-mediated tissue degradation and attenuates downstream cytokine signaling.

## VI. RATIONALE FOR A TOPICAL GEL DELIVERY SYSTEM

### 6.1 Overcoming Limitations of Conventional Oral Therapeutics

Oral administration of synthetic nonsteroidal anti-inflammatory drugs (NSAIDs) remains the clinical standard for managing peripheral inflammatory disorders; however, its utility is severely restricted by systemic pharmacokinetics and toxicities. Orally ingested active ingredients undergo rigorous enzymatic breakdown in the gastrointestinal tract and first-pass hepatic biotransformation, demanding elevated systemic dosages to achieve therapeutic concentrations at peripheral joint and musculoskeletal target sites. Consequently, systemic COX-1 inhibition triggers severe gastrointestinal mucosal erosion, ulceration, hemorrhagic events, hepatotoxicity, and renal vasoconstriction. Formulating a topical vehicle avoids first-pass hepatic metabolism entirely, reduces systemic drug burden, and delivers concentrated therapeutic bioactives directly to the target tissue.

### 6.2 Advantages of Carbopol-Based Hydrogel Systems

Carbopol 940-based hydrogels provide specific pharmaceutical, structural, and physiological benefits over alternative semisolid systems:

- Hydrophilic, Non-Greasy Architecture: Comprising an interconnected three-dimensional network hydrated with an aqueous vehicle, the hydrogel dries smoothly without sticky or greasy residue, facilitating patient comfort and ease of washing.
- Pseudoplastic Rheology and Superior Spreadability: The hydrogel exhibits high static viscosity that prevents product leakage from primary containers, while undergoing immediate shear-thinning under minimal frictional stress. This enables uniform, thin-layer spreadability across tender, inflamed cutaneous surfaces without inducing mechanical pain.
- Enhanced Epidermal Hydration and Permeation: The high water fraction, combined with propylene glycol as a humectant, hydrates the stratum corneum, loosening dense lipid packing and promoting the transdermal diffusion of bioactive polyphenols into viable underlying epidermal and dermal strata.
- Controlled, Sustained Local Delivery: The cross-linked polymeric matrix entrains the botanical extract, regulating dissolution and diffusion rates to provide prolonged localized exposure.

### 6.3 Clinical Relevance and Patient Compliance

Topical administration allows targeted therapy directly over afflicted anatomical regions, such as arthritic joints, sprained ligaments, and localized inflammatory swellings. By avoiding gastrointestinal irritation, minimizing systemic adverse effects, and offering an intuitive, non-invasive method of application, topical Pyrus pashia hydrogel represents a therapeutically sound and patient-compliant strategy for managing local inflammatory disorders.

## VII. PROPOSED FORMULATION INGREDIENTS AND EXCIPIENTS

### 7.1 Active Pharmaceutical Ingredient (Botanical Extract)

The primary active therapeutic component is the standardized hydroethanolic extract obtained from the ripe fruits of Pyrus pashia Buch.-Ham. ex D. Don. Incorporated at a target concentration of 1.0% w/w, the extract serves as a concentrated reservoir of bioactive secondary metabolites—chiefly bioflavonoids (quercetin, rutin), polyphenolic acids, and condensed tannins—which provide localized anti-inflammatory, free-radical scavenging, and membrane-stabilizing activities.

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**7.2 Gelling Matrix (Carbopol 940)**

Carbopol 940 (cross-linked polyacrylic acid polymer) is selected as the primary structural hydrogel matrix. Evaluated across three distinct concentrations—1.0% w/w (Formulation F1), 1.5% w/w (Formulation F2), and 2.0% w/w (Formulation F3)—Carbopol 940 provides the high static yield stress and pseudoplastic (shear-thinning) flow essential for topical hydrogels. In its unneutralized state, the polymer chains remain coiled and acidic; upon neutralization, ionizing carboxyl groups generate electrostatic repulsion, expanding into a stable, transparent, three-dimensional viscoelastic network.

**7.3 Functional Excipients and Additives**

- Propylene Glycol (5.0% w/w): Acts as a multifunctional excipient, functioning as a humectant to retain water within the applied gel matrix and as a skin penetration enhancer to facilitate the diffusion of polar phytoconstituents across the stratum corneum.
- Ethanol (95% v/v, 5.0% w/w): Functions as a secondary co-solvent to ensure complete solubilization and homogenous dispersion of the semi-solid herbal extract prior to incorporation into the aqueous polymer dispersion.
- Triethanolamine (Quantity Sufficient, approximately 1.0% to 1.5% w/w): Serves as the primary alkalizing and cross-linking neutralizing agent. It converts the acidic polyacrylic acid dispersion into an isotropic, clear, viscoelastic hydrogel while buffering the final pH to physiological dermal compatibility.
- Methylparaben (0.1% w/w) and Propylparaben (0.02% w/w): Act as broad-spectrum antimicrobial preservatives, preventing bacterial, mold, and yeast proliferation within the water-rich gel vehicle during storage.
- Purified Distilled Water (Quantity Sufficient to 100% w/w): Serves as the continuous aqueous vehicle supporting polymer hydration and swelling.

Composition of Formulations (per 100 g):

- Formulation F1: Pyrus pashia extract (1.0 g), Carbopol 940 (1.0 g), Propylene glycol (5.0 g), Ethanol (5.0 g), Methylparaben (0.1 g), Propylparaben (0.02 g), Triethanolamine (q.s. to pH 6.4 – 6.8), Purified water (q.s. to 100 g).
- Formulation F2: Pyrus pashia extract (1.0 g), Carbopol 940 (1.5 g), Propylene glycol (5.0 g), Ethanol (5.0 g), Methylparaben (0.1 g), Propylparaben (0.02 g), Triethanolamine (q.s. to pH 6.4 – 6.8), Purified water (q.s. to 100 g).
- Formulation F3: Pyrus pashia extract (1.0 g), Carbopol 940 (2.0 g), Propylene glycol (5.0 g), Ethanol (5.0 g), Methylparaben (0.1 g), Propylparaben (0.02 g), Triethanolamine (q.s. to pH 6.4 – 6.8), Purified water (q.s. to 100 g).

## VIII. GENERAL METHOD OF PREPARATION

**8.1 Collection, Authentication, and Processing of Plant Material**

Fresh, disease-free ripe fruits of Pyrus pashia were collected from natural wild habitats in the temperate mid-Himalayan belt of Mandi District, Himachal Pradesh, India. The botanical specimen was systematically authenticated by qualified taxonomists at the Department of Pharmacognosy, Abhilashi University, with a voucher specimen deposited in the institutional herbarium for future reference.

The collected pomes were manually inspected, washed thoroughly with running tap water followed by rinsed distilled water to eliminate superficial dirt, dust, and microbial debris, and sliced into uniform longitudinal segments. The fruit pieces were subjected to shade drying at ambient room temperature (22°C to 25°C) for 14 days under controlled low humidity to prevent enzymatic or thermal degradation of thermolabile bioflavonoids. Once dehydrated to a brittle consistency, the dried fruits were milled in a mechanical grinder and passed through an Indian Standard Sieve (Mesh No. 40) to obtain a moderately coarse, uniform powder suitable for liquid-solid extraction.

**8.2 Extraction Procedure**

The powdered fruit material (100 g) was subjected to hydroethanolic extraction using a 70:30 (% v/v) ethanol-water solvent mixture:

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● Cold Maceration: The coarse powder was initially soaked in 70% v/v ethanol in a closed conical flask at room temperature for 48 hours with intermittent manual shaking to promote cell wall swelling and initial solute diffusion.

● Hot Soxhlet Extraction: The pre-macerated marc and solvent were transferred into a Soxhlet extraction apparatus and subjected to continuous hot extraction for 24 hours (roughly 30 to 35 siphon cycles) until the siphoning liquid emerged completely colorless.

● Concentration and Drying: The combined extracts were filtered through double-layered Whatman No. 1 filter paper to eliminate micro-particulates. The clear filtrate was concentrated under reduced pressure utilizing a rotary vacuum evaporator at a regulated temperature below 45°C. The resulting semi-solid viscous mass was dried completely in a vacuum desiccator over anhydrous calcium chloride, providing a final dark brownish resinous extract with an extraction yield of 12.4% w/w. The dried extract was transferred into amber glass containers and stored in a desiccator until formulation compounding.

**8.3 Preparation of the Polymeric Gelling Matrix**

The aqueous polymeric base was prepared by dispersing accurately weighed quantities of Carbopol 940 (1.0 g for F1, 1.5 g for F2, and 2.0 g for F3) into approximately 60 mL of warm purified distilled water. To ensure rapid hydration and prevent the formation of unhydrated polymer agglomerates (fish-eyes), the polymer was sifted slowly over the vortex of the water under continuous mechanical stirring at 800 to 1,000 rpm using an overhead paddle stirrer. The resulting milky dispersion was allowed to stand undisturbed for 24 hours at room temperature to achieve complete macromolecular hydration, chain relaxation, and passive de-aeration of entrapped air bubbles.

**8.4 Incorporation of Botanical Extract and Additives**

In a separate clean vessel, the required quantities of methylparaben (0.1 g) and propylparaben (0.02 g) were dissolved in a co-solvent mixture of propylene glycol (5.0 g) and 95% ethanol (5.0 g) under gentle magnetic stirring. Accurately weighed Pyrus pashia fruit extract (1.0 g) was added slowly to this organic phase, stirring continuously until a clear, uniform, lump-free botanical concentrate was obtained.

This concentrated extract solution was then incorporated dropwise into the hydrated Carbopol dispersion under moderate, unidirectional stirring (300 to 500 rpm) to ensure thorough homogeneous distribution without inducing mechanical shear degradation of the polymer chains.

**8.5 Neutralization, Gelation, and De-Aeration**

The homogeneous acidic mixture was neutralized by the slow, dropwise addition of pure triethanolamine under steady, gentle agitation. As the pH approached the neutral range (6.4 to 6.8), instantaneous cross-linking and ionization of the carboxyl groups occurred, transitioning the fluid dispersion into an optically translucent, highly viscous, cohesive hydrogel. The total weight was adjusted to 100 g with purified distilled water.

The finalized hydrogel was transferred to an ultrasonic bath and sonicated at 40 kHz for 15 minutes to eliminate remaining entrapped micro-air bubbles. The finished preparations were filled into clean, collapsible lacquered aluminum tubes, crimped securely, and stored at controlled room temperature (25 ± 2°C) for subsequent physicochemical characterization and pharmacological evaluation.

## IX. EVALUATION PARAMETERS AND QUALITY TESTING

**9.1 Physical Appearance, Clarity, and Homogeneity**

The developed polyherbal gel formulations (F1, F2, and F3) were visually inspected for their organoleptic characteristics, including color, clarity, odor, and physical state. Homogeneity was evaluated by visual examination of the gels after settling in transparent glass containers to detect any aggregate formation, phase separation, or syneresis. In addition, a small quantity of each formulation was pressed between the thumb and index finger to assess consistency, greasiness, stickiness, and the presence of coarse or gritty particles.

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**9.2 Determination of pH**

The pH of topical hydrogel formulations is a critical quality attribute that governs epidermal tolerance and prevents contact dermatitis or cutaneous irritation. The pH was determined using a standardized digital benchtop pH meter equipped with a combined glass-calomel electrode. One gram of gel was accurately weighed and dispersed in 100 mL of freshly boiled and cooled neutral distilled water. The dispersion was magnetically stirred for 15 minutes to achieve equilibrium. The electrode was calibrated using standard buffer solutions of pH 4.0, 7.0, and 9.2 prior to immersion into the test samples. Triplicate measurements were recorded at 25 ± 1°C, and the mean values with standard deviations were calculated. The target acceptable physiological range was established between 6.4 and 6.8 to match normal skin surface tolerance.

**9.3 Dynamic Viscosity and Rheological Flow Behavior**

Rheological properties directly dictate the flow, packaging fill, tube retention, and spreading dynamics of topical preparations. The dynamic viscosity of formulations F1, F2, and F3 was quantified using a rotational Brookfield digital viscometer (Model DV-E or RVT) fitted with an appropriate spindle (Spindle No. 6 or 7). Approximately 50 g of gel was placed in a 100 mL wide-mouth glass beaker and allowed to equilibrate at a thermostatically controlled temperature of 25 ± 0.5°C for 30 minutes. Viscosity measurements were taken at varied rotational speeds ranging from 10 to 100 rpm to establish the shear-dependent flow profile. The spindle was allowed to rotate in each sample for 2 minutes before the dial reading was recorded. All assessments were executed in triplicate, confirming the pseudoplastic, non-Newtonian shear-thinning characteristics of the cross-linked polyacrylic matrix.

**9.4 Spreadability Determination**

Spreadability denotes the extent of surface area over which the gel readily disperses upon application to skin or affected joint tissues, directly influencing therapeutic coverage and patient ease of application. Spreadability was quantified using the classic parallel glass slide apparatus.

A standardized mass of 1.0 g of the formulated gel was placed on a pre-marked circular zone (1 cm diameter) on a fixed lower glass plate. A second movable glass plate of identical dimensions was placed over the gel. A standardized weight of 500 g was placed on top of the upper slide for 5 minutes to expel entrapped air and establish a uniform, circular gel film. After 5 minutes, the weight was removed, and the upper slide was attached via a non-elastic thread over a frictionless pulley to a loading pan carrying an 80 g weight. The time (T, in seconds) required for the upper slide to displace a distance of 7.5 cm (L) across the lower fixed plate was recorded.

Spreadability was calculated using the formula:

$$S = (M \times L) / T$$

Where: S = Spreadability of the formulation (g·cm/sec); M = Weight tied to the upper slide / pan (80 g); L = Distance traversed by the glass plate (7.5 cm); T = Time elapsed in seconds to complete slide separation.

Alternatively, the spread diameter of the compressed gel mass was measured across perpendicular axes and expressed directly as the mean spread diameter (cm).

**9.5 Extrudability Assessment**

Extrudability measures the force required to expel the semisolid formulation from a collapsible tube container, serving as an operational index of packaging performance and ease of patient dispensing. Clean, lacquered aluminum collapsible tubes were filled with 20 g of each gel formulation and crimped securely. The filled tubes were clamped horizontally between two glass plates. A uniform weight of 1.0 kg was applied evenly across the tube surface for 30 seconds.

The amount of gel extruded from the 0.5 cm orifice was collected and weighed. Extrudability was rated based on the percentage of gel mass expelled:

- Excellent: Greater than 90% extrusion
- Good: Between 80% and 90% extrusion
- Fair/Poor: Less than 80% extrusion

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**9.6 Drug and Phytochemical Content Uniformity**

To confirm the homogeneous dispersion of active botanical phytoconstituents across the polymeric matrix, content uniformity testing was performed using UV-Visible spectrophotometry. An accurately weighed sample of 1.0 g of gel was transferred into a 100 mL volumetric flask, dissolved in approximately 50 mL of 70% v/v ethanol, and sonicated in an ultrasonic bath for 20 minutes to achieve complete extraction of active bioflavonoids from the cross-linked polymer network.

The volume was adjusted to 100 mL with 70% ethanol, mixed thoroughly, and filtered through Whatman No. 41 filter paper. Appropriate serial dilutions were prepared using phosphate-buffered saline (pH 6.8). The absorbance of the resulting solution was measured against a blank gel preparation (formulated identically without plant extract) at the predetermined wavelength of maximum absorption (λmax at 356 nm, corresponding to the flavonol conjugated chromophore).

Total marker content was quantified using a pre-constructed calibration curve of standardized Pyrus pashia extract and expressed as a percentage of the nominal 1.0% w/w loading.

**9.7 In-Vitro Anti-Inflammatory Assays**

**9.7.1 Inhibition of Albumin Protein Denaturation Assay**

Tissue protein denaturation is a well-established pathological hallmark of inflammatory and arthritic disorders, leading to the generation of auto-antigens [23]. The anti-denaturation efficacy of the formulations was evaluated using the egg albumin model [24].

The standard assay reaction mixture (5.0 mL total volume) comprised:

- 0.2 mL of fresh hen's egg albumin (filtered)
- 2.8 mL of phosphate-buffered saline (PBS, pH 6.4)
- 2.0 mL of the test gel solution (reconstituted in PBS to yield concentrations ranging from 100 to 500 mcg/mL), or reference standard solution (diclofenac sodium at equivalent concentrations), or control (PBS with equivalent solvent without active extract).

The reaction mixtures were incubated in a biochemical incubator at 37 ± 1°C for 15 minutes to allow molecular binding, followed by heating at 70°C in a precision water bath for 5 minutes to induce thermal denaturation of albumin. After heating, the tubes were rapidly cooled under running tap water to ambient temperature. The turbidity of the denatured protein solutions was determined spectrophotometrically by measuring absorbance at 660 nm against an appropriate blank.

The percentage inhibition of protein denaturation was calculated according to the equation:

Percentage Inhibition = [(Absorbance of Control - Absorbance of Formulation) / Absorbance of Control] × 100

**9.7.2 Human Red Blood Cell (HRBC) Membrane Stabilization Assay**

Because erythrocyte membranes are structurally and functionally homologous to lysosomal membranes, protection against hypotonicity-induced erythrocyte hemolysis serves as a reliable surrogate index for lysosomal membrane stabilization and anti-inflammatory activity [25, 26].

Fresh human blood collected from healthy volunteers who had refrained from NSAID consumption for two weeks was mixed with equal volumes of sterilized Alsever's solution (2% dextrose, 0.8% sodium citrate, 0.05% citric acid, and 0.42% sodium chloride). The blood suspension was centrifuged at 3,000 rpm for 10 minutes, and the packed cells were washed three times with sterile isosaline (0.9% w/v NaCl). A 10% v/v cell suspension was prepared with isosaline.

The assay reaction mixture consisted of:

- 1.0 mL of 10 mM phosphate buffer (pH 7.4)
- 2.0 mL of hyposaline (0.36% w/v NaCl)
- 1.0 mL of test gel solution (100 to 500 mcg/mL) or standard diclofenac sodium solution
- 0.5 mL of the 10% HRBC suspension

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A control tube was prepared replacing the test solution with distilled water (representing 100% hypotonic lysis). The tubes were incubated at 37°C for 30 minutes and subsequently centrifuged at 3,000 rpm for 20 minutes. The supernatant was collected, and hemoglobin release was analyzed spectrophotometrically at 560 nm. The percentage of membrane protection was calculated using:

Percentage Protection = [1 - (Absorbance of Test Sample / Absorbance of Control)] × 100

**9.8 Stability Testing Protocol (ICH Guidelines)**

To evaluate the physical integrity, chemical stability, and shelf-life of the optimized formulation, stability testing was structured in accordance with International Council for Harmonisation (ICH) Q1A(R2) guidelines [27].

Samples of the optimized gel formulation (sealed in lacquered aluminum collapsible tubes) were stored in temperature- and humidity-controlled stability chambers under two environmental conditions:

- Real-Time (Long-Term) Storage: Maintained at 25 ± 2° C and 60 ± 5% relative humidity (RH) over a test period of 3 months.
- Accelerated Storage: Maintained under elevated thermal and humidity stress at 40 ± 2° C and 75 ± 5% RH over a test period of 3 months.

Samples were withdrawn periodically at 0, 30, 60, and 90 days of storage and re-evaluated for physical appearance, phase stability (centrifugation at 4,000 rpm for 30 minutes), pH drift, rheological viscosity, spreadability, marker content retention, and retained in-vitro anti-inflammatory activity.

## X. RESULTS AND DISCUSSION

**10.1 Extraction Yield and Phytochemical Confirmation**

Hydroethanolic extraction (70% v/v ethanol) of 100 g coarse fruit powder of Pyrus pashia yielded 12.4 g of semi-solid resinous extract, representing an extraction yield of 12.4% w/w. The extraction efficiency is attributed to the synergistic polarity of the hydroethanolic binary solvent system, which facilitates the dissolution of both polar glycosides and moderately polar aglycone flavonoids. Phytochemical screening confirmed substantial presence of phenolics, flavonoids (quercetin, rutin), condensed tannins, and saponins, which serve as the active bioactive foundation of the formulation.

**10.2 Organoleptic Characteristics and Physical Appearance**

All prepared polyherbal gel formulations (F1, F2, and F3) exhibited a homogeneous, smooth texture with a light brownish-translucent color and a pleasant, characteristic herbal aroma. None of the batches displayed syneresis, grittiness, phase separation, or particulate settling during initial inspection and subsequent storage. Formulations F1 and F2 demonstrated an elegant, non-greasy cosmetic appeal with a soothing, cooling sensation upon topical application, whereas formulation F3 presented a slightly stiff, excessively rigid consistency due to higher polymer density.

**10.3 pH Determination**

The pH values for formulations F1, F2, and F3 were found to be 6.42 ± 0.08, 6.64 ± 0.11, and 6.78 ± 0.09, respectively. All three formulations fall safely within the physiological human skin pH threshold (5.5 to 7.0). Maintaining this physiological neutrality avoids cutaneous irritation, erythema, and barrier disruption, confirming that the triethanolamine cross-linking concentration effectively buffered the polyacrylic matrix for safe topical application.

**10.4 Rheological Flow Behavior and Viscosity**

The dynamic viscosity of the formulations showed a direct concentration-dependent increase with Carbopol 940 content:

- Formulation F1 (1.0% Carbopol 940): 4,150 ± 140 cps at 20 rpm
- Formulation F2 (1.5% Carbopol 940): 5,800 ± 210 cps at 20 rpm
- Formulation F3 (2.0% Carbopol 940): 7,920 ± 260 cps at 20 rpm Rheological evaluation across rotational speeds from 10 to 100 rpm confirmed that all

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formulations exhibited non-Newtonian, pseudoplastic (shear-thinning) flow. As shear rate increased, viscosity decreased markedly, facilitating easy, smooth spreadability across sensitive, inflamed tissues under minimal applied force while retaining structural consistency at rest to prevent tube leakage. Formulation F2 offered the ideal rheological profile, balancing the structural body with smooth flow under shear.

**10.5 Spreadability and Extrudability Performance**

Spreadability values were inversely proportional to polymer concentration:

- Formulation F1: 6.8 ± 0.22 cm spread diameter (Spreadability coefficient: 18.2 ± 0.6 g • cm/sec)
- Formulation F2: 5.5 ± 0.18 cm spread diameter (Spreadability coefficient: 14.5 ± 0.5 g • cm/sec)
- Formulation F3: 4.1 ± 0.15 cm spread diameter (Spreadability coefficient: 10.8 ± 0.4 g • cm/sec)

Formulation F1 spread rapidly but was excessively fluid, running the risk of dripping away from the application site. Formulation F3 required significant mechanical effort to spread, which could cause discomfort when applied to tender, inflamed joints. Formulation F2 demonstrated optimal spreadability, forming a uniform, cohesive thin film with minimal frictional resistance.

Extrudability testing confirmed this relationship:

- Formulation F1: Exhibited greater than 95% extrusion (rated Excellent), though slightly too fluid.
- Formulation F2: Exhibited 91.4% ± 1.2% extrusion (rated Excellent), delivering smooth, uniform ribbons without spitting.
- Formulation F3: Exhibited 76.5% ± 2.1% extrusion (rated Fair), requiring excessive manual pressure to expel through the nozzle.

**10.6 Drug Content Uniformity**

Phytochemical marker assay performed at 356 nm revealed uniform extract distribution across all batches:

- Formulation F1: 96.8% ± 1.4%
- Formulation F2: 98.4% ± 1.1%
- Formulation F3: 95.2% ± 1.8%

These findings confirm that the co-solvent incorporation technique (propylene glycol and ethanol pre-mix) ensured complete, homogeneous solubilization and macromolecular dispersion of the botanical extract throughout the Carbopol hydrogel network.

**10.7 In-Vitro Anti-Inflammatory Efficacy**

**10.7.1 Inhibition of Albumin Protein Denaturation**

Denaturation of tissue proteins is a key pathogenic event in chronic inflammatory and arthritic disorders. The polyherbal gel formulations exhibited concentration-dependent inhibition of thermal albumin denaturation:

- Formulation F1: Maximum inhibition of 62.1% ± 1.8% at 500 mcg/mL
- Formulation F2: Maximum inhibition of 78.4% ± 1.5% at 500 mcg/mL (IC50 = 245.6 mcg/ mL)
- Formulation F3: Maximum inhibition of 71.5% ± 1.7% at 500 mcg/mL
- Standard Diclofenac Sodium Gel: Maximum inhibition of 85.2% ± 1.2% at 500 mcg/mL (IC50 = 182.4 mcg/mL)

Formulation F2 demonstrated anti-inflammatory activity comparable to the synthetic standard diclofenac sodium. The slightly lower activity observed in F3 is likely due to the higher polymer network density retarding active phytoconstituent diffusion into the aqueous assay buffer.

**10.7.2 HRBC Membrane Stabilization Assay**

Hypotonic hemolysis of human erythrocytes was inhibited by all tested formulations:

- Formulation F1: 58.6% ± 1.9% protection
- Formulation F2: 74.2% ± 1.6% protection
- Formulation F3: 67.8% ± 1.7% protection
- Standard Diclofenac Sodium: 81.6% ± 1.3% protection

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Because erythrocyte membranes are structurally homologous to lysosomal membranes, these findings indicate that Pyrus pashia bioflavonoids protect biological membranes against osmotic stress and shear lysis, thereby preventing the extracellular release of destructive lysosomal proteases at inflammatory sites.

**10.8 Stability Testing (ICH Q1A Guidelines)**

Formulation F2, selected as the optimized batch, was evaluated over a 3-month stability protocol at real-time (25 ± 2°C / 60 ± 5% RH) and accelerated (40 ± 2°C / 75 ± 5% RH) conditions:

- Physical Stability: The gel remained clear, homogeneous, and free from syneresis, discoloration, or microbial growth throughout the 90-day period. Centrifugation at 4,000 rpm for 30 minutes produced no phase separation.
- pH Stability: The pH exhibited minimal drift, moving from an initial 6.64 ± 0.11 to 6.58 ± 0.08 at real-time conditions and 6.51 ± 0.10 under accelerated conditions, remaining well within physiological limits.
- Viscosity and Spreadability: Rheological properties showed negligible degradation (less than 3.5% variation in dynamic viscosity and spread diameter).
- Bioactive Content and Activity: Active flavonoid marker content remained above 95.8% of the initial value, and in-vitro anti-inflammatory protein denaturation inhibition showed no statistically significant reduction (76.8% retained inhibition after 90 days).

## XI. LIMITATIONS AND FUTURE SCOPE

Although the in-vitro evaluations confirm the anti-inflammatory efficacy and structural stability of formulation F2, several translational aspects warrant further investigation:

1. In-Vivo Pharmacodynamic Validation: Preclinical animal studies, including the carrageenan-induced rat paw edema model and the cotton pellet-induced granuloma model, are necessary to validate acute and chronic anti-inflammatory efficacy in living tissue systems.
2. Dermal Safety and Toxicity Profiling: While the physiological pH and traditional history of Pyrus pashia suggest high biocompatibility, structured Primary Dermal Irritation Index (PDII) testing under OECD Guideline 404 should be completed to formally rule out erythema, edema, and allergic sensitization [28].
3. Ex-Vivo Permeation Kinetics: Percutaneous transport studies using Franz diffusion cells mounted with excised mammalian or human skin will be essential to establish steady-state flux, permeability coefficients, and drug deposition within the epidermal layers.
4. Standardization and Analytical Fingerprinting: High-Performance Liquid Chromatography (HPLC) and Liquid Chromatography-Mass Spectrometry (LC-MS) fingerprinting should be established to isolate, identify, and quantify specific marker compounds (such as quercetin-3-O-rutinoside and chlorogenic acid) for consistent commercial scale-up and batch release testing.

## XII. CONCLUSION

The present investigation successfully formulated and evaluated a stable, cosmetically elegant, topical polyherbal anti-inflammatory hydrogel incorporating hydroethanolic fruit extract of Pyrus pashia (Kainth). Among the evaluated batches, formulation F2—compounded with 1.5% w/w Carbopol 940, 5% propylene glycol, and neutralized with triethanolamine—demonstrated the optimal pharmaceutical profile, combining physiologically compatible pH (6.64), balanced pseudoplastic viscosity (5,800 cps), uniform spreadability, and high extrudability.

In-vitro pharmacological assays established that formulation F2 produces pronounced membrane stabilization and potent inhibition of albumin denaturation (78.4%), closely approaching the therapeutic efficacy of standard diclofenac sodium gel (85.2%). Stability testing in accordance with ICH guidelines confirmed that the formulation preserves physical, rheological, and chemical integrity over time. These results demonstrate that Pyrus pashia fruit extract formulated in a Carbopol hydrogel offers a promising, safe, and effective topical alternative to synthetic NSAIDs for localized inflammatory conditions.

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