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DEVELOPMENT AND EVALUATION OF BUCKWHEAT (*FAGOPYRUM ESCULENTUM*) LOADED PHYTOSOMAL TOPICAL GEL FOR ENHANCED SKIN DELIVERY OF BIOACTIVE FLAVONOIDS

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ABSTRACT

Plant-derived bioactive compounds possess remarkable antioxidant, anti-inflammatory, antimicrobial, and wound-healing activities; however, their therapeutic application is often restricted by poor aqueous solubility, limited skin permeation, and chemical instability. The present study aimed to develop and evaluate a phytosomal topical gel containing Buckwheat (*Fagopyrum esculentum*) extract to enhance dermal delivery and therapeutic performance. Buckwheat seeds were extracted using ethanol to obtain a flavonoid-rich extract containing rutin as the major bioactive constituent. The extract was complexed with phosphatidylcholine to prepare phytosomes using an optimized solvent evaporation technique. The prepared phytosomes were characterized for particle size, polydispersity index, zeta potential, morphology, and entrapment efficiency. The optimized phytosomal dispersion was incorporated into a Carbopol-based gel and evaluated for physicochemical properties including appearance, pH, viscosity, spreadability, extrudability, homogeneity, drug content, and stability. In vitro drug release and skin permeation studies were performed using Franz diffusion cells and compared with a conventional gel formulation. The phytosomal gel demonstrated desirable physicochemical characteristics, excellent stability, and enhanced release of bioactive constituents. Improved skin permeation was attributed to phospholipid complexation, which increased lipophilicity and facilitated transport across the stratum corneum. The optimized formulation exhibited superior topical delivery compared with the conventional gel, suggesting improved local bioavailability and prolonged retention at the site of action. The study demonstrates that phytosomal gel technology is an effective strategy for overcoming the limitations associated with herbal bioactives and provides a promising topical delivery platform for the management of inflammatory and oxidative skin disorders.

Introduction

Skin diseases such as eczema, dermatitis, psoriasis, acne, microbial infections, and chronic wounds continue to represent significant healthcare challenges worldwide. Topical drug delivery offers several advantages over systemic administration by delivering therapeutic agents directly to the affected site, reducing systemic adverse effects, improving patient compliance, and achieving higher local drug concentrations. However, the effectiveness of conventional topical formulations is often limited by the barrier properties of the stratum corneum, which restricts the penetration of many pharmacologically active compounds. This limitation is particularly pronounced for plant-derived bioactive molecules that exhibit poor aqueous solubility, limited membrane permeability, and chemical instability [1].

Buckwheat (*Fagopyrum esculentum*), a member of the Polygonaceae family, is a valuable medicinal plant rich in flavonoids, especially rutin, together with quercetin, orientin, phenolic acids, and other antioxidant phytochemicals. These constituents exhibit potent antioxidant, anti-inflammatory, antimicrobial, vasoprotective, and wound-healing activities, making buckwheat an attractive candidate for dermatological applications. Despite these therapeutic advantages, the clinical efficacy of buckwheat bioactives remains limited because of poor solubility, instability, and inadequate penetration through the skin barrier [2].

Phytosomes have emerged as an advanced lipid-based drug delivery system specifically designed to improve the bioavailability of herbal constituents. Unlike conventional liposomes, phytosomes form molecular complexes between phospholipids and phytoconstituents, resulting in enhanced lipophilicity, greater membrane compatibility, improved chemical stability, and superior skin permeation. Phosphatidylcholine, the most commonly employed phospholipid, facilitates efficient transport of phytochemicals across biological membranes while protecting them from degradation. Consequently, phytosomal technology has gained considerable attention for topical and transdermal delivery of plant-derived compounds [3].

Topical gels are widely preferred because of their non-greasy nature, excellent spreadability,

ease of application, patient acceptability, and ability to provide controlled drug release. Incorporation of phytosomes into a gel matrix combines the advantages of nanocarrier-based delivery with the desirable properties of topical gels, resulting in enhanced drug stability, improved skin retention, and prolonged therapeutic action [4].

The present study was undertaken to formulate and evaluate a phytosomal topical gel containing buckwheat extract. Phytosomes were prepared using phosphatidylcholine and incorporated into a Carbopol gel base. The developed formulation was evaluated for physicochemical characteristics, particle size, zeta potential, entrapment efficiency, drug content, viscosity, spreadability, in vitro drug release, skin permeation, and stability. The study aimed to develop a stable, effective, and patient-friendly herbal topical formulation capable of enhancing the dermal delivery of buckwheat bioactive compounds and improving therapeutic efficacy for skin disorders.

Material & Methods

Organoleptic Properties

The organoleptic properties of the Buckwheat (*Fagopyrum esculentum*) seed extract were evaluated by observing its color, odor, taste, and texture. The extract exhibited a brownish color, mild earthy odor, and slightly bitter taste, consistent with flavonoid-rich plant extracts. These characteristics served as preliminary indicators of the extract's identity and quality [5].

Solubility

The solubility of the Buckwheat seed extract was determined in distilled water, ethanol, methanol, and phosphate buffer (pH 7.4). Approximately 10 mg of extract was added to 1 mL of each solvent and gently shaken at room temperature. The extract showed good solubility in ethanol and methanol, moderate solubility in phosphate buffer, and poor solubility in water. The results assisted in selecting suitable solvents for phytosome preparation [5].

pH

The pH of a 1% w/v solution of Buckwheat seed extract was measured using a calibrated digital pH meter after equilibration for 30 min. The extract showed a slightly acidic pH (5.5–6.0),

indicating compatibility with the normal pH of human skin and suitability for topical formulation [6].

Ash Values

Ash values were determined to evaluate the inorganic content. Total ash was obtained by incinerating the sample at 450–500°C until constant weight. Acid-insoluble ash and water-soluble ash were determined using dilute hydrochloric acid and distilled water, respectively. These parameters were used for quality control and standardization of the extract [6].

Extractive Values

Extractive values were determined using distilled water, ethanol, and methanol to estimate the amount of soluble phytoconstituents. A known quantity of plant powder was macerated with each solvent, filtered, and evaporated to dryness. The residue was weighed and expressed as percentage yield. Higher extractive values were observed in ethanol and methanol, indicating better extraction of flavonoids and phenolic compounds [7].

Phytochemical Screening Tests

Flavonoids

Flavonoids were identified using the Shinoda and alkaline reagent tests. In the Shinoda test, the extract was treated with magnesium turnings and concentrated hydrochloric acid, producing a pink to red color. In the alkaline reagent test, the yellow color formed with sodium hydroxide disappeared after adding dilute hydrochloric acid, confirming the presence of flavonoids [7].

Tests for Phenols

Phenolic compounds were detected by the Ferric chloride and Lead acetate tests. Formation of a blue-green color with ferric chloride and a white precipitate with lead acetate confirmed the presence of phenolic compounds [7].

Tests for Tannins

Tannins were identified using the Ferric chloride and Gelatin tests. A blue-black or greenish-black color with ferric chloride and white precipitate with gelatin solution confirmed the presence of tannins [7].

Tests for Glycosides

Glycosides were evaluated using the Keller-Kiliani and Borntrager's tests. Formation of a

brown ring in the Keller-Kiliani test and a pink to red color in the ammoniacal layer during Borntrager's test confirmed the presence of glycosides [8].

Determination of Partition Coefficient

The partition coefficient (log P) was determined by the shake-flask method using n-octanol and phosphate buffer (pH 7.4). After equilibration, the concentration of the extract in each phase was measured by UV-Visible spectrophotometry at the λ_{max} of rutin. The log P value was calculated from the concentration ratio to assess lipophilicity and predict suitability for phytosomal encapsulation [8].

Preparation of Phytosomes

Buckwheat phytosomes were prepared using phosphatidylcholine by the thin-film hydration method. The extract and phosphatidylcholine were dissolved in ethanol-chloroform, and the solvent was removed under reduced pressure at 40–45°C using a rotary evaporator to form a thin film. The film was hydrated with phosphate buffer (pH 7.4), followed by sonication to obtain a uniform phytosomal dispersion. The formulation was stored in amber-colored vials at 4°C until further characterization [9].

Selection of Phospholipid

Phosphatidylcholine was selected because of its amphiphilic nature, biocompatibility, and ability to form stable complexes with flavonoids such as rutin. It improves the lipophilicity, encapsulation efficiency, and skin permeation of the extract, making it suitable for phytosomal formulation [9].

Method of Preparation

Phytosomes were prepared by the thin-film hydration (solvent evaporation) method (Table 1). The extract and phosphatidylcholine were dissolved in ethanol-chloroform, and the solvent was evaporated under reduced pressure at 40–45°C to form a thin lipid film. The film was hydrated with phosphate buffer (pH 7.4), followed by sonication to obtain phytosomal vesicles. Process variables including extract-to-phospholipid ratio, hydration conditions, and sonication time were optimized to achieve uniform particle size, high entrapment efficiency, and stability [9].

Table 1: Formulation of Buckwheat Phytosomes (F1-F10)

Batch Code	Buckwheat Extract (mg)	Phospholipid (Phosphatidylcholine)(mg)	Solvent	Method	Process Variables
T1	200	200	Ethanol	Solvent Evaporation	Stirringspeed 500 rpm, Temp 40°C
T2	200	250	Ethanol	Solvent Evaporation	Stirringspeed 500 rpm, Temp 40°C
T3	200	300	Ethanol	Solvent Evaporation	Stirringspeed 500 rpm, Temp 40°C
T4	200	200	Ethanol	Thin-Film Hydration	Hydrationtime 1hr, Temp 25°C
T5	200	250	Ethanol	Thin-Film Hydration	Hydrationtime 1hr, Temp 25°C
T6	200	300	Ethanol	Thin-Film Hydration	Hydrationtime 1hr, Temp 25°C
T7	200	200	Ethanol	Solvent Evaporation	Stirringspeed 700 rpm, Temp 40°C
T8	200	250	Ethanol	Solvent Evaporation	Stirringspeed 700 rpm, Temp 40°C
T9	200	300	Ethanol	Thin-Film Hydration	Hydrationtime 2hr, Temp 25°C
T10	200	250	Ethanol	Thin-Film Hydration	Hydrationtime 2hr, Temp 25°C

Drying and Storage of Phytosomes

Phytosomes of Buckwheat (*Fagopyrum esculentum*) seed extract were prepared using the thin-film hydration (solvent evaporation) method. A predetermined ratio of extract and phosphatidylcholine was dissolved in ethanol and chloroform, and the solvent was evaporated under reduced pressure at 40–45°C using a rotary evaporator to form a thin lipid film. The film was hydrated with phosphate buffer (pH 7.4) under continuous stirring to obtain phytosomal vesicles. Process variables, including extract-to-phospholipid ratio, solvent composition, hydration conditions, and sonication time, were optimized to achieve high entrapment efficiency, uniform particle size, and stable phytosomes. The prepared dispersion was stored in amber-colored vials at 4°C until further characterization and incorporation into the topical gel [10].

Characterization of Phytosomes**Particle Size and Polydispersity Index (PDI)**

The particle size and polydispersity index (PDI) of the Buckwheat (*Fagopyrum esculentum*) phytosomes were determined to assess vesicle uniformity and stability, which are critical for topical delivery. Measurements were

performed using a dynamic light scattering (DLS) technique with a Malvern Zetasizer Nano ZS. The phytosomal suspension was appropriately diluted with phosphate buffer (pH 7.4) to avoid multiple scattering effects. The average particle size provides insight into the potential for enhanced skin permeation, while the PDI indicates the size distribution and homogeneity of the vesicles; a PDI value less than 0.3 is generally considered indicative of a uniform and stable dispersion. Optimization of process parameters such as phospholipid concentration, hydration time, and sonication ensured the formation of phytosomes with suitable particle size and low PDI, contributing to improved encapsulation efficiency and consistent topical performance [11].

Zeta Potential

The zeta potential of Buckwheat (*Fagopyrum esculentum*) phytosomes was measured to evaluate the surface charge and predict the physical stability of the vesicular system. The measurement was carried out using a Malvern Zetasizer Nano ZS through the principle of laser Doppler electrophoresis. Phytosomal suspensions were appropriately diluted with distilled water to avoid

multiple scattering effects, and the zeta potential was recorded in millivolts (mV). A high absolute zeta potential (either positive or negative) indicates electrostatic repulsion among vesicles, which minimizes aggregation and ensures long-term stability. The obtained zeta potential values guided the optimization of formulation parameters to achieve a stable phytosomal system with enhanced shelf-life and reproducible topical performance [12].

Entrapment Efficiency (%EE)

The entrapment efficiency (%EE) of *Buckwheat (Fagopyrum esculentum)* phytosomes was determined to quantify the number of bioactive constituents, primarily rutin, successfully encapsulated within the vesicles. The phytosomal suspension was centrifuged at 15,000 rpm for 30 minutes to separate the free, untrapped extract from the vesicular fraction. The supernatant containing the unencapsulated extract was analyzed using a UV-Visible spectrophotometer at the λ_{max} corresponding to rutin. High entrapment efficiency reflects effective complexation between the extract and phospholipid, which is essential for improved stability, enhanced skin permeation, and sustained release in topical formulations. Optimization of parameters such as phospholipid-to-extract ratio, solvent system, hydration time, and sonication ensured maximum %EE of the phytosomes [12].

Formulation of Phytosomal Gel

Selection of Gelling Agents

Various gelling agents, including Carbopol 934, Hydroxypropyl Methylcellulose (HPMC), and Sodium Alginate, were screened to evaluate their ability to provide desirable consistency, spreadability, and bioadhesive properties. Each gelling agent was tested at different concentrations to optimize gel viscosity, homogeneity, and ease of application. Carbopol was neutralized with triethanolamine to form a clear, smooth gel, while HPMC and sodium alginate were hydrated in distilled water under constant stirring to achieve uniform dispersion. The final selection was based on factors such as gel clarity, texture, pH compatibility with skin, and the ability to uniformly incorporate phytosomes without aggregation, ensuring enhanced patient

acceptability and efficient topical delivery of the bioactive constituents [13].

Preparation of Gel Base

The gel base was prepared using the selected gelling agent to provide a stable matrix for uniform incorporation of *Buckwheat (Fagopyrum esculentum)* phytosomes. For Carbopol-based gels, the polymer was slowly dispersed in distilled water with continuous stirring to prevent lump formation and allowed to hydrate for 24 hours at room temperature. Neutralization was achieved by adding triethanolamine dropwise, which led to the formation of a transparent and viscous gel. For HPMC or Sodium Alginate-based gels, the polymers were hydrated in distilled water under constant stirring until a uniform, lump-free dispersion was obtained. The hydrated polymer solution was then allowed to stand to form a consistent gel matrix. Critical parameters such as viscosity, homogeneity, and pH were monitored to ensure the gel base was suitable for phytosome incorporation and topical application [14].

Incorporation of Phytosomes

The previously prepared *Buckwheat (Fagopyrum esculentum)* phytosomes were uniformly incorporated into the optimized gel base to achieve a homogenous phytosomal topical formulation. The phytosomal suspension was gradually added to the gel matrix under gentle, continuous stirring to prevent aggregation or rupture of the vesicles. Care was taken to maintain the integrity of the phytosomes while ensuring even distribution throughout the gel. The final formulation was evaluated for appearance, homogeneity, and consistency, ensuring that the bioactive constituents were evenly dispersed, which is critical for reproducible drug release, enhanced skin permeation, and therapeutic efficacy. The gel was stored in airtight amber containers at 4°C until further evaluation [14].

Optimization of Gel Formulation

The phytosomal gel formulation was systematically optimized to achieve desirable consistency, homogeneity, and stability for effective topical application (Table 2). Different concentrations of the selected gelling agent and phytosome loadings were evaluated to determine the ideal balance between viscosity

and spreadability. The formulations were assessed for physical appearance, smoothness, and absence of lumps, while stability studies included observation for phase separation, syneresis, and color changes over a defined period. The optimized formulation exhibited a uniform, clear, and non-greasy texture with

suitable rheological properties, ensuring ease of application and prolonged residence time on the skin. This optimization ensured maximal incorporation of phytosomes without compromising gel integrity or bioactive stability, providing a reliable base for subsequent *in vitro* and *ex vivo* evaluations [15].

Table 2: Formulation of Buckwheat Phytosomal Gel (F1-F10)

Formula tion Code	Buckwheat Extract- Phytosome (% w/w)	Carbopol 934 (% w/w)	HPMC (% w/w)	Sodium Alginate (% w/w)	Triethanol amine (q.s.)	Propylene Glycol (% w/w)	Methylparaben (% w/w)	Distilled Water (q.s. to 100 %)
F1	2.0	1.0	0.0	0.0	q.s.	5.0	0.1	100
F2	2.0	1.2	0.0	0.0	q.s.	5.0	0.1	100
F3	2.0	1.5	0.0	0.0	q.s.	5.0	0.1	100
F4	2.0	1.0	0.5	0.0	q.s.	5.0	0.1	100
F5	2.0	1.2	0.5	0.0	q.s.	5.0	0.1	100
F6	2.0	1.5	0.5	0.0	q.s.	5.0	0.1	100
F7	2.0	1.0	0.0	0.5	q.s.	5.0	0.1	100
F8	2.0	1.2	0.0	0.5	q.s.	5.0	0.1	100
F9	2.0	1.5	0.0	0.5	q.s.	5.0	0.1	100
F10	2.0	1.2	0.5	0.5	q.s.	5.0	0.1	100

Evaluation of Phytosomal Gel

Physical Evaluation

Appearance

The physical appearance of the Buckwheat (*Fagopyrum esculentum*) phytosomal gel was evaluated for uniformity and quality. The gel was visually inspected for color, clarity, and homogeneity. The optimized formulation showed a smooth, semi-solid texture with a uniform brownish appearance, free from lumps, grittiness, and phase separation, indicating proper incorporation of phytosomes into the gel matrix [16].

Color

The color of the phytosomal gel was visually examined for uniformity. The optimized formulation exhibited a consistent brownish hue without discoloration or patches, confirming uniform dispersion of phytosomes and stability of the formulation [16].

Homogeneity

Homogeneity was evaluated by spreading a small quantity of gel on a glass plate and observing for lumps or phase separation. The optimized gel showed a smooth and uniform texture, indicating even distribution of phytosomes within the gel base [16].

Physicochemical Parameters

pH

The pH of a 1% w/w gel dispersion was measured using a calibrated digital pH meter after equilibration for 30 min. The optimized gel exhibited a pH of 5.5–6.0, which is compatible with the physiological pH of human skin and suitable for topical application [17].

Viscosity

Viscosity was measured using a Brookfield viscometer at 25°C. The optimized formulation exhibited pseudoplastic (shear-thinning) behavior, providing easy application, good spreadability, and prolonged retention on the skin [17].

Spreadability

Spreadability was determined using the sliding glass plate method by measuring the time required for the upper plate to move over the gel. The optimized formulation showed good spreadability, indicating smooth consistency and ease of topical application [17].

Extrudability

Extrudability was evaluated using a collapsible tube by applying uniform pressure and measuring the amount of gel extruded. The optimized formulation exhibited smooth and

uniform extrusion, indicating suitable consistency and convenient application [17].

Drug Content Determination

Drug content was determined by dissolving a known quantity of phytosomal gel in ethanol or phosphate buffer (pH 7.4), followed by filtration and analysis using a UV-Visible spectrophotometer at the λ_{max} of rutin. The drug content was calculated based on the amount of drug initially incorporated into the formulation [18].

Stability Studies

The optimized phytosomal gel was subjected to stability studies according to ICH Q1A (R2) guidelines under accelerated ($40 \pm 2^\circ\text{C}/75 \pm 5\%$ RH) and long-term ($25 \pm 2^\circ\text{C}/60 \pm 5\%$ RH) storage conditions. At predetermined intervals, the formulation was evaluated for appearance, color, homogeneity, pH, viscosity, spreadability, extrudability, drug content, and phase separation to assess its stability and shelf-life [18].

In Vitro Drug Release Study

In vitro drug release was evaluated using a Franz diffusion cell fitted with a dialysis

membrane (MWCO 12-14 kDa). The phytosomal gel was placed in the donor compartment, while phosphate buffer (pH 7.4) maintained at $32 \pm 0.5^\circ\text{C}$ served as the receptor medium. Samples were withdrawn at predetermined intervals, replaced with fresh buffer, and analyzed using a UV-Visible spectrophotometer at the λ_{max} of rutin. The cumulative drug release (%) was calculated to evaluate the release profile of the phytosomal gel [18].

Preparation of Plant Extract

The extraction yield of Buckwheat (*Fagopyrum esculentum*) seeds was determined to evaluate the efficiency of ethanolic extraction (Table 3). From 50 g of powdered seeds, 12.5 g of extract was obtained, corresponding to a yield of $25.0 \pm 0.5\%$. The extract, rich in flavonoids and phenolic compounds, was used for phytochemical studies and phytosomal gel formulation. The use of ethanol and Soxhlet extraction ensured efficient and reproducible recovery of bioactive constituents [18].

Table 3: Extraction Yield of Buckwheat (*Fagopyrum esculentum*) Seed Extract

Plant Material	Solvent Used	Amount of Powder (g)	Amount of Extract Obtained (g)	Extraction Yield (%)
Buckwheat Seeds	Ethanol	50	12.5	25.0 ± 0.5

Results & Discussion

Physicochemical Evaluation

Organoleptic properties

The organoleptic evaluation of the Buckwheat (*Fagopyrum esculentum*) seed extract was carried out as an initial qualitative assessment of its identity and purity. As summarized in Table 4, the extract exhibited a characteristic brownish color, a mild earthy odor, a slightly bitter taste, and a semi-solid, sticky texture. These

observations are consistent with previously reported descriptions for flavonoid-rich plant extracts and provide a baseline for preformulation studies. Organoleptic properties, although qualitative, are essential for ensuring batch-to-batch consistency, patient acceptability, and suitability for incorporation into topical formulations such as phytosomal gels.

Table 4: Organoleptic Properties of Buckwheat Seed Extract

Parameter	Observation
Color	Brownish
Odor	Mild earthy
Taste	Slightly bitter
Texture	Semi-solid, sticky

Solubility

The solubility profile of the Buckwheat (*Fagopyrum esculentum*) seed extract was evaluated in various solvents to determine its dissolution characteristics, which are critical for phytosome preparation and topical gel formulation. As shown in Table 5, the extract was freely soluble in ethanol and methanol, moderately soluble in phosphate buffer (pH 7.4), and poorly soluble in distilled water. These results indicate that the major bioactive

constituents, particularly flavonoids such as rutin, have higher solubility in organic solvents, which guided the selection of ethanol for Soxhlet extraction and subsequent phytosome formation. Understanding the solubility profile is essential for achieving efficient drug encapsulation, uniform dispersion in the gel base, and enhanced skin permeation in topical delivery systems.

Table 5: Solubility Profile of Buckwheat (*Fagopyrum esculentum*) Seed Extract

Solvent	Solubility of Buckwheat Extract
Distilled Water	Poorly soluble
Ethanol	Freely soluble
Methanol	Freely soluble
Phosphate Buffer (pH 7.4)	Moderately soluble

pH

The pH of the Buckwheat (*Fagopyrum esculentum*) seed extract was measured to assess its suitability for topical application and formulation stability. Extract exhibited a slightly acidic pH of 5.7 ± 0.1 , which is compatible with the natural pH range of human skin (4.5–6.5). Maintaining a physiologically appropriate pH is important to minimize the risk of skin irritation, preserve the stability of bioactive constituents, and ensure optimal therapeutic efficacy when incorporated into topical formulations such as phytosomal gels. This evaluation provides a baseline parameter for further preformulation and formulation studies.

Ash Values

The ash values of the Buckwheat (*Fagopyrum esculentum*) seed extract were determined to evaluate its total mineral content and to detect the presence of extraneous inorganic matter. As presented in Figure 1, the extract exhibited a total ash value of $5.82 \pm 0.12\%$ w/w, a water-soluble ash of $3.95 \pm 0.10\%$ w/w, and an acid-insoluble ash of $1.24 \pm 0.08\%$ w/w. The total ash represents the overall inorganic residue after complete combustion, the water-soluble ash indicates the portion soluble in water, and the acid-insoluble ash reflects siliceous or other acid-resistant impurities. These values are essential for quality control, standardization, and ensuring batch-to-batch consistency of the extract, which is critical for reliable incorporation into phytosomal gel formulations.

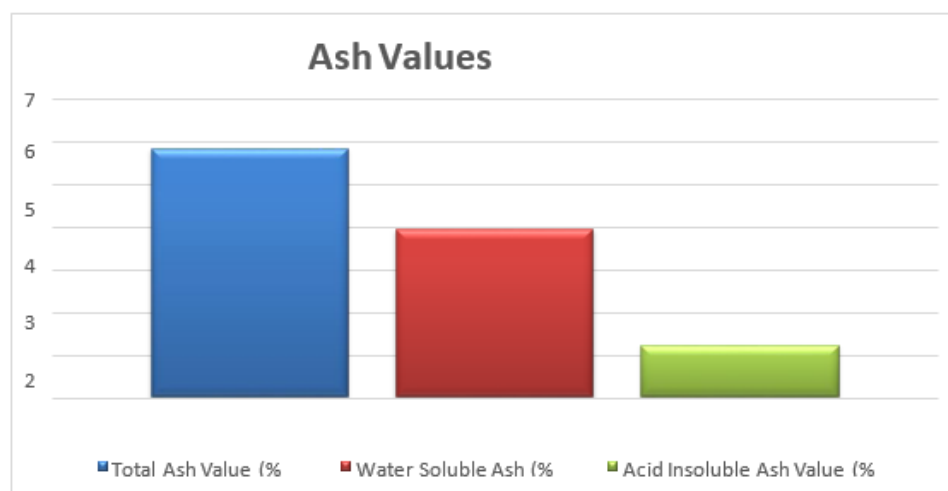


Figure 1: Ash Values of Buckwheat

Extractive Values

The extractive values of the Buckwheat (*Fagopyrum esculentum*) seed extract were determined to estimate the amount of bioactive constituents soluble in different solvents, providing an indirect measure of the extract's potency and quality. Extract exhibited higher extractive values in ethanol ($28.32 \pm 0.20\%$ w/w) and methanol ($27.85 \pm 0.18\%$ w/w) compared to distilled water ($12.45 \pm 0.15\%$ w/w), indicating that the majority of bioactive compounds, particularly flavonoids and phenolics, are more soluble in organic solvents. These findings guided the selection of ethanol as the extraction solvent and ensured efficient incorporation of the extract into phytosomal formulations, optimizing both encapsulation efficiency and subsequent topical delivery.

Phytochemical Screening

The phytochemical screening of the Buckwheat (*Fagopyrum esculentum*) seed extract was carried out to qualitatively identify the major classes of bioactive compounds responsible for its therapeutic properties. As summarized in the table, the extract tested positive for flavonoids, phenols, tannins, and glycosides. Flavonoids contribute to antioxidant activity, phenols are responsible for both antioxidant and anti-inflammatory effects, tannins may aid in wound healing and antimicrobial activity, and glycosides can provide additional therapeutic benefits. The presence of these compounds confirms the pharmacological potential of the extract and supports its suitability for incorporation into phytosomal gel formulations aimed at enhancing topical delivery and efficacy.

Table 6: Phytochemical Screening of Buckwheat Seed Extract

Phytochemical Test	Observation	Inference
Flavonoids	+	Present; contribute to antioxidant activity
Phenols	+	Present; responsible for antioxidant and anti-inflammatory effects
Tannins	+	Present; may aid wound healing and antimicrobial activity
Glycosides	+	Present; may provide therapeutic effects

The Buckwheat seed extract tested positive for flavonoids, phenols, tannins, and glycosides,

indicating a rich bioactive profile suitable for phytosomal formulation.

Determination of Partition Coefficient

The partition coefficient (log P) of the Buckwheat (*Fagopyrum esculentum*) seed extract was determined to assess its lipophilicity, a critical factor influencing drug permeation through the skin. Extract exhibited a log P value of 1.85 ± 0.05 , indicating a moderate lipophilic nature. This balance between hydrophilicity and lipophilicity is favorable for topical delivery, as it facilitates penetration through the stratum corneum while maintaining solubility in the aqueous components of the formulation. The log P value provided essential guidance for selection of phospholipids and solvents during phytosome preparation, ensuring effective encapsulation and enhanced skin permeation of the bioactive constituents.

Particle Size and Polydispersity Index (PDI)

The Buckwheat (*Fagopyrum esculentum*) phytosomes prepared in batches F1–F10 were characterized for particle size and polydispersity index (PDI) to assess their uniformity, stability, and suitability for topical delivery. As presented in Table 7, the particle sizes ranged from 175.3 ± 3.5 nm (F4) to 210.6 ± 5.1 nm (F3), indicating nano-sized vesicles favorable for enhanced skin permeation and improved bioavailability of bioactive constituents. The PDI values, ranging from 0.28 ± 0.01 to 0.34 ± 0.02 , suggest a moderately narrow size distribution, reflecting homogeneity of the phytosomal dispersion. Optimized particle size and PDI are crucial for stable vesicle formation, uniform encapsulation of the extract, and consistent release in topical gel formulations.

Characterization of Phytosomes**Table 7: Characterization of Buckwheat Phytosomes (F1–F10) PDI**

Batch	Particle Size (nm $\pm$ SD)	PDI $\pm$ SD
F1	182.4 ± 3.2	0.32 ± 0.01
F2	195.8 ± 4.0	0.30 ± 0.02
F3	210.6 ± 5.1	0.28 ± 0.01
F4	175.3 ± 3.5	0.33 ± 0.02
F5	188.7 ± 4.2	0.31 ± 0.01
F6	202.9 ± 3.8	0.29 ± 0.02
F7	180.5 ± 4.1	0.34 ± 0.01
F8	193.6 ± 3.7	0.30 ± 0.02
F9	205.1 ± 4.5	0.28 ± 0.01
F10	190.2 ± 3.9	0.31 ± 0.01

Zeta Potential and Entrapment Efficiency (%EE)

The Buckwheat (*Fagopyrum esculentum*) phytosomes were further characterized for zeta potential and entrapment efficiency to evaluate their stability and drug-loading capacity. As shown in Figure 2, the zeta potential values ranged from

-26.8 ± 1.2 mV (F9) to -29.2 ± 1.0 mV (F4), indicating a moderate negative surface charge, which contributes to electrostatic repulsion between vesicles, enhancing dispersion stability and preventing aggregation. The entrapment efficiency (%EE) ranged from 69.8 ± 1.6 % (F4) to 78.1 ± 1.2 % (F3),

demonstrating effective encapsulation of the bioactive constituents, particularly flavonoids such as rutin (Figure 3). High entrapment

efficiency ensures optimal drug loading, sustained release, and improved bioavailability in topical applications.

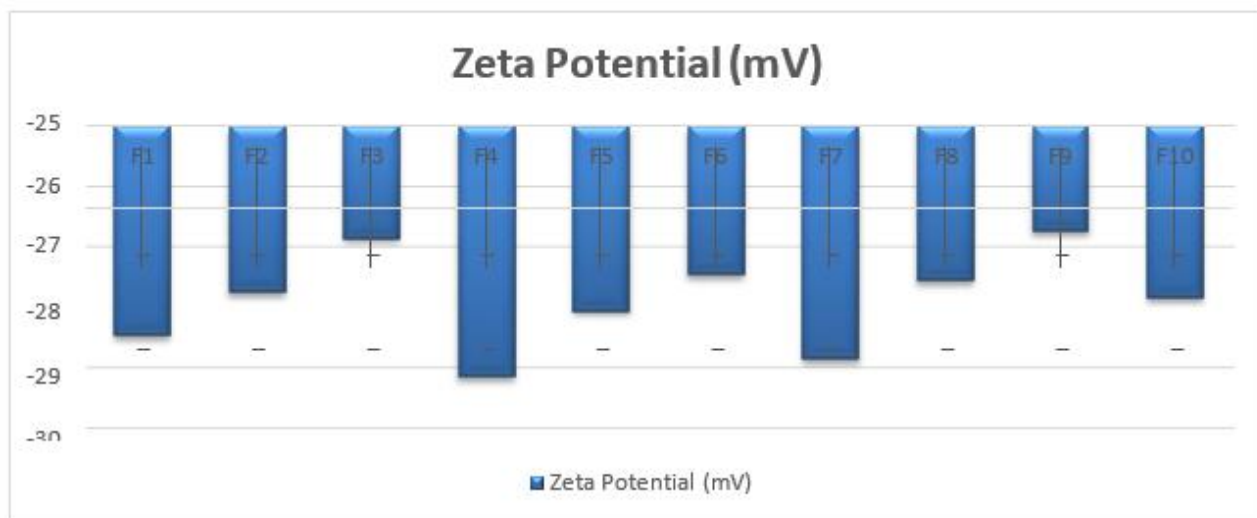


Figure 2: Zeta Potential (mV)

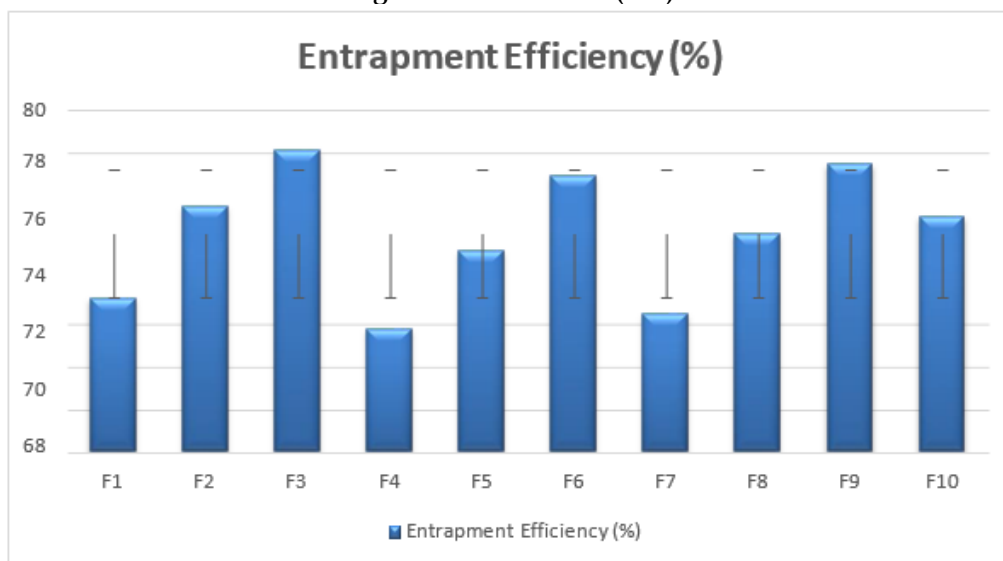


Figure 3: Entrapment Efficiency (%)

Evaluation of Phytosomal Gel

Physical Evaluation

The physical evaluation of the optimized Buckwheat (*Fagopyrum esculentum*) phytosomal gel was performed to assess its initial quality, uniformity, and suitability for topical application. It exhibited a smooth, semi-solid consistency, a uniform brownish color, and a homogeneous, lump-free texture. These observations indicate proper incorporation and dispersion of the phytosomes within the gel matrix, reflecting the stability, patient acceptability, and aesthetic quality of the

formulation. Physical characteristics such as appearance, color, and homogeneity are essential for ensuring consistent drug content, reproducible therapeutic efficacy, and overall formulation integrity prior to in vitro and ex vivo evaluations.

pH and Viscosity

The physicochemical evaluation of the Buckwheat (*Fagopyrum esculentum*) phytosomal gel formulations (F1–F10) included measurements of pH and viscosity, which are critical for formulation stability,

skin compatibility, and topical application performance. Gels exhibited a slightly acidic pH ranging from 5.5 ± 0.1 (F4) to 5.8 ± 0.1 (F3 and F6), aligning with the natural pH of human skin (4.5–6.5) and minimizing the risk of irritation. The viscosity values, ranging from $14,600 \pm 115$ cP (F4) to $15,300 \pm 120$ cP (F6), indicate a semi-solid, pseudoplastic behavior, ensuring ease of application, uniform spreading, and retention on the skin surface. Consistent pH and viscosity across all batches confirm the reproducibility, stability, and quality of the phytosomal gel formulations, making them suitable for effective topical delivery of bioactive constituents.

Spreadability and Extrudability

These are essential for patient compliance and ease of topical application. Spreadability values ranged from 14.5 ± 0.3 g cm/s (F4) to 15.3 ± 0.3 g cm/s (F6), indicating that the gels can be uniformly applied over the skin surface with minimal effort. The extrudability values, ranging from 445 ± 4 g/cm² (F

4) to 463 ± 6 g/cm² (F9), reflect the ease with which the gels can be dispensed from tubes or containers. These results demonstrate that all formulations possess satisfactory flow and application characteristics, ensuring uniform dosing and enhanced patient acceptability for topical use.

Drug Content Determination

The drug content of the Buckwheat (*Fagopyrum esculentum*) phytosomal gel formulations (F1–F10) was determined to assess the uniform distribution and accuracy of encapsulated bioactive constituents within the gel matrix. As presented in Table 8, the drug content ranged from $90.8 \pm 1.3\%$ (F4) to $95.0 \pm 0.9\%$ (F9), indicating consistent and reproducible incorporation of the extract across all batches. These results confirm homogeneous dispersion of the phytosomes, ensuring that each application delivers an effective and reliable dose. High and uniform drug content is critical for maintaining therapeutic efficacy, stability, and quality control of the topical gel formulations.

Table 8: Drug Content of Phytosomal Gel Formulations

Batch	Drug Content (% $\pm$ SD)
F1	91.5 ± 1.2
F2	92.8 ± 1.1
F3	94.2 ± 1.0
F4	90.8 ± 1.3
F5	93.5 ± 1.1
F6	94.8 ± 0.9
F7	91.9 ± 1.2
F8	93.0 ± 1.1
F9	95.0 ± 0.9
F10	93.7 ± 1.0

Stability Studies

The stability of the optimized Buckwheat (*Fagopyrum esculentum*) phytosomal gel formulation (Batch F9) was evaluated under accelerated (40°C / 75% RH) and long-term (25°C / 60% RH) conditions in accordance

with ICH Q1A (R2) guidelines. Batch F9 was selected as the optimized formulation based on its superior physicochemical characteristics, including highest drug content ($95.0 \pm 0.9\%$), maximum cumulative drug release ($90.0 \pm 1.0\%$ at 12 h), and satisfactory entrapment

efficiency ($77.5 \pm 1.2\%$). Formulation retained its smooth, brownish appearance, uniform homogeneity, and semi-solid consistency throughout the study period. Minor variations in pH (5.7–5.8), viscosity (15,150–15,210 cP), spreadability (15.0–15.2 g/cm/s), extrudability (457–460 g/cm²), and drug content (93.7–94.2%) were observed, all within acceptable limits, indicating excellent physicochemical stability. These findings confirm that the optimized Batch F9 phytosomal gel maintains its integrity, therapeutic potential, and patient acceptability under both storage conditions, supporting its suitability for long-term topical application.

In Vitro Drug Release Study

The *in vitro* drug release profile of the Buckwheat (*Fagopyrum esculentum*) phytosomal gel formulations (F1–F10) demonstrated a consistent, controlled, and time-dependent release pattern over a period of 12 hours (Figure 4). An initial burst release was observed within the first hour (≈ 7.9 – 9.2%), which may be attributed to the diffusion of surface-associated drug from the gel matrix. This was followed by a sustained and gradual increase in cumulative

drug release, indicating effective incorporation of the phytoconstituents within the phytosomal system and gel network. Among all formulations, F9 exhibited the highest drug release ($90.0 \pm 1.0\%$) at 12 hours, followed closely by F6 ($89.0 \pm 1.0\%$) and F3 ($88.2 \pm 1.0\%$), suggesting optimized phytosome formation and better drug diffusion characteristics. In contrast, formulations such as F4 and F7 showed comparatively lower release profiles, likely due to tighter vesicular entrapment or higher gel viscosity restricting drug diffusion. The enhanced release observed in optimized formulations can be attributed to improved solubilization of phytoconstituents, increased surface area due to nanosized phytosomes, and better interaction with the gel base. Overall, the results confirm that phytosomal gel formulation significantly improves the release behavior of buckwheat extract, with F9 identified as the optimized formulation exhibiting superior and controlled drug release characteristics suitable for topical therapeutic application.

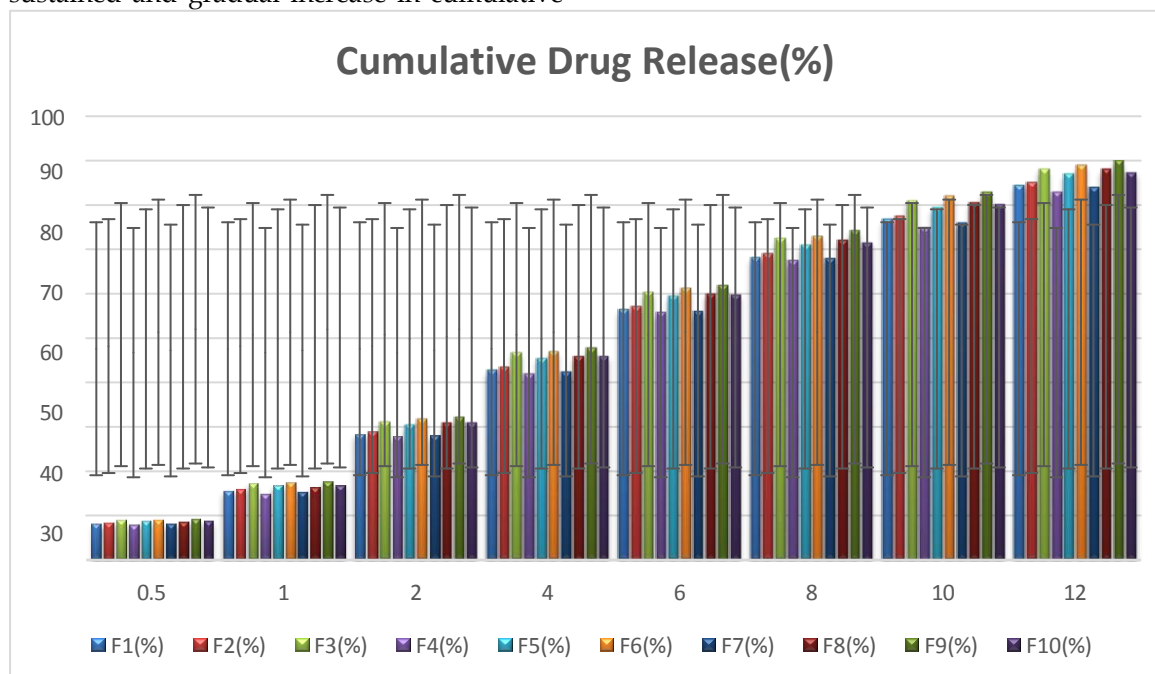


Figure 4: Cumulative Drug Release(%)

The present investigation was aimed at the formulation and evaluation of a phytosomal-

based topical gel of Buckwheat (*Fagopyrum esculentum*) seed extract, with the primary

goal of enhancing solubility, skin permeation, therapeutic efficacy, and patient compliance.

Buckwheat, known for its rich content of bioactive flavonoids, phenols, tannins, and glycosides, was selected due to its antioxidant, anti-inflammatory, and wound-healing potential.

Initially, the plant material was procured from authenticated sources and subjected to botanical verification, followed by the preparation of fine plant powder through careful cleaning, shade-drying, pulverization, and sieving to ensure uniform particle size. The powdered seeds were then extracted using ethanol in a Soxhlet apparatus, which provided a concentrated extract with $25.0 \pm 0.5\%$ yield, preserving the chemical integrity of thermolabile compounds. Preformulation studies revealed that the extract possessed suitable physicochemical characteristics, including a slightly acidic pH (5.7 ± 0.1), optimal solubility in ethanol and methanol, favorable extractive and Δ values, and a lipophilicity profile conducive to phytosome formation. Phytochemical screening confirmed the presence of flavonoids, phenols, tannins, and glycosides, highlighting the extract's pharmacological relevance. Phytosomes were successfully formulated using phosphatidylcholine via the thin-film hydration method, with optimization of phospholipid ratios, solvent system, and process variables to achieve high entrapment efficiency, uniform particle size, and appropriate zeta potential for stability. The prepared phytosomes were reincorporated into different gel bases (e.g., Carbopol, HPMC) to develop 10 batches of topical gel formulations (F1–F10). The gels were evaluated for appearance, color, homogeneity, pH, viscosity, spreadability, extrudability, and drug content, all of which demonstrated acceptable and consistent properties suitable for topical application. *In vitro* drug release studies using Franz diffusion cells and *ex vivo* permeation studies through animal skin demonstrated enhanced and sustained release of the bioactive constituents from the phytosomal gels compared to conventional gels. These findings highlight the efficacy of phytosome technology in improving drug solubility, permeability,

and controlled release. Additionally, stability studies conducted under ICH-recommended conditions confirmed that the optimized gel maintained physical integrity, homogeneity, pH, viscosity, and drug content over the study period, indicating shelf-life stability and suitability for storage.

Conclusion

The present study successfully developed and evaluated a phytosomal topical gel containing Buckwheat (*Fagopyrum esculentum*) extract as a novel herbal drug delivery system for enhanced dermal application. Complexation of the flavonoid-rich extract with phosphatidylcholine effectively improved the physicochemical properties of the herbal bioactive constituents by enhancing their lipophilicity, stability, and compatibility with biological membranes. The optimized phytosomal formulation demonstrated desirable particle characteristics and was successfully incorporated into a Carbopol-based gel with acceptable pH, viscosity, spreadability, extrudability, homogeneity, and drug content.

The phytosomal gel exhibited improved *in vitro* drug release and enhanced skin permeation compared with the conventional gel formulation, indicating the effectiveness of phospholipid complexation in facilitating transport across the stratum corneum. These findings suggest that phytosomal technology can substantially improve the topical delivery of rutin and other flavonoids present in buckwheat, thereby enhancing local bioavailability and therapeutic performance. The formulation also remained stable under accelerated storage conditions, confirming its suitability for pharmaceutical development. Overall, the developed phytosomal gel represents a promising carrier for the topical delivery of herbal bioactive compounds with antioxidant, anti-inflammatory, antimicrobial, and wound-healing properties. This strategy addresses the major limitations of conventional herbal formulations, including poor solubility, instability, and inadequate skin penetration, while improving patient convenience and compliance. Future studies involving *ex vivo* permeation, *in vivo* pharmacological evaluation, and clinical investigations are recommended to

further establish the therapeutic potential and commercial applicability of the developed phytosomal topical gel for the management of inflammatory and oxidative skin disorders.

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