IJBPAS, June, 2026, 15(6): 2960-2975

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

FORMULATION AND EVALUATION OF A PHYTOSOMAL GEL CONTAINING "*PUNICA GRANATUM*" LEAF EXTRACT

JEEVITHA K B[1], ASHVINI H M[2*] AND MARIYA SANJANA A[3]

Department of Pharmaceutics, Mallige College of Pharmacy, #71Silvepura, Chikkabanavara Post, Bangalore-560090, Karnataka, India

***Corresponding Author: Dr. Ashvini H M: E Mail: ashvinimcp@gmail.com**

Received 7th May 2025; Revised 8th June 2025; Accepted 28th Aug. 2025; Available online 1st June 2026

https://doi.org/10.31032/IJBPAS/2026/15.6.10303

ABSTRACT

The present study aimed to formulate and evaluate a phytosomal gel of *Punica granatum* leaves for antimicrobial activity. Ethanolic extracts of *Punica granatum* leaves were prepared and screened for active phytoconstituents through phytochemical tests and GC-MS analysis. Phytosomes were formulated using the salting-out method with varying concentrations of soya lecithin and evaluated for entrapment efficiency, drug content, in-vitro drug release, and particle size. Among the formulations, F4 was identified as the best, exhibiting high entrapment efficiency (96.4 ± 1.5%), maximum drug content (95.05 ± 1.5%), and superior in-vitro drug release (96.54 ± 0.57% at 10 hours). This optimized formulation was incorporated into a Carbopol 940 gel base and further evaluated for pH, viscosity (53,468 cps), spreadability, drug content (95.41%), in-vitro drug release (96.45% at 9 hours), and antimicrobial activity against *Staphylococcus aureus*, showing a significant zone of inhibition at a 1.0 mg concentration. The short-term stability study confirmed the formulation's stability. In conclusion, the F4 phytosomal formulation incorporated into Carbopol 940 gel demonstrated excellent physicochemical properties and enhanced antimicrobial activity, making it a promising candidate for topical applications.

Keywords: *Punica granatum* extract, Phytosomes, Physical parameters, Phytosomal gel, Anti-microbial activity, Drug release

INTRODUCTION

In developing nations where the majority of the population relies on natural remedies for primary healthcare, the use of complementary and alternative medicine has grown in popularity worldwide. The World Health Organization (WHO) states that traditional medicine is still an essential part of healthcare systems, particularly in areas where access to traditional medical care is scarce **[1]**.

One of the many medicinal plants is the pomegranate, *Punica granatum*, which belongs to the Lythraceae family and is known for its wide range of pharmacological profiles and rich phytochemical composition. Originally from the Himalayas, *Punica granatum* has spread to many temperate and tropical regions across the world. The leaf extract contains a variety of bioactive substances, such as flavonoids, tannins, glycosides, alkaloids, terpenoids, phenolic compounds, steroids, and saponins, according to phytochemical analysis. A variety of therapeutic qualities, including anti-inflammatory, antioxidant, antibacterial, anticancer, and antidiabetic effects, are attributed to these constituents. Furthermore, even at high dosages, acute toxicity studies have demonstrated that the leaf extract is safe and non-toxic **[2]**.

Despite these promising pharmacological attributes, a significant challenge in herbal medicine remains the poor bioavailability of many phytoconstituents due to limited solubility, stability, and permeability. To address this limitation, novel drug delivery systems such as phytosomes have been developed. Phytosomes are vesicular systems formed by complexing phytoconstituents with phospholipids, enhancing the solubility, stability, and absorption of poorly bioavailable plant actives **[3]**. These complexes improve the oil-water partition coefficient and facilitate better membrane permeability, resulting in improved systemic availability of the active ingredients **[4]**. Recent studies have shown that phytosomal formulations not only enhance bioavailability but also offer a sustained release profile and better therapeutic efficacy compared to traditional extracts **[5]**.

MATERIALS AND METHODS

Materials:

Fresh *Punica granatum* leaves were collected from local areas of Bengaluru, India, and authenticated by a botanist. Soya lecithin, Carbopol, Chloroform was procured from Yarrow chemicals, Mumbai, India. Dichloromethane (DCM), Triethanol-amine, Propylene glycol Methyl paraben and Propyl paraben were also sourced from Karnataka fine Chem, Bengaluru, India. All other chemicals and reagents used were of analytical grade.

Methods:

Extraction of Plant Material

Collected *Punica granatum* leaves were washed, shade-dried for 20 days, and coarsely powdered. Ethanolic extraction was performed using a Soxhlet apparatus (1:10 w/v ratio), and the extract was concentrated on a water bath at 50°C. The dry extract was stored in a desiccator until use **[6]**.

Preformulation Studies

The initial step in creating a drug substance's dosage form is a preformulation study, which is a stage of research and development in which the physiochemical properties of a novel drug substance are ascertained by applying biopharmaceutical principles.

Preliminary phytochemical screening of extract:

To determine the presence of different phytochemicals such as alkaloids, tannins, flavonoids, phenols, carbohydrates, proteins, steroids, and terpenoids, a phytochemical screening was conducted on an extract of *Punica granatum* leaves **[7]**.

GC-MS Analysis:

Based on peaks and component areas, the GC-MS analysis was carried out to verify the existence of the extract's major chemical components **[8]**.

Determination of Absorption Maxima:

A standard stock solution was prepared by accurately weighing 25 mg (0.025 g) of *Punica granatum* leaf extract and transferring it into a 25 mL volumetric flask. The extract was dissolved and diluted with pH 6.8 phosphate buffer which acts as solvent. Then Sample was kept for analysis and scanned between 200-400nm and absorption maxima was determined

Calibration curve of *Punica granatum* Leaf Extract:

From above stock solution, serial dilutions were prepared to obtain standard concentrations of 2, 4, 6, 8, and 10 µg/Ml. The absorbance of each dilution was measured at 300 nm using a UV-Visible spectrophotometer **[9]**.

Fourier transforms infrared (FT-IR) spectroscopy

To investigate the interaction between *Punica granatum* leaf extract and phospholipids in the phytosomal suspension, Fourier-transform infrared (FTIR) spectroscopy was employed using an FTIR microscope **[10]**.

Formulation of *Punica granatum* loaded phytosomes

The phytosomes were prepared by salting out method and *Punica granatum* loaded phytosomes formulation can be seen in **Table 1**. This method uses two phases in varying amounts. One phase contains the medicine (an extract from the leaves of the plant, *Punica granatum*), which is dissolved in 15 ml of alcohol. Another phase contains soy lecithin, which is dissolved in the

necessary quantity of dichloromethane. After that, the solutions from the two phases were combined and stirred magnetically for a predetermined amount of time until a homogenous solution was formed. The necessary quantity of n-hexane was added to that homogenous solution, and the resulting precipitates. After filtering, the precipitates were placed in a desiccator for 48 hours to dry. When phytosomes are dried and kept in a desiccator, any remaining solvents are guaranteed to be eliminated **[11]**.

Table 1: Composition Of *Punica granatum* Leaf Extract-Loaded Phytosome

Sl.no	Ingredients	F1	F2	F3	F4
01	*Punica granatum*	1	1	1	1
	extract(g)	0.5	1	1.2	2
02	Soya lecithin (g)	15	15	15	15
03	Alcohol (ml)	10	15	20	25
04	DCM (ml)	Q.s.	Q.s.	Q.s.	Q.s.
05	n-hexane (ml)				

EVALUATION OF *PUNICA GRANATUM* LOADED PHYTOSOMES

Percentage yield:

The percentage yield of the prepared phytosomes was calculated to evaluate the efficiency of the formulation process. After completion of the salting-out method and drying, the total weight of the phytosomal complex obtained was recorded as the practical yield. The theoretical yield was calculated based on the total amount of starting materials used i.e, the weight of *Punica granatum* leaf extract and phospholipids.

Entrapment Efficiency:

To determine the entrapment efficiency of the *Punica granatum* leaf extract-loaded phytosomes, 10 mg of the freeze-dried phytosomal complex was dispersed in 10 mL of pH 6.8 phosphate buffer. The dispersion was centrifuged at a predetermined speed of 15,000 rpm for 30 - 1 hr minutes to separate the unentrapped drug present in the supernatant from the entrapped drug bound within the phytosomal vesicles. A 1 mL aliquot of the supernatant was withdrawn and diluted to 10 mL with the same buffer. The absorbance of the diluted supernatant was measured at 300 nm using a UV-Visible spectrophotometer against pH 6.8 phosphate buffer as a blank. The concentration of the free drug in the supernatant was determined using a calibration curve **[12]**.

Particle size, Polydispersity index analysis and Zeta potential:

The physicochemical characteristics of the formulated *Punica granatum* phytosomes specifically particle size, polydispersity index (PDI), and zeta potential were determined using Dynamic Light Scattering (DLS) with a Malvern Zetasizer **[13]**.

Drug Content:

To determine the drug content of the *Punica granatum* -loaded phytosomes, 25 mg of the prepared phytosomes were dissolved in 25 ml of pH 6.8 phosphate buffer using a bath sonicator for 20 minutes. The resulting solution was filtered through Whatman filter paper. From the filtrate, 1 ml of the stock solution was pipetted and diluted with 10 ml of pH 6.8 phosphate buffer. The concentration of *Punica granatum* in the ethanolic extract was then measured using a UV-Visible spectrophotometer at a wavelength of 300 nm, with pH 6.8 phosphate buffer used as the blank **[14]**.

Surface Morphology:

Particle size and surface topography were examined using scanning electron microscopy (SEM), which was run at 15 kV acceleration voltage **[15]**.

DSC Analysis:

Drugs' physical characteristics and the compatibility of the drug with excipients can both be assessed using Differential Scanning Calorimetry (DSC) **[16]**.

***In-vitro* drug release studies:**

An in vitro drug release study of the *Punica granatum* -loaded phytosomes was conducted using a Dissolution Apparatus Type II (basket type). A precisely weighed amount of phytosomes equivalent to 100 mg of *Punica granatum* extract was placed on a sanitized muslin cloth. This was then suspended in 900 mL of pH 6.8 phosphate buffer, maintained at 37 ± 0.5 °C, with the basket rotating at 75 rpm. At predetermined intervals of one hour over a period of ten hours, samples were withdrawn from the dissolution medium and analyzed spectrophotometrically at 300 nm to determine the release of *Punica granatum* extract. The experiment was repeated three times to ensure reproducibility. A graph was plotted showing the cumulative percentage of drug release versus time **[17]**.

FORMULATION OF PHYTOSOMES LOADED TOPICAL GEL

The gel base was initially prepared by soaking Carbopol 940 in distilled water overnight for complete hydration. The pH of the dispersion was then neutralized by the gradual addition of triethanolamine to form a clear gel. Subsequently, the previously optimized *Punica granatum* -loaded phytosomes were incorporated into the gel base, along with preservatives such as methyl paraben and propyl paraben, and a permeation enhancer, propylene glycol. The mixture was stirred thoroughly to ensure uniform distribution of all components **[18]**. The composition of various formulations of *Punica granatum* phytosomal gel is presented in **Table 2**.

Table 2: Formulation Table of *Punica granatum* Phytosomal Gel

Sl no.	Ingredients	Quantity
01	*Punica granatum* loaded Phytosomes(mg)	100
02	Carbopol 940 (g)	1
03	Triethanolamine (ml)	Q.s.
04	Propylene glycol (ml)	5
05	Methyl paraben (g)	0.03
06	Propyl paraben (g)	0.02
07	Distilled water(ml)	100

EVALUATION OF PHYTOSOMES LOADED TOPICAL GEL:

Determination of Viscosity:

The viscosity of the prepared gel was measured using a Brookfield viscometer **[19]**.

Determination of pH of Gels:

The pH of the prepared gel was measured three times independently using a calibrated digital pH meter, and the average value was recorded **[20]**.

Spreadability:

The apparatus consisted of two glass slides, one fixed to a wooden board and the other movable. The movable slide was weighted and connected to a thread that passed over a pulley. A 0.5 g sample of the formulation was placed on one side of the fixed glass slide. To eliminate trapped air and ensure a uniform layer of the formulation, a 100 g weight was placed on the upper slide for one to two minutes. After removing this weight, a 30 g weight was attached over the pulley to apply a pulling force on the top slide. Spreadability was defined as the time (in seconds) required for the movable slide to travel a fixed distance of 6.5 cm **[21]**.

Drug content:

One gram of the phytosomal gel was dissolved in ethanol and diluted to 100 ml in a volumetric flask. The mixture was then sonicated for 10 minutes to ensure complete dissolution. From this solution, 1 ml was taken and further diluted to 10 ml using the same solvent. The absorbance of the resulting solution was measured at 300 nm using a UV-visible spectrophotometer **[22]**.

In-vitro diffusion study:

Drug release studies were performed using a Franz diffusion cell. The surface of an egg membrane was coated with 1 g of the phytosomal gel and clamped securely between the donor and receptor chambers of the diffusion cell. Freshly prepared phosphate buffer (pH 6.8) was added to the receptor chamber to solubilize the drug. The receptor compartment was continuously stirred using a magnetic stirrer. At predetermined time intervals, 5.0 ml aliquots of the receptor solution were withdrawn and immediately replaced with an equal volume of fresh phosphate buffer to maintain sink conditions. After appropriate dilution, the samples were analyzed for drug release by measuring absorbance at 300 nm using a UV-visible spectrophotometer **[23]**.

***In-vitro* release kinetics:**

The kinetic drug release study was performed using a Differential Dissolution (DD) solver to analyze the release profile of the *Punica granatum* -loaded phytosomal gel. The release data were fitted to various kinetic models to understand the mechanism and rate of drug release from the formulation. The goodness of fit parameters for each model were calculated to determine the most appropriate model describing the drug release behavior **[24]**.

Anti-microbial studies:

The in vitro antibacterial activity of the optimized formulation was evaluated using Muller Hinton agar plates. The agar medium was prepared by dissolving 28 grams of powder in 1 liter of deionized water, mixed thoroughly, and sterilized by autoclaving at 121°C (15 psi) for 15 minutes. After cooling to 47°C, the medium was poured into sterile Petri dishes under aseptic conditions and allowed to solidify at room temperature. A bacterial suspension of *Staphylococcus aureus* with a standardized turbidity of 10^6 CFU/mL was evenly spread over the agar surface using a sterilized glass spreader. Wells of 6 mm diameter were aseptically created in the agar using a cork borer. Four different concentrations of the optimized formulation were then introduced into the wells using a sterile syringe. The plates were incubated at 37°C for 24 hours, and the zones of inhibition around each well were measured in millimeters **[25]**.

Stability studies:

A stability study was carried out to evaluate any significant changes that might occur in the formulation during storage. The stability of the gel was assessed by monitoring parameters such as viscosity, spreadability, drug content, pH, visual appearance, and in vitro drug release **[26]**.

RESULTS AND DISCUSSION

Extraction of whole plant *Punica granatum* leaves:

Ethanolic extraction was performed using a Soxhlet apparatus and after extraction the percentage yield was found to be 7.56 %.

Phytochemical screening:

The preliminary phytochemical screening of the *Punica granatum* leaf extract revealed the presence of several bioactive constituents. The extract tested positive for alkaloids, flavonoids, tannins, saponins, terpenoids, and phenolic compounds, while Amino acids, Anthraquinone were absent.

GC-MS analysis:

The GC-MS analysis of the methanolic extract of *Punica granatum* leaves revealed several bioactive phytoconstituents, as indicated by distinct peaks at specific retention times in the total ion chromatogram as represented in **Figure 1**.

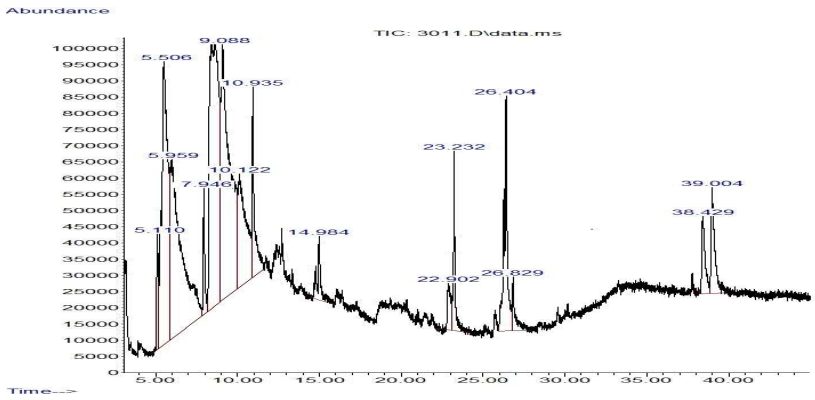

Figure 1: chromatographic profile of *Punica granatum* leaf extract

Determination of wavelength maxima (λmax)and Calibration Curve of drug :

The UV spectra of the drug were acquired through the scanning of drug solutions with a concentration of 10 µg/mL**,** revealing a peak absorption at 300 nm. A standard calibration curve was prepared by measuring the absorbance of different concentrations of the standard solution ranging from 2 to 10 µg/mL. The plot of absorbance versus concentration yielded a straight line, demonstrating a linear relationship. The linear regression equation obtained was y = 0.083x − 0.0267**,** with a correlation coefficient **(R^2)** of 0.9985 (**Figure 2**).

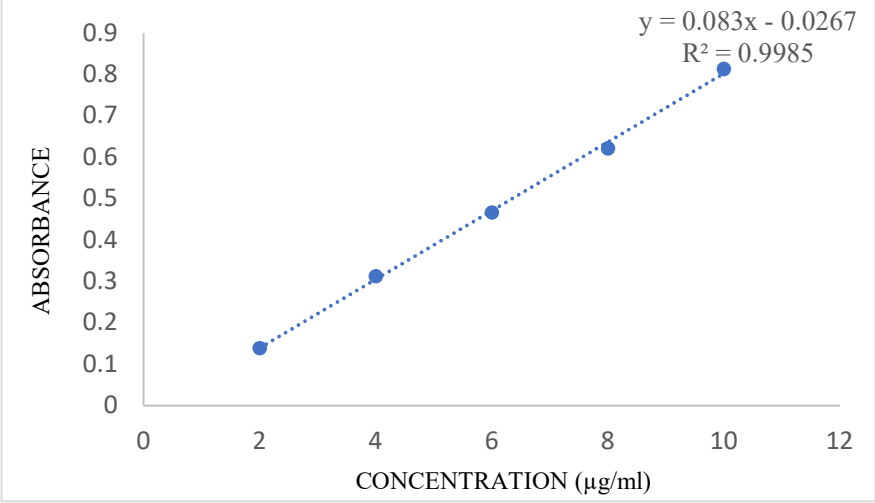

Figure 2: calibration curve for standard drug concentration vs absorbance

Drug-Polymer Compatibility Studies:

The FTIR spectrum of the *Punica granatum* extract revealed prominent absorption bands, including a broad peak at 3401.90 cm^{-1} due to O–H stretching, a peak at 2923.02 cm^{-1} due to aliphatic CH_2 stretching, and a strong C=O band at 1690.06 cm^{-1}, indicating the presence of phenolic and ketonic functional groups. Upon addition of soya lecithin, noticeable

shifts were observed in the carbonyl and hydroxyl regions, particularly the C=O band shifting to 1738.04 cm^{-1}, suggesting hydrogen bonding or electrostatic interactions between the phospholipids and bioactive compounds of the extract. When Carbopol 940 powder was added to the extract-lecithin mixture, further shifts in the C=O band to 1715.85 cm^{-1} and the C–N band to 1114.10 cm^{-1} were observed. These changes indicate possible physical interactions (e.g., hydrogen bonding) between the polymer matrix of Carbopol and the phytosomal complex, without any major chemical modifications to the functional groups of the extract. The FTIR spectra are presented in **Figure 3A, 3B, 3C**.

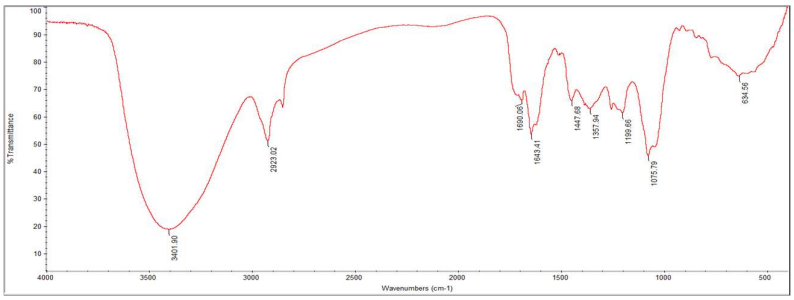

Figure 3A: FTIR spectrum of *Punica granatum* leaf extract

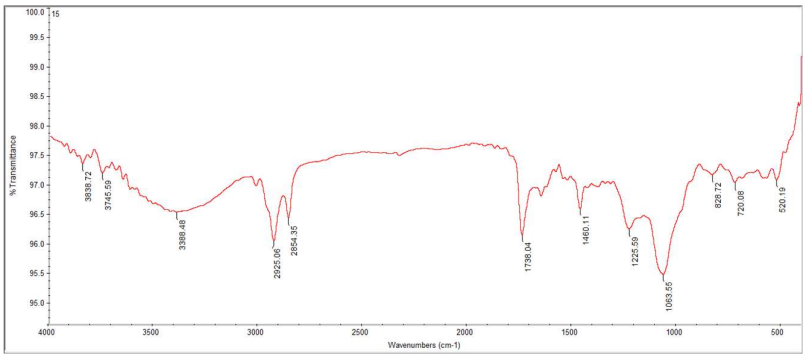

Figure 3B: FTIR spectrum of mixture of *Punica granatum* leaf extract and soya lecithin

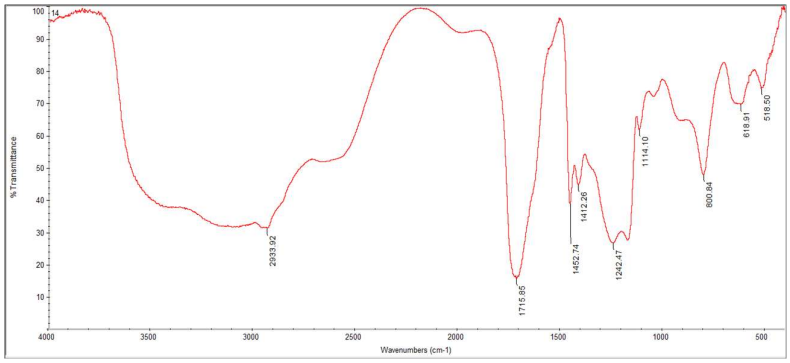

Figure 3C: FTIR spectrum of mixture of *Punica granatum* leaf extract and Carbopol

Evaluation of *Punica granatum* Loaded Phytosomes

Determination of Entrapment efficiency:

The formulations F1 to F4 were evaluated for entrapment efficiency. Among the formulations tested, F4 exhibited the highest entrapment efficiency in F4 (90.09 ± 0.51%) indicating a more efficient preparation process compared to the others.

Determination of *In-vitro* drug release study of phytosomes:

The USP type-II dissolution device was used to investigate the drug release from the produced phytosomes. Using a pH 6.8 phosphate buffer, *Punica granatum 's in-vitro* drug release was conducted for 10 h. It was discovered that the phytosome formulations' percentage cumulative drug release increased progressively over the course of 10 h. At the 10^{th} h, the F4 formulation demonstrated the highest drug release i.e., 96.54%.

The release profile of *Punica granatum* from the phytosomes over 10 hours is illustrated in **Figure 4**.

Determination of Particle size distribution, Poly-dispersibility index and Zeta potential:

The average particle size of the formulated phytosomes was found to be 252.1 ± 141.2 nm, with a polydispersity index (PDI) of 0.253, as determined using a Malvern Zetasizer . The zeta potential was measured at –28.9 ± 3.86 mV, indicating good physical stability of the formulation and represented in **Figure 5**.

Surface Morphology of Phytosomes :

SEM analysis of the formulated phytosomes was performed to evaluate the surface morphology of the phytosomes. The Phytosomes obtained shows disclosed discrete particles with ideal smooth surface. The morphological characteristics of the phytosomal formulation are shown in **Figure 6**.

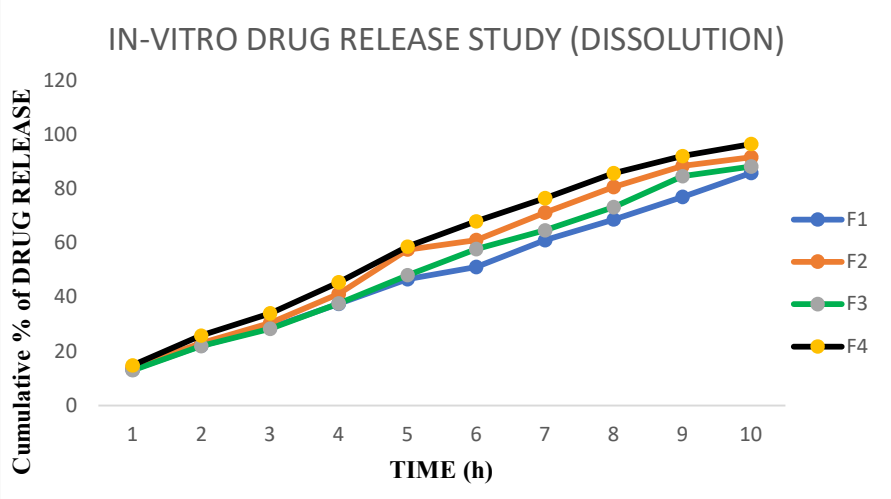

Figure 4: Comparative In-vitro Drug Release Profile of Phytosomal Gel Formulations

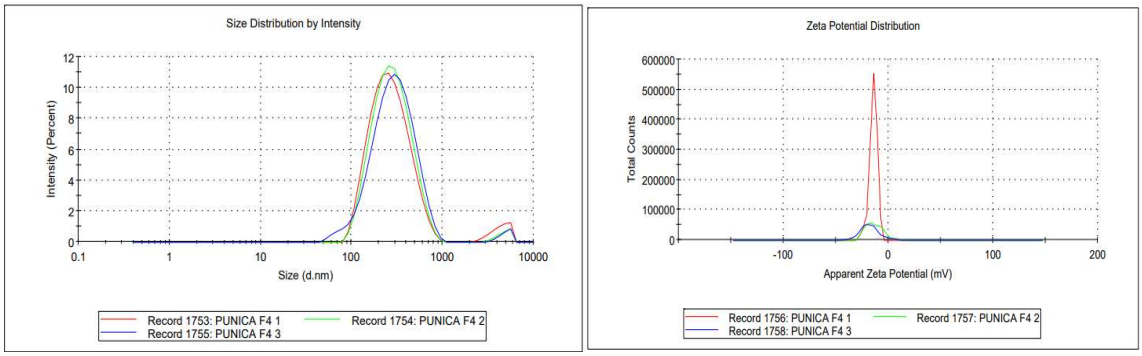

Figure 5: Particle Size Distribution and Zeta potential distribution of Phytosomal Formulation f4 by intensity

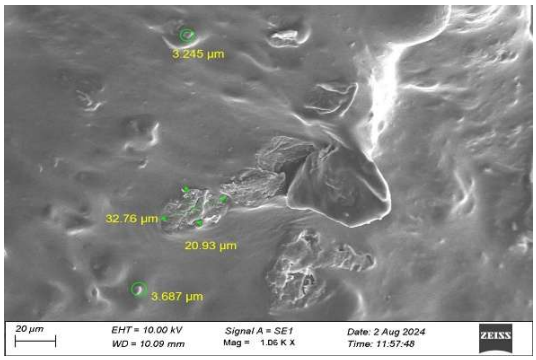

Figure 6 : Scanning Electron Microscopy (sem) image of phytosomal gel formulation

Differential Scanning Calorimetry (DSC) Study:

Thermal behaviour of the best Phytosomes formulation containing *Punica granatum* leaves extract and soya lecithin were studied with the help of DSC. The DSC thermogram shows multiple thermal transitions in the sample. A major endothermic peak at 133.01 °C (ΔH = -694.63 J/g) indicates a possible melting point or loss of volatile components.

The DSC thermograms of the extract, phospholipid, and phytosomal complex are presented in **Figure 7**.

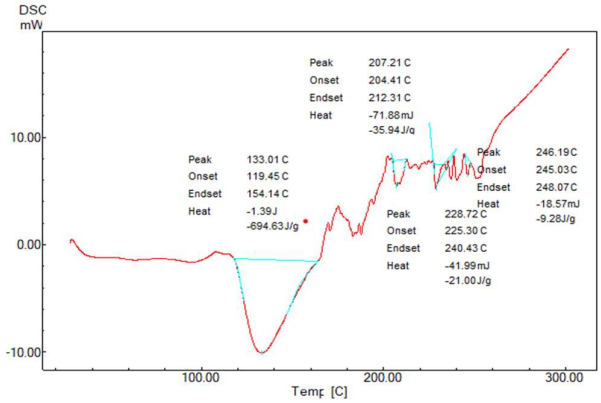

Figure 7: DSC thermograph of best Phytosomes formulation (F4)

IJBPAS, June, 2026, 15(6): 2960-2975

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

Evaluation of *Punica granatum* Loaded Phytosomal Gel

Measurement of pH:

The pH of the gel was found to be 6.25 ± 0.025, which is close to the natural pH of human skin (around 5.5 to 6.5). This indicates that the formulation is mild and skin-friendly, reducing the risk of irritation or allergic reactions upon topical application.

Determination of viscosity :

The viscosity was measured as 53,468 CPS**,** indicating that the gel has a thick but smooth consistency**.** This is important because it ensures the gel stays in place after application without running off, while still being easy to spread. An optimal viscosity also contributes to controlled drug release and good patient compliance**.**

Determination of Spreadability:

The spreadability of the gel was 26.43 ± 0.46 g/cm/s**,** which reflects how easily the gel spreads over the skin surface. A higher spreadability value means the gel can be evenly applied with minimal effort**,** ensuring better coverage and ease of use for the patient.

Determination of *In-vitro* drug release study of Phytosomal gel:

The **Figure 8** represents the in-vitro drug diffusion profile of the gel formulation over a period of 9 hours. The results clearly show a gradual and sustained increase in drug release. This trend continued, and at the 9th hour, the gel formulation showed a maximum cumulative drug release of 96.45%.

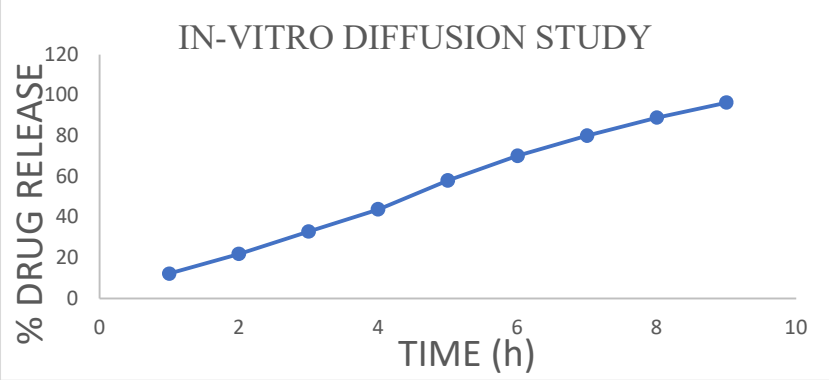

Figure 8: In-vitro Drug Diffusion Profile of Phytosomal Gel Formulation

Release Kinetic profile for Phytosomal gel:

The drug release data from the phytosomal gel was analyzed using different kinetic models. The Korsmeyer-Peppas model showed the best fit with the highest correlation (R^2 = 0.9955) and lowest error, indicating it best describes the release mechanism. Overall, the formulation shows controlled, sustained drug release, ideal for topical delivery and represented in **Table 3**.

Table 3: Kinetic Drug Release Study of Phytosomal Gel Analyzed Using DD Solver Software

Model	Goodness of fit parameters						
	R_obs-pre	Rsqr	MSE	MSE_ root	SS	AIC	MSC
Zero-order	0.9975	0.9947	4.8344	2.1987	38.6748	34.8967	5.0147
First-order	0.9828	0.9026	88.5240	9.4087	708.1917	61.0644	2.1071
Higuchi	0.9910	0.8270	157.294	12.5417	1258.3541	66.2380	1.5323
Korsmeyer-Peppas	0.9978	0.9955	4.6749	2.1622	32.7246	35.3931	4.9595

Antimicrobial Study of Phytosomal gel:

The *Punica granatum* loaded phytosomal gel formulation demonstrated antimicrobial activity against *Staphylococcus aureus*. No zone of inhibition was observed at concentrations of 0.25 mg and 0.50 mg, while a measurable zone appeared at higher concentrations. At 0.75 mg, the zone of inhibition was 2 mm, increasing to 2.5 mm at 1.0 mg concentration, indicating a concentration-dependent antimicrobial effect. These results represented in **Figure 9** confirm the formulation's potential as an effective antimicrobial agent.

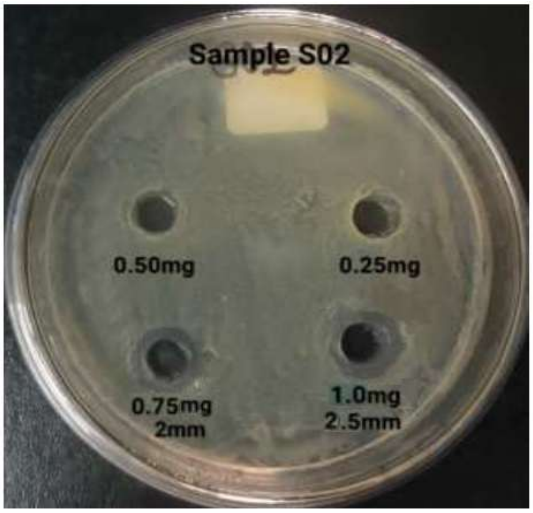

Figure 9: Antibacterial activity of *Punica granatum* -loaded phytosomal gel formulation

Stability Studies:

Stability studies of the optimized phytosomal gel formulation showed no significant changes in key parameters over the study period. The gel maintained its green color and consistent visual appearance, indicating physical stability.

Acknowledgments

I would like to sincerely thank Dr.Ashvini HM, my guide, for her invaluable advice, encouragement, and support during the writing of this review article. Her knowledge and experience have been crucial in determining the focus and caliber of this work.

Authors' Contributions

Jeevitha K B designed the study, wrote the protocol, and prepared the first draft of the manuscript. Ashvini H M and Mariya Sanjana A managed the analyses of the study. Mariya Sanjana A conducted the literature searches. All authors read and approved the final manuscript.

REFERENCES

[1] World Health Organization. Traditional Medicine Strategy 2002–2005. Geneva: WHO Publications; 2002.

[2] Kaur G, Jabbar Z, Athar M, Alam MS. *Punica granatum* (Pomegranate) fruit as a chemopreventive agent: a review of the evidence. Toxicology 2006;228(2–3):202–16.

[3] Bombardelli E, Patri G. Phytosomes: a new delivery system for herbal extracts. Herba Italia 1991;1(3):12–6.

[4] Semalty A, Semalty M, Rawat MSM, Franceschi F. Phytophospholipid complex of catechins in green tea: physicochemical and pharmacokinetic characterization. Phytomedicine 2010;17(6):345–52.

[5] Jain S, Tiwary AK. Topical phytosome-loaded gels: a novel approach for improved skin delivery of herbal extracts. AAPS PharmSciTech 2014;15(3):716–25.

[6] Sreedevi P, Vijayalakshmi K, Venkateswari R. Phytochemical evaluation of *Punica granatum* L. leaf extract. Int J Curr Pharm Res 2017;9(4):14–8.

[7] Usha T, Middha SK, Shanmugarajan D, Babu D, Goyal AK, Yusufoglu HS, *et al*. Gas chromatography-mass spectrometry metabolic profiling, molecular simulation and dynamics of diverse phytochemicals of *Punica granatum* L. leaves against estrogen receptor. Front Biosci (Landmark Ed) 2021;26(9):423–41.

[8] Acquadro S, Civra A, Cagliero C, Marengo A, Rittà M, Francese R, *et al*. *Punica granatum* leaf ethanolic extract and ellagic acid as inhibitors of Zika virus infection. Planta Med 2020;86(18):1363–74.

[9] Kumar M, Dandapat S, Ranjan R, Kumar A, Sinha MP. Plant mediated synthesis of silver nanoparticles using *Punica granatum* aqueous leaf extract. J Microbiol Exp 2018;6(4):175–8.

[10] Nanavati B. Phytosome: a novel approach to enhance the bioavailability of phytoconstituent. Asian J Pharm 2017;11(3):453–61.

[11] Pande SD, Wagh AS, Bhagure LB, Patil SG, Deshmukh AR. Preparation and evaluation of phytosomes of pomegranate peels. Res J Pharm Technol 2015;8(4):416–22.

[12] Udapurkar PP, Bhusnure OG, Kamble SR. Diosmin phytosomes: development, optimization and physicochemical characterization. Indian J Pharm Educ Res 2018;52(4):29–36.

[13] Hindarto CK, Surini S, Permana AH, Redjeki S, Irawan C. Effect of mole ratio on physicochemical properties of luteolin-loaded phytosome. J Pharm Innov 2017;6(12):96–101.

[14] Hou Z, Li Y, Huang Y, Zhou C, Lin J, Wang Y, *et al*. Phytosomes loaded with mitomycin C–soybean phosphatidylcholine complex developed for drug delivery. Mol Pharm 2013;10(1):90–101.

[15] Das MK, Kalita B. Design and evaluation of phyto-phospholipid complexes (phytosomes) of rutin for transdermal application. J Appl Pharm Sci 2014;4(10):51–7.

[16] Shriram RG, Moin A, Alotaibi HF, Khafagy ES, Al Saqr A, Abu Lila AS, *et al*. Phytosomes as a plausible nano-delivery system for enhanced oral bioavailability and improved hepatoprotective activity of silymarin. Pharmaceuticals 2022;15(7):1–20.

[17] Gahandule MB, Jadhav SJ, Gadhave MV, Gaikwad DD. Formulation and development of hepato-protective *Butea monosperma*-phytosome. Int J Res Pharm Pharm Sci 2016;1(4):21–7.

[18] Raj MP, Reichal CR, Manju S, Shobana M, Sangeetha M. Formulation and characterization of phythosomal topical gel of *Ocimum basilicum*. Res J Pharm Technol 2022;15(10):4649–54.

[19] Bharati R, Badola A. Formulation and evaluation of phytosomal gel of *Camellia sinensis* for treatment of skin ageing. World J Pharm Res 2022;11(1):845–56.

[20] Joshua JM, Anilkumar A, Cu VE, Vasudevan DE, Surendran SA. Formulation and evaluation of

antiaging phytosomal gel. Asian J Pharm Clin Res 2018;11(3):409–22.

[21] Rao M, Sukre G, Aghav S, Kumar M. Optimization of metronidazole emulgel. J Pharm Sci 2013;13(1):1–9.

[22] El-Menshawe SF, Ali AA, Rabeh MA, Khalil NM. Nanosized soy phytosome-based thermogel as topical anti-obesity formulation: an approach for acceptable level of evidence of an effective novel herbal weight loss product. Int J Nanomedicine 2018;9(4):307–18.

[23] Fatima Z, Shahidulla SM. Formulation, optimization and evaluation of hexadecanoic acid phytosomal gel for anti-fungal activity. Int J Pharm Sci Res 2023;14(1):519–29.

[24] Mannan A, Begum S, Rasheed A. Formulation, development and evaluation of phytosomal gel of thymoquinone. Int J Pharm Biol Sci 2019;9(4):419–31.

[25] Ray N, Chouksey R, Malviya K, Sahu AR. Development and evaluation of polyherbal phytosome with potential effect against microbes. Aegaeum J 2020;8(3):1123–33.

[26] Roy D, Nagori M, Jain V, Pal P. Development, characterization and evaluation of phytosomal gel of curcumin for the treatment of topical fungal infection. Int J Newgen Res Pharm Healthc 2023;1(1):62–9.