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Research Article

Development and Characterization of Phytosomal Mucoadhesive Oral Gel of *Camellia sinensis* Polyphenols

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Abstract

Background: Epigallocatechin-3-gallate is a polyphenol obtained from *Camellia sinesis.* Which acts as an antioxidant and Anti-inflammatory. It exhibits poor water solubility, low lipophilicity (log P ≈ 1.2), and extensive first-pass metabolism, highlighting the need for improved drug delivery methods.

Aim: To formulate a stable phytosomal delivery system for EGCG and incorporate it into a mucoadhesive oral gel suitable for effective oral mucosal and topical applications.

Materials and Methods: Phytosomes were prepared by the solvent-evaporation technique using phosphatidylcholine as the lipid carrier to form stable phyto-complexes. The resulting vesicles were characterised for their morphological and physicochemical properties using Scanning Electron Microscopy (SEM) and particle size analysis. The prepared phytosomal gels (F1–F3) were further evaluated for pH, viscosity, spreadability, and drug content uniformity. In vitro diffusion studies were performed in phosphate buffer (pH 6.8). Kinetic modelling and stability testing at 25 °C ± 2 °C / 60 % ± 5 % RH for 45 days were also conducted.

Results: SEM revealed uniformly shaped spherical vesicles with smooth surfaces. Formulation F8 exhibited the smallest mean particle size of 244 nm, suggesting improved permeation and stability. In vitro diffusion studies demonstrated a sustained-release profile extending over 12 hours, with cumulative drug release ranging from 96.37% to 98.88%. Kinetic modelling of the optimised formulation (F2) indicated diffusion-controlled release consistent with the Higuchi model. Stability testing showed negligible variations in physicochemical parameters and only a slight reduction in drug release (from 98.88% to 94.37%), confirming the formulation's robustness.

Conclusion: The developed phytosomal mucoadhesive gel offers a promising delivery system for EGCG, capable of improving its therapeutic potential and bioavailability for effective oral mucosal and topical applications.

Keywords: Camellia sinensis, solvent evaporation method, *in vitro* drug release, phytosomal gel, mucoadhesive system.

1. INTRODUCTION

Green tea (Camellia sinensis) is a rich source of naturally occurring polyphenolic compounds, primarily catechins such as (−) epigallocatechin-3-gallate (EGCG), (−)-epigallocatechin (EGC), and (−)-epicatechin gallate (ECG), which are known for their potent antioxidant, anti-inflammatory, antimicrobial, and anticancer activities.[1] In a phytosomal complex, the polyphenolic compounds form hydrogen bonds with the polar head of phospholipids, typically phosphatidylcholine, resulting in a lipid-compatible molecular complex. This unique arrangement improves lipophilicity, membrane permeability, and stability, thereby overcoming the limitations associated with conventional extracts. Phytosomal technology has been successfully applied to various herbal bioactive, significantly improving their pharmacokinetic and pharmacodynamic profiles.[2] Mucoadhesive drug delivery systems have gained substantial attention as an effective approach for enhancing the residence time of formulations at mucosal sites, ensuring sustained drug release and improved therapeutic efficiency. Oral mucoadhesive gels offer several advantages, including ease of administration, enhanced patient compliance, controlled release behaviour, and the ability to bypass hepatic first-pass metabolism when applied to the oral mucosa.[3] Incorporating phytosomal complexes into mucoadhesive gels can provide dual benefits improved absorption of the bioactive compound and prolonged mucosal contact, ensuring better therapeutic outcomes. Hence, the present research focuses on the development and characterization of a phytosomal mucoadhesive oral gel containing Camellia sinensis polyphenols.[4] The study aims to formulate a stable, bioavailable, and effective oral gel system by combining phytosome technology with mucoadhesive delivery principles. The prepared formulations will be evaluated for physicochemical

properties, drug excipient compatibility, in vitro release, mucoadhesive strength, and stability studies to establish a suitable platform for enhanced delivery of Camellia sinensis polyphenols through the oral mucosa.

2. MATERIALS AND METHODS

Green tea (Camellia sinensis), Soya lecithin and Cholesterol were procured from Synpharma Research Labs, Hyderabad, and other chemicals and reagents used were of analytical grade.

A.Extraction of dried powdered Camellia sinensis:

In the first stage of the study, the dried powdered leaves was extracted with either 95% ethanol, 50% ethanol or water by maceration with (1:10) dried powdered leaves to extraction solvent ratio at 45 °C ± 2 °C for 48 h. One hundred˚ grams of powdered leaves was placed in a glass flask, 1000 ml of either extraction solvents was added, the flask was covered with aluminium foil and transferred into water bath with occasional shake. At the end of maceration period the extracts were filtered using Whatman No.1 filter paper, concentrated by rotary evaporator to about 10% of the original volume. The process was repeated twice more , and the concentrated extracts were combined together. Thereafter, the concentrated extracts were dried in a drying oven at 45 °C ± 2 °C Until a constant weight of dry mass is obtained .The collected dried extracts were used to determine the best extraction solvent. [5]

2.1 PRE-FORMULATION STUDIES

Ways to Describe Epigallocatechin-3-gallate (EGCG)

2.1.1Physical characteristics

The extract's colour, smell, and taste were noted.

2.1.2 Studies on solubility

The solubility test method involves trying to dissolve compounds in different solvents using mechanical methods that are more and more difficult. We found out how soluble EGCG was in both water and organic solvents.

2.1.3 Finding the melting point: The capillary technique was used to get the M. P of EGCG.

2.1.4 Making a phosphate buffer

To bring the pH to 7.4, 28.85 grammes of di-sodium hydrogen orthophosphate and 11.45 grammes of potassium dihydrogen phosphate were weighed out and added to 1000 ml of water. Then, ortho phosphoric acid was used to change the pH.

Making a standard solution of EGCG

A 100 ml volumetric flask was filled with 100 mg of EGCG that had been weighed correctly. We added 7.4 phosphate buffer to the volume until it reached 100 ml, which generated a 1000 mcg/ml solution.

Stock solution II: To make 100mcg/ml, 10ml of stock solution I was put into a 100ml volumetric flask and mixed with 7.4 phosphate buffer to make 10ml.

Stock solution-III: A 1ml aliquote from stock solution-II was built up to 10ml to achieve 10mcg/ml.

Similar dilutions were made from stock solution -I in several types of media, such as buffer solutions with a pH of 7.4.

Finding the absorption maxima (λmax) for EGCG

We used a twin beam spectrophotometer to scan a 10mcg/ml standard solution of EGCG against the appropriate media blanks. All solutions had an absorption maximum (λmax) of 274 nm, which was used to make the standard curve.

2.1.5 Standard curves for EGCG:

Standard graph of EGCG in phosphate buffer 7.4:

We made a standard stock solution of EGCG (1mg/ml) by mixing 100mg of EGCG with 100ml of 7.4 phosphate buffer. By adding phosphate buffer 7.4 to the normal stock solution, a solution with a concentration of 100 µg/ml was produced. We created 10, 20, 30, 40, 50, 60, 70, 80, and 90 µg/ml concentrations by serially diluting this solution with phosphate buffer 7.4.

Finding the absorption maxima (λmax) for EGCG

A 10 mcg/ml standard solution of EGCG was analysed using a double beam spectrophotometer in comparison to the corresponding media blanks.

2.1.5 FTIR Studies

FT-IR spectroscopy was used to look at how drugs and polymers interact with each other. Weighing and mixing one to two milligrammes of medication, polymer, and physical mixes of samples until they were all the same. By exerting pressure, a little amount of the powder was turned into a thin, semi-transparent pellet. We captured the IR spectra of the pellet from 400 to 4000 cm1, using air as a reference, and then compared the two to see whether there was any interference.

3. FORMULATION DEVELOPMENT:

Table 1: Formulation development of phytosomes

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Extract equivalent to 100mg of EGCG (mg)	100	100	100	100	100	100	100	100
Soya lecithin(mg)	100	100	100	200	200	200	300	300
Cholesterol (mg)	25	50	75	25	50	75	25	50
Dichloromethane(ml)	10	10	10	10	10	10	10	10
Ethanol(ml)	30	30	30	30	30	30	30	30
Phosphate buffer pH 7.4	50	50	50	50	50	50	50	50
Distilled water (v/v)	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

B. Preparation of phytosomes - Dissolve the weighed amount of phosphatidylcholine in ethanol in a round-bottom flask. Heat gently (30–40 °C) if needed to solubilize. Dissolve the calculated amount of Camellia sinensis extract in ethanol and add to the PC solution. For improved complexation, add the extract slowly while stirring. Optionally add a small amount of cholesterol to improve membrane rigidity. Attach the flask to a rotary evaporator and evaporate the solvent under reduced pressure at 40–45 °C to form a thin lipid film on the flask wall. Keep the flask under vacuum for 30–60 min to remove residual solvent. Hydrate the thin film with phosphate buffer pH 7.4 at room temperature with gentle rotation to yield a suspension. Sonicate the suspension (probe sonicator) in an ice bath for 5–10 min (pulse mode) to reduce particle size and obtain uniform vesicles. Optionally extrude through polycarbonate membranes for size control. Store the phytosomal suspension at 4 °C for further characterization.[6]

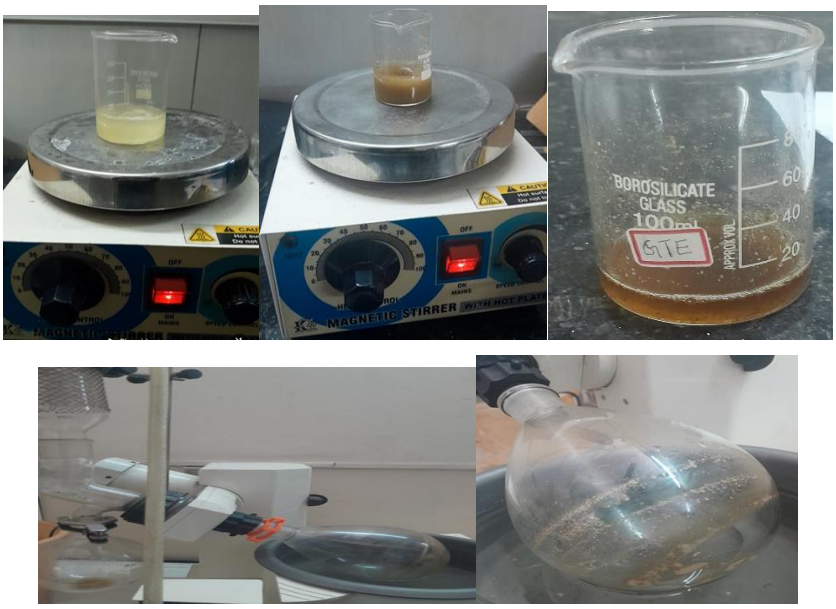

Figure 1: Pictorial representation of formulation and evaluation of phytosomes

3.1. Formulation of phytosomal gel

A predetermined amount of Carbopol 940 was introduced into distilled water, followed by the addition of Glycerine and subsequent stirring until complete dissolution was achieved Subsequently, the solution underwent neutralization and was rendered viscous through the inclusion of triethanolamine. The amalgamationn was agitated incessantly for a duration of one hour until it coalesces into a lucid gel, as reported in reference. Separately, an amount of phytosomal dispersion equivalent to 500 mg of EGCG was was generated and subsequently introduced gradually into the pre-existing polymer gel. The ultimate amount was adjusted to utilizing distilled water. The gels that were produced were subsequently stored in appropriate receptacles at ambient temperature in order to facilitate subsequent investigations.[7]

Table 2: Formulation development of phytosomal gel

Ingredients	F1	F2	F3
Phytosomes(mg)equivalent of EGCG	500	500	500
Carbopol 934 (%)	0.5	1.0	1.5
Methyl paraben (ml)	0.01	0.01	0.01
Glycerine (ml)	1	1	1
Water	q.s	q.s	q.s

3.2 CHARACTERIZATION OF PHYTOSOMES

Particle Size-The particle size of the phytosomes were determined using Particle Size Analyzer (PSA) with the dynamic light scattering (DLS) method. The measurements were performed using Horiba Scientific SZ-100, with the sample diluted 10 times in aqueous medium at room temperature.[8]

Zeta-potential:

The sample was diluted with distilled water (1:100 (V/V)) and zeta potential was determined using Malvern zetasizer (Nano ZS, Malvern Instruments, United Kingdom). Measurement was based on the electrophoretic mobility of the particles, which was converted to the zeta potential by inbuilt software based on the Helmholtz-Smoluchowski equation.[9]

SEM analysis

The shape, surface characteristics, and size of the phytosomal gel were observed by scanning electron microscopy. Once again, 0.2 g of the phytosomal gel in a glass tube was diluted with 10 ml of pH 7.4 phosphate buffer. The phytosomal gel were mounted on an aluminium stub using double-sided adhesive carbon tape. Then the vesicles were sputter-coated with gold palladium (Au/Pd) using a vacuum evaporator (Edwards) and examined using a scanning electron microscope (Hitachi 3700N, Germany) equipped with a digital camera, at 10 kV accelerating voltage.[10]

Yield of phytosomes

The practical yield of phytosomes refers to the percentage of product actually obtained after preparation compared to the total theoretical amount of drug and phospholipid used in the formulation process.[11]

It is calculated using the following formula:

Practical Yield (%) =Weight of dried phytosomes obtained / Total weight of drug + phospholipid taken x100

Drug entrapment efficiency and drug loading

The drug entrapment efficiency (EE) of the phytosomal formulations was determined to evaluate the amount of Camellia sinensis extract successfully encapsulated within the vesicles. An accurately weighed amount of phytosomal suspension was centrifuged at 10,000 rpm for 30 minutes at 4°C to separate the unentrapped free drug in the supernatant. The concentration of free drug in the supernatant was then quantified using a UV–Visible spectrophotometer at 274 nm, based on a pre-established calibration curve of EGCG .[12] The entrapment efficiency (%) was calculated using the formula:

EE (%) = Total drug – Free drug /Total drug× 100

Similarly, the drug loading (DL%) of the phytosomes was determined to assess the proportion of drug relative to the total weight of the vesicles. The drug loading was calculated using the formula:

DL (%) = Amount of drug in phytosomes/ Total weight of phytosomes × 100

These measurements provide crucial information about the efficiency of drug encapsulation and the capacity of the vesicles to carry the active phytoconstituents.

***In vitro* drug release studies**

The *in-vitro* release of Extract equivalent of EGCG (mg) from phytosomal formulations was carried out using a Franz diffusion cell. A known amount of phytosomal suspension was placed in a pre-soaked dialysis membrane (with appropriate molecular weight cut off) and immersed in 50 ml of phosphate buffer pH 6.8 maintained at 37 ± 0.5°C with continuous stirring at 100 rpm. At predetermined time intervals (e.g., 1, 2, 3, 4, 6, 8, 10, and 12 hours), 2 ml of the release medium was withdrawn and replaced with an equal volume of fresh buffer to maintain sink conditions. The withdrawn samples were analyzed spectrophotometrically at 274 nm, and the cumulative percentage of drug released was calculated using the calibration curve of Camellia sinensis extract. This method provides insight into the drug release kinetics, rate, and mechanism from the phytosomal vesicles, ensuring sustained and controlled delivery of the active compound.[13]

3.3 CHARACTERIZATION OF PHYTOSOMAL GEL[14,15]

Physical evaluation: The formulation was manually examined to check any variations in the color, odor, and texture.

Measurement of pH: PH of each formulation was determined by using pH meter. This was calibrated before with buffer solutions of pH 4, 7 and 9.

Determination of viscosity: The viscosity measurement of phytosomal gels was determined by using a Brookfield viscometer. 30gm of gel preparation was kept in 50ml beaker, set at room temperature and spindle at 5, 10, 20, 50, and 100rpm.

Homogeneity: All developed gels were tested for uniformity by visual inspection after setting into containers. They were tested for their appearance and presence of any aggregates.

Spreadability: Two sets of glass slides of standard dimensions were taken. The herbal gel formulation was placed over one of the slides. The other slide was placed on the top of the gel, such that the gel was sandwiched between the two slides in an area occupied by a distance of 7.5 cm along the slides. Hundred g weight of gel was placed on the upper slides so that the gel was between the two slides was pressed uniformly to form a thin layer. The weight was removed and the excess of gel adhering

to the slides was scrapped off. The two slides in position were fixed to a stand without slightest disturbance and in such a way that only upper slides to slip off freely by the force of weight tied on it. A 20 g weight was tied to the upper slide carefully. The time taken for the upper slide to travel the distance of 7.5 cm and separated away from the lower slide under the influence of the weight was noted. The experiment was repeated for three times and the mean time was taken for calculation.

Spread ability was calculated by using the following formula: S= m × l/t

where,

S= spread ability, m-weight tied to upper slides (20 g),

l- Length of the glass slide (7.5 cm), t- time taken in sec.

Drug content : Each formulation (1 g) was taken in a 50 mL volumetric flask and made up to volume with Ethanol and shaken well to dissolve the active constituents in methanol. The solution was filtered through Whatman filter paper and 0.1 mL of the filtrate was pipetted out and diluted to 10 mL with methanol. The content of active constituents was estimated spectro photometrically by using standard curve plotted. (λ max of active constituents in the extracts).

***In vitro* diffusion profile:** *In vitro* release study of the formulated phytosomal mucoadhesive oral gel was carried out by using diffusion cell through membrane as a dialysis membrane. Diffusion cell with inner diameter 24mm was used for the study. 1 mL formulation was placed in donor compartment and freshly prepared pH 6.8 phosphate buffer was placed in receptor compartment. Dialysis membrane was mounted in between donor and receptor compartment. The position of the donor compartment was adjusted so that the membrane just touches the diffusion medium. The whole assembly was placed on the thermostatically controlled magnetic stirrer. The temperature of the medium was maintained at 37°C ± 0.5°C. 1mL of sample was withdrawn from receiver compartment after 12 hrs and same volume of fresh medium was replaced. The withdrawn samples were diluted to 10mL in a volumetric flask with distilled water and analysed by UV spectrophotometer.

Drug release kinetics : The models used were zero order (equation 1) First order (equation 2) and Higuchi model (equation 3) and Koresmeyer Peppas model (equation 4).

i) Zero order kinetics:

$$R = K_o t \quad \text{-- (1)}$$

R=cumulative percent drug

Ko=zero order rate constant

ii) First order kinetics

$$\log C = \log C_o - K_1 t / 2.303 \quad \text{-- (2)}$$

where C = cumulative percent drug

K_1 = first order rate constant

iii) Higuchi model

$$R = K_H t^{0.5} \quad \text{-- (3)}$$

Where R = cumulative percent drug

K_H = higuchi model rate constant

iv) Korsmeyer peppas model:

$$M t / M \alpha = K_k t^n$$

$$\log M t / M \alpha = \log K_k + n \log t \quad \text{-- (4)}$$

where K_k = korsermeyer peppas rate constant

'M t / M α' is the fractional drug , n = diffusional exponent, which characterizes the mechanism of drug.

The obtained regression co-efficient (which neared 0.999) was used to understand the pattern of the drug from the phytosomal gel.

3.4 Stability studies: The main objective of the stability testing is to provide evidence on how the quality of the drug product varies with time under the influence of temperature and humidity. The stability study for the phytosomal mucoadhesive oral gel formulation was done as per ICH guidelines in a stability chamber for a period of 45 days.

4. RESULTS AND DISCUSSION:

1. Pre-formulation studies:

4.1.1 Organoleptic evaluation:

Table 3: Organoleptic properties of Camellia sinensis Polyphenols

Properties	Results
Description	Fine powder
Taste	Bitter
Odor	Characteristic herbal
Color	Light to dark green or greenish-brown

The extract was found to be a fine powder, bitter in taste, with a characteristic herbal odor, and green to brownish color, which complies with literature reports.

4.1.2. Determination of Melting point:

TABLE 4: Melting point

MELTING POINT OF CAMELLIA SINENSIS Polyphenols	REFERENCE RANGE	OBSERVED RESULTS
Melting point of Camellia sinensis polyphenols was found in which complied with the standard, indicating purity of the drug sample.	235°C	238°C

The melting point was recorded at around 238 °C, indicating purity of the phytoconstituent without signs of degradation or impurity contamination.

Semi-soluble in water, better in warm water or alcohol.

Discussion: Solubility studies showed that Camellia sinensis polyphenols is somewhat soluble in water and more soluble in warm water and alcohols. This shows that phytosome formulation that increases lipophilicity might improve bioavailability.

4.1.3. Solubility:

Semi-soluble in water, better in warm water or alcohol.

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4.2. Standard curve of Epigallocatechin-3-gallate [EGCG]

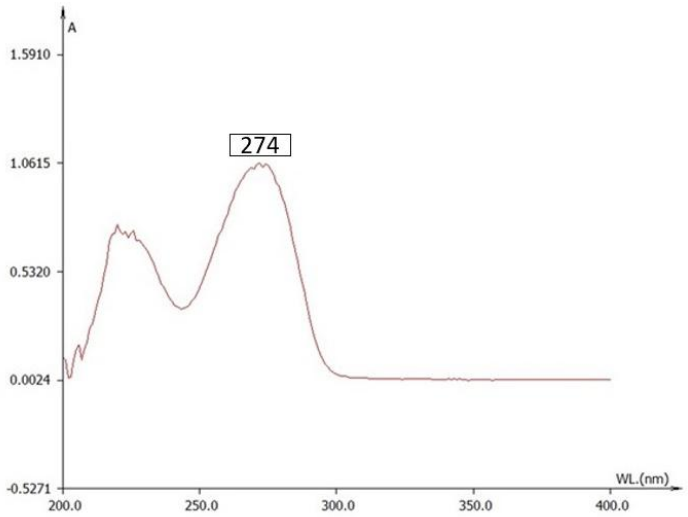

Figure 2 : Standard curve of Epigallocatechin-3-gallate (EGCG)

Standard curve of Camellia sinensis leaf was determined by plotting absorbance V/s concentration using phosphate buffer pH 7.4 at 274 nm. And it follows the Beer's law. The R^2 value is 0.9964.

Table 5: Preparation of Calibration curve of [EGCG]:

Concentration (µg/ml)	Absorbance
0	0±0.000
10	0.125±0.003
20	0.240 ±0.004
30	0.337 ±0.005
40	0.441 ±0.006
50	0.528 ±0.004

Measured at 274nm ,mean ± SD (n = 3)

4.3: Calibration curve of EGCG

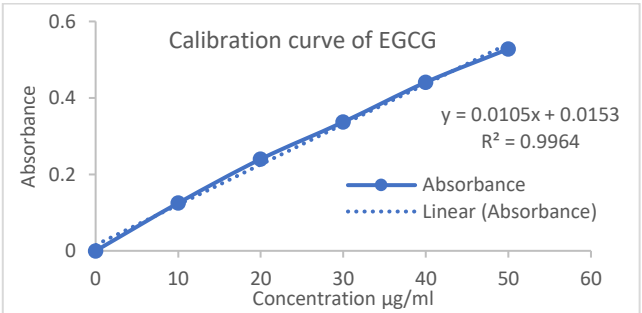

Figure 3: Calibration curve of EGCG

Discussion

The maximum wavelength (λmax) for EGCG was found to be 274 nm. This number matches what is already known about the catechin and polyphenol chemicals in Camellia sinensis, which confirms that the analytical wavelength chosen is correct. A calibration curve made in phosphate buffer (pH 7.4) showed great linearity throughout a concentration range of 10–50 µg/ml, with a correlation value (R^2) of 0.997. This strong linear connection shows that the analytical approach follows the Beer-Lambert law, making it a dependable and accurate way to measure EGCG in future in vitro research.

4.4: FT – IR Studies of EGCG

Compatibility study (IR spectroscopy)

FTIR analysis was performed in order to study the compatibility of ingredients used in the preparation of nanoparticles, using a Shimadzu FTIR spectrophotometer (Prestige21, Shimadzu Corporation, Kyoto, Japan). Camellia sinensis extract and Excipients their mixture with ratio (1:1) was evaluated using FTIR spectrophotometer using potassium bromide disc technique where 1mg of the sample is mixed with 100 mg of dry powdered KBr, the mixture is pressed into a transparent disc and was inserted in the apparatus for IR scan.

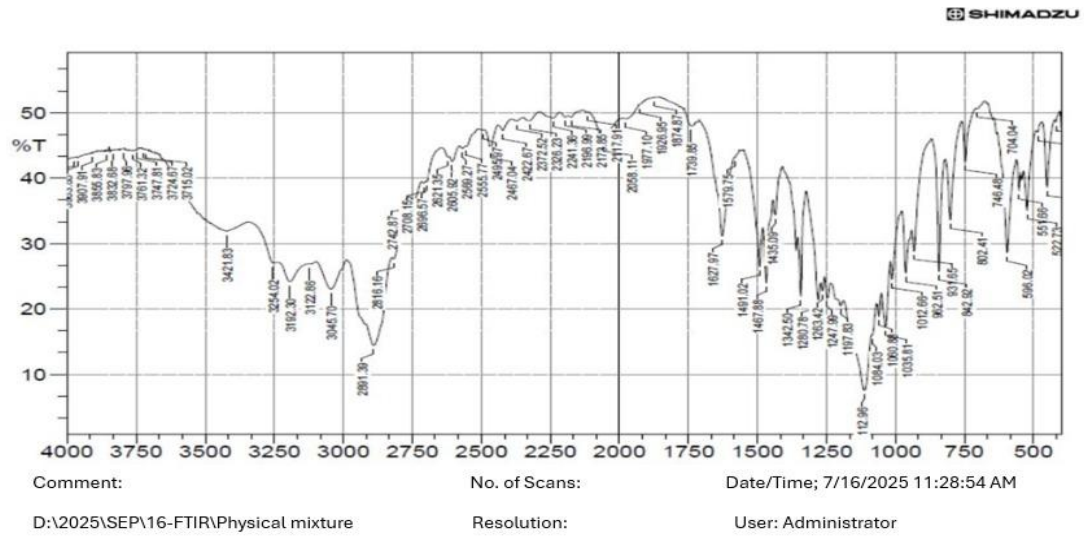

Figure 4: FT-IR Spectra for EGCG

Table 6: Characteristic Peaks and frequency of Camellia Sinensis Extract

S. No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	**OH stretching**	**4000-3500**	**3855.83**
2	OH Bending	3000-2750	2891.39
3	C-H stretching	1750-1250	1342.50
4	C-N stretching	1250-1000	1112.96

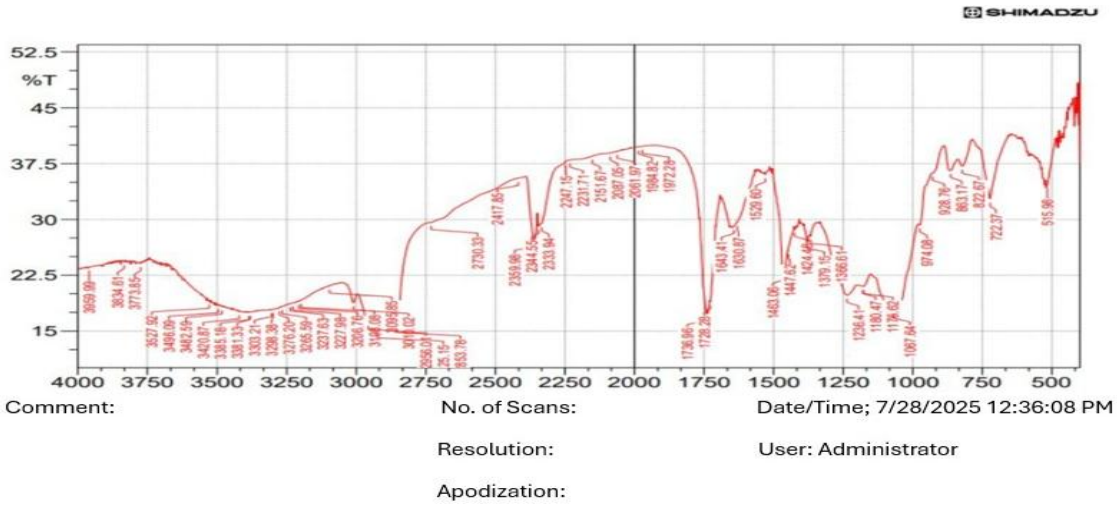

Figure 5: FT-IR of EGCG Sample for Optimized formulation

Table 7: Characteristic Peaks and frequency of Optimized formulation

S. No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	**OH stretching**	**4000-3500**	**3834.61**
2	OH Bending	3500-2750	3227.98
3	C-H stretching	1750-1250	1463.06
4	C-N stretching	1250-1000	1180.47

Discussion: FTIR spectra of pure extract showed prominent peaks corresponding to –OH, C–H, and C–N stretching vibrations, confirming the presence of phenolic and aromatic compounds. The optimized formulation retained these characteristic peaks without significant shifting or disappearance, demonstrating no chemical interaction between the extract and excipients. This confirms excipient compatibility for phytosomal gel formulation.

4.5. EVALUATIONS OF PHYTOSOMES:

a)Determination of Vesicle Morphology and Size

The morphological characteristics of formulated phytosomes were carried by using Scanning Electron Microscopy (SEM). A small drop of Phytosomal suspension was placed between two rivets fixed on a gold-plated copper sample holder. The whole system was slushed under vacuum in liquid nitrogen. The sample was heated to -85^{0}C for 30 min to sublime the surface moisture. Finally the sample was coated with gold and allowed the SEM to capture the images at a temperature of - 120^{0}c and a voltage of 5kV.

SCANNING ELECTRON MICRSCOPY[SEM]

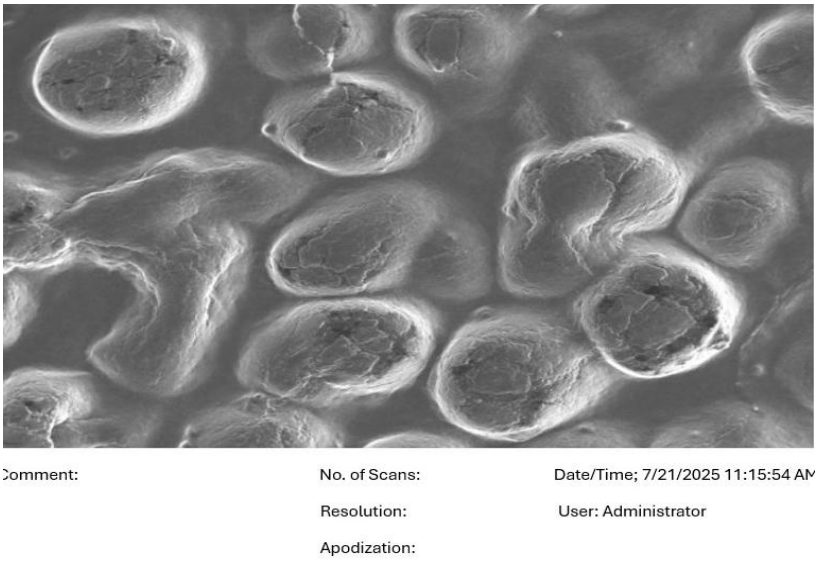

Figure 6: SEM analysis of phytosomes.

Discussion: SEM analysis demonstrated spherical vesicles with smooth morphology. The particle size analysis revealed vesicles in the range of 244–295 nm, which is optimal for dermal delivery and ensures uniform drug distribution. Among the formulations, F8 showed the smallest particle size (244 nm), which is expected to favor better permeation and stability.

b) Entrapment Efficiency of phytosomes :

Table 8: Drug entrapment efficiency

F.NO	F1	F2	F3	F4	F5	F6	F7	F8
Drug entrapment efficiency	78.96	77.50	80.21	81.36	79.82	76.88	83.60	**85.26**

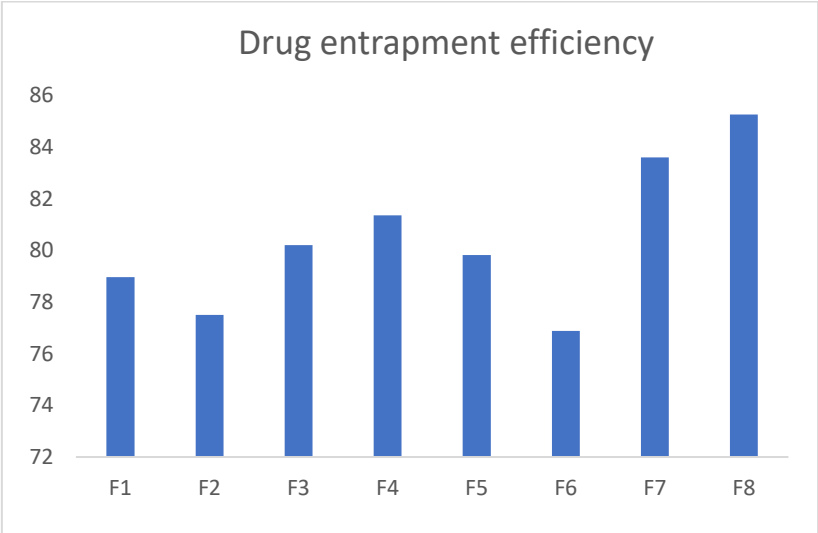

Figure 7: Drug entrapment efficiency of all formulation

c) Zeta potential

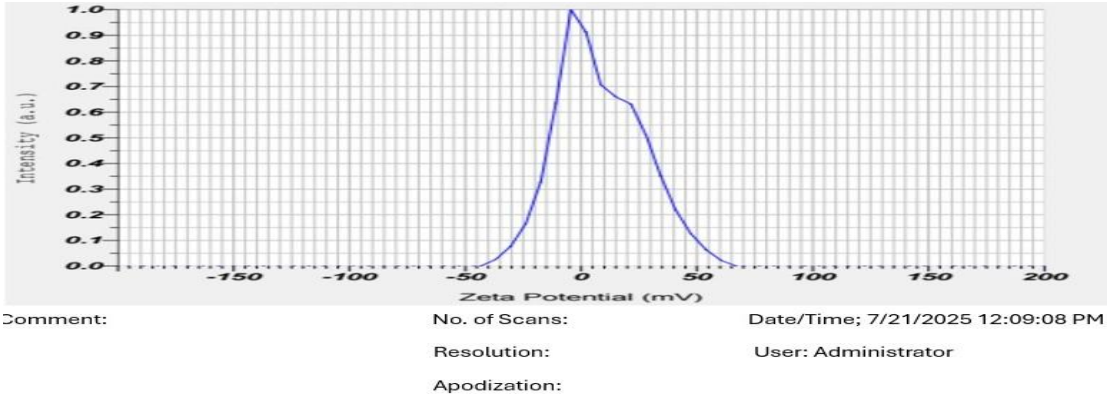

Figure 8: Zeta potential of Phytosomes

Discussion: The zeta potential values ranged between –18 to –29 mV, confirming moderate stability of phytosomal dispersions due to sufficient electrostatic repulsion. F3 (–29 mV) and F8 (–25 mV) showed the most stable vesicles, reducing the chances of aggregation during storage.

Table 9: Evaluation Studies of particle size and Zeta potential Pytosomes

F.NO	F1	F2	F3	F4	F5	F6	F7	F8
Particle size [nm]	259	262	278	295	279	253	260	**244**
Zeta potential	-20	-23	**-29**	-25	-18	-23	-20	-25

d) Particle Size Analysis

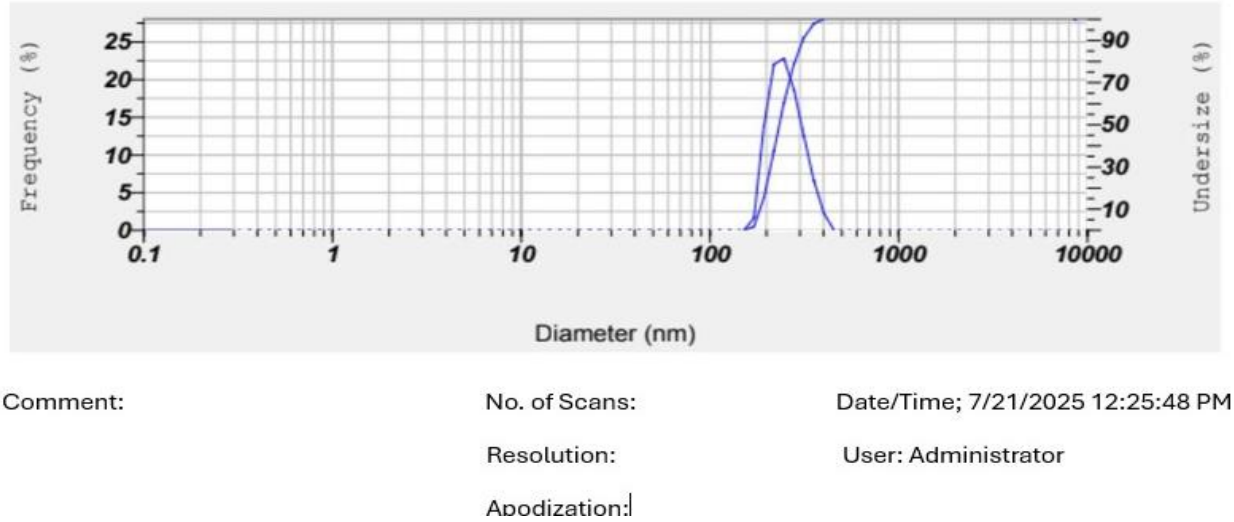

Figure 9: Particle size Analysis of Phytosomes

e) Drug loading of phytosomes

Table 10: Drug loading efficiency

F.NO	F1	F2	F3	F4	F5	F6	F7	F8
Drug entrapment efficiency	66.98	71.25	69.37	73.50	69.35	70.15	74.53	**79.80**

4.6. In vitro drug release studies of Phytosomes.

Table 11: *in-vitro* drug release studies of phytsomes

Time (hrs.)	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
1	16.36	15.60	14.50	14.36	15.91	13.65	15.16	14.93
2	27.15	25.36	24.53	22.39	23.67	25.19	26.37	26.15
3	35.69	38.43	40.16	40.10	42.37	43.67	45.37	42.13
4	53.25	54.50	55.36	51.37	53.69	55.95	52.10	55.50
6	67.56	67.53	66.37	65.69	67.42	68.92	67.89	66.97
8	74.91	72.39	70.10	72.15	73.10	75.38	74.69	73.65
10	82.25	80.15	83.19	80.22	82.12	83.25	85.16	81.25
12	93.50	94.59	91.25	94.53	94.57	95.67	92.35	96.38

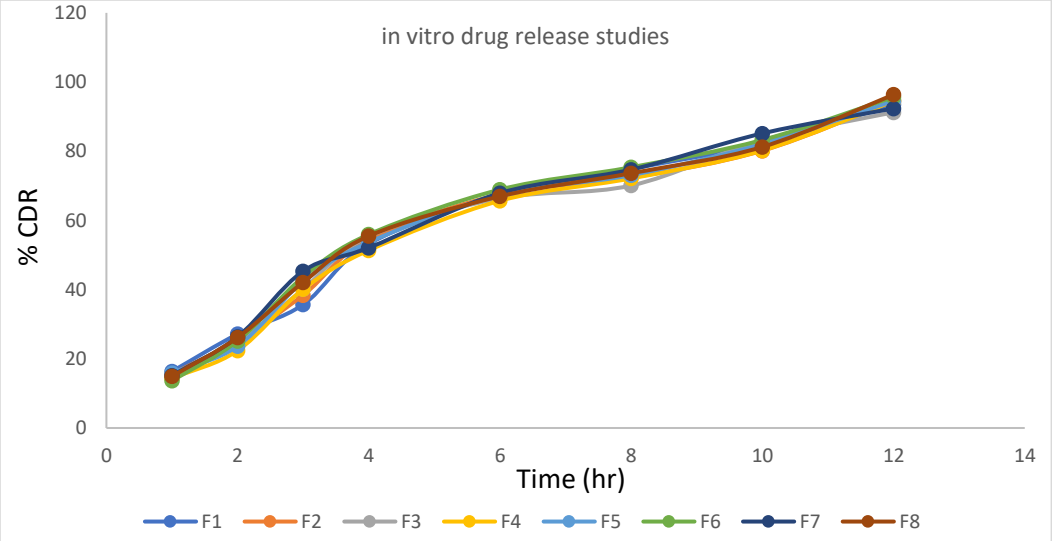

Figure 10: *In vitro* drug release studies of Phytosome

4.7. PHYTOSOMAL GEL EVALUATION PARAMETERS:

a) Physical evaluation

The prepared phytosomal gel of Camellia sinensis exhibited a green-to-brownish colour and a homogeneous appearance.

b) Measurement of pH and Viscosity:

Table 12: PH and Viscosity values of formulations

F.NO	F1	F2	F3
pH	6.5	**7.4**	7.2
VISCOSITY	22,184	21,398	**23,146**

c) Spreadability :

Table 13: Spread ability values of formulations

F.NO	F1	F2	F3
Spread ability (g.cm/sec)	5.86	6.13	**6.84**

d) Drug content:

Table 14: Drug content values of all formulations

F.NO	F1	F2	F3
Drug content	68.12	**73.35**	70.22

4.8. In vitro release study:

Phosphate buffer pH 6.8 was used as medium for the release studies and good linearity was observed in the plotted standard graph with a correlation coefficient of 0.998. The drug release profiles of Phytosomal gel containing different ratios of synthetic polymer. It was cleared from the release profiles of formulations, that the drug release was governed by polymer nature and content.

Table15: *In vitro* drug release profiles of Phytosomal gel (F1-F3)

Time (hr)	F1	F2	F3
0	0	0	0
1	20.12	20.10	15.58
2	29.82	28.15	25.17
3	36.75	37.48	38.10
4	45.19	53.69	50.12
6	67.52	67.82	68.95
8	77.19	79.52	79.81
10	85.69	89.35	83.69
12	97.82	98.88	96.37

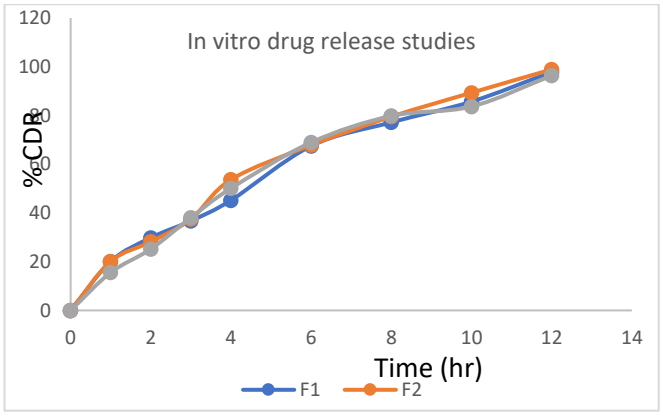

Figure 11: *In vitro* drug release studies of F1-F3 formulations

Kinetic modelling of drug release

All the 3 formulations of the prepared phytosomal gel of Camellia Sinensis Extract were subjected to in vitro release studies these studies were carried out using a Franz diffusion apparatus.

a). Zero-order kinetics

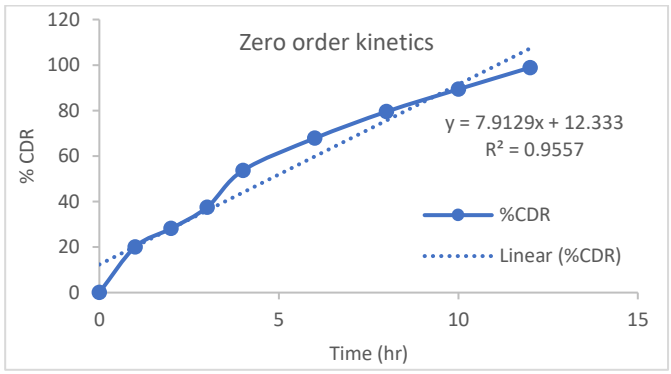

Figure 12: Zero order kinetics of optimized formulation

b).First order kinetics

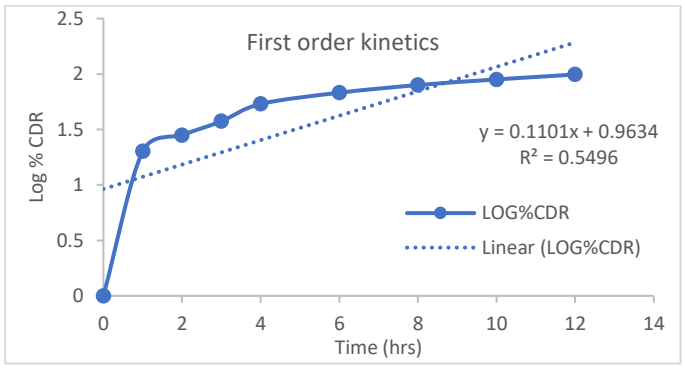

Figure 13: First order kinetics of optimized formulation

c). Higuchi model

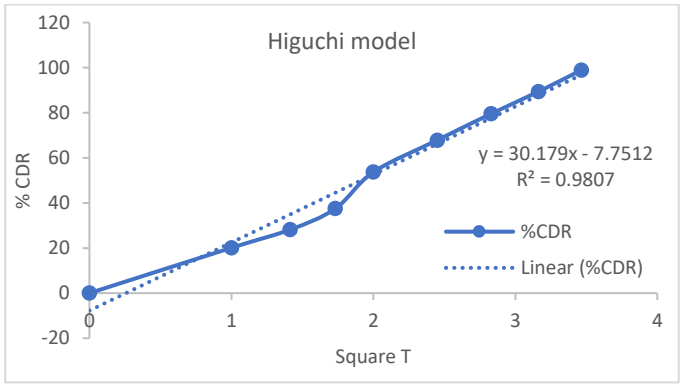

Figure 14: Higuchi model of optimized formulation

d). Korsmeyer-peppas

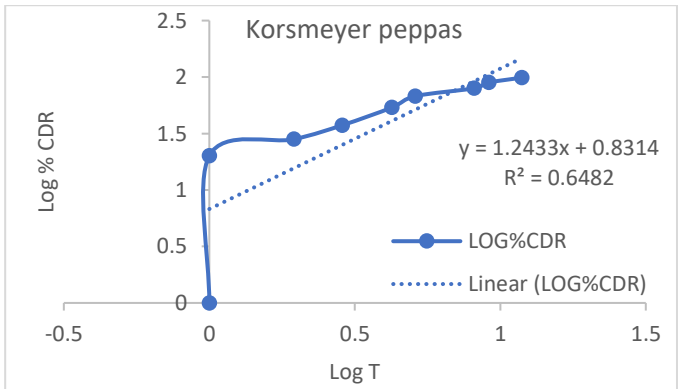

Figure 15: Korsmeyer-peppas model

The kinetic data obtained for formulation F2 were analyzed using various mathematical models to determine the drug release mechanism. The regression coefficient (R^2) values were found to be higher for the first-order release kinetics, indicating that the optimized formulation of *Camellia sinensis* extract follows the Higuchi model release mechanism.

4.9. Stability Studies:

Table 16: Stability studies of optimized formulations at 25^{0}C/60%RH % Release for 45 days

SI.NO	Parameters	Initial	30th Day	45th Day
1.	Homogeneity	Good	Good	Good
2.	Drug Content (%)	91.71	91.67	91.64
3.	pH	6	6	6
4.	Spreadability	4.5	4.5	4.4
5.	Viscosity	9641	9638	9630
6.	% Cumulative Release	98.85	98.80	97.71

DISCUSSION

Organoleptic Evaluation

Camellia sinensis polyphenols was evaluated for its physicochemical characteristics. The extract appeared as a fine powder, bitter in taste, with a characteristic herbal odour and a green to brownish color. These observations are consistent with literature reports, confirming the authenticity and quality of the extract.

Determination of Melting Point

The melting point of green tea polyphenols was determined to be 238°C, which falls within the reference range of 235°C, indicating the purity of the extract and absence of degradation or impurity contamination.

Solubility Studies

Camellia sinensis polyphenols was found to be partially soluble in water, with improved solubility in warm water and alcohols (ethanol, methanol).

UV Spectrophotometric Analysis and Standard Curve λmax of EGCG

The λmax of EGCG was determined to be 274 nm in phosphate buffer (pH 7.4), consistent with reported values for catechins and polyphenols. A calibration curve was plotted for concentrations ranging from 10–50 µg/ml, showing a linear relationship with an R^2 value of 0.997, thus following Beer–Lambert's law.

FTIR Studies (Drug–Excipient Compatibility)

The optimised formulation showed similar peaks at 3834 cm^{-1}, 3227 cm^{-1}, 1463 cm^{-1}, and 1180 cm^{-1} without major shifts, indicating no chemical interaction between the extract and excipients.

Vesicle Morphology and Particle Size (SEM Analysis)

SEM analysis revealed spherical vesicles with smooth morphology. The particle size of the phytosomes ranged between 244–295 nm, with the F8 formulation showing the smallest vesicles (244 nm).

Zeta Potential

The zeta potential values of phytosomal formulations ranged between -18 to -29 mV. The formulations F3 (–29 mV) and F8 (–25 mV) showed the highest negative potential, indicating moderate electrostatic stability and reduced aggregation tendency during storage.

Entrapment Efficiency

The entrapment efficiency of the formulations varied between 76.88% and 85.26%. The F8 formulation demonstrated the highest entrapment (85.26%), indicating effective encapsulation of the active constituents within the phytosomal matrix.

Drug Loading Efficiency

Drug loading efficiency ranged from 66.98% to 79.80%, with F8 showing the highest loading (79.80%).

In-vitro Drug Release Studies

The *in-vitro* release profile of the phytosomal formulations was evaluated over 12 hours. The results showed a sustained release pattern, with cumulative drug release ranging from 91% to 96% at the 12th hour. The optimised formulation (F8) exhibited a controlled and prolonged release (≈93%), ensuring continuous delivery of the active constituents.

The prepared gels had a pH in the range of 6.5–7.4, which is within the acceptable dermal application range, ensuring minimal skin irritation. Viscosity ranged between (21,398–23,146 cP), providing optimal consistency for easy application and patient compliance.

Physicochemical Evaluation of gel: The pH of the formulations ranged from 6.5 to 7.4, which is near the physiological pH of the skin, indicating that the gels are unlikely to cause irritation upon topical application. Viscosity values (21,398–23,146 cP) suggested that the gels had an adequate consistency, which ensures that they remain on the skin surface after application while allowing ease of spread. The spreadability values (5.86–6.84 g.cm/sec) indicated that the gels could be applied

uniformly over the skin, which is critical for proper dosing and efficacy.

The drug content of the gels ranged from 68.12% to 73.35%, indicating uniform distribution of Camellia sinensis polyphenols within the gel matrix. The slight variation in drug content could be attributed to differences in polymer concentration and the interaction between the polymer and the phytosomal complex during gel formation.

***In Vitro* Drug Release:**

The *in vitro* release studies were conducted using phosphate buffer (pH 6.8). All formulations exhibited sustained release over 12 hours, with cumulative release values ranging from 96.37% (F3) to 98.88% (F2). The release profiles demonstrated that drug release was influenced by both the nature and concentration of the polymer. F2 exhibited the highest release, possibly due to a lower polymer concentration or a polymer type that allowed faster diffusion, whereas F3 showed a slightly slower but controlled release, indicating a more sustained effect.

Drug Release Kinetics:

Formulation F2, identified as the optimised formulation, was subjected to kinetic modelling. The regression analysis revealed that the release followed the Higuchi model (r^2 = 0.980), suggesting that the drug release is primarily governed by diffusion through the polymer matrix. Zero-order kinetics (r^2 = 0.955) also indicated that the drug was released in a relatively consistent manner over time, while Korsmeyer-Peppas analysis (r^2 = 0.648) suggested a combination of diffusion and polymer relaxation mechanisms. These findings demonstrate that the optimised gel provides controlled drug release, which is desirable for sustained therapeutic effects.

Stability Studies:

The optimised gel (F2) was evaluated under stability conditions (25°C/60% RH) for 45 days. The drug release slightly decreased from 98.85% to 97.71%, indicating minor degradation but still remaining within acceptable limits (>85%). This confirms that the formulation maintains its integrity and efficacy under normal storage conditions, suggesting good shelf-life potential

CONCLUSION

The study successfully formulated and evaluated a phytosomal gel incorporating *Camellia sinensis* polyphenols to overcome the limitations associated with their poor solubility and bioavailability. Phosphatidylcholine-based phytosomes were efficiently developed using the solvent - evaporation technique, achieving favourable particle size, zeta potential, and high entrapment efficiency. The optimised formulation (F2) exhibited excellent physicochemical stability, suitable rheological characteristics, and uniform drug distribution. *In vitro* diffusion studies confirmed a controlled and prolonged release following Higuchi diffusion kinetics, indicating sustained delivery of EGCG from the gel matrix. Stability results demonstrated that the gel retained its homogeneity, pH, viscosity, and release characteristics with minimal degradation over 45 days of storage. Overall, the formulated phytosomal gel of *Camellia sinensis* represents a stable, effective, and patient-friendly system that enhances the therapeutic efficacy and bioavailability of natural polyphenols.

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Syed Abdul Azeez: Supervision and review-editing.

Dr. Abdul Mannan**:** Data curation and investigation.

All authors have reviewed and approved the final manuscript.

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REFERENCES

1. Andrews GP, Laverty TP, Jones DS. Mucoadhesive polymeric platforms for controlled drug delivery. Eur J Pharm Biopharm. 2009;71(3):505-18. https://doi.org/10.1016/j.ejpb.2008.09.028 PMid:18984051

2. Bombardelli E. Phytosome: New cosmetic delivery system. Boll Chim Farm. 2005;144(12):431-8.

3. Khan N, Mukhtar H. Tea polyphenols in promotion of human health. Nutrients. 2018;11(1):39. https://doi.org/10.3390/nu11010039 PMid:30585192 PMCid:PMC6356332

4. Maiti K, Mukherjee K, Gantait A, Saha BP, Mukherjee PK. Curcumin-phospholipid complex: Preparation, therapeutic evaluation and pharmacokinetic study in rats. Int J Pharm. 2006;330(1-2):155-63. https://doi.org/10.1016/j.ijpharm.2006.09.025 PMid:17112692

5. Patel VF, Liu F, Brown MB. Advances in oral transmucosal drug delivery. J Control Release. 2011;153(2):106-16. https://doi.org/10.1016/j.jconrel.2011.01.027 PMid:21300115

6. Sabu MC, Smitha P. Green tea polyphenols: Chemistry, bioavailability, and pharmacological effects. J Pharm Bioallied Sci. 2020;12(2):89-97.

7. Yanyu X, Yunmei S, Zhipeng C, Qineng P. Preparation of silybin-phospholipid complex and study on its pharmacokinetics in rats. Int J Pharm. 2006;307(1):77-82. https://doi.org/10.1016/j.ijpharm.2005.10.001 PMid:16300915

8. Pagano C, Giovagnoli S, Perioli L, Tiralti MC, Ricci M. Development and characterization of mucoadhesive-thermoresponsive gels for treatment of oral mucosa diseases. Eur J Pharm Sci. 2020;142:105125. https://doi.org/10.1016/j.ejps.2019.105125 PMid:31682975

9. Mane VB, Killedar SG, More HN. Formulation and evaluation of phytosomal gel of Camellia sinensis for treatment of skin ageing. Res J Pharm Technol. 2022;15(1):165-70.

10. Mane VB, Killedar SG, More HN. Evaluation of acute oral toxicity of Camellia sinensis phytosome formulation in female Wistar rats. Int J Health Sci. 2022;6(S8):912-22. https://doi.org/10.53730/ijhs.v6nS8.11579

11. Wahyuni IS, Sufiawati I, Shafuria A, Nittayananta W, Levita J. Formulation and evaluation of mucoadhesive oral care gel containing Kaempferia galanga extract. Pharmaceutics. 2024;16(3):421. https://doi.org/10.3390/pharmaceutics16030421 PMid:38543315 PMCid:PMC10975056

12. Singh BN, Shankar S, Srivastava RK. Green tea catechin epigallocatechin-3-gallate: Mechanisms, perspectives, and clinical applications. Biochem Pharmacol. 2011;82(12):1807-21. https://doi.org/10.1016/j.bcp.2011.07.093 PMid:21827739 PMCid:PMC4082721

13. Narayana Charyulu R, Parvathy Devi P, Jobin Jose, Veena Shetty A. Formulation and evaluation of mucoadhesive oral gel containing miconazole nitrate for oral candidiasis. Res J Pharm Technol. 2013;6(11):1251-7.

14. Danaei M, Dehghankhold M, Ataei S, Davarani FH, Javanmard R, Dokhani A, et al. Impact of particle size and polydispersity index on clinical applications of lipidic nanocarrier systems. Pharmaceutics. 2018;10(2):57. https://doi.org/10.3390/pharmaceutics10020057 PMid:29783687 PMCid:PMC6027495