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Management of Psoriasis by *Psoralea corylifolia* laden nanoparticulate gel

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ABSTRACT

The aim of the current research is to create and assess an in-situ gel drug delivery system using nanoparticulates, i.e., an in-situ gel containing ethanol extract from P. corylifolia, for the management and treatment of psoriasis. The physicochemical and phytochemical characteristics of P. corylifolia seeds were investigated. Based on initial phytochemical screening of the seeds, a high concentration of flavonoids, tannins, steroids, glycosides, and saponins is present in the ethanolic extract, which might play a major role in the anti-psoriatic action. Preformulation investigations were carried out in order to create an in-situ gel comprising a nanoparticulate of P. corylifolia ethanol extract. A number of parameters, including vesicle size and shape and entrapment effectiveness, were evaluated and optimized for the generated nanoparticle formulation. By using scanning electron microscopy to determine the form of the vesicle, it was found that the nanoparticles were spherical in shape. The F8 batch of produced nanoparticles had the smallest particle size, with vesicles ranging in size from 185 to 243 nm. The P. corylifolia loaded nanoparticles that were created demonstrated an encapsulation efficiency ranging from 19.05±1.0 to 73.06±0.1. Out of the several batches, batch F8 had the highest encapsulation efficiency. The percentage of drug release was found to be between 82.75% and 96.33% in the in-vitro dissolution investigation carried out on produced nanoparticles. F8 batch demonstrated the highest release. In situ gel formulation was prepared by batch (F8). The prepared in situ gel's pH was determined to be between 6.68 and 7.4. Since the pH values of all the created formulations fell within the region of neutral pH, it is possible to use them without risking irritation. The percentage of drug loading varied from 85.57 to 95.39%. According to the in vitro drug release results for Nanoparticulate in situ gel, batch B3 had the maximum release, with a considerable rise in release observed up to 12 hours, ranging from 71.84 to 91.89%. According to the stability investigations, the chosen formulation batch (B3) of nanoparticulate in situ gel remained stable for three months at room temperature (25 ± 2 º C) and 75% ± 5% relative humidity. This study's findings showed that the use of P. corylifolia ethanol extract with nanoparticle in-situ gel was an excellent method for managing psoriasis and enhancing the delivery of topical medications.

Keywords: *Psoriasis, Psoralea corylifolia, nanoparticulate gel, topical, medication*

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1. Introduction

Psoriasis is a long-term inflammatory skin condition that causes thick, scaly patches on the skin's surface due to fast multiplication of skin cells. Millions of people worldwide suffer from this autoimmune disease, which is extremely difficult to control since it relapses and may have negative side effects from prolonged therapy. Conventional treatments, such as systemic immunomodulators, topical corticosteroids, and vitamin D analogs, frequently offer momentary relief but have side effects that make long-term usage of them difficult.[1-2]

Traditionally employed in Chinese and Ayurvedic medicine, *Psoralea corylifolia*, sometimes referred to as Babchi, is a medicinal plant. Psoralen is a bioactive substance found in *Psoralea corylifolia* seeds that has been shown to have photochemotherapeutic effects. The treatment known as PUVA therapy, which combines psoralen with ultraviolet A light, has shown promise in the management of a number of skin conditions, including psoriasis. The capacity of *Psoralea corylifolia* to regulate immune responses, reduce inflammation, and encourage skin healing makes it a promising treatment for psoriasis.[3-5]

The application of nanotechnology in medication delivery has created new opportunities to raise the bioactive chemicals' therapeutic effectiveness. By increasing phytochemical solubility, stability, and bioavailability, nanoparticulate systems allow for targeted and regulated release. *Psoralea corylifolia* extracts' limited solubility and inadequate skin penetration are two drawbacks of conventional formulations that may be solved by encasing the extracts in nanoparticle form. A targeted and prolonged release of the active ingredients can be achieved with a nanoparticulate gel formulation, improving therapeutic results and reducing systemic exposure and adverse effects.[6-8]

The stratum corneum, the skin's outermost layer, may be easily penetrated by nanoparticles because of their tiny size and great surface area. This allows the active substances to be delivered straight to the deeper layers of the skin, where they can exercise their therapeutic effects. *Psoralea corylifolia* has anti-inflammatory and immunomodulatory properties that can be strengthened by this tailored administration, making it a more potent and patient-friendly psoriasis therapy choice.[9-10]

Psoralea corylifolia extracts are first added to a nanoparticle matrix and then dispersed in an appropriate gel basis to create a *Psoralea corylifolia*-laden nanoparticulate gel. In addition to stabilizing the nanoparticles, the gel matrix makes the skin application smooth and non-greasy, which increases patient compliance. To increase the therapeutic efficacy and enrich the whole treatment experience, additional skin-beneficial components including moisturizers and calming agents can be added to the gel composition.[11-12]

In summary, the application of *Psoralea corylifolia*-loaded nanoparticulate gel offers a novel method of treating psoriasis. This formulation offers a focused, effective, and maybe safer treatment approach by combining the traditional medicinal characteristics of *Psoralea corylifolia* with the cutting-edge drug delivery capabilities of nanoparticles. This innovative formulation may provide substantial advantages in the management of psoriasis, enhancement of patient outcomes, and improvement of quality of life as research in this field advances.[13-14]

2. Materials and Methods

2.1 Materials

All chemical and reagent used in the study, including solvents and other materials for the preparation of formulation were obtained from different reputed companies.

2.2 Adopted Method

2.2.1 Preformulation Studies

2.2.1.1 Collection of the plant material

In February, the seed of *Psoralea corylifolia* seeds bought from market. The botanist then recognized the plant using its colloquial nomenclature and compared it to the department's herbarium. For later usage, the collected materials were ground into a powder.

2.2.1.2 Processing of Crude Drug

In a soxhlet mechanical assembly, the dried powder of seeds was gradually extracted using separate solutions of petroleum ether, chloroform, ethanol, and refined water. Refining removed the solvents and removed the remaining remnants of the dissolvable under lower tension.

2.2.1.3 Soxhlet Extraction

By using solvents to separate the ingredients from raw medicine, extraction is the most popular method of obtaining the components. The unrefined medication's various phytoconstituents were extracted from the powdered substance using a suitable solvent or mixture of solvents.[15] The soxhlation, which is listed in the following table, was used to do the extraction. 6.1. 400 grams of seed powder were utilized to do soxhlation extraction at a certain temperature and duration using various solvents, as shown in the accompanying table. A percentage yield of each extraction was calculated by measuring the dried residues.

Table 1. Successive solvent extraction using different solvent with time duration and temperature

S. No.	Solvents	Quantity(ml).	Duration	Temperature (℃)
1.	Petroleum Ether	500ml	3hrs	60
2.	Chloroform	500ml	3hrs	60
3.	Methanol	500ml	6hrs	70
4.	Ethanol	500ml	5hrs	70
5.	Water	500ml	5hrs	100

2.2.1.4 Extract Characterization

Colour, odour and physical appearance were examined for extracts.

2.2.1.4.1 Phytochemical Screening

The ethanolic extract were analyzed by the following procedures.[16]

A Test for alkaloids: Dragendorff's test

To 1 ml of the concentrate, add 1 ml of Dragendorff's reagent (Potassium Bismuth iodide arrangement). An orange-red encourage shows the presence of alkaloids.

B Test for saponins

Measure out a little quantity of each watery and alcoholic concentration separately, add 20ml of purified water, and shake in a graduated chamber for fifteen minutes. A layer of foam 1 cm thick indicates the presence of saponins.

C Test for Glycosides: Legal test

To make the concentrate soluble, break it up with pyridine and add sodium nitroprusside solution. The existence of glycosides is indicated by the arrangement of the pink red to red coloring.

D Test for carbohydrates: Molisch's test
Concentrated sulfuric acid should be added through the test tube's side to 2ml of concentrate and 1ml of α-napthol arrangement. The presence of carbohydrates is indicated by a purple or fiery violet tone where the two fluids converge.

E Test for triterpenoids: Noller's test
Break up a few grains or tin metal in a 2ml thionyl chloride solution. The presence of triterpenoids is then shown by the arrangement of pink tones after 1ml of the concentrate has been added to the test tube and heated.

F Test for flavonoids: Shinoda's test
The significant cherry red color of the alcoholic powder concentration treated with magnesium foil and HCl indicates the presence of flavonones, whereas the orange red color indicates the presence of flavonols.

G Test for steroids: Libermann-Burchard test
1gm of the test material was broken up in a few drops of chloroform, followed by the addition of 3ml of acidic anhydride, 3ml of frosty acidic corrosive, and some warming and cooling under the faucet. Concentrated sulfuric corrosive drops were then placed at the test tube's edges. The presence of steroids is indicated by the appearance of faint blue-green shading.

H Test for tannins
Take the little amount of test arrangement and blended in with essential lead acetic acid derivation arrangement. Development of white accelerates demonstrates the presence of tannins.

2.2.1.4.2 Determination of λ_{max}

Using UV-1800, Shimadzu, the UV spectrum of psoralen was obtained spectrophotometrically. Psoralen (around 10 mg) was precisely weighed, dissolved in enough ethanol, and the final volume was brought to 100 ml. After diluting the stock solution to a concentration of 1000 µg/ml, 2.5 ml of an aliquot was taken out, and ethanol was added to the volume to make it to 25 ml, which resulted in a concentration of 100 µg/ml.[17] To determine the value of λmax, the resulting solution was scanned from 200 to 600 nm, and the spectra was recorded.

2.2.1.4.3 Preparation of Standard Curve of Psoralen in Ethanol.

1ml of psoralen was dissolved in 10 mL of ethanol to create the stock psoralen solution. Serial dilutions on 10 µg/ml, 20 µg/ml, 30 µg/ml, 40 µg/ml, and 50 µg/ml were made from this stock solution. At 247 nm, the UV absorbance was measured, and a calibration curve was created.

2.2.1.4.4 Determination of total Psoralen content

The aluminium chloride colorimetric method was used to determine the sample's total psoralen concentration. Psoralen was used to create the standard calibration curve for the measurement of total psoralen. Separately, 0.6 mL of 2 percent aluminium chloride and 0.6 mL of diluted standard psoralen solutions or extracts were mixed. The mixture was mixed and then allowed to sit at room temperature for sixty minutes. The absorbance of the reaction solutions was measured at 247 nm wavelength using a UV-Vis spectrophotometer (Shimadzu UV 1800 Spectrophotometer) against a blank.[18] The total psoralen content in the test samples was ascertained using the calibration plot.

2.2.1.5 Compatibility Studies

2.2.1.5.1 FTIR Spectroscopy

IR Spectroscopy is often used as a tool for the determination of identity of pharmaceutical compounds. FT-IR spectroscopy helps in confirming the formation of the complex between the polymer and drug by comparing it with the individual spectrum of polymer and drug with the spectrum of polymer-drug complex.[19] A specific amount of standard drug was weighed and the sample was placed directly on IR Spectrophotometer (Bruker 1800) and the spectrum was taken. To this standard drug, formulated blend of Nanoparticulate in-situ gel was compared for compatibility studies.

2.2.2 Formulation and Development

2.2.2.1 Preparation of Nanoparticle by Solvent Injection Technique

Using the solvent injection technique, solid lipid nanoparticles were produced The extract of *P.corylifolia* were dissolved in 15 ml of distilled water along with the help of sonicator. A specific quantity of GMS and Psoralen (15 mg) were dissolved in a specific volume of IPA (81°C to 83°C boiling point) and heated to the melting point of GMS, 52°C, before being added. In IPA, GMS dissolves quite easily; however, it requires a bit of heat to do so. A 10 ml aqueous phase with poloxamer 407 was added to the dispersion and agitated at 400 rpm for 30 minutes on a magnetic stirrer. 0.1 N HCl (4 ml) was added to the dispersion to lower the pH to roughly 1.5 to 2 to trigger the aggregation of SLNs for easier separation. The dispersion was then centrifuged at 10,000 rpm for 30 minutes at 10°C in a Remi cooling centrifuge & the aggregates were purified by dialysis bag and resuspended in 10 ml distilled water containing 4 percent poloxamer 407 (by weight) as stabilizing agent along with the stirring at 1,000 rpm for 10 minutes. Table 6.2 shows the

formulation design of *P.corylifolia* extract-loaded nanoparticle. Formulations of SLNs (F1 to F8) were prepare as stated to the using different ratios.

Table 2. Different nanoparticle formulations prepared for ethanolic extract of *P.corylifolia* encapsulation

Batch	Polaxmer 407	IPA (ml)	GMS (mg)	Amt. of Extract (ml)
F1	0.8%	1	100	8.5
F2	0.8%	2	100	8.5
F3	2%	1	100	8.5
F4	2%	2	100	8.5
F5	0.8%	1	200	8.5
F6	0.8%	2	200	8.5
F7	2%	1	200	8.5
F8	2%	2	200	8.5

*Equivalent to 25 mg Psoralen

2.2.3 Evaluation of Nanoparticle

2.2.3.1 Organoleptic properties

The prepared nanoparticle was investigated for morphological structure, visual size estimate, etc. using an optical microscope set to 45x magnification.

2.2.3.2 Morphology

The produced nanoparticle was investigated for morphological structure, visual size estimate, etc. using an optical microscope set to 45x magnification.

2.2.3.3 Vesicle size and zeta potential

Zeta potential and vesicle size of nanoparticles was determined by Zeta sizer (Malvern Zetasizer).

2.2.3.4 SEM

A scanning electron microscope was used to measure and take pictures of the formulation's particle size.

2.2.3.5 Entrapment Efficiency

By measuring the amount of free drug in the supernatant after the nanoparticles were centrifuged, the % entrapment efficiency (EE%) was determined. The suspension of nanoparticles was subjected to a 30-minute ultracentrifugation at 11,000 rpm and 4°C. They collected the

supernatant. UV spectrophotometry at 247 nm was used to evaluate the unentrapped drug fixation in supernatant. There was an EE% difference in Lawsone content between formulations and free Lawsone. It was calculated by the following formula:

Drug entrapment efficiency (%) = [Amount of drug entrapped / Total amount of drug added] × 100

2.2.3.6 In vitro drug release of Nanoparticles

The produced solid lipid nanoparticles were subjected to in-vitro release tests using the dialysis bag technique. After cleaning, a dialysis bag was placed in distilled water to soak. The dialysis sac was filled with a predetermined amount of SLNs, and the opening was closed with thread. The dialysis bag was sealed and then placed in a beaker containing 500 mL of pH 7.4 PBS. By keeping the beaker over a magnetic stirrer running at 50 rpm, the temperature was maintained at 37°C ± 0.5°C. Samples were collected at different times. Fresh PBS was used in place of the withdrawn sample to preserve the sink condition throughout the process. Drug content was measured after samples were diluted and measured at 247 nm using a UV-visible spectrophotometer.

2.2.4 Formulation of Nanoparticulate In-situ gel

Nanoparticulate in situ gel was created based on the form and efficacy of drug entrapment. For the in situ gel preparation, the batch of nanoparticles with the best surface shape and entrapment was selected. Using a glass rod to swirl continuously and prevent lump formation, the appropriate amounts of Carbopol 940 and HPMC were sprinkled over the nanoparticle dispersion and left to hydrate. A suitable amount of benzalkolium chloride is added as a preservative, and sodium chloride is added to change the pH.

Table 3. Composition of Nanoparticulate In-situ gel using selected batch (F8) of nanoparticles (Ingredients in %w/v or v/v).

Batch	HPMC	Carbopol 940	EDTA	Benzolkonium chloride	Sodium chloride	Phosphate buffer (ml)	Drug
B1	0.4	0.2	0.1	0.01	0.9	100	8.5 ml
B2	0.4	0.4	0.1	0.01	0.9	100	8.5 ml
B3	0.2	0.2	0.1	0.01	0.9	100	8.5 ml
B4	0.2	0.4	0.1	0.01	0.9	100	8.5 ml

2.2.4.1 Evaluation of Nanoparticulate In-situ gel

The produced nanoparticle in situ gel formulation was assessed for drug content, rheological tests, spreadability test, pH, drug content, and in vitro drug release.

2.2.4.2 Visual Appearance

For clarity, the in situ gel solutions were created and evaluated visually on black and white backdrops in low light.

2.2.4.3 pH

With a few minor adjustments, the digital pH meter was used to measure the gels' pH. First, neutral pH 7.0 was used to calibrate the pH meter. The electrode was fully dried with tissue paper after being properly cleaned with distilled water. After obtaining the precise amount of sample (30 gm gel formulation), the electrode was submerged in it. An average of three readings were obtained (n = 3). The created formulation's pH value of 6.8 is deemed adequate to minimize the possibility of skin irritation upon application.

2.2.4.4 Estimation of Drug Content

By adding a weighed quantity of in situ gel formulation containing 10 mg of psoralen into a 100 mL volumetric flask, the drug content of the in situ gel formulations was determined. The volumetric flask was filled with a 50 mL phosphate buffer solution (pH 6.8) and shaken constantly until the gel was fully dissolved and a clear solution was obtained. The solution was filtered after the final volume was adjusted to 100 ml using phosphate buffer pH 6.8. The amount of medication in the filtrated solution was measured at 247 nm using the UV-Visible spectrophotometer.

2.2.4.5 Spreadability Test

Using a spreadability apparatus made up of two glass slides, one of which was mounted into a wooden board and the other of which was mobile and attached to a threat that passed over a completely carrying weight, the spreadability of the nanoparticulate in-situ gel formulation was assessed. The gel was poured between two glass slides in an amount of around 2 g. The time it took to separate the two slides, measured in seconds, was recorded after the top glass slide was removed horizontally. Better spreadability requires less time to separate the two slides. The spreadability values in Table 3 demonstrated that a decrease in spreadability was invariably correlated with an increase in the concentration of any of the gelling agents. The following formula may be used to calculate spreadability: $S = M \times L/T$, where M is the weight attached to the top slide, L is the length of the glass slides, and T is the amount of time (in seconds) needed to fully separate the slides from one another.

2.2.4.6 In vitro drug release of Nanoparticulate In-situ gel

The release media for the nanoparticulate in situ gel in vitro release assays was phosphate buffer (pH 7.4) at 37°C. 5ml of psoralen-containing nanoparticle in situ gel were carefully weighed before being added to the dialysis membrane. The gel was gently rubbed on the surface of the dialysis membrane to establish contact. Phosphate buffer (1 mL, pH 7.4) was added to the reservoir compartment to wet the gel; the dialysis membrane was then submerged in the buffer, which performed the role of the receiving compartment. The receiving container was put in a 100 rpm magnetic stirrer set at 37°C. A spectrophotometer designed to detect psoralen released from the nanoparticle in situ gel was used to gather 1 mL samples from the receiving compartment on a regular basis. The sample size was 247 nm. Following the removal of each sample, an equivalent volume of phosphate buffer was supplied to the receiving compartment.

2.2.4.7 Stability Studies

The ICH guidelines were followed in the course of the stability investigations. In order to assess the stability of the nanoparticulate in-situ gel, amber-colored vials were kept in a stability chamber for three months under accelerated storage settings (25 ± 2˚C/75% ± 5% relative humidity). The samples were removed and evaluated for key physicochemical characteristics at different intervals, such as pH, color, and in vitro drug release `1on the first day of storage and at the conclusion of the 1, 2, 3 month storage periods.

3. Results and Discussion

3.1 Preformulation Studies

3.1.1 Extract Characterization

3.1.1.1 Organoleptic Properties

The organoleptic properties of different extracts of *Psoralea corylifolia* seeds were observed and were found to be acceptable which is shown in Table 4.

Table 4. Organoleptic properties of the Extract.

Solvent	Colour	Odour	Texture
Petroleum Ether	Light Brown	Pungent	Slightly rough
Chloroform	Dark Brown	Odourless	Slightly rough
Methanol	Dirty Brown	Chemical	Slightly rough

Ethanol	Dark brownish black	Characteristic	Rough

3.1.1.2 Phytochemical Screening

The findings of a qualitative phytochemical study indicated that bioactive components were found in *Psoralea corylifolia* seeds extract. The results of phytochemical screening are summarized in table 5.

Table 5. Phytochemical screening for secondary metabolites

Test	Petroleum ether extract.	Chloroform extract.	Methanolic extract.	Ethanolic extract.	Water extract.
Carbohydrate	-	-	+	+	-
Alkaloids	-	-	+	+	+
Triterpenoids	+	+	+	+	-
Glycosides	-	-	+	+	-
Saponins	-	-	+	+	+
Flavanoids	-	-	+	+	-
Steroids	+	-	-	-	-
Tannins	-	+	-	+	+

3.1.1.3 Determination of λ_{max}

The λ_{max} of 20µg/ml solution of psoralen solution in ethanol was found to be 247nm.

3.1.1.4 Compatibility Studies

3.1.1.4.1 FTIR

By contrasting it with the individual spectra of the excipient and extract and the spectrum of the herbal extract-excipient complex, FT-IR spectroscopy aids in verifying the development of the complex between the excipient and extract.

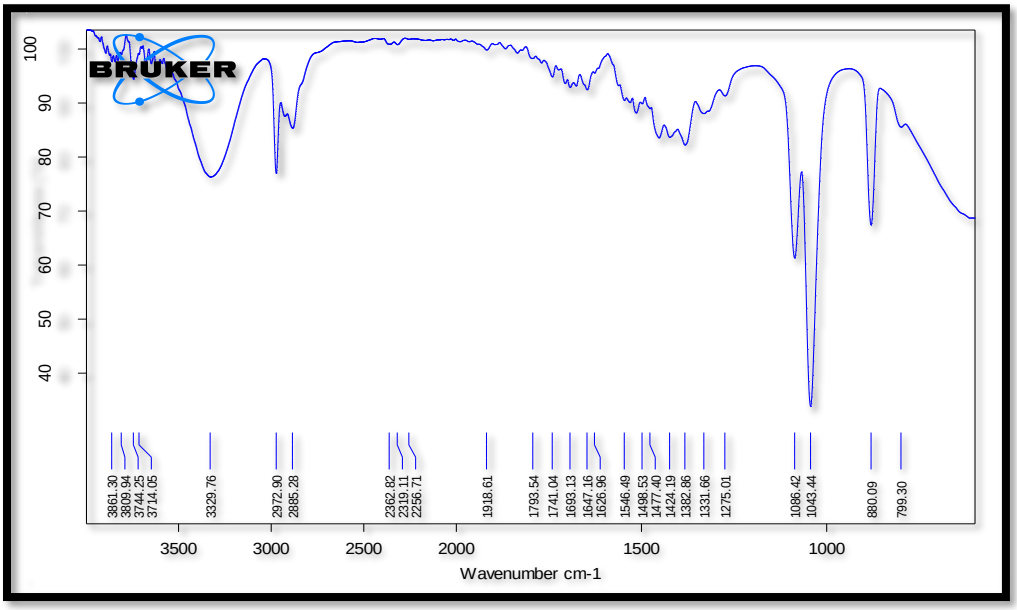

Figure 1. FTIR spectra of standard Psoralen

Table 6. Interpretation of FTIR Spectra for functional group

S. No.	Wavenumber (cm^{-1})	Bond	Functional Group
1.	1746,1719	C=O	Carbonyl group
2.	1043	C-O-C	Ether group
3.	2972,2885	C-H	Aromatic and vinyl hydrocarbon group

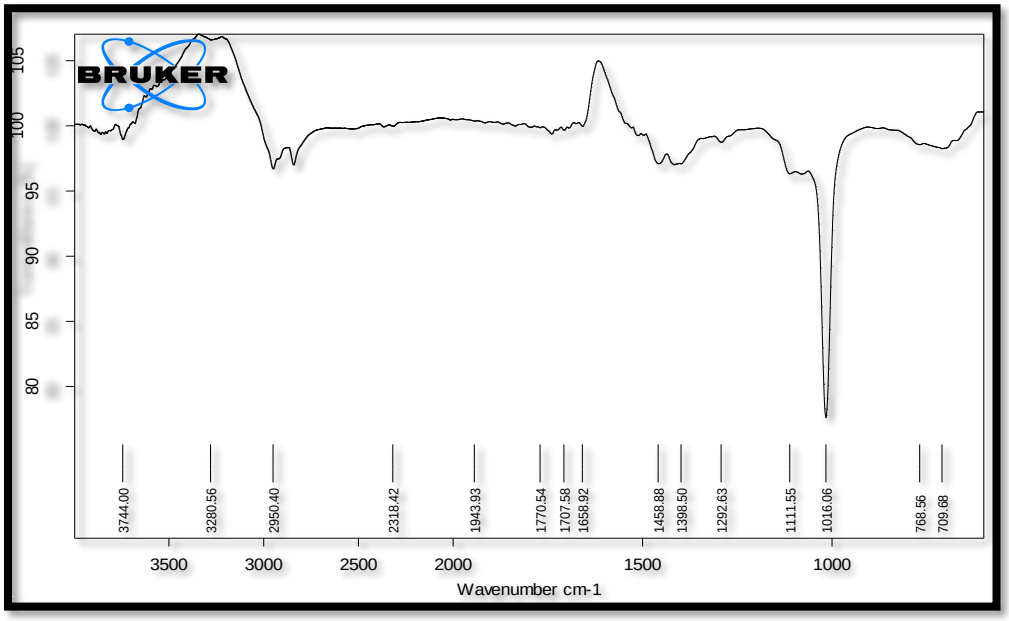

Figure 2. FTIR of formulation blend

The FT-IR spectra of Nanoparticulate in-situ gel formulation blend shows the stretching at 2950 cm^{-1}, 1770 cm^{-1} and 1675 cm^{-1} showing no major shifts in band. There are no indications of an interaction between the extract and excipient combination according to the IR research. This indicates that there was no incompatibility.

3.1.2 Evaluation of Nanoparticle

3.1.2.1 Organoleptic properties of Nanoparticles

After the formulated nanoparticles were examined for organoleptic properties, it was discovered that the suspension was odourless and rather hazy.

3.1.2.2 Microscopic evaluation

Under microscopy, the synthesized and formed psoralen nanoparticle dispersion demonstrated the presence of projected round/spherical shaped vesicles (Figure 3) at a 45x magnification.

Figure 3. Microscopic view of Nanoparticle 45x

3.1.2.3 Vesicle size and Zeta potential

Zeta potential of prepared Nanoparticle batches were ranged between (-19.0) to (-26.0).

Table 7. Vesicle size and Zeta potential of nanoparticles of *Psoralea corylifolia*

S. No.	Formulation batch	Vesicle size (nm)	Zeta potential
1	F1	193	-20.0
2	F2	211	-22.5
3	F3	185	-21.0
4	F4	196	-23.0
5	F5	199	-21.5
6	F6	240	-24.0
7	F7	243	-23.0
8	F8	185	-19.0

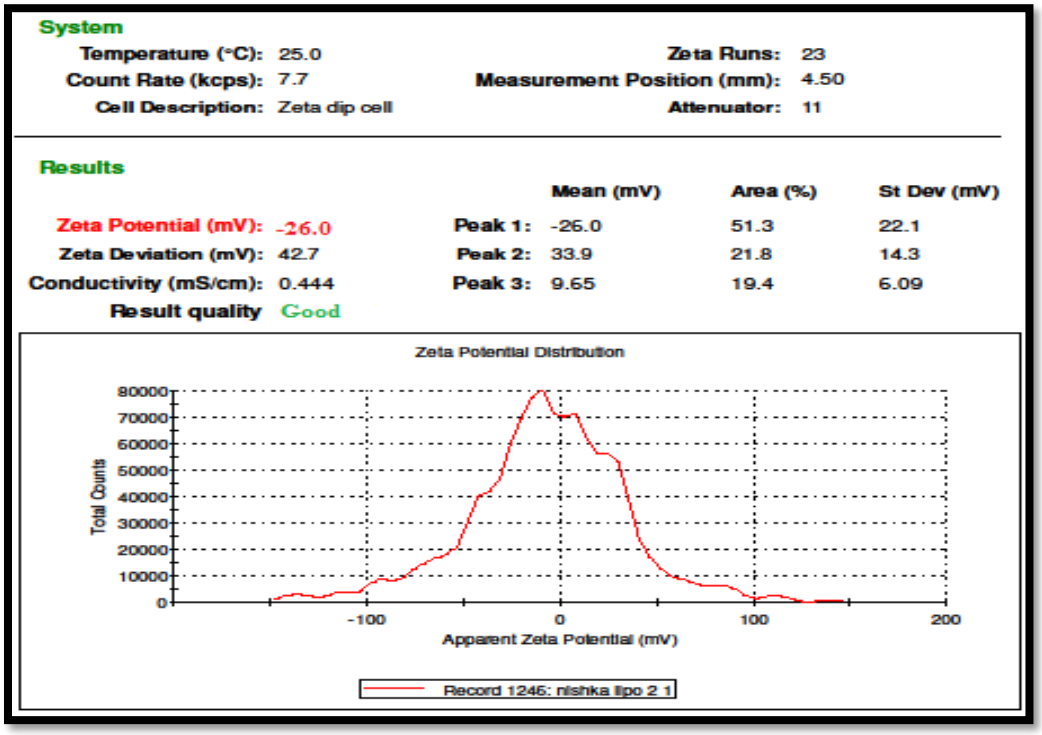

Figure 4. Zeta potential and particle size distribution of solid lipid nanoparticles formulations

3.1.2.3 SEM

The SEM images were seen for the formulated nanoparticle formulations. The results are shown in figure 5.

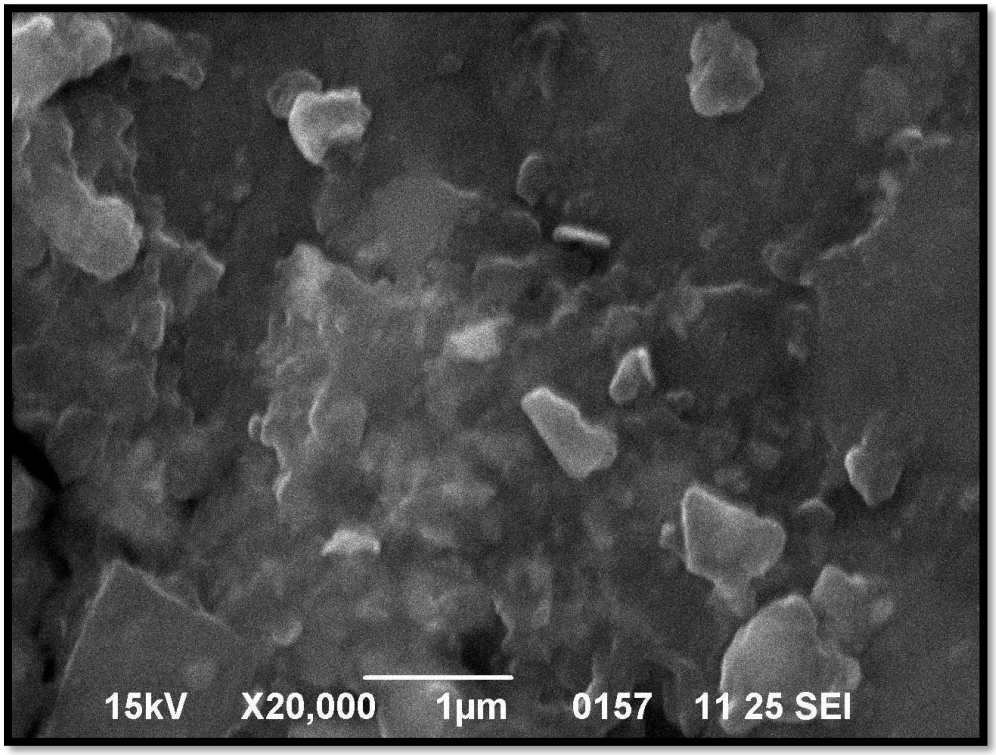

Figure 5. SEM image of Nanoparticle formulation (F8)

3.1.2.4 Encapsulation Efficiency

Next, with a UV spectrophotometer set at 247 nm to measure the quantity of active component in the supernatant, absorbance data were utilized to compute the amount of free drug, so determining the EE%. Table 8 lists the results of the calculation of the EE% for each batch.

Table 8. EE% of different batches of formulated Nanoparticles

Batch	Encapsulation Efficiency (EE%)
F1	19.05±1.0
F2	54.45±1.2
F3	50.42±0.6

F4	32.73±0.8
F5	69.37±1.2
F6	59.82±0.8
F7	46.97±1.0
F8	73.06±0.1

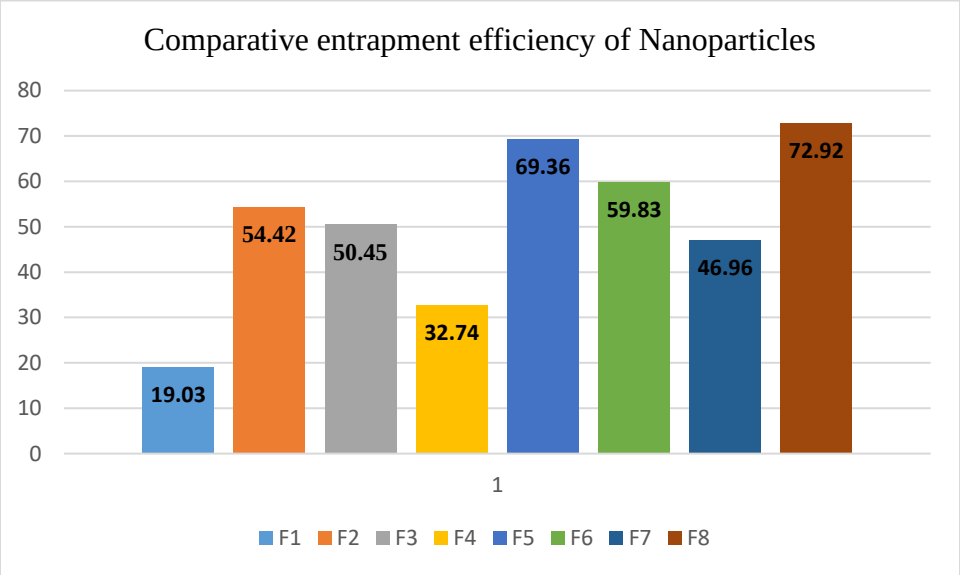

Figure 6. Comparative entrapment efficiency of different batches of nanoparticles

3.1.2.5 In vitro drug release of nanoparticles

P. corylifolia ethanolic extract solid lipid nanoparticle formulation batches' in vitro drug release profiles are shown in Table 9. Up to 12 hours, the findings demonstrated a considerable improvement in the nanoparticle formulation's in vitro drug release. Highest release was demonstrated by formulation F8. Within a day, 96.33% of the medication was taken out of the SLNs.

Table 9. *In vitro* release profile of formulated batches of SLNs (F1-F8)

Time (hrs)	**F0**	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
0	0	0	0	0	0	0	0	0	0
1	5.46	6.03	5.88	7.33	6.66	5.02	7.69	6.84	5.92
2	10.33	11.11	10.59	13.62	12.89	9.69	14.72	12.52	10.22
3	17.69	19.40	16.92	18.9	18.52	18.74	19.46	17.69	17.45
4	24.28	27.83	22.16	25.24	27.31	26.51	28.13	24.18	24.56
5	38.38	37.76	36.75	39.56	38.08	29.49	38.84	31.22	26.27
6	45.59	48.09	42.56	46.97	49.68	38.36	47.86	42.43	39.66
7	65.86	63.08	61.97	67.79	58.34	49.64	68.27	61.71	50.84
8	72.96	69.68	69.78	74.58	65.86	58.45	75.28	69.99	59.27
9	78.97	72.77	76.08	80.13	72.88	65.72	81.32	72.55	66.81
10	85.47	78.88	83.74	88.94	83.79	73.98	87.94	83.82	76.85
12	92.18	86.31	90.87	91.62	93.15	82.75	91.99	94.63	96.33

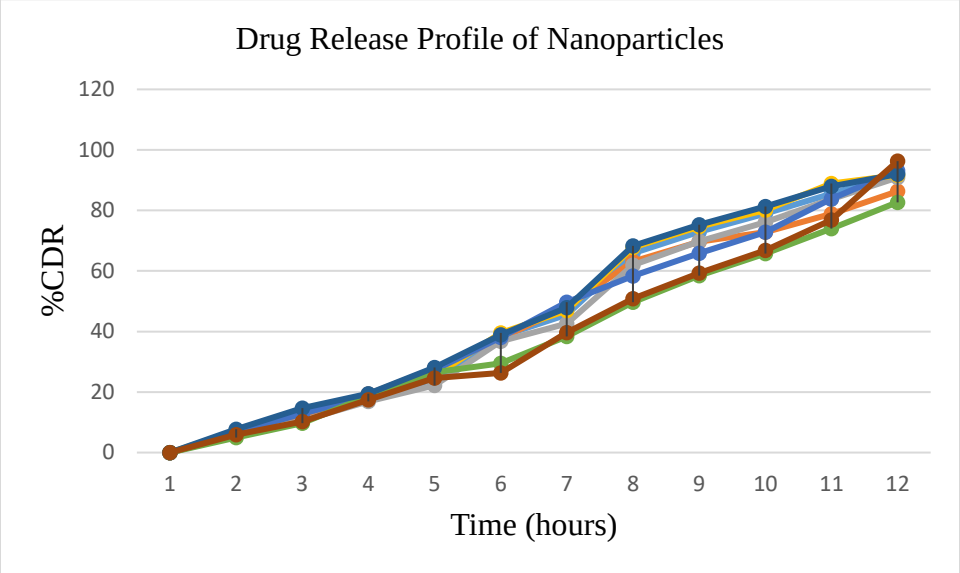

Figure 7. Cumulative % Drug release of formulated batches of SLNs (F1-F8) at different time intervals

3.1.3 Evaluation of Nanoparticulate in-situ gel

3.1.3.1 Visual Examination

All the prepared batches were found to be clear.

3.1.3.2 pH

The in situ gel's pH was discovered to be between 6.68 and 7.4. Since the pH values of all the created formulations fell within the region of neutral pH, they can all be used without irritating the skin.

3.1.3.3 Estimation of Drug Content

Drug content (% loading) of the nanoparticulate in-situ gel batches was estimated by UV spectrophotometer at 247 nm in methanol and it was found to be 95.38% (w/w) as shown in the table below (Table 10).

Table 10. Drug content (% loading) of different batches of nanoparticulate in-situ gel

Batch	Drug Content%
B1	85.57
B2	87.16

B3	95.39
B4	91.21

3.1.3.4 Spreadability

The spreadability of the Nanoparticulate in situ gel is given in Table 11.

Table 11. Spreadability of the formulated batches of Nanoparticulate in situ gel

Batch	Spreadability
B1	17.34
B2	22.30
B3	32.58
B4	19.26

3.1.3.5 Drug release

Table 12 shows the in vitro drug release characteristics of the nanoparticulate in-situ gel formulation that contained extract from *Psoralea corylifolia*. The results demonstrated a considerable increase in the nanoparticle formulation's in vitro drug release for up to 12 hours.

Table 12. *In vitro* release profile of nanoparticulate in-situ gel formulation containing psoralen

Time (hours)	B1	B2	B3	B4
0	0	0	0	0
1	4.25	5.09	6.85	6.13
2	8.68	10.23	13.69	12.11
3	17.63	17.45	20.11	19.42
4	29.87	26.29	38.87	37.77
5	37.86	39.68	51.09	49.88
6	46.97	50.84	65.68	63.11

8	56.33	59.28	71.46	69.70
10	61.97	65.61	77.91	75.97
12	71.84	73.98	91.89	84.96

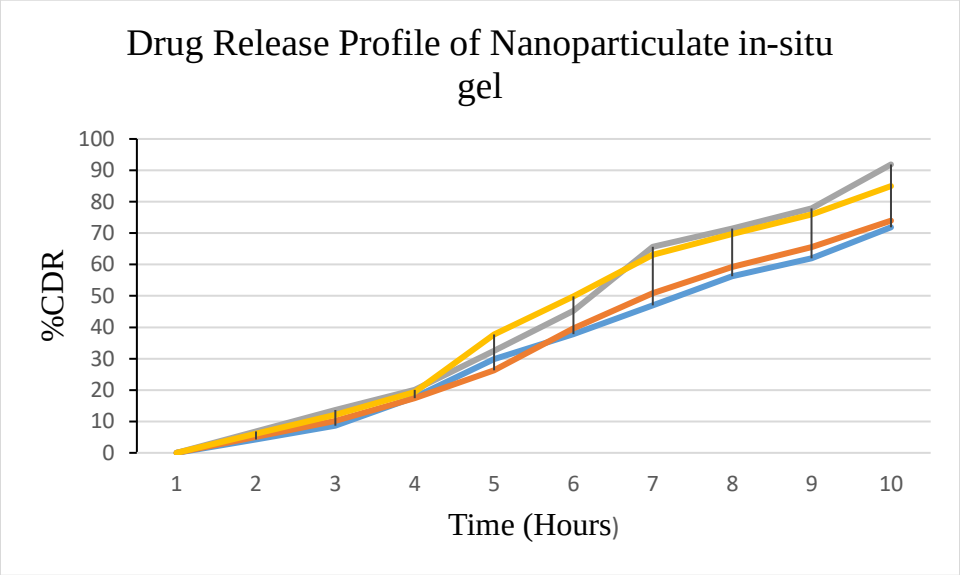

Figure 8. Cumulative % Drug release from of nanoparticulate in-situ gel formulation at different time intervals

3.1.3.6 Stability Studies

Stability testing was conducted by monitoring three parameters: pH, color, and in-vitro drug release investigations. In vitro drug release studies, pH, color, and storage times of one, two, three, and six months are displayed in The established formulations are stable and do not exhibit drug degradation while stored at room temperature, as shown by the characteristics examined for their stability, which are presented in Table 13.

Table 13. Results of different parameters for Nanoparticulate in-situ gel formulation stored at (25 ± 2˚C/75% ± 5% relative humidity) RH

S. No.	**Parameter**	**Result**			
		Day 1	**1 month**	**2 months**	**3 months**

1.	**pH**	7.2	7.2	7.2	7.1
2.	**Colour**	Clear	Clear	Clear	Clear
3.	**% CDR (12 hrs)**	91.87%	91.82%	91.76%	91.71%

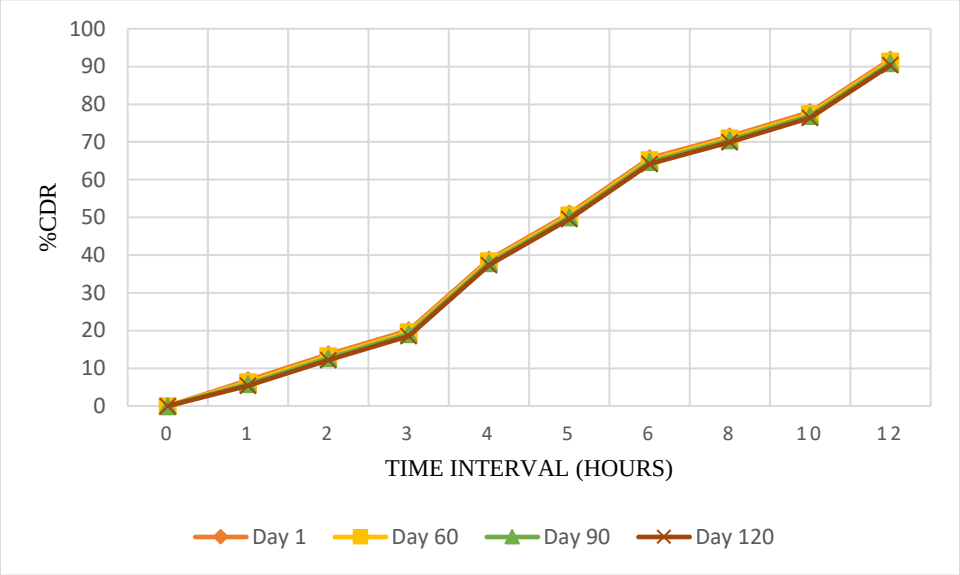

Figure 9. Comparative release profile Nanoparticulate in-situ gel on stability stored at 25 ± 2˚C/75% ± 5% RH

4. Conclusion

The current research aims to develop and evaluate an in-situ gel drug delivery system using nanoparticulates containing ethanol extract from *Psoralea corylifolia* for treating psoriasis. The physicochemical and phytochemical properties of *P. corylifolia* seeds were analyzed, revealing high concentrations of flavonoids, tannins, steroids, glycosides, and saponins in the extract, which may contribute to its anti-psoriatic effects. Preformulation studies focused on creating an in-situ gel with nanoparticulates, optimizing parameters like vesicle size, shape, and entrapment efficiency. The F8 batch of nanoparticles, with sizes ranging from 185 to 243 nm, showed the highest encapsulation efficiency at 73.06±0.1%. In vitro drug release studies demonstrated a release range of 82.75% to 96.33%, with the F8 batch achieving the highest release. The resulting in-situ gel had a pH of 6.68 to 7.4, making it suitable for non-irritating topical application. Drug loading varied between 85.57% and 95.39%. Batch B3 of the nanoparticulate in-situ gel exhibited

the highest drug release, sustaining up to 12 hours with a release range of 71.84% to 91.89%. Stability studies confirmed that batch B3 remained stable for three months. The study concluded that using *P. corylifolia* ethanol extract in a nanoparticulate in-situ gel is a promising method for managing psoriasis and enhancing topical drug delivery.

5. Conflict of interest

The authors have no conflict of interest.

6. Acknowledgement

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