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RESEARCH ARTICLE

A Research Article on Nanogel as Topical Promising Drug Delivery for Psoriasis

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ABSTRACT

Background: Transdermal medication administration seems promising, but it is a difficult method to implement for both local and systemic drug effects.

Objective: This study aimed to create a nanogel with a smaller particle size to increase the bioavailability of curcumin, an anti-inflammatory and anti- psoriasis medication.

Methods: This research aims to create nanosize Curcumin dispersion using an emulsion-solvent diffusion technique with the addition of a gelling agent to create a nanogel. Particle sizes in the formulation range from 100 to 400 nanometers. Curcumin is a medication used to treat psoriasis and chronic inflammatory disorders.

Results: The glycerol:water co-solvent system was chosen to prepare curcumin nanogels with various polymers because it has a higher permeability coefficient than the alcohol:water co-solvent system. In a franz diffusion cell, permeation across the cellophane membrane was achieved using 0.9% w/v sodium chloride as the receptor fluid. Curcumin-containing gels with eudragit polymer had a higher permeability coefficient.

Conclusion: Compared to nanogels made with HPMC and methyl cellulose, curcumin nanogels produced with carbopol with permeation enhancer showed greater flux improvement. Curcumin nanogels with carbopol 940 as a gelling agent and Eudragit S-100 as a permeation enhancer.

Keywords: Carbopol-940, Cellophane membrane, Curcumin, Eudragit S-100, Glycerol, TDDS.

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INTRODUCTION

Transdermal medication administration seems promising, but it is a difficult method to implement for both local and systemic drug effects.[1] Drug can enter the stratum corneum via the intercellular, transcellular, or appendageal routes. The intercellular route is the most frequent route for drug absorption through the skin.[2] Nanogel is a dispersion of hydrogel of nanoscale size caused by a physical and chemical cross-linking polymer.[3] Nanogels have characteristics that are similar to both solids and liquids. It comprises a limited number of solid components entangled with polymers scattered in a vast volume of liquid, with the solids creating a 3D network with a nanoscale size, resulting in a huge surface area and bi-conjugation of active targeting sites.[4] Nanogels combine the benefits of hydrogels with the nanoscale size characteristic. Nanogel networks have a high specific form that allows them to house and preserve medicinal molecules.[5] The incorporation of high-affinity functional groups can help in drug molecule release. Nanogels can transport encapsulated drug molecules to specific tissues or cell structures without causing the medication to leak prematurely into the bloodstream or other tissues. Nanogel is a kind of material with a size range of 1–100 nm. Nanogels have been utilized to shield unstable peptides from harsh manufacturing and physiological conditions and improve drug absorption at particular locations in oral drug administration.[6] Curcumin nanogels have been utilized as nonsteroidal anti-inflammatory drugs (NSAIDs) because of their anti-inflammatory, analgesic, and anti-psoriasis properties. The oral method irritates the mouth and raises blood pressure. Curcumin with a high degree of skin permeation can be used to treat not just inflamed tissues but also inflammatory pain and skin disorders.[7] This work aimed to create and test a Curcumin nanogel that offers extended release, increases drug residence time on the skin, and improves bioavailability.

MATERIALS AND METHOD

Evonik Industries, Mumbai, provided Curcumin and Eudragit S-100. Loba Chemie Pvt. Ltd., Mumbai, sent Carbopol 940 and Glycerol as a gift sample. Tween 80 was acquired from Mumbai-based S.D. Fine Chemical Ltd. Spectrochem in Mumbai provided the triethanolamine.

METHOD

Preparation of Curcumin Nanogel

Drug, Eudragit S-100 (polymer), and Tween-80 as stabilizers are accurately weighed and dissolved in glycerol while stirring. An aqueous phase containing

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Carbopol-940 dissolved in water was prepared with constant stirring and heat. On an ultrasonic bath sonicator, the drug-containing phase is sonicated.[8] During homogenization, the drug phase is introduced drop by drop into the aqueous phase to produce an emulsion. The homogenizer transformed the emulsion into nanodroplets, resulting in an O/W emulsion. Homogenization was carried out for an additional hour.[9] Triethanolamine was added to produce the gel, which was then stirred continuously to generate a nanogel. Batches A1, A2, and A3 were made with various compositions at the maximum rpm of 8000.[10] Using a homogenizer, prototype batches B1, B2, B3 and C1, C2, C3 were produced at varied rpms of 5000, 6000, and 7000, respectively (Tables 1 to 3).

Evaluation Parameters

Appearance: The clarity, color, and presence of any particles in the produced gel bases were visually examined.

Homogeneity

After the gels had been set in the container, all of the produced gels were visually inspected for homogeneity. They were examined for the appearance of aggregates and the existence of any.[11]

Measurement of Particle Size of Formulation

The Malvern Mastersizer 2000 MS was used to calculate the mean size of the chosen nanogels. The average particle size was taken down.

Measurement of pH

The pH was measured using a calibrated digital type pH metre by completely immersing the glass electrode and the reference electrode in the gel system to cover the electrodes.

Composition of the Drug

Curcumin was extracted from 1-gm of gel formulation using 50 mL of phosphate buffer 5.8 and filtered through a membrane filter (pore size 0.45 m) for drug estimation in gel. 2 mL was pipette out and built up to 10 mL from this. The sample's absorbance was measured spectrophotometrically at 276 nm. The calibration curve was used to quantify Curcumin content.

Release Studies *In-vitro*

The drug release from the formulation was measured using the Franz Diffusion Cell, which consists of a cylindrical glass tube with two openings on each ends.[12] 1-g of gel equating to 10 mg of curcumin was evenly placed on the surface of a cellophane membrane (previously soaked in medium for 24 hours) and attached to one end of the tube. The entire system was adjusted such that the bottom end of the tube containing the gel just touched (1–2 mm deep) the surface of the diffusion medium, which was 100 mL of pH 6.8 phosphate buffer in a 100 mL beaker. The contents were swirled using a magnetic bar at 100 rpm for 24 hours, and 5 mL of samples were extracted at different time intervals. The assembly was put on a thermostatic hot plate with magnetic stirrer and kept at 37.2°C. This 5 mL was diluted in 10 mL of new phosphate buffer (pH 6.8) before being analyzed for curcumin at 276 nm in a UV-vis spectrophotometer.

Irritation Test on the Skin

Human volunteers were used in the irritation test. Four volunteers were chosen for each gel, and 1.0 g of prepared gel was sprayed on the back of the hand in a two square inches region. Lesions or irritation were seen on the volunteers.[13]

Spreadability

Mutimer's recommended equipment is used to determine spreadability. It comprises a wooden block with a pulley

Table 1: Curcumin Nanogel (Composition of Batch A)

Comosition	*A-1*	*A-2*	*A-3*
Curcumin (g)	100	100	100
Eudragit S-100 (g)	0.15	0.2	0.25
Tween-80 (ml)	0.1	0.3	0.5
Glycerol (ml)	5	10	15
Carbopol (g)	0.5	0.1	0.3
Water (ml)	70	30	50
Triethanolamine (ml)	2	3	4

Table 2: Curcumin Nanogel (Composition of Batch B)

Composition	*B-1*	*B-2*	*B-3*
Curcumin (g)	100	100	100
Eudragit S-100 (g)	0.15	0.15	0.15
Tween-80 (ml)	0.1	0.1	0.1
Glycerol (ml)	5	5	5
Carbopol (g)	0.1	0.1	0.1
Water (ml)	30	30	30
Triethanolamine (ml)	2	2	2

Table 3: Curcumin Nanogel (Composition of Batch C)

Composition	*C-1*	*C-2*	*C-3*
Curcumin (g)	100	100	100
Eudragit S-100 (g)	0.15	0.15	0.15
Tween-80 (mL)	0.1	0.1	0.1
Glycerol (mL)	5	5	5
Carbopol (g)	0.1	0.1	0.1
Water (mL)	30	30	30
Triethanolamine (mL)	2	2	2

attached to one end. Spreadability is assessed with this approach using the terms "Slip" and "Drag." On this block is a ground glass slide. A 0.1 g sample of nanogel under investigation is put on this ground slide. The beach formula gel was squeezed between two slides, and a 1 kg weight was put on top of two slides for around 5 minutes to evacuate air and produce a uniform coating of nanogel between the two slides. The excess gel is scraped away from the edges. It was determined using the method, with a shorter interval indicating higher spreadability.[14]

$$S=M.L/T,$$

Where, S= Spreadability, L=Length of glass slide, M=Weight tied to upper slide, T=Time taken to separate the slides

Extrudability

This common empirical test is used to determine how much force is needed to extrude a material from a tube. This method determines the amount of applied shear in the rheogram area corresponding to a shear rate greater than the yield value and plug flow. The technique used to evaluate nanogel formulations for extrudability is based on the amount of nanogel in % and nanogel extruded from a lacquered aluminum collapsible tube with a weight in grams requirement of at least 0.5 cm ribbon of nanogel in ten seconds. Each formulation's extrudability is measured three times, and the average value is reported.[15]

Table 4: Interpretation of FTIR spectrum of pure curcumin.

Peaks cm-1	*Groups*
3351	O-H
1208	C-O
2936	Aliphatic C-H
1179	Asymmetric C-O-C
1042	Symmetric C-O-C

Table 5: Effect of pH on λ_{max}.

Drug solution in pH	*λmax*
6.8	276 nm
7.4	276 nm

Table 6: Calibration curve of curcumin.

Sr. No.	*Concentration (µg/mL)*	*Absorbance*
1	0	0
2	4	0.1548
3	8	0.3173
4	12	0.4842
5	16	0.6303
6	20	0.7963
R^2	0.9971	
Slope	25.61	
Intercept	-0.1020	

Extrudability = Applied weight to extrude the nanogel from tube (in gm) / Area (in cm^2)

Brookfield viscometer was utilized for the rheological experiments. The spindle was first dipped into the gel until the notch on the spindle made contact with the gel's surface. In the investigation, 3 gm of gel I and gel II (Stability chamber and room temperature) were utilized. The spindle numbers 61, 63, and 64 were chosen depending on the gel's viscosity. At 50, 100, 150, and 250 rpm, dial readings were obtained, and viscosity was measured.[2,4-7]

The outcome of the evaluation parameter done for the three prototype batches was determined to be good in all aspects, and therefore batch A-1 was chosen for trial batches. Tables 7 to 9 illustrate the results.

The results of evaluation of various pharmaceutical parameters for Batch A, B and C were recorded in Tables 7 to 9.

RESULTS AND DISCUSSIONS

FTIR Spectroscopy

Figure 1 shows the FTIR spectrum for curcumin, while Table 4 shows the interpretation of FTIR spectra for curcumin.

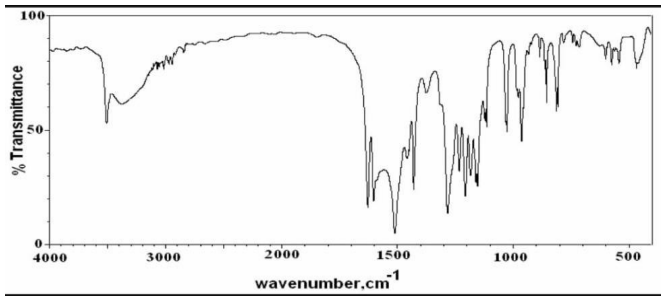

Figure 1: FTIR spectrum of pure curcumin

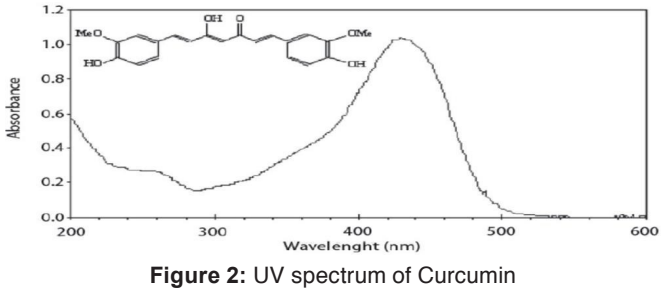

Figure 2: UV spectrum of Curcumin

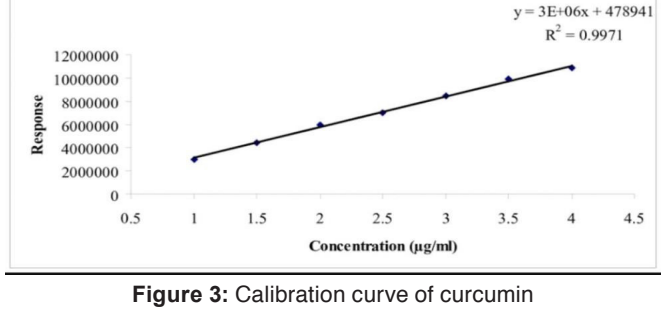

Figure 3: Calibration curve of curcumin

Table 7: Evaluation Parameters of Batch A

Evaluation parameters	*A-1*	*A-2*	*A-3*
Appearance	Clear	Clear	Clear
Homogenicity	Homogeneous	Homogenous	Homogenous
Particle size (nm)	165	189	213
pH	6.9 ± 0.00	6.5 ± 0.02	6.2 ± 0.20
Drug content±SD	98.8 ± 0.02	96.5 ± 0.02	97.8 ± 0.04
In vitro drug release (%)	96.72 ± 0.0784	94.75 ± 0.963	92.78 ± 0.77
Skin irritation test	No irritation	No irritation	No irritation
Spreadability (g.cm/s)	6.3 ± 0.5	6.7 ± 0.6	6.0 ± 0.6
Extrudability (g)	279 ± 0.7	268 ± 0.5	254 ± 0.7
Viscosity in cp at 50 (rpm)	9563	8562	8000

Table 8: Evaluation Parameters of Batch B

Evaluation parameters	*B-1*	*B-2*	*B-3*
Appearance	Clear	Clear	Clear
Homogenicity	Homogenous	Homogenous	Homogenous
Particle size (nm)	165	175	220
pH	6.8 ± 0.00	6.7 ± 0.02	6.5 ± 0.20
Drug content±SD	98.8 ± 0.02	98.5 ± 0.02	98.8 ± 0.04
In vitro drug release (%)	96.72 ± 0.0784	95.75 ± 0.963	95.78 ± 0.77
Skin irritation test	No irritation	No irritation	No irritation
Spreadability (g.cm/s)	6.6 ± 0.5	6.5 ± 0.6	6.7 ± 0.6
Extrudability (g)	279 ± 0.7	270 ± 0.5	260 ± 0.7
Viscosity in cp at 50 (rpm)	9863	9582	9888

Table 9: Evaluation Parameters of Batch C

Evaluation parameters	C-1	C-2	C-3
Appearance	Clear	Less clear	Clear
Homogenicity	Homogeneous	Homogeneous	Homogeneous
Particle size (nm)	165	160	160
pH	6.5 ± 2	6.7 ± 1	6.2 ± 2
Drug content±SD	98.2 ± 0.029	98.6 ± 0.04	98.5 ± 0.072
In vitro drug release (%)	93.25 ± 0.903	95.72 ± 0.861	94.3 ± 0.85
Spreadability (g.cm/s)	6.3	6.4	6.3
Extrudability (g)	254	243	254
Viscosity in cp at 50 (rpm)	9585	9588	8500

The FTIR spectrum of the medication sample revealed all of the peaks that corresponded to the functional groups found in curcumin's structure. The drug sample was found to be pure based on the FTIR spectrum.

Differential Scanning Calorimetry Studies

Pure drug- Curcumin

Polymer- Eudragit S-100 Binary Mixture- Drug + polymer

Figure 4 shows the DSC thermogram of Curcumin. DSC analyses reveal a prominent endothermic peak at 282^{o}C, which corresponds to the sample's melting point and is identical to the melting point of curcumin, showing that the substance is pure.

It may be concluded from the DSC overlay thermogram of pure drug and physical mixture with Eudragit S-100 that the excipients and drug have no interaction. The Medicine also did not create a compound with the excipients, as the endothermic peaks remained in the same place.

UV Spectroscopy

UV Spectroscopy is a kind of spectroscopy that uses ultraviolet light. Curcumin has absorbances at 226 and 276 nm. However, according to the UV spectra, the greatest absorbance is at 276 nm when the solution is produced in distilled water. As a result, 276 nm was chosen as the maximum wavelength. Figure 2 shows the UV spectrum of curcumin.

Table 10: Stability data of Optimized Formulation

Time period	*Particle size(nm)*	*Total drug content(%)*
Initial	165	98.2 ± 0.029
After storage (40 ± 2°C and 75 ± 5%RH)		
1 Month	162	95.72 ± 0.861
2 Month	160	94.3 ± 0.85
3Month	164	93.25 ± 0.903

Effect of Change in pH on λ_{max}

The impact of changing the pH on the drug's λ_{max}. λ_{max} was investigated by preparing its solution at various pH levels. Table 5 shows the outcome of the same. There was no significant difference in curcumin's maximum concentration at varying pH levels. Although the release assessment medium is phosphate buffer pH 7.4, a calibration plot may be produced using pure water and utilized for quantitative evaluation.

Curcumin Calibration Curve

Figure 3 shows the curcumin calibration curve in phosphate buffer 6.8 and Table 6 shows the observation values. In the concentration range of 4–24 g/mL at 276 nm, the graph of absorbance vs. concentration was found to be linear. The calibration curve's R2 was determined to be 0.999.

Evaluation of Batches Stability

The stability tests were conducted out on a formulation that was optimized. According to ICH standards, the samples were kept for three months at 40°C2°C and 75% relative humidity. Samples were taken after 1, 2, and 3 months and evaluated for appearance, pH, particle size, drug content, spreadability, extrudability, and viscosity.

Data on the Stability of Optimized Formulation

The following evaluation parameters were used for the trial batches (B and C): appearance, homogeneity, particle size measurement, pH measurement, drug entrapment efficiency, drug content, in vitro drug release, skin irritation study, spreadability, extrudability, rheological study, and stability batches. We identified Batch-A1 as the optimum batch based on the evaluation parameter results of trial batches, and a further experimental design was created (Figure 5 and Table 10).

CONCLUSION

Curcumin nanogel formulation was effectively produced and demonstrated to be efficacious and a superior carrier for transdermal/topical preparation. The homogenicity, particle size, pH, drug content, *in vitro* drug release, skin irritation test, spreadability, extrudability, and viscosity of the created nanogel were optimized. The advantages of administering this through the dermal route are that

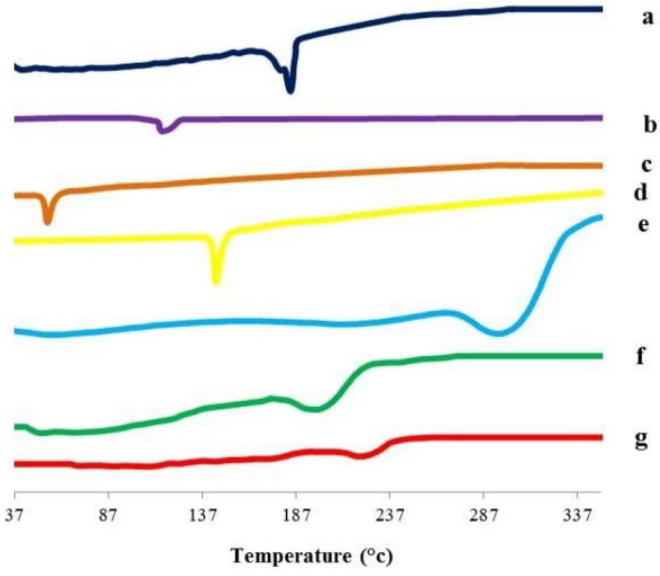

Figure 4: DSC thermogram of (a) Curcumin, (b) Eudragit S-100, (c) Tween 80, (a) Glycerol, (e) Carbopol, (f) Triethanolamine, and (g) the optimized Curcumin proniosomal formula.

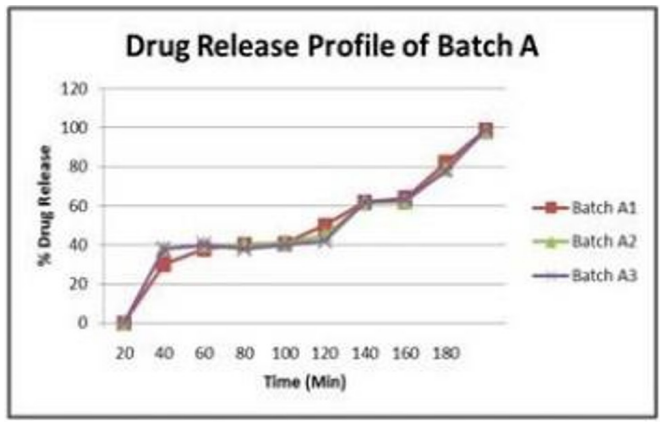

Figure 5: Drug release profile of Batch A

it avoids the drawbacks of administering it through the oral route and maintains constant plasma levels for a single dose of treatment. The initial release rate from each formulation was very fast, which might be attributed to incomplete gel formation in the early period, but following complete gel formation, the release became sluggish. The release profiles showed an inflection point, indicating gel formation on the diffusion membrane in the diffusion cell's donor compartment. The formulation was converted to the gel phase during gel formation, slowing drug release. The results revealed that the gels produced may hold curcumin for an extended period. The formulation's manufacturing is more efficient and cost-effective than oral dose forms.

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