Development and Evaluation of Curcumin Transferosomal Hydrogel: - A Promising Treatment for Psoriasis

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ABSTRACT

The aim of this work to develop curcumin transferosomal gel for the better treatment of Psoriasis through skin. The transferosome prepared by Modified Hand Shaking Method. In this method Soya-phosphatidylcholine, Span 80 and Salicylic acid were dissolved alcohol. Then solution was put in a round bottom flask. These were then dissolved by shaking. The mixture is subjected to evaporation to remove the organic solvent using temperature above the transition temperature of lipid by hand shaking. The characterization of trasferosome were further evaluated for vesicle size, drug entrapment efficiency, Shape and surface characterization by Microscopic observation. The vesicle size of all transfersomes varied between 178.89 and 245.65 nm whereas entrapment efficiency was found between 61.15 to 75.65%. the characterization of transferosomal gel were further evaluated for pH, viscosity, spreadability, drug content and invitro release study. The Viscosity of optimized formulation was found to be was in the range of 2361 ± 0.046 - 2772 ± 0.058 cps. *In-vitro* diffusion study of the transfersomes gel (F1-F6) was performed using modified Franz diffusion cell with dialysis membrane in phosphate buffer pH 7.4 for a period of 12 hours. In vitro release of the drug was found in the rage of 80.269-89.230.

Keywords: Curcumin, Transferosome, Soya-phosphatidylcholine, *invitro* release study.

INTRODUCTION

Transferosomes are the optimized ultra-deformable lipid supramolecular aggregates able to penetrate mammalian skin. The edge activator is incorporated into the layers such as span 80, tween 80. They consist of at least inner aqueous phase surrounded by lipid bilayer.¹ A Transfersome carrier is an artificial vesicle designed to exhibit the characteristics of a cell vesicle or a cell engaged in exocytosis, and thus suitable for controlled and, potentially, targeted drug delivery.² A Transfersome carrier is an artificial vesicle designed to exhibit the

characteristics of a cell vesicle or a cell engaged in exocytosis, and thus suitable for controlled and, potentially, targeted drug delivery.³

Hydrogels are water swollen polymer matrices, with a tendency to imbibe water when placed in aqueous environment.⁴ This ability to swell, under biological conditions, makes it an ideal material for use in drug delivery and immobilization of proteins, peptides, and other biological compounds. Due to their high water content, these gels resemble natural living tissue more than any other type of synthetic biomaterial. These networks, have a three dimensional structure, cross-linked together either physically (entanglements, crystallites), or chemically (tie-points, junctions).^{5,6}

Curcumin is chemically (1E, 6E)-1, 7-bis (4-hydroxy-3- methoxyphenyl) hepta-1, 6-diene-3, 5-Dione. Curcumin is used for the treatment of anti-cancer, anti-oxidant, antiinflammatory, hyperlipidemic, antibacterial, wound healing and hepatoprotective activities. Apart from its pharmacological actions, it has also been investigated as photostabilizing agent to protect photolabile drugs in solution, topical preparations and soft gelatin capsules. Despite the presence of large number of pharmacological actions, the therapeutic efficacy of curcumin is limited due to its poor oral bioavailability. The poor oral bioavailability of curcumin has been attributed to its poor aqueous solubility as its partition coefficient 3.2 and extensive first pass metabolism.⁷

The objective of the study to develop hydrogel of curcumin in the form of transfersome to get enhanced bioavailability and long term treatment of psoriasis. The safety and efficacy of a novel occlusive hydrogel dressing was assessed in an open-label, bilaterally controlled study that compared the use of hydrogel dressing alone vs hydrogel dressing in conjunction with topical medications (hydrocortisone cream; tacrolimus ointment; triamcinolone cream 0.1%; calcipotriene cream 0.05%; halobetasol propionate cream 0.05% and calcipotriene cream 0.005%) in the treatment of plaque psoriasis.

MATERIALS AND METHODS

Material

Curcumin was purchased on himedia lab, Mumbai, Soya Lecithin and span 80 purchase from HIMEDIA Lab Mumbai. Carbopol and PEG purchased from Loba Chem. Pvt. Ltd., Mumbai Tween 80 was purchase from HIMEDIA Laboratories Pvt. Ltd, Mumbai, All other chemicals were locally procured and solvents of merck grade were used.

Method

Formulation and Development of Curcumin Transferosome

Soya lecithin and span 80 are taken at different ratios. After that 100mg drug is added, dissolving in a mixture of chloroform and methanol with ratio 1:1. The mixture is evaporated to remove organic solvent above the transition temperature of liquid by hand shaking. A thin film is formed which is left over night to ensure complete removal of solvent. A buffer capsule is tore into a 100 ml of beaker with 10 ml water. Gently shake the solution for 5 minutes. Makeup the volume upto 100 ml. The film is hydrated with buffer water in gentle hand shaking for 15 min. The suspension formed is further hydrated at 40°C for 40 min. Brownish colored transferosomal suspension is formed.^{8,9}

Table 1: Formulation code and variable used in preparation of transferosome.

S.NO	FORMULATION CODE	SL:S	DRUG(MG)
1	SP1	95:05	100
2	SP2	90:10	100
3	SP3	85:15	100
4	SP4	80:20	100
5	TW5	80:20	100
6	TW6	85:15	100
7	TW7	90:10	100
8	TW8	95:05	100

(SP-Span 80, TW-Tween 80, SL-Soya lecithin, S-surfactant)

Characterization of Curcumin-loaded transfersomes:

Vesicle size distribution and zeta potential ^{10,11}

Vesicle size, size distribution and zeta potential were determined by Dynamic Light Scattering system by Malvern Zetasizer.

Vesicle morphology

The diameter of vesicle in a transferosome can be determined by dynamic light scattering method. The samples are passed through 0.2mm diameter of membrane filter. Before the samples are

prepared by distilled water. Filtered sample is diluted with saline which is also filtered. Then size measurement is done by dynamic scattering method. Although the vesicle of transfersome can be visualized by TEM. Stability of the vesicle determined by size and structure of the vesicle. Mean size of the vesicles is performed by DLS method. System by Malvern Zetasizer.

Entrapment efficiency¹²

Percentage of drug which are entrapped into a delivery system is known as entrapment efficiency. By the use Mini column centrifugation method the first separation of the untrapped drug can be determined. After centrifugation, the vesicles were disrupted using 0.1% Triton X-100 or 50% n-propanol. The entrapment efficiency is expressed as:

$$\text{Entrapment efficiency} = (\text{Amount entrapped} / \text{Total amount added}) \times 100$$

Surface charge and charge density

Surface charge and charge density of Transfersomes can be determined using zetasizer.

PREPARATION OF TRANSFERSOME HYDROGELS

For the preparation of hydrogel, the gel-forming polymer Carbopol 971P (2%) was dispersed in distilled water, stirred for 10 min at 1500 rpm and neutralized by triethanolamine until pH 6.0. Hydrogel were further allowed to equilibrate for 24 hours at room temperature and then used to disperse a freshly prepared tropical hydrogel. Transfersomal dispersion and hydrogel were mixed in a high speed stirrer (Remi, Mumbai, India) at 1000 rpm for the next 5 min. The gel was allowed to stand overnight to remove entrapped air.

Table 2. Formulation of topical hydrogel

Formulation	Topical Hydrogel formulations			
	HG1	HG2	HG3	HG4
Transfersome	Eqv. To 2% of drug	Eqv. To 2% of drug	Eqv. To 2% of drug	Eqv. To 2% of drug
Carbopol971P	0.5%	1.0%	1.5%	2.0%
Propylene Glycol	10%	10%	10%	10%
Glycerol	30%	30%	30%	30%
Distilled water	q.s			

CHARACTERIZATION OF TOPICAL HYDROGEL

Determination of pH¹³:

The value of pH of topical hydrogels was measured by using digital pH meter (EL. Alpha 01 pH meter) at the room temperature.

In-vitro drug release of transferosomal hydrogel

An in-vitro drug release study was performed using modified Franz diffusion cell. Dialysis membrane (Hi Media, Molecular weight 5000 Daltons) was placed between receptor and donor compartments. Transfersomes hydrogel equivalent to 500 mg of curcumin was placed in the donor compartment and the receptor compartment was filled with phosphate buffer, pH 7.4 (24 ml). The diffusion cells were maintained at $37 \pm 0.5^\circ\text{C}$ with stirring at 50 rpm throughout the experiment. At different time interval, 5 ml of aliquots were withdrawn from receiver compartment through side tube and analyzed for drug content by UV Visible spectrophotometer 424 nm (Rizwan *et al.*, 2004). The quantitative analysis of the values obtained in dissolution/release tests is easier when mathematical formulas that express the dissolution results as a function of some of the dosage forms characteristics are used ^{14,15}.

RESULTS AND DISCUSSION

Characterization of Transferosomal hydrogel

Vesicle Size and Entrapment Efficiency:

Table includes the value of vesicle size, and entrapment efficiency. The vesicle size of all transfersomes varied between 178.89 and 245.65nm whereas entrapment efficiency was found between 61.15 to 75.65%.

Table.3. Vesicle size and Entrapment Efficiency

S.No.	Formulation	Vesicle Size (nm)	Entrapment Efficient (%)
1	F1	230.39 $\pm$ 0.94	61.98 $\pm$ 0.62
2	F2	211.71 $\pm$ 0.25	66.01 $\pm$ 0.68
3	F3	182.94$\pm$0.48	70.67$\pm$1.56
4	F4	196.29 $\pm$ 0.20	60.63 $\pm$ 1.26
5	F5	223.32 $\pm$ 0.72	63.13 $\pm$ 1.49
6	F6	231.48 $\pm$ 0.49	68.14 $\pm$ 1.35

Table 4: Vesicle size and entrapment efficiency of optimized formulation

Formulation Code	Vesicle size (nm)	Entrapment efficiency (%)	Zeta potential (mv)
F3	182.94±0.48	70.67±1.56	-25.1

Figure 1. Zeta potential of optimize formulation

Microscopic observation

The photomicrographs showed the presence of spherically shaped vesicles dispersed in all the batches prepared.

Figure 2: Microscopic observation of transfersomes of optimized formulations (F3)

Evaluation of Transfersomal Hydrogel:

Determination of pH

The pH of the formulations was found to be satisfactory and was in the range of 6.7 ± 0.038 – 6.9 ± 0.039 , as shown in Table 5. The preparations were fluid at room temperature and at the pH formulated. Terminal sterilization via autoclaving had no impact on the pH.

Viscosity measurements

The viscosity of gels was determined by using a Brookfield viscometer DV-II model. T-Bar spindle in combination with a helipath stand was used to measure the viscosity and have accurate readings.

The Viscosity of optimized formulation was found to be was in the range of 2361 ± 0.046 – 2772 ± 0.058 cps.

Spreadability

A modified apparatus was used for determining spreadability. The spreadability was measured on the basis of slip and drug characteristics of the gels and was in the range of 10.29 ± 0.046 – 11.57 ± 0.053 gms. cm. /sec. The gels should have optimum spreadability because very high and very low spreadability values indicate that the application of the gel to the site is difficult. The spreadability of optimized formulation F-3 was found to be 11.57 ± 0.053 .

Drug content

Drug content is most important in transfersomes formulation and the data found are satisfactory. It was found to be 96.61 ± 0.028 to $98.58 \pm 0.036\%$ which shows the good capacity of formulation to hold the drug. The maximum drug content was found in formulation F-3 ($98.38 \pm 0.043\%$).

Table 5: Results of transfersomes hydrogel formulations

S.No.	Formulation	pH	Viscosity	Spreadability(G m.cm/sec.)	Drug content (%)
1	HG1	6.9 ± 0.039	2659 ± 0.075	11.08 ± 0.042	97.51 ± 0.017
2	HG2	6.8 ± 0.038	2737 ± 0.042	10.75 ± 0.059	96.61 ± 0.028
3	HG3	6.9 ± 0.021	2687 ± 0.059	11.57 ± 0.053	98.38 ± 0.043
4	HG4	6.7 ± 0.038	2772 ± 0.058	10.83 ± 0.058	98.53 ± 0.033

In-vitro drug release study

In-vitro diffusion study of the transfersomes hydrogel (F1-F6) was performed using modified Franz diffusion cell with dialysis membrane in phosphate buffer pH 7.4 for a period of 12 hours. In vitro release of the drug was found in the range of 80.269-89.230. (**Table 6**). In vitro release of the drug was fitted into different kinetic models like Zero-order, First-order, Higuchi model and Korsmeyer Peppas model. The zero-order plots were observed to be genuinely linear. In request to determine the precise system of medication discharge from curcumin gel the *In-vitro* discharge information was fitted to Korsmeyer Peppas was determined. As per the above research it was shown that the transfersome gel was discharged medication in controlled release way in 12hour.

Table 6: *In vitro* release data of transfersosomal using phosphate buffer 7.4

S. No	Time (hr)	HG1	HG2	HG3	HG4
1	0	0	0	0	0
2	0.5	13.568	11.890	14.973	8.274
3	1	22.336	20.210	19.709	14.115
4	2	34.050	32.087	34.042	24.729
5	4	48.638	44.733	49.684	41.461
6	6	66.993	64.560	68.397	60.568
7	8	78.074	74.046	77.553	70.648
8	10	83.419	83.145	83.949	74.021
9	12	89.230	88.446	87.462	87.777

Figure 3: Release Pattern of Various Formulations
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CONCLUSION:

From this study, it was concluded that the transfersomal formulations of curcumin, with high EE % and small particle size. Also, the preparation of curcumin as transfersomal gel has the ability to overcome the barrier properties of the skin and increase the drug release.

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