Available online on 15.12.2023 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Full Text Article

Research Article

Formulation Development and *In-Vitro* Evaluation of Transferosomal Gel of Mometasone Furoate

Arshiya Begum*[1], Syed Abdul Azeez Basha[2], Shahid Mohammed[3], Arjumand Begum[4]

Department of Pharmaceutics, Deccan School of Pharmacy, Osmania University, Hyderabad, India-500001

Article Info:

Article History:

Received 23 Sep 2023
Reviewed 04 Nov 2023
Accepted 03 Dec 2023
Published 15 Dec 2023

Cite this article as:

Begum A, Basha SAA, Mohammed S, Begum A, Formulation Development and *In-Vitro* Evaluation of Transferosomal Gel of Mometasone Furoate, Journal of Drug Delivery and Therapeutics. 2023; 13(12):91-102

DOI: http://dx.doi.org/10.22270/jddt.v13i12.6101

*Address for Correspondence:

Arshiya Begum, Department of Pharmaceutics, Deccan School of Pharmacy, Osmania University, Hyderabad, India-500001

Abstract

The main aim of the study is to formulate and evaluate transferosomal gel formulation for effective topical delivery of Mometasone furoate. The transferosomes was prepared using thin film hydration technique by various proportions of Soya phosphatidylcholine, tween 80. The drug was encapsulated into eight different Transferosomal formulations from F1-F8. The optimized formulation F4 showed small particle size (152.48 nm), entrapment efficiency % EE of 87.16%, zeta potential of -32mV, 0.252 PDI and % Cumulative Drug Release of (97.14%). SEM of optimized Transferosome appeared as spherical, well identified, Unilamellar vesicles. The optimized formulation of Transferosomes was further formulated to transferosomal gel with Carbopol-940 (0.2 to 0.8% w/w), HPMC k15 (0.2 to 0.8% w/w), Propylene glycol, Triethanolamine and Isopropyl alcohol. Among these, F4 formulation with Carbopol-940 0.8%w/w transferosomal gel is the optimized transferosomal gel and showed Spreadability value 0.229±0.01gm.cm/sec, pH value 5.8. The actual drug content of the Transferosomal gel was found to be 98.90%, which represents good content uniformity. The viscosity of optimized Transferosomal gel was found to 55417cps. The percentage drug release for Transferosomal gel was 98.22%. And the formulation was stable throughout the stability studies. This research suggests that Mometasone Furoate loaded transferosomal gel can be potentially used as a transdermal drug delivery system for effective topical delivery.

Keywords: Mometasone Furoate, Transfersomes, Soya phosphatidyl choline and Tween 80.

1. INTRODUCTION

Innovations in the area of drug delivery are taking place at a much faster pace. Improved patient compliance and effectiveness are inextricable aspects of new drug delivery systems. Transdermal drug delivery system (TDDS) is one of the systems lying under the category of controlled drug delivery, in which the aim is to deliver the drug through the skin in a predetermined and controlled rate.[1] TDDS are adhesive drug-containing devices of defined surface area that deliver a predetermined amount of drug to the surface of intact skin at a programmed rate to reach the systemic circulation. [2,3]

The name Transferosome means “carrying body” and is derived from the Latin word ‘transferre,’ meaning ‘to carry across’ and the Greek word 'soma', meaning 'a body'.[4] In broadest sense, a transfersome is a highly adaptable and stress-responsive, complex aggregate. Interdependency of local composition and shape of the bilayer makes the vesicle both self-regulating and self-optimising. This enables the transfersome to cross various transport barriers efficiently, and then act as a drug carrier for non-invasive targeted drug delivery and sustained release of therapeutic agents.[5]

A gel consists of a polymer which swells in the presence of fluid and perhaps within its structure. The rigidity of the gel is determined by the amount of fluid it entraps.[6] The clarity ranges from clear to a whitish translucent.[7] The extensive studies on release properties of gels have revealed that the active ingredients in gel-based formulations are better percutaneous absorbed than from creams and ointment bases. Thus, facts have clearly indicated that a formulation and development of a gel based topical dosage form for dermal conditions will be proved to be worthwhile.[8]

Mometasone furoate is a medium potency topical corticosteroid which presents an improved risk/benefit ratio. It is therefore of great value for inflammatory skin diseases, showing a strong anti-inflammatory action, rapid onset of action and low systemic bioavailability after topical application.[9]

Mometasone furoate is a 17-ester of 16α-methyl analogue of beclomethasone shows better potency with higher anti-inflammatory effect to a longer duration of action. A prodrug of free mometasone, is a non-fluorinated synthetic corticosteroid which is mainly used topically to reduce skin inflammation in psoriasis and eczema. It has anti-inflammatory, antipruritic and anti-hyperproliferative activity.[10]

Psoriasis is a chronic inflammatory skin disease characterized by skin thickening, scaling and epidermal alterations including inflammatory infiltrate in the epidermal and dermal region. For the management of psoriasis, topical therapy is most commonly used in majority of patients.[11]

Mometasone furoate transferosomal gel permeates the drug into stratum corneum and rise therapeutic concentration of

drug into skin without going in systemic circulation so it avoids further systemic effect. [12]

2. MATERIALS AND METHODS

2.1 Collection of drug and excipients: Mometasone Furoate (Provided by SARACA Laboratories), HPMC K15, Carbopol-940, Propylene Glycol (Merck Limited), Triethanolamine, Isopropyl Alcohol, Soya phosphatidylcholine, Cholesterol (S.D. Fine Chem Ltd.), Dicetyl phosphate (DCP), Methanol (Merck Limited). All the chemicals and reagents used were of analytical grade.

2.2 Preformulation Studies:

Organoleptic properties:

Take a small quantity of sample and spread it on the white paper and examine it visually for Color, odour, and texture.

Determination of Melting point:

The melting point of Mometasone Furoate was determined by capillary tube method according to the USP. A sufficient quantity of Mometasone Furoate powder was introduced into the capillary tube to give a compact column of 4-6 mm in height. The tube was introduced in electrical melting point apparatus and the temperature was raised. The melting point was recorded, which is the temperature at which the last solid particle of Mometasone Furoate in the tube passed into liquid phase.

Solubility Studies:

Drug sample (10mg) was suspended separately in a 10 ml of different solvents at room temperature in tight closed test tube and shaken by wrist action. The samples were filtered through Whatman filter paper and diluted appropriately with same solvent and concentration was determined by UV- vis spectroscopy.

Determination of maximum absorbance (λ max):

A solution containing the concentration 10 µg/ml drug was prepared in 6.8 phosphate buffer and UV spectrum was taken using Lab India Double beam UV-vis spectrophotometer (Lab India UV 3000+). The solution was scanned in the range of 200 – 400 nm.

Construction of standard graph:

100 mg of Mometasone Furoate was dissolved in 100 mL of pH 6.8 phosphate buffer to give a concentration in 1mg/mL (1000µg/mL), 1 ml was taken and diluted to 100 ml with pH 6.8 phosphate buffer to give a concentration of 0.01 mg/ml (10µg/ml). From this stock solution aliquots of 0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml, 1 ml, were pipette out in 10 ml volumetric flask and volume was made up to the mark with pH 6.8 phosphate buffer to produce concentration of 2, 4, 6, 8 and 10 µg/ml respectively. The absorbance of each concentration was measured at respective λmax.

Drug – excipient compatibility study: FTIR

The formulations were subjected to FTIR studies to find out the possible interaction between the drug and the excipients during the time of preparation. FTIR analysis of the pure drug and optimized formulation were carried out using an FT-IR spectrophotometer (Bruker FT-IR -Germany).

2.3 FORMULATION AND DEVELOPMENT

Formulation development of Mometasone Furoate loaded transferosomes- thin film hydration method:

Start by creating a thin film, this film is likely composed of phospholipids and a surfactant. The mixture of vesicles forming ingredients, that is phospholipids, surfactants and the Drug were dissolved in volatile organic solvent (chloroform-methanol). The organic solvent is then evaporated, this is typically done above the lipid transition temperature using a rotary evaporator, leaving behind a lipid film. Any remaining traces of the organic solvent were removed under vacuum conditions overnight. This step ensures that the final vesicle product is free from solvent residues. The deposited lipid films were hydrated with buffer (pH 6.8) by rotation at 60 rpm/min for 1hour at the corresponding temperature. The resulting vesicles were allowed to swell for 2 hours at room temperature. This swelling process helps the vesicles reach their optimal size and stability. To prepare small vesicles, the resulting LMVs were probe sonicated for 30 min at room temperature. The sonicated vesicles were homogenized by manually extruding them through a membrane filter. This step aids in achieving a uniform size and structure for the final vesicles.

Table 1: Formulation code of transferosomes

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Mometasone Furoate (%)	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Soya phosphatidylcholine (mg)	20	40	60	80	20	40	60	80
Cholesterol (mg)	20	20	20	20	40	40	40	40
Tween-80 (mg)	30	30	30	30	60	60	60	60
Dicetyl phosphate (mg)	8	8	8	8	8	8	8	8
Coconut oil (mg)	4	4	4	4	4	4	4	4
Methanol (mL)	5	5	5	5	5	5	5	5
Chloroform (mL)	10	10	10	10	10	10	10	10

2.4 PREPARATION OF TRANSFEROSOMAL GEL:

Optimization of Transferosomal gel was done on the basis of concentration of HPMC K15 and Carbopol-940 (0.2% to 0.8%) as described in the table below.

HPMC K15 and Carbopol-940 were dispersed in Isopropyl Alcohol. Then the mixture was stirred until it gets thickened. After complete dispersion, propylene glycol was added slowly into the aqueous dispersion of HPMC K15, and Carbopol-940 and other ingredients, such as Propylene Glycol and triethanolamine were added. 10 ml of transferosomes dispersion was incorporated into HPMC K15 and Carbopol-940 gel with continuous stirring. Quantity sufficient distilled water was added to make up the volume up to 0.1% of gel.

Table 2: Formulation code of transferosomal gel

INGREDIENTS (%)	FORMULATION CODE							
	F1	F2	F3	F4	F5	F6	F7	F8
Mometasone Furoate	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Carbopol-940	0.2	0.4	0.6	0.8	-	-	-	-
HPMC K15	-	-	-	-	0.2	0.4	0.6	0.8
Propylene Glycol	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Triethanolamine	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Isopropyl Alcohol	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

2.5 CHARACTERIZATION OF TRANSFEROSOMES:

Particle Size and Zeta Potential: [13,14]

Zeta sizer was used to measure the mean particle size and Zeta potential (ZP) of the transferosome. The mean particle size is an important parameter that governs the degree of permeation through the skin. The stability of the colloidal system in terms of particle size was evaluated based on Zeta Potential values and was established based on a Dynamic light scattering technique. For each formulation, three replicate analyses were performed, and data were presented as mean± S.D.

Polydispersity index: [15]

PDI is a measure of heterogenicity of a sample based on size, polydispersity can occur because of agglomeration of sample. PDI can be obtained by Dynamic light scattering microscopy (DLS). PDI of less than 0.1 is considered as homogenous and ≥0.4 as heterogenous.

Entrapment efficiency: [16]

The entrapment efficiency was determined by using direct method. Detergents are used to break the transferosome membranes 1 ml of 0.1% Triton X- 100(Triton X-100 dissolved in phosphate buffer) was added to 0.1 ml Transfersomes preparations and made up to 5 ml with phosphate buffer then it was incubated at 37oC for 1.5 hrs to complete breakup of the transfersome membrane and to release the entrapped material. The sample was filtered through a Millipore membrane filter (0.25) µm and the filtrate was measured at 240 nm for Mometasone furoate. The amount of Lamivudine was derived from the calibration curve.

The entrapment efficiency is expressed as:

$$\textbf{\% Entrapment efficiency} = \frac{\textbf{Amount of the drug entrapped}}{\textbf{Total amount of the drug}} \times \textbf{100.}$$

2.6 EVALUATION OF TRANSFEROSOMAL GEL:

Physical appearance:

All prepared gel formulations have been observed for their visual appearance, such as transparency, colour, texture, grittiness, greasiness, stickiness, smoothness, stiffness, and tackiness. The prepared gels were also evaluated for the presence of any particles. Smears of gels were prepared on glass slide and observed under the microscope for the presence of any particle or grittiness.

pH of Formulation: [17,18]

pH measurement of the gel was carried out by using a digital pH meter. pH of the topical gel formulation should be between 4-6 to treat the skin infections.

Determination of viscosity:

Viscosity of the gels were determined by using Brookfield Viscometer (model- RVTP). Spindle type, RV-7 at 100 rpm.

Spreadability: [18,19]

A modified apparatus suggested was used for determining spreadability. The spreadability was measured on the basis of slip and drag characteristics of the gels. The modified apparatus was fabricated and consisted of two glass slides, the lower one was fixed to a wooden plate and the upper one was attached by a hook to a balance. The spreadability was determined by using the formula:

$$s=ml/t,$$

where s, is spread ability, m is weight in the pan tied to upper slide and t is the time, l is the distance travelled. for the practical purpose the mass, length was kept constant and 't' was determined.

Homogeneity: [20]

All developed gels were tested for homogeneity by visual inspection after the gels have been set in the container for their appearance and presence of any aggregate.

Drug Content:

Gel formulations (100 mg) was dissolved in suitable solvent and filtered and the volume was made. The resultant solution was suitably diluted with solvent and absorbance were measured at 240 nm using UV-Visible spectrophotometer. Drug content was determined from calibration curve.

***In-vitro* diffusion studies:** [21]

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. Transferosomal gel was placed in the donor compartment and the receptor compartment was filled with phosphate buffer, pH 6.8 (24 ml). The diffusion cells were maintained at 37±0.5°c with stirring at 50 rpm throughout the experiment. At different time intervals, 5 ml of aliquots were withdrawn from receiver compartment through side tube and analyzed for drug content by UV visible spectrophotometer and analyzed spectrophotometrically at 240 nm using phosphate buffer pH 6.8 as blank.

Kinetic modelling of *In -vitro* release rates of formulations: [22]

The results of *in-vitro* release profile obtained for all the formulations were plotted in modes of data

treatment as follows: -

Zero-order kinetic model-cumulative percentage drug release versus time.

First- order kinetic model-log cumulative percentage drug release remaining versus time.

Higuchi's model-cumulative percentage drug released versus square root of time.

Korsmeyer's equation/Peppa's model-log cumulative percentage drug released versus log time.

Stability Studies: [12]

Stability studies have been carried to point out any physical visual or chemical stability of optimized batch at 25°C ± 2°C/ 60% RH ± 5% RH as per ICH guidelines for 3 months. Samples are taken out at various days 0th, 30th, 60th and 90th and checked their physical property and drug content.

3. RESULTS AND DISCUSSION

3.1 Preformulation Studies:

a. Organoleptic Properties:

Table 3: Organoleptic Properties of Mometasone furoate

S.no	Properties	Observed Results
1	State	Solid
2	Colour	White to off-white powder
3	Odour	Odourless
4	Taste	Bitter or Unpleasant

b. Melting point determination:

Table 4: Melting point determination

Reported Melting Point	Observed Melting Point
215-220°C	215°C

Observation: The Melting point of Mometasone Furoate was found to be 215ºC. This indicates the purity of drug sample, any impurity if present will cause variation in the melting point of given drug substance.

c. Solubility Studies:

Table 5: Solubility of drug in different solvents

S.no	Solvents	Solubility
1	Water	10.8±0.13
2	Methanol	49.41 ±0.65
3	Acetonitrile	58.46 ± 0.57
4	Dimethyl formamide	71.61 ± 0.63
5	pH 6.8 Phosphate Buffer	82.25 ±0.52
6	Ethanol	89.08 ± 0.51

3.2 UV-Spectroscopy-Analysis of Drug

d. Determination of maximum absorbance (λ max):

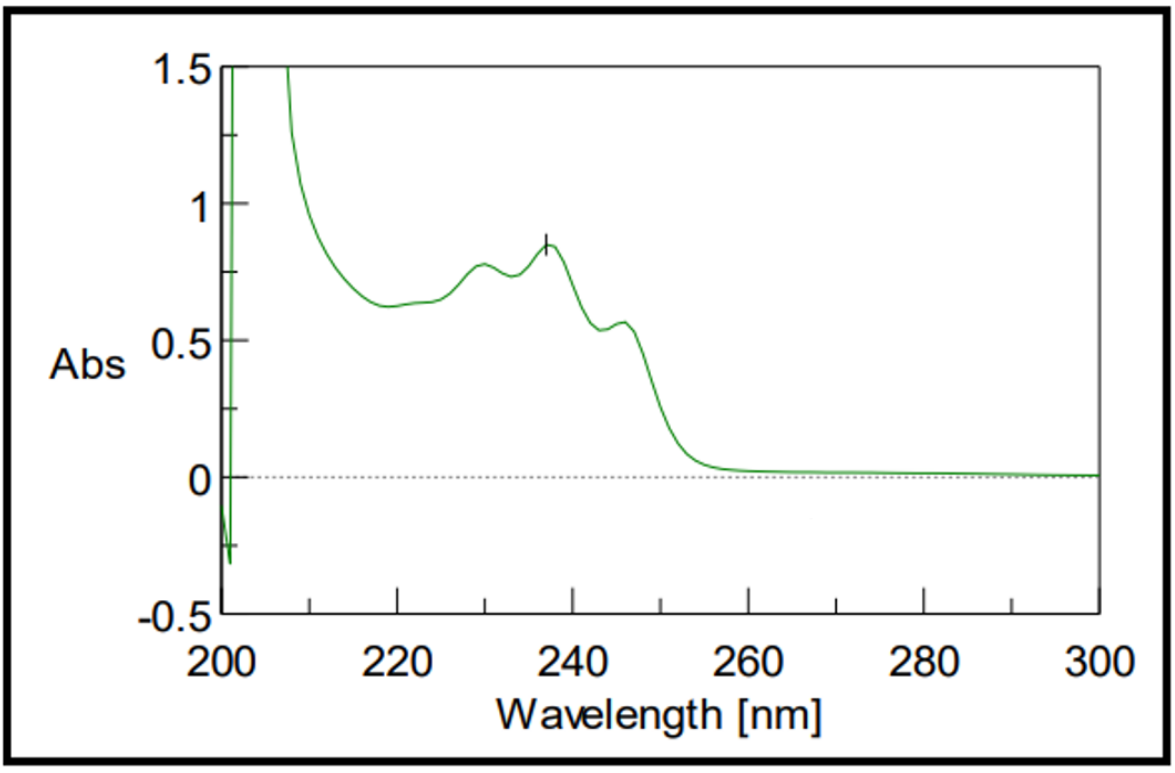

Figure 1: Lambda max determination of Mometasone furoate

Observation: UV-vis spectra of Mometasone Furoate were measured from 200 to 300 nm and the absorption spectrum was found to be sharp and maximum at wavelength of **240 nm**, therefore, it was used as the optimum wavelength throughout the experiment.

e. Calibration curve:

Table 6: Construction of Calibration curve:

Concentration (µg/ ml)	Absorbance
0	0
2	0.228±0.10
4	0.424±0.05
6	0.636±0.12
8	0.811±0.09
10	0.999±0.03

All values are expressed as mean, ± SD(n=3)

Calibration curve:

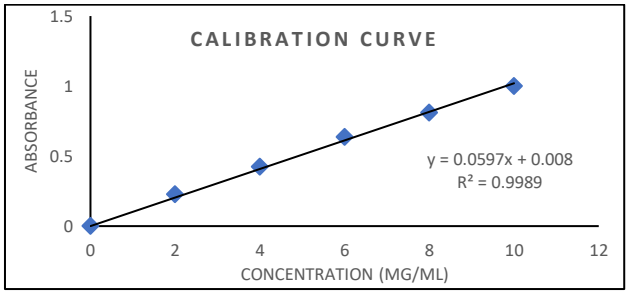

Figure 2: Standard calibration curve of Mometasone Furoate

Observation: The standard graph of Mometasone Furoate showed good linearity with R^2 of 0.998, which indicates that it, obeys "Beer- Lamberts" law.

f. FTIR

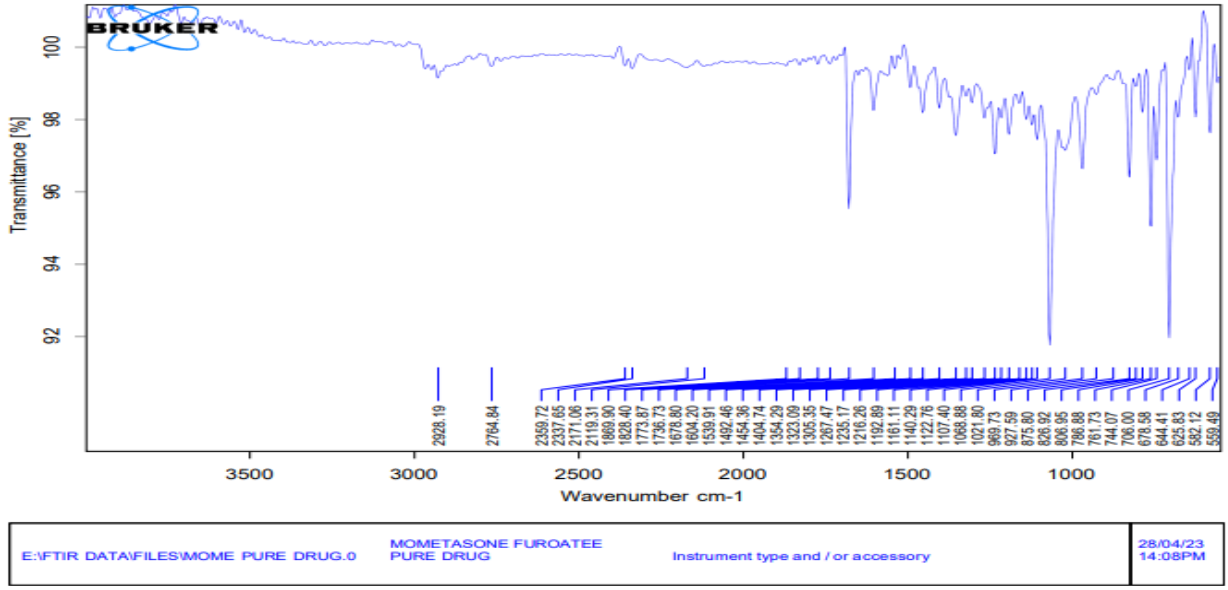

Figure 3: FTIR of Pure Drug-Mometasone furoate

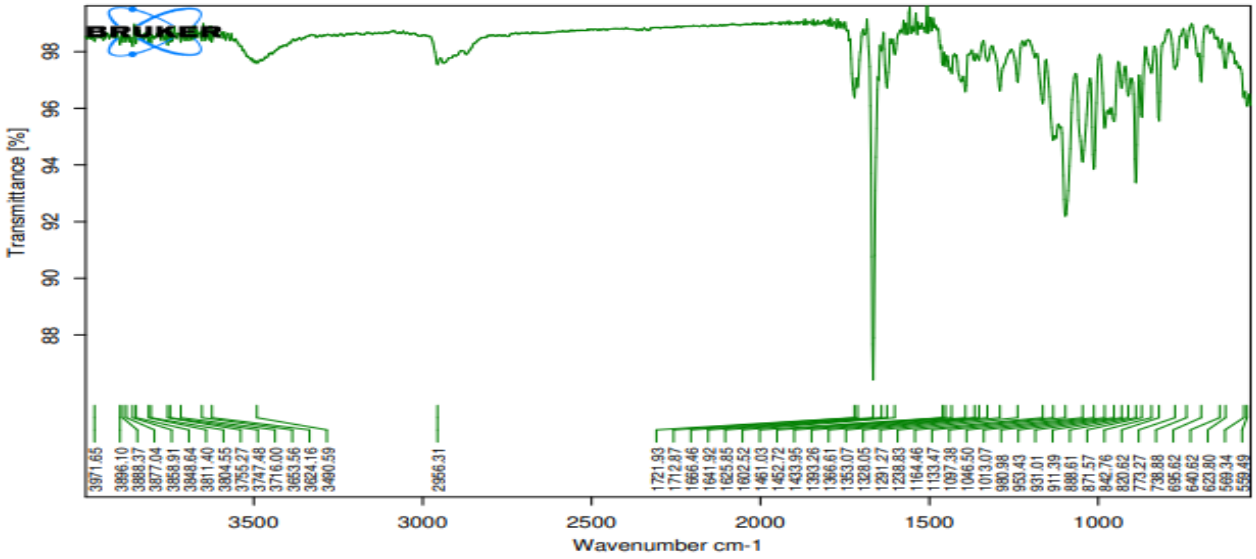

Figure 4: FTIR of Drug with Excipients

Observation: Infrared studies were carried out to confirm the compatibility between the drug and selected excipients. From the spectra, it was observed that there was no major shifting, as well as, no loss of functional peaks between the spectra of the drug and transferosomal gel. This indicated no interaction between the drug and other excipients.

3.3 CHARACTERIZATION OF PREPARED TRANSFEROSOMES:

Table 7: Particle size, PDI, Zeta potential and entrapment efficiency of all formulations

Formulation	Particle Size	PDI	Zeta Potential	Entrapment efficiency	Drug content
F1	171.57±2.10	0.503	-5.44	60.31±1.15	75.43±0.05
F2	162.61±2.35	0.378	-20.62	72.39±0.26	82.19±5.10
F3	160.38±4.13	0.313	-12.93	79.05±3.02	87.76±1.26
F4	**152.48±2.61**	**0.252**	**-32.55**	**87.16±2.10**	**97.45±2.12**
F5	192.89±3.16	0.987	-18.21	59.22±1.24	66.31±1.41
F6	197.93±2.27	1.235	-10.46	61.79±5.87	78.14±0.25
F7	182.54±1.20	1.503	-16.67	75.63±2.11	88.01±3.40
F8	171.68±3.32	1.378	-15.10	85.48±1.30	91.35±2.09

SD±(n=3)

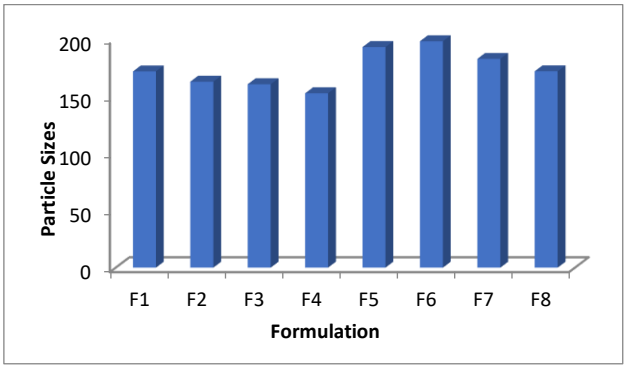

Figure 5: Particles size graph of Mometasone furoate Transferosomes (All Formulations)

Observation: Particle Size of Prepared F4 formulation showed the least particle size of 152.48±2.61 nm.

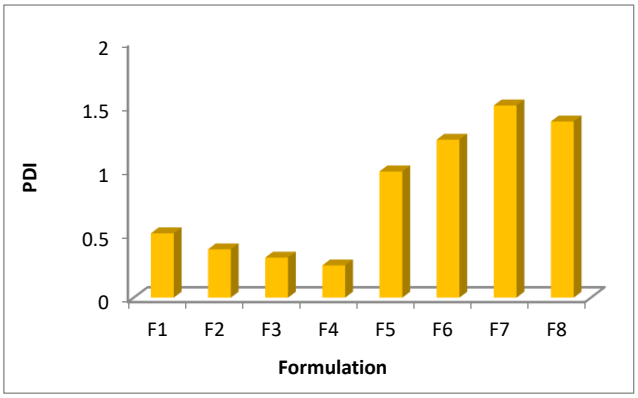

Figure 6: PDI graph of Mometasone furoate Transferosomes (All Formulations)

Observation: PDI of F4 formulation is least when compared to other formulations.

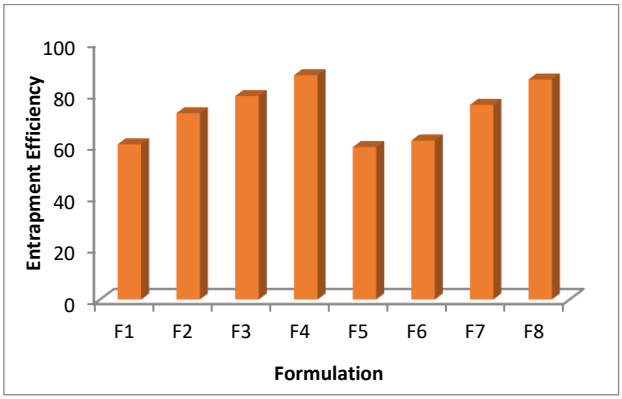

Figure 7: Entrapment efficiency graph of Mometasone furoate Transferosomes (All Formulations)

Observation: F4 formulation showed the highest Entrapment efficiency of **87.16±2.10**

***IN-VITRO* DIFFUSION STUDIES:**

Table 8: *In-vitro* diffusion studies of F1-F8 Transferosomes formulations in percentage

Time (hour)	CUMULATIVE PERCENT DRUG RELEASE							
	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
1	21.16±0.07	28.10±0.10	32.93±0.02	40.52±0.08	36.60±0.05	28.42±0.11	25.93±0.09	20.40±0.06
2	36.02±0.01	32.36±0.02	43.30±0.12	49.89±0.02	44.56±0.01	35.97±0.05	30.47±0.02	26.99±0.09
3	52.97±0.12	40.29±0.06	49.02±0.06	55.54±0.06	51.06±0.13	42.68±0.15	36.65±0.05	31.02±0.10
4	50.24±0.09	48.95±0.05	56.91±0.15	65.26±0.10	60.30±0.00	48.99±0.09	40.24±0.19	38.87±0.09
5	67.11±0.05	56.61±0.12	65.65±0.12	72.72±0.09	73.49±0.01	59.47±0.02	48.76±0.06	42.24±0.10
8	78.69±0.01	69.61±0.25	72.72±0.09	83.14±0.15	78.20±0.08	64.26±0.06	52.34±0.16	50.34±0.15
9	90.19±0.11	78.20±0.14	82.53±0.12	86.63±0.18	86.16±0.06	76.97±0.04	60.87±0.10	56.91±0.13
10		86.97±0.01	90.26±0.10	95.43±0.05	90.78±0.09	82.34±0.05	71.51±0.15	65.80±0.05
12		91.36±0.14	91.59±0.09	**97.14±0.10**	95.36±0.02	92.92±0.09	85.01±0.12	80.69±0.02

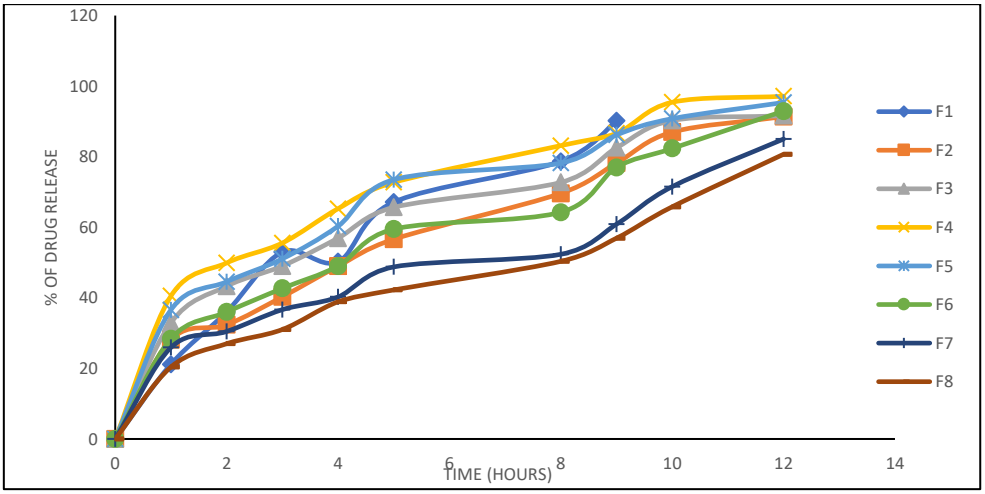

Figure 8: *In-vitro* diffusion studies of F1-F8 Transferosomes formulations in percentage

Observation: The Mometasone Furoate Transferosomes F4 showed a better release profile of **97.14%** by 12 hours. The prolonged release at 12 hours can be attributed to slow diffusion of drug from lipid matrix.

3.4 CHARACTERIZATION OF OPTIMIZED FORMULATION:

Surface morphology of optimized formulation:

SEM, was used to characterize the size and shape of the transfersomes. The size of the spherical, small Unilamellar vesicles was revealed by microscopic analysis.

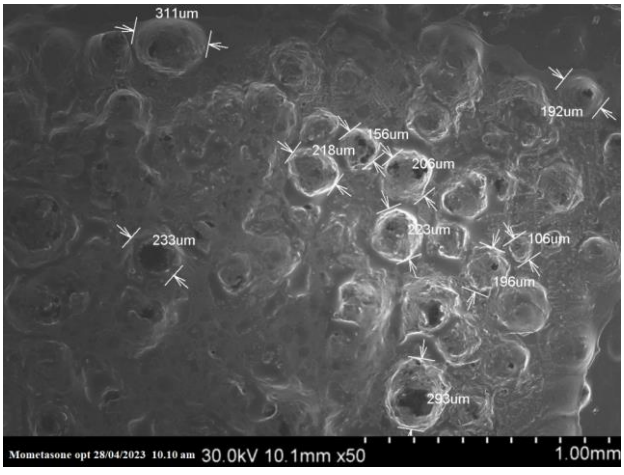

Figure 9: SEM Photograph of Mometasone Furoate Transferosome (Formulation-4)

Particle Size:

2023.04.28 11:13:25

201707121200311.nsz

Measurement Results

Date	: 28 April 2023 11:13:25
Measurement Type	: Particle Size Sura Labs
Sample Name	: MOMETASONE optimized
Scattering Angle	: 90
Temperature of the holder	: 25.0 deg. C
T% before meas.	: 20
Viscosity of the dispersion medium	: 0.884 mPa.s
Form Of Distribution	: |Standard|
Representation of result	: Scattering Light Intensity
Count rate	: 1317kCPS

Calculation Results

Peak No.	S.P.Area Ratio	Mean	S. D.	Mode
1	1.00	152.48 nm	18.2 nm	152.48 nm
2	---	--- nm	--- nm	--- nm
3	---	--- nm	--- nm	--- nm
Total	1.00	152.48 nm	18.2 nm	152.48 nm

Cumulant Operations

Z-Average	: 152.48 nm
PI	: 0.252

Molecular weight measurement

Molecular weight	: ---
Mark-Houwink-Sakurada parameters	: ---

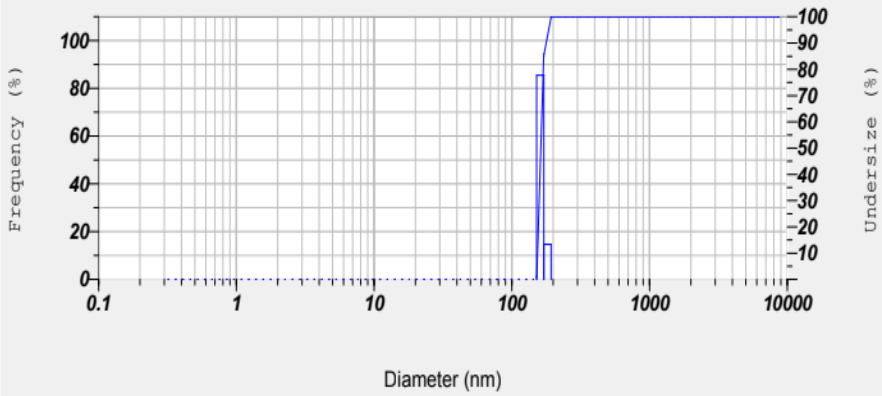

Figure 10: Particle Size of F4 formulation

Zeta Potential:

2022.04.26 10:40:31

Measurement Results

Mometasone optimized-Zeta.nzt

Measurement Results

Date	: 28 April 2023 10:40:31
Measurement Type	: Zeta Potential Sura Labs
Sample Name	: Mometasone optimized
Temperature of the holder	: 25.0 deg. C
Viscosity of the dispersion medium	: 0.814 mPa.s
Conductivity	: 0.123 mS/cm
Electrode Voltage	: 3.6V

Calculation Results

Peak No.	Zeta Potential	Electrophoretic Mobility
1	-32.55 mV	-0.000333 cm2/Vs
2	--- mV	--- cm2/Vs
3	--- mV	--- cm2/Vs

Zeta Potential (Mean)	: -32.55 mV
Electrophoretic Mobility mean	: -0.000333 cm/Vs

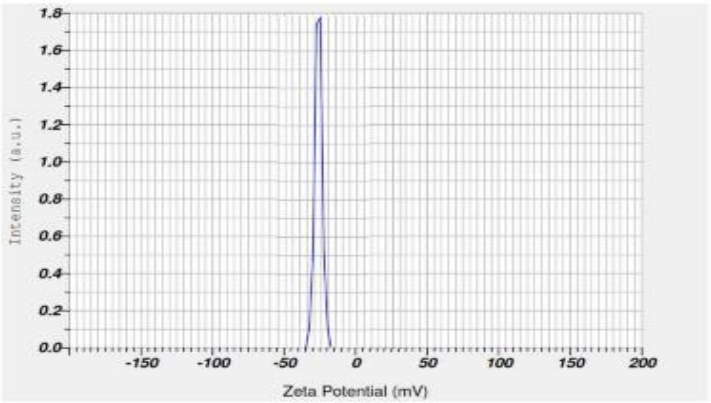

Figure 11: Zeta Potential of F4 formulation

3.5 CHARACTERIZATION OF TRANSFEROSOMAL GEL:

Table 9: Gel evaluation Parameters

Polymer	Formulation	pH	Viscosity (centipoise)	Extrudability	Homogeneity	Drug Content	Skin Irritation test
Carbopol-940	F4 optimized 0.2 %	6.5	52325	+	Satisfactory	93.29	No
	F4 optimized 0.4%	6.2	53425	+	Satisfactory	95.56	No
	F4 optimized 0.6%	5.9	54360	+	Satisfactory	96.06	No
	F4 optimized 0.8%	5.8	**55417**	**++**	**Excellent**	98.90	No
HPMC K15	F4 optimized 0.2 %	6.6	50368	+	Satisfactory	92.19	No
	F4 optimized 0.4%	6.4	51117	+	Satisfactory	95.22	No
	F4 optimized 0.6%	6.1	51392	+	Satisfactory	96.21	No
	F4 optimized 0.8%	6.0	51871	+	Satisfactory	96.05	No

Table 10: Physical evaluation of Mometasone Furoate Transferosomal gel

Polymer	Formulation	Colour	Spreadability (g.cm/sec)
Carbopol-940	F4 optimized 0.2%	White to off white	0.456±0.01
	F4 optimized 0.4%	White to off white	0.320±0.12
	F4 optimized 0.6%	White to off white	0.258±0.09
	F4 optimized 0.8%	**White to off white**	**0.229±0.01**
HPMC K15	F4 optimized 0.2%	White to off white	0.570±0.05
	F4 optimized 0.4%	White to off white	0.590±0.09
	F4 optimized 0.6%	White to off white	0.578±0.06
	F4 optimized 0.8%	White to off white	0.490±0.03

***In-vitro* diffusion studies:**

Table 11: *In-vitro* diffusion studies of Transferosomal gel

Polymer	Carbopol-940				HPMC K15			
Time (hrs)	**F4 optimized 0.2 %**	**F4 optimized 0.4%**	**F4 optimized 0.6%**	**F4 optimized 0.8%**	**F4 optimized 0.2 %**	**F4 optimized 0.4%**	**F4 optimized 0.6%**	**F4 optimized 0.8%**
0	0	0	0	0	0	0	0	0
1	40.62±0.01	34.89±0.09	35.96±0.11	30.99±0.04	37.20±0.16	41.98±0.02	32.01±0.02	28.92±0.16
2	45.10±0.05	40.92±0.02	41.60±0.08	38.06±0.13	42.95±0.06	46.93±0.05	40.53±0.16	34.64±0.10
4	71.91±0.09	46.06±0.05	48.14±0.05	45.36±0.00	60.41±0.02	55.54±0.09	45.20±0.19	40.05±0.05
5	76.82±0.13	53.86±0.04	55.30±0.02	56.12±0.05	67.56±0.09	63.63±0.11	49.16±0.10	44.13±0.02
6	80.86±0.10	69.11±0.03	70.82±0.09	60.79±0.02	74.99±0.17	70.15±0.18	56.99±0.03	53.92±0.15
8	94.01±0.04	75.70±0.01	78.14±0.10	75.66±0.09	89.82±0.10	90.83±0.16	62.82±0.05	60.46±0.06
10		82.59±0.08	85.97±0.09	80.90±0.15	92.88±0.11	93.25±0.12	74.61±0.09	64.58±0.02
11		97.05±0.10	90.36±0.02	95.36±0.10		95.14±0.10	80.79±0.04	75.11±0.06
12			93.75±0.04	**98.22±0.12**			95.26±0.11	90.62±0.02

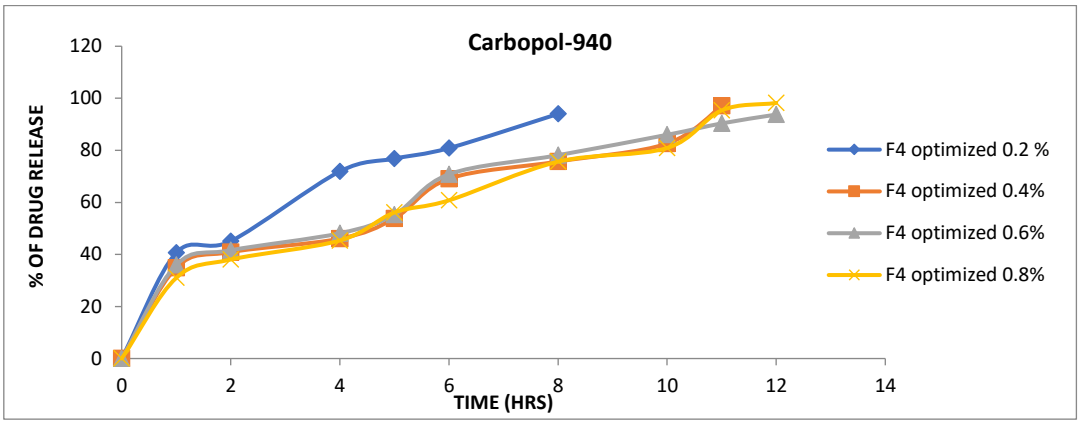

Figure 12: *In-vitro* diffusion studies for Transferosomal gel with different concentrations of Carbopol-940.

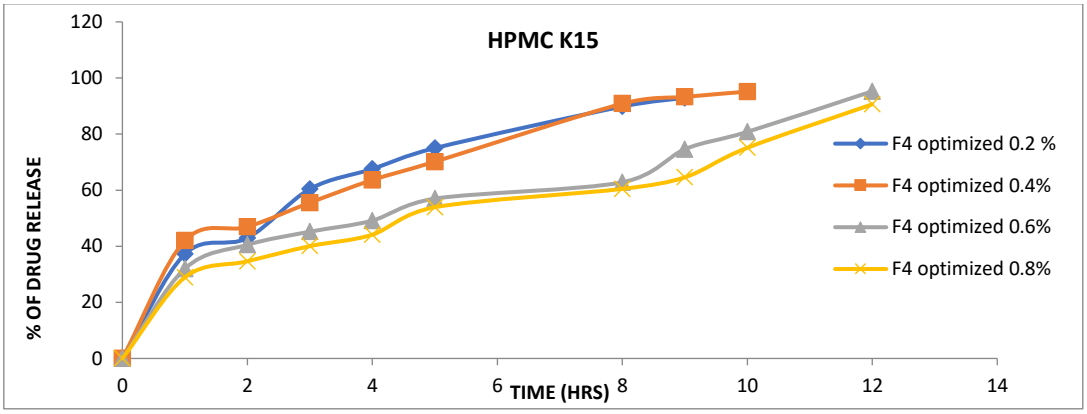

Figure 13: *In-vitro* diffusion studies for Transferosomal gel with different concentrations of HPMC K15.

Observation: F4 optimized 0.8% Carbopol-940 gel showed highest drug release (98.22 % for 12 hours), good Homogeneity, highest drug content, Proper viscosity. Hence, it was considered as optimized formulation.

Kinetic Studies:

Table 12: Release kinetics of optimized formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG (%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
30.99	1	1.000	1.491	0.000	1.839	30.990	0.0323	-0.509	69.01	4.642	4.102	0.540
38.06	2	1.414	1.580	0.301	1.792	19.030	0.0263	-0.420	61.94	4.642	3.957	0.685
45.36	4	2.000	1.657	0.602	1.738	11.340	0.0220	-0.343	54.64	4.642	3.795	0.847
56.12	5	2.236	1.749	0.699	1.642	11.224	0.0178	-0.251	43.88	4.642	3.527	1.114
60.79	6	2.449	1.784	0.778	1.593	10.132	0.0165	-0.216	39.21	4.642	3.397	1.244
75.66	8	2.828	1.879	0.903	1.386	9.458	0.0132	-0.121	24.34	4.642	2.898	1.744
80.9	10	3.162	1.908	1.000	1.281	8.090	0.0124	-0.092	19.1	4.642	2.673	1.969
95.36	11	3.317	1.979	1.041	0.667	8.669	0.0105	-0.021	4.64	4.642	1.668	2.974
98.22	12	3.464	1.992	1.079	0.250	8.185	0.0102	-0.008	1.78	4.642	1.212	3.430

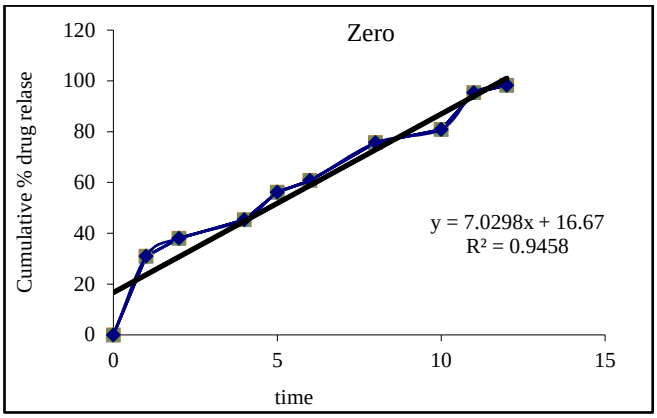

Figure 14: Zero order release kinetics

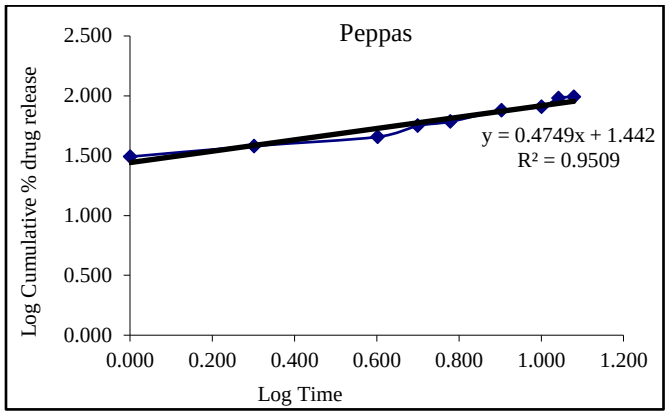

Figure 16: Peppas release kinetics

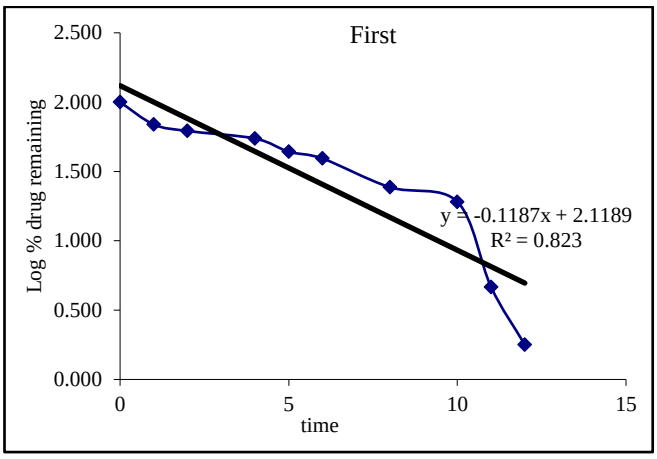

Figure 15: First order release kinetics

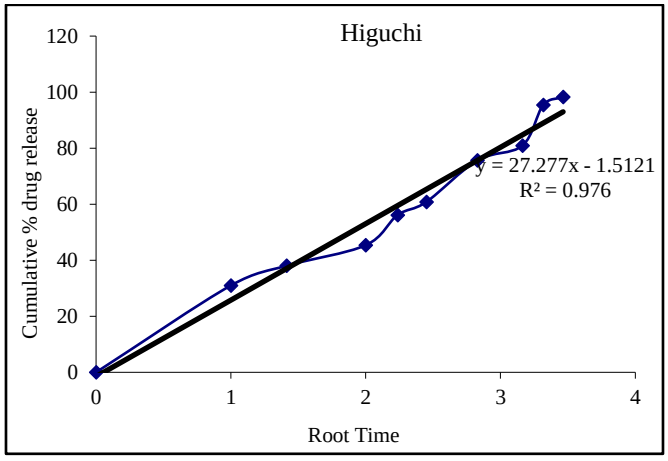

Figure 17: Higuchi release kinetics

Observation: The optimized formulation F4 optimized 0.8% Carbopol-940 Transfersomes gel was analyzed for the drug release mechanism. The best correlation coefficient value (0.976) indicates the best release mechanism (Higuchi release kinetics).

Stability Studies:

The stability study of the Transfersomal gels was performed as per ICH guidelines. Freshly prepared formulations were divided into groups and kept at specified storage conditions as per ICH guidelines. The sample was withdrawn periodically and tested for various evaluation parameters. The results of the stability study are tabulated in table respectively

Table 13: Stability Study of F4 Transferosomal Gel

Formulation	**F4**			
Storage Condition	**25℃± 2℃/ 60 % RH ± 5 % RH**			
Time interval (days)	**0**	**30**	**60**	**90**
Colour	White to off white	White to off white	White to off white	White to off white
Homogeneity	+++	+++	+++	+++
pH	5.8	6.0	6.0	6.1
Viscosity (cP)	55417	54120	54012	52059
Spreadability (g.cm/sec)	0.229±0.01	0.226±0.05	0.225±0.02	0.224±0.06
Extrudability	++	++	++	++
Drug content uniformity (%)	98.90	98.82	98.72	98.60
+++ Excellent, **++** Good, **+** Satisfactory, **-** Poor, **--** Fail				

Discussion: There was not much more variation in the properties of transferosomal gel F4 under stability study as the formulation retained all the properties when stored at specified storage conditions over a while, indicating that the transferosomal gel was very much stable.

4. CONCLUSION:

The aim of the research was to formulate and evaluate Transferosomal gel of Mometasone furoate. Preformulation studies shows high solubility in phosphate buffer pH 6.8 and ethanol, Absorption maxima of Mometasone furoate was found to be 240 nm whereas, FTIR shows no interaction between the drug and studied excipients. Total Eight formulations (F1 to F8) were formulated by thin film hydration technique and the optimized formulation F4 showed small particle size (152.48 nm), entrapment efficiency %EE of 87.16%, and %Cumulative Drug Release of (97.14%). SEM of optimized Transferosome appeared as spherical, well identified, Unilamellar vesicles. The optimized formulation of Transferosomes was further formulated to gel with Carbopol-940 (0.2 to 0.8% w/w), HPMC k15 (0.2 to 0.8% w/w), Propylene glycol, Triethanolamine and Isopropyl alcohol. Among these, F4 formulation with Carbopol-940 0.8%w/w transferosomal gel is the optimized transferosomal gel and showed Spreadability value 0.229±0.01gm.cm/sec, pH value 5.8. The actual drug content of the Transferosomal gel was found to be 98.90%, which represents good content uniformity. The viscosity of optimized Transferosomal gel was found to 55417cps. The percentage drug release for Transferosomal gel was 98.22%. The stability studies showed it was stable throughout the shelf life of the product and revealed it follows Higuchi order kinetics. In the end, it is proved to be valid that Mometasone Furoate transferosomal gel is clinically beneficial of management for localized skin infections and is likely to be profitably developed as an industrial item to enhance the anti-inflammatory and immunosuppressant abilities.

Conflicts of Interest:

The authors have no conflicts of interest regarding this investigation.

REFERENCES:

1. Rastogi V, Yadav P, "Transdermal drug delivery system: An overview" Asian Journal of Pharmaceutics, 2012; 6(3):161-170. DOI:10.4103/0973-8398.104828 https://doi.org/10.4103/0973-8398.104828

2. Ansel HC, Allen LV and Popovich NG. Pharmaceutical dosage forms and drug delivery system. 7th ed. New York: Lipponcott Williams and Wilkins; 2002.

3. Patel RP, Baria AH, "Formulation and evaluation consideration of transdermal drug delivery system" Int J Pharm Res, 2011; 3:1-9.

4. Solanki D, Kushwah L, Mohit Motiwale and Vicky Chouhan, "Transferosomes - A Review" World Journal of Pharmacy and Pharmaceutical Sciences, 2016; 5(10):435-449. https://doi.org/10.20959/wjpps201610-7845

5. Eldhose MP, Mathew F, Mathew NJ, "Transfersomes - A Review" International Journal of Pharmacy and Pharmaceutical Research, 2016; 6(4): 436-452.

6. Prajapati ST, Patel CG, Patel CN, 'Transferosomes: A Vesicular Carrier System for Transdermal Drug Delivery', Asian Journal of Biochemical and Pharmaceutical Research, 2011; 2(1):507-524. https://doi.org/10.4103/2231-4040.85524 PMid:22171309 PMCid:PMC3217704

7. Kumari K, Sara UVS, Sachdeva M, "Formulation and Evaluation of Topical Hydrogel of Mometasone Furoate using Different Polymers" International Journal of Pharmaceutical and Chemical Sciences, 2013; 2(1):89-100.

8. Chandira RM and Pradeep Pasupathi A., "Design, Development and Formulation of Antiacne Dermatological Gel" Journal of Chemical and Pharmaceutical Research, 2010; 2(1):401-404.

9. Patel RP, Patel GI, and Kamani R. Formulation, "Optimization and Evaluation of Mometasone Furoate Gel" Journal of Pharmacy Research, 2009; 2(11):720-724.

10. Madan RJ, Khude PA, Dua K, "Development and evaluation of solid lipid nanoparticles of mometasone furoate for topical delivery" International Journal of Pharmaceutical Investigation, 2014; 4(2):60-64. https://doi.org/10.4103/2230-973X.133047 PMid:25006550 PMCid:PMC4083535

11. Mendonca CO, Burden AD, "Current concepts in psoriasis and its treatment" Pharmacology & Therapeutics, 2003; 99(2):133-147. https://doi.org/10.1016/S0163-7258(03)00041-X PMid:12888109

12. Patel TJ, Khan AM, Shah DP, "Formulation and Characterization of Nanosponge Loaded Gel of Mometasone Furoate for Topical Delivery" International Journal of Modern Pharmaceutical Research, 2022; 6(11):116-122.

13. Khalid M, Fathy I, Ahmed E, Abd E, Alaa E, "Diacerein niosomal gel for topical delivery: development, in vitro and in vivo assessment" J Liposome Res, 2015;1-12.

14. Rehman M, Madni A, Ihsan A, Khan WS, Khan MI, Mahmood MA, Ashfaq M, Bajwa SZ, Shakir I, "Solid and liquid lipid-based binary solid lipid nanoparticles of diacerein: in vitro evaluation of sustained release, simultaneous loading of gold nanoparticles, and potential thermos responsive behavior" International Journal of Nanomedicine, 2015; 10(1):2805-2814. https://doi.org/10.2147/IJN.S67147 PMid:25897224 PMCid:PMC4396646

15. Chien YW and Banga AK, 'Iontophoretic (transdermal) delivery of drugs: overview of historical development' Journal of Pharmaceutical Sciences, 1989; 78(5):353-354. https://doi.org/10.1002/jps.2600780502 PMid:2664122

16. Yameen SH, Shahidulla SM, "Formulation and evaluation of Lamivudine transferosomal gel" Journal of Drug Delivery and Therapeutics, 2022; 12(6):163-170. https://doi.org/10.22270/jddt.v12i4-S.5768

17. Farooqui N, Kar M, Jain S, "Development and evaluation of proniosomes as drug carriers for transdermal delivery of ketorolac tromethamine" Journal of Drug Delivery and Therapeutics, 2017; 7(7):38-40. https://doi.org/10.22270/jddt.v7i7.1580

18. Nimker V, Jamal H, Ghosh P, Jain S, Beotra A, "Liposomes: drug delivery system or possible doping agent?" Journal of Drug Delivery and Therapeutics, 2017; 7(1):25-29. https://doi.org/10.22270/jddt.v7i1.1369

19. Mishra M. and Biswal P, "Complexation, Optimization, Formulation development and characterization of clindamycin phosphate gel using zinc acetate dehydrate" International journal of pharmacy, 2012; 2(3):472-486.

20. Gupta A, Mishra AK, Singh AK, Gupta V and Bansal P, "Formulation and evaluation of topical gel of Diclofenac sodium using different polymers" Drug Invention Today, 2010; 2(5):250-253.

21. Jivrani Shilpa D, Patel Vijay K, Formulation, "Development and Evaluation of Niosomal Drug Delivery System for Clindamycin Phosphate" Pharma Science Monitor, 2014; 5(2):256-274.

22. Kurmi S, Khangar PK, Jain V, Jain DK, "Formulation, Development and Evaluation of Transfersomal Gel of Miconazole Nitrate" IAJPS, 2022; 09(04):344-351. https://zenodo.org/records/6487369