Journal of Chemical and Pharmaceutical Sciences

Journal of Chemical and Pharmaceutical Sciences-JCHPS (2024) 17 (3): 01-12
Online ISSN: Online 2349-8552, Print ISSN: 0974-2115
Research Article | Chemical Sciences | MCI Approved | Peer-Reviewed | Referred | OA Journal |

Enhanced Delivery Systems: Formulating and Evaluating Topical Ciprofloxacin Pharmacosomal Gels

Aravind Nandini [1]*, Shiva Kumar Ravula [2], Priyanka Gannarapu [2], Vivek Sagar P [3]
[1]Department of Pharmaceutics, Vikas College of Pharmacy, Telangana, India.
[2]Department of Pharmaceutics, Vaagdevi Pharmacy College, Warangal, Telangana, India.
[3]Department of Pharmaceutical Analysis, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Secunderabad, Telangana, India.

Received: 6 May 2024 / Accepted: 10 Jun 2024 / Published online: 01 Jul 2024
*Corresponding Author Email: nandiniaravind@gmail.com

ABSTRACT

Compared to conventional gels, the pharmacosomal gel offers several advantages which are enhanced penetration and residence time of drug at the infection site, Improved drug release kinetics and skin permeation, Sustained release profile, reducing dosing frequency, bypassing first-pass metabolism, potentially increasing drug efficacy. Ciprofloxacin, a broad-spectrum antibiotic, has been formulated into a topical pharmacosomal gel to improve its delivery for treating skin infections. This research investigated the effectiveness of pharmacosomes as carriers for topical ciprofloxacin delivery. Pharmacosomal formulation developed and optimized for ciprofloxacin (F6) with high drug entrapment efficiency (96.41%). This formulation showed sustained release of the drug (98.27% over 24 hours) and desirable characteristics like a spherical shape, smooth surface, and negative zeta potential.In-vivo tests further confirmed the benefits of the ciprofloxacin pharmacosomal gel. It exhibited significant wound healing activity, reduced inflammation, and provided a depot effect for sustained drug delivery compared to a plain ciprofloxacin gel. These findings suggest that ciprofloxacin pharmacosomal gel is a promising and potentially superior alternative to existing treatments for topical bacterial infections and wound healing.

KEY WORDS: Ciprofloxacin, Pharmacosomal gel, *In vitro* Release studies.

INTRODUCTION:

Topical drug delivery systems have gained significant attention in recent years due to their ability to deliver drugs directly to the target site, thereby enhancing efficacy and minimizing systemic side effects. Ciprofloxacin, a broad spectrum antibiotic, is widely used for the treatment of various bacterial infections. However, its topical application has been limited due to factors such as low skin permeability and rapid drug degradation. To overcome the challenges associated with topical delivery of ciprofloxacin, the development of an efficient and sustained-release drug delivery system is essential. Pharmacosomes, as novel drug carriers, have shown promise in enhancing drug delivery to the skin. Ciprofloxacin, its empirical formula is $C_{17}H_{18}FN_3O_3$. HCl. H_2O (Figure 1) is a fluoroquinolone, since it contains a fluorine atom at position 6 of the 4-quinolone nucleus Fluoroquinolones have an expanded spectrum of activity and increased antibacterial potency compared with non-fluorinated quinolones (e.g., cinoxacin, nalidixic acid, oxolinic acid) [9]. Ciprofloxacin, like other fluoroquinolones, contains a piperazine group at position 7 of the 4-quinolone nucleus, which results in antipseudomonal activity. The drug also contains a cyclopropyl group at position1, which enhances antimicrobial activity [10]. Ciprofloxacin inhibits DNA gyrase enzyme of bacteria which is responsible for the continuous introduction of negative supercoils into DNA, so ciprofloxacin is considered a bactericidal agent. The concentration needed to inhibit gyrase –mediated DNA super coiling is between (0.1-10 µg/ml)

The primary objective of this study is to formulate and evaluate topical ciprofloxacin-loaded pharmacosomal gel formulations. The research aims to improve the drug's skin penetration, prolong its residence time at the application site, and consequently enhance its therapeutic efficacy. It is hypothesized that the incorporation of ciprofloxacin into pharmacosomes will significantly enhance its transdermal delivery compared to conventional gel formulations. The

Journal of Chemical and Pharmaceutical Sciences -JCHPS (2024) 17 (3): 01-12
Online ISSN: Online 2349-8552, Print ISSN: 0974-2115
Research Article | Chemical Sciences | MCI Approved | Peer-Reviewed | Referred | OA Journal |

pharmacosomal gel is expected to exhibit improved drug release kinetics, better skin permeation, and enhanced therapeutic efficacy.

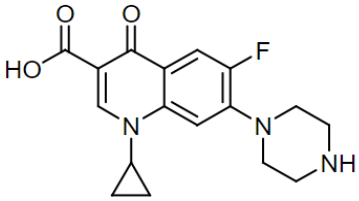

Figure 1: Ciprofloxacin HCl Chemical Structure

2. MATERIALS AND METHODS:

Important equipment utilized in this study included a weighing balance for precise measurement, a UV-visible spectrophotometer for drug quantification, a pH meter for pH determination, an FT-IR spectrophotometer for material characterization, a scanning electron microscope (SEM) for morphological analysis of pharmacosomes, a homogenizer for formulation preparation, a lyophilizer for drying, a particle size analyzer for particle size distribution, a zeta potential analyzer for determining zeta potential, and a viscometer for viscosity measurement.

Analytical Method Development

Preparation Of Calibration Curve: For the preparation of calibration curve stock solution was prepared by dissolving100 mg of accurately weighed drug in 100ml of methanol (1mg/ml). Further 1ml of the stock solution was pipette out into a 100ml volumetric flask and volume was made up with phosphate buffer (7.4 PH). From this stock solution pipette out 1ml and dilute to 10 ml with phosphate buffer and subject for UV scanning in the range of 200-400 nm using double beam UV spectrophotometer. The absorption maximum was obtained at 329 nm with a characteristic peak. Preparation of calibration curve: Methanol was used for solubilizing the drug. Stock solution (1 mg/mL) of Ciprofloxacin was prepared in methanol and subsequent working standards (2, 4, 6, 8 and 10 µg/ml) were prepared by dilution with phosphate buffer of pH-7.4. These solutions were used for the estimation Ciprofloxacin by UV method. The whole procedure was repeated three times, and the average peak area was calculated. Calibration plot was drawn between concentrations and peak area. Calibration equation and R2 value are reported.

Preparation of pharmacosomal gel

Preparation of Ciprofloxacin loaded pharmacosomes

Ciprofloxacin (CPX) is acidified with 1N HCl, this will result in the formation of drug acid that contains free carboxyl group. Free CPX extracted into chloroform by shake flask method. This aqueous solution of drug is then transferred into a 100 ml of separating funnel with chloroform and shaken well for 30 minutes. Then the separating funnel is kept for about 24 hours. CPX extracted into chloroform mixed with methanol in which phosphatidylcholine was dissolved in a 250 ml round bottom flask and refluxed for 3hours at 45°C. After 3 hrs. this mixed solution is transferred into Round Bottom Flask (RBF) and subjected to solvent evaporation, a thin film of solid mixture is deposited on the wall of RBF. Film is hydrated with buffer solution followed by sonication. The resultant Pharmacosomes are collected and placed in a vacuum desiccator overnight and then subjected to characterization.

Table 1: Composition of Ciprofloxacin pharmacosomes formulations (F1 to F6)

Ingredients	F1	F2	F3	F4	F5	F6
Ciprofloxacin HCI (mg)	100	100	100	100	100	100
Soya lecithin (mg)	88	176	264	352	440	528
Chloroform + Methanol 1:1 (ml)	20	20	20	20	20	20
HCL (ml)	5	5	5	-	-	.
Dichloromethane (ml)	-	-	-	10	10	10
Sodium benzoate (mg)	5	5	5	5	5	5
7.4 Phosphate buffer	15	15	15	15	15	15

Preparation Pharmacosomal gel of Ciprofloxacin:

A 5% W/W Ciprofloxacin Pharmacosomal gel is formulated using 1% Carbopol 934 as a gelling agent. The accurately weighed polymer is sprinkled into a beaker containing 60 mL boiling distilled water, and then soaking is allowed overnight. The Pharmacosomal dispersion containing 5% Ciprofloxacin is added with continuous stirring to allow homogeneous distribution of Ciprofloxacin Pharmacosomes within the gel base. Sodium benzoate is used as preservatives. The dispersion is neutralized by addition of Triethanolamine drop wise, with continuous mixing until a homogenous gel is obtained.

Characterization of pharmacosomes:

FTIR Spectroscopy

The formation of Complex is confirmed by comparing the infrared spectra of conjugate with individual components and physical mixtures. The spectrum of conjugates differs significantly from that of individual components or physical mixtures due to chemical interactions between the drug and the phospholipid, which result in the formation of new bonds. XRPD X-ray powder diffraction was used to determine the crystalline state of CPXHCL. An aluminum sample holder was used to hold the powder sample. The X-ray generator used the Ka lines of copper as the radiation source and ran at 40kV tube voltages and 30mA tube current. Scanning angles ranged from 10 to 80 degrees, with 2θ in step scan mode. X-ray diffraction was used to examine the drug, phosphatidylcholine and pharmacosome.

Particle shape:

Scanning Electron Microscopy (SEM) was used to examine the surface morphology (roundness, smoothness, and aggregation formation) of Pharmacosomes Particle size, poly dispersity index and zetapotential Zetasizernano S90 is used to measure vesicle size and surface charge of the particles. Zeta potential measurements are routinely used to determine colloidal system stability. If all of the particles in suspension have a large negative or positive zeta potential, they will resist each other, and no aggregation will occur. If the particles have a low zeta potential, however, there will be no force to prevent them from flocculating. A laser is utilized to produce a light source that illuminates particles within the samples in order to detect the zeta potential. Particle suspensions with zeta potentials greater than or equal to +30 mV are considered stable.

Entrapment efficiency:

The entrapment efficiency of Pharmacosomes is measured using the centrifugation method. Laboratory centrifuge, an aliquot of Pharmacosomal suspension is centrifuged at 5000 rpm for 35minutes at 4°C. The unentrapped drug is carefully separated from the clear supernatant, and the absorbance is measured. The sediment in the centrifuge tube is washed three times with a suitable solvent and then diluted to 5 mL with the same solvent before being tested for absorbance. To generate a calibration curve, different concentrations of appropriate solvents (1g/mL-10 /10 mL) are used. The supernatant and sediment are used to calculate the total quantity of drug in a 1 mL suspension.

Entrapment efficiency % = Total drug –free drug/ Total Drug (100)

Pharmacosomes are dispersed insufficient dichloromethane (5 ml/mg Ciprofloxacin). The complex and phospholipids both were easily checked up in the dichloromethane. The Ciprofloxacin non-complexes are sediment and separated into assay. The yield of Ciprofloxacin present as a complex (%) was defined using the following formula equation. Where, a is the content of Ciprofloxacin present as a complex, b is the content of Ciprofloxacin no present as a complex‖ in the complex

Evaluation of Pharmacosomal gel of Ciprofloxacin:

Physical appearance and homogenesity

It is important for patient compliance to determine the homogeneity of semisolid dosage forms which are applied topically on the skin. This is done by pressing a small quantity of gels between the thumb and the index finger. Consistency is determined as homogeneous or not.

Viscosity:

The viscosity of gel was measured by a Brookfield viscometer (Brookfield DVE) using spindle number S64 rotated at a speed of 12 rpm for a 10-s run time at 37°C.

pH Measurement:

One gram of gel is dispersed in 20 mL of distilled water, and a digital pH meter is used to determine the pH value. The measurement is performed three times and the mean ±SD was calculated.

Spreadability:

The Spreadability of gel formulations is determined by measuring the spreading diameter of 1g of gel between two horizontal plates (20 cm × 20 cm).

$$S = M \times L/T$$

Where, S is the Spreadability in g/s, M is the mass in grams L is the length of gel spread and T is the time in seconds.

Drug Content:

The Ciprofloxacin content is measured by placing 1 g of gel onto a clean volumetric flask (100 mL) and completing the volume with 7.4 pH buffer. This is then stirred for 2 h. Solution is filtered, and samples are analyzed spectrophotometrically at specific wavelength.

In-Vitro diffusion studies:

A diffusion study of Ciprofloxacin loaded Pharmacosomal gel is carried out using Franz diffusion cell through dialysis membrane. Dialysis membrane is soaked in distilled water for 24 hours. The receptor compartment is filled with phosphate buffer pH 7.4 and donor compartment contain 1g of Pharmacosomal gel (equivalent to 5mg) on dialysis membrane with exposure area of 2cm2 to receptor medium and whole assembly is kept on magnetic stirrer at 600rpm for a period of 10 hours and samples are withdrawn at specified time interval of 1 hr. and replaced with equal volume of buffer. Samples were appropriately diluted with buffer and analyzed using UV spectrophotometer at 247n. Steady state Flux (Jss) is calculated from the slop of the linear part of the cumulative amount of drug permeated per unit area (µg/cm2) against a time (h) plot.

Permeability coefficient (Kp) =Jss/Co, (Co = initial CPX concentration.

Stability studies:

The stability studies of Ciprofloxacin Pharmacosomal gel of optimize formulationare conducted at refrigerated temperature (4°C) and room temperature as per Guidelines of International Conference on Harmonization (ICH). Samples are analyzed for physical appearance, drug content, entrapment efficiencyand in vitro diffusion studies after 30 days.

Release kinetic Profile of Pharmacosomal Gel of Ciprofloxacin:

Zero order kinetics:

Zero order release would be predicted by the following equation:

$$A_t = A_0 - K0_t$$

Where, At= Drug release at time 't' A0= Initial drug concentration

K0= Zero-order rate constant (hr^{-1})

When the data is plotted as cumulative percent drug release versus time, if the plot is linear then the data obeys zero-order kinetics, and its slope is equal to zero order release constant K_0.

First order kinetics:

First order kinetics could be predicted by the following equation:

$$\text{Log } C = \log C_0 - K_t / 2.303$$

Where, C= Amount of drug remained at Time _t. C_0= Initial amount of drug. K= First order rate constant (hr^{-1})

When the data plotted as log cumulative percent drug remaining versus time yields a straight line, indicating that the release follow first order kinetics. The constant K_t can be obtained by multiplying 2.303 with the slope value.

Higuchi's model:

Journal of Chemical and Pharmaceutical Sciences -JCHPS (2024) 17 (3): 01-12
Online ISSN: Online 2349-8552, Print ISSN: 0974-2115
Research Article | Chemical Sciences | MCI Approved | Peer-Reviewed | Referred | OA Journal |

Drug release from the matrix devices by diffusion has been described by following

Higuchi's classical diffusion equation:

$$Q= [D\epsilon/\tau\ (2A-\epsilon CS)\ CS_t]1/2$$

Where, Q= Amount of drug release at time 't'. D= Diffusion coefficient of the drug in the matrix. A= Total amount of drug in unit volume of matrix. CS = Solubility of drug in matrix. Є= Porosity of the matrix. T= Tortuosity. t = Time (hrs. at which q amount of drug is released).

3. RESULTS AND DISCUSSION

CALIBRATION PLOT OF CIPROFLOXACIN IN PHOSPHATE BUFFER OF pH 7.4:

Standard graph of Ciprofloxacin HCL was plotted as per the procedure in experimental method and its linearity is shown in following Table 1 and Figure 2. The standard graph of Ciprofloxacin HCL showed good linearity with R2 of 0.999, which indicates that it obeys "Beer- Lamberts" law.

Table 1: Calibration curve of Ciprofloxacin HCL in phosphate buffer pH 7.4

Concentration (µg/mL)	Absorbance
0	0.000
2	0.134
4	0.237
6	0.347
8	0.468
10	0.589

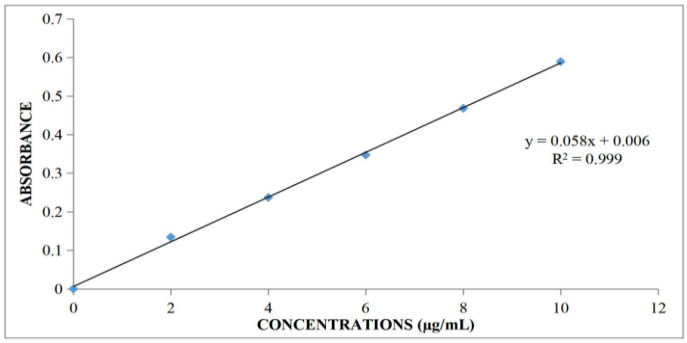

Figure 2: Standard graph of Ciprofloxacin

Characterization of pharmacosomes:

Table 2: Percentage yield, Drug Content, Entrapment Efficiency of all pharmacosomes formulations.

Formulation Code	Percentage yield (%)	Drug Content (%)	Entrapment Efficiency (%)
F1	68.01	71.16	63.54
F2	75.96	75.34	72.43
F3	80.5	89.26	86.6
F4	83.34	86.99	90.11
F5	92.16	93.76	93.34
F6	97.37	98.53	96.41

Journal of Chemical and Pharmaceutical Sciences -JCHPS (2024) 17 (3): 01-12
Online ISSN: Online 2349-8552, Print ISSN: 0974-2115
Research Article | Chemical Sciences | MCI Approved | Peer-Reviewed | Referred | OA Journal |

Table 3: Vesicles size, PDI, Zeta Potential of all pharmacosomes formulations

Formulation	Average Vesicles Size (µm)	PDI	Zeta Potential (mV)
F1	1.63	3.525	-4.31
F2	1.89	2.89	-6.29
F3	3.1	2.536	-8.1
F4	1.99	1.26	-25.43
F5	2.04	1.201	-28.82
F6	3.56	1.125	-32.97

The particle size of the all formulations was observed in the range of 1.63 to 3.56 µm. The average particle size, PDI observed in the F6 formulation i.e., 3.56µm, 1.125 respectively. The particle size was found to be increased with increase in soya lecithin concentration but as the Dichloromethane concentration was increased the size range of pharmacosomes was decreased, Dichloromethane probably caused an alteration of the net charge of the system and conferred it some extent of steric stabilization that might finally lead to a reduction in the vesicle size. Depending upon the size range the order for the formulationwasF1<F2<F4<F5<F3

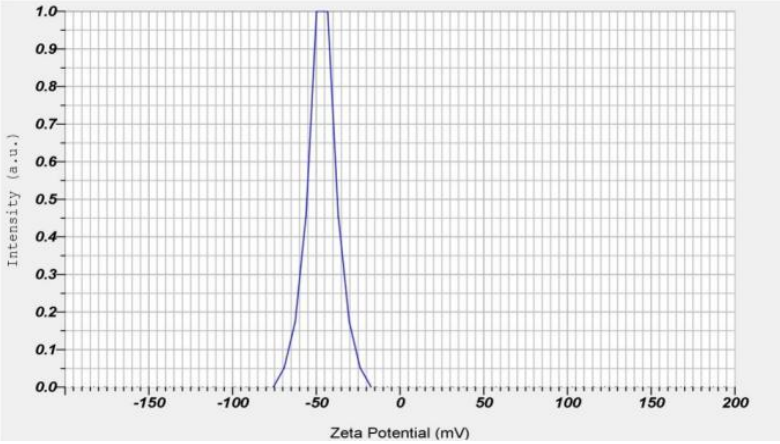

Figure 3: Zeta potential of F6 formulation

SEM

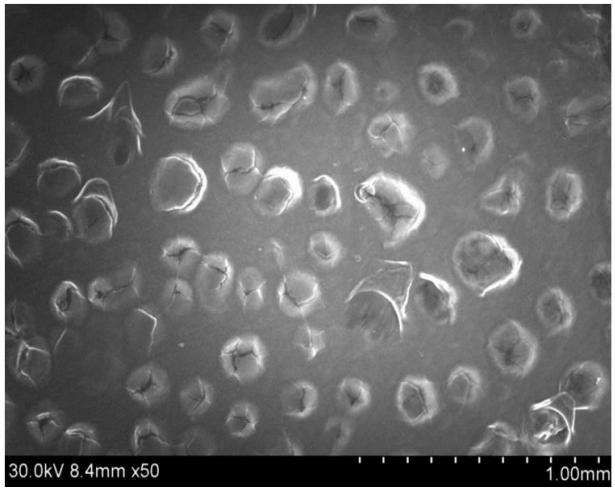

Figure 4: Ciprofloxacin HCl F6 optimised Pharmacosomes

SEM studies showed that the Ciprofloxacin HCl Pharmacosomes had a spherical shape withasmooth surface as shown in Figure 4.

Journal of Chemical and Pharmaceutical Sciences -JCHPS (2024) 17 (3): 01-12
Online ISSN: Online 2349-8552, Print ISSN: 0974-2115
Research Article | Chemical Sciences | MCI Approved | Peer-Reviewed | Referred | OA Journal |

DSC:

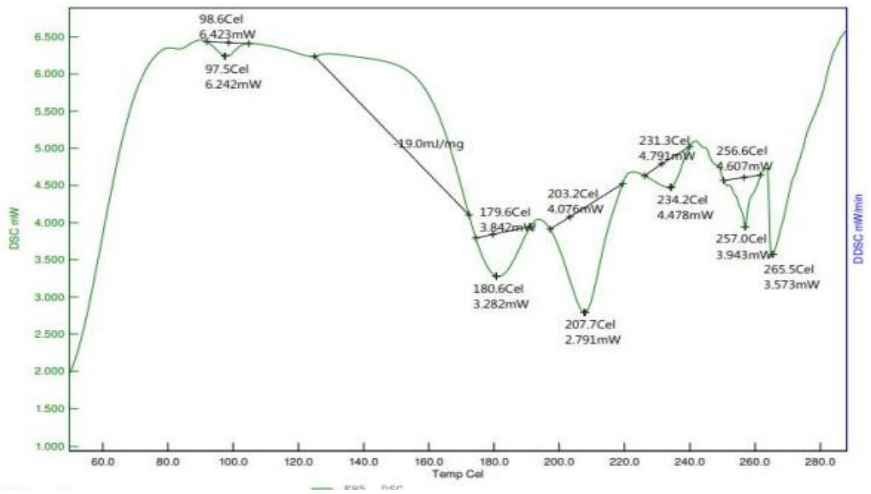

Figure 5: DSC Ciprofloxacin HCl drug

Powder X-ray Diffraction Studies (PXRD)

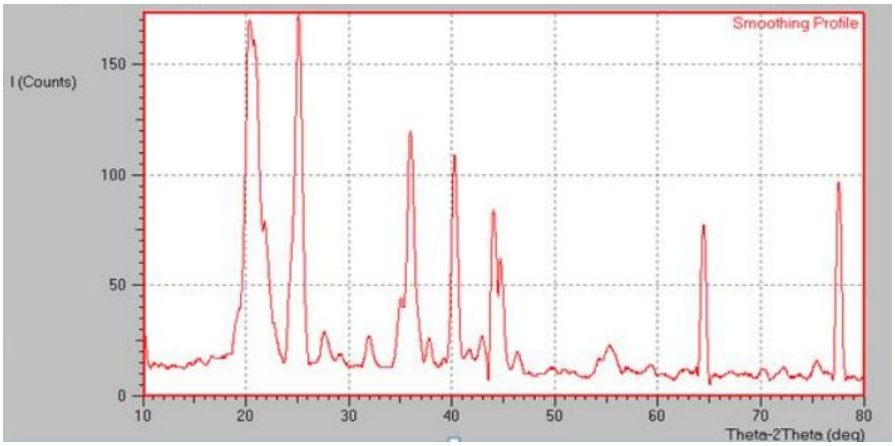

Figure 6: XRD for optimized formulation

In vitro dissolution studies of F1-F6 pharmacosomes formulations:

Table 4: In vitro dissolution studies of F1-F6 pharmacosomes formulations in percentage

Time (hour)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	12.96	18.36	22.09	23.2	32.96	45.12
2	23.43	28.92	36.25	30.59	40.24	52.98
4	30.3	34.01	47.29	46.61	52.35	65.89
6	38.16	49.26	55.76	53.03	63.99	78.14
8	47.89	56.74	62.12	63.9	76.13	85.22
10	52.6	67.96	82.96	75.83	81.75	87.53
12	65.14	81.55	87.03	82.34	89.69	94.69
24	82.76	90.46	93.54	86.27	94.82	97.89

Journal of Chemical and Pharmaceutical Sciences -JCHPS (2024) 17 (3): 01-12
Online ISSN: Online 2349-8552, Print ISSN: 0974-2115
Research Article | Chemical Sciences | MCI Approved | Peer-Reviewed | Referred | OA Journal |

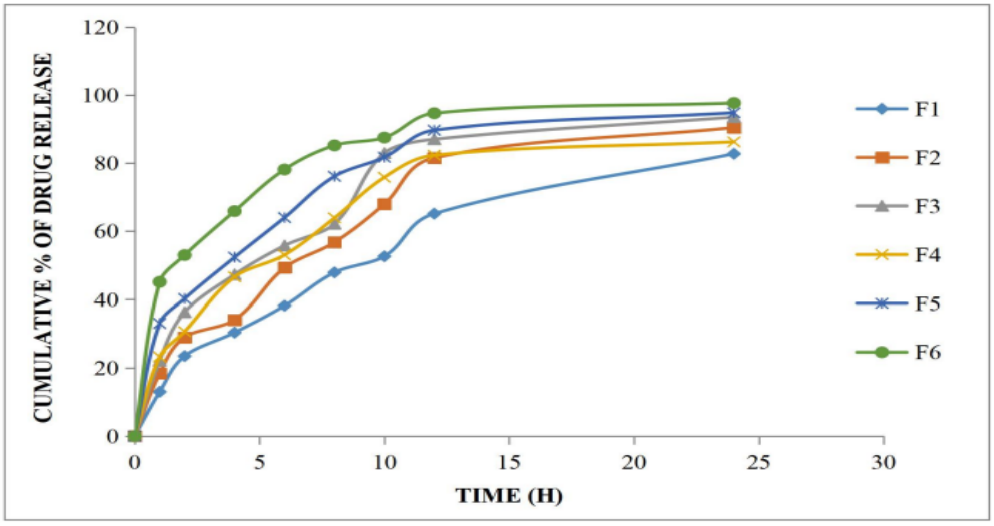

Figure 7: In vitro dissolution studies of F1-F6 pharmacosomes formulations

In vitro drug release study of the selected pharmacosomes (F1, F2, F3, F4, F5 and F6) was carried out. The pharmacosomes exhibited 24 hours sustained release pattern. Formulations F1, F2 and F3 were prepared with 5mL HCL and 1:1, 1:2, 1:3 of drug: Lecithin (Soya lecithin). Formulations F1, F2 and F3 were prepared with 10mL Dichloromethane and 1:1, 1:2, 1:3of drug: Lecithin (Soya lecithin). Formulations F1, F2, F3 were prepared with HCL quantity of 5 mL, 88 mg, 176 mg and264mgof Lecithin showed the cumulative percentage of drug release 82.76 %, 90.46 % and 93.54 % respectively at the end of 24 hours. Formulations F4, F5 and F6 were prepared with Dichloromethane quantity of 10mL, 352mg, 440 mg and 528 mg of Lecithin showed the cumulative percentage of drug release 86.27%, 94.82% and 97.89% respectively at the end of 24 hours. The Ciprofloxacin -loaded pharmacosomes F6 showed a better release profile of 97.89% by 24 hours. It was considered as optimized formulation.

PHARMACOSOMAL GEL EVALAUTION PARAMETERS

Immediately after the formulations were prepared their physical characteristics of formulations were studied and the data was shown in Table 5. Thus, all the formulations exhibited good characteristics like homogeneity in colour, and appearance. Topical gel formulation was prepared by 1% Carbopol 934 the concentration of polymer. For the formulations pH was determined and the results were shown in Table 5. From the results it was found that, pH of gel formulations was in the range 5 to 6 which lies in the skin normal pH range (5.7 and 6.2). The minimum pH of the gels should be less than neutral i.e., 7.0. The tests were performed using a Brookfield viscometer. The viscosity of the prepared gel showed direct proportion with the concentration of polymer. The order of viscosity of the formulations indicates the concentration of Carbopol agent higher will be viscosity. The results are shown in Table 5. Viscosity of formulation (F6) 1% Carbopol 934 is 56241cps which is of proper viscosity. The percentage drug content was found to be in between 80% to 100%CiprofloxacinHCl indicating good content uniformity in formulations (F6) means drug was uniformly distributed throughout the gel.

Table 5: Pharmacosomal Gel Evalaution Parameters

Formulation	pH	Viscosity (cp)	Clarity	Extrudability	Homogeneity	Drug Content (%)	Spreadability (g.cm/sec)
F6	5.93	56241	++	Very Good	Excellent	98.34	0.102±0.06

Journal of Chemical and Pharmaceutical Sciences -JCHPS (2024) 17 (3): 01-12
Online ISSN: Online 2349-8552, Print ISSN: 0974-2115
Research Article | Chemical Sciences | MCI Approved | Peer-Reviewed | Referred | OA Journal |

Table 6: *In vitro* permeation studies of Pharmacosomal gel:

Time (hrs)	0	1	2	4	6	8	10	12	24
F6	0	41.39	48.16	61.9	69.82	76.11	85.67	90.39	98.27

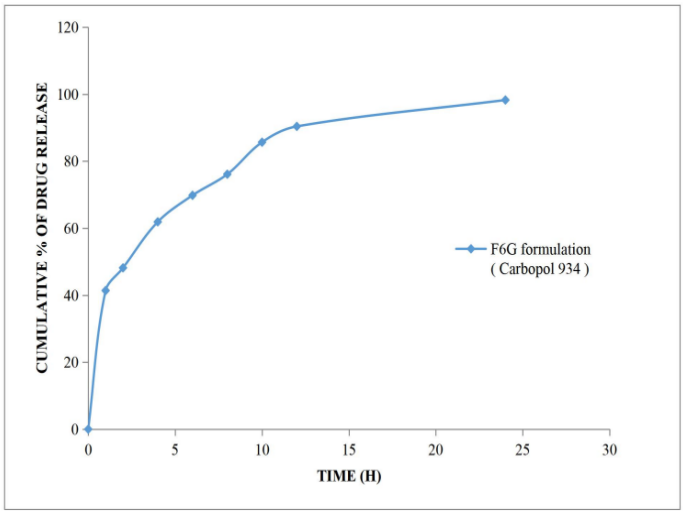

Figure- 8: *In vitro* permeation studies for Pharmacosomal gel with different polymers of Carbopol 934

F6 optimized 1% Carbopol 934 gel highest drug release (98.27% for 24 hours), good Homogenity, highest drug content, Proper viscosity. Hence it was considered as optimized formulation

Release Kinetics

To analyze the drug release mechanism the in vitro release was fitted into various release equations and kinetic models first order, zero order, Higuchi and Korsmeyer-peppas. The release kinetics of optimized formulation F6 (1% Carbopol 934 gel) is shown in Table 7 and in following Figures.

Table- 7: Release kinetics of optimised 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	4.64	4.64	0.00
41.39	I	1.00	1.617	0.00	1.768	41.390	0.0242	-0.383	58.61	4.64	3.88	0.75
48.16	2	1,41	1,683	0.30	1.715	24.080	0.0208	-0.317	51.84	4,64	3,72	0.91
61.9	4	2.00	1,792	0.60	1.581	15.475	0.0162	-0.208	38.1	4,64	3.36	1.27
69.82	6	2,44	1,844	0.77	1.480	11.637	0.0143	-0.156	30.18	4.64	3.11	1.52
76.11	8	2.82	1.881	0.90	1.378	9.514	0.0131	-0.119	23.89	4.64	2.88	1,7
85.67	10	3.16	1.933	1.00	1,156	8,567	0.0117	-0.067	14.33	4,64	2,42	2,21
90.39	12	3.46	1,956	1,07	0.983	7.533	0.0111	-0.044	9.61	4,6	2,12	2,51
98.27	24	4.89	1,992	1,38	0.238	4.095	0.0102	-0.008	1.73	4.64	1.20	3.44

The prepared F6 optimized 1% Carbopol 934 gel was subjected to the drug release kinetics and release mechanism. The formulations were studied by fitting the drug release time profile with the various equations such as Zero order, First order, Higuchi and Korsmeyer pappas. The data revealed a better fit to the First order release model

Journal of Chemical and Pharmaceutical Sciences -JCHPS (2024) 17 (3): 01-12
Online ISSN: Online 2349-8552, Print ISSN: 0974-2115
Research Article | Chemical Sciences | MCI Approved | Peer-Reviewed | Referred | OA Journal |

FTIR

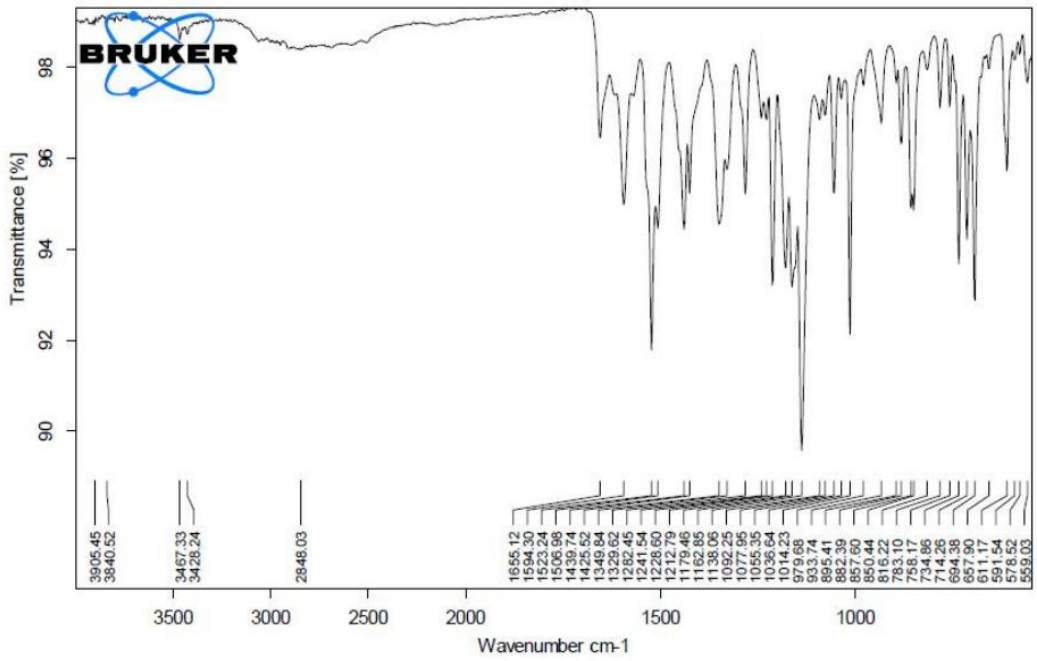

Figure 9: Ciprofloxacin HCl Pure drug FTIR

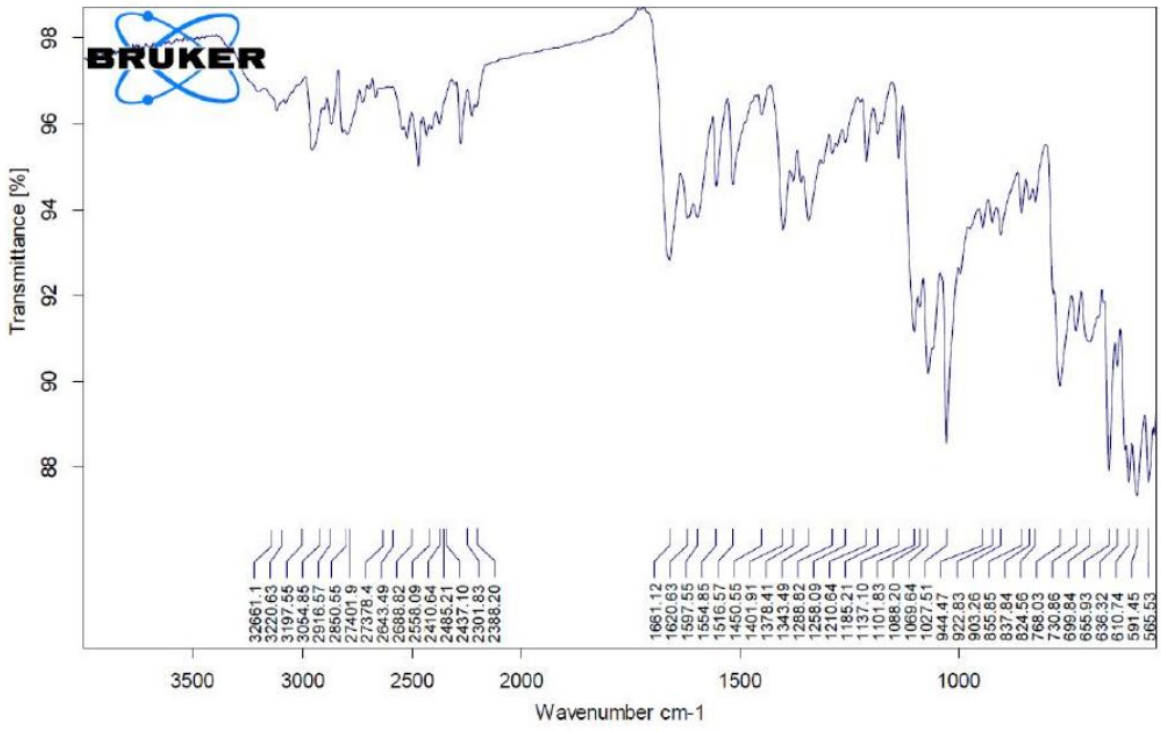

Figure 10: Ciprofloxacin F6 optimized 1% Carbopol 934 gel FTIR

Infrared studies were carried out to confirm the compatibility between the lipid, 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 drug-loaded Pharmacosomal gel. This indicated no interaction between the drug and other excipients.

STABILITY STUDIES

Stability studies of best formulation (F6) were carried out at a Refrigerated temperatureof4°C± 2°C for 30 days and Room temperature (25°C). After 30 days the sample was evaluated for the Drug content, and invitro drug release studies. The values are as shown in Table 8.

Table 8: Stability Studies at Refrigerated temperature (4°C) 30 days

Formulation	pH	Viscosity (cp)	Clarity	Extrudability	Homogeneity	Drug Content (%)	Spreadability (g.cm/sec)
F6	5.86	55135	++	Very Good	Excellent	98.12	0.105±1.09

After the study for 30 days, it was concluded that there was no major changes in the various parameters evaluated like physical appearance, percentage drug content and invitro permeation study of F6 at 4°C± 2°C and Room temperature 25°C. Thus, it can be conducted that F6 is stable at a 4°C± 2°C and Room temperature 25°C for a period of 30 days.

5. CONCLUSION

Novel vesicular drug delivery systems (Pharmacosomes) offer more advantages as compared to conventional drug delivery systems. Moreover, they are non-invasive, non-irritant and offers better functionality. Pharmacosomal systems are novel lipid vesicular carriers containing a relatively of HCL and Dichloromethane. These nanocarriers are especially designed for the efficient delivery of therapeutic agents with different physicochemical properties into deeps in layers and across the skin. Pharmacosomal were prepared by and optimized on the base of average vesicle size, % drug entrapment and drug release. The optimized formulation was further incorporated with gel base (Carbopol 934 gel) and characterized for their viscosity, pH, % drug content and drug release study. Optimized formulation (F6) of Pharmacosomes resulted in average vesicle size as 3.56µm, zeta potential as -32.97 mv, and % EE as 96.41%. Prepared gel of optimized formulation viscosity was 56241cps, pH was 5.93, %drug content was 98.53, and in vitro drug release found as 97.89 % in 24 h, respectively. It can be concluded that prepared gel containing Ciprofloxacin-loaded Pharmacosomal formulation was optimized and successfully formulated in the gel form can be use for topical preparation. The data shows that Ciprofloxacin Pharmacosomal gel provides sustained release profile as well as it is nonirritant in nature. The transdermal system offers complete bypass of first pass metabolism. Ciprofloxacin pharmacosomal gel showed greater stability when storedunderrefrigerated conditions and can be suitably used in pharmacotherapy of bacterial infections.

6. REFERENCES

1. Keith, A.D., 1983. Polymer matrix consideration for transdermal devices. Drug. Dev. Ind. Pharm., 9, 605-621.
2. Jain, A.K., Thomas, N.S., Panchagula, R., 2001. Transdermal drug delivery of imipramine hydrochloride.I. Effect of terpenes. J. controlled release, 79, 93-101.
3. Willams, A.C., Barry, B.W., 2004. Penetration Enhancers. Adv. Drug Del. Rev., 56, 603-618.
4. Pellet, M., Raghavan, S.L., Hadgraft, J., Davis, A., 2003. Application of Supersaturated Systems to Percutaneous Drag Delivery. In: Guy RH, Hadgraft J (Eds.) Transdermal Drug Delivery. 2nd Edition, 305-326. Marcel Dekker, NewYork.
5. Sharma, N., Agarwa, G., Rana, A.C., Bhat, Z.A., Kumar, D., 2011a. A Review: Transdermal Drug Delivery System: A Tool for Novel Drug Delivery System. Int. J. Drug Dev. & Res., 3, 70-84.

6. Allen, L.V., Popovich, N.G., Ansel, H.C., 2002. Pharmaceutical dosage forms and drug delivery systems, 7th edition, Lippincott Williams and Wilkins, 263-278.
7. Ramesh, G., Vamshi, V.Y., Kishan, V., Madhusudan, R.Y., 2007. Development of nitrendipine transdermal patches: in vitro and ex vivo characterization. Current Drug Del, 4, 69-76.
8. Ramesh, G., Vamshi, V.Y., Kishan, V., Madhusudan, R.Y., 2007b. Studies on the influence of penetration enhancers on in vitro permeation of carvedilol across rat abdominal skin. Current Trends in Biotechnology and Pharmacy, 1, 62-69.
9. Sharma, T., Rawal G., 2011b. Transdermal Therapeutic Systems: An Overview. Int. J. Pharm. Bio. Arch., 2, 1581-1587.
10. Chein, Y.W., 2005. Transdermal Drug Delivery, In: Swarbick J. editor, Novel Drug Delivery Systems, 2nd edition, New York: Marcel Dekker, 50, 301–380.
11. Barry B., 2002. Transdermal Drug Delivery, In: Aulton M. E., editor, Pharmaceutics: The Science of Dosage Form Design, Churchill Livingstone 499 – 533.Ltd.,
12. Bodae, H.E., De Hnn, F.H.N., 1994. Drug Permeation Enhancement: Theory and Application, In : Hsieh DS editor, Drugs and Pharmaceutical Sciences, New York : Marcel Dekker, 62, 59 – 90.
13. Zhou, Y., Wu, X.Y., 1997. Fine element analysis of diffusional drug release from complex matrix system. J. control Rel., 49, 277–288.
14. Misra, A.N., 1997. Transdermal Drug Delivery, In : Jain N.K., editor, Controlled and Novel Drug Delivery, first edition, CBS publication, 100 – 129.
15. Berner, B., John, V.A., 1994. Pharmacokinetic characterization of Transdermal delivery systems. Jour. Clinical pharmacokinetics, 26, 121-34.
16. Tsai, J.C., Guy, R.H., Thornfeldt, C.R., Gao,W.N., Feingold, K.R., Elias, P.M., 1998.Metabolic Approaches to Enhance Transdermal drug delivery. J. Pharm. Sci., 85,643-648.
17. Brown, M.B., Jones, S.A., 2000. Hyaluronic acid: a unique topical vehicle for localized drug delivery of drugs to the skin. JEDV; 19, 308-318.
18. Baker, W., Heller, J., 1989. Material Selection for Transdermal Delivery Systems, in Transdermal Drug Delivery: Developmental Issues and Research Initiatives. J. Hadgraft and R.H. Guys, Eds. New York: Marcel Dekker, 293-311.
19. Wiechers, J., 1992. Use of chemical penetration enhancers in Transdermal drug delivery- possibilities and difficulties. Acta pharm., 4, 123.
20. Yamamoto, T., Katakabe, K., Akiyoshi, K., Kan, K. Asano, T., 1990. Topical application of glibenclamide lowers blood glucose levels in rats. Diabetes res. Clin. Pract., 8, 19-22.
21. Al- Khamis, K., Davis, S.S., Hadgraft, J., 1986. Micro viscosity and drug release fromtopical gel formulations. Pharm. Res., 3, 214-217.
22. Anon, 1980. Transdermal delivery systems-general drug release standards. Pharmacopeial Forum., 14, 3860-3865. 24. Mayorga, P., Puisieux, F., Couarraze, G., 1996. Formulation study of Transdermal delivery system of primaquine. Int. J. Pharm., 132, 71-79. 25.
23. Deo, M.R., Sant, V.P., Parekh, S.R, Khopade, A.J. Banakar, U.V., 1997. Proliposome- based Transdermal delivery of levonorgestrel. J. Biomat. Appl., 12, 77-88. 26.
24. Crawford, R.R., Esmerian, O.K., 1997. Effect of plasticizers on some physical properties of cellulose acetate phthalate films. J. Pharm. Sci., 60, 312- 314. 27. Amidon, G.L., Lennernas, H., Shah, V.P., Crison, J.R., 1995.
25. A theoretical basis for a biopharmaceutic drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. Pharm. Res., 12, 413-420