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DESIGN AND DEVELOPMENT OF TRANSDERMAL GEL OF FEMCYCLOVIR

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ABSTRACT

Famciclovir is an antiviral drug widely used in the treatment of herpes simplex and herpes zoster infections; however, its oral administration is associated with frequent dosing and variable bioavailability. The present study aimed to formulate and evaluate a transdermal gel of famciclovir for sustained drug release and enhanced skin permeation. Preformulation studies, including organoleptic evaluation, melting point determination, solubility analysis, partition coefficient, UV spectrophotometric analysis, and FT-IR compatibility studies, confirmed the suitability of the drug and excipients for formulation development. Transdermal gels were prepared using Carbopol 940, HPMC K100M, aloe vera powder, and disodium EDTA as a penetration enhancer and were evaluated for physicochemical properties, pH, viscosity, spreadability, drug content, in vitro drug release, permeation using a Franz diffusion cell, release kinetics, and accelerated stability. Among all formulations, CHF-4 exhibited optimum characteristics with a pH of 7.3, viscosity of 6832 cP, spreadability of 12.722 g·cm/s, drug content of 98.42%, and cumulative drug release of 94.39% after 10 h. The optimized formulation demonstrated an enhancement ratio of 2.034 compared with the control formulation and followed the Higuchi diffusion model (R^2 = 0.982), indicating diffusion-controlled drug release. Stability studies showed no significant changes in the physicochemical characteristics or drug release profile after one month under accelerated storage conditions. The findings suggest that the optimized famciclovir transdermal gel is a promising alternative to conventional oral therapy, providing sustained drug release, improved transdermal permeation, and the potential to enhance therapeutic efficacy and patient compliance.

KEYWORDS: Famciclovir; Transdermal gel; Transdermal drug delivery system (TDDS); Antiviral.

1. INTRODUCTION

Transdermal drug delivery system is convenient route for the delivery of drugs having short biological half life. Transdermal drug delivery is based on absorption of drugs into the skin after topical application. Transdermal patches are pharmaceutical preparation of varying sizes containing one or more active ingredients that when applied to skin deliver drug directly into systemic circulation after passing through skin barrier [1].

Transdermal patches are delivered the drug through the skin in controlled and predetermined manner in order to increase the therapeutic efficacy of drug and reduced side effect of drug. Controlled drug release can be achieved by transdermal drug delivery systems (TDDS, Which can deliver the drug via the skin portal to systemic circulation at a predetermined rate over a prolonged period of time[2]. Transdermal formulation maintain drug concentration within the therapeutic window for prolong period of time ensuring that drug levels neither fall below the minimum effective concentration nor exceed the maximum effective concentration [2,3].

1.1. Structure of Skin

The human skin is a multilayered organ composed of many histological layers. Skin is most accessible organ in body [4]. Its major functions are; protection of major or vital internal organs from the external influences, temperature regulations, control of water output and sensation. The skin of an average adult body covers approximately surface area of two square meters and receives about one-third of the blood circulating through the body. Skin is the complex organ and allows the passage of various chemicals into and across the skin. Skin serves as the point of administration for systemically active drugs, the drug applied topically will be absorbed, first into the systemic circulation and then transported to target tissues [5,6].

1.2. Herpes Simplex Virus

Herpes simplex virus types 1 and 2 (HSV-1 and HSV-2) cause prevalent, chronic infections that have serious outcomes in some individuals. Neonatal herpes may occur when the infant traverses the cervix during maternal genital herpes. Genital herpes is a major risk factor for human immunodeficiency virus type 1 transmission. Considerable efforts have been made to design and test vaccines for HSV, focusing on genital infection with HSV-2.7 [7].

Herpes simplex virus (HSV) is a ubiquitous, enveloped, and doublestranded DNA virus,

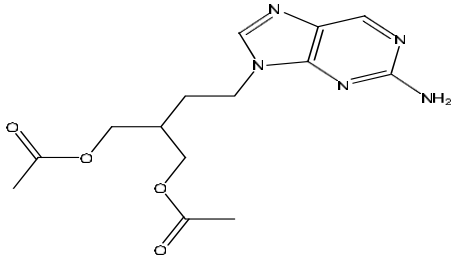
belonging to the family of Herpesviridae transmitted across mucosal membranes and nonintact skin, that migrate to nerve tissues, where they persist in a latent state. HSV-1 predominates in orofacial lesions, and it is typically found in the trigeminal ganglia, whereas HSV-2 is most commonly found in the lumbosacral ganglia [8]. Nevertheless these viruses can infect orofacial areas and the genital tract. In some developed countries type 1 has recently emerged as the prominent causative agent in genital lesions. Changes in sexual behaviours of young adults may partly explain its higher incidence. A first primary infection develops when a susceptible person (lacking of preexisting HSV-1 and HSV-2 antibodies) is exposed to HSV. Indeed, a first nonprimary episode occurs when a person with preexisting HSV antibodies (against type 1 or 2) experiences a first episode with the opposite HSV type. Recurrent infection occurs in a person with preexisting antibodies against the same HSV type8. Infections during pregnancy may be transmitted to newborns: HSV-1 and HSV-2 may cause eye or skin lesions, meningoencephalitis, disseminated infections, or foetal malformations. [9,10]

1.3. Famciclovir

Famciclovir is used to treat infections caused by certain types of viruses. It treats shingles caused by herpes zoster. It also treats outbreaks of herpes simplex that cause cold sores around the mouth, sores around the anus, and genital herpes. In people with frequent outbreaks of genital herpes, famciclovir is used to help reduce the number of future episodes [11,12].

Synonyms: Famvir, famciclovir

Structure:



IUPAC name: 2-[2-(2-amino-9H-purin-9-yl)ethyl]-1,3-propanediol diacetate

Molecular formula: C14H19N5O4

Molecular weight:321.33

Description: A white to pale yellow solid. M.P. 103°C

Solubility: It is freely soluble in acetone and methanol and sparingly soluble in ethanol and

isopropanol.

Storage: Store in air tight containers. Protect from light and moisture.

Category: Antiviral

2. MATERIALS AND METHODS

2.1. Materials

All chemicals and excipients used in this study were of analytical reagent (AR) grade. Aloevera powder, Carbopol 940, HPMC K100M, methanol, methyl paraben, and potassium dihydrogen orthophosphate were procured from HiMedia Laboratories Pvt. Ltd., Mumbai, India. Disodium EDTA and propylene glycol were obtained from Oxford Laboratories, Mumbai, India. Ethanol was purchased from Jiangsu Huaxi International Trade Co. Ltd. Ethyl acetate, *n*-octanol, polyethylene glycol, propyl paraben, thiourea, and urea were procured from Finar Chemical (India) Pvt. Ltd., Ahmedabad, India. Famciclovir was kindly gifted by Ipca Laboratories, India.

2.2. Methodology

2.2.1. Preformulation studies

Organoleptic Properties: The drug (famciclovir) powder was examined for its organoleptic properties like color, odour and taste it was observed.

Determination of Solubility: Solubility study should be performed for famciclovir to determine in which solvent it is soluble.

Melting Point Determination: The Melting point was determined by the capillary method using Digital Melting point apparatus.

Analytical Estimation by U V-spectrophotometer

Determination of Wavelength of Maximum Absorbance (λmax)

10 µg/ml solution of was scanned in UV-spectrophotometer range from 200-400nm using double beam visible spectrophotometer.

Preparation of Calibration Curve: The absorbance of the solutions of drug was taken on double beam U V spectrophotometer using λmax at 306 nm. The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibration curve. Same procedure was fallowed for every solvent.

Partition coefficient

In the pharmaceutical sciences, a partition (P) (also called distribution coefficient (D)) is the ratio of concentrations of a drug in the two immiscible phase mixture at equilibrium. Normally one of the solvents chosen is water (hydrophilic) while the second is hydrophobic

such as n-Octenol.

Drug and Excipients Compatibility Study:

FT-IR Spectra Analysis

FT-IR Spectroscopy used to investigate and predict any physicochemical interactions between different components, in a formulation and therefore it applied to selection of suitable chemically compatible excipient. While selecting the ingredients, we would choose those which are stable, compatible and therapeutically acceptable. The aim of compatibility study was to test, whether there is any interaction between the excipients and the drug and compatibility between the drug and excipients.

2.3. Formulation Development

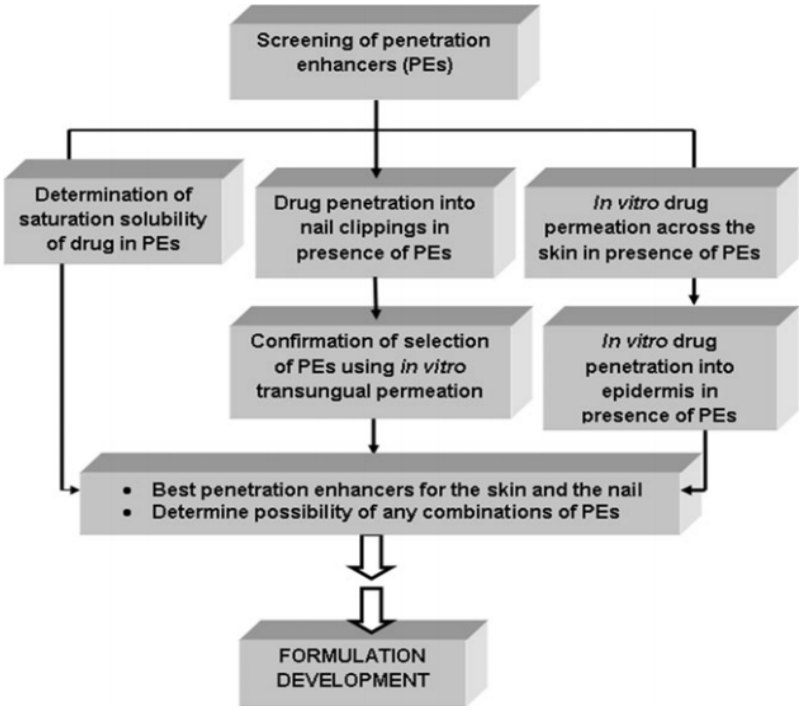


Figure no. 1: Selection of penetration enhancer.

2.3.1. Method of Preparation of Transdermal Gel

Accurately, weighed amount of polymers (Carbopol 940, HPMC K100M, aloe vera powder) according to formula were dispersed in purified water and allowed to swell overnight. Drug dissolved in solutions of selected penetration enhancers (Di sodium EDTA). After swelling polymers mix the solution with magnetic stirrer and drug-penetration enhancer solution was added in it with string and preservatives solution were also added. Final volume was made up and prepared gels were subjected for further characterization.

2.3.2. Characterization of famciclovir loaded Transdermal Gels

Visual observation: Those properties of formulations which were observed visually e.g. color, consistency, homogeneity, clearance and phase separation.

Determination of pH: The pH of formulated gel was determined by using digital pH meter at ambient (room) temperature. Prepared gels were accurately weighed and dispersed in 50ml purified water to make 10% solution. The calibration of pH meter was done with buffered solution before each use.

Viscosity: A cone and plate viscometer with spindle C75-2 (Brookfield) at 100rpm was used to determine viscosity of different formulated gels.

Spreadability study: Spreadability of prepared gel was determined by placing 0.5 g of gel within a circle of 1 cm diameter pre-marked on a glass plate. The slides were pressed upon each other so as to displace any air present and the adhering gel was wiped off. The two slides were placed onto a stand such that only the lower slide is held firm by the opposite fangs of the clamp allowing the upper slide to slip off freely by the force of weight tied to it. 20 gm weight was tied to the upper slide carefully. The time taken by the upper slide to completely detach from the lower slide was noted.

% Drug Content determination

The % drug content of prepared Gel was determined by dissolving of gel equivalent to 10 mg famciclovir in 10 ml methanol, sonicated in bath sonicator then filtered by filter paper. After preparation of suitable dilutions with pH 7.4 phosphate buffer, absorbance was determined using double beam UV-spectrophotometer with pH 7.4 phosphate buffer as blank at wavelength 306nm.

Diffusion study

The diffusion of famciclovir from gel formulations was studied through and cellophane membrane using the Franz diffusion apparatus. The donor cell was filled with gel formulation equivalent to 4 mg of drug. The receptor compartment was filled with phosphate buffer of pH 7.4. The temperature of the receptor compartment was maintained at 37 ± 0.5 oC by circulating hot water through the jacket of Franz diffusion cell. Orifice size of Franz diffusion cell was 11.28 mm diameter and surface area was calculated as 1.00 cm2 and receptor compartment volume was 8ml. The samples were removed at predetermined intervals of time and replaced immediately with equal volume of receptor solution to maintain sink conditions. The aliquots were analyzed at 306 nm by UV spectrophotometer.

Stability study: Stability study is performed for F5 as the formulation shows greatest drug

release and hence can be termed as 'best formulation' from within those that are developed. Stability study was carried out for 1 month, the formulation was kept in stability chamber at 40oC and at 75% relative humidity. After one month the formulation was checked for following parameters.

Kinetics models of drug release

There are several models to represent the drug dissolution profiles where f (t) is a function of time related to the amount of drug dissolved from the pharmaceutical dosage form.

3. RESULT AND DISCUSSION

3.1. Preformulation studies

Organoleptic properties of famciclovir

Table no. 1: Organoleptic properties of pure drug famciclovir

Test	Specification	Observations
Color	White	Complies
Taste	Characteristic	Complies
Odor	Odorless	Complies
Physical state	Solid pellets	Solid amorphous powder

Determination Melting Point

Table no. 2: Melting point of drug famciclovir.

Sr. No	Material	Specification	Melting point
1.	Famciclovir	102 - 104 ^{0}C	102 ^{0}C

Solubility study

Table no. 3: Solubility profile of famciclovir in different solvent.

S. No.	Solvents	Solubility
1.	Distilled water	Sparingly Soluble
2.	Ethanol	Slightly Soluble
3.	Methanol	Freely Soluble
4.	Ethyl acetate	Sparingly soluble
5.	pH 7.4 Phosphate Buffer	Soluble, dispersible

Determination of Wavelenth of Maximum Absorbance (□max)

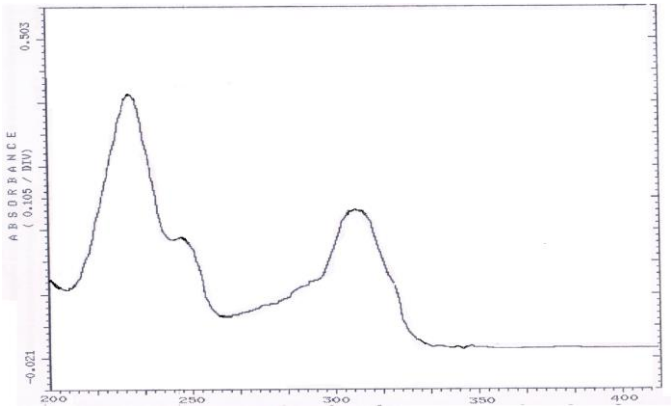


Figure no. 2: Scanning of Wavelenth of famciclovir Table no. 7: Wavelength of Maximum Absorbance (λ_{max})

Conc. (µg/mL)	Scanning range (nm)	Peaks Observed (nm)	Selected □max
10	200-400	224, 244, 306	**306 nm**

Preparation of the Calibration Curves of famciclovir

Table no. 4: Linearity of famciclovir 7.4 pH buffer.

Conc. (µg/ml)	0	10	20	30	40	50
Absorbance	0	0.109	0.228	0.352	0.472	0.605

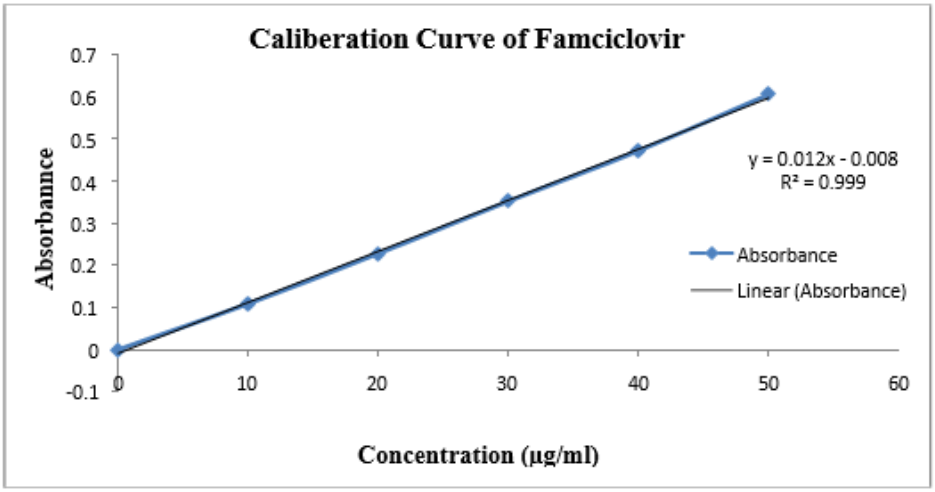


Fig. no. 3: Calibration Curve of famciclovir in 7.4 pH buffer Linearity Equation.

Partition Co-efficient

Table no. 5: Partition Co-efficient.

Sr. No.	Solvents	Absorbance
1.	Water	0.754
2.	n- Octanol	1.363

Compatibility Study

Physical Compatibility Study

Table no. 6: Physical Compatibility Study of Famciclovir with polymer.

S. No.	Material	Storage at room temperature	Storage at 45^0C - 50^0C	Storage at 2^0C - 8^0C
1	Pure Drug (10mg)	Stable	Stable	Stable
2	Famciclovir + Di sodium EDTA	Stable	Stable	Stable
3	Famciclovir + HPMC + Carbopol	Stable	Stable	Stable
4	Famciclovir + Di sodium EDTA + HPMC + Carbopol	Stable	Stable	Stable

Chemical Compatibility Study by FT-IR

Table no. 7: FT-IR Peaks of Famciclovir.

Standard Peaks(Cm^{-1})	Observed Peaks(Cm^{-1})	Peak Assigned
3500-3000	3441	N-H_2 str, sharp
3200-3000	3184	N-H str, sharp
3000-2840	2858	CH_3 str
1750-1710	1714	C-O str. (Ester)
1650-1600	1634	C=C str
1210-1163	1181	C-O str (Ester)

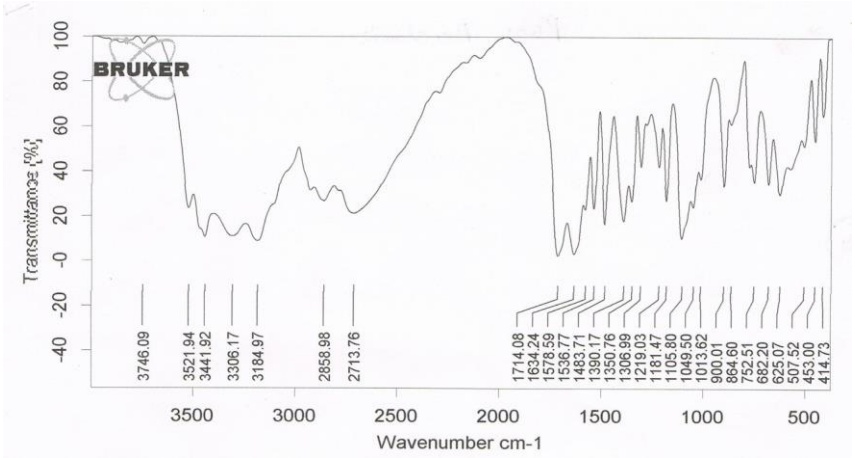


Figure no. 4: FT-IR spectrum of famciclovir pure.

3.2. Formulation development

Selection of penetration by saturation solubility

Table no. 8: Solubility of famciclovir in different oils at 25 ^{o}C.

S. No.	Oil	Drug solubility (mg/ml)
01	0.02 % Di sodium EDTA	14.0
02	Propylene glycol	11.0
03	Poly ethylene glycol	10.8
04	Urea	10.5
05	Thiourea	09.3
06	Nerolidol	07.0

Result: 0.02 % di Sodium EDTA was selected as penetration enhancer for further procedure to development of gel formulation.

Optimization of Formulation

Different trial formulations were prepared and studied for their physicochemical characterization and visual observation and finally got the optimized formulations. The trial formulations of gel were prepared in three batches, formulations prepared according to following formulae:

Trial batch- 01: In first trial batch, drug famciclovir and penetration enhancer percentage remains constant and the percentage of polymer(s) was gradually increased.

Table no. 9: Formulations of trial batch- 01.

S. No.	Ingredients	CF-1	CF-2	CF-3	CF-4	CF-5
1	Famciclovir (mg)	100	100	100	100	100
2	Carbopol 940 (%w/v)	0.2	0.4	0.6	0.8	1.0
3	*Aloe vera* powder (%w/v)	0.5	0.5	0.5	0.5	0.5
4	Disodium EDTA solution (%w/v)	0.02	0.02	0.02	0.02	0.02
5	Methyl paraben (%w/v)	0.02	0.02	0.02	0.02	0.02
6	Propyl paraben(%w/v)	0.1	0.1	0.1	0.1	0.1
7	Purified Water q.s. to produce 100ml	100	100	100	100	100

Trial batch- 02: In second trial batch, drug famciclovir and oil concentration percentage remains constant and the percentage of Smix (1:1) will gradually increase.

Table no. 10: Formulations of trial batch-02.

S. No.	Ingredients	HF-1	HF-2	HF-3	HF-4	HF-5
1	Famciclovir (mg)	100	100	100	100	100
2	HPMC K100M (%w/v)	0.2	0.4	0.6	0.8	1.0
3	*Aloe vera* powder (%w/v)	0.5	0.5	0.5	0.5	0.5
4	Disodium EDTA solution (%w/v)	0.02	0.02	0.02	0.02	0.02

5	Methyl paraben (%w/v)	0.02	0.02	0.02	0.02	0.02
6	Propyl paraben(%w/v)	0.1	0.1	0.1	0.1	0.1
7	Purified Water q.s. to produce 100ml	100	100	100	100	100

Trial batch- 03: In second trial batch, drug famciclovir and oil concentration percentage remains constant and the percentage of Smix (1:1) will gradually increase.

Table no. 11: Formulations of trial batch-03.

S. No.	Ingredients	CHF-1	CHF-2	CHF-3	CHF-4	CHF-5	CHF-0
1	Famciclovir (mg)	100	100	100	100	100	100
2	Carbopol 940 (%w/v)	0.2	0.4	0.6	0.8	1.0	0.8
3	HPMC K100M (%w/v)	0.8	0.6	0.4	0.2	0.0	0.2
4	*Aloe vera* powder (%w/v)	0.5	0.5	0.5	0.5	0.5	0.5
5	Disodium EDTA solution (%w/v)	0.02	0.02	0.02	0.02	0.02	0.00
6	Methyl paraben (%w/v)	0.02	0.02	0.02	0.02	0.02	0.02
7	Propyl paraben(%w/v)	0.1	0.1	0.1	0.1	0.1	0.1
8	Purified Water q.s. to produce 100ml	100	100	100	100	100	100

Optimization results of all prepared formulation

Table no. 12: Optimization of all prepared formulation.

S. No.	Code of formulation	Visual observation	Thermo dynamic Stability
1	CF-1	Yellowish, Coludy	Phase separation
2	CF-2	Yellowish, Coludy	Phase separation
3	CF-3	White, Coludy	Phase separation
4	CF-4	Clear	Stable
5	CF-5	Clear	Stable
6	HF-1	Light yellow, Clear	Phase separation
7	HF-2	Light yellow, Clear	Phase separation
8	HF-3	Light yellow, Clear	Phase separation
9	HF-4	Clear	Stable
10	HF-5	Clear	Stable
11	CHF-1	Yellowish, Clear	Stable
12	CHF-2	Yellowish, Clear	Stable
13	CHF-3	Clear	Stable
14	CHF-4	Clear	Stable
15	CHF-5	Clear	Stable

Result: From the study reported in above tables, formulations **CF-4, CF-5, HF-4, HF-5 and CHF-1** to **CHF-5** were selected for further studies. Rests of formulations were discarded because they were thermodynamically unstable and phase separation occurred within 7 days. It was also observed during this study that as the concentration of polymer increased stability

and clearness of formulations was improved.

3.3. Evaluation of prepared Gel formulations

Physical Observation and properties of prepared Gel formulations

Table no.13: Physical Observation, pH, Viscosity and Spreadability of prepared Gels.

Gel formulation Code	Physical Observation	pH	Viscosity (cp)	Spreadability gm.cm/sec	% Drug content
CF-4	Clear	6.2	4718	9.334	86.32
CF-5	Clear	6.8	5543	10.334	89.53
HF-4	Clear	7.1	5455	9.341	87.44
HF-5	Clear	6.6	5531	10.326	87.98
CHF-1	Yellowish, Clear	6.9	4548	7.265	90.21
CHF-2	Yellowish, Clear	6.5	4623	8.331	94.53
CHF-3	Clear	6.6	5342	9.314	93.31
CHF-4	Clear	7.3	6832	12.722	98.42
CHF-5	Clear	6.7	7638	11.421	96.81

Result: Formulations CF-4, CF-5, HF-4 and HF-5 showed % Drug content less than 90% that's why these were not considered for further study.

***In-vitro* cumulative %drug release (permeation) study of formulated gel preparations**

Table no. 14: *In-vitro* cumulative %drug release of gel preparations.

	Cumulative %drug release of gels				
Time (hrs)	CHF-1	CHF-2	CHF-3	CHF-4	CHF-5
0	0	0	0	0	0
1	14.14	14.49	19.77	17.12	18.45
2	29.33	29.44	39.02	34.23	36.99
4	51.69	51.57	67.61	57.20	67.25
6	66.76	65.57	87.82	75.97	87.10
8	75.50	73.34	88.99	84.83	89.71
10	81.23	79.79	90.90	94.39	92.82

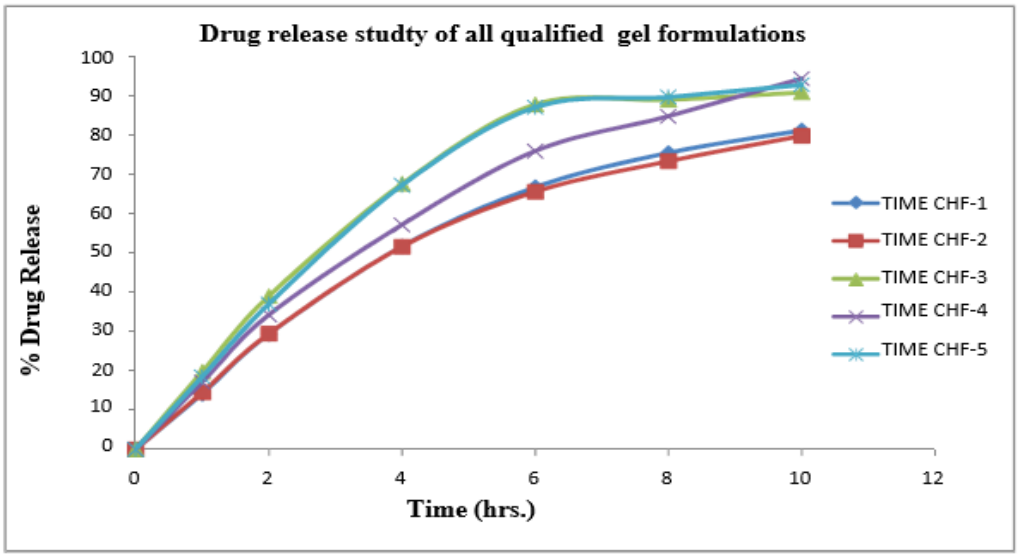


Figure no 5: *in-vitro* cumulative % drug release of gel preparations.

Table no. 15: R^2 values of all Transdermal gel preparations.

Model	Equation	R^2
CHF-1	y = 8.185x + 9.270	R^2 = 0.937
CHF-2	y = 7.958x + 9.641	R^2 = 0.933
CHF-3	y = 9.206x + 15.52	R^2 = 0.866
CHF-4	y = 9.34x + 10.6	R^2 = 0.946
CHF-5	y = 9.466x + 14.12	R^2 = 0.883

Results: On the basis of % drug release study, regression (R^2) values of all gel formulations showed that formulation CHF-4 possessed excellent release profile.

Optimization of effect of penetration enhancer

Preparation of blank formulation

Formulation **CHF-0** was the blank formulation which was same as the CHF- 4 without penetration enhancer intended for comparison in permeability.

Table no. 16: General evaluation of Formulation CHF-0 and Formulation CHF-4.

S. No.	Code of formulation	Visual observation	Thermo dynamic Stability
1	CHF-4	Clear	Stable
2	CHF-0	Clear	Stable

3.3.1. Comparative permeation study between gel batch CHF-4 and blank gel batch CHF-0

Equivalent to 4 mg of famciclovir gel batch CHF-4 and CHF-0 were filled into the donor

compartment of Franz Diffusion cell and 8ml of phosphate buffer pH 7.4 filled in receptor compartment for each experiment separately.

Table no. 17: *In-vitro* drug release profile of optimized gel formulation. (CHF-4)

Time (hr.)	S.R.T.	Log T.	Abs.	Conc (µg/ml)	Amt. in 1ml (mg)	Amt. in 8ml (mg)	Correction factor	% C.R	Log % C.R	% Drug remaining	Log% drug remaining
0	0	0	0	0	0	0	0	0	0	100	2
1	1	0	0.120	10.7	0.0107	0.0856	-	17.12	1.234	82.88	1.918
2	1.141	0.301	0.265	22.7	0.0227	0.1819	0.0107	34.23	1.534	65.77	1.818
4	2	0.602	0.455	38.6	0.0386	0.3087	0.0227	57.20	1.757	42.80	1.631
6	2.449	0.777	0.620	52.3	0.0523	0.4185	0.0386	75.97	1.881	24.03	1.381
8	2.828	0.903	0.707	59.6	0.0596	0.4765	0.0523	84.83	1.929	15.17	1.181
10	3.162	1.000	0.789	66.41	0.0665	0.5316	0.0596	94.39	1.975	05.61	0.749

Table no. 18: I*n-vitro* drug release profile of Blank gel formulation. (CHF-0)

Time (hr.)	S. R.T	Log T	Abs.	Conc (µg/ml)	Amt. in 1ml (mg)	Amt. in 8ml (mg)	Correction factor	% C.R	Log % C.R	% Drug remaining	Log% drug remaining
0	0	0	0	0	0	0	0	0	0	100	2
1	1	0	0.032	3.34	0.0034	0.0267	-	05.34	0.728	94.66	1.976
2	1.141	0.301	0.127	11.25	0.0113	0.0900	0.0034	17.32	1.239	82.68	1.917
4	2	0.602	0.223	19.25	0.0192	0.1539	0.0113	28.53	1.455	71.47	1.854
6	2.449	0.777	0.317	27.08	0.0271	0.2165	0.0192	39.46	1.596	60.54	1.782
8	2.828	0.903	0.358	30.50	0.0305	0.2437	0.0271	43.32	1.637	56.68	1.734
10	3.162	1.000	0.385	32.80	0.0328	0.2626	0.0305	46.42	1.667	53.58	1.729

Comparison of drug permeation on different parameters

Table no. 19: Results of drug permeation parameters across membrane.

Formulation code	Q_{10} (mg/cm^2)	Jss (mg/cm^2)/hr	Kp(x 10^{-3})	ER
CHF-0	1.8568	0.18568	46.42	-
CHF-4	3.776	0.3776	94.40	2.034

Kinetics modeling for optimized gel batch CHF-4

Zero Order model

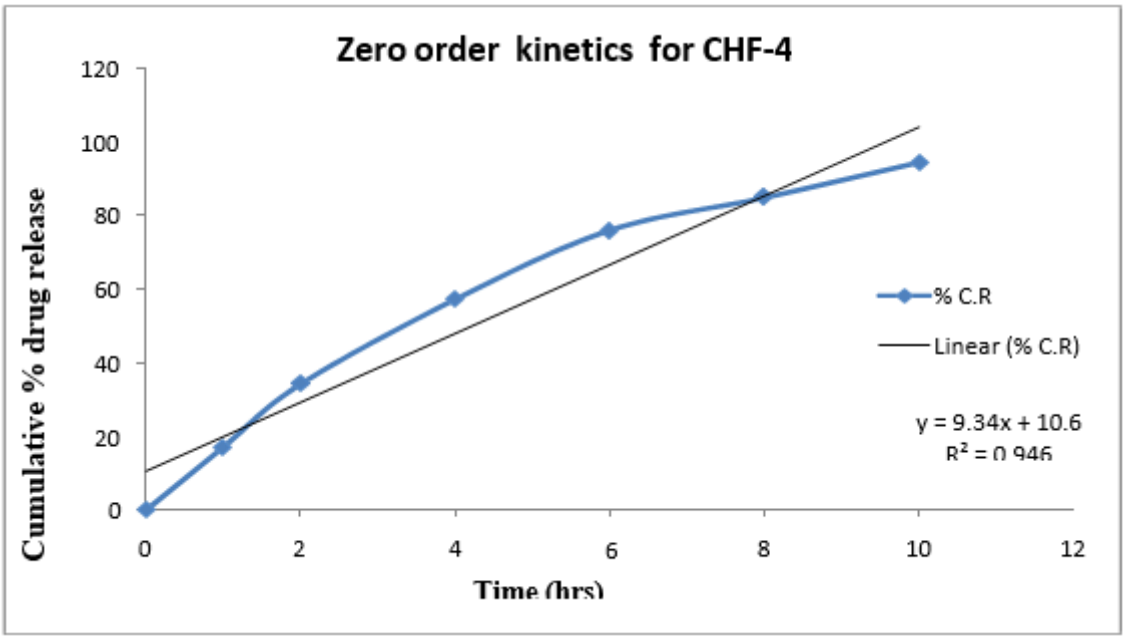


Fig. no. 6: Zero Order For model for CHF-4.

First Order model

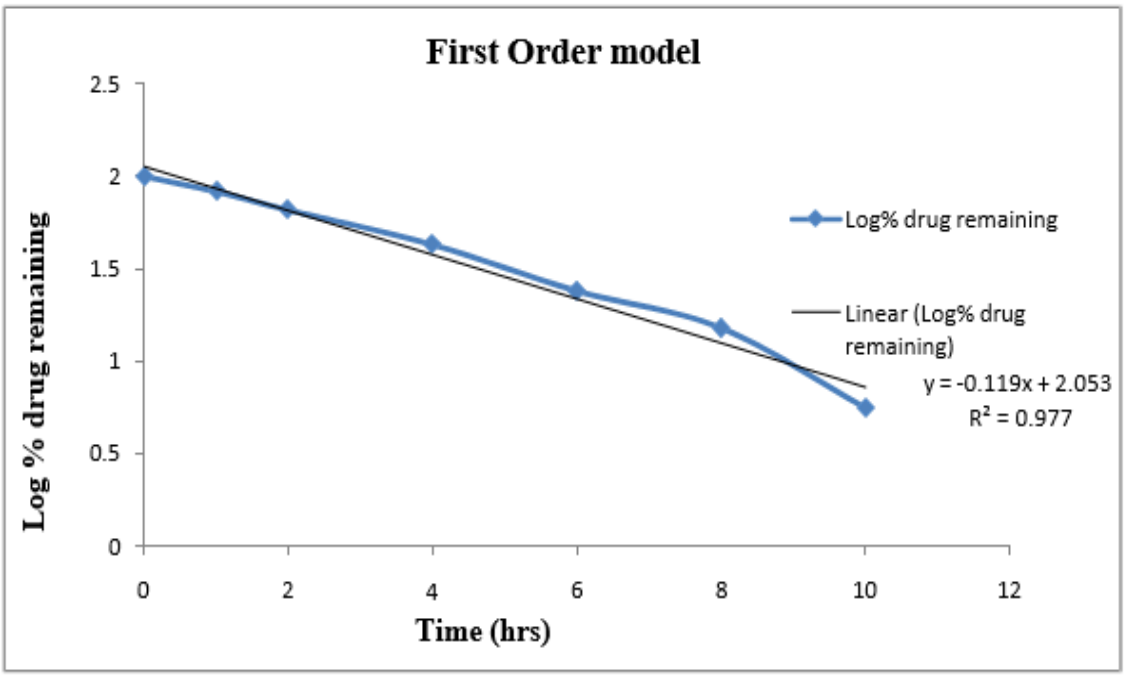


Fig. no. 7: First order model for CHF-4.

Higuchi model

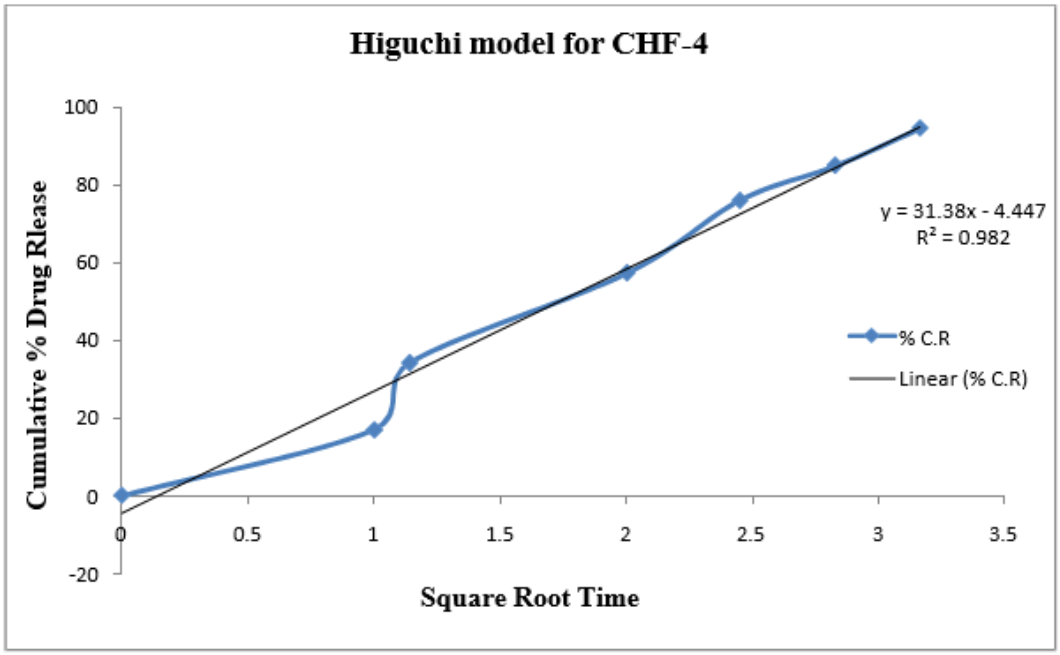


Fig. no. 8: Higuchi model for CHF-4.

Korsmeyer-Peppas model

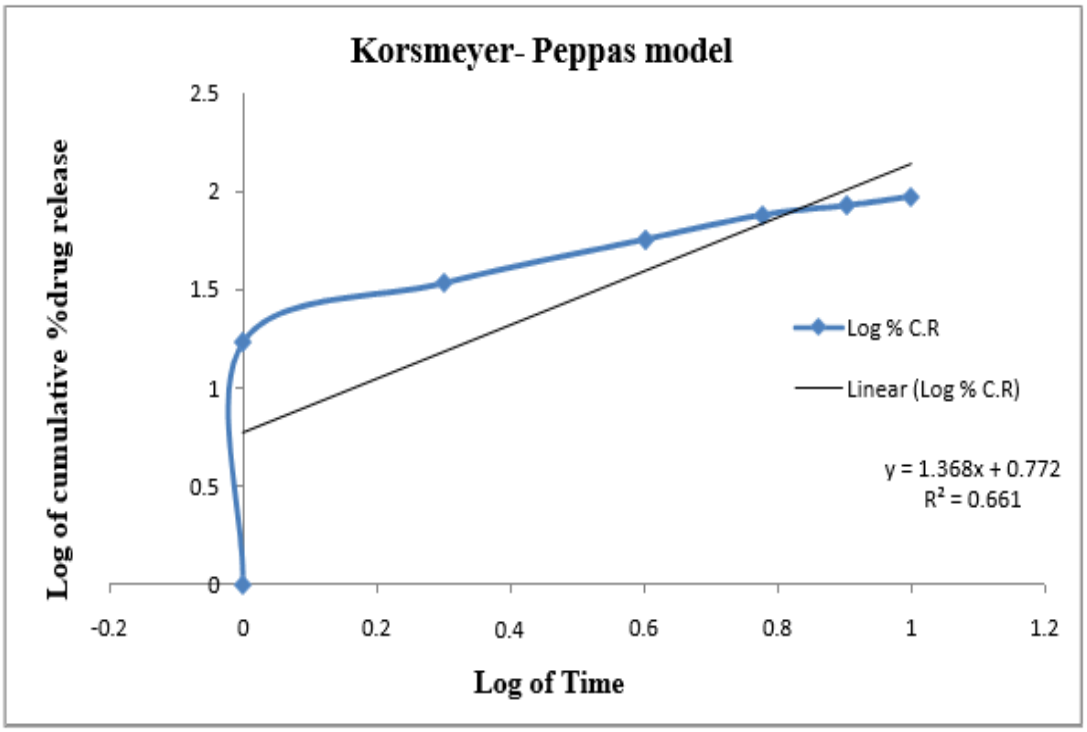


Fig. no. 9: Korsmeyer- Peppas model for CHF-4.

Table no. 20: I*n-vitro* curve fits for various release systems for optimized gel CHF-4.

Model	Equation	R^2
Zero order	y = 9.34x + 10.6	R^2 = 0.946
First order	y = -0.119x + 2.053	R^2 = 0.977
Higuchi	y = 31.38x - 4.447	R^2 = 0.982
Korsmeyer –Peppas	y = 1.368x + 0.772	R^2 = 0.661

3.4. Stability Studies

Table no. 21: Stability studies of optimized gel batch CHF-4.

Time (Days)	% Drug release		
	4 °C	25 °C	40 °C
0	94.39	94.39	94.39
15	92.41	91.31	91.32
30	90.02	91.14	91.06

4. CONCLUSION

The present study successfully developed and optimized a transdermal gel of famciclovir using Carbopol 940, HPMC K100M, aloe vera powder, and disodium EDTA as a penetration enhancer. The optimized formulation (CHF-4) exhibited desirable physicochemical characteristics, high drug content, satisfactory spreadability and viscosity, enhanced transdermal permeation, and sustained drug release. Drug release was best explained by the Higuchi kinetic model, indicating diffusion-controlled release from the gel matrix. The optimized formulation also remained stable during accelerated stability testing, demonstrating its suitability for pharmaceutical application. Overall, the developed transdermal gel represents a promising alternative to conventional oral therapy for famciclovir, with the potential to improve drug delivery, maintain sustained therapeutic levels, and enhance patient compliance. Further in vivo and clinical studies are recommended to establish its therapeutic efficacy and safety.

5. REFERENCES

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