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TO STUDY THE EFFECT OF COW GHEE AND ALOE VERA ON THE PERMEATION OF ACYCLOVIR

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ABSTRACT

For transdermal delivery to be effective, drugs have to enter into the viable skin in sufficient quantities to produce a therapeutic effect. The objective of present research work is to formulate acyclovir gel which shows the potential in the topical delivery of a hydrophilic drug and reduces the dosing frequency, side effects, increases the therapeutic efficacy and improves the patient compliance. Acyclovir is a potent and highly selective inhibitor of viruses of herpes group, such as herpes simplex virus type 1 (HSV1) and type 2 (HSV2), varicella zoster virus, and to a lesser extent against Epstein Barr virus and cytomegalovirus. pH of all formulas was found to be up to 6.9, practical yield above and up to 95%, spreadability was found to be 10.9, viscosities of all the formulations were found in the range of 18300 to 62830 cps and lying within the limit of 50-50,000 cps.pH, drug content were also found to be have satisfactory results with low standards deviation values. Viscosity studied indicate that increase the viscosity with increase the conc. With cow ghee and increase the permeability of drug through skin. In-vitro drug diffusion of acyclovir from gel & Ex-vivo drug release profile of acyclovir from gel was monitored wasobserved that its increase the permeability of drug in comparision of without cow ghee formulation. The method devised to prepare gel was effective and reproducible. The result of present investigation indicated that Transdermal gel of acyclovir prepared with combination of polymer (carbopol 934P), and different permeation enhancer is possible.

KEYWORDS: Cow ghee, Acyclovir, Aloe vera, penetration, transdermal.

INTRODUCTION

Although the skin is the most accessible organ of the body to superficial investigations, the direct measurement of penetrating substances has long posed major hurdles for detailed mechanistic studies.[1-4] Skin acts as a barrier against diffusion of substances through the underlying tissue.

A disadvantage of this route for drug delivery is that a relatively high dose is required to deliver therapeutic amounts across the skin and therefore evaluation of the potential for enhancement of skin penetration is of great practical importance.

There are two main ways to attack the problem of formulating a successful topical dosage form.

1. Directing drugs to the viable skin tissue without using oral, systemic or other routes of therapy.
2. The other approaches use skin delivery for systemic treatment. For example, transdermal therapeutic system provides systemic therapy for conditions such as motion sickness and pain.

For transdermal delivery to be effective, drugs have to enter into the viable skin in sufficient quantities to produce a therapeutic effect.[5]

The diffusional resistance of the SC is a challenge that has been accepted by the pharmaceutical scientist and considerable activity has been directed towards percutaneous penetration enhancement technologies. Overcoming this natural barrier is the main challenge in dermal or transdermal delivery of drugs to produce a systemic effect, TDD requires that suitable quantities of drug be transported through the skin. This has proved to be a challenge and has led to the development of a large repertoire of penetration enhancer compounds and physical techniques that, to different degrees, facilitate drug penetration across the skin.

A. Cow ghee

The cow ghee contains many fatty acids with varying physicochemical properties. [6-7] The lipoid nature of this substance aids passage of many drugs through many physiological barriers because barriers are lipoidal. it can be used for permeability Enhancement in Transdermal preparation.

B. Aloe vera

Aloe vera gel increased the in vitro skin penetration of compounds depending on their molecular weights, with an apparent inverse correlation between enhancement ratio and molecular weight of the compound.[5]

Acyclovir is an analogue of 2'-deoxyguanosine that exerts its antiviral effect after being metabolized to acyclovir triphosphate. Acyclovir has proved effective for the treatment of infections caused by herpes simplex virus types 1 and 2 and varicella zoster virus and for the suppression of some forms of cytomegalovirus disease. The objective of present research work is to formulate acyclovir gel which shows the potential in the topical delivery of a hydrophilic drug and reduces the dosing frequency, side effects, increases the therapeutic efficacy and improves the patient compliance.[8-11]

The Main Aims of the present work were set as.

1. To enhance permeability of Acyclovir.
2. To study the permeability of acyclovir by using cow ghee and Aloe Vera.
3. To study in-vitro drug release profile of the formulation.
4. To study Ex-vivo drug release profile of the formulation.

MATERIALS AND METHODS

Acyclovir was a gift sample from Medico Remedies Pvt. Ltd., Mumbai, Carbopol 934P was used as a polymer. Triethanolamine was used as a Surfactant. All other chemicals and reagents used were of high analytical grade.

Preparation of carbopol gel 934p (f1)

Carbopol 934P was dispersed in distilled water, by stirring at 800 rpm for 60 minutes, during stirring drug also added to it slowly.[11] Then Propylene glycol was added and mixture was neutralized by drop wise addition of triethanolamine, mixing was continued until a transparent gel prepared. While the amount of base was adjusted to achieve a gel with pH 5.5.

Preparation of Aloe Vera Gel (F3)

Slice off an outer leaf of an aloe plant. drain the resin for 10 min, peel the leaves, scoop the gel out with spoon or knife, consider mixing the gel with a natural preservative by using vit.C during mixing drug also added to it slowly, E (500 mg) for every ¼ cup of gel, place the gel in a sterillised, clean glass jar. Use the gel upto 2 month, stored in refrigerator.

Preparation of aloe vera gel with carbopol 934P (F3)

To prepare aloe vera gel with carbopol 934P, Triethanolamine was slowly added to the dispersion with continuous stirring which resulted in a stiff gel. Aloe vera gel was added to it and stirred for 15 min. Volume was made with water and stirred continuously till a uniform gel was formed.

Preparation of aloe vera gel, carbopol 934p with cow ghee

To prepare Aloe vera gel with carbopol gel, Sodium metabisulphite, Methyl paraben sodium and Propyl paraben sodium were dissolved in water. Carbopol gel was added to it cow ghee also added to it, and stirred continuously till it got swollen completely,during mixing drug also added to it slowly. Triethanolamine was slowly added to the dispersion with continuous stirring which resulted in a stiff gel. Aloe vera gel was added to it and stirred for 15 min. Volume was made with water and stirred continuously till a uniform gel was formed as shown in table 1.

Table 1: Formula for preparation of aloe vera gel, carbopol 934p with cow ghee (F4).

Sr.No.	Ingredients	Quantity
1.	Acyclovir	250 mg
2.	Carbopol 934P	0.05 ml
3.	Aloe extract	3.55 gm
4.	Coe ghee	0.2 gm
5.	Triethanolamine	Dropise
6.	Sodium metabisulphide	0.01 gm
7.	Methyl paraben sodium, or Propyl paraben sodium	0.001 gm
8.	Water	Upto 1.19 ml

COMPATIBILITY STUDIES

FT-IR study was carried out to check the compatibility between drug and polymer. The FTIR spectra of drug with polymers were compared with the standard FTIR spectrum of the pure drug.

EVALUATION OF GEL[12-13]

Determination of pH

The pH meter was calibrated with buffered solution at 4.0, 7.0 and 9.2 before starting pH determination.

Percentage yield

The empty container was weighed in which the gel formulation to be stored and again the container was weighed with gel formulation.

Homogeneacity

Homogeneacity was checked by visual inspection.

Spreadability

The Spreadability of all formulations was determined by using horizontal plate method. 1 g of gel was placed between two horizontal glass plates and standard weight (125 g) was tied on the upper glass plate. The whole set was hold in the vertical position. The time was noted for the plate to slide off from the other plate. The spreadability was calculated from the following formula, $S = (m \times l) / t$

Where 'S' is the spreadability coefficient, 'm' is the weight tied to the upper slide, 'l' is the length of glass slide and't' is the time taken.

Skin Irritancy Test

This test was performed on human volunteers. Twenty volunteers were chosen for single formulation and study was performed after taking their informed consent. It was performed by applying gel on an area of 2 square inch to the back of hand. Then the examination for the presence of lesion or irritation was done.

Drug Content Studies

Accurately weighed 1 g of gel was transferred into 100 ml volumetric flask containing 20 ml of saline phosphate buffer (pH 6.8) and stirred for 30 min followed by sonication. The volume was made up to 100 ml with saline phosphate buffer (pH 6.8). After suitable dilution the absorbance was measured using Shimadzu 1700 UV Visible spectrophotometer at 253 nm.

Viscosity Measurement

Viscosity of the gel was determined by using Brookfield viscometer.

In Vitrodiffusion Studies

In-vitrodiffusion study was carried out in a Modified Franz diffusion cell using cellophane membrane which is soaked overnight in distilled water.

Ex-Vivo Drug Permeation Study

Ex vivo permeation study was conducted using a Franz diffusion cell. The receptor phase (containing pH 6.8 phosphate buffer) was continuously stirred and kept at a temperature of 37±10 ^{0}C during experiments. The freshly excised rat skin was mounted on the donor compartment. 1 g of gel (containing 1 mg Acyclovir) was placed on the donor compartment of rat skin.

Each experiment was run in 3 independent cells and each sample was withdrawn from the receiver compartment in one hour interval.

Stability studies

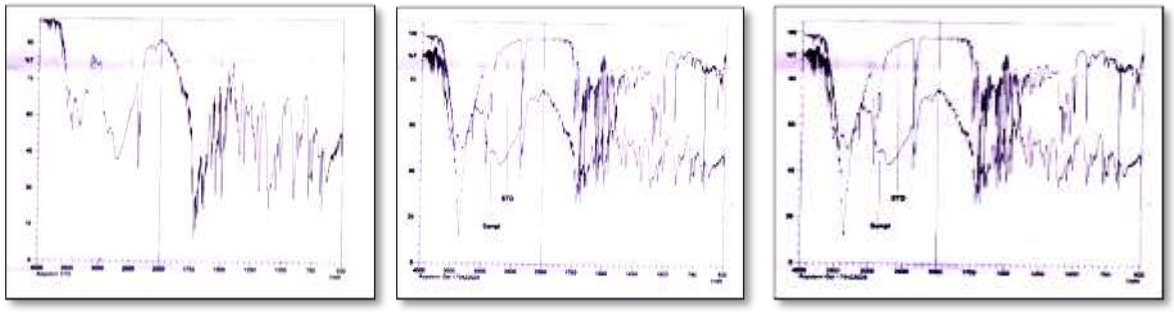
Stability studies were carried out on optimized formulation at 37 ± 2°C, 25 ± 2°C, room temperature in stability chamber (Thermo lab) and 2-8°C in refrigerator for 2 months. The optimized formulation stored in the sealed in aluminium foil. After 2 months, *in vitro* drug release studies were carried out.

RESULTS AND DISCUSSION

Drugs and other chemicals were procured from the source or suppliers.

The UV scanning of Acyclovir showed maximum absorbance i.e. 253 nm (λmax) which complies with the specification given in USP monograph.

The FTIR spectrum of Acyclovir was characterized by the presence of strong absorption band absorption at 3000 cm^{-1} (CH_2 Stretching), 3442 cm^{-1} (N-H-NH2 stretching) and 1710 cm^{-1} (C=O stretching) 3300 cm^{-1} (OH Stretching), 1700 cm^{-1} (CN-Stretching). The observation of the infrared spectroscopy (IR) spectra of physical mixture of formulation acyclovir gel and showed all the major peaks of the Acyclovir, indicating that there was no interaction between the Acyclovir and Acyclovir gel as shown in figure 1.



A **B** **C**

Figure 1: FTIR spectrum of A. Acyclovir B. Acyclovir gel C. physical mixture of acyclovir and acyclovir gel.

By comparing the peak of drug observed in drug spectrum and Acyclovir gel spectra shown in table, it was observed that no significant changes occur in the spectra of drug and acyclovir gel Hence it was concluded that acyclovir was found to be compatible with acyclovir gel.

Evaluation of Gel

The gel obtained were examined and characterized for the parameters shown in table 2.

Table 2: Evaluation parameter of formulation containing different concentration.

Parameters	Conc. of cow ghee- 250 mg	Conc. Of cow ghee – 500 mg	Conc. Of cow ghee – 750 mg
P^H	6.9	6.9	7.4
Practical yield	96.21 %	94.96%	93.71%
Homogeniacity	Good	Good	Good
Spredability	10.98	10.9	12.5
Skin irritancy test	Pass	pass	Pass

The percentage yield all the formulations were found in the range of 93.71% to 96.21 % and lying within limit. P^H and spreadability of all the formulations were found in the range of 6.8 to 7.4 and 10.90 to 12.5 gm.cm/sec respectively. The pH of all formulations was found near to the skin Ph value.

Viscosity of gel

Viscosities of gel can concluded with the help of different concentration of gel, the results are shown in table 3.

Table 3: Viscosity of gel.

SPEED (RPM)	SPINDLE	CP	TORQUE (%)
30	S64	18760	93.8
20	S64	18300	61.0
0.5	S92	62830	83.6

Viscosities of all the formulations were found in the range of 18300 to 62830 cps and lying within the limit of 50-50,000 cps. The viscosities of formulated gels were found more than the marketed cream. The results showed as the concentration of Cow ghee increases viscosity increases. All the formulations showed a gelling capacity of +++.From the result obtained it was observed that viscosity increases with the increasing concentration of cow ghee containing higher concentration of cow ghee showed maximum viscosity.

7. IN-VITRO DRUG RELEASE STUDY

In-vitro drug release study was carried out the using the Franz diffusion cell in pH 6.8 phosphate buffer. In-vitro release profile of Acyclovir from gel was monitored for 48 hrs

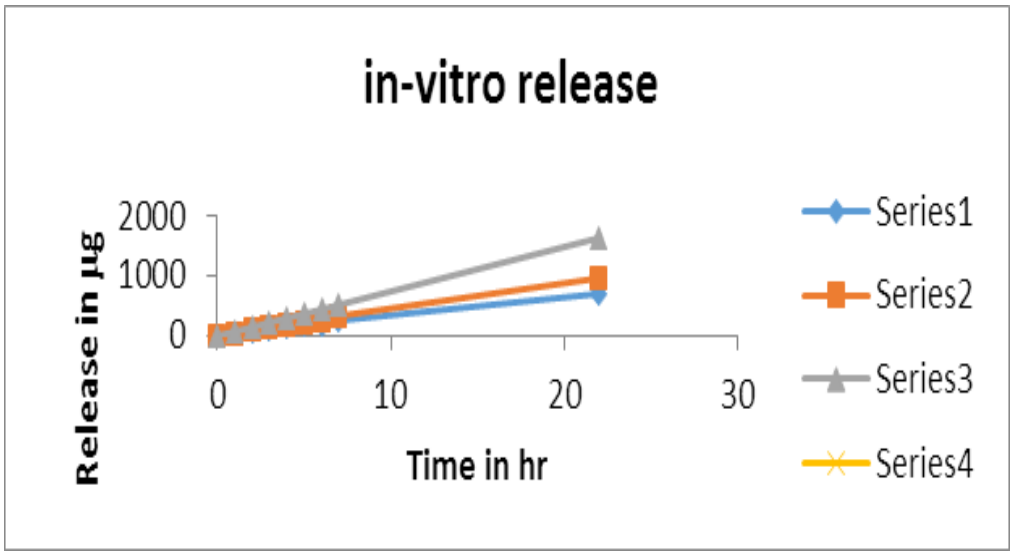


Figure 2: In-Vitro release of drug.

In the comparision of marketed preparation results of the maximum in-vitro release study was revealed that formulation F1 (696.330 %), F2 (803.80%), F3 (924.77%) and F4 (1494.49 %) was achieved more drug release in 48 hours. Whereas Formulation F4 was achieved 14 times more drug release in comparision of marketed preparation in 48 hours.

The results indicated that the formulation four showed better sustaining effect amongst all formulations. Results indicated that, the drug release was significantly prolonged by addition of the cow ghee and aloe vera as shown in figure 2.

The increase in the permeation is in permeation is in order of aloe vera with carbopol with cow ghee> aloe vera gel > aloe vera gel with carbopol gel > carbopol gel. The reason may be constitution of aloe vera where which reversibly remove the barrier resistance of the stratum corneum and allow drugs to penetrate more readily to the viable tissues and thus enter the systemic circulation. and The cow ghee contains many fatty acids with varying physicochemical properties. The lipoid nature of this substance aids passage of many drugs through many physiological barriers because barriers are lipoidal.

Ex-Vitro Drug Permeation Study

Ex-Vitro drug release study was carried out the using the Franz diffusion cell in pH 6.8 phosphate buffer.

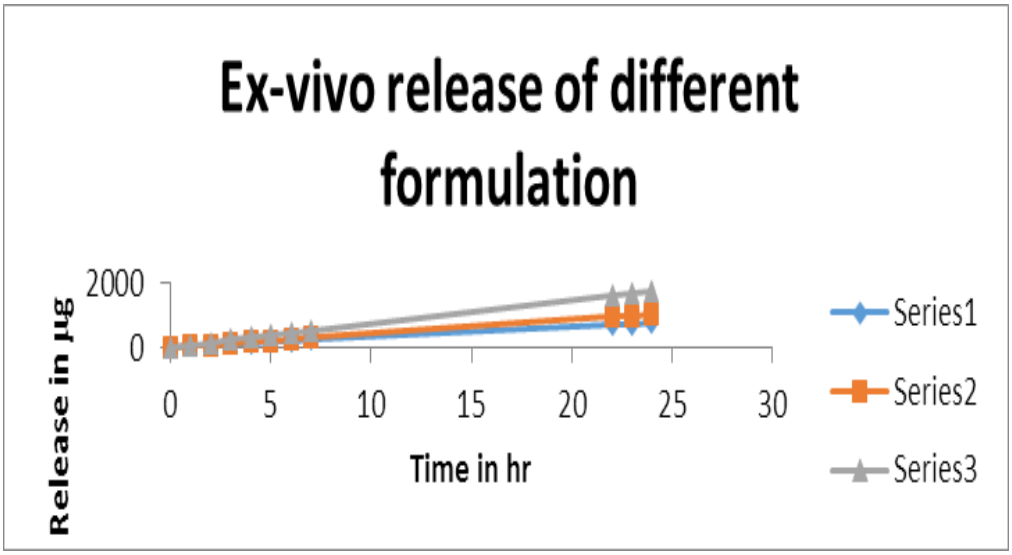


Figure 3: Ex-vivo of drug permeation through rat skin.

Ex-vivo drug release study was carried out the using the Franz diffusion cell in pH 6.8 phosphate buffer. Ex-vivo drug release profile of acyclovir from gel was monitored for 24 hrs. Result of ex-vivo permeation study was revealed that F1 (685.32 %), F2 (953.21%) have achieved F3(1618.34%) of drug release on 24 hrs. Formulation F3 shows maximum release and more than 1618.34 % release at 24 hours and indicating that increase in concentration of cow ghee Increase the release of drug as shown in figure 3.

Kinetics and mechanism of drug release

Release data were fitted to kinetic models in order to investigate the drug release kinetics and results shown. For the optimized batch i.e. F4, it was found that, in vitro drug release was best fitted to Peppas kinetic model, as compared to First order (0.9016) and zero order model (0.8896). The corresponding plot of Korsmeyer-Peppa's model indicated a good linearity of regression coefficients (R^2 = 0.9170). Release exponent (n) was found to be 1.0627 as shown in table 4.

Table 4: Kinetic model fitting.

FORMULAT-ION CODE	ZERO ORDER (R^2)	FIRST ORDER (R^2)	HIGUCHI (R^2)	HIX-CROWEL	PEPPAS	
					(R^2)	(n^2)
F4	0.8896	0.9016	0.9012	0.8978	0.9170	1.0627

For the optimized batch i.e. F4, it was found that, in vitro drug release was best fitted to Peppas kinetic model, as the plot showed highest linearity regression coefficient (R^2) is (0.9170) compared to First order (0.9016) and zero order model (0.8896). Release data was also fitted to Hix-crowel model, to investigate mechanism of drug release from microspheres formulation. The corresponding plot of Korsmeyer-Peppa's model indicated a good linearity of regression coefficients (R^2 = 0.9170). Release exponent (n) was found to be 1.0627 as shown in Table.

Stability studies

Stability studies were carried out at 25±2ºC and 37±2ºC and Room Temperature for optimized acyclovir gel for 30 days. The results of the stability study are shown in figure 4.

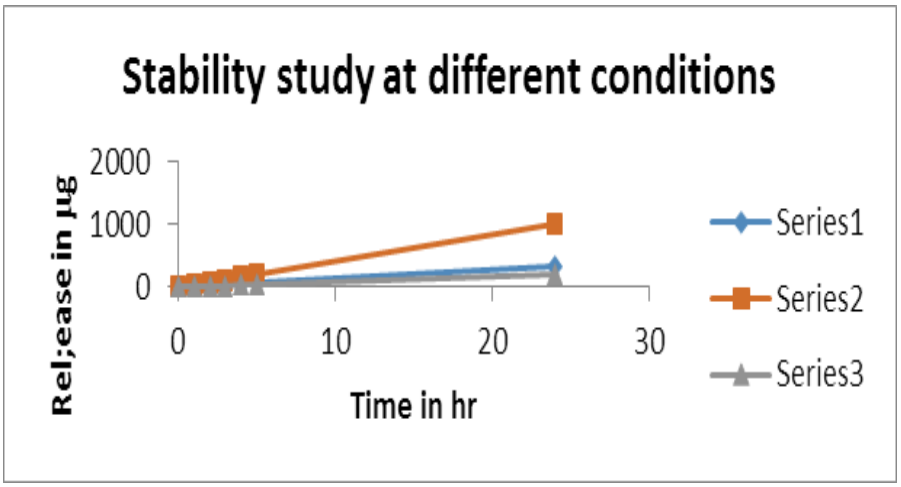


Figure 4: Effect of Drug Release at Different Conditions.

The results showed no significant difference between the initial, after 30 days of In case of In vitro drug release at 37 ± 2 ºC, slightly significant difference between the initial, after 30 days of In case of In vitro drug release at 25 ± 2 ºC, But in case of In vitro drug release at Room Temprature, significant difference between the initial, after 30 days, it gives odour, bad smell, and totally degraded in the environment due to degradation of ingredients in up to temp 45^0C. So finally conclusion is that, the formulation is degraded in high temp so it stored always below 25 ± 2 ºC or upto 25 ± 2 ºC.

REFERENCES

1. Robinso JR, Lee VL. Controlled drug delivery", Fundamental and applications. 2nded. Marcel Dekker: New York, 1987; 29-53.
2. Aulton ME. In "Transdermal drug delivery", Pharmaceutics: The science of dosage form design. 2 ed. Churchill Livingstone, New York, 2002; 499-33.
3. Schnetz E, Fartasch M. Microdialysis for the evaluation of penetration through the human skin barrier - a promising tool for future research. European J of Pharma Sci, 2001; 12: 165-74.
4. Hadgraft J. Skin, the final frontier. International Journal of Pharmaceutics, 2001; 2(24): 1-18.
5. Sharma K, Mittal A, Chauhan N. "Aloe Vera as Penetration Enhancer". Int. J. Drug Dev. & Res, 2015; 7(1): 31-43.
6. Biyani DM. "Formulation and Evaluation of Ayurvedic preparation containing cow ghee". PHD Thesis, 2015; 24.
7. Dumore MN, Mishra MR, Dumore NG, Mahajan UN, "Formulation of Ophthalmic Ointement using cow ghee as a base and penetration enhancer". Int research j of pharmacy, 2016; 7(7): 13-4.
8. Henry HB, Alfour JR. "Antiviral drugs", 340; 16: 1257.
9. Khushal MA, Shelat PK. "Formulation and Development of topical neosomal gel BCS Class–3 Antiviral Drug for better efficacy as herpes treatment". Int Research J of Pharmacy, 2012; 3(3): 272-6.
10. Parchuri DB, Shantha Kumar GS, Goli D, Karki R. "Formulation and Evaluation of nanoparticulate drug delivery system of Acyclovir for topical drug delivery. World journal of pharmacy and pharmaceutical sciences, 2013; 2(6): 5602-17.

11. Dey S, Mazumder B, Patel JR. “Enhanced Percutaneous Permeability og Acyclovir by DMSO from Topical Gel Formulation”. Int J of Pharma Sci and Drug Research, 2009; 1(1): 13-8.
12. Jacob S, Nair AB, Al-Dhubiab BE. “Preparation an evaluation of niosome gel containing acyclovir for enhanced dermal deposition”. J of Liposome Research, 2016; 2(3): 1-22.
13. Coceani N, Colombob I. “Acyclovir permeation through rat skin: mathematical modeling and in vitro experiments”, Int J of Pharmaceutics, 2003; 2(54): 197-210.