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FORMULATION OF ACYCLOVIR TRANSDERMAL GEL USING ALEOVERA AS PENETRATION ENHANCER FOR HERPES TREATMENT

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ABSTRACT

The aim of this study was to investigate the in-vitro permeation enhancement effects of the gel and Aloe vera using acyclovir as a marker compound. Aloevera, acyclovir and Polysorbate 80 were used for preparation of gel. The perepared grl was evaluated for Determination of pH, Determination of Viscosity, Drug Content, Spreadability and *In vitro* drug release study. Incorporation of penetration enhancer (polysorbate 80) showed modified or improved in-vitro permeability and enhancement of the drug. In the formulation greatest permeation is achieved at 4 % concentration of penetration enhancer (polysorbate 80) and hence S4 can be termed as the best formulation among those that are developed. In the formulation use of aloe vera gel as absorption base it posses soothing, moisturizing and healing properties, aloe vera gel contain of lignins, that allows for penetrative properties.

KEYWORDS: Aloevera, Acyclovir, Transdermal gel, formulation, Penetration enhancer.

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.[3-4]

Aloe vera (L.) Burm.f. (*Aloe barbadensis* Miller) is a perennial succulent xerophyte, which develops water storage tissue in the leaves to survive in dry areas of low or erratic rainfall. The innermost part of the leaf is a clear, soft, moist, and slippery tissue that consists of large thin-walled parenchyma cells in which water is held in the form of a viscous mucilage.[5] Therefore, the thick fleshy leaves of aloe plants contain not only cell wall carbohydrates such as cellulose and hemicellulose but also storage carbohydrates such as acetylated mannans.[6]

Acyclovir (ACV) is a guanosine antiviral drug and is one of the antiviral drugs most commonly used for treatment of herpes simplex virus infection, as well as varicella zoster (chickenpox) and herpes zoster (shingles). Topical application of ACV is limited by low transdermal penetration and poor solubility in water. Many strategies have been used to improve the therapeutic efficacy of ACV, including chemical modification, liposomes and nanoparticles.[7-8]

The aim of present work is, to formulate of transdermal aloevera gel by using Polysorbate80 as a penetration enhancer for localization action with minimize its side effects and benefacial for unconscious patients. Also investigate the effect of polysorbate 80 on penetration of Acyclovir in the form of transdermal gel formulation. Then compare the prepared formulation with marketed product for its flux and penetration enhancement property. Aloevera are used in formulation it posses soothing, moisturizing and healing properties. The anthraquinones in aloevera breakup residue of lifeless cells, and bring blood to the region of wound and ulcer. lignins a important structural materials of cellulose which allows for penetration properties.

MATERIAL AND METHODS

Material

All chemicals purchased from CDH chemical Pvt. Ltd. New Delhi. Dialysis membrane of Mol Wt cutoff 1200 was purchased from Himedia Laboratory, Mumbai. All other chemicals

and reagents used were of analytical reagent grade.

Methods

Formulation of acyclovir Aloevera gel

Aloevera gel (50g) was taken in a pestle morter, to this required amount of drug acyclovir (2.5g) dispersed in water. Polysorbate 80 (3%) was added in above mixture. Which used as a penetration enhancer. After that methyl paraben (0.15%) and propyl paraben (0.05%) used as a preservative, were added slowly with continuous gentletrituration until the homogenous gel formed.[9]

Table 1: Design of formulations.

Formulation Code	Acyclovir (g)	Polysorbate 80 (% w/w)	Methyl paraben (% w/w)	Propyl paraben (% w/w)	Aloe veragel (g)
S1	2.5	1	0.15	0.05	50
S2	2.5	2	0.15	0.05	50
S3	2.5	3	0.15	0.05	50
S4	2.5	4	0.15	0.05	50

Evaluation of prepared gel formulations

Determination of pH

pH was determined of each formulation by using pH meter (pH meter Henna industries H198107) pH meter was calibrated before with buffer solutions of pH 4, 7 and 9.[10]

Determination of Viscosity

Viscosity determined of each formulation by using Brookfield viscometer (Brookfield viscometer; type DV-E) with spindle at room temperature and at 5, 10, 20, 50and 100 rpm.[11]

Drug Content

1gm of the gel formulation was taken in 100 ml volumetric flask which contains 20 ml of phosphate buffer pH 7.4 and stirred for 30 minutes. Volume was made upto 100 ml. 1ml of above solution was further dilute to 10 ml by using phosphate buffer of pH 7.4.The resultant solution was subjected to UV spectrophotometric analysis at 251.3 nm and the absorbance was noted.[12]

Spreadability

Spreadability determined of the gel formulations, two glass slides of known standard dimensions are selected. Formulation whose spreadability to be determined was place on one

slide and then other slide was kept over its top such that the gel is sandwiched between the two slides. 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 one opposite fangs of the clamp clips and allows the upper slide to slip freely over it by the force of weight tied Tiethe 20 gm weight to the upper slide carefully. The time taken by the upper slide to completely detach from the lower slide was noted. The spreadability was calculated by using the following formula.[13]

$$\text{Spreadability} = m.l/t$$

Spreadability = Value s is spreadibility, m is the weight tied to the upper slides, l is the length of glassslide, and t is the time taken.

In vitro drug release study

The in vitro release of acyclovir from gel formulation (S3) and the amount of drug that is permeated through cellophane membrane using the diffusion apparatus. The donor cell was filled with 300 mg of gel formulation. The receptor compartment was filled with phosphate buffer pH 7.4. The temperature of the receptor compartment was maintained at 37 ± 0.5^{o}C by hot water using water bath. The samples were removed at predetermined intervals at 0.5, 1, 2, 4, 6 hours and replaced immediately with equal volume of receptor solution to maintain sink conditions. The removed samples were analyzed at 251.3 nm on UV spectrophotometer.[13]

RESULTS AND DISCUSSION

Aloe vera based transdermal gel were successfully prepared by the trituration method in the presence of PE (Penetration enhancer) polysorbate 80. In this formulation the aloevera concentration, polysorbate 80 concentration, were optimized to optain transdermal gel**.**

The use of penetration enhancer is capable approach to enhance the permeation of drugs which having low permeability. Incorporation of penetration enhancer (polysorbate 80) showed modified or improved in-vitro permeability and enhancement of the drug. In the formulation greatest permeation is achieved at 3 % concentration of penetration enhancer (polysorbate80) and hence S3 can be termed as the best formulation among those that are developed. No significant change in in-vitro drug release was obtained when taken 4% penetration enhancer.

In the formulation pH was determined the pH meter. In the formulations pH is found to be

around 6.66 to 6.43 so pH is found in the range of 6 which is compatible withskin. In case the range of pH of the formulation are found in above range of pH 6 so which is not compatible with skin and causes irritation with skin.

Rheological properties showed that viscosity is inversely proportional to the rate of shear and thus the system shows pseudoplastic characteristics or behaviour. It is observed that the viscosity of the formulations goes on decreasing as the rpm increases an inverse relationship exists between the viscosity and the shear rate. Viscosity is found in the range of 30195 to 31545 cp. Drug content was found within the range of 98 to 99 % for all the formulations. Spreadibility of the formulations is found within the range of 11.43 to 12.56 gm.cm/sec.

Drug release study of the formulation is found in the range of 1290.82(µg/cm^2) it is shown better result compare to the marketed formulation (1195µg/cm^2).Stability studies had shown that the formulation is stable at 40^{o}C at 75% RH for a one month of period time. The result of the present study proved that the drug was easily penetrate the dermis. The result clearly suggests that antiviral drug incorporated gel formulation could be utilize for the herpes virus infectious disease.

Table 2: Evaluation of prepared gel.

Sr. no.	Formulation code	pH	Viscosity (cp) at 10 rpm	Drug content (%)	Spreadibility (gm.cm/sec)
1.	S1	6.66	30195	96.27 ±1.2	12.56
2.	S2	6.67	31545	97.53 ±1.3	11.75
3.	S3	6.68	30723	98.12 ±1.1	11.43
4.	S4	6.55	30616	99.23 ±1.6	12.23

Table 3: Cumulative amount of drug released (Q) /cm^2 at different time intervals across cellophane membrane.

Time (hr)	Q (µg/cm^2)				
	S1	S2	S3	S4	Marketed
0.5	171.3±4.3	195.49±3.4	260.55±4.6	265.02±6.0	244.01±7.6
1	324.24±8.1	345.25±6.0	376.01±6.6	382.03±8.6	336.89±9.5
2	585.68±14.6	635.89±11.1	693.40±12.1	703.04±15.8	647.75±14.0
4	854.69±21.4	1007.0±17.6	1163.15±20.4	1172.00±26.4	999.00±19.3
6	1072.75±26.8	1165.07±20.4	1285.05±22.5	1290.82±29.0	1195.05±24.2

CONCLUSION

The Result obtained from all the experimental analysis as a part of project work suggested that it is possible to prepare optimized formulation of transdermal gel preparation. In this

method we have used of penetration enhancer is a capable approach to enhance the permeation of drugs which having low permeability. Incorporation of penetration enhancer (polysorbate 80) showed modified or improved in-vitro permeabilityand enhancement of the drug. In the formulation greatest permeation is achieved at 4 % concentration of penetration enhancer (polysorbate 80) and hence S4 can be termed as the best formulation among those that are developed. In the formulation use of aloe vera gel as absorption base it posses soothing, moisturizing and healing properties, aloe vera gel contain of lignins, that allows for penetrative properties. Lignins action is associated with excellent penetration abilities of aloe into the human skin so the aloevera gel based formulation is advantageous indelivering the entire drug safely to the skin.

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