

PREPARATION AND CHARACTERIZATION OF ANTIVIRAL GEL

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ABSTRACT

The study was to develop an antiviral gel for topical application. The topical application of drug has many advantages over the intravenous and oral administration. It prevents metabolism of drug from liver and avoid the risk of gastrointestinal disorder and inconvenience of intravenous therapy pain. When the drug is applied topically it can penetrate deeper into the skin hence show better absorption and bio-availability. The wide variety of pharmaceutical dosage form are available for topical drug delivery system. The most used one is gel, ointment and cream. Herpes Simplex Virus (HSV) are widely spread that cause infections. There are two types of this virus, one is HSV-1 usually causes sore around the lip or inside the mouth that are sometime called fever blisters or cold sore and the second is HSV-2, it causes sore on the genitals (private part). Acyclovir (ACV) is an effective and selective antiviral drug.

The study of its toxicology and use of appropriate detection technique to control its toxicity at safe levels are important for human health. Acyclovir remains the gold standard in the treatment of Herpes Simplex Virus infections, mainly due to emerging new drug delivery systems which are improving the bio-availability and less side effects. The gel was prepared by using different types of polymers viz. Carbopol-934, Carbopol-940, HPMC and Na-CMC. The gel formulation was evaluated for physical and chemical characterization. The recent study is about the preparation and characterization of the Acyclovir for the antiviral action.

KEYWORDS

Acyclovir (ACV), Antiviral activity, Herpes Simplex Virus (HSV), Carbapol-934, Carbapol-940, HPMC, Na-CMC.

INTRODUCTION

Parenteral route of administration is used to avoid the first pass effect/metabolism and also to maintain the constant level of drug into the body. The drug reaches into the systemic circulation directly but it has certain disadvantages.¹

One of the disadvantages of parenteral administration is invasive nature which can be overcome with topical route of administration¹.

The topical route of administration is noninvasive drug delivery at the point of application, so adequate amount of drug is absorbed into the systemic circulation to provide therapeutic action. To give continuous drug infusion through intact skin, there are many topical preparations are used like "Gel".

The ideal characteristics of topical application include:

1. Formation of gel should have both physical and chemical stability.
2. Formulation should have acceptability of the patient.
3. Formulation consisting one or more components should be non-sensitizing and non-irritating.
4. Formulation must have ability to release therapeutic agents within therapeutic window.

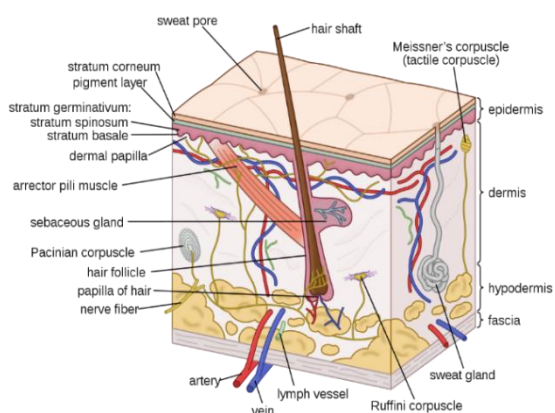
SKIN CHARACTERISTICS²

The purpose of topical application of dosage form is to suitably delivery of drug across the localized area of the skin. Drug or medication are applied to the skin in a many pharmaceutical dosage forms like ointment, cream, gel, etc. the absorption occurs outside the skin including entry into the blood stream is known as the percutaneous absorption. It's necessary to determine skin characteristic to develop an ideal topical dosage form.

SKIN STRUCTURE³

The skin is largest surface area of the body. the average of adult it occupied a surface area approximately 2 sq. m. (3000 sq inches). Structurally, the skin composed of mainly two layers. The outer most layer is thinner portion it consists of epithelium, is called as epidermis. It contains five layers stratum corneum, s. granulation, s. lucidum, s. spinosum, and basal layer. The epidermis is cemented on the inner thicker layer (Connective tissue) called dermis.

Beneath the dermis connected with subcutaneous layer it is also known as a superficial fascia or hypodermis, consist of areolar and adipose tissues.



Gels are “semisolid dosage form, in this system liquid phase trapped within 3D polymer matrix in which a high degree of chemical and physical

cross linking is present” this matrix network create a resistance to flow of fluid due to the entrapment and immobilization of solvent molecules.⁴

FACTORS AFFECT THE TRANSDERMAL PERMEATION⁵

The main principal of transport mechanism through skin is passive diffusion. The factors influencing can be classified into three major categories.

1. Physico-chemical properties of drug delivery system.
2. Pathological and physiological condition of skin.
3. Physico-chemical properties of penetrates.

There are many other factors also affect the penetration of drug⁶ and the physico-chemical properties of drug like partition co-efficient, concentration of vehicle, molecular size and molecular weight etc.⁷

DRUG DIFFUSION MECHANISM THROUGH THE STRATUM CORNEUM²

Stratum corneum contain many intercellular membranes and the intercellular region are filled with lipid rich amorphous material. In case of dry membrane, the intercellular volume is about 5% of total volume. Although molecules diffuse through intercellular region, the available evidence indicate that for polar or non-electrolyte, water soluble drug not diffuse primarily through intercellular. The transcellular permeation is explained on the basis of relatively smaller diffusion constant. Molecule also penetrates through transcellular mechanism.

Stratum corneum has a finite thickness and there is a period of transient diffusion (lag time) after applying drug on the skin, rate of drug transfer through skin increase to reach a steady state. Lag time (t), is related to the thickness of the membrane (h), and the diffusion constant (D) of the drug, by relationship, $t = h^2/6D$.

Physical destruction or damage of the stratum corneum barrier or cracking of the skin,

increase the absorption. stratum corneum is a main physical diffusion barrier.

PERCUTANEOUS ABSORPTION MECHANISM⁴

The percutaneous absorption mechanism for topical dosage form, is important for entire drug delivery system than drug alone. Important consideration.

1. Diffusion of drug
2. Drug dissolution process in the vehicle

Fick's law gives better understanding of these factors, which describes drug transport across the skin to this,

$$J = P \cdot C$$

J = the flux (is the amount of material cross the barrier per unit area per unit time)

C= the difference in concentration on both sides of the membrane)

P = permeability constant

$$P = K_m \cdot D_m/h$$

Where,

K_m = permeability constant of the drug molecule between the membrane and the vehicle in which the drug is dissolved.

D_m = diffusion constant of drug in the skin

h = thickness of the membrane

TOPICAL APPLICATION OF GEL

Gels are come under semisolid system; this form a network structure which is responsible for gel resistance to change its form (deformation)⁷ and clear transparent as water, and visually appealingly pleasing as in gelatin dessert, as whitish translucent.⁸

It contains preservatives depending upon the use of the gelling agent it includes the parabens (0.2%), benzoic acid (0.2%) and chlorocresol (0.1%).

The gel has several properties because of these properties being used more frequently in therapeutic and cosmetics industries.⁹ The properties are: -

1. High degree of clarity
2. Semisolid state
3. Ease of removal and use
4. Ease of application.

GEL CHARACTERISTICS

Ideally gelling agents are safe, inert, and non-reactive to other excipients.¹⁰ It provides reasonable solid like nature during storage, that can be broken easily by applying shear stress generated by squeezing a tube or during topical application of medication. The gel should exhibit little viscous change under the temperature difference of normal use or during storage. The characteristic of gel should match to intended use. It should not be tacky.¹¹

FORMULATION CONSIDERATIONS¹²

In the formation of gel, the efficiency of gel is dependent on the composition of the vehicles. It must have ability to penetrate through skin barriers and exert their effect into the site of action. It called "vehicle effects" the consequences of these two diffusional processes. These two processes are closely related and are dependent upon physico-chemical properties of the drug, vehicle, and the barriers.

SCOPE AND PLAN OF WORK

Acyclovir is a broad spectrum anti-viral agent used against Varicella Zoster Virus (VZV) and Herpes Simplex Virus (HSV). This virus infects the mucous membrane, neurons and skin, two conditions like chicken pox and shingles caused by VZV. Acyclovir has low aqueous solubility and poor oral bioavailability therefore for intravenous or topical application are necessary for inhibition of virus growth, topical semisolid dosage form is prepared to produce local activity. Gels, creams, ointment and pastes are some examples of semi solid use for many years.¹³

Gels have better absorption than other formulation of semi solid dosage form. Consequently, a study on formulation and evaluation of acyclovir gel was as a main objective for their anti-viral action. It is well tolerated. It prevents the spread of the HSV into

the body. So, the aim of this study to develop gel preparation containing Acyclovir.¹⁴

The main consideration of research work objectives is following: -

1. Compatibility study of drug with different polymers like Hydroxypropyl methyl cellulose, Carbopol and Sodium carboxy methyl cellulose.
2. Optimization of the formula to attain all gel characteristics.
3. Designing the trial formula for different concentration of each polymer
4. Selection of suitable formula from each polymer and preparation of gel formulations
5. Evaluation of the prepared gels for
 - PH
 - Drug content
 - Spreadability
 - Extrudability
 - viscosity
6. In-vitro drug release for each gel formulation, study the effect of permeation enhancer for each formulation. From this the best formulation is considered for further studies.
7. In-vitro evaluation of the selected formulation to perform by using Albino Rabbits and comparison with marketed acyclovir topical preparation.
8. Stability study of selected formulation to perform on them in different storage condition.¹⁵

PROFILE OF DRUG AND CHEMICALS

ACYCLOVIR – Drug profile¹⁶

Chemistry

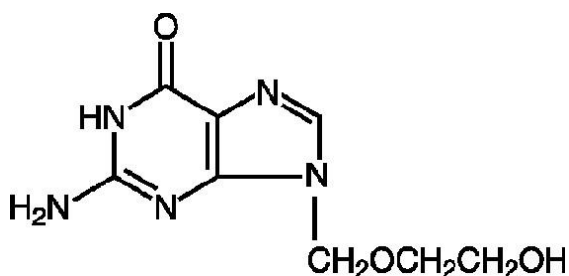


Figure: 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy) methyl]-6H-purin-6-one

Description¹⁷

Colour : White crystalline powder

Odour : Characteristics

Taste : Bitter to alkaline

Solubility: low solubility with water, very slightly soluble in alcohol, dilute solution with mineral acid and freely soluble in di methyl sulfoxide.

CLINICAL PHARMACOLOGY¹⁸

Acyclovir contains a partial nucleoside structure; the sugar ring is replaced by an open chain structure. It is selectively converted into acyclo-guanosine monophosphate (acyclo-GMP) by viral thymidine kinase, which is far more effective (3000 time) in phosphorylation than cellular thymidine kinase. Further it converted into its active triphosphate form, acyclo-guanosine triphosphate (acyclo-GTP), by cellular kinase. It is a potent inhibitor of viral DNA polymerase, it has approximately 100 times more affinity for viral than cellular polymerase by chain termination

Acyclovir is specific used for viral infection it is used mainly because it is less toxic than its earlier generation it shows major therapeutic advantages. It also called as prodrug, it works as a less active, its metabolite shows more action after administration.

Acyclovir is active against herpes virus family, in ascending order of activity:

- Activity is predominantly against HSV and VZV, it is only limited efficiency against EBV and CMV.
- Cyto-megalo virus (CMV)
- Varicella zoster virus (VZV)
- Herpes simplex virus type II (HSV-2)
- Herpes simplex virus I (HSV-1)

Pharmacokinetics

Acyclovir is poor water soluble and has poor oral bioavailability, hence intravenous and oral administration is necessary it require high concentrations When orally administered.

- Metabolism - Viral thymidine kinase
- Bioavailability - 10-20%

- Protein binding - 30%
- Excretion - renally excreted, partly by glomerular filtration and partly by tubular secretion
- Elimination half-life – 2-3 hour
- t_{max} - 1-2 hour
- Acyclovir has a high of dissolution rate

Therapeutic use: Anti-viral activity against Herpes Simplex Virus and Varicella Zoster Virus infections in immunosuppressed patient.

Toxicity: It has teratogenic action in pregnant women.

Drug interaction: Probenecid or zidovudine prolong its half-life and increase CNS toxicity.

Dosage form: Intravenous infusion; Capsule; Tablet; Suspension; Topical cream; Topical Ointment.

Dose¹⁹: Oral - 200mg times daily every four for 5-10days

400mg 5 times daily for 5 days in severely immunosuppressed patients

800mg 4-5 times daily for 5-7 days.

Contraindication: Hypersensitivity

CARBOMER²⁰

Structural formula

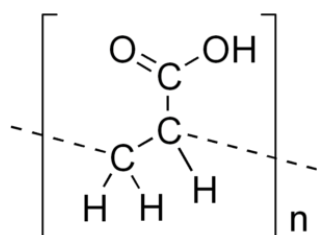


Figure: Poly (acrylic acid), poly(1-carboxyethylene)

Carbomer polymer are formed from a unit of acrylic acid. The monomer unit is shown above. The polymer chains are crosslinked with allyl sucrose or allyl pentaerythritol, it contains carboxylic acid (COOH) about (56%-68%).

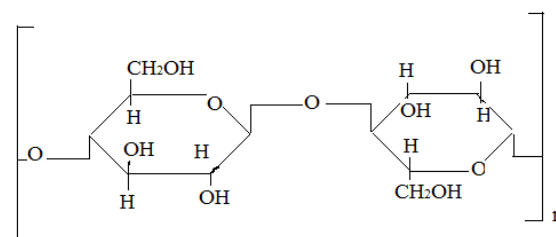
Synonyms: Acritamer, acrylic acid, carboxy poly methylene, polyacrylic acid, pemulen, etc.

Molecular weight; 7×10^5 to 4×10^9

Description: White-colored 'fluffy', acidic hygroscopic powder, characteristic odor.

Application in pharmaceutical preparation: It mainly used in liquid or semisolid pharmaceutical formulation as suspending or viscosity-increasing agent.

HYDROXY PROPYL METHYL CELLULOSE²⁰



Structure of Cellulose, 2-hydroxypropyl methyl ether

Synonyms: benecel MHPC; hydroxypropyl methyl ether; HPMC; methocel; etc.

Molecular weight: 10,000-1,500,000

Description: Odorless and tasteless, white or creamy-white fibrous or granular powder

Solubility: soluble in cold water and insoluble in hot water; practically insoluble in chloroform,

Carboxy methyl cellulose-sodium²⁰

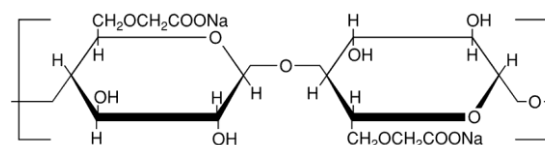


Figure: Carboxy methyl cellulose sodium

Molecular weight: 90,000-700,000

Description: almost white, odorless, granular powder.

EXPERIMENTAL WORK

Materials	Source
Carbapol-940	Kemphasol, Mumbai
Acyclovir	Microlabs hosur

Carbapol-934	Kemphasol, Mumbai
HPMC	HIMEDIA LBS Mumbai
CMC-Na	Kemphasol, Mumbai
Propyl paraben	NATIONAL CHEMICALS
Methyl paraben	NATIONAL CHEMICALS
Triethanol amine	REACHEM LAB, CHENNAI

Table 1: material used in research work

Instruments and equipment's	makers
UV-Spectrometer	SHIMADZU UV-1700, Japan
Remi stirrer	REMI Equipment's, Mumbai,
pH meter	ELICO, LI120
Viscometer	Brookfield
refrigerator	ALLWYN
Semi Centrifuge	REMI Equipment's, Mumbai

Table 2: Instruments and Equipment's used in research work

0.1M HCl acid Preparation

0.1M HCl solution was prepared by diluting 8.5ml of HCl in 1000ml with water.²¹

FORMULATION OF GELS²²

Acyclovir gels are prepared by using different polymers like Carbapol 934, carbapol940, Hydroxy propyl methyl cellulose, etc. different concentration of polymer used in preparation of gels.²³

Preparation of Corbapol-934 gels

Ingredients	Formula for 100gms		
	P ₁ (gm)	P ₂ (gm)	P ₃ (gm)
Acyclovir	1.0	1.0	1.0
Carbapol-934	0.4	1.1	1.6
Triethanolamine	0.5	0.5	0.5
Purified water	98	97.5	97
Methyl paraben	0.001	0.003	0.002

Table 3: Formulations with different carbapol-934 concentrations

Procedure

1. Accurately weigh the quantity of acyclovir is mixed in purified water with constant stirring and heat it at 50°C.
2. Add methyl paraben as preservative.
3. Add carbapol-934 to solution with continuous stirring at 50°C temperature.
4. Then add triethanolamine to the solution to maintain pH, stir until a clear gel was obtained.

Preparation of carbapol-940 gels: Repeat the same procedure and same amounts for carbapol-940 gel preparation.

Ingredients	Formula for 100gms		
	P ₁ (gm)	P ₂ (gm)	P ₃ (gm)
Acyclovir	1.0	1.0	1.0
Carbapol-940	0.4	1.1	1.6
Triethanolamine	0.5	0.5	0.5
Purified water	98	97.5	97
Methyl paraben	0.001	0.003	0.002

Table 4: Formulation with varying Carbapol-940

Preparation of Sodium Carboxy methyl cellulose gel

Ingredients	Formula for 100gms		
	A ₁ (gm)		A ₁ (gm)
Acyclovir	1.0	Acyclovir	1.0
Sodium carboxy methyl	2.5	Sodium carboxy methyl	2.5
Purified water	98	Purified water	98
Methyl paraben	0.004	Methyl paraben	0.004

Table 5: Formulation with varying Na-CMC concentrations

Procedure:

1. Accurately weighed quantity of acyclovir was dispersed in purified water with constant stirring

- Na-CMC was added in solution with continuous stirring. Add methyl paraben is used as preservatives by stirring.
- Stand it for complete hydration of Na-CMC. Adjust weight to 10gm by adding purified water.

EVALUATION PARAMETER OF GELS

The gels were evaluated in the following parameter are Drug content, pH, Viscosity, Extrudability, Spreadability In-vitro release of drug by using Albino Rabbit.

Determination of Drug content

1gm of Acyclovir gel was dissolved in 0.1M HCl and volume make up to 100ml. then 1ml of solution is dilute with 10ml of 0.1M HCl solution. Absorbance was measured in a form of standard calibration curve at 255nm by using UV spectrophotometer.

Formulation	Drug content (mg)	Drug content (%)
P ₁	10.173	101.73
P ₂	9.82	98.2
P ₃	9.68	96.8

Table 6: Drug content in the gel formulation

pH Measurements: This is done by using digital pH meter as per procedure.

Formulation	pH
P ₁	6.8
P ₂	7.3
P ₃	6.9

Table 7: pH of gel formulations

Estimation of viscosity: The viscosity of gel is determined by using Brookfield Viscometer (model-RVTP).

Formulation	Viscosity in cps
P ₁	43,500
P ₂	41,400
P ₃	51,600

Table 8: Viscosity of gel preparations

Extrudability: It is a test to measure the force to extrude the material from a tube.

Formulation	Extrudability
P ₁	++++
P ₂	++
P ₃	+++

++++Estimation, +++Good, +Not satisfactory

Table 9: extrudability of gel

Determination of Spreadability

The ideal quality of gel should possess good spreadability. Take about 1gm of gel formulation and kept it on a center of glass plate [standard dimensions(10x10cm)] and another glass plate place over it carefully, and put 2kg weight at center of glass plate (avoid sliding of plate). Diameter is measured after 30 minutes in cm.

formulation	Time taken (minutes)	Spreadability (cm)
P ₁	30	8.2
P ₂	30	7.9
P ₃	30	7.6

Table 10: determination of spreadability

STABILITY STUDY²⁵

The stability is a test is used to check the capability of any formulation to retain its chemical, physical and therapeutic specification, in an accelerated condition. In which the formulation is subjected to elevated temperature, humidity and atmospheric conditions.

Methods

The selected formulation was filled into aluminum collapsible tubes and stored at different temperature for an interval of three months. After this the physical parameter should be checked.

- Room temperature
- 37± 5°C
- 4-5°C

Physical parameters and Chemical parameters

1. Visual appearance
2. pH
3. Extrudability
4. Phase separation
5. Viscosity
6. Leakage
7. Nature
8. Drug content

Parameters	Room Temp.	37 ±5°C	4-5°C
Visual Appearance			
Initial	Trans.	Trans.	Trans.
final	Trans.	Trans.	Trans.
pH			
initial	6.8	6.8	6.8
final	7.1	7.0	7.1
Viscosity			
Initial	43,500	43,500	43,500
final	43,500	43,500	43,400
Extrudability			
Initial	++++	++++	++++
final	++++	++++	++++
Phase separation			
Initial	No	No	No
final	No	No	No
Leakage			
Initial	No	No	No
final	No	No	No
Nature			
Initial	Smooth	Smooth	Smooth
final	Smooth	Smooth	Smooth
Drug content			
Initial	101.73	101.73	101.73
final	100.40	100.86	100.54

Table 11: Physical parameters of gel

Skin irritation test²⁶

Take a healthy Albino rabbit weight 2.0-3.3kg. and then primary test of skin irritation test was performed on them, the gel was prepared and used a test patch, as a control, this test is performed on the skin of rabbit. The test and control patch are placed in left and right dorsal surface of rabbit respectively, after 24 hours removed the patch by help of alcohol swab and examined the skin conditions²⁷

In-vivo studies of selected gel formulation

Selection of animal model

Rabbit animal model is chosen because it had advantage of handling safety and experimentation.

Experiment

Study is performed by using Albino rabbits' weight from 1.5-2.0kg selected and fed them vegetable and water. The animal is divided into two groups, each group contains six animals.

The groups under treatment were designed as follows,

Group-I: Marketed ACIVIR cream as Standard

Group-II: Selected gel formulation as Test

The test and standard sample were applied at the unbraided area of the skin. After administration exactly 1ml of blood sample is collected from marginal ear vein of rabbits using sterile butterfly needles and syringes, at 1hour interval from 0hour to 2 biological half-lives of drug. Then plasma was separated from blood by centrifugation at 3000rpm for ten minutes, then collect supernatant plasma and kept it on refrigerator till sample were analyzed.

Determination of plasma concentration

The drug plasma level was determined by using Shimadzu UV-spectrophotometer. Then each sample is diluted with equal quantity of distilled water. Then prepared solution is analyzed in UV-spectrophotometer at 255nm. That are shown in table 10-11, and the result is shown in table 12.

Pharmacokinetic parameters²⁸

From all above data obtained. (AUC) Area Under Curve (AUC) was plotted in a graph taking a time (in hour) on X-axis and plasma drug concentration($\mu\text{g/ml}$) in Y-axis.

Elimination rate constant (Ke)

This can be calculated by the following formula equation $Ke = 0.693/t_{1/2}$

Elimination half-life($t_{1/2}$)

The ($t_{1/2}$) values are obtained by extrapolation of Time Vs plasma concentration curve

Peak plasma concentration (C_{max})

C_{max} was obtained from the Time Vs Plasma concentration curve.

t_{max} was obtained from the Time Vs Plasma concentration curve.

Relative Bioavailability

This can be determined by using following formula

$$\text{Relative Bioavailability} = \frac{\text{AUC for test}}{\text{AUC for standard}}$$

Absorption rate constant (K_a)

The (k_a) value were obtained by the extrapolation of Time Vs log concentration in semilogarithmic curve by Residual (or) feathering methods.

Time (hours)	Absorption at 255nm	Conc. ($\mu\text{g/ml}$)	AUC ($\mu\text{g hr/ml}$)
0	0	0	0
1	0.646	4.408	10.666
2	0.984	17.084	19.403
3	1.304	21.862	17.470
4	0.916	13.879	10.651
5	0.512	7.824	7.422
6	0.673	6.821	6.546

Table 12: Plasma drug conc. At different time intervals for standard (ACIVIR cream)

Time (hours)	Absorption at 255nm	Conc. ($\mu\text{g/ml}$)	AUC ($\mu\text{g hr/ml}$)
0	0	0	0
1	0.594	7.450	3.975
2	1.774	19.588	13.420
3	1.619	24.429	21.878
4	1.202	19.764	22.196
5	0.874	17.330	18.647
6	0.821	12.224	14.727

Table 13: Plasma drug conc. At different time intervals for Test-A₂ (1% Carbopol gel formulation)

Pharmacokinetic parameters	Unit	Std.	Test
AUC	($\mu\text{g hr/ml}$)	98.03	146.32
Relative bioavailability		2.523	1.492
C_{max}	($\mu\text{g/ml}$)	21.96	24.329
t_{max}	Hour	3	3
Ke	Hour-1	0.234	0.230
$T_{1/2}$	Hour	2.96	3.01
Ka	Hour-1	0.621	0.575

Table 14: Pharmacokinetic parameter for standard (ACIVIR cream) and test (Acyclovir gel)

RESULT AND DISCUSSION

Compatibility study

The Acyclovir drug was compatible with all the polymers namely Hydroxypropyl methyl cellulose, Carbopol, Na carboxy methyl cellulose was used in the gel formulation and also used as a gelling agent.

Evaluation of Acyclovir gels

Prepared gel undergoes to evaluation studies

Estimation of drug content

The drug content in gel formulation 1% carbopol-934(A₂) showed the maximum drug content (101.73%) as compare to another formulations result shown in table 6.

pH Measurements

The pH measurement of gel is done by using Digital pH meter. The pH range of the formulations was from 6.8 to 7.3, the result shown in table 7.

Determine the viscosity of gel

Viscosity is measure by using Brookfield Viscometer. The viscosity of the gels was ranged from 41,400 to 51,600cps and the result shown in table 8.

Extrudability

The extrudability of gel was determined according to procedure. Extrudability of Carbopol and HPMC gels were excellent than Na-CMC the result is shown in table 9.

Spreadability

The spreadability of gel was determined as per the procedure. The spreadability data of the formulation with 1% Carbopol-934 showed maximum (8.2cm), then other formulation was showed in table 10.

In vitro study

In vitro drug release of gel formulation was carried out as per procedure. Every formulation has different percentage of drug release and it determined at end of 8hr. 1% Carbopol -934 shows maximum release (64.91%). DMSO used as permeation enhancer in gel formulation. 1% Carbopol-940 show release was lesser (51.47%). In case of HPMC and Na-CMC gels shows lesser release than Carbopol gels.

Stability study

Stability study for the best formulation was done as per the procedure. The gels are physically and chemically stable at 4-5⁰C and 37±5⁰C room temperature. Result shown in table 10.

Skin irritation test

Skin irritation test was carried out as per the procedure, there was no erythema and edema and any kind of reaction. The gel is safer for topical use.

In vivo studies for the selected gel formulation

In vivo studies are carried out as per procedure. The blood samples are taken at different time intervals for standard and test group of animals and analysed the absorbance at 255nm in UV-spectrophotometer. Bioavailability is measure by determining the AUC, the relative bioavailability was estimated. The bioavailability of test was more than standard.

The t_{max} was 3hr for both test and standard and C_{max} was found to be 24.329 to 21.962 respectively. The elimination rate constant (Ke) for standard and test was found to be 0.230 and 0.234 hour⁻¹.

CONCLUSION

This study demonstrates that a gel formulation can be used to improve the solubility, permeability, bioavailability of acyclovir and it overcome the difficulties arises with its use in the clinic. On the bases of analysis different polymers Carbapol-934, Carbpol-940, HPMC and Na-CMC are used in the gel formulation.

The prepared formulations exhibit all properties of gel. The selected formulation was evaluated for stability, viscosity, spreadability, drug content, and the pH study. The result suggest that the optimised formulation was stable at different temperature and the study shows that the prepared formulation is one of the formulations which has higher permeability, solubility and the bioavailability. The present work aimed to developing a successful Gel formulation for the topical treatment of Herpes Simplex Virus infections. In this study we got success in development and evaluation of gel.

The study shows a successful development of gel formulation by using varying type of polymer (Carbapol-934, Carbpol-940, Na-CMC and HPMC). The gel containing Carbapol-934 shows higher drug content, stability and shows better properties than other polymer containing formulations.

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DECLATION OF INTERESTS

The authors declare no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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