**PREPRATION 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 drug metabolism from liver and minimize the danger of gastrointestinal disorder and inconvenience of intravenous therapy pain. When the drug is applied topically it might pierce the skin more deeply. Hence show improved absorption and bio-availability. The wide variety of pharmaceutical dosage form are available for topical drug delivery system. A majority used one is gel, ointment and cream. Herpes Simplex Virus (HSV) are widely spread that cause infections. There are two varieties of this virus HSV-2 causes sores on the genitals (private area), while HSV-1 typically causes blisters around the lips or inside the mouth that are sometimes known as fever blisters or cold sores. Acyclovir (ACV) is a potent and specific antiviral medication. For the sake of human health, it is crucial to understand its toxicology and apply the proper detection methods to keep its toxicity under control. 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**

To prevent the first pass effect and metabolism and to maintain a steady amount of medication in the body, the parenteral route of delivery is employed. 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 adminstration1.

The topical route of administration is noninvasive drug delivery at the point of application, so adequate amount of drug to deliver therapeutic effect is absorbed into the systemic circulation. There are numerous topical preparations like "Gel" that are used to continuously administer drugs via undamaged skin.

The ideal characteristics of topical application include:

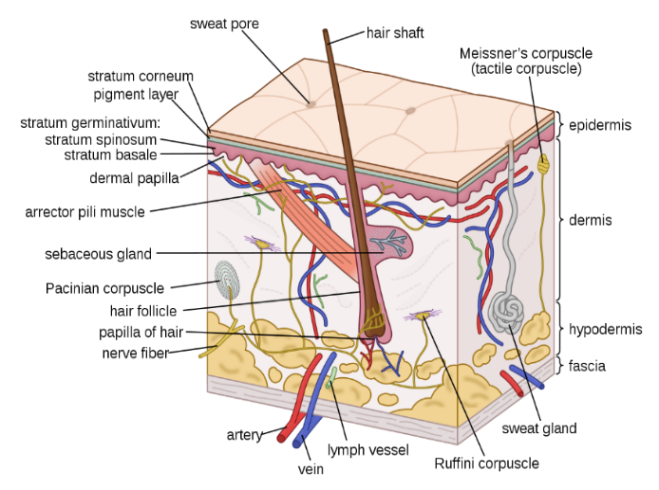
1. Gel formation needs to be chemically and physically stable.
2. Formulation should have acceptability of the patient.
3. A mixture made up of one or more ingredients should not irritate or sensitise people.
4. Formulation must have ability to release therapeutic agents within therapeutic window.

**SKIN CHARACTORSTICS2**

The objective of topical dosage form application is to effectively administer medication across the targeted area of skin. Drug or medication are applied to the skin in a many pharmaceutical dosage forms like ointment, cream, gel, etc. Percutaneous absorption refers to absorption that happens via the skin and into the bloodstream. To create the best topical dose form, skin characteristics must be identified.

**SKIN STRUCTURE3**

The skin surface is largest surface area of the body. The average of adult it occupied a surface area of about 2 square metres (3000 square 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 inner, thicker layer (Connective tissue) known as the dermis is adhered to by the epidermis.

A superficial fascia or hypodermis, which is made up of areolar and adipose tissues, is the layer that lies beneath the dermis and connects to the subcutaneous layer. 

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 divided into three main groups.

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 drug's physico-chemical characteristics, such as its partition coefficient, vehicle concentration, molecular weight, and others7.

**DRUG DIFFUTION MECHANISM THROUGH THE STRATUM CORNEUM 2**

Stratum corneum contain many intercellular membranes and the intercellular space is filled with amorphous, lipid-rich material. The intercellular volume of a dry membrane makes up around 5% of the total volume. Despite the fact that molecules spread over the intercellular space indicate that for polar or non-electrolyte, water soluble drug not diffuse primarily through intercellular. The substantially lower diffusion constant is used to explain transcellular permeation. Additionally, molecules enter cells via a transcellular method. After administering a medicine to the skin, the rate of drug transfer through the stratum corneum increases to achieve a steady state after a brief period of transitory diffusion (lag time). The relationship between lag time (t), membrane thickness (h), and drug diffusion constant (D) is t=h2/6D.

Physical destruction or damage of the skin's stratum corneum barrier or skin breaking, 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 a drug delivery method as opposed to just the medicine. 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. 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 = Km. Dm/h

Where,

Km is the drug's molecule's permeability constant between a membrane and the solvent it dissolves in.

Dm = the skin's drug diffusion constant

h = thickness of the membrane

**TOPICL APPLICATION OF GEL**

Gels fall under the category of semisolid systems; this creates a network structure that gives gels their resistance to changing their shape (deformation), making them clear, transparent, and visually appealing, as the whitish translucent gelatin desert8.

Depending on the gelling agent used, it may contain preservatives such as 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.9The properties are: -

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

**GEL CHARACTERISTICS**

Ideally gelling agent 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 shouldn't change significantly in viscosity when used normally or while stored at different temperatures. Gel should have properties appropriate for its intended purpose. It shouldn't be obnoxious.11

**FORMULATION COSIDERATIONS12**

The vehicles' chemical make-up affects the gel's ability to form and its effectiveness. It must be able to pass through skin barriers in order to exert its effects at the target site. It referred to the results of these two diffusional processes as "vehicle effects". These two procedures depend on the physico-chemical characteristics of the drug, the vehicle, and the barriers. They are also closely related to one another.

**SCOPE AND PLAN OF WORK**

Acyclovir is a broad spectrum anti-viral agent use against Varicella Zoster Virus (VZV) and Herpes Simplex Virus (HSV). This virus infects the mucous membrane, neurons and skin two VZV-related conditions, such as chicken pox and shingles. Acyclovir has low aqueous solubility and poor oral bioavailability there for intravenous or topical application are necessary for inhibition of virus growth, topical semi-solid dosage form is prepared to produce local activity. Pastes, creams, gels, and ointments are a few examples of semi-solids that have been around for a while.13Gels have better absorption than other formulation of semi solid dosage form. Consequently, the main goal for their anti-viral action was a study on the formulation and assessment of acyclovir gel. It is tolerated well. It prevents the spread of the HSV into the body. Consequently, this study's goal is to create a gel preparation that contains acyclovir.14

The main consideration of research work objectives is following: -

1. Drug compatibility research with various polymers, including sodium carboxy methyl cellulose, carbopol, and hydroxypropyl methyl cellulose.
2. Optimization of the formula to attain all gel characteristics.
3. Creating a test formula with various polymer concentrations
4. Selection of suitable formula from each polymer and preparation of gel formulations
5. Evaluation of the prepared gels for

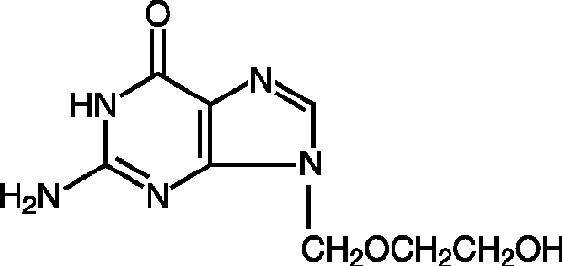
* PH
* Drug content
* Spreadability
* Extrudability
* viscosity

1. Study the impact of the permeation enhancer for each formulation using in-vitro drug release for each gel formulation. The most effective formulation is chosen from this for additional research.
2. In-vitro testing of the chosen formulation using albino rabbits and comparison to commercially available acyclovir topical preparation.
3. A stability study of the chosen formulation will be carried out on them in various storage conditions.

**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**

The sugar ring is replaced by an open chain structure in acyclovir's partial nucleoside structure. Viral thymidine kinase, which is much more efficient in phosphorylation than cellular thymidine kinase (3000 times), selectively converts it into acyclo-guanosine monophosphate (acyclo-GMP). Cellular kinase then converted it into acyclo-guanosine triphosphate (acyclo-GTP), which is its active triphosphate form. It is a strong inhibitor of viral DNA polymerase and, by chain termination, has an affinity for viral polymerase that is approximately 100 times greater than that of cellular polymerase.

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 primarily targets HSV and VZV; EBV and CMV are only partially effective..
* Cyto-megalo virus (CMV)
* Varicella zoster virus (VZV)
* Herpes simplex virus type II (HSV-2)
* Herpes simplex virus I (HSV-1)

**Pharmacokinetics**

* Because acyclovir is poorly soluble in water and has a low oral bioavailability, it must be administered intravenously and orally at high concentrations. Whenever taken orally. 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
* tmax - 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

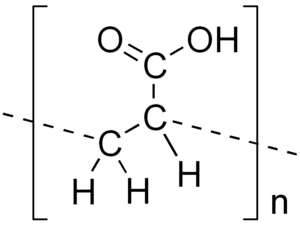
400mg 5 times daily for 5 days in severely immunosuppressed patients

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%).

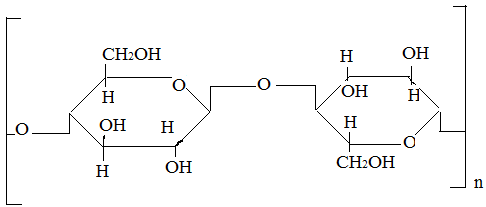
**Synonyms:** Acritamer, acrylic acid, carboxy poly methylene, polyacrylic acid, pemulen, etc.

**Molecular weight;** 7x105 to 4x109

**Description:** White-colored ‘fluffy’, acidic hygroscopic powder, characteristicodor.

**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**

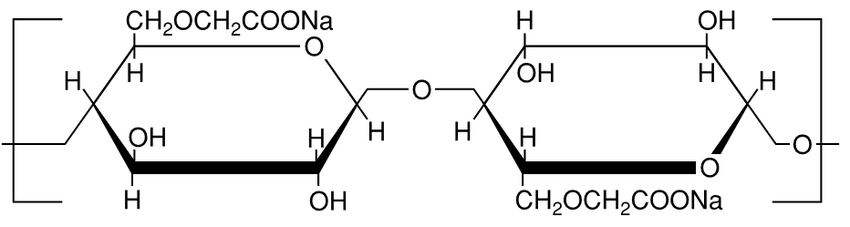
**Synonyms:** benecel MHPC; hydroxypropyl methyl ether; HPMC; methocel; etc.

**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 Carbopol 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** | | |
|  | **P1**  **(gm)** | **P2**  **(gm)** | **P3**  **(gm)** |
| Acyclovir | 1.0 | 1.0 | 1.0 |
| Carbopol-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. Weigh the acyclovir accurately, stir it continuously, and heat it to 500°C in purified water.
2. Include the preservative methyl paraben.
3. Add carbapol-934 to solution with continuous stirring at 500C 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** | | |
|  | **P1**  **(gm)** | **P2**  **(gm)** | **P3**  **(gm)** |
| Acyclovir | 1.0 | 1.0 | 1.0 |
| Carbopol-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** | | |
|  | **A1**  (gm) |  | **A1**  (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. With constant stirring, an exact amount of acyclovir was dissolved in purified water.
      2. Na-CMC was added in solution with continuous stirring. Add methyl paraben is used as preservatives by stirring.
      3. Stand it for complete hydration of Na-CMC. Adjust weight to 10gm by including distilled water.

**EVALUATION PARAMETER OF GELS**

The gels' drug content, pH, viscosity, extrudability, and spreadability were all evaluated. drug release in vitro using albino rabbits.

**Determination of Drug content**

Acyclovir gel weighing 1gm was dissolved in 100ml of 0.1M HCl. 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**  **(%)** |
| **P1** | 10.173 | 101.73 |
| **P2** | 9.82 | 98.2 |
| **P3** | 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** |
| **P1** | 6.8 |
| **P2** | 7.3 |
| **P3** | 6.9 |

**Table 7: pH of gel formulations**

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

|  |  |
| --- | --- |
| **Formulation** | **Viscosity in cps** |
| **P1** | 43,500 |
| **P2** | 41,400 |
| **P3** | 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 |
| **P1** | ++++ |
| **P2** | ++ |
| **P3** | +++ |

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

**Table 9: extrudability of gel**

**Determination of Spreadability**

Gel of the best kind should be easily spreadable. Take about 1gm of the gel formulation and place it in the middle of a glass plate with the standard (10x10cm) dimensions. and carefully place a second glass plate on top of it, placing a 2 kg weight in the middle to prevent the glass plate from sliding. After 30 minutes, the diameter is measured in cm.

|  |  |  |
| --- | --- | --- |
| **formulation** | **Time taken**  **(minutes)** | **Spreadability**  **(cm)** |
| **P1** | 30 | 8.2 |
| **P2** | 30 | 7.9 |
| **P3** | 30 | 7.6 |

**Table 10: determination of spreadability**

**STABILITY STUDY25**

The stability test determines whether a formulation can maintain its intended chemical, physical, and therapeutic properties under accelerated conditions. 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.

1. Room temperature
2. 37± 50C
3. 4-50C

**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**  **±50C** | **4-50C** |
| **Visual**  **Appearance**  Initial  final | Trans.  Trans. | Trans.  Trans. | Trans.  Trans. |
| **pH**  initial  final | 6.8  7.1 | 6.8  7.0 | 6.8  7.1 |
| **Viscosity**  Initial  final | 43,500  43,500 | 43,500  43,500 | 43,500  43,400 |
| **Extrudability**  Initial  final | ++++  ++++ | ++++  ++++ | ++++  ++++ |
| **Phase separation**  Initial  final | No  No | No  No | No  No |
| **Leakage**  Initial  final | No  No | No  No | No  No |
| **Nature**  Initial  final | Smooth  Smooth | Smooth  Smooth | Smooth  Smooth |
| **Drug content**  Initial  final | 101.73  100.40 | 101.73  100.86 | 101.73  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**

Albino rabbits weighing 1.5 to 2.0 kg were chosen for the study and given vegetables and water. The animal is split into two groups, each of which has six creatures.

The treatment groups were created as follows:

Group-I: Marketed ACIVIR cream as Standard

Group-II: Selected gel formulation as Test

On the skin's unbraided area, the test sample and reference sample were applied. Following administration, exactly 1ml of blood is taken from a rabbit's marginal ear vein using sterile butterfly needles and syringes, at intervals of 1 hour between the biological half-lives of the drug (0 and 2). Following a ten-minute centrifugation process at 3000 rpm to separate the plasma from the blood, the supernatant plasma was collected and refrigerated while the sample was being analysed.

**Determination of plasma concentration**

Shimadzu UV-spectrophotometer was used to measure the drug's plasma level. Then an equal amount of distilled water is added to each sample to dilute it. The prepared solution is then examined at 255nm in a UV spectrophotometer. that are displayed in tables 10 and 11, and table 12 displays the outcome.

**Pharmacokinetic parameters28**

From the information gathered above. Area Under Curve (AUC) graphs were created with time (in hours) on the X-axis and plasma drug concentration (in g/ml) on the Y-axis..

**Elimination rate constant (Ke)**

This can be calculated by the following formula equation Ke = 0.693/t1/2

**Elimination half-life(t1/2)**

The (t1/2) values are obtained by extrapolation of Time Vs plasma concentration curve

**Peak plasma concentration (Cmax)**

**Cmax** was obtained from the Time Vs Plasma concentration curve.

**tmax** was obtained from the Time Vs Plasma concentration curve.

**Relative Bioavailability**

This can be determined by using following formula

Relative Bioavailability = AUC for test

AUC for standard

**Absorption rate constant (Ka)**

The (ka) 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.**  **(µg/ml)** | **AUC**  **(µg 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.**  **(µg/ml)** | **AUC**  **(µg 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 | (µg hr/ml) | 98.03 | 146.32 |
| Relative  bioavailability |  | 2.523 | 1.492 |
| Cmax | (µg/ml) | 21.96 | 24.329 |
| tmax | Hour | 3 | 3 |
| Ke | Hour-1 | 0.234 | 0.230 |
| T1/2 | 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**

From the information gathered above. Area Under Curve (AUC) graphs were created with time (in hours) on the X-axis and plasma drug concentration (in g/ml) on the Y-axis.

**Evaluation of Acyclovir gels**

Prepared gel undergoes to evaluation studies

**Estimation of drug content**

Comparatively to the other formulations, the gel formulation of 1% carbapol-934 (A2) showed the highest drug content (101.73%).

**pH Measurements**

Digital pH metres are used to determine the gel's pH. The formulations' pH ranged from 6.8 to 7.3, with the results displayed in table 7.

**Determine the viscosity of gel**

The Brookfield Viscometer is used to measure viscosity. The gels' viscosities ranged from 41,400 to 51,600 cps, with the results displayed in table 8.

**Extrudability**

According to protocol, the extrudability of gel was determined. Carbopol and HPMC gels had superior extrudability to Na-CMC. Table 9 displays the outcome.

**Spreadability**

The procedure was used to determine the gel's spreadability. The formulation containing 1% Carbopol-934 had the highest spreadability data (8.2 cm), which was followed by other formulations 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**

According to protocol, a stability study was conducted for the ideal formulation. At 4 to 50 °C and 37 to 50 °C, the gels are physically and chemically stable. Table 10 displays the outcome.

**Skin irritation test**

According to protocol, a skin irritation test was performed; there were no erythema, edoema, or other adverse reactions. Use of the gel topically is safer.

**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 tmax was 3hr for both test and standard and Cmax 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 shows that a gel formulation can be used to increase the solubility, permeability, and bioavailability of acyclovir and to get around the problems that come up when using it in clinical settings. The formulation of the gel uses a variety of polymers, including Carbapol-934, Carbpol-940, HPMC, and Na-CMC, based on the analysis.

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 goal of the current research was to create an effective gel formulation for the topical treatment of herpes simplex virus infections. We were successful in developing and evaluating gel in this study.

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.

**ACKNOWLEDGEMENT**

The authors are very much thankful to the ITM University Gwalior (M. P.) 474001 India for providing a facility to carrying out this research work.

**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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