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Formulation and Evaluation of Topical Adapalene Emulgel

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ABSTRACT

Topical drug delivery systems have been utilized for centuries for the treatment of local skin disorders. One side the topical applications of the drug provides the potential advantages of delivering drug straightly to the site of action and delivering drug for extended period of time at the effected site that mainly acts at the related regions. On the other hand, topical delivery system elevates the contact time and mean resident time of drug. The aim of the work is to develop & characterize adapalene emulgel formulation. Adapalene emulgel formulations were prepared by dispersing Carbopol 934 in distilled water with constant stirring at a moderate speed, then the pH was adjusted to 6 - 6.5 using Triethanolamine. Evaluation of the adapalene emulgel was carried out for Physical appearance, Rheological study, pH values, Spreadability, Drug content determination, In vitro release study, Accelerated stability studies. It was noticed that all formulations were liquefied and diluted at the end of the experiments, indicating water diffusion through the membrane. The accelerated stability studies were performed according to ICH guidelines for three months & emulgels were found to be stable in differing temperature. The results demonstrate that the release of the drug is dependent on viscosity of the polymer used.

Keywords: Emulsion, Emulgel, Adapalene, Transdermal gel, water-in-oil system.

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INTRODUCTION

Delivering medicine to the common circulation through the skin is seen as a desirable alternative to taking it by mouth or oral route. Patients often forget to take their medicine and also they get tired of swallowing pills. Additionally escaping the gastrointestinal tract would obviate the GI irritation that frequently occurs & avoid partial 1st pass inactivation by a liver. Further, steady absorption of drug over hours or days is usually preferable to blood level spikes and troughs created by oral dosage forms. These advantages are offered by the currently marketed transdermal products. A trans-dermal drug delivery is defined as self-contained, discrete dosage forms which when applied to intact skin deliver the drug at controlled rate to the systemic circulation.[1, 2]

An emulsion can be defined as biphasic system consisting of two immiscible liquids, one of which (the dispersed phase) is finely & uniformly dispersed as globules throughout the second phase (the continuous phase). Since emulsions are a thermodynamically unstable system, a 3rd agent, the emulsifier is added to stabilize the system. Emulsifier stabilizes the system by making a thin film around the globules of dispersed phase. Either the dispersed phase or the continuous phase may differ in consistency from that of a mobile liquid to semisolid. Thus, pharmaceutical emulsions range from lotions to creams. The particle size of the dispersed phase commonly ranges from 0.1 to 100 μm.[3]

Gels are relatively new class of dosage form created by entrapment of large amounts of aqueous or hydro alcoholic fluid in network of colloidal solid particles. Gel formulation provides faster drug release compared with ointment and cream. In spite of many advantages of gel, a vital limitation is in the delivery of hydrophobic drugs. So to overcome this restriction emulgels are prepared and with their use even a hydrophobic drug can enjoy the unique properties of gels. When gels & emulsions are used as a combination, the dosage forms are referred as Emulgels. In the presence of a gelling agent in water phase transform an emulsion into an emulgel. Direct (oil-in-water) system is used to deliver hydrophobic drugs whereas hydrophilic drugs are encapsulated in the reverse (water-in-oil) system. Emulsions consist of a certain degree of elegance and are simply washed off whenever desired.[4]

MATERIALS AND METHOD

Adapalene was obtained as a gift sample from Torrent Pharmaceutical Ltd. Carbopol 934, Light paraffin, Tween 80 and Almond oil was procured from Arihant Trading Co., Mumbai.

Fabrication of Adapalen Emulgel[5]

Emulgel was made in 2 steps. The first step was made of oil in water emulsion and base of gel.

The second step was mixed of the emulsion and gel base. The oil phase emulsion was made by dissolving Span 20, Adapalene in almond oil. The water phase was made by dissolving Tween 80 in distilled water. Methyl and propyl paraben was dissolved in isopropyl alcohol and mixed in water phase. Each phase was heated at a temperature of 70-75 °C. After each phase reaches a temperature 70-75 °C, oil phase was mixed to the water phase. Then, the mixture was stirred using a homogenizer with a speed of 1500 rpm until the room temperature and the emulsion was formed. Then the emulsion was mixed into base gel consisting of 0.7% carbopol 934 bit by bit using a homogenizer stirring 1000 rpm until a homogeneous mass of emulgel was formed.

Table 1: Composition of various emulgel formulations

Ingredients	F1	F2	F3	F4	F5	F6
Adapalene	0.10	0.10	0.10	0.10	0.10	0.10
Almond oil	3	4	5	6	7	8
Tween 80	2	3	4	5	6	6
Span 20	1	1	1.5	2	2.5	3
Light paraffin	4	4	4	4	4	4
Isopropyl Alcohol	5	5	5	5	5	5
Carbopol 934	1	1	1	1	1	1
Water up to	100	100	100	100	100	100

Evaluation of the Adapalene Emulgel [6, 7, 8, 9, 10, 11]

- **Physical appearance**

The prepared adapalene Emulgel formulations were inspected visually for their color, homogeneity, consistency and pH values of 1% aqueous solutions of the prepared Emulgel were measured by a pH meter.

- **Spreadability**

One of the criteria of Emulgel to meet the ideal quantities is that it should possess good spreadability. The term is expressed to represent the extent of area to which gel readily spread on application to skin or affected part. The therapeutic efficacy of the formulation is relying upon its spreading value. Spreadability is expressed by time in seconds taken by two slides to slip off from emulgel and deposited in between the slides under the direction of certain load. Minimum time taken for separation of 2 slides, better the spreadability. It is calculated by using formula.

$S = M. L / T$

Where M = Weight tied to a upper slide

L = Length of glass slides

T = Time taken to separate the slides.

- **Extrudability study**

To carry outing the test, a closed collapsible tube containing above 20 grams of gel was squeezed firmly at a crimped end and a clam was applied to prevent any rollback. The cap was removed and the microencapsulated emulgel was extrudes until the pressure was dissipated.

- **Rheological study**

The viscosity of different Gellified emulsion formulations were determined at 37˚c using an instrument brook field viscometer.

- **Drug content determination:**

Drug concentration in Emulgel was measured by UV spectrophotometer. Adapalene content in emulgel was studied by dissolving known quantity of gellified emulsion in solvent (methanol) by sonication. Absorbance was measured after suitable dissolution at 315 nm in UV/ visible spectrophotometer.

- ***In vitro* release study:**

Franz diffusion was used for the drug release studies. Gellified emulsion (200mg) was applied on to cellophane membrane .The cellophane membrane was clamped between donor and receptor chamber of diffusion cell. The receptor chamber was filled with freshly prepared Phosphate buffer 7.4 solutions to solubilize the drug. The receptor chamber was stirred by magnetic stirrer. The samples were collected at suitable time interval sample were analyzed for drug content by UV visible spectrophotometer at 315 nm after appropriate dilutions. Cumulative corrections were made to obtain the total amount of drug release at each time interval. The percent cumulative drug release across the cellophane membrane was determined as a function of time

- **Accelerated stability study**

Emulgel Stability studies were performed according to ICH guidelines. The formulations were stored in hot air oven at 37 ± 2°C, 45 ± 2°C and 60 ± 2°C for three months. The samples were analyzed for drug content every two weeks by UV-Visible spectrophotometer at 315 nm. Stability study was also carried out by measuring the change in pH of gel at regular interval of time.

RESULTS AND DISCUSSION

- **Physical appearance**

The prepared adapalene Gellified Emulsion formulations were white viscous creamy preparation with a smooth and considered satisfactory to avoid the chance of irritation upon application to the skin. The results of pH, Spreadability, Extrudability, Homogeneity of the formulations was obtained as indicated in Table 2.

Table 2: Results of pH, Extrudability, Homogeneity, Spreadability

	pH	Extrudability	Homogeneity	Spreadability (g.cm/sec)
F1	6.34	Easily extrudable	Good	20.35
F2	6.28	Easily extrudable	Good	25.54
F3	6.44	Easily extrudable	Good	22.12
F4	6.23	Easily extrudable	Good	24.71
F5	6.47	Easily extrudable	Good	23.67
F6	6.21	Easily extrudable	Good	21.27

- **Rheological studies & Drug content determination**

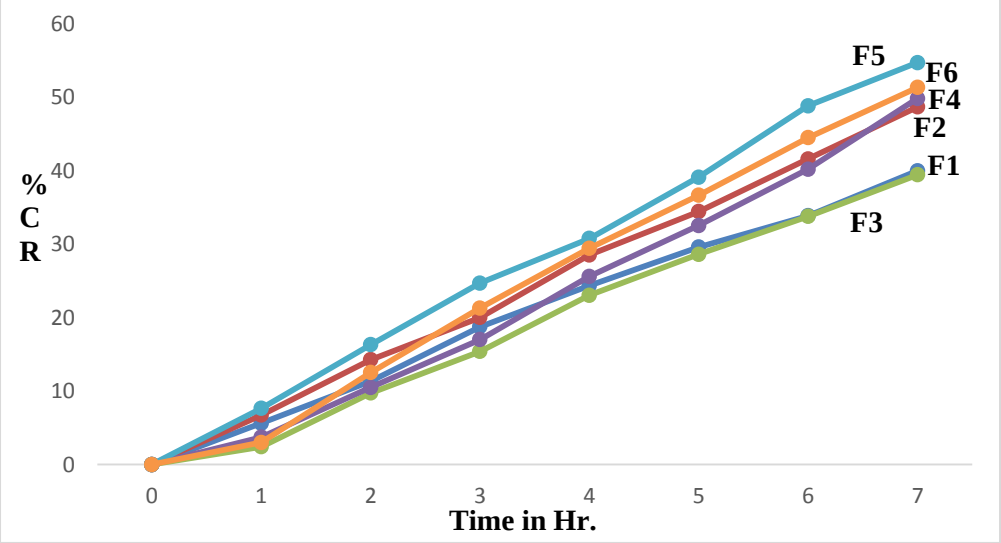
The measurement of viscosity of the prepared Adapalene Emulgel was done with Brookfield viscometer (Brookfield DV-E viscometer. 1g of the prepared Emulgel was mixed with 100 ml of suitable solvent. Aliquots of different concentration were prepared by proper dilution after sonication and filtering the stock solution and absorbance was measured. Drug content was calculated using equation, which was obtained by linear regression analysis of calibration curve. The result of viscosity and Drug content determination of formulations was obtained as indicated in Table 3.

Table 3: Results of Viscosity& Drug content determination

Formulation	Drug Content (Mean % ± SD)	Viscosity At 10 RPM
F1	98.48± 1.2	5234
F2	98.64± 1.6	4753
F3	99.83± 1.9	5244
F4	97.35± 2.1	4358
F5	99.57±. 2.3	5471
F6	97.61± 1.5	4190

- ***In vitro* Drug release**

The in vitro release profiles of adapalene from its various Emulgel formulations are represented in figure. It was observed that all the formulation had become diluted and liquefied at the end of the experiments, indicating water diffusion through the cellophane membrane. In general, it can be observed from figures that the better release of the drug from all Emulgel formulation. From results of in vitro diffusion studies, it can be concluded that F5 had better sustained release than the other formulations as shown in Graph 1



Graph 1 shows drug Release Profile of F1-F6

Accelerated stability studies

The accelerated stability studies were performed as per ICH guidelines for 3 months and the results were found to be stable in varying temperature.

CONCLUSION

The present study reports for the development of Adapalene emulgel for topical release of the drug. The results demonstrate that the release of the drug is dependent on viscosity of the polymer used. It can be conclusively stated that the adapalene emulgel formulation appears to be the promising system for the topical delivery of adapalene to avoid the disturbances of the conventional routes of administration.

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