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FORMULATION, DEVELOPMENT AND EVALUATION OF TRETINOIN EMULGEL FOR EFFECTIVE TRANSDERMAL DRUG DELIVERY

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Abstract

Acne vulgaris (or simply acne) is an infectious disease and one of the most prevalent human diseases. Topical drug delivery refers to the application of a drug-containing formulation to the skin to treat a cutaneous condition. Emulgel is a stable and superior system that incorporates poor water-soluble drugs. Emulgel has both gel and emulsion properties and functions as a dual control release system. Thus, the aim of this study is to formulate & evaluate emulgel of Tretinoin. Emulgel was formulated by standard method and evaluated for various parameters. The results showed that emulgel formed has good washibility spreadability, and consistency. The drug content of prepared emulgel formulation was found to be near to 100%. The drug content of formulation F1, F2, F3, F4, F5 and F6 was found to be 98.12±0.25, 97.85±0.32, 99.45±0.15, 97.65±0.22, 95.85±0.34 and 96.45±0.25 percent. The drug release of drug through prehydrated cellophane membrane was found to be 25.45, 39.98, 56.65, 72.23, 85.65 and 98.98 for formulation F1, F2, F3, F4, F5 and F6 after 240 minute. The optimized batch F3 of emulgel showed good drug release of 98.84% after 4 hrs. The R^2 value for zero order was found to be 0.771 while for first order it is found to be 0.989 respectively. From these results it can be said that the reaction follows first order kinetic. So, it can be concluded that the formed emulgel of Tretinoin have all ideal characteristics and can be used for acne treatment.

Keywords: Emulgel, Anti acne, Topical drug delivery, Tretinoin

Introduction

Acne vulgaris (or simply acne) is an infectious disease and one of the most prevalent human diseases. It is characterized by different areas of scaly red skin (seborrhea), pinheads (papules), blackheads and whiteheads (comedones), large papules (nodules), and sometimes scarring (piples). Severe acne is usually inflammatory, however it may also be non-inflammatory. In acne, the skin changes, due to changes in pilosebaceous unit skin structures including hair follicles and their associated sebaceous glands (Suva *et al*., 2014; Kamra *et al*., 2017).

Topical drug delivery refers to the application of a drug-containing formulation to the skin to treat a cutaneous condition. This system is used when other routes of drug administration (such as oral, sublingual, rectal, and parental) fail, or when a local skin infection, such as a fungal infection, occurs. Topical drug administration is a common treatment method for both local and systemic conditions. In the topical delivery system, the drug is absorbed by the skin and reaches the site of action to provide a therapeutic effect. The rate of drug release from a topical preparation is dependent directly on the physiological features of the carrier. The primary benefit of a topical delivery system is that it avoids the first-pass metabolism. The term microemulsion is based on particle size. Due to their smaller size, the drug particles can easily diffuse through the skin and reach their site of action. The gel will hold the microemulsion for a long time and will aid in the sustained release of the drug (Das *et al*., 2019; Kumar *et al*., 2019).

Emulgel is known as an emulsion that has been gelled by using a gelling agent. They can be made either o/w or w/o type. Emulgel is a stable and superior system that incorporates poor water-soluble drugs. In brief, emulgel is a combination of emulsion and gel. Despite the numerous advantages of gels, one significant disadvantage is the delivery of hydrophobic medications. As a result, an emulsion-based solution is being used to overcome this limitation, allowing even hydrophobic therapeutic moieties to benefit from the unique properties of the gel (Light and Karboune,2021; Mohammed,2013).

Emulgel can deliver both hydrophilic and lipophilic drugs due to the presence of both aqueous and non-aqueous phases. In recent years, they have been used as a control release formulation. These are biphasic systems that have better drug loading capacity

and better stability . Emulgel has several good properties, such as good spreadability, greaseless, thixotropic, good shelf life, odorless, and a pleasant appearance over the conventional topical formulation. Emulgel has both gel and emulsion properties and functions as a dual control release system(Satya Lakshmi *et al*., 2021; Poonuru *et al*., 2021). This study deals with the formation of emulgel of Tretinoin.

Material and Methods

Preparation of emulsion

The simple method was employed for preparation of an emulsion was as follows: The oil phase was prepared by dissolving Span 20 in liquid paraffin in the different ration given in table 7.1 while the aqueous phase was prepared by dissolving Tween 20 in purified water[54]. 1 gram of Tretinoin was dissolved in 5 ml of ethanol, while 0.15 g of methylparaben and 0.05 g of propylparaben were dissolved in 5 gm of propylene glycol and both were mixed with aqueous phase. Both the oily and aqueous phases were separately heated to 70-80°C. Then, the oil phase was added to the aqueous phase with continuous stirring at 500 rpm until cooled to room temperature.

Preparation of carbopol gel

Fifty (50) grams of the carbopol gel was prepared by dispersing 1 gram of carbopol powder in 50 ml purified water with aid of moderate speed stirrer (50 rpm), and then the pH was adjusted to 6.5-6.8 using 0.5 N of sodium hydroxide (Kaur *et al*., 2014).

Formulation of Tretinoin emulgel

Six formulations of Tretinoin were prepared by dispersing the obtained emulsions with the gel in 1:1 ratio with gentle stirring until get homogenous emulgel (Jain *et al*., 2010).

Table 1: Different formulations of Tretinoin emulgel (% w/w)

Formulation	Tretinoin (mg)	Carbomer 941	Liquid paraffin	Span 20	Tween 20	Propylene glycol	water
F1	500	0.5	5	2	5	5	50
F2	500	0.5	5	2	10	5	50
F3	500	1.0	10	4	5	5	50
F4	500	1.0	10	4	10	5	50
F5	500	1.5	5	2	5	5	50
F6	500	1.5	5	2	10	5	50

Evaluation of emulgel

Physical characteristic

The physical characteristic was checked for emulgel formulations (colour, clogging, homogeneity and texture) and observations were noted.

Determination of pH

The pH of the emulgel was determined by digital pH meter. One gram of gel was dissolved in 25 ml of distilled water and the electrode was then dipped in to gel formulation for 30 min until constant reading obtained. And constant reading was noted. The measurements of pH of each formulation were replicated two times (Jivani *et al*., 2018).

Washability

Formulations were applied on the skin and then ease and extent of washing with water were checked manually and observations were noted (Pawbake *et al*., 2020).

Extrudability study

The emulgel formulations were filled into collapsible metal tubes or aluminium collapsible tubes. The tubes were pressed to extrude the material and the extrudability of the formulation was checked (Suman *et al*., 2020).

Spreadability

Two glass slides of standard dimensions (6×2) were selected. The emulgel formulation whose spreadability had to be determined was placed over one of the slides. The second slide was placed over the slide in such a way that the formulation was sandwiched between them across a length of 6 cms along the slide. 100 grams of weight was placed up on the upper slide so that the emulgel formulation between the two slides was traced uniformly to form a thin layer.

The weight was removed and the excess of the emulgel formulation adhering to the slides was scrapped off. The lower slide was fixed on the board of the apparatus and one end of the upper slide was tied to a string to which 20 gram load could be applied 50 with the help of a simple pulley. The time taken for the upper slide to travel the distance of 6 cms and separate away from lower slide under the direction of the weight was

noted. The experiment was repeated and the average of 6 such determinations was calculated for each emulgel formulation

Viscosity

The measurement of viscosity of the prepared gel was done using Brookfield digital Viscometer. The viscosity was measured using spindle no. 6 at 10 rpm and 25^0C. The sufficient quantity of gel was filled in appropriate wide mouth container. The gel was filled in the wide mouth container in such way that it should sufficiently allow to dip the spindle of the Viscometer. Samples of the gels were allowed to settle over 30 min at the constant temperature (25 ±/1^0C) before the measurements (Chaitali *et al*., 2015).

Drug content

1 gm. of the prepared gel was mixed with 100 ml. of ethanol. Aliquots of different concentrations were prepared by suitable dilutions after filtering the stock solution and the absorbance was measured at 322 nm. Drug content was calculated by linear regression analysis of the calibration curve.

***In-vitro* drug release studies using the prehydrated cellophane membrane**

Preparation of cellophane membrane for the diffusion studies:

The cellophane membrane approximately 25 cm x 2cm was taken and washed in the running water. It was then soaked in distilled water for 24 hours, before used for diffusion studies to remove glycerin present on it and was mounted on the diffusion cell for further studies.

Diffusion Studies:

The *in-vitro* diffusion of drug from the different gel preparations were studied using the classical standard cylindrical tube fabricated in the laboratory; a simple modification of the cell is a glass tube of 15 mm internal diameter and 100 mm height. The diffusion cell membrane was applied with 1 gram of the formulation and was tied securely to one end of the tube, the other end kept open to ambient conditions which acted as donor compartment. The cell was inverted and immersed slightly in 250 ml of beaker containing neutralizing 7.4 pH phosphate buffer, freshly prepared as a receptor base

and the system was maintained for 2 hrs at 37± 0.5° C. The media was stirred using magnetic stirrer. Aliquots, each of 5 ml volume were withdrawn periodically at predetermined time interval of upto 12 hrs and replaced by an equal volume of the receptor medium. The aliquots were suitably diluted with the receptor medium and analyzed by UV-Vis spectrophotometer at 322.0 nm using neutralizing 7.4 pH phosphate buffer as blank.

Results & Discussion

All the prepared formulation were found to be white, clogging was found to be absent and having good homogeneity. Spreadability of formulation F1, F2, F3, F4, F5 and F6 was found to be 12.50, 11.45, 11.15, 10.24, 13.14 and 12.74 g cm/sec respectively.

The pH of all formulation was found to be near to skin pH. The pH of formulation F1, F2, F3, F4, F5 and F6 was found to be 6.85±0.15, 6.92±0.12, 6.78±0.17, 6.74±0.22, 6.82±0.11 and 6.65±0.17respectively.

The Viscosity of formulation F1, F2, F3, F4, F5 and F6 was found to be 3525±10, 3325±15, 4215±08, 3895±12, 4025±25 and 3715±21 cps respectively.

The drug content of prepared emulgel formulation was found to be near to 100%. The drug content of formulation F1, F2, F3, F4, F5 and F6 was found to be 98.12±0.25, 97.85±0.32, 99.45±0.15, 97.65±0.22, 95.85±0.34 and 96.45±0.25 percent.

The drug release of drug through prehydrated cellophane membrane was found to be 25.45, 39.98, 56.65, 72.23, 85.65 and 98.98 for formulation F1, F2, F3, F4, F5 and F6 after 240 minute.

The R^2 value for zero order was found to be 0.771 while for first order it is found to be 0.989 respectively. From these results it can be said that the reaction follows first order kinetic.

Table 2: Psychorheological characteristic

Formulation code	Washability	Observation	Clogging	Homogeneity
F1	+++	white cream	Absent	Good
F2	+++	white cream	Absent	Good
F3	+++	white cream	Absent	Good
F4	+++	white cream	Absent	Good
F5	+++	white cream	Present	Average
F6	+++	white cream	Present	Average

Table 3: Extrudability and Spreadability study

Formulation code	Extrudability	Spreadability (gcm/sec)
F1	++	12.50
F2	++	11.45
F3	+++	11.15
F4	+++	10.24
F5	+	13.14
F6	+	12.74

Table 4: Viscosity and pH

Formulation code	Viscosity (cps)	pH
F1	3525±10	6.85±0.15
F2	3325±15	6.92±0.12
F3	4215±08	6.78±0.17
F4	3895±12	6.74±0.22
F5	4025±25	6.82±0.11
F6	3715±21	6.65±0.17

Results of drug content of emulgel

Table 5: Results of drug content of emulgel

Formulation code	% Drug content
F1	98.12±0.25
F2	97.85±0.32
F3	99.45±0.15
F4	97.65±0.22
F5	95.85±0.34
F6	96.45±0.25

Table 6: *In vitro* drug release data for optimized formulation F3

S. No.	Time (min)	Square Root of Time	Log Time	Cumulative* Percentage Drug Release ± SD	Log Cumulative Percentage Drug Release	Cumulative Percent Drug Remaining	Log cumulative Percent Drug Remaining
1	15	3.873	0.588	25.45	1.406	74.55	1.872
2	30	5.477	0.739	39.98	1.602	60.02	1.778
3	45	6.708	0.827	56.65	1.753	43.35	1.637
4	60	7.746	0.889	72.23	1.859	27.77	1.444
5	120	10.954	1.04	85.65	1.933	14.35	1.157
6	240	15.492	1.19	98.98	1.996	1.02	0.009

Conclusion

In conclusion Tretinoin emulgel is a topical medication used to treat acne, wrinkles, and other skin conditions. It contains a form of vitamin A, which helps to reduce inflammation and increase the production of new skin cells. The medication can be used alone or in combination with other topical treatments. Tretinoin emulgel is generally well-tolerated and can be effective in treating mild to moderate acne. However, it should be used with caution and only as directed, as it may cause skin irritation and sensitivity to sunlight. It can be concluded from the above results and discussion that Tretinoin emulgel formulations prepared with Carbomer 941, Liquid paraffin, Span 20, Tween 20 and Propylene glycol showed acceptable physical properties, drug content and drug release. The optimized batch F3 of emulgel showed good drug release of 98.84% after 4 hrs.

References

1. Suva MA, Patel AM, Sharma N, Bhattacharya C, Mangi RK. A brief review on acne vulgaris: pathogenesis, diagnosis and treatment. Research & Reviews: Journal of Pharmacology. 2014;4(3):1-2.
2. Kamra M, Diwan A. Acne: current perspective. Journal of Applied Pharmaceutical Research. 2017 Jul 15;5(3):01-7.
3. Das S K, Khanum A, Ghosh A. Microemulsion based gel Technique- A Novel Approach for Sustained Delivery to Treat Fungal Infection. Indo American Journal of Pharmaceutical Research. 2019; 8 (2): 1958.
4. Kumar N, Saxena C, A Novel Approach for Topical Drug Delivery System -Emulgel Trends in Pharmaceutical and Nanotechnology. 2019, 1 (2), 27-28.
5. Light k, Karboune S. Emulsion, hydrogel and Emulgel system and novel application in cannabinoid delivery: a review. Taylor & Francis Group. 2021; 22:1-31
6. Mohammed Haneefa P K. Emulgel: An Advance Review. Journal of Pharmaceutical Science and Research, 2013;5 (12): 254 – 258.
7. Satya Lakshmi S, Divya R, Srinivasa Rao Y, Kamala Kumari PV, Deepthi K. Emulgel-Novel Trend in Topical Drug Delivery System – Review Article. Research J. Pharm. and Tech. 2021; 14 (5): 2903-2906.

8. Poonuru R, Cheruku R, Thippani G, Bommakanti R. Emulgel Based Skin Delivery of Adapalene for Treatment of Acne. InProceedings of International Conference on Drug Discovery (ICDD) 2020 Feb 2.
9. Darshan Kaur, Aparajita Raina, Nirmal Singh. Formulation and evaluation of carbopol 940 based glibenclamide transdermal gel. Int J Pharm Pharm Sci, 2014; Vol 6, Issue 8, 434-440.
10. Jain A, Gautam S P, Gupta Y, Khambete H, Jain S, Development and characterization of ketoconazole emulgel for topical drug delivery, Pelagia Research Library Der, 2010; 1(3): 221- 231.
11. Jivani M N, Patel C P, Prajapat B G, Nanoemulgel Innovative Approach for Topical Gel Based Formulation, Research and Reviews on Healthcare: Open Access Journal, 2018: 18-22.
12. Pawbake G R, Shirolkar S V, Microemulgel: A Promising Approach to Improve the Therapeutic Efficacy of Drug, J ournal of Critical Reviews, 2020; 7(14): 1138-1142.