Formulation And Evaluation of Metronidazole Emulgel For Topical Drug Delivery

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Abstract

The skin may be directly accessed for diagnosis and therapy without worrying about going through first pass metabolism thanks to topical medication administration. Emulgel is one of the cutting-edge medical technologies that is frequently used for skin conditions like psoriasis, acne, and fungal infections. Emulgel is an emulsion that can be either o/w or w/o in nature. When mixed with a gelling agent, such as Carbapol, HPMC, etc. to form a gel. The primary goal of emulgel is to use the skin to transfer hydrophobic medications to the bloodstream. It benefits from a dual release control mechanism, which includes emulsion and gel. Emulgels are beneficial for dermatological usage because they are thixotropic, greaseless, readily spreadable, easily removed, emollient, non-staining, water-soluble, have a longer shelf life, are bio-friendly, and have a clear and appealing appearance. New polymers are utilised, can serve as an emulsifier and thickener because their ability to gel results in stable emulsions and creams by lowering surface and interfacial tension and simultaneously raising aqueous phase viscosity. The effects of several permeation enhancers can be potentiated.

Keyword: *Emulgel, Metronidazole, antiacne drug, topical drug delivery.*

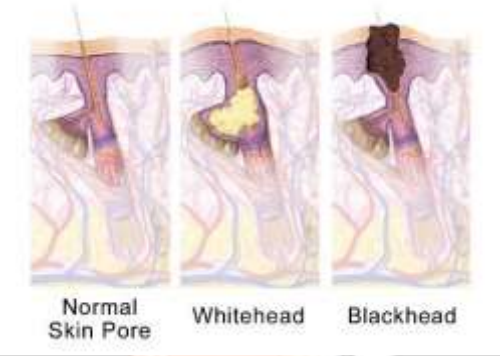
Introduction :

Localised drug administration through the skin, vagina, rectal, and ocular cavities is known as topical drug delivery. These apply a variety of cosmetic and dermatological preparations to their healthy or diseased skin1.Emulgels, which have the benefits of both gels and emulsions, serve as a controlled drug delivery mechanism for medications that are topically applied. They are either water in oil or oil in water emulsions that are gelled by combining with a gelling agent. Gels' mucoadhesive properties allow them to prolong the time that medication is in touch with the skin. Topical preparations use both types of emulsions—water in oil and oil in water—as water washable preparations and as emollients for dry skin, respectively. If the emulsion's natural state changes, the penetration process becomes simple. less viscous, or less thixotropic, when sheared. Emulgels are created by jellifying an emulsion in a gel foundation to boost its stability and capacity to penetrate the stratum corneum. Compared to creams and ointments, gels in dermatological preparations are easier to apply and give higher stability2.According to the BCS classification of the four drug classes, class II drugs have high permeability and poor solubility. It is evident that class II medicines' poor ability to dissolve is a bigger drawback to their overall rate and amount of absorption than their capacity to pass across the membrane. Emulgels may therefore be a better option when it comes to the topical distribution of medications that are not highly water-soluble. Emulsified gel is used for medications that are hydrophobic or poorly soluble in water.

Disease Profile :-

Acne vulgaris, usually referred to as acne, is a chronic skin condition that develops when the hair follicles become clogged with dead skin cells and skin oil. Blackheads, whiteheads, pimples, and oily skin are signs of acne, which can leave scars in some cases. The outcome can cause anxiety, low self esteem, and, in severe situations, depression or suicidal thoughts.

Pathophysiology :-



Anatomy of a hair follicle depicting a whitehead, or closed comedone, on the left, a blackhead, or open comedone, on the right, and a healthy hair follicle on the left. Skin inflammation vulgaris is a persistent skin sickness of the pilosebaceous unit and creates because of blockages in the skin's hair follicles. These blockages are thought to happen because of thefollowing four unusual cycles: a higher-than-normal amount of sebum production (caused by androgens), an excessive accumulation of the protein keratin that results in the formation of comedones, the colonization of the follicle by the bacteria Propionibacterium acnes (P. acnes), and the local release of chemicals that cause inflammation in the skin.

Material and Methods :-

Collection of plant material :-

Metronidazole is obtained from Samarth Institute of Pharmacy [Belhe] , including other chemicals too.

Ingredients	**F1**	**F2**	**F3**
Metronidazole	3gm	3gm	3gm
Carbopol 934	1.5gm	1.5gm	1.5gm
Clove Oil	5ml	-	-
Mentha Oil	-	5ml	-
Liquid Paraffin	-	-	5ml

Propyl Paraben	0.02ml	0.02ml	0.02ml
Methyl Paraben	0.02ml	0.02ml	0.02ml
Tween 80	1ml	1ml	1ml
Propylene Glycol	2.5ml	2.5ml	2.5ml
Triethanolamine	Qs	Qs	Qs
Dist. water	Qs	Qs	Qs

Topical emulgel formulation (15 g) table

Preparation of Emulgel :-

The methodology for preparation of emulgel include three steps :

Step 1: Formulation of gel base: The gel phase is set up by dissolving the polymer in the purified water with enduring mixing at moderate speed using mechanical shaker and the pH was adjusted to 6-6.5 using triethanolamine or NaOH.

Step 2: Formulation of o/w or w/o kind of emulsion: Oil phase of the emulsion is set up by dissolving emulsifier e.g. span in oil vehicle like liquid paraffin while the water phase is set up by dissolving hydrophilic emulsifier like tween in purified water. Methyl paraben and propyl paraben are dissolved in humectant like propylene glycol and drug is dissolved in ethanol and both the prepared solutions are mixed with watery phase with consistent blending. Both the oily and aqueous phase are freely warmed to 70°C to 80°C, then the oily phase is added to aqueous phase with constant blending. This mix is allowed to cooled to room temperature to shape an emulsion.

Step 3: Incorporation of emulsion into gel base with steady blending: the gel stage is mixed into the emulsion stage in the extent of 1:1 to procure emulgel

Evaluation of topical emulgel Formulation :-

- **Physical Evaluation**

Physical parameters such as color and appearance were checked.

1. Measurement of pH

pH of the gel was measured by using pH meter.

2. Spreadibility

Spreadibility was determined by the apparatus which consists of a wooden block, which was provided by a pulley at one end. By this method spreadibility was measured on the basis of slip and drag characteristics of gels. An excess of gel (about 2 g) under study was placed on this ground slide. The gel was then sandwiched between this slide and another glass slide having the dimension of fixed ground slide and provided with the hook. A 1 kg weighted was

placed on the top of the two slides for 5 minutes to expel air and to provide a uniform film of the gel between the slides. Excess of the gel was scrapped off from the edges. The top plate was then subjected to pull of 80 g. With the help of string attached to the hook and the time (in seconds) required by the top slide to cover a distance of 7.5 cm be noted. A shorter interval indicates better spreadibility. Spreadibility was calculated using the following formula: **S = M × L / T**

Where, S = Spreadibility,

M = Weight in the pan (tied to the upper slide),

L = Length moved by the glass slide and

T = Time (in sec.) taken to separate the slide completely each other.

3. Homogeneity

All developed gels were tested for homogeneity by visual inspection after the gels have been set in the container. They were tested for their appearance and presence of any aggregates.[19]

4. Viscosity

The viscocity of prepared emulgel formulation was determined at ambient temperature by using Brookfield Viscometer(DV-E version-1) with spindle no.5 at 10,30,50,60 and 100 rpm..[20]

5. Stability study

The stability study was performed as per ICH guidelines. The formulated gel were filled in the collapsible tubes and stored at different temperatures and humidity conditions, viz. 25ºC ± 2ºC / 60% ± 5% RH, 30º C ± 2ºC / 65% ± 5% RH, 40ºC ± 2ºC / 75% ± 5% RH for a period of three months and studied for appearance, pH, viscosity and spreadibility.[21, 22]

6. Swelling Index

The Swelling Index of prepared topical emulgel is performed by taking weighed 1 gm of emulgel on porous aluminium foil and then kept aside undisturbed in a 50-ml beaker containing 10 ml 0.1 N NaOH. Then at different time intervals the sample is removed from beaker and put it on dry place for some time and reweighed it. Swelling index is calculated by using following formula:

$$\boldsymbol{SW}\% = \frac{[\mathbf{Wt} - \mathbf{Wo}] * \mathbf{100}}{\mathbf{Wo}}$$

Where, SW% = Equilibrium percent swelling Wo = Initial weight of emulgel at time zero Wt = Weight of swollen emulgel after time. Syneresis measurement

7. Phase Separation

The emulgel formulation are subjected to centrifugation at 10,000 rpm for 10 min and examined for any change in phase separation

8. Drug Content Determination

A known quantity of 1 gm of prepared emulgel formulation is dissolved in 100 ml methanol by mean of sonication. It is kept for 2 hours in a volumetric flask and shaken well with the help of shaker to mix it properly. Then solution is filtered through Millipore filter paper. UV/VIS spectrophotometer is used to measure the absorbance after suitable dilutions

Conclusion :-

Emulgels have proven as most convenient, better and effective delivery system. It provides gel like property due to its non-greasy nature and lacks oily bases therefore it provides better release of drugs as compared to other topical drug delivery system. Incorporation of emulsion into gel makes it a dual control release system and solves the further problem such as phase separation, creaming associated with emulsion gets resolved and its stability improves. Emulgel loaded with specific drugs has been found effective in some topical disorders and it is emerging as potential drug delivery system in area of dermatology. In future Emulgel will provide a solution for topical delivery of hydrophobic drugs. Many of drugs that have utility in treatment of skin disorders are hydrophobic in nature. Such drugs can be delivered in the form of Emulgel where they can be incorporated in oil phase of emulsion and combined with gel.

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