FORMULATION & EVALUATION OF VORICONAZOLE OINTMENT FOR TOPICAL DELIVERY

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ABSTRACT

The present study was undertaken to develop ointment containing voriconazole selectively inhibits 14-alpha-lanosterol demethylation in fungi, preventing the production of ergosterol, an essential constituent of the fungal cell membrane, and resulting in fungal cell lysis. (NCI04). The ointment containing voriconazole was prepared by a fusion method., The specified concentration of polyethylene glycol (PEG) 4000, PEG400 and PEG 600 The amount of voriconazole remains fixed (5 mg) for all the eight formulations whereas the amounts of PEG400 will be used for first four formulations i.e. F-1,F-2,F-3,F-4,and PEG 600 for F-5,F-6,F7 & F-8 formulations respectively. The prepared ointments were evaluated for Physical Examination, Determination of pH, Measurement of viscosity, Spreadability Extrudability In-vitro Drug release study. We can conclude that all the parameters were within the acceptable limits.

KEYWORDS:- *voriconazole,polyethylene glycols,antifungal activity*

1.INTRODUCTION:

The studies were conducted with an object to develop a desired ointment for treatment of fungal infection like eczema itching, purities'. Main objective of this study is to formulate the ointment with different ointment bases having good consistency, diffusion, antifungal and antiseptic properties. To assess the efficacy of formulations assay, spread ability, permeability, drug release, uniformity, viscosity, diffusivity, stability, and other physical characteristics were evaluated. The ointment base was prepared and formulation of ointment was done by incorporating the active ingredients in most effective ratio in the base by fusion method. The PEG ointments were prepared with changing the type of the liquid PEG (low molecular weight). Then, the viscosity and the voriconazole release from the prepared formulations were studied.[1,2]

1.1 Characteristics of an ideal ointment[3,4,5]

1. It should be physically and chemically stable.
2. The base of ointment should possess no therapeutic action.
3. In ointment base, finely divided active ingredient should be uniformly distributed.
4. The ointment should be sooth and free from grittiness

1.2 Types Of Ointments Bases

The medicated stuff or the ingredients present inside the ointment is actually the main base of ointments. There are ointment bases:

1. Hydrocarbon bases. e.g. hard paraffin and paraffin, microcrystalline wax and ceresine.
2. Absorption bases. e.g. wool fat, beeswax.
3. Water soluble bases. e.g. PEG 200, 300, 400.
4. Emulsifying bases. e.g. Emulsifying wax, Vegetable oils like as coconut oil, sesame oil, olive oil, almond oil and peanut oil [6] .

1.3 Two type of method for preparation of ointments.

1. Mechanical method: This method also called trituration method. The quantity of ointment is not more than 50g, white porcelain or marble ointment should be used in conjunction with a flexible steel spatula. A steel spatula should not be used as medicament may react with the metal. the substance react with metal such as mercury compounds, tannic acid, salicylic acid and iodine [7,8] .

2. Fusion method: Ointment containing hard paraffin, beeswax, emulsified wax, wool alcohol are prepared by melting ingredients in a porcelain dish over a water bath. In this process higher melting point substance should be melted first and add then other ingredients of the bases in order of their melting point[9,10]

2. MATERIALS AND METHOD

Materials Voriconazole was procured from Jaipur pharmaceutical works. PEG400 and PEG600 was procured from Maharishi Arvind Institute of Pharmacy, mansarovar, Jaipur. All other chemicals were used of analytical grade and without any further chemical modification.

2.1 Method

The ointment containing voriconazole was prepared by a fusion method. The specified concentration of polyethylene glycol (PEG) 4000 was melted in a porcelain dish over a boiling water bath. PEG 400 or PEG 600 was heated to decrease order temperature and added to the melted PEG 4000. The mixture was then removed from heat and stirred. Then, voriconazole (5% w/w) dissolved in 20% propylene glycol (which is slightly heated) was added to the PEGs mixture and stirred until congealing. The excipients were taken according to drug weight. The different forms of ointment preparation together with their compositions are given in following tables.

Table 1: Composition of Voriconazole Ointment

Formulation	F1	F2	F3	F4	F5	F6	F7	F8
Drug	5	5	5	5	5	5	5	5
PEG 4000	20	20	20	20	20	20	20	20
PEG 400	10	20	30	40	-	-	-	-
PEG 600	-	-	-	-	10	20	30	40
Methanol	2	2	2	2	2	2	2	2
Propylene glycol	20	20	20	20	20	20	20	20
Methyl paraben	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Propyl paraben	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

3. EVALUATION OF OINTMENT

3.1 Fourier transforms infra red spectroscopy (FTIR): The primary objective of this investigation was to identify a stable storage condition for drug in solid state and identification of compatible excipients for formulation. The FTIR spectra of voriconazole was done and given in Fig. 1

3.2 Physical Examination: The Prepared ointment formulations were inspected visually for their colour, homogeneity, consistency.

3.3 Determination of pH: 2.5gm Ointment sample was taken in 100 ml dry beaker, 50 ml water was added to it. Beaker was heated on water bath maintained at about 60ºC to 70ºC for 10 minutes, cooled to room temperature, and then centrifuged at 3000 rpm for 10 minutes. The pH of water extract was measured by using pH meter. The pH measurements were done by using a digital type pH meter by dipping the glass electrode into the ointment formulation.

3.4 Measurement of viscosity: The viscosity of the prepared ointment formulations was determined using BrookField viscometer DV-III ULTRA (Brookfield Engineering laboratories, USA) using spindle no. 64. The viscosity was measured in centipoises (cps) at 10 rpm for 1 minute and temperature 25ºC using 20 gram sample4 .

3.5 Spreadability: The spreadability is expressed in terms of time in seconds taken by two slides to slip off from ointment, placed in between two slides under the direction of certain load. Lesser the time taken for separation of two slides, better the spreadability of ointment.

The spreadability was calculated by using the following formula.

$$S=M\times L/T$$

Where,

M = weight tied to upper slide

L = length of glass slides

T = time taken to separate the slides

3.6 Extrudability: Extrudability test is the measure of the force required to extrude the material from a collapsible tube when certain amount of force has been applied on it in the form of weight. In the present study the quantity in percentage of ointment extruded from the tube on application of certain load was determined. The extruadibility of prepared ointment formulations was calculated by using following formula.

$$\textbf{Extrudability} = \frac{\text{Amount of ointment extruaded from the tube} \times 100}{\text{Total amount of ointment filled in the tube}}$$

3.7 In-vitro Drug release study: The in vitro release of voriconazole from the prepared formulations was studied using dialysis method. 1 gram sample of each formulation was accurately weighed and placed on a semi permeable cellophane membrane immersed in phosphate buffer pH 7.4 for 24 hours. The loaded membrane (donor compartment) was firmly stretched over the lower open end of a glass tube of 2.5 cm internal diameter and made watertight by rubber band. The tube was then immersed in a beaker containing 25 ml of phosphate buffer pH 7.4 which is the release medium (receptor compartment). The system was maintained for 3 hours at 37 ± 0.5ºC in a thermostatic shaking water bath at 50 rpm. Samples of 5 ml were withdrawn at intervals of 1, 2, 3, 4, 5, and 6 hours. The volume of each sample was replaced by the same volume of fresh buffer (kept at the same temperature) to maintain constant volume

4. RESULTS AND DISCUSSION:

4.1 Physical Appearance:

Table 2: Physical Appearance

S. No.	Formulation Code	Colour	Homogeneity	Consistency
1	F1	White	Good	++
2	F2	White	Excellent	+++
3	F3	White	Excellent	+++
4	F4	White	Excellent	+++
5	F5	White	Poor	+
6	F6	White	Poor	++
7	F7	White	Good	++
8	F8	White	Good	+++

4.2 Determination of pH:

Table 3: Determination of pH

S. No.	Formulation Code	pH*
1	F1	6.36±0.3
2	F2	6.27±0.1
3	F3	7.09±0.6
4	F4	6.53±0.5
5	F5	6.09±0.18
6	F6	7.2±0.23
7	F7	7.12±0.4
8	F8	6.8±0.9

4.3 Rheological Study:

Table 4: Rheological Study

S. no.	Formulation Code	Viscosity (CP) *
1	F1	29,840±7.3
2	F2	32,646±16.4
3	F3	33,284±22.8
4	F4	34,028±17.7
5	F5	37,416±9.5
6	F6	37,996±11.3
7	F7	39,728±22.4
8	F8	41,176±18.5

4.4 Spreadability:

Table 5: Spreadability

S. No.	Formulation Code	Spreadability*
1	F1	28.49±0.7
2	F2	36.31±0.58
3	F3	39.54±1.39
4	F4	42.38±0.75
5	F5	18.7±1.04
6	F6	22.15±1.39
7	F7	29.64±0.94
8	F8	32.87±1.8

4.5 Extrudability:

Table 6: Extrudability

S. No.	Formulation Code	Extrudability
1	F1	Easily Extrudable
2	F2	Easily Extrudable
3	F3	Easily Extrudable
4	F4	Easily Extrudable
5	F5	Easily Extrudable
6	F6	Easily Extrudable
7	F7	Easily Extrudable
8	F8	Easily Extrudable

4.6 *In-vitro* drug release study:

Table 7: *In-vitro* drug release study

Formulation	% CDR (6hr)*	Drug content*
F1	72.38±1.14	96.1±0.46
F2	86.108±1.04	98.2±0.73
F3	89.722±0.75	98.7±0.39
F4	91.014±1.09	99.6±0.48
F5	63.079±0.95	95.3±0.35
F6	69.256±1.29	95.8±0.95
F7	78.871±1.26	96.3±0.57
F8	82.201±1.05	97.5±0.64

5. CONCLUSION:

Voriconazole ointment were successfully formulated using the mixture of PEG 4000, PEG 400, PEG 600 and propylene glycol for delivery of drug to produce local effect. Ointment could increase the drug permeability across the skin and fast release of the drug could be successfully achieved. The obtained results showed that the PEG ointment formulations exhibited better Voriconazole release formulation. For PEG ointments, the nature of the base itself may be adjunctive to the efficacy of the used antifungal agent. So, PEG ointments could be a promising topical antifungal drug.

6. REFERENCES

[1]. Upadhyay Mihir R., Design & Evaluation of Aceclofenac Loaded Microsponge for Topical Delivery, thesis for Degree of Master of Pharmacy at KLE University, Karnataka (2011), P.n.1-10

[2]. Jain N.K., Sharma N.K., A text book of professional pharmacy fifth edition, vallabh prakashan, (2007) P.n. 264-279

[3]. Jain N.K., Pharmacrutical product development second edition, CBH publishers, (2010) P.n. 269-286

[4]. Mekkawy I.A.A., Fathy M., Shanawany S., Study of Fluconazole Release from O/W Cream and Water Soluble Ointment Bases, British Journal of Pharmaceutical Research, Vol.3, Issue-1, (2013) P.n. 1-12

[5]. Yeu Chun Kim, Transdermal Drug Delivery Enhanced by Magainin Peptide, P.hd thesis at Georgia Institute of Technology (2007), P.n. 42-48.

[6]. www.drugbank.com

[7]. Pandey A., Jagtap J.V., Formulation and evaluation of anti-bacterial and anti-fungal activity of a herbal ointment containing Aloe-vera, Azadirachta indica and Curcuma- longa, Journal of Chemical and Pharmaceutical Research, Vol.2, Issue-3, (2010), P.n. 182-186

[8]. Ju M., Xu A., Duan Y., study of calcipotriol betamethasone ointment in the treatment of patients with refractory chronic eczema, Asian Journal of Pharmaceutical and Clinical Research, Vol.6, (2007), P.n. 34-40

[9]. Nagai H., Teramachi H., Tuchiya T., Recent Advances in the Development of Anti-allergic Drugs, Department of Clinical Pharmacology, Gifu Pharmaceutical University, Gifu, Japan, Vol.55, Issue 1, (2006), P.n. 35-42

[10]. Pasupathi A., Formulation, Development, Evaluation Of Calcitriol And Clobetasol Propionate Ointment, Indian Journal of Research in Pharmacy and Biotechnology, VoL.1, Issue-1, P.n. 95-105.