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RESEARCH ARTICLE

FORMULATION AND EVALUATION OF OXICONAZOLE EMULGEL FOR TOPICAL DRUG DELIVERY

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ABSTRACT

Emulgel is one of the emerging topical drug delivery system for the delivery of hydrophobic drugs which overcome various disadvantages of ointments and creams such as greasiness and phase inversion. The aim of present work was to develop and evaluate Oxiconazole emulgel with controlled release. The oxiconazole used in treatment of various fungal infections such as cutaneous and subcutaneous diseases like acne and psoriasis. Different formulations (F1-F4) of Oxiconazole emulgel was prepared by using carbopol 934 as gelling agent with varying concentrations of oily phase such as liquid paraffin and Tween-80 and Span-80 as a emulsifying agent. The prepared emulgels were evaluated for physical appearance, pH, drug content, *In-vitro* diffusion studies, microbiological assay and skin irritation test. By the *In-vitro* diffusion studies it was observed that formulation F1 showed 47.2% and marketed formulation (Oxistat cream) showed 42.1% of drug release after 10 hours and results concluded that the formulation F1 showed better releasing of drug than comparison with marketed cream.

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INTRODUCTION

Topical drug delivery system have been very useful for centuries for the treatment of local skin disorders without undergoing first pass metabolism and acid or enzymatic degradations. Emulgel is one of the interesting topical drug delivery system which drug is randomly distributed as oil micro droplets. The oxiconazole is broad spectrum antifungal used for the treatment of fungal diseases like tinea vermicular, athletes foot, jock itch etc. The aim of the work was to formulate Oxiconazole emulgel with sustained drug release in controlled manner and evaluate their characteristics.

MATERIALS

Oxiconazole Nitrate, Carbopol 934, Liquid Paraffin, Potassium Dihydrogen Phthalate and Sodium Hydroxide were procured from Research Lab Fine Chem Industries, Mumbai; Tri Ethanol Amine, Citric Acid and Dichloromethane were procured from Merch Specialities Pvt. Ltd, Mumbai; Span 80 from Qualikems Fine Chem Pvt. Ltd, Vadodara; All chemicals were pharmaceutical grade and used without further modification.

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METHODS

Standard Curve of Oxiconazole

The stock solution (1 mg/ml) was prepared by weighed accurately 50 mg of Oxiconazole nitrate and transferred to a 50 ml volumetric flask then makeup the final volume with methanol. Different concentrations (2, 4, 6, 8, and10µg/ml) of solutions were prepared from the stock and measure the absorbance at 427 nm by using UV-Visible spectrophotometer and reagent blank. Graphs were plotted taking concentration on X-axis and absorption on Y-axis to give linear curve and the method obeyed Beer's law.

Preparation of Oxiconazole Emulgel

The gel was prepared by dispersing Carbopol 934 in purified water with constant stirring and adjusted the pH to 6 to 6.5 using Tri Ethanol Amine (TEA) (Ramakanth Ambala and Sateesh Kumar Vemula, 2015; Ranga Priya *et al.*, 2012). The oil phase of the emulsion were prepared by dissolving Span 80 in light liquid paraffin while the aqueous phase was prepared by dissolving tween 80 in purified water. Methyl and Propyl paraben were dissolved in propylene glycol whereas drug was dissolved in ethanol and both solutions mixed with the aqueous phase.

Table 1. Standard Curve of Oxiconazole

S. No	Concentration (µg /ml)	Absorbance
1	0	0
2	2	0.067
3	4	0.153
4	6	0.239
5	8	0.327
6	10	0.413

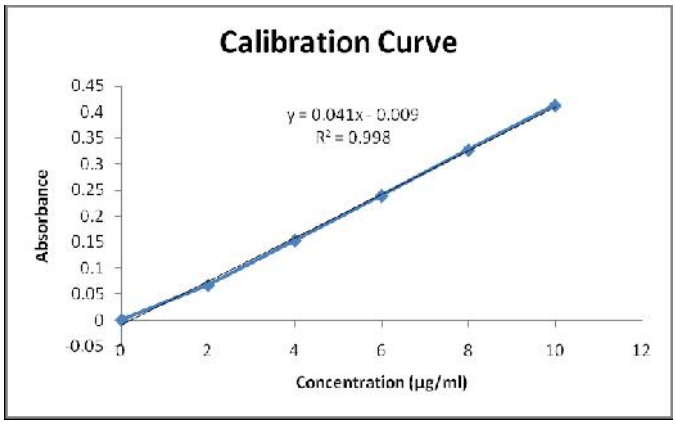

Fig. 1. Standard Curve of Oxiconazole

Both the oily and aqueous phases were separately heated to 70° to 80°C; then the oily phase were added to the aqueous phase with continuous stirring until cooled and add glutaraldehyde during the mixing of gel and emulsion in ratio 1:1 to obtain the emulgel (Ramakanth Ambala and Sateesh Kumar Vemula, 2015).

Table 2. Formulation of Oxiconazole Emulgel

Ingredients (%w/w)	F1	F2	F3	F4
Oxiconazole	1	1	1	1
Carbopol 934	0.5	0.5	0.5	0.5
Liquid paraffin	2.5	3.75	2.5	3.75
Tween 80	0.3	0.3	0.5	0.5
Span 80	0.45	0.45	0.75	0.75
Propylene glycol	2.5	2.5	2.5	2.5
Ethanol	2	2	2	2
Methyl paraben	0.01	0.01	0.01	0.01
Propyl paraben	0.005	0.005	0.005	0.005
Gluteraldehyde	0.05	0.05	0.05	0.05
Purified water	Q.S	Q.S	Q.S	Q.S

Evaluation parameters

- **Physical Appearance:** The prepared Oxiconazole emulgel formulations were inspected visually for their color, homogeneity, consistency, grittiness and phase separation (Ramakanth Ambala and Sateesh Kumar Vemula, 2015; Joshi Baibhav *et al.,* 2011).
- **Measurement of pH:** The pH of emulgel formulations was determined by using digital pH meter (Asmit Kamble *et al.,* 2014).
- **Drug Content:** Oxiconazole content in emulgel was measured by dissolving known quantity of emulgel in solvent by sonication in a separator funnel and add 3 ml 0.1M citric acid solution, 2 ml of 0.1% methyl orange and 10 ml of dichloromethane. The organic extracts were collected to measure the absorbance at 427 nm by using UV-Visible spectrophotometer and reagent blank (Ramakanth Ambala and Sateesh Kumar Vemula, 2015; Asmit Kamble *et al.,* 2014; Joshi Baibhav *et al.,* 2011).
- ***In vitro* Release Study:** Franz diffusion cell (with effective diffusion area 3.14 cm^2 and 15.5 ml cell volume) was used for the drug release studies. 200 mg of emulgel from each formulation was applied onto the surface of egg membrane and clamped between the donor and the receptor chamber of diffusion cell (Ramakanth Ambala and Sateesh Kumar Vemula, 2015). The receptor chamber was filled with freshly prepared phosphate buffer solution (pH 5.5) and stirr the solution by using magnetic stirrer. Then collect the samples (1.0 ml aliquots) at suitable time interval (Ranga Priya *et al.,* 2012; Yehia *et al.,* 2011). Take each sample in a separator funnel and add 3 ml 0.1M citric acid solution, 2 ml of 0.1% methyl orange and 10 ml of dichloromethane. The organic extracts were collected to measure the absorbance at 427 nm by using UV-Visible spectrophotometer and reagent blank. The cumulative amount of drug release across the egg membrane was determined as a function of time (Asmit Kamble *et al.,* 2014). Same procedure is repeated for marketed Oxistat cream to determine the cumulative amount of drug release for comparative studies.

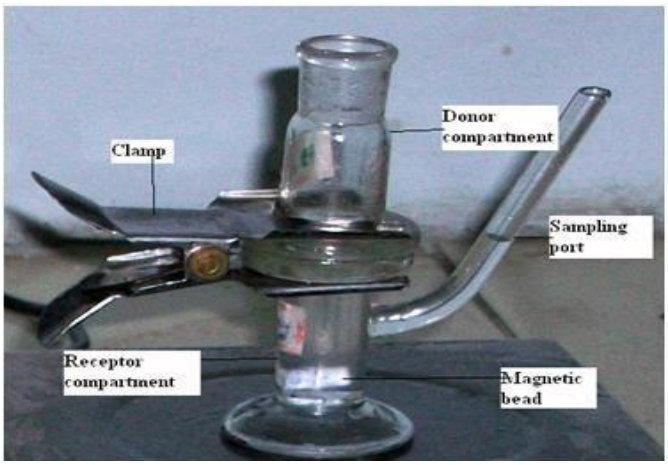

Fig 2. Experimental setup for *In vitro* diffusion studies

Microbiological Assay

Ditch plate technique was used. In which previously prepared Sabouraud's agar dried plates were used. Three grams of the emulgel are placed in a ditch cut in the plate and freshly prepared culture loops are streaked across the agar at a right angle from the ditch to the edge of the plate (Joshi Baibhav *et al.,* 2011). After incubation for 18 to 24 hours at 25°C, the fungal growth was observed and the percentage inhibition was measured as follows

$$\%\text{inhibition} = L2 / L1 \times 100$$

Where L1 = Total length of the streaked culture, and L2 = Length of inhibition.

Skin Irritation Test (Patch Test)

A set of 4 rats was used in the study. A 0.5 gm of emulgel formulation was applied on the properly shaven area of skin approximately 1" x 1" (2.54 x 2.54 cm) $square^2$. When the undesirable changes like skin color; change in skin morphology was checked for a period of 24 hr^3.

Table 3. Drug content in formulations

S.No	Formulation code	Sample Volume (ml)	Dilution Factor	Absorbance	Amount Present (mg)	% drug Content (%)
1	F1	10	100	0.336	8.44	84.4
2	F2	10	100	0.316	7.95	79.5
3	F3	10	100	0.292	7.34	73.4
4	F4	10	100	0.248	6.25	62.5

RESULTS AND DISCUSSION

- **Physical Examination:** The prepared Oxiconazole emulgel formulations were white, viscous, creamy preparation with a smooth, homogeneous, good consistency and without any gritty particles.
- **Measurement of pH:** The pH of the Emulgel formulations was in the range of 5.8 to 6.0 and there was no significant change in pH values as a function of time for all formulations.
- **Drug Content:** The formulation F1 showed higher drug content of 84.4% and it may be due to the low concentration of liquid paraffin and emulsifying agent. The formulation F4 showed lower drug content of 62.5%.

Table 4. *In Vitro* Diffusion Data of Oxiconazole from Formulation F1, F2, F3, F4 & M.F

Time in Hours	% Cumulative drug release				
	F1	F2	F3	F4	M.F
1	22.70	07.65	18.63	10.32	16.54
2	24.30	09.55	21.55	12.70	19.75
3	27.95	11.65	24.40	15.00	22.65
4	30.35	13.10	27.35	18.15	25.50
5	32.05	16.10	29.65	22.20	28.45
6	34.05	19.30	32.75	24.95	31.50
7	37.00	23.30	35.20	27.80	33.90
8	40.00	26.05	37.70	30.75	36.35
9	43.70	28.90	40.25	35.30	38.85
10	47.20	33.35	43.60	40.05	42.1

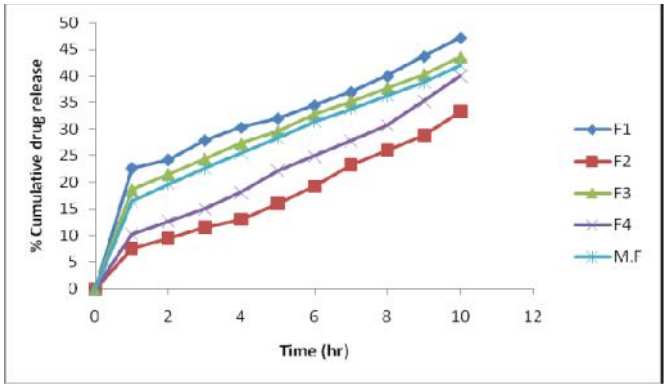

Fig. 3. Comparative Release Profile of Formulations F1, F2, F3, F4 & M.F

- ***In vitro* drug release:** The diffusion data for the formulations F1 to F4 and marketed Oxistat cream is as follows. The better release of the drug from all emulgel formulation can be observed and the can be ranked in the following descending order: F1 > F3 > F4 >F2.
- **Microbiological assay:** The antifungal activity of Oxiconazole in different emulgel formulations was passed in which Percentage inhibition was taken as a measure of the drug antifungal activity. Thus, the highest activity was observed with F1, where the percentage inhibition found to be 48.48, while the lowest activity was found with F2, where the percentage inhibition was 33.33.Whereas the percentage inhibition of marketed product was found to be 42.42.
- **Skin Irritation Test:** The allergic symptoms like inflammation, redness, irritation, erythema and edema are not appeared on rats up to 24hr.

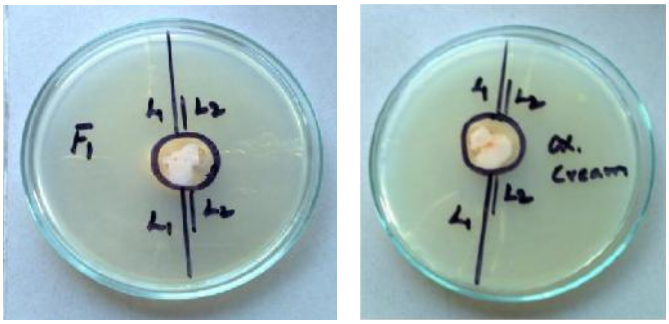

Fig. 4. Microbial Assay of F1 and Oxistat Cream

Conclusion

Oxiconazole can be formulated as emulgel with proper consistency, pH, anti-microbial activity and drug release. The emulgel formulation with lower concentrations of oily phase and emulsifying agent showed better release than compared with marketed formulation.

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