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DEVELOPMENT AND CHARACTERIZATION OF EMULGEL FOR TOPICAL APPLICATION

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ABSTRACT:
In the present study, an attempt has been made to develop the topical drug delivery system of fluconazole as Emulgel. Fluconazole is an antifungal medicine used to treat a variety of fungal skin infections. When taken by mouth, this medication has a low absorption rate. To counter this, topical drug delivery is favored, as it prevents the drug's first-pass metabolism. Emulgel of Fluconazole was prepared by the emulsification technique using gelling agent carbapol 940; Span 20 and tween 20 as Emulsifiers; Propylene glycol as penetration enhancer; Methyl paraben used as preservative. The major objective behind this formulation is to enhance topical delivery of Fluconazole which is hydrophobic in nature.The prepared emulgel were evaluated for their physical appearance, viscosity, spread-ability, % drug diffusion and drug content. Physical characteristics of all the prepared emulgels were acceptable. % Drug diffusion reveals a maximum release of 96.4 percent in 4 hours and the drug content was found to be 88.59 in F9 formulations. When compared to all other formulations, the formulation batch F9 shows better drug release. The formulation was found to be stable over the stability period.From the study conducted, it can be concluded that emulgel of Fluconazole can be better alternative for conventional topical gel. However thorough clinical studies need to prove its actual human use.

KEYWORDS:Emulgel; Fluconazole; % Drug content; % Drug diffusion; Stabilitystudy.

INTRODUCTION:

Topical drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. These are applying a wide spectrum of preparations for both cosmetic and dermatological, to their healthy or diseased skin.[1] Skin is one of the most read accessible organs on human body for topical administration and is the main route of top drug delivery system.

Topical drug delivery is the potential route to deliver the drug producing low side effect in comparison with any other dosage form. They are various example of drug delivered to topically include corticosteroid, antifungals, antivirals, antibiotics, antiseptic, local anesthetics. Several antifungal agents are available in the market as cream, ointment, gel, powders, lotions etc.[2]

Fungal infections are very common in human beings, especially in the tropical regions.[3] Fungi produce a wide spectrum of human infections ranging from superficial skin infections affecting the outer layers of skin, hair, nails and mucous membranes.

Whenever, it is used for fungal disease for topical delivery system so it is good for compare to oral delivery.[4]Through the ages, Diseases affect the health of human beings by various types of diseases. The effort has taken to give newer drug molecules by various administration methods for different routes. The route of administration selected depending upon the severity of the disease, type of disease, emergency of treatment and location of the disease. Each type of drug delivery and route of administration has the merits and demerits.

When emulsion and gel are used in combined form the dosage form is referred as 'emulgel'.In spite of many advantages of gels a major limitation is in the delivery of hydrophobic drugs. The presence of gelling agent in the water phase converts a classical emulsion into an emulgel.[5]

Emulsion itself is a controlled release system where entrapped drug particles in internal phase pass through the external phase to the skin and slowly get absorbed.[6] Internal phases act as reservoir of drug and slowly release drug in controlled way through the external phase to the skin. Gel forms cross linked network where it captures small drug particles and provides its release in a controlled manner.Due to its bio adhesive property it prolongs the contact period of medication over the skin. Since emulgel possesses the property of both emulsion and gel, it actsas dual control release system.

MATERIALS AND METHODS:

A. Materials:

Fluconazole sample obtained from Yarrow chem products Mumbai, India. Other chemicals used are Carbapol 940, Liquid paraffin, Tween 20, Span 20, Propylene Glycol, Ethanol, Methyl paraben,Triethanolamine, etc.

B. Methods:

Preformulation:

UV-Spectroscopy:

Fluconazole 1000 µg/ml solution prepared using PBS 7.4. From this solution 1 ml was withdrawn and dilutedupto 10 ml to make 100µg/ml. By using this stock; working dilutions of 2, 4, 6, 8, 10 µg/ml concentrations were prepared and analyzed on UV.Calibration curves were then constructed to plot linearity.[11,12]

Fluconazole shows maximum absorption at wavelength 260 nm in a phosphate buffer solution of pH 7.4. Calibration curves data were figured below.

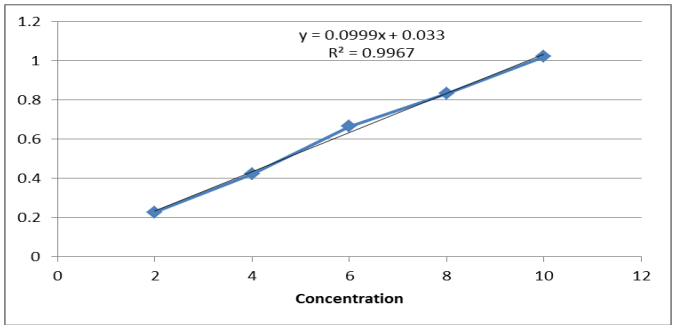

Figure 1: Calibration curve

FTIR spectroscopy:

FTIR spectroscopy conducted to identify drug excipient study using Perkin Elmer FTIR instrument. Results concluded drug sample is pure and is compatible with all the excipients.

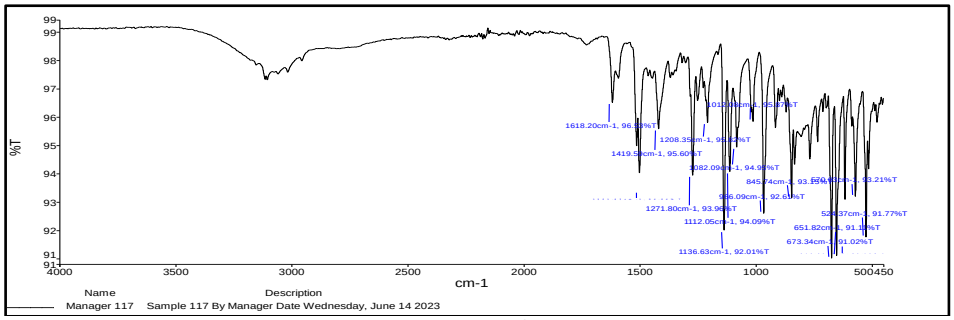

Figure 2: FTIR of Drug

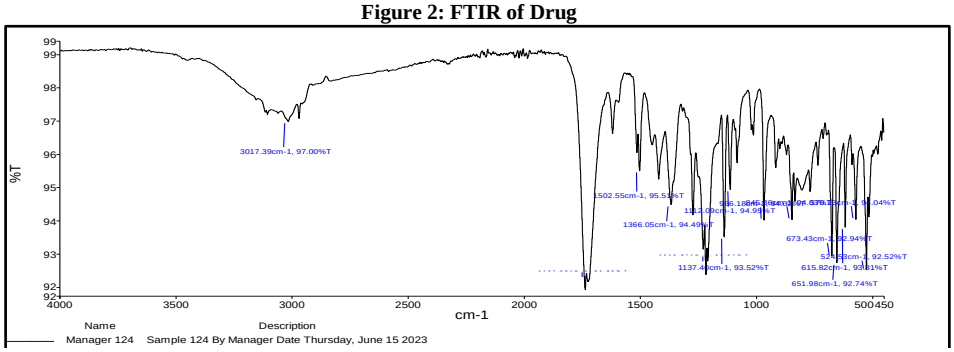

Figure 3: FTIR of Drug & Excipients physical mixture

Formulation:

Firstly drug loaded emulsion were developed by using varying concentration/ quantity of oil i.e. Light liquid paraffin (as solvent for drug dissolution) & emulsifying agents Tween 20 & Span 20.[7,8]Carbapol 940 is swollen & uniformly mixed with previously prepared emulsion.Preservative, penetration enhancer, as well as humectant was finally added.[13,14] Kept aside prepared emulgelfor a day and evaluated for physicochemical stability.

Table 1: Formulation table

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Fluconazole(gm)	1	1	1	1	1	1	1	1	1
Carbapol 940(gm)	0.5	0.5	0.5	0.75	0.75	0.75	1	1	1
Light liquid paraffin(ml)	2.5	3	3.5	2.5	3	3.5	2.5	3	3.5
Tween 20 (ml)	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Span 20(ml)	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4
Propylene glycol(ml)	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Ethanol(ml)	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25
Methyl paraben(mg)	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Purified water (q.s.)	50	50	50	50	50	50	50	50	50

Characterization:

Appearance &Homogeneity:

The emulgel was observed for appearance and clarity by visual testing.Emulgels found were homogeneous with absence of any particulate matter and lumps.

Results are figured below.

Figure 4: Result of Appearance & Homogeneity

Viscosity &Spread-ability:

20 gm of emulgel was subjected to the viscosity determination on Brookfield viscometer using spindle no. 6 at RPM 50.

Spreadability of emulgel was determined by sandwiching 5gm sample in between two glass slides and applying weight to the upper slide. A shorter interval indicates better spreadability, which is calculated by as S=M.L/T.[7,8]

Results obtained are mentioned in table 2

% Drug content:

2 gmof emulgel sample were taken in 100 ml flask having 10ml ethanol and stirred by magnetic stirrer for 5 minutes. The solutions were filtered using Whatmann filter paper. The absorbance of the solution was estimated spectrophotometrically (UV 1800, Shimadzu) to calculate % drug content in emulgel.[12]

Table 2: Results of rheological parameters & drug content

Formulation code	Viscosity (cps)	Spread-ability (gm.cm/sec)	Drug content (%)
F1	2161±9.01	14	37.37
F2	2168±4.58	15.21	39.07
F3	2190±6.50	13.46	47.33
F4	2272±7.54	16.66	50
F5	2287±7.93	14.58	54.61
F6	2295±5.29	15.21	64.56
F7	2325±5.03	16.66	71.35
F8	2341±6.50	15.90	86.4
F9	2345±2.08	17.50	88.59

% Drug diffusion:

The diffusion studies of the prepared emulgel were carried out in diffusion cell membrane assembly. Gel sample (0.5g) was taken in cellophane membrane and the diffusion studies were carried out at 37±1°C using 250 ml of phosphate buffer (pH 7.4) as the dissolution medium.5ml of each sample was withdrawn periodically at 0.5, 1, 2,3,&4 hrs and each sample was replaced with equal volume of fresh dissolution medium in order to maintain sink condition. Samples were analyzed by UV-visible spectrophotometer at 260 nm for drug content.[8-16]

Table 3: Results of % drug diffusion

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	9.67	9.76	9.84	9.88	10.17	10.3	10.79	11.25	12.16
1	23	23.86	24.57	25.6	26.14	26.8	27.55	28.29	29.32
2	30.99	32.32	38.43	34.59	40.25	46.45	47.28	48.07	49.14
3	36.16	40.74	46.06	37.3	48.05	50.41	60.49	71.42	82.93
4	57.24	59.08	60.51	51.83	52.62	64.03	71.1	80.64	96.21

Due to composition of varying quantities of polymer and oil the large difference has to be seen in results of % drug diffusion. As F1 is sustaining drug release while F2 and F3 are immediately releases. As like F1<F2<F3 drug release pattern is same in F7<F8<F9 but somewhat in large quantity drug has released. Among all F9 is considered as optimized with maximum drug release at 4hr.

Stability study:

Optimized emulgelF9 is placed in collapsible tubes with proper sealing for accelerated stability study as per ICH Guidelines at 40±2°C, 75±5%RH.[17]The formulation was withdrawn after particular period of interval; the physical stability was evaluated for physical appearance, rheological properties, % drug content, and % drug diffused.

No significant change was noticed in the parameters evaluated after stability. Results are tabulated below.

Table 4: Results of stability study

Month	Physical appearance	Viscosity (cps)	Drug content (%)	Drug diffused (%)
Initial	White homogeneousemulgel	2345	88.59	96.21
Final	No change	2318	88.14	95.89

CONFLICT OF INTEREST:

The authors have no conflicts of interest regarding this investigation**.**

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CONCLUSION:

Fluconazole emulgel was prepared by the emulsification technique and was evaluated for various physicochemical tests and results were found within the accepted limits. Among all the formulations of emulgel; F9 was the best formulation, showed better drug content, % drug diffusion. The formulation was found to be stable over the stability period. It can be concluded that emulgel of Fluconazole can be better alternative for conventional topical gel. However thorough clinical studies need to prove its actual human use.

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