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Formulation and Evaluation of Vegetable Oil Based Emulgel of Fluconazole

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ABSTRACT

Aim: The aim of the study was to prepare an emulgel formulation of fluconazole using vegetable oil (sesame oil) and compare with liquid paraffin Fluconazole emulgel. Emulgel has emerged as a promising drug delivery system for delivery of hydrophobic drug. Fluconazole is an anti- fungal medication use for a number of fungal infections it belong to a group of medicine called azole antibiotics. The edible oil is used as it has no side effects.

Method: The oil phase of emulsion was prepared by dissolving span 20 in light liquid paraffin and vegetable oil & drug. The aqeous phase is prepared by dissolving tween 80 in purified water. Methyl & Propyl gel phase was prepared by dispersing carbopol 940 in purified water & both phases are mixed with continuous stirring. The pH is adjusted using TEA (tri-ethanol-amine).

Results: The prepared emulgel was also evaluated for their physical properties, pH, drug content, viscosity, spreadability and swelling index. The pH of formulation with liquid paraffin & vegetable oil. The pH of formulation with liquid paraffin & edible oil pH in range 5 to 7.0 and the viscosity of both emulgel are almost same in range of 1134-2000 centipoises.

Conclusion: It was concluded that vegetable oil based emulgel are stable and effective and can be used instead of liquid paraffin based emulgel.

Keywords: Emulgel, Hydrophobic drug, Vegetable oil, Fluconazole, Topical drug delivery.

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INTRODUCTION

Topical drug administration is that the simplest and best route of localized drug delivery anywhere within the body by routes as ophthalmic, rectal, vagina and skin without undergoing first pass metabolism and acid or enzymatic degradations. As the name suggest, Emulgel are the combination of emulsion and gel. To penetrate the skin emulgel have high permeability. For dermatological use emulgel have many favorable properties like being thixotropic, greaseless, simply removable, simply spreadable, emollient & bio-friendly [1]. Emulgel formulation can incorporate hydrophobic drug which is not possible by simple hydrogel i.e. only by formulating emulgel. Emulgel overcome the problems associated with emulsion (i.e. stability) and gel (i.e. syneresis) alone. Fluconazole is hydrophobic in nature therefore it reports a problem of solubility in water this can be solved by adding drugs in oil phase of emulsion. Sesame oil is a vegetable oil obtains from sesame seeds. The oil from the nutrient rich seeds is popular in alternative medicine, from traditional massages [2].

MATERIAL AND METHOD

MATERIAL

Fluconazole (syncom Pharma Ltd.), Tween 80 (Lobal Chemie Lab. Reagent & Fine Chemicals), Span 20 (Lobal Chemie Lab. Reagent & Fine Chemicals), Propyl paraben, Methyl paraben (RFCL Ltd.), Propylene glycol (Lobal Chemie Lab. Reagent & Fine Chemicals), Carbopol 940 (Lobal Chemie Lab. Reagent & Fine Chemicals), TEA (tri-ethanol-amine), (Lobal Chemie Lab. Reagent & Fine Chemicals), Liquid Paraffin (Lobal Chemie Lab. Reagent & Fine Chemicals), Sesame oil (Deepak Agencies).

METHOD

Preparation of emulsion phase: The oil phase of emulsion was prepared by dissolving span 20 in light weight liquid

paraffin/ oil (sesame oil) with required quantity of Fluconazole. The aqueous phase is prepared was prepared by dissolving tween 80 in pure water. Methyl paraben and Propyl paraben was added in Propylene glycol and mixed with aqueous phase. The oil phase and aqueous phase was mixed at 70^{0}C with continuous stirring [3].

Preparation of gel: The gel phase was ready by dispersing carbopol 940 in pure water with constant stirring using mechanical shaker. To maintain the consistency of gel, more distilled water is added in it. The pH of the formulation was adjusted to 6.0 to 7.0 using triethonalamine [4].

Formulation of emulgel: Each phase were separately heated, then mixed with the continuous stirring and allowed to cool down to room temperature. The obtained emulsion was mixed with the gel in 1:1 ratio with mild stirring to get the Fluconazole emulgel formulation [5].

Table No.1 Composition of Emulgel of Fluconazole Formulation (% w/w)

Ingredients	Formulation code							
	F_{1L}	F_{2L}	F_{3L}	F_{4L}	$F_{1\ Oil}$	$F_{2\ Oil}$	$F_{3\ Oil}$	$F_{4\ Oil}$
Liquid paraffin	7.5	10	12.5	15				
Sesame oil					7.5	10	12.5	15
Span 20	1.0	2.0	3.0	4.0	1.0	2.0	3.0	4.0
Tween 80	0.5	0.75	1.0	1.25	0.5	0.75	1.0	1.25
Propylene Glycol	5	5	5	5	5	5	5	5
Propylene Paraben	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Methyl Paraben	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Carbopol 940	1	1	1	1	1	1	1	1
Tri-ethanol	pH was adjusted to 6-6.5							

EVALUATION OF EMULGEL

Preparation of standard curve of Fluconazole: Phosphate buffer 7.4 pH was prepared by dissolving 10.1045gm of sodium phosphate dibasic and 1.697gm of sodium phosphate monobasic in 800ml of distilled water in a beaker. Adjust solution to final desired pH using Hcl and NaOH. Add distilled water until volume is one liter. Standard curve of Fluconazole was prepared by accurately weighing 100mg of Fluconazole. The Fluconazole was dissolved in phosphate buffer 7.4pH in 100ml volumetric flask. The volume was made up to 100ml by same solvent mixture to get stock solution with 1mg/ml. From this stock solution, aliquots 0.5ml, 1ml, 1.5ml, 2ml, 2.5ml, 3ml, 3.5ml, 4ml, 4.5ml, 5ml were taken in10ml volumetric flask and volume made up to 10ml with phosphate buffer to get dilution with concentration ranging from 2µg/ml to 20µg/ml respectively. The absorbance of these dilutions was measured at 260nm against blank phosphate buffer. Standard curve was plotted between concentration (µg/ml) and absorbance [6].

Physical appearance: The prepared emulgel formulations were inspected visually for their color, homogeneity, consistency and phase separation [7].

Determination of pH: The pH of the formulation was determined by using digital pH meter; pH meter electrode was washed by distilled water and then dipped into the formulation to measure pH. The pH of the topical formulation should be between 3-9 to treat the skin infection [8].

Measurement of viscosity: The viscosity of the formulation was determined using a Brookfield Viscometer. The prepared emulgel was added to the beaker and allowed to settle down for 30 min. at the room temperature before the measurement was taken [9].

Spreadability: Spreadability of emulgel depends on its viscosity. The greater the viscosity the longer will be the time taken for spreading. A weighed quality (500mg) of emulgel is taken on one glass plate and another glass plate is dropped from a distance of 5cm. The spread emulgel diameter of the circle is measured [10].

Drug content: Weighed 1gm of each formulation and dissolved in 100ml of PBS (7.4pH) in volumetric flask and shaken well. Filter it to obtain clear solution. Determine its absorbance using ultraviolet illumination photometer at 260nm. The drug content was determined using following formula [11].

Drug Content = (Concentration × Volume taken× Dilution Factor) × Conversion Factor

Swelling index: Take 1g of emulgel in a porous aluminum foil and dipped in 0.1N NaOH kept in a 50ml beaker. At different time intervals samples are withdrawn and kept for drying and it is reweighed. Swelling index is calculated as follows [12-13]:

Swelling index = {Wt-Wo/Wo} 1003.

In-vitro Study: Franz diffusion cell is used for the study. Emulgel is applied on the surface of egg membrane is clamped between the donor and receptor chamber of diffusion cell [14]. The receptor chamber contains freshly prepared PBS (pH 7.4) solution to solubilize the drug. The receptor chamber is stirred using magnetic stirrer. The samples (1.0ml aliquots) are collected at different time interval and analyzed for drug content by UV-Visible spectrophotometer at 260 nm after applicable dilutions [15-16].

RESULTS

1. Physical Appearance of formulation:

Emulgel formulations were white viscous creamy preparation with a smooth homogeneous texture and glossy appearance. Results have been discussed in **Table 2**

Table:-2 Physical Appearance of formulation

Formulation	Color	Phase Separation	Homogeneity	Consistency
With Liquid Paraffin:-				
F_{1L}	Milky	None	Excellent	Good
F_{2L}	Milky	None	Excellent	Good
F_{3L}	Milky	None	Good	Excellent
F_{4L}	Milky	None	Excellent	Good
With Vegetable Oil (Sesame Oil):-				
$F_{5\ il}$	Milky	None	Excellent	Excellent
$F_{6\ Oil}$	Milky	None	Excellent	Good
$F_{7\ Oil}$	Milky	None	Excellent	Excellent
$F_{8\ Oil}$	Milky	None	Excellent	Excellent

2. pH of Determination

The pH of prepared formulations was measured by using pH meter. The pH of the formulations was in range of 5.0-7.0 which considered acceptable to avoid the risk of skin irritation upon application to skin.

Table 3: pH of formulation

Formulation	pH
With Liquid Paraffin	
F_{1L}	5.0
F_{2L}	6.1
F_{3L}	6.6
F_{4L}	6.2
With Vegetable Oil (Sesame Oil):-	
$F_{5\ Oil}$	5.1
$F_{6\ Oil}$	6.0
$F_{7\ Oil}$	7.0
$F_{8\ Oil}$	6.7

3. Spreadability of emulgel formulation

The Speadability of various emulgel formulations are given below in **Table 4**. It was concluded that all the developed formulation showed acceptable spreadability.

Table: 4 Spreadability of emulgel formulation

Formulation	Spreadability (cm)
With Liquid Paraffin	
F_{1L}	4.4
F_{2L}	4.1
F_{3L}	4
F_{4L}	5.2
With Vegetable Oil (Sesame Oil):-	
$F_{5\ Oil}$	6
$F_{6\ Oil}$	4
$F_{7\ Oil}$	7.2
$F_{8\ Oil}$	6.3

4. Viscosity of emulgel formulation

The tests were performed by using Brook-field viscometer. Results are given in **Table 5**

Table: 5 Viscosity of emulgel formulation

Formulation	Viscosity (centipoises)
With Liquid Paraffin	
F_{1L}	1134
F_{2L}	1110
F_{3L}	1570
F_{4L}	2082
With Vegetable Oil (Sesame Oil):-	
$F_{5\ Oil}$	2009
$F_{6\ Oil}$	1570
$F_{7\ Oil}$	1213
$F_{8\ Oil}$	2165

5. Swelling index of emulgel Formulation

Swelling index of all formulations are represented in **Table 6.**

Table: 6 Swelling index of emulgel Formulation

Formulation	Time (min)	Swelling index (%)
With liquid paraffin:-		
F_{1L}	30	113.33
	60	119.33
F_{2L}	30	91.11
	60	100.03
F_{3L}	30	77.77
	60	112.02
F_{4L}	30	88.88
	60	96.03
With Sesame Oil:-		
$F_{5\ Oil}$	30	73.33
	60	80
$F_{6\ Oil}$	30	97.77
	60	103.00
$F_{7\ Oil}$	30	80.00
	60	88.05
$F_{8\ Oil}$	30	110.04
	60	124.08

6. Drug Content of Emulgel Formulation

The drug content of different emulgel formulation was estimated by using UV spectrophotometer at 260 nm range. Results are discussed in **Table 6.**

Table: 6 Drug Content of Emulgel Formulation

Formulations	Drug Content (%)
With liquid paraffin	
F_{1L}	89.40
F_{2L}	91.1
F_{3L}	98.9
F_{4L}	99.4
With Sesame Oil	
$F_{5\ Oil}$	96.82
$F_{6\ Oil}$	97.65
$F_{7\ Oil}$	98.25
$F_{8\ Oil}$	98.06

7. In vitro % release data of Formulation

The study revel that, the release of the drugs from emulsified gel formulation the amounts of drug release after 150 min were shown in Table 7

Table: 7 In vitro % release data of Formulation

	Time (min)					
Formulations	**0**	**30**	**60**	**90**	**120**	**150**
With liquid paraffin						
F_{1L}	0	13.65	38.96	45.89	55.71	63.70
F_{2L}	0	16.42	32.07	45.89	56.24	60.01
F_{3L}	0	14.66	30.69	40.54	55.73	62.21
F_{4L}	0	13.42	30.71	40.83	50.03	59.06
With Sesame Oil						
$F_{5\ Oil}$	0	12.95	39.51	47.02	56.59	62.48
$F_{6\ Oil}$	0	16.87	44.93	48.94	56.05	61.34
$F_{7\ Oil}$	0	14.88	40.20	40.76	57.45	63.59
$F_{8\ Oil}$	0	14.03	43.75	56.01	58.65	62.31

CONCLUSION

In the coming years, topical drug delivery will be used extensively to impart better patient compliance. Since emulgel is helpful in enhancing spreadability, adhesion, viscosity and extrusion, this novel drug delivery become popular. Moreover, they will become a solution for loading hydrophobic drugs in water soluble gel bases for the long term stability. Similarly in the study, topical emulgels of Fluconazole were formulated and subjected to physicochemical studies i.e. rheological studies, spreading coefficient studies and in vitro release studies. In this research work we formulated liquid paraffin and vegetable oil based emulgels of Fluconazole. It was concluded that vegetable oil based emulgel are stable and effective and can be used instead of liquid paraffin based emulgel.

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