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DESIGN AND OPTIMIZATION OF EMULGEL FOR EFFICIENT DRUG DELIVERY THROUGH THE SKIN

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Abstract:

The study aimed to enhance the topical delivery of Itraconazole through emulgel formulations using Carbopol 934 and Carbopol 940 as gelling agents. A 2^3 factorial design was employed to study the effects of gelling agent type, oil phase concentration, and emulsifying agent concentrationondrugrelease.The formulationswereevaluatedforphysicalproperties,viscosity, drug release, globule size, skin irritation, antifungal activity, transmission electron microscopy, and stability. Results showed all formulations exhibited acceptable physical characteristics, including color, homogeneity, spreadability, and pH. The optimized formulation demonstrated 95.08% drug release over 48 hours, with enhanced antifungal activity compared to commercial Itraconazole cream. Skin irritation tests showed no signs of edema or erythema on rat skin. Stabilitystudiesconfirmedtheformulationsretainedtheirpropertiesafterthreemonthsofstorage. Overall, the study concluded that the optimized emulgel ensures sustained drug delivery in a controlled manner.

Keyword: Itraconazole, Emulgel, Topical drug delivery, Carbopol934, Carbopol940, Factorial design, Drug release.

1. Introduction

Topical drug delivery systems have gained significant attention due to their ability to deliver drugs directly to the site of action, reducing systemic side effects and improving patient compliance. Among various formulations, emulgels have emerged as a promising approach for delivering hydrophobic drugs, offering advantages such as enhanced drug release, better penetration, and prolonged retention at the application site.[1-4]

The delivery of hydrophobic drugs like Itraconazole, an antifungal agent, is often challenging due to their poor solubility and limited bioavailability. Traditional topical formulations, such as creams and ointments, may lack the necessaryconsistency and

penetration capabilities. Emulgels, a combination of emulsion and gel, overcome these limitations by incorporating hydrophobic drugs into a stable emulsion systemwhile providing a gel's spreading and stability benefits.[4-6]

The conceptofcombining emulsionsand gelswas first exploredto enhance the solubility and stability of drugs. Early research in topical formulations focused on improving drug penetrationthroughtheskin.Withtheadvancementofpolymerscience,agentslikeCarbopol934 and940wereintroduced,whichimprovedtheviscosity,spreadability,anddrugretentionoftopical formulations. Over the years, emulgels have been widely studied for various therapeutic applications, including antifungal, anti-inflammatory, and cosmetic uses.[7-9]

This study aims to investigate the potential of emulgel formulations in improving the topicaldeliveryofItraconazole.Emulgelswerepreparedusingtwogellingagents—Carbopol934 and Carbopol 940—while evaluating the influence of formulation components using a factorial design. Keyparameterssuchasdrugrelease, antifungalactivity, stability, andskinirritationwere systematicallyassessed, withcomparisons made to a commerciallyavailable Itraconazole cream.

2. MaterialsandMethods

Materials

Thechemicalswereobtained fromdifferent sourcesandusedasreceived. Itraconazolewasagift sample fromMylan laboratories Ltd. Nashik. Propylene glycol, Carbopol940, Tween80, Propyl paraben, Liquid paraffin, Span80, Triethanolamine, Ethanolpurchased fromS .D fine chemicals Mumbai. India.

Pre-formulationStudy:SolubilityofItraconazole:

The solubility of Itraconazole in various solvents was carried out and the solubility was determined.ExcessamountofItraconazole(100mg)wasaddedto10mlofeachsolventandtaken in a 25ml Stoppared conical flask and the mixture was shaken for 24 hrs at room temperature (28±10 0 C) on a rotary flask shaker. After 24 hrs ofshaking, 2 ml aliquots were withdrawn at 1 hr intervaland filtered using Watman filter paper. The filtered samples were diluted suitablyand assayed for Itraconazole by UV spectrophotometric method. Shaking was continued until two consecutive estimations are same. The solubility experiments were conducted in triplicate.[10-13]

PreparationofstandardcurveofItraconazole:

Anaccuratelyweighedamountof Itraconazoleequivalentto10mgwasdissolvedinsmallvolume ofmethanol, in10 mlvolumetric flask. Aseries ofstandard solutioncontaining 2.0to 16µg/ml ofItraconazolewerepreparedandabsorbancewasmeasuredat282nm,against reagentblank.All spectral absorbance measurements were made on Shimadzu-1700 UV-visible spectrophotometer.[14-15]

Drugcontentandcontent uniformity:-

Take 1gm of emulgel mix it in 10ml of methanol. Filter it to obtain clear solution .Drug

concentration in emulgel was measured by spectrophotometer. Itraconazole content inemulgel was measured by dissolving known quantity of emulgel in solvent by sonication. Absorbance was measured after suitable dissolution at 282nm in UV/visible spectrophotometer.[16-18]

Invitrodrugdiffusionstudy:-

Topicalgel formulations were expected to release the drug quicklywhen theyare applied to the skin for a quick relief. Totest the patternofreleaseofdrug fromformulations in vitro diffusion studies were carried out. The apparatus consist of a cylindrical glass tube(with22mm internal diameter and 76 mm height) which was opened at both the ends.1gm of gel formulation was spread uniformly on the surface of cellophane membrane (previously soaked in water for overnight) and was fixed to the one end of tube such that the preparation occupies inner circumferenceofthetube.Thewholeassemblywasfixedinsuchawaythatthelowerendof tubecontaining gelwas just touched (1-2 mmdeep)thesurfaceofdiffusion medium i.e., 100ml pH5.5phosphatebuffercontained in100mlbeakerwhichwasplaced inwaterbathand maintained at 37±2 °C. The cellophane membrane acts as a barrier between the gel phase and pH 5.5 phosphatebuffers(sinkphase).Aquantityof1mlsampleswerewithdrawsfromreceptorfluidat thetimeintervalof1,2,3,4,5,6,7and8hrs.Thereleaseddrugwasestimatedbyusing Shimadzu UV–visiblespectrophotometerat282nmand1mlphosphatebufferpH5.5wasreplacedeach time.[19-21]

ViscosityDetermination:-

The viscosityofthe gels prepared was determined using Brookfield viscometer model(LVDV- II+),the gelsample was filled inthe sample holder andthe particular spindle immersed intothe sample, the spindle is attached to the viscometer and then it is allowed to rotate at a particular speed then viscosity of the formulation was measured after 2 minutes.[22]

AcceleratedstabilitystudiesofEmulgel:-

Stability studies were performed according to ICH guidelines. The formulations were stored in hot air oven at 37 ± 2° C, 45 ± 2° C and 60 ± 2° C for a period of 3 months. The samples were analyzedfordrugcontenteverytwoweeksbyUV-Visiblespectrophotometerat282nm.Stability studywas also carried out by measuring the change in pH ofgelat regular intervaloftime.[23-24]

Table1:FormulationtableforItraconazoleEmulgel

IN GR ED IE NT	BATCHS				
	F 1	F 2	F 3	F 4	F 5

S					
Itraconazole(mg)	200	200	200	200	200
Propylenegylcol(ml)	1	1	1	1	1
Carbapol940(mg)	300	400	500	600	700
Tween80(ml)	0.5	0.5	1	1	1
Propylparaben(mg)	0.03	0.03	0.03	0.03	0.03
Liquid paraffin(ml)	1.5	1.5	1.5	1.5	1.5
Span80(ml)	1	1	1	1	1
Triethanolamine	Qs	Qs	Qs	Qs	Qs
Ethanol(ml)	2	2	2	2	2
Purified	Qs	Qs	Qs	Qs	Qs

water QS					

Result

Pre-formulationStudy:

Solubility of Itraconazole: Itraconazole was soluble in ethanol and methanol.

Evaluationofgels:

AppearanceTest:

Table2.Appearance test of various formulations.

Formulation	**Appearance**
F1	white
F2	white
F3	white
F4	white

F5	white

pHTest:

The prepared Itraconazole emulgel formulations were white viscous creamy preparation with a smooth and homogeneous appearance. The pH values ofall prepared formulation ranged from5 to 5.7, whichare considered acceptable to avoid the risk of irritationupon applicationto the skin because adult skin pH is 5.5.

Table3-pHdeterminationtestofvariousformulations

Formulation	**pH**
F1	5
F2	5.5
F3	5.6
F4	5.7
F5	5.5

Rheological properties:

SpreadabilityTest:F3 batch showed good spreadability

Table4: Spreadability of various formulations

Formulation	**Spreadability(cm)**
F1.	2.3
F2.	2.5
F3.	3.1
F4.	2.6
F5.	2.8

Extrudability Test:

All Formulation show good extrudability.

Table5: Extrudability of various formulations

Formulatio	**Extrudability(gm/cm2)**	**Comment**

n		
F1.	3.8	Good
F2.	3.7	Good
F3.	4.2	Good
F4.	3.9	Good
F5.	4.0	Good

Viscosity Determination:

The measurement of viscosity of the prepared emulgel was done with Brookfield viscometer (Brookfield DV-Eviscometer).Theemulgel were rotated at10(min.)and100(max.)rotation per minute with spindle 61.At each speed,the corresponding dial reading was noted.The viscosity of the emulgel was obtained.

Tableno6: Viscosityofvarious formulations

Formulation	**Viscosity (centipoise)**
F1.	1739.45
F	2356

2.	.44
F3.	1845.56
F4.	1340.42
F5.	2145.32

Accelerated stability studies of Emulgel:

The stability study of the prepared emulgel was carried out according to ICH guidelines at 45±20 C/60±5% RH, for 3 month by storing the samples in stability chamber.

Parameters evaluated

a. Drug content

b. Dissolution profile

c. pH

Tableno.7. Accelerated stabilityformulation

Sr. No	**Parameter**	**Initial Results**	**After stability Study**
1.	Drug Content	96.45%	96.39%
2	pH	5.	5.4

		6	
3	% Drug release	89.15±0.61	89.03 ±0.54

Drugcontentuniformity:

10 mg ofthe prepared emulgelwas mixed with10 ml of suitable solvent (methanol). Aliquotsof different concentration were prepared by suitable dilutionafter Sonication and filtering the stock solution and absorbance was measured. Drug content was calculated using the equation, which was obtained by linear regression analysis of calibration curve. The drug content of emulgel formulation is given below.

Table8:Drug content uniformity of various formulations

Formulation	**Drug content**
F1	91.13±0.16
F2	93.78

	± 0. 2 7
F 3 .	9 5. 1 2 ± 0. 6 7
F 4	9 0. 7 6 ± 0. 7 9
F 5	9 4. 2 4 ± 0. 4 6

***In vitro* drug diffusion study:**

The in vitro release profiles ofItraconazole fromits various Gellified Emulsion formulations are represented in . It was observed that all the formulation had become liquefied and diluted at the end of the experiments, indicating water diffusion through the membrane. In general, it can be observed fromfigures thatthe betterrelease ofthe drugfromallGellified Emulsion formulation. The release of the drugs from its Gellified Emulsion formulation can be ranked in the following descendingorder: F3≥F5≥F2≥F4≥F1,Where the amounts of the drug release of the drug released

after24hourswere,67.89,70.7,92.15,70.16,and63.15.respectively.Thusthehigherdrugrelease was observed with formulations F3.

Table9: Cumulative%DrugReleaseProfileof variousGels.

Time in hr	BATCHES				
	F1	F2	F3	F4	F5
0	0	0	0	0	0
1	12.26±0.13	11±0.16	12.29±0.026	16.38±0.19	24.77±0.14
2	14.05±.26	12.26±0.22	24.88±0.50	20.02±0.05	30.02±0.16
3	15.01±.31	13.63±0.33	27.38±0.37	20.98±0.53	32.61±0.56
4	15.5	13.7	31.1	23.9	33.6

	±.22	7±0.007	±0.9	±0.49	3±0.53
5	16.2±.15	14.6±0.31	31.13±0.10	26.97±0.53	34.51±0.58
6	17.35±0.12	15.02±0.006	33.81±0.57	28.95±0.51	35.22±0.59
7	20.01±0.21	16.21±0.12	36.35±0.17	32.26±0.13	37.26±0.45
8	21.97±0.	17.36±0.	39.7±0.2	39.63±0.	40.22±0.

	60	37	5	31	32
9	22.51±0.48	21.22±0.48	43.61±0.79	43.51±0.25	44.06±0.61
10	30.65±0.30	23.41±0.59	46.97±0.92	48.87±0.45	47.11±0.21
11	34.33±0.16	27.6±0.52	55.83±0.92	50.88±0.13	48.22±0.22
12	36.36±0.18	30.61±0.64	61.77±0.94	52.2±0.27	48.52±0.31
13	41.0	33.4	65.1	50.2	50.2

	8±0.23	1±0.22	±0.02	6±0.0	6±0.52
14	45.36±0.28	35.76±0.32	71.32±0.50	51.27±0.50	51.27±0.42
15	48.96±0.27	41.95±0.51	77.56±0.37	53.85±0.37	53.85±0.41
16	53.51±0.41	48.0±0.41	79.33±0.79	55.82±12	55.82±36
17	58.12±0.23	53.01±0.35	81.37±0.68	63.81±32	56.63±25

18	63.53±0.32	57.4±0.42	84±0.42	65.1±56	58.38±52
19	66.02±0.61	61.45±0.12	86.27±0.57	67.7±54	62.03±33
20	67.88±.056	66.96±0.33	87.38±0.46	70.15±41	65.33±33
21	70.32±.0.3	70.7±0.18	92.05±0.61	73.33±12	69.41±65

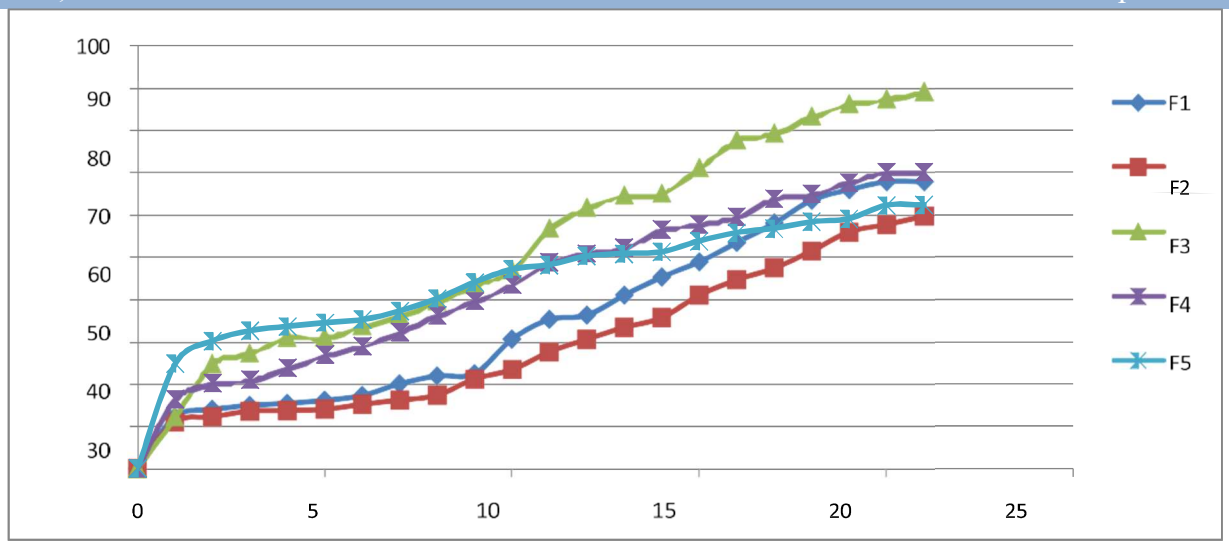

Figure1. Graph showing percentage in vitro drug release of Emulgel

Evaluation of Anti-fungal activity

Table10 Anti-fungal activity formulation

COMPNAME	**SPECIES**	**CONC**	
		50µg/ml	**100µg/ml**
Std (pur	Candida Albicans	++	+++

edrug)			
F3	Candida Albicans	+	++

Table.11 Anti-fungalactivity formulation

+++	Highly active	7-9mm
++	moderate	4-6mm
+	slightly	3mm

-	inactive	Less than 3mm

Skin irritation test:-No Erythema and Edema was monitored.

Table12. Skinirritationtest formulation

No of Rat	**Erythema**	**Edema**
Experimental (4)	No	No
Con	-	-

t r o l (4)		

3. Conclusion:

The project was undertaken with the aim to formulate anti-fungal emulgel of Itraconazole was mainlyusedforvarioussideeffectsoffungaldisease.Itraconazoleisavailableinthe conventional dosage form like Tablet, Capsules, Gel; etc .A common problem associated with itraconazole conventional therapy is a high incidence of gastrointestinal side ulceration, and also risk of first pass effect. The rationale behind the formulation development of the anti-fungal emulgel of Itraconazole with desired release profile. There are numerous procedures reported to prepare an anti-fungal emulgel among those the procedures that uses polymers, penetration enhancers and drug are selected. The rheologyofsuspensionsystemis a very important criteria, the rheological behavior was therefore studied using Brookfield viscometer. The viscosity also found to beoptimum to withdraw the formulation from container. The prepared formulation of it emulgel was found to be effective.

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