FORMULATION AND EVALUATION OF TOPICAL ANTIFUNGAL GEL OF FLUCONAZOLE USING ALOE VERA GEL

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Abstract: The Present research is based on developing Topical gel formulation of fluconazole with the help of natural Aloe Vera gel. Fluconazole is a Triazoles derivative and used to prevent and treat candidiasis. Taking fluconazole by oral administration is not considered appropriate as it has many side effects. Commercially fluconazole topical gel preparations are available in market which is formulated with the help of synthetic polymer. Thus, this formulation is made for better patient compliance and to reduce the dose of drug and to avoid side effect like liver damage kidney damage and safe in pregnancy.
Methods: The gel was formulated by changing the synthetic polymer. Various formulations like (F1, F2, F3, F4, F5 and F6) were developed by using natural polymer aloe Vera. The formulation was evaluated for % yield, spread ability, extrudability, wash ability and viscosity in vitro release study, Skin irritation study, stability testing.
Result: Carried out viscosity studies of various formulations evident that formulation F1 was better to compare to other. From among all the developed formulation F1 show better drug diffusion, good rheological properties, pH of F5formulation is sufficient to treat the skin infection. Result indicated that the concentration of aloe Vera significantly affected drug release and rheological properties of the gel.
Conclusion: it was calculated that formulation F1 was the best formulation among this formulation. Hence formulation F1 should be further developed for scale-up to industrial production.

Keywords: Anti-fungal activity, Fluconazole, Aloe-vera,

INTRODUCTION:

Fluconazole is a triazole derivative, chemically known as 2-(2,4 diflurophenyl)-1,3 bis (1H-1,2,4- Triazole -1-yl) propanol used in the treatment of fungal infection [1]. Fluconazole is a broad-spectrum antifungal agent [2]. Fluconazole drugs is administered various route rectal, ophthalmic, vaginal and skin as topical route. fluconazole drug is fighting the against the work of fungi and other HIV agents [3]. Fluconazole is active and against the work of following micro-organism specially name Blastomyces dermatitidis candida SPP. It is primary fungistatic [4]. Fluconazole is most important drug of fungal infection. These drugs inhibit the human cytochrome p450 system, particularly enzyme CYP2C 9 [5]. Fluconazole is a white color powder and slowly soluble in water and soluble in alcohol, it is a new drug, used in various fungal infection e.g. vaginal fungal infection in women and these are treating the oral pharyngeal fungi in patients [6]. Fluconazole treats the various infection like vaginal yeast infection, diabetes oral candidiasis, fever desert, Blastomycosis, candidiasis and histiocytosis and fungal infection of vaginal yeast [7,8]. Candida is a common infection, in human onset of almost all mucous membrane (skin) [9]. candida infection is harmful for body is a member of the normal human microbiome candida albicans affect the human, it is very harmful for eyes [10].

ALOEVERA:

Aloe vera has been used for over 9000 years. aloe vera is a species of aloe that is famous for medicinal properties [11]. The name of aloe vera is derives from the Arabic word ‘Alloeh’ ’which means shining bitter substance and vera means’ true; that is a Latin word. Fresh aloe vera Jel is used as cathartic, stomachic, anthelmintic, skin disease and hairs problems. Various species found in various countries like India, Rajasthan, Andhra Pradesh, Gujrat, Maharashtra and Tamil Nadu, commercially cultivated in Aruba, Hati, India and South Africa [12,13]. Aloe vera is obtained from fresh leaves gel, also known as ‘aloe Barbadensis’. The Sanskrit name of aloe vera is ‘’Ghee Kunwar’’, member of Liliaceae family. The various shaped of plant like Lance shaped, sharp- pointed and jagged and edged leaves [14].

Figure no. 1 Fresh leaf of aloe-vera

MORPHOLOGY OF ALOE VERA:

- Colour : greenish to yellow
- Odour : slightly aromatic
- Taste : bitter
- Size : 30-50cm long and 10cm width
- Shape : lancet

TAXONOMY:

- Kingdom : Plantae
- Order : Asparagales
- Division: Spermatophyta
- Class : Monocotyledoneae
- Family : Liliaceae
- Species : Barbadensis [15,16]

ADVANTAGES OF HERBAL FLUCONAZOLE GEL

- Effective cost
- No side effect
- Easy preparation
- No expensive
- Easily available
- Decrease the dose to be administered
- Increase the patient's compliance
- Decrease the gastrointestinal effect

TYPE OF FUNGAL INFECTION

1. **Skin infection:** Foot, hand (ring worm)
2. **Mucosal infection:** Vaginal infection
3. **Systemic infection:** Fungus present in the blood [17].

MATERIALS AND METHODS

Apparatus: dissolution bath, UV -visible spectrophotometer (shimadzer). computer, electronic balance, ph. meter, magnetic stirrer, viscometer (Brookfield) [18,19].

Materials: Fluconazole API, hydrochloric acid, acetic acid, sodium chloride, calcium chloride, urea, glucose, glycerol, di sodium hydrogen phosphate, aloe vera, alcohol, methyl paraben [20, 21].

PREPARARTION OF GEL BASE:

We are prepared fluconazole gel with 6 different batches of formulation that is F1, F2, F3, F4, F5 and F6 in which changing of polymers ratio, by using natural polymer of aloe vera. these formulations developed by using natural polymer aloe vera. Constant value show in table-1. carbapol 934 (2,3,4,5,6 w/w) was taken purified in beaker, these are allowed to soak for 24 hours and required amount of drug (2 gm) was dispersed in water, then Aloe vera was neutralized with sufficient of NAOH. after this preparation add glycerin, as a moisturing agent and methyl paraben and propyl paraben as preservatives were added slowly with continuous shaking and homogeneous gel was formed [22,23,24,25].

Table 1: Ratio of ingredients for different-different batches for preparation of fluconazole gel [26].

Ingredients	F1	F2	F3	F4	F5	F6
Fluconazole	2	2	2	2	2	2
Aloe vera for Carbapol 934	0.8	2.5	-	5	-	-
Aloe vera for HPMC	3	-	1.5	2	-	-
Glycerin	12	12	12	12	12	12
Propylene glycol	22	22	22	22	22	22
Methyl paraben	0.05	0.05	0.05	0.05	0.05	0.05
Purified water	100	100	100	100	100	100

Evaluation parameters

1. **Viscosity:** viscosity of herbal gel of fluconazole determined by Brookfield viscometer at 5, 10, 20, 50, 70 and 90 rpm at room temperature. Spindle no. 6 was dipped in the preparation and rotated at 5, 10, 20, 50, 70 and 90 at room temperature. Various factor like temperature, pressure affect the viscosity and particles size. [27].
2. **PH:** Measurement of P_H of fluconazole gel is determined by P_H METER and with different standard P_H 3-7 of buffer solution. 40 gm weight of gel formulation and transferred in 10 ml beaker. Gel formulation between 4-7 treat the fungal infection **[**[28].
3. **Skin Irritancy studies:** These are the most important parameter of fluconazole gel, check the skin irritancy test. Skin irritancy test were conducted in rabbits to determine. 0.6 gm fluconazole gel is applied on 2 rabbits for 24 HRS, after 24hs removed the gel. skin was graded for formation of edema and erythema's scoring was repeated 72h later. these formulations were graded as non-irritant test, irritant and highly irritant [29, 30].
4. **Stability studies:** Maintain the stability studies. maintain the formulation at an ambient condition for 3-4 months. these drug contents were determined after 1st, 2nd, 3rd, months after completed formulation of topical gel [31].

Table 2: Percentage (%) drug content at different time interval

Days	Percent drug content					
	F1	F2	F3	F4	F5	F6
0	99.88	98.75	98.92	97.98	95.6	98.75
15	98.85	98.66	98.82	97.85	95.51	98.61
30	98.71	98.5	98.5	97.88	95.57	97.15
45	97.99	98.80	98.90	97.75	95.37	97.37
60	98.73	98.35	98.52	97.65	95.11	96.37
75	98.55	98.11	98.41	97.60	94.90	96.15
90	98.57	97.99	98.10	97.5	94.85	96.02

5. **Spreadability**: These test important parameter for all Gel formulation. these tests were estimated by wooden block with scale and 2 glass slides having a pan mounted on a pulley. These formulations were applied 2 slide and 100g weight was placed on the upper glass slide for 5 min. for maintain uniform thickness formulation ,100gm weight added to the pan. After this process, time in second separated the slide and measure the Spreadability test. The results are show in table no .5

   The Spreadability was calculated by using the following formula:

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

S= Spreadability
M= weight tied to the upper slides
L= length of glass slide and
T= time in second [32]

6. **Thermal test**: these tests was studied the against the heat, after 48h, of the preparation. Three samples of these preparation were placed different temperature at different room temperature like 4^{0C}, 25^{0C} and 45^{0C} at 24h,1 week and 1 month [33].
7. **Visual test:** Prepared gel were inspected visually for their color, separation and syneresis, the complete preparation was much clear and transparent. these gels show good homogeneity. The result are show table no.5 [34]
8. **FT-IR STUDY:** FT-IR study of herbal gel of fluconazole shown in figure-1
FT-IR study were used for the compatibility of the ingredients, these ingredients used in this formulation. FT-IR check the compatibility. Compatibility is the most important in ingredients.

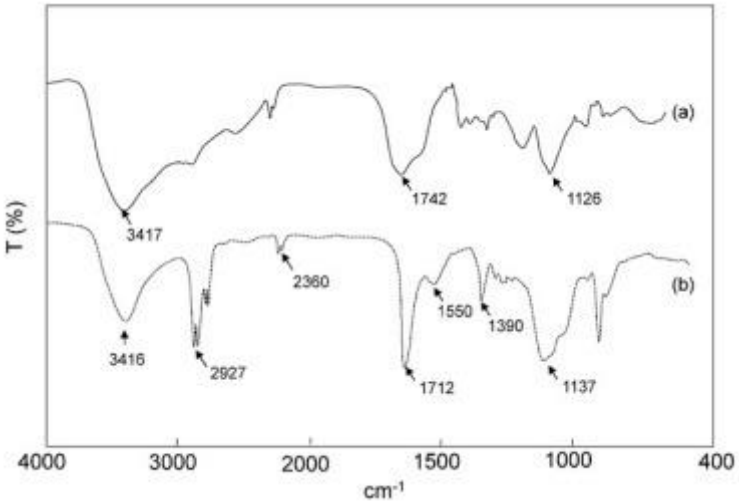
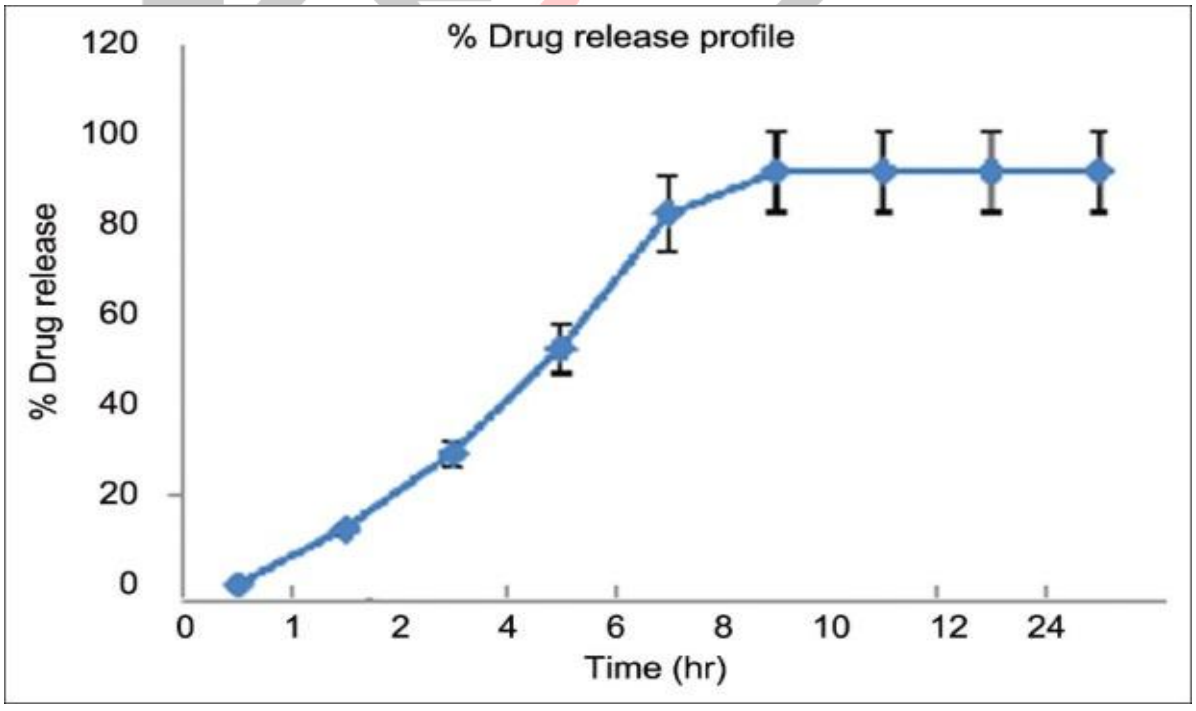


Figure 2: FT-IR study for (a) Fluconazole and (b) Aloe Ver

IN-vitro release study: In – vitro studies were carried out by dialysis method. 2 gm sample of fluconazole exact weight and placed on semi permeable cellophane membrane in phosphate buffer at 7.5 ph. for 24hrs. The loaded membrane was tightly stretched over open the lower end of a glass tube of 2.6148 cm internal diameter. The tube absorbed in a beaker containing phosphate buffer at ph. 7.5 which is release the medium. This method is maintaining for 3 hrs. at 37°C and put in thermostatic water bath at 50 rpm. 5 ml samples were withdrawing at 150 intervals of 0, 1 2,4, 6 , 8 10, 12 and 14 hours. The volume of each sample replaced by the same volume of fresh buffer at same temperature. Sample was analyzed by Spectroscopy at λmax 259 nm [35]



RESULTS AND DISCUSSION:

Measure the viscosity: Measured all formulation (F1-F2) of fluconazole gel was by using the Brookfield Viscometer (PRO-II extra model, Brookfield Viscometer, USA). The received value show in this table no. 3.

Table no. 3 Measure the viscosity (cps)

Formulation	Values (viscosity cps)
F1	70,365.12
F2	80,245.00
F3	97,123.19
F4	98,158.47
F5	77,789.47
F6	92,125.45

PH Measurement: Measure the PH determination of all formulations was complete by PH meter (global electronics DPH 500). The PH value show in table no.4.

Table no. 4 measurement of PH Determination

Formulation	**Ph**
F1	**6.9**
F2	**7.2**
F3	**6.8**
F4	**7.0**
F5	**6.5**
F6	**7.1**

Drug content: After prepared six formulation of fluconazole gel od drug content was done by UV spectroscopy at 259 nm in alcohol. The result show in table no.5 and minimum drug content show in formulation F4(96.45) and maximum F6(99.85).

Formulation	Drug content
F1	97.78
F2	98.02
F3	98.52
F4	96.45
F5	97.99
F6	99.85

Visual examination and Spreadability test

Formulation	Colour	Spreadability
F1	Milky	7
F2	Buff	6.1
F3	Cream	5.2
F4	Greenish	6.55
F5	Milky	6.14
F6	Milky	4.22

Discussion: The present formulation of fluconazole gel was prepared by aloe vera, API, methyl paraben, Alcohol and distill water. we were prepared only six formulation. The received data from various paraments like PH, viscosity studies and in-vitro release study.

CONCLISION: The results indicate that the studies of formulation and evaluation for topical antifungal gel of fluconazole using aloe vera gel has potential for avoid side effect like liver damage, kidney damage and safe in pregnancy. It was calculated that formulation F1 was best formulation as compare other formulation. The basic gel definitely succeeding and the proficient development and production of excellence pharmaceutical gel depends on their base knowledge of physiochemical properties and stability.

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CONFLICT OF INTEREST

The author has declared that no conflicts of interest exist.

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ETHICAL APPROVAL
Not required.

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