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PREPARATION, CHARACTERIZATION AND EVALUATION STUDY OF FLUCONAZOLE VANISHING CREAM

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ABSTRACT

The purpose of this article is to overcome the systemic adverse effect of fluconazole that is hepatotoxicity and nephrotoxicity by topical application of fluconazole. Fluconazole is an azole antifungal and used in the treatment of local and systemic fungal infections like tinea corporis, onychomycosis and dermatophytosis. For efficient delivery of drug to skin tissue, a fluconazole vanishing cream was not develop till date. But we can found various formulations like fluconazole capsule, tablets etc. Skin creams are generally W/O and O/W. In the sin cream various vitamins like vit. A, E and D3 and fatty acid used. The objective of the research article study is to treat various fungal diseases. Physical mixture of the surfactant base and fluconazole was also prepared as a control formulation to evaluate the various effects. The vanishing cream was made based on the various evaluation parameter and types of polymer used. So, Fluconazole vanishing cream formulation was developed in this study and is promising for better patient compliance as no any traces when applied.

KEYWORDS: Fluconazole, Emollients, Dermatophytosis, Candida krusei.

1. INTRODUCTION

Cream

Pharmaceuticals semisolid dosage preparation includes

Vanishing cream: A cream in which one or more one active ingredients are dispersed, dissolved in a suitable excipients like as paste or ointment and also suitable bases like antimicrobial agents, stabilizing agents emulsifier, etc.[1,2] Cream that leaves no any visible

trace or seem to be disappear while rubbing or while spraying on skin is known as vanishing cream. Where other system of drug administration fails there topical drug delivery system is used or it is mainly used in pain and urinary disturbance. The various formulation aspects, various tests, various tests, various challenges of topical drug delivery describes. Cream perhaps the commonest prescribed topical medicament. As it is less oily, messy and sticky, most patients find it more user-friendly.[1] Fungal infection son scalf are common and some of them causes serious illness. The scalf infections such as Tinea versocolar, (pityriasis, versicolar), Seborrhoea dermatitis, pityriasis capititis have been mentioned as a scaling disorders, will affect scalf and hair abruptly. The genus malassezia responsible for variety of superficial cutaneous as well as systemic fungal infections and pityriasis versicolor is the most commonly presenting diseases.[2]

It is of two types.

- **External topical:** Generally that dispersed and spread on to the cutaneous tissue to cover the affected area.
- **Internal topical:** Generally that applied on the mucus membrane orally and through vagina for local activity.[4]

Advantages of vanishing cream

- They give prolonged contact in their site of application than other doses form formulations.
- When applied to skin it give no irritation and easily water washable.
- Efficacy with lower daily dosage of drug by continuous drug input can be achived.
- More safely drug deliver to a specific site.
- Physiological and pharmacological response is increased.
- It has large area of application in comparison with buccal or nasal cavity.
- The main objective of study is to treat fungal infection like Candida krusei Candida albicans, Candida tropcialis, Cryptococcus neoformans, Candida glabrata.
- Prolonged contact in their site of application can give than other doses forms.

Disadvantages of vanishing cream

- Allergy such as skin may occur at site of application due to drug /excipients.
- Larger particles cannot be absorbed absorbed from topical doses forms.
- When applied to skin, inflammation may occur.

- Small plasma concentration drug cannot be used.

Types of cream

1. Oil in water (o/w) cream, example. Vanishing cream
2. Water in oil (w/o) cream, example. Cold cream

Advantages of topical use of fluconazole

1) When applied to skin it give no irritation and easily water washable.
2) Drug level is minimum in inter and intra patient variation by fluctuation.
3) More safely drug deliver to a specific site.
4) Physiological and pharmacological response is increased.
5) A relatively large area of application in comparison with buccal or nasal cavity.
6) The main objective of study is to treat fungal infection like Candida krusei Candida albicans, Candida tropcialis, Cryptococcus neoformans, Candida glabrata.
7) To avoid the first pass hepatic metabolism.
8) The drug Bio-availability is increased.
9) Better patient compliance can be achived.[6]

Disadvantages of vanishing cream

- Due to drug /excipients allergy such as skin may occur at site of application.
- From the topical doses forms larger particles cannot be absorbed.
- Inflammation may occur when applied to skin,.

Ideal properties of semisolid dosage forms

Physical properties

- Smooth texture
- Elegant in appearance
- Non dehydrating
- Non greasy and non-staining
- Non hygroscopic

Physiological properties

- Non irritating
- Do not alter membrane / skin functioning
- Miscible with skin secretion

- Have low sensitization index

Application properties

- Easily applicable with efficient drug release
- High aqueous washability

Mode of action of semisolid

- **Local and Topical**

In intimate contact with skin with the site of action for a period of time e.g. sunscreen

- **Localized systemic action**

Penetrate through skin.

Release drugs from base and penetrate across different layers of skin.

Reach local circulation underneath skin o e.g. acne

Classification of topical drug delivery systems

Classification of Semi-solid doses form are given below

- Ointment
- Cream
- Jelly
- Gel
- Suppository
- Ointment

1.1 Physiology of the skin

Skin is the largest organ of the body. The outermost part of the body is known as skin. Skin has several layers such as outer layer is epidermis, which layer below the epidermis is dermis, which contain several network of blood vessels, sweet gland, hair follicles and sebaceous gland. The subcutaneous fatty tissues lies beneath the dermis.

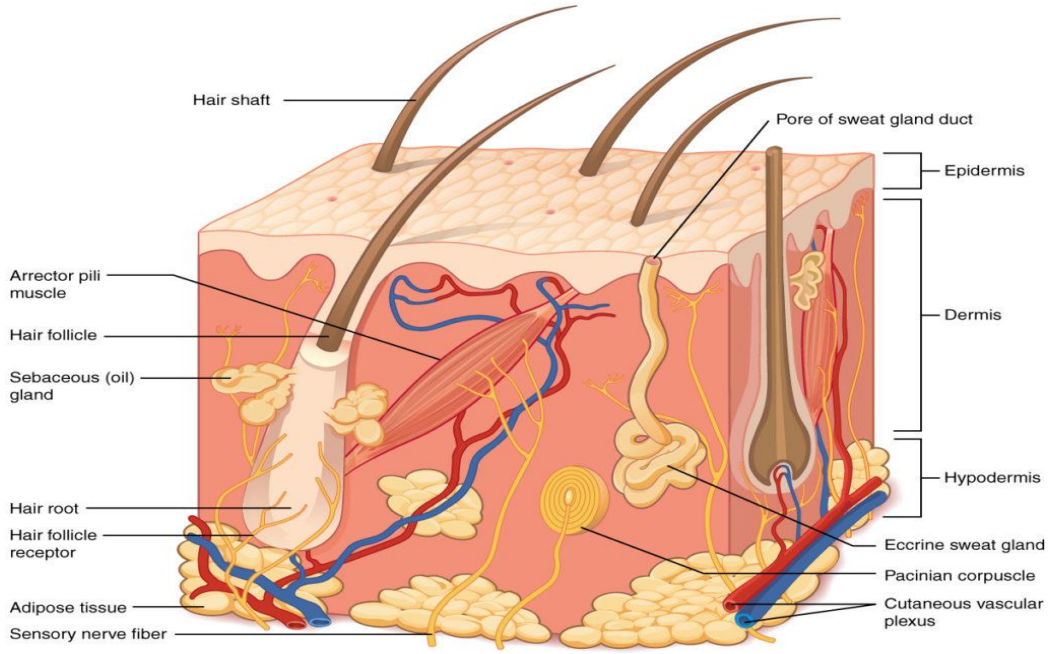

Figure 1.2: Anatomy of human Skin.

Functions of skin

- Skin protects from external and internal environment**.**
- It contain body fluid and and tissues.
- It protects from external stimuli like pollution, chemicals, light, radiation, heat, cold,
- It helps in the synthesis of biochemical.
- It helps in metabolism and disposal of biochemical wastes.
- It helps to maintain body temperature and controlling of blood pressure.
- It also works as cushions against mechanical shock.
- It helps to prevents from loss of moisture.
- It reduces harmful effects of UV radiation.
- Skin also acts as a sensory organ (touch, feel, detects temperature).
- It helps to regulate body temperature.
- Skin also works as an immune organ which detects infections etc.

Biochemistry of skin

Epidermis

The outer layer of skin which acts water-proof barrier of the body is known as epidermis. Squamous epithelial tissue having four kinds of cells is composed of the epidermis layer of skin. Marker cells, Langerhans, Melanocytes and last one is keratinocytes. Our body or internal organ through the external environmental condition such as microbes and other

external elements is protected by epidermal layer. To produce keratin protein which helps to keep safe the skin and tissue from heat, microbes and other external chemicals keratinocytes of epidermal layer are responsible. Source of energy for the lower portion of epidermis and lactic acid is end product of the metabolism that accumulates in the skin is glucose. For the pigmentation of skin and brown- black and yellow-red pigment melanin is liable. Melanin supply skin color is produced by melanocytes of epidermal layer. Stratum basal, stratum granulose, stratum spin sum, stratum lucidum and stratum corneum fifth layer present in the epidermal cells as. The entire cellular make-up changes during differentiation from basal cells to stratum conium by degradation of the existing cellular components. Host enzyme of lysosomes an release for intracellular lies is lytic enzymes and the epidermis is reservoir.[8-11]

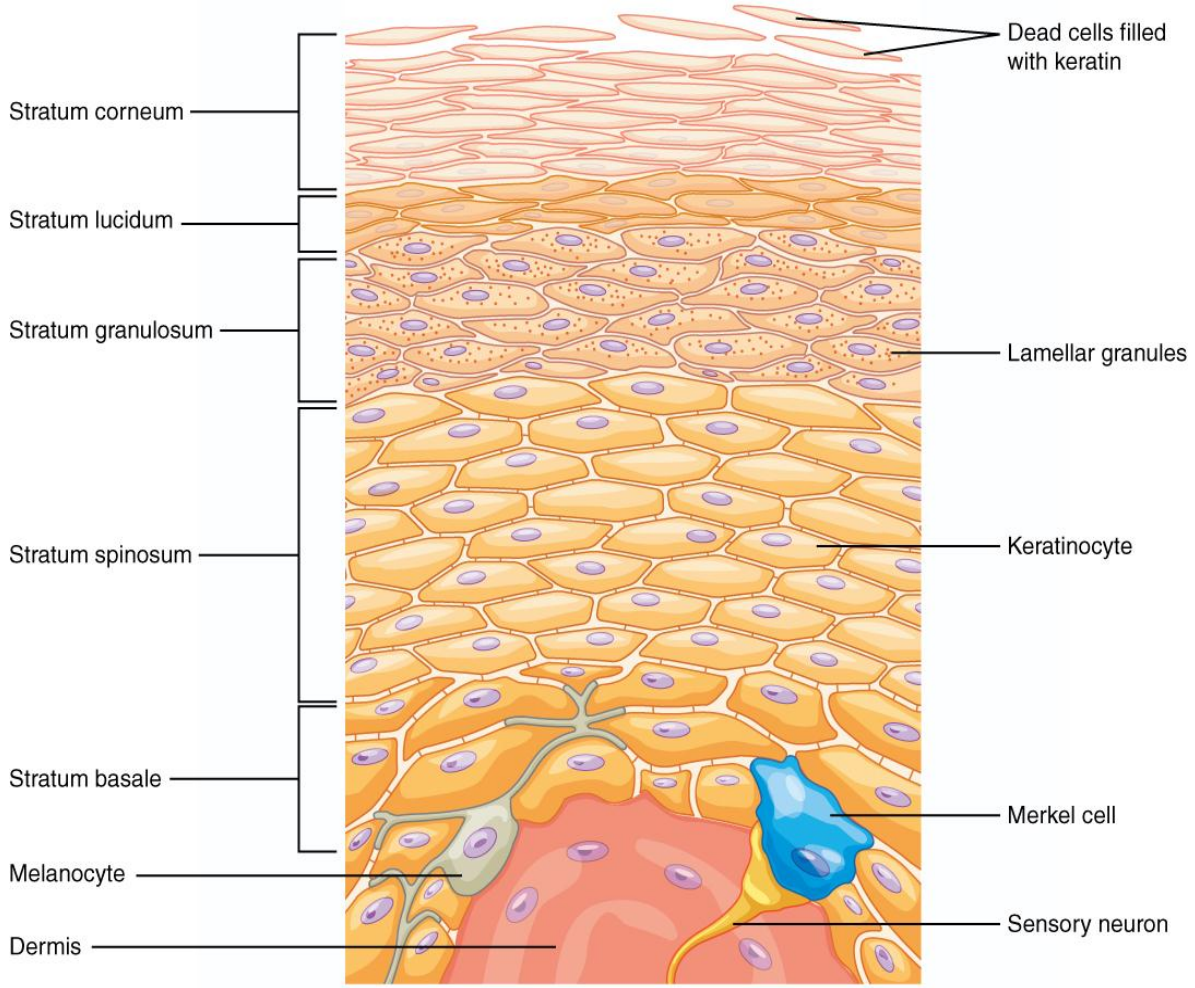

Figure 1.3: Epidermis layer of skin.

Dermis

Beneath the epidermis layer and subcutaneous layer the inner layer of skin which is found is known as dermis and despite its larger area of skin, Cellular and a cellular structure is

comprising by dermis and composed of hair follicles, blood vessels, nerve, amorphous and fibrous connective tissue, dermal cells and receptors. Due to dermal papillae the surface area of dermis is large. For Several cell types including multi-functional cells of the immune system like macrophages and mast cells the dermis is home.[12,13]

Hypodermis

Hypodermis layer composed of the cells called adipose tissue, fibroblast, fat cells, microphages and blood vessels. Hypodermis layer is made up of areolar and adipose tissue.[14]

Absorption through skin

Absorption route are identified by two basic pathways.

- **Pathway 1 (Trans-epidermal absorption)**

Forcross the skin pathway 1 act by diffusing principle and responsible. At the stratum conium when a permeating drug exists at the stratum conium, it enters the wet cell mass of the epidermis and no direct blood supply by the epidermis. A single field of diffusion in models is considered as a viable epidermis.[17-20]

- **Pathway 2 (Shunt pathway) absorption**

A "diffusional resistor." membranes act as Resistance(R) which is proportional to the thickness (h) and inversely proportional to the diffusive mobility of matter to the diffusion coefficient (D), where there is more than one (F) to the fractional area of a route and to the carrying capacity of a phase.[22,22]

R=H/FDK

R =Resistance of diffusion resistor

H = Thickness

F = Fractional area

K = Relative capacity

D = diffusivity

Basic principle of permeation

Drugs molecules may penetrate the skin along the hair follicles or sweat ducts in the starting diffusion stage and then be absorbed through the sebaceous glands and follicular epithelium.

Diffusion through stratum corneum due to dominant pathway is initiated through Steady state. Under steady condition the membrane-limited flux (J) is described by expression

$$J = \frac{DAKO/W\ r\ C}{\text{----------}}$$

Where:

J = Amount of drug passing through the membrane system per unit area, per unit area per unit time.

A= Area of the membrane

D= Diffusion coefficient

Ko/w= Membranes / vehicle partition coefficient

C= Concentration gradient

h= Thickness of the membrane.

Following are the factor affecting topical permeation

Physicochemical properties of drug substances

Drug solubility

Partition coefficient

pH- condition

Particle size

Concentration

Molecular weight

Polymorphism

Penetration enhancer

Chemical penetration enhancer

These are classified into following types

Solvents

For penetration enhancer solvents play an important role. Increased penetration of these compound possibly by pump the polar pathway and/or by fluidizing lipids. Propylene glycol, isopropyl alcohol, glycerine, transcutol-p, water, alcohols, methanol and ethanol.

Surface active agent

Agents that increase the polar pathway transport, especially of hydrophilic drugs are surface active agents. To change or alter the penetration function of polar head group and the hydrocarbon chain length is the function of surface acting agents.[29]

Anionic surfactant

Surfactants having negative charge on their hydrophilic head that responds to provide excellent detergency properties due to ability to bind positive charge particles are known as anionic surfactant. Interact strongly with skin theses surfactant can penetrate. Some examples of anionic surfactants sinclude are alkyl ether sulfates, sodium dodecyl sulfate, benzyl sulfonates, Decodecylmethyl sulphoxide, Sodium lauryl sulphate, etc.[30]

Cationic surfactant

These having negative charge on their water loving head unlike to anionic surfactants but is not widely used as skin penetration enhancer so these are known as cationic surfactant. Examples: Dodecyl trimethyl ammonium chloride.

Non-ionic surfactant

Examples include: castor oil ethoxylate amines, Pluronic F68 etc.

Binary system

Examples are 1, 4-butane diol- linoleic acid and Prolylene glycol -oleic acid.

Miscellaneous chemicals

Miscellaneous includes N, N-dimethyl-m-toluamide, urea, calcium thioglycolate etc.

Physicochemical properties of topical

Nature of vehicle

In this, water hating vehicle (lipophobic) decrease permeation of drug molecule and Water soluble vehicle (Lipophilic) increase permeation of drug molecule.

Composition of drug delivery system

In this delivery system, low molecular weight that leads to decrease in permeation is Polyethylene glycols.

Release characteristics

In the drug release system, The drug molecules are dissolved or suspended in the delivery system release of drugs depends. From delivery systems to the skin pH of the vehicle the interfacial partition coefficient of drug.

Penetration enhancer

These can be achived by two ways either by chemical enhancer or by physical method.

Chemical penetration enhancer

These are classified into following types

Solvents

For penetration enhancer solvents play an important role. Increased penetration of these compound possibly by pump the polar pathway and/or by fluidizing lipids. Propylene glycol, isopropyl alcohol, glycerine, transcutol-p, water, alcohols, methanol and ethanol; dimethyl sulfoxide, alkyl methyl sulfoxide, alkyl homologs of methyl sulfide, and dimethylformamide and dimethyl acetamide; pyrrolidones- 2 -pyrrolidone, (Azone), miseellancous solvents-glyeerol, silicone fluids, propnylene glycol, isopropyl palmitate.sss, These are the some of the examples.

Surface active agent

Agents that increase the polar pathway transport, especially of hydrophilic drugs are surface active agents. To change or alter the penetration function of polar head group and the hydrocarbon chain length is the function of surface acting agents.[25]

Anionic surfactant

Surfactants having negative charge on their hydrophilic head that responds to provide excellent detergency properties due to ability to bind positive charge particles are known as anionic surfactant. Interact strongly with skin theses surfactant can penetrate. Some examples of anionic surfactants sinclude are alkyl ether sulfates, sodium dodecyl sulfate, benzyl sulfonates, Decodecylmethyl sulphoxide, Sodium lauryl sulphate, etc.[26]

Cationic surfactant

These having negative charge on their water loving head unlike to anionic surfactants but is not widely used as skin penetration enhancer so these are known as cationic surfactant. Examples: Dodecyl trimethyl ammonium chloride.

Non-ionic surfactant

Least potential for irritation are the properties of non-ionic surfactant.

Examples include: castor oil ethoxylate, Ethoxylated amines, and Pluronic F68 etc.

Binary system

Binary system, heterogeneous multilaminated pathway as well as the continuous pathways these systems apparentely includes. Examples are 1,4-butane diol- linoleic acid and Prolylene glycol -oleic acid.

Miscellaneous chemicals

Miscellaneous includes N, N-dimethyl-m-toluamide, urea, calcium thioglycolate etc.

Physical method of topical drug delivery

Through intact skin by the passage of direct or periodic weak electric current, using an appropriate electrode polarity through an electrolyte solution containing the ionic molecules to be delivered in this process the ionic drug molecule can be transported.

Phonophoresis

Phonophoresis is the movement of drugs through living intact skin and into soft tissues under the ultrasound application is called phonophoresis.

Sonophoresis

In this process, the drug delivery process that involves the usage of the ultrasound waves is called sonophoresis. In permeation of low frequency ultrasound the ultrasound application has resulted was shown to increase the permeability of human skin by several orders of magnitude too many drugs are included high molecular weight.

Physicochemical properties of topical

Nature of vehicle

In this, water hating vehicle (lipophobic) decrease permeation of drug molecule and Water soluble vehicle (Lipophilic) increase permeation of drug molecule.

Composition of drug delivery system

In this delivery system, low molecular weight that leads to decrease in permeation is Polyethylene glycols.

Evaluation parameter

Identification of drug

- IR Spectroscopy
- Solubility Studies of drug molecules
- Melting Point determination
- Partition-Coefficient
- Compatibility Studies of drug
- Physical Identification of Drug

Physical identification of drug

By the physical properties of drug like odour, colour, taste,their texture, organoleptic properties the drug molecules was identified.

Melting point determination

In this appratus small amount of drug molecules fluconazole was taken in clean and empty capillary tube and after that the capillary tube is sealed at one side. After that the capillary tube was kept on visual melting point apparatus or on heater at which the sample was start to melt and the temperature of melting of drug was noted.

Infra-red spectrum studies

The absorption of infrared light by molecule for the determination of function group present in the sample or molecule caries in this studies. In this identification, the comparision between two sample to each other was identified.

Partition coefficient

In this, Partition coefficient is used to identify the hydrophilic/Lipophilic nature of drug molecules which can affect extend of drug absorption as well as the rate of absorption of drug. By the lipophilicity, the partition coefficient of drug is measured and it also have the tendency to cross biological membrane.The log p value of lipophilic drug is much greater than 1 and the hydrophilic drugs has partition coefficient value always less than 1.

Pw/o = (C aqueous/ organic)

Po/w = (C organic/C aqueous)

For partition coefficient using n-Octanol/ buffer and n-Octanol/ water general procedure should followed and at the 250nm the absorbance was taken.

Drug -excipient compatibility studies

In this, the drug- excipient is mixed with together in 1:1 ratio and placed it in the borosilicate colored glass vials and in the humidity chamber by maintaining at 400C these vials are placed at 75% Relative Humidity (RH) for 21 days. After these all the sample was observed after 7, 14 and 21 days for identification of any lump formation as well as color change formation. Therefore the FTIR studies are carried out by these all mixtures.

PH of the formulation

The pH of formulation was measured by using Ph meter or Ph paper.[27,28,29]

Viscosity measurement

Viscosities of formulations were measured by using Brookfield DV-I viscometer.[30]

Drug content

The drug content was determined by UV Spectrophotometry.

Basic principle of permeation

Drugs molecules may penetrate the skin along the hair follicles or sweat ducts in the starting diffusion stage and then be absorbed through the sebaceous glands and follicular epithelium. Diffusion through stratum corneum due to dominant pathway is initiated through Steady state. Under steady condition the membrane-limited flux (J) is described by expression

$$J = \frac{DAKO/W\ r\ C}{\text{----------}}$$

Where:

J = Amount of drug passing through the membrane system per unit area, per unit area per unit time.

A= Area of the membrane

D= Diffusion coefficient

Ko/w= Membranes / vehicle partition coefficient

C= Concentration gradient

h= Thickness of the membrane.

Kinetics of permeation

For the development of topical formulation, knowledge of skin permeation play the vital to the successful development.

The following steps involves during the permeation of a drug,

- By stratum corneum Sorption,
- Through viable epidermis penetration of drug,
- By the capillary network in the dermal papillary layer ussptake of the drug.

Due to physicochemical properties drug molecule permeation can be possible only.

The skin (dQ/dt) the rate of permeation across is given by:

$dQdt=Ps(Cd-Cr)$

Where,

The concentrations of skin penetrate in the donor compartment and in the receptor compartment are Cd and Cr (e.g., body) respectively.

Ps is permeability coefficient.

By the relationship this permeability coefficient is given:

$Ps=KsDss/Hs$[23,24]

Physicochemical properties of drug substances

Drug solubility

Partition coefficient

pH- condition

Particle size

Concentration

Molecular weight

Polymorphism

Candida krusei

Frequent use of fluconazole can select for the emergence of *Candida krusei* as a commonly isolated opportunistic pathogen in some medical centers. Frequent use of fluconazole cause Candida Krusei.[7]

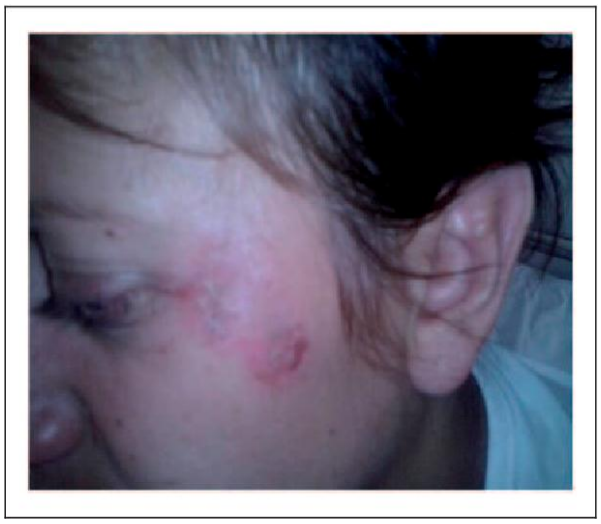

Fig. 1: Candida krusei,

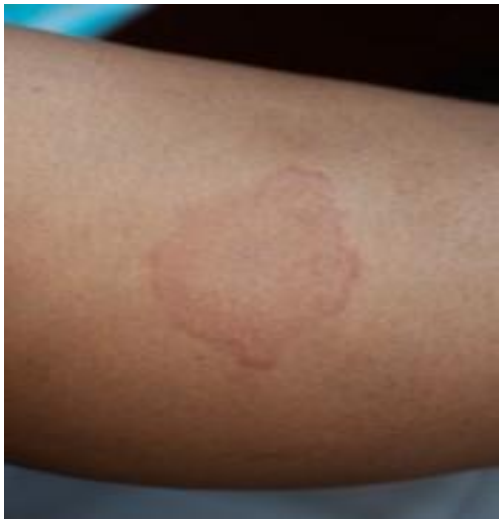

Fig. 2: Candida glabrata.

Mechanism of fluconazole resistance in candida krusei

The first one is an alteration in the target enzyme is called, 14a-demethylase.An accumulation of C14 methylated sterols which likely disrupt membrane structure Inhibition of this enzyme by azoles causes. The another second mechanism is decreased drug accumulation, it mediated by either increased efflux of the drug or diminished uptake *C. krusei* for the determination if fluconazole resistance in *C. krusei* is mediated by one or more of these mechanisms, In addition, fluconazole uptake and cytochrome P-450 content of these organisms were measured. fluconazole resistance is a 14a-demethylase.

Objective of research

The objective of this research work was to formulate and evaluate the fluconazole vanishing cream which does not cause any side effects or adverse reactions and also acts as an antifungal properties.To treat fungal infection is the main objective of study,like tinea corporis, dermatophytosis, onychomycosis and dermatophytosis. Emulsion which are viscous, liquid or semisolid emulsion is called cream. Fluconazole is an azole antifungal drug and used in the treatment of local as well as systemic fungal infections like tinea corporis, onychomycosis and dermatophytosis. The topical formulation is designed in such a way is used to introduced the drug into the skin or mucous membrane of the skin and also for the different skin disorders. For efficient delivery of drug to skin tissues , a fluconazole vanishing cream was not develop till date. But we can found various formulations in market like fluconazole capsule, tablets etc.

The main objective of the study is to treat fungal infections. The vanishing cream was designed in based on solubility measurement of fluconazole in various types of polymers. To evaluate the effects of the solubilized state of fluconazole in vanishing cream base physical mixture of the surfactant base and fluconazole was also prepared as a control for formulation on the in vitro skin deposition behavior of fluconazole. So, For better patient compliance as no any traces when applied Fluconazole vanishing cream formulation was developed in this study and is promising.

Drug profile

Structural formula

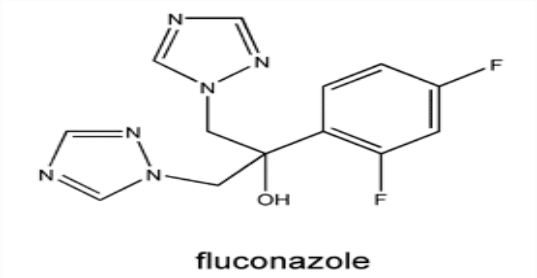

Fig. 3: Structure of fluconazole.

IUPAC name: 2-(2, 4-Difluorophényl)-1,3-di(1H-1,2,4-triazol-1-yl)-2-propanol

Table 1: Physiological properties.

Appearance	**A odorless white powder**		
Chemical formula	C13H12F2N6		
Molecular weight	306.271 g/mol		
Metabolism	Hepatic metabolism.		
Synonyms :	Biozolene, Diflucan, Elazor, Triflucan		
Description	Fluconazole, the first of a new subclass of synthetic triazole for the treatment of systemic and surface fungal infections.		
Solubility	Fluconazole solubility is in various solvent system at room temprature below 25℃.		
	S.no.	**Solvent**	**Solubility**
	1	Methanol	soluble
	2	Ethanol	soluble
	3	Chloroform	soluble
	4	Ethyl acetate	soluble
	5	Water	Slightly soluble
	6	Dimethyl formamide	Soluble
Dose	100-400mgTab.		
Melting point	138-140°C		
Metabolism	Hepatic metabolism		
Route of administration	Oral administration, Topical administration,		

Side effects	Muscle or joint pain, rash, itching, flushing, Fatigue, Dizziness, tiredness etc.
Pharmacodynamic	Fluconazole is a triazole antifungal which act by inhibiting fungal cytochrome P450 3A dependent enzyme, decreases ergosterol synthesis and inhibits cell membrane formation.The Cytochrome P450 3A4 isoenzyme system fluconazole is a potent inhibitor of this. when concomitantly administering fluconazole with drugs that have narrow therapeutic windows and are substrates of the CYP3A4 substrates caution should be exercised and monitoring is suggested. Patients with renal and hepatic dysfunction or previous hepatotoxicity from other azole derivatives precautions should be used in caution. From the gastrointestinal tract it readily absorbed because fluconazole is water-soluble. Oral bioavailability of fluconazole is 80-90% an urinary excretion data indicate that this. The mechanisms of fluconazole is that is act by interferes with the cytochrome P-450-dependent enzyme C-14.

Pharmacokinetic	
Absorption	80- 90%.
Half life	Approximately 30 hours
Bioavailability	Oral oioavailability of Fluconazole between 80- 90%.
Protein Binding	Protein binding of Fluconazole is approximately 14%.
Affected organism	Fungi, yeast and protozoans
Distribution	Distributed to various sites, including sputum, blister fluid, CNS, saliva, urine, normal skin, nails, and blister skin.
Metabolism	Fluconazole is primarily metabolized hepatically. Excretion: Primarily excreted via the kidneys.
Route of elimination	Fluconazole route of elimination is by renal excretion, with approximately 80% .
Mechanism of Action	Fluconazole is a triazole antifungal which acts by inhibiting fungal cytochrome P450 3A dependent enzyme, decreases ergo sterol synthesis and inhibits cell membrane formation. The Cytochrome P450 3A4 is enzyme system fluconazole is a potent inhibitor of this. When concomitantly administering fluconazole with drugs that have narrow therapeutic windows and are substrates of the CYP3A4 substrates caution should be exercised and monitoring is suggested. Patients with renal and hepatic dysfunction or previous hepatotoxicity from other azole derivatives precautions should be used in caution. From the gastrointestinal tract it readily absorbed because fluconazole is water-soluble. Oral bioavailability of fluconazole is 80-90% an urinary excretion data indicate that this. The mechanisms of fluconazole is that is act by interferes with the cytochrome P-450-dependent enzyme C-14.
Drug interaction	Using warfarin together with fluconazole may cause you to bleed more easily, Concomitant use of fluconazole and erythromycin has the potential to increase the risk of cardiotoxicity (prolonged QT interval, torsade de pointes) and consequently sudden death.
Food interaction	Avoid grapefruit products. Avoid multivalent ions.

Excretion	Renal
State	Solid
Contradication	Peripheral neuropathy, chronic heart failure decrease kidney function

MATERIALS AND METHODS

Materials

Fluconazole, Propylene Glycol, Glycerin, Methyl Paraben, Propyl Paraben, Disodium EDTA, Transcutol-P, Flowcare ET-36V, Cetronella Flavour.

Method

Formulation of fluconazole vanishing cream

Vanishing cream formulations were prepared containing 1.42%w/w of Fluconazole using flowcare ET-36V as polymer base according to the formula mentioned in the table 1.

Procedure

1) 421.78g Purified water was taken in SS container and slowly Flow care ET -36V was added with Continuous stirring to form viscous cream.
2) In another SS container, Transcutol-P and Propylene Glycol was heated at temperature 700C over Heating mantle and dissolve Disodium EDTA, Methyl Paraben and Propyl paraben till clear Solution was formed.
3) Then slowly Fluconazole was dispersed in step 2 with continuous stirring till Fluconazole dissolve completely.
4) Step 2 was added in step 1 with continuous stirring by passing through 80#.
5) Glycerin was added when temperature was fall at 400C and cooling is continuing till temperature is decrease to 300C.
6) After that Cetronella Flavour was added with continuous stirring.
7) Finally after stirring PH was Checked.

Table 1: List of formulation.

Batch size 500g

S. no.	Ingredients used	Grade	Content%	Quantity used(g)
1.	Fluconazole	IP	1.42	5
2.	Propylene Glycol	IP	10	35
3.	Methyl Paraben	IP	0.15	0.12
4.	Propyl Pababen	IP	0.05	0.32
5.	Disodium EDTA	IP	0.01	0.08

6.	Glycerin	IP	2.14	7.49
7.	Flow care ET-36	IH	3	15
8.	Transcutol-P	BP	3	15
9.	Citronella Flavor	IHS	0.062	0.21
10.	Purified Water	IP	Q.S.	421.78

Evaluation of fluconazole vanishing cream

1) Drug content analysis

Weigh accurately about 1 gm of sample in 100ml of volumetric flask. Add diluents about 50 ml and heat to melt complete dispersion in heating mantle. After that it was cooled to room temperature and make up the volume with Diluents up to the mark.

2) Measurement of pH

Accurately 10 g of sample was taken in a beaker and 100 ml of distilled water was addedwith continuous stirring, when all the cream formed into liquid form then only with the pre calibrated Ph meter the Ph was determined. The ph of cream was found to be 6.3.

3) Spreadability

Spreadability of Fluconazole vanishing cream was detected by the measured diameter 2gm of cream placed between the plates for 3 minutes. After that Cream made a uniform layer between plates by the spreading, then after weighed the upper plate tie cream and calculated that by using of bellowing formula.

$S=M\times L/T$

S= Spreadability (gcm-1/sec)

M=weight of tied vanishing cream on the upper plate

L=length of glass slide

T=Time

4) Determination of organoleptic properties: The organoleptic properties was determined by physical appearance of the cream

5) Appearance: It is determined by observing its color, opacity.

6) Determination of viscosity: The viscosity of fluconazole cream was determined by using a Brookfield Viscometer (DV II+ Pro model.

7) In-vitro release Study

By using 1g of cream formulation in a Franz cell at static mode using dialysis membrane the in vitro release study was determined.

8) Physical identification of drug

By the physical properties of drug like odour, colour, taste,their texture, organoleptic properties the drug molecules was identified.

9) Melting point determination

The Melting point of fluconazole vanishing cream is determined by the melting point apparatus. In this appratus small amount of drug molecules fluconazole was taken in clean and empty capillary tube and after that the capillary tube is sealed at one side. After that the capillary tube was kept on visual melting point apparatus or on heater at which the sample was start to melt and the temperature of melting of drug was noted.

10) Drug content

The drug content was determined by UV Spectrophotometry.

RESULTS AND DISCUSSION

Preformulation studies

Physiochemical properties

The organoleptic properties results are reported in table 6.1

Table 1: Results of organoleptic properties.

S. no.	Property	Observation
1	Color	White
2	Taste	Bitter
3	Odor	Odorless
4	Form	Fine powder

Determination of melting point

Table 2: Determination of melting point.

	Melting point		
S. no.	Drug sample	Average	Standard
1	139°C (282 °F)	139.59°C	139°C
2	139.6°C		
3	140°C		

Partition coefficient of fluconazole

Table 3: Partition coefficient of fluconazole.

S. no.	Partition Coefficient (Log P)	Average
1	1.16	4.72
2	1.32	
3	1.28	
4	0.96	

Solubility studies of fluconazole

Table 4: Solubility study of fluconazole.

Solvent	Solubility (µg/ml)
Ethanol	61mg/ml
Dimethylsulfoxide	33mg/ml
Dimethyl formamide	16mg/ml
Water	1mg/mL.

Moisture content of fluconazole

Fluconazole moisture content was found to be 0.3%.

Standard curve of fluconazole

In phosphate buffer the standard curve of the drug was prepared in phosphate buffer pH 6.

Table 5: Standard curve data in phosphate buffer pH 6.8.

S. no.	Concentration (µg/ml)	Absorbance
1	0	0
2	0.5	0.126
3	1.0	0.248
4	1.5	0.362
5	2.0	0.487
6	2.5	0.599

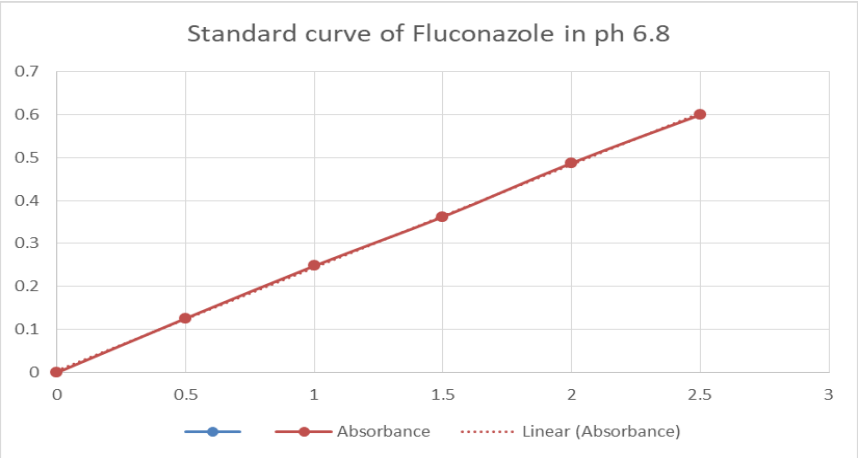

Figure 1: The standard curve of Fluconazole in pH 6.8.

Drug Excipient and Drug identification compatibility study

Identification of drug

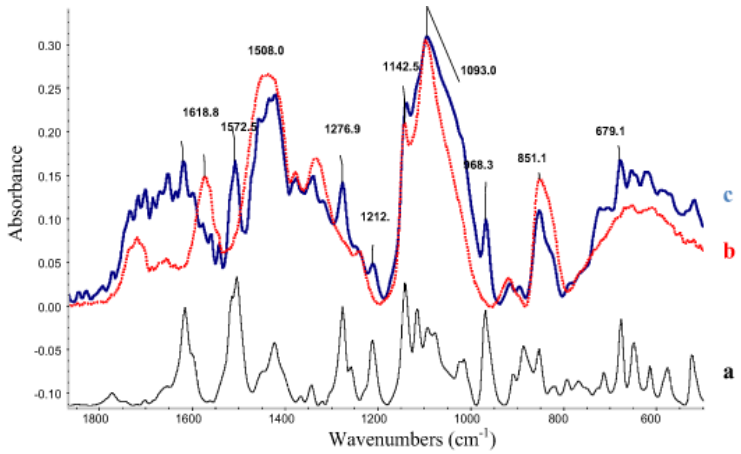

Figure 2: FTIR Spectra of a fluconazole, b PVA nanofiber, c fluconazole incorporated PVA nanofiber.

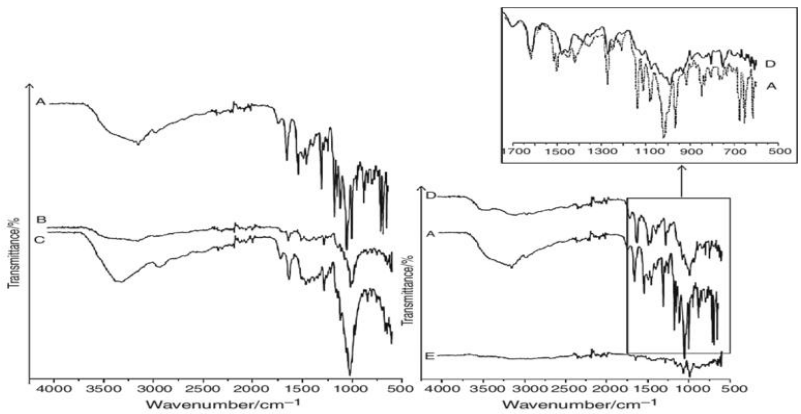

Figure 3: FTIR spectra of fluconazole (A), microcrystalline cellulose (B), fluconazole/ microcrystalline cellulose (C), fluconazole/ calcium hydrogen phosphate dihydrate (D), calcium hydrogen phosphate dihydrate (E).

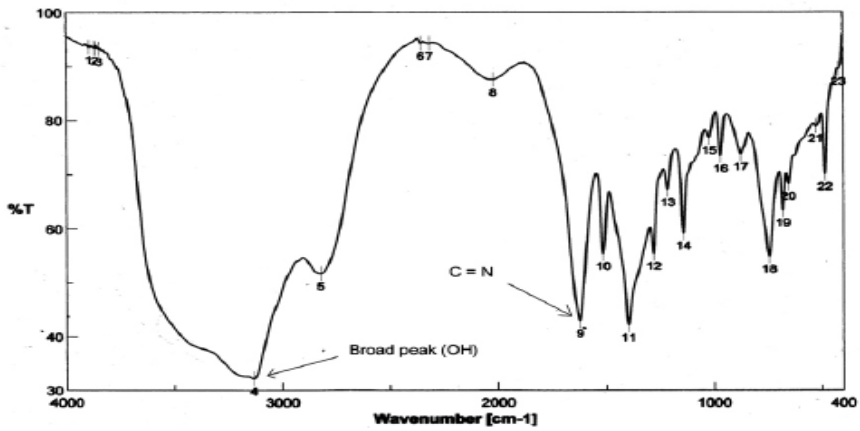

Figure 4: Infra red spectra of fluconazole.

CONCLUSION

The new designed formulation of fluconazole vanishing cream was developed for the anti-fungal properties/ activity. By using the Flowcare ET-36V the formulation of fluconazole cream was done. The confirmed the drug was done by FTIR spectra. The compatability properties between excipients and drug it also reveals. The vanishing properties was seen by the formulation 5 and there is no any residue or traces when applied to the skin that means this formulation which was made was a vanishing cream. Again at accelerated (40˚C±2˚C, 75% ±5% RH) and real (30˚C±2˚C, 75% ±5% RH) the stability studies were conducted. The results revealed that the product, formulation 5 complies at all parameters like drug content, Ph, leak test, antifungal activity, release kinetics, stability study. This product also showed good stability properties, hence this formulation is good for future approach and valuable.

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