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FORMULATION AND EVALUATION OF LULICONAZOLE SOLID DISPERSION INCORPORATED GELS

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ABSTRACT

Drug Luliconazole is a topical antifungal drug used for fungal infection treatment. Luliconazole is a novel topical antifungal imidazole with broad spectrum and potent antifungal activity. The purpose of the present research was to formulate Luliconazole solid dispersion incorporated gels. Solid dispersion was prepared in various ratios using each carrier. Solubility study and dissolution study showed that as the concentration of the carrier increase, the solubility and dissolution rate of Luliconazole increases. The particle size and surface morphology of solid dispersion were studied by SEM. IR studies showed that no chemical reaction was taken place between drug and excipient in solid dispersion.

KEYWORDS: Solid Dispersion, Luliconazole, Carrier, Solubility, Dissolution.

INTRODUCTION

The Skin is the largest organ of the body, accounting for more than 10% of body mass, and the one that enable the body to interact most intimately with its environment. The integumentary system is formed by the skin and its derivative structure.

Many agents are applied to the skin either deliberately or accidentally, with either beneficial or deleterious outcome. The outer most level, the epidermis consists of specific constellation of cells known as keratinocytes, which function to synthesize keratin, a long threadlike protein with a protective role. The middle layer, the dermis is fundamentally made up of the fibrillar structural protein known as collagen. The dermis lies on the subcutaneous tissue, or panniculus which contain small lobes of fat cells known as lipocytes. The thickness of these layers varies considerably, depending on the geographic location on the anatomy of the body.[1]

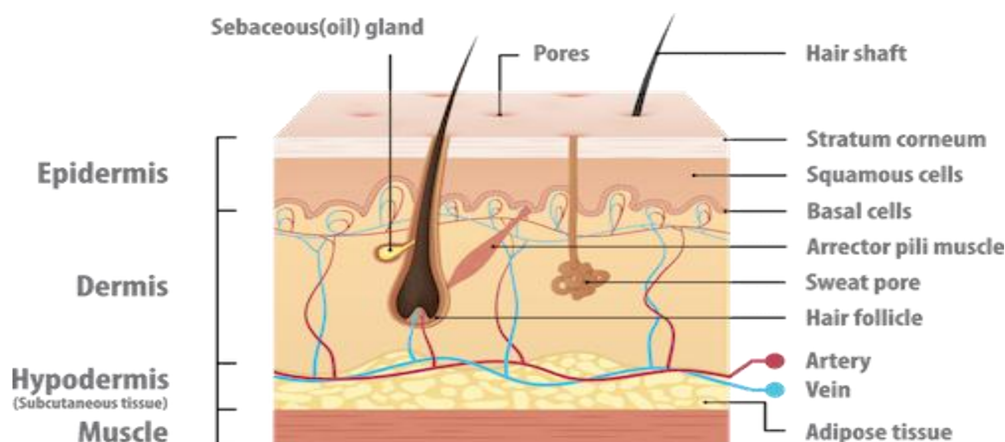


Fig. 1: Structure of the Skin (2).

Epidermis

The epidermis is the outer layer of the skin, defined as a stratified squamous epithelium, primarily comprising keratinocytes in progressive stages of differentiation. Keratinocytes produce the protein keratin and the major building blocks of the epidermis.As the epideremis is a

vascular; it is entirely dependent on the underlying dermis for nutrient delivery and waste disposal through the basement membrane.

The primary function of the epidermis is to act as a physical and biological barrier to the external environment, preventing penetration by irritants and allergens. The epidermis is composed of layer; most body part have four layers, but those with the thickest skin have five. The layers are;

Stratum corneum (horny layer)
Stratum lucidum (only found in thick skin that is palms of the hands, the soles of the feet and the digits)
Stratum granulosum (granular layer)
Stratum spinosum (prickle cell layer)
Stratum basale (germinative layer)

The epidermis also contains other cell structures. Keratinocytes make up around 95% of the epidermal cell population, the others being melanocytes, langerhans cells and merkel cells.
Dermis

The dermis forms the inner layer of the skin and is much thicker than the epidermis.The basement membrane zone and the subcutaneous layer, the primary role of the dermis is to sustain and support the epidermis.

The main functions of the dermis are
Protection
Cushioning the deeper structure from mechanical injury.
Providing nourishment to the epidermis
Playing an important role in wound healing

The epidermal appendages also lie within the dermis or subcutaneous layers, but connect with the surface of the skin.

Layers of dermis, the dermis is made up of two layers;
- The more superficial papillary dermis
- The deeper reticular dermis.

The papillary dermis is the thinner layer, consisting of loose connective tissue containing capillaries, elastic fibres and some collagen. The reticular dermis consists of a thicker layer of dense connective tissue containing larger blood vessels, closely interlaced elastic fibres and thicker bundles of collagen.

It also contains fibroblasts, mast cells, nerve endings, lymphatics and epidermal appendages. Surrounding these structures is a viscous gel that;
- Allows nutrients, hormones and waste products to pass through the dermis.
- Provides lubrication between the collagen and elastic fibre networks.
- Gives bulk, allowing the dermis to act as a shock absorber.

Hypodermis
The hypodermis is the subcutaneous layer lying below the dermis; it consists largely of fat. It provides the main structural support for the skin, as well as insulating the body from cold and aiding shock absorption. It is interlaced with blood vessels and nerves.[3]

Structure of the skin
The skin is the largest organ organ of the body. It has three main layers, the epidermis, the dermis and the subcutaneous layer.

The epidermis is an elastic layer on the outside that is continually being regenerated. It includes the following
- Keratinocytes

The main cells of the epidermis formed by cell division at its base. New cells continually move towards the surface. As they move they gradually die and become flattened.

- Corneocytes

The flattened dead keratinocytes that together make up the very outer layer of the epidermis is called the stratum corneum or horny layer. This protective layer is continually worn away or shed.

- Melanocytes

Melanocytes produce the pigment melanin that protects against UV radiation and gives skin its colour.
The dermis is the inner Layer that includes the following:

- Sweat gland

It produces sweat that travels via sweat ducts to opening in the epidermis called pores.
They play a role in temperature regulation.

- Hair follicles

Hair follicles are pits in which hair grow. Hairs also play a role in temperature regulation.

- Sebaceous gland

Sebaceous gland produces sebum to keep hairs free from dust and bacteria.
Sebum and sweat make up the surface film.

- Subcutaneous layer

The subcutaneous layer under the dermis is made up of connective tissue and fat.

Function of the skin
- Provides a protective barrier against mechanical, thermal and physical injury and hazardous substances.
- Prevents loss of moisture.
- Reduces harmful effect of UV radiation.
- Acts as a sensory organ
- Helps regulate temperature.
- An immune organ to detect infections.
- Production of vitamin D.[4]

Luliconazole may represent effective topical drug for the treatment of Tinea Corporis, Jock itch and athelts foot.

Luliconazole is a topical antifungal agent that acts by unknown mechanism but is postulated to involve altering the synthesis of fungi cell membranes. It was approved by
The FDA in November 2013.

Luliconazole kills the organism Trichophyton rubrum and Epidermophyton floccosum, most likely by altering their fungal cell membranes.

Mechanism of action

The exact mechanism of action for luliconazole's anti-fungal activity is still not known, but Luliconazole is thought to inhibit the enzyme lanosterol demethylase. Lanosterol demethylasa is needed for the synthesis of ergosterol, which is a major component of the fungus cell membranes.(5)

Uses

Luliconazole is used to treat skin infections such as athlete's foot, jock itch and ringworm.
Luliconazole is an azole antifungal that works by preventing the growth of fungus.(6)

The fungal infection treated by Luliconazole is as follows:

- Interdigital tinea pedis (athletes foot)-

Fungal infection that occurs between the toes.

- Tinea cruris (jock itch)

Fungal infections that occurs on the skin in the groin, buttocks and inner aspects of the thighs.

- Tinea Corporis (ringworm)-

Fungal infection that form red scaly rashes on the body.[7]

Topical delivery can be defined as the application of a drug containing formulation to the skin to directly treat cutaneous disorders of a general disease with the intent of containing the pharmacological or other effect of the drug to the surface of the skin. Among the topical formulations clear transparent gels have widely accepted in both cosmetics and pharmaceuticals.[8]

Gels have gained more and more importance because the gel-bases formulations are better percutaneously absorbed than cream and ointment bases. The percutaneous absorption of drugs involves two consecutive processes the release of the drug from the topical formulation, and its absorption into the skin at the site of application.

Solid dispersion defined as the dispersion of one or more active pharmaceutical ingredient in a carrier at solid state and an efficient technique to improve dissolution of poorly water soluble drug to enhance their bioavailability.

Solid dispersion is an effective technique which can easily enhance the dissolution rate of drugs. This technique involves one or more hydrophobic drugs in an inert hydrophilic carrier or hydrophilic matrix at solid state.

Advantages of Solid dispersion

1. To reduced particle size and thus the surface area are improved and increased dissolution rate is attentained. Hence bioavailability is increases.
2. The carrier used in the solid dispersions plays a major role in improve wettability results in increased solubility thus improving the bioavailability.
3. To decrease the crystalline structure of drug in to amorphous form.
4. To improve dissolvability in water of a poorly water- soluble drug in a pharmaceutical.

Disadvantages of Solid dispersion

1. Sometimes it is not easy to handle because of tackiness.
2. Major disadvantages are their Instability. They show changes in crystalline and decreases in dissolution rate with ageing.
3. Temperature and moisture have more deteriorating effect on solid dispersions than on physical mixtures.
4. Difficulty in handling because of tackiness.[9]

Applications

- To increase the solubility, dissolution rate, absorption and bioavailability.
- Improved the solubility and stability.
- To reduce side effect of certain drugs.
- Improvement of drug release from ointment, creams.

Types of Solid Dispersion

1. Binary Solid dispersion

It consists of drug and a polymeric carrier.

2. Ternary Solid dispersion

It consists of drug, a polymeric carrier and a surfactant.
Generally used surfactant is polysorbate 80 which plays an important role in dissolution of the solid dispersion both the binary and ternary solid dispersion enhanced the dissolution of poorly water soluble drugs.

3. Surface Solid dispersion

Surface solid dispersion is formulated with polymers such as polyvinyl pyrrolidone, polyethylene glycol and polyvinyl pyrrolidone – vinyl acetate copolymer by fusion technique to improve its solubility.

Uses of solid dispersion

- Drug is formulated with hydrophilic carrier as a solid dispersion to increase its aqueous solubility and dissolution.

- Solid dispersion improves dissolvability in water of poorly water soluble drug in a pharmaceutical composition.

Selection of carrier

- The carrier should be freely soluble in water with a high rate of dissolution.
- It should be pharmacologically inert.
- It should possess chemical compatibility with drug.
- It should be non toxic in nature.[10]

Method of preparation

- Fusion method
- Solvent evaporation method
- Melting solvent method
- Kneading method
- Super critical fluid technology
- Spray drying
- Gel entrapment technique
- Hot melt extrusion
- Co-Grinding method

Fusion Method

The first solid dispersions are created for pharmaceutical applications were prepared by the fusion method. In Fusion method, the molecular dispersion is formed due to the mixing caused by molecular mobility of drug and carrier molecules which are greatest at the melting point of the two components of the dispersion.

- **Solvent Evaporation Method**

In this method, the thermal decomposition of drugs or carrier can be prevented since organic solvent evaporation occurs at low temperature. A basic process of preparing solid dispersion of this type consists of dissolving the drug and polymer carrier in a common solvent.

- **Melting Solvent Method**

It involves preparation of solid dispersion by dissolving the drug in a suitable liquid solvent and then incorporating the solution directly into the melt of polyethylene glycol, which is then evaporated until a clear solvent free film is left.[11]

- **Kneading Method**

A mixture of accurately weighed and carrier is wetted with solvent and kneaded thoroughly for some time in a glass mortar. The paste formed is dried and sieved.

- **Super Critical Fluid Technology**

The super critical fluid process involves the spraying of the solution composed of the solute and of the organic solvent into a continuous super critical phase flowing concurrently. Super critical fluid methods are mostly applied with carbon dioxide which is used as either a solvent for drug and matrix or as an anti-solvent.

- **Spray Drying**

Accurately weighed amount of drug with lipid carrier are dissolved in methanol to obtain a clear solution. This solution is then dried using laboratory scale dryer.

- **Gel entrapment Technique**

Carrier for example hydroxyl propyl methyl cellulose is dissolved in organic solvent to form a clear and transparent gel.

- **Hot melt extrusion**

In hot –melt extrusion, a blend of polymer and excipients in powder form is transferred by a rotating screw through the heated barrel in the extruder. The molten mass is continuously pumped through the die at the end of the extruder and rapidly solidifying when exiting the machine.

- **Co-Grinding method**

Accurately weighed pure powder and the carrier are physically mixed for some time using a blender at a specified speed. The mixture is then charged into the chamber of vibration ball mill. The powder mixture is ground. Then the sample is collected and kept at room temperature in a screw capped glass vials until use.[12]

MATERIAL AND METHODS

Material

The following Materials were Used : Luliconazole, Beta- Cyclodextrin, Triethanolamine, Propylene glycol, methyl paraben.

Methods

1. Preformulation Study

Preformulation study is the development of dosage form of drug.

It is a step in which investigation of physicochemical properties of drug sample is carried out alone and combined with the excipient.

The objective of study to identify and confirmed the respective sample and this information is useful for formulation development.

- **Organoleptic Properties of drug**

The drug sample was studied for characterization of colour, odour and physical appearance.

- **Determination of melting point**

Drug sample of Luliconazole was studied for melting point analysis for confirmation of drug sample.

It was determined by capillary method.

For this a small quantity drug sample was filled into the sealed capillary and it was tied to thermometer and heated in the theils tube.

The temperature at which drug melted was recorded.

- **Solubility analysis of drug**

The solubility analysis of drug Luliconazole was carried out in different solvent such as, methanol, Ethanol and phosphate buffer

Preparation of Solid Dispersion

Kneading Method

Solid dispersion of drug in β cyclodextrin containing three ratios (1:1, 1:2, 1:3 w/w) was prepared by kneading method. The β – cyclodextrin was taken in mortar and little amount of ethanol was added and triturated to obtained a homogenous slurry like consistency.slowly the drug was incorporated into the slurry and trituration was continued for 1 hour Then dried at 25°C for 2 hours, pulverized sieved through mesh no. 100.

Characterization of Drug

1) U.V Spectrophotometric Method

The standard calibration curve was performed by preparing stock solution, 10 mg was weighed and transferred to 100ml volumetric flask and were dissolved in methanol and volume was made. From these stock solutions further dilution was made in 10 ml volumetric flask (2, 4, 6, 8 and 10) and volume was made with respective solvent and absorbance of samples was recorded on UV spectrophotometer at respective wavelength of maximum absorbance with use of corresponding solvents as blank.

2) FTIR Spectroscopy

The interaction between drug sample used for the formulation and excipients were studied using FTIR. The FTIR Spectrum of pure Luliconazole, Beta cyclodextrin physical mixture of drug and beta cyclodextrin were analysed for compatibility study.

Evaluation of Solid Dispersion

1) Pre – Compression parameter

Pre-compression study an important while formulating the dosage form.

Bulk density

The sample was weighed accurately and filled to the graduated measuring cylinder. The volume occupied by the granules recorded as the bulk volume. Bulk density can be calculated by using formula.

$$\text{Bulk density} = \frac{\text{Weight of powder}}{\text{Bulk volume}}$$

Tapped density

The weighed powder blend was transferred to the measuring cylinder. The tapping was carried out about 100 times the changes in volume of powder after tapping was noted as tapped volume.

$$\text{Tapped density} = \frac{\text{weight of powder}}{\text{Tapped volume}}$$

Compressibility index

The Carr's compressibility index was calculated using tapped density and bulk density. Compressibility index was calculated by formula.

$$\text{Carr's index} = \frac{\text{Tapped density-bulk density}}{\text{Tapped density}} \times 100$$

Hausner ratio

Hausner ratio can be calculated using formula,

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Bulk density}} \times 100$$

Angle of repose

Angle of repose was carried using the funnel method. The funnel and free standing cone method employ a funnel that is secured with its tip at a given height. The height and diameter of resulting cone were determined and angle of repose calculated by using the formula.

$\tan \Theta = h/r$

Where, r is the radius of cone

H is height

2) Percentage practical yield

Percentage practical yield was calculated to know about percent yield.

Solid dispersion was collected and weighed to determine practical yield from the following equation.

$$\text{Percentage practical yield} = \frac{\text{Practical mass (solid dispersion)} \times 100}{\text{Theoretical mass (Drug +carrier)}}$$

3) Drug Content

The drug content in solid dispersion was determined by taking weighed quantity of 50mg in 50 ml methanol.

The solution was further diluted and absorbance of solution was determined by UV- Spectrophotometer at 296nm.

4) Scanning Electron Microscopy

A Scanning electron microscope is a type of electron microscope that produces images of a sample by scanning the surface with a focused beam of electrons. The electrons interact with atom in the sample, producing various signals that contain information about the surface topography and composition of the sample.

Study shows complete disappearance of crystal of drugs and confirms that drug is totally solubilised in solid dispersion system.

5) X- Ray Diffraction

X ray diffraction is a technique used to find out the nature of the materials as crystalline or amorphous. XRD works by irradiating a material with incident x-ray and then measuring the leave the material. The primary use of x ray diffraction analysis is the identification of material based on their diffraction pattern.

6) *In-vitro* drug release study

The dissolution studies of solid dispersion were performed using USP dissolution apparatus type I. Dissolution study was performed in 900 ml phosphate buffer pH 7.4. The stirring speed was 50 rpm and the temperature was maintained at37ºC ±0.5ºC. The sample were withdrawn at time interval and replenished with fresh dissolution medium. The samples were filtered, diluted ananalyzed by UV spectrophotometer at 302nm. Dissolution studies of solid dispersion were carried out.

Preparation of Gel Formulation

The formulation was prepared by soaking carbopol in water for 24 hrs triethanolamine was added to neutralize the PH. Weigh accurately solid dispersion dissolve in methanol, propylene glycol and methyl paraben.
This solution was added to neutralize carbopol with continuous stirring to form clear gel.

Evaluation of Gels

1) Appearance

The prepared gels were inspected visually for clarity, colour and presence of any particle.

2) PH

The PH of gel was determined using digital PH meter.
1gm of gel in 20 ml distilled water.

3) Spreadability

Spreadability was determined by wooden block and glass slide apparatus.
For the determination of spreadability excess of sample was applied in between two glass slide and was compressed to uniform thickness by placing 100 gm weight for 5 minutes. Weight was added to pan. The time required to separate the two slides, the time in which the upper glass slide moves over the lower plates was taken as measure of spreadability.

Spreadability was calculated by using formula.
S=ML/T

Where,
S = Spreadability
M =Weight tide to upper slide.
L =Length moved on the glass slide.
T =Time taken to separate the slide.

4) Viscosity

Viscosity of the gel was determined by using Brook field viscometer. The spindle number 4 was rotated at 15 rpm

5) Drug content

The gel of 20 mg was dissolved in 20 ml methanol. The volumetric flask containing gel solution was shaken for 2hr on mechanical shaker in order to get complete solubility of drug. From this 1ml was pipette out and made upto 10ml with methanol. This solution was filtered and analyzes by UV spectrophotometer at 296 nm.

6) Skin irritation test

Irritation test was carried out to determine possible localised reaction of selected formula on the skin.

Skin irritation study was performed on albino Wister rat. 1 gm gel was applied on the dorsal surface of the rat skin.
The visual inspection was observed for 3 days to check any evidence of redness and swelling on the rat skin.

7) *In Vitro* Diffusion Study

Phosphate buffer of PH 7.4 was used for *In vitro* release as a receptor medium.

1 gm gel was placed on donor compartment and receiver compartment filled with PH 7.4 phosphate buffer solution with constant stirring.

Samples were withdrawn at interval of 1hr. Then equal quantity of fresh phosphate buffer PH 7.4 is replaced after each sampling. The samples further diluted and analysed by UV spectrophotometer.

8) *In vitro* Antifungal test-

The suspension of candida albicans was poured evenly on plated of sabouruds dextrose agar .Agar wells were cut from the seeded agar medium using a sterile cork borer.

These wells were filled with 10 mg of formulated gel Prepared with 1% drug and also without drug.10 mg of marketed gel was used for comparison. A plate was then incubated at 37ºC for about 3 days and compared the zone of inhibition. A plate was then incubated at 37ºC for about 3 days and compared the zone of inhibition.

RESULT AND DISCUSSION

1.Preformulation studies

Organoleptic Properties-

Table 1: Organoleptic properties of drug.

Parameter	Observation
Color	White
Odor	Odourless
Appearance	Crystalline

2.Determination of Melting point

Drug sample of Luliconazole was determined by capillary method. Theils tube was used for determination of melting point. Melting point of Luliconazole was observed in range of 154ºCwhich is comply with the reported melting rang of 150-154ºC.

Table 2: Determination of Melting point.

Reported Melting point	Observed melting point
	153ºC
150-154ºC	154ºC
	154ºC

3.Determination of Solubility

Luliconazole drug soluble in methanol, ethanol and posphate buffer.

Table 3: Determination of Solubility.

Solvent	Solubility
Methanol	Readily soluble
Ethanol	Readily soluble
Water	Practically insoluble
Phosphate buffer	Soluble

4.U.V.analysis

The Construction of standard calibration curve was performed by preparing stock solution.

10mg drug sample was weighed accurately and transferred to 100ml volumetric flask and diluted up to the mark with methanol.

From these stock solution further dilutions was made in 10ml volumetric flask (2, 4, 6, 8 and 10) and volume was made with respective solvent and absorbance of sample was recorded on UV spectrophotometer at respective wavelength.

Table 4: Calibration curve in methanol.

Sr No.	Concentration(PPM)	Absorbance
1.	2	0.2584
2.	4	0.4267
3.	6	0.6274
4.	8	0.8264
5.	10	0.9226

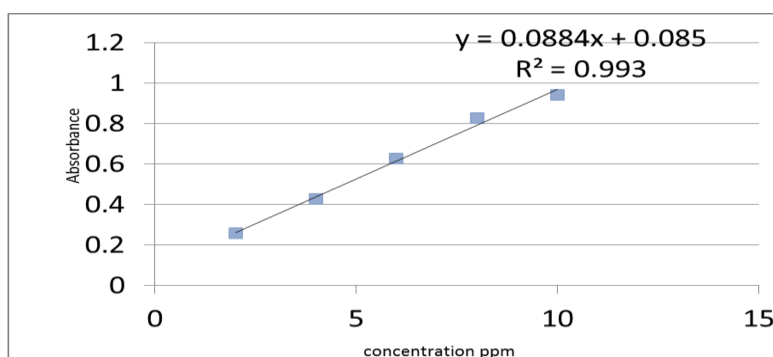


Fig. 2: Calibration curve in methanol.

5.Fourier Transform Infrared Spectroscopy (FT-IR)

Characterization and confirmation of the functional group in representative sample carried out by FTIR study.

Following are the peak observed at different wave numbers and the functional group associated with these peaks.

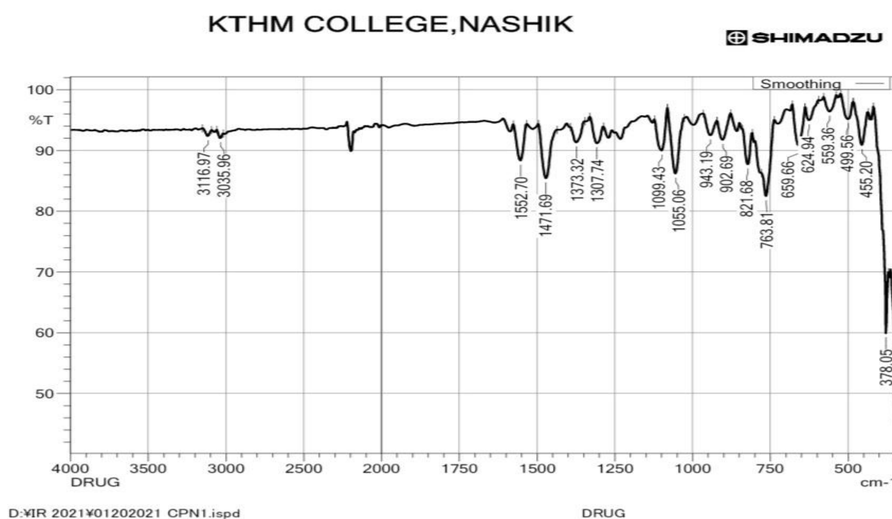


Fig. 3: FT-IR Spectra of drug Luliconazole.

Table 5: Interpretation of FT-IR spectra of Luliconazole.

Functional groups	Peak reported cm^{-1}	Peak observed cm^{-1}
C-H	1300-1600	1471.69

C-O	1085-1050	1055.06
N-O	1600-1300	1552.70
OH	2500-3300	3035.96

6.FT-IR spectra oF Excipient

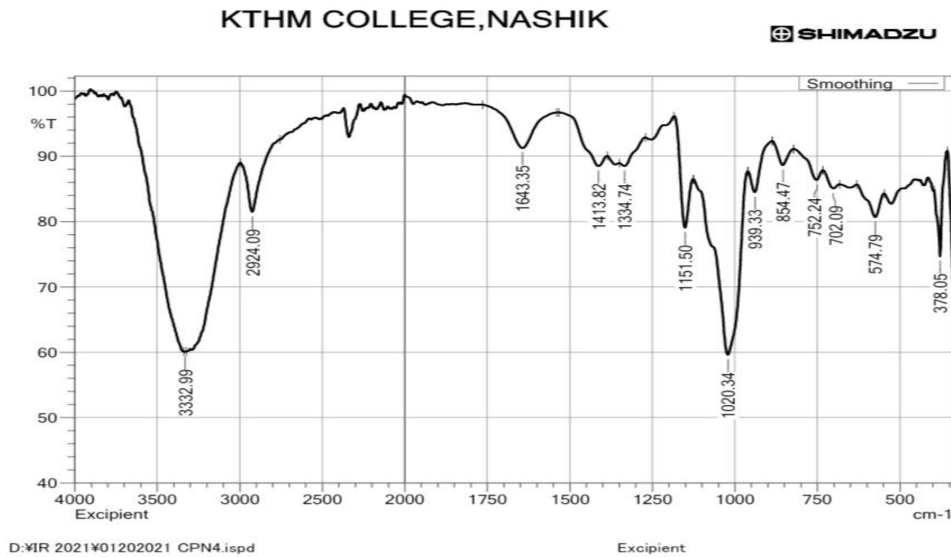


Fig. 4: FT-IR Spectra of Excipient.

Table 6: Interpretation of FT-IR spectra of β cyclodextrin.

Functional group	Peak reported cm^{-1}	Peak observed cm^{-1}
O-H	3400-3200	3332.99
O-H	2500-3300	2924.09
C-O	1020-1075	1020.34.
C-F	1400-1000	1151.50
C=C	1650-1600	1643.35

Drug-Excipient Compatibility study

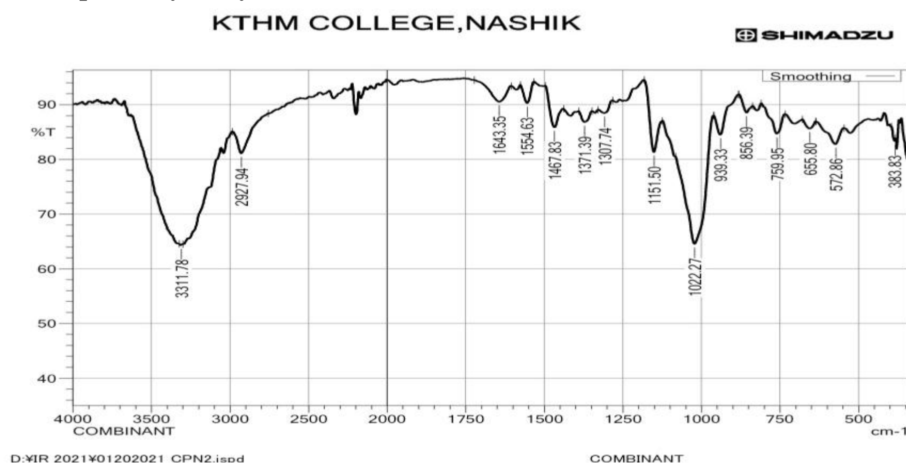


Fig. 5: FT-IR Spectra of Drug excipient compatibility.

Table 7: Interpretation of FT-IR spectra of drug-excipient compatibility.

Functional group	Peak reported cm^{-1}	Peak observed cm^{-1}
O-H	3400-3200	3311.78
O-H	2500-3300	2927.94
C-O	1020-1075	1022.27
C-F	1400-1000	1151.50
C=C	1650-1600	1643.35

The characteristic peak obtained after FT-IR indicates that there is chemical interaction between drugs, excipient both is compatible to each other at different conditions.

Evaluation of Solid Dispersion

1. Pre- Compression study

Table 8: Pre-compression study of solid dispersion.

Batch number	Bulk density(g/ml)	Tapped density (g/ml)	Compressibility index (%)	Hausner's ratio	Angle of repose(θ)
F1	1	-	-	-	-
F2	1	1.7	10.47	1.11	20.30
F3	1	1.12	10.71	1.12	21.30

Pre-Compression study is an imported parameter in formulation of dosage form.
This study was used to perform for all 3 batches it was found that batch F3 shows better result than other.

2. Percent Practical Yield

Percent practical yield was calculated to know the percent yield , it helps in selection of appropriate method of production.

Table 9: Determination of percent practical yield.

Formulation	Percent practical yield
F1	-
F2	94%
F3	95%

3. Drug content

The drug content of the prepared solid dispersion was calculated by using a standard calibration curve of solid dispersion in methanol .The drug content of all solid dispersion formulation was found to be in rang 89.07 to 97.76%

Table 10: Determination of % Drug content.

Sr.No	Formulations	% Drug content
1.	F1	-
2.	F2	89.07%
3.	F3	97.76%

4. Scanning Electron Microscopy

The shape and surface morphology of the solid dispersion was studied by scanning electron microscopy. The result shows changes in crystal pattern ,network form and three dimensional structures of the drug in solid dispersion and gels.

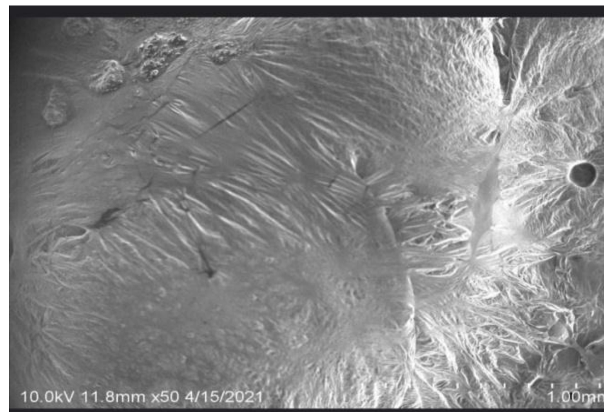


Fig. 6: SEM of Solid dispersion.

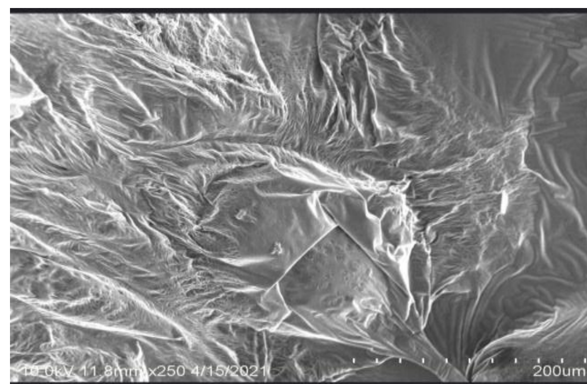


Fig. 6.1 SEM of Gel.

5. X-ray diffraction

The Diffraction angles are similar as far as both X-ray diffraction patterns are concerned. Only a decrease in reflection intensities can be pointed out for the solid dispersion sample.

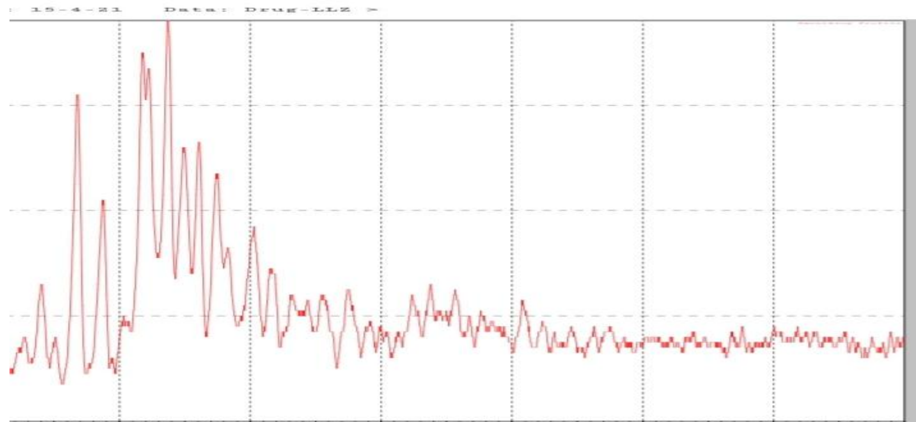


Fig. 7: X ray diffraction of drug.

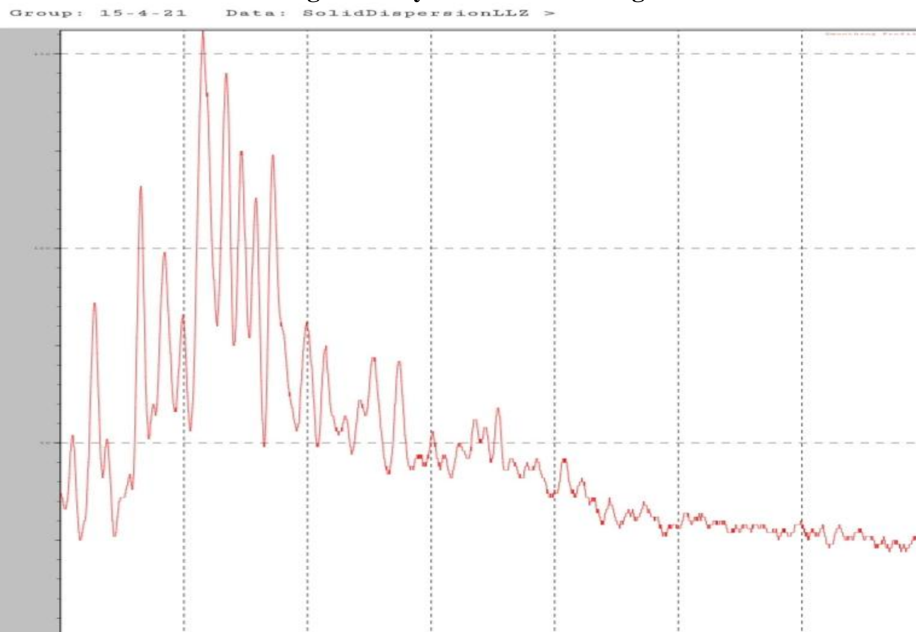


Fig. 7.1: X-ray diffraction of solid dispersion.

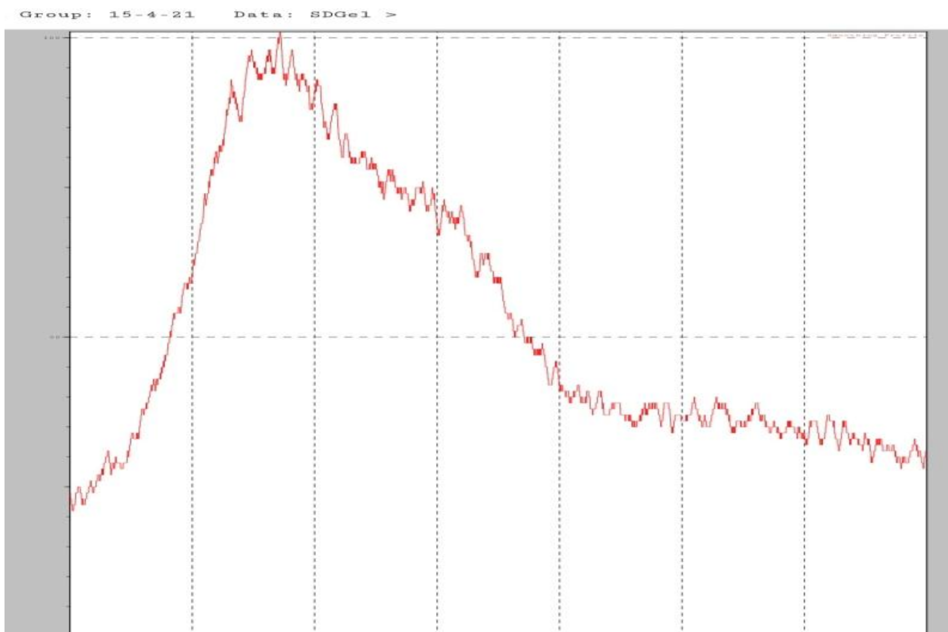


Fig. 7.2: X-ray diffraction of gel.

6. *In vitro* drug release study of solid dispersion

In vitro drug release study was performed using USP type 1 dissolution apparatus, phosphate buffer PH7.4 was used.

Table 11: % Cumulative drug release of all batches up to 60 min.

Sr No.	Time (min)	% Cumulative Drug Release	
		F2	F3
1.	5	13.34	13.36
2.	10	19.99	20.23
3	15	26.98	30.20
4.	30	46.28	47.33
5.	45	65.41	68.21
6.	60	84.92	95.58

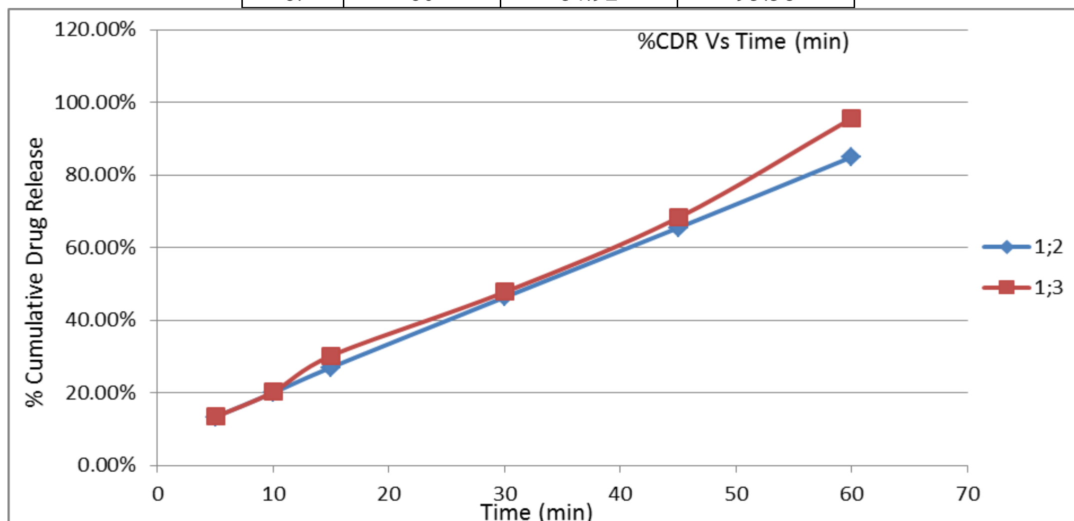


Fig. 8 Graphical representation of % CDR vs.Time in min.

Table 12: Different batches of Luliconazole Solid dispersion formulation.

Sr.No	Ingredients	F1	F2	F3
1.	Luliconazole (%W/W)	1	-	-
2.	Solid dispersion of Luliconazole	-	1	1
3.	β-Cyclodextrin	-	1	2
4.	Dimethyl Sulfoxide	2.5	2.5	2.5
5.	Carbopol 940	10	10	10
6.	Methanol	7.5	7.5	7.5
7.	Propylene glycol	5	5	5
8.	Methyl paraben	0.25	0.25	0.25
9.	Triethanolamine	q.s	q.s	q.s
10.	Distilled water	q.s to 100 ml	q.s to 100 ml	q.s to 100 ml

Evaluation of solid dispersion incorporated gel-

1) Appearance-

The colour of formulated gel was found be white.
Colour – White

2) PH-

The PH of the sample will be measured by digital PH meter at room temperature..

Table 13: Determination of PH.

Formulation code	PH
F1	7.06±0.2144
F2	7.13±0.2509
F3	7.32±0.2932

3) Spreadability

Determination of Spreadability using wooden block and glass slide apparatus. The concentration increases, Spreadability is decreases.
It was calculated using formula,
S=M.L/T

Table 14: Determination of Spreadability.

Formulation code	Spreadability
F1	10.10±0.1702
F2	10.11±0.1923

F3	10.17.0.2097

4) Viscosity

Determination of viscosity using brook field viscometer. The RPM increases viscosity is decreases

Table 15: Determination of viscosity.

Formulation code	viscosity
F1	31080±2.724
F2	30983±2.723
F3	29427±2.733

5) Drug content

% Drug Content of prepared Luliconazole gel formulation was calculated by using a standard calibration curve of Luliconazole in methanol. The drug content of all gel formulations was found to be in the range of 88.80%-90.68%. The results indicate that there is a uniform distribution of Luliconazole in the prepared formulation base.

Table 16: Determination of % Drug content.

Formulation code	% Drug content
F1	88.80
F2	89.72
F3	90.68

6) *In-vitro* drug release study of formulated gels

In – vitro drug release study of different gel formulations were carried out in Phosphate buffer PH 7.4.

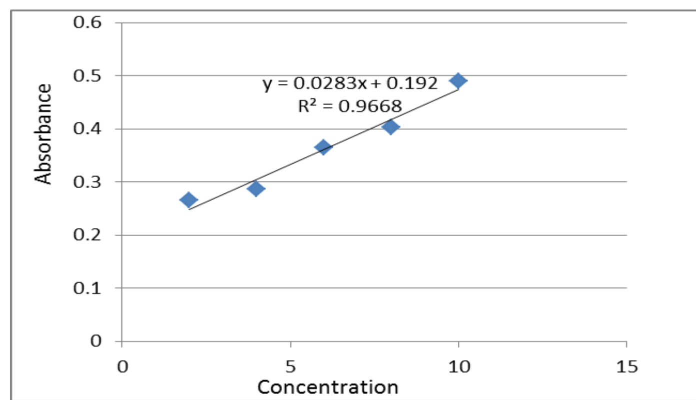


Fig. 9: Calibration curve of solid dispersion in phosphate buffer PH 7.4.

Table 17: UV Calibration of solid dispersion.

Sr.No.	Concentration	Absorbance
1	2	0.2648
2	4	0.2864
3	6	0.3649
4	8	0.4022
5	10	0.4894

Table 18: % Cumulative drug release of all batches.

Sr.No	Time (min)	% Cumulative Drug Release		
		F1	F2	F3
1.	5	7.42	9.45	9.12
2.	10	20.63	13.72	15.02
3.	15	22.68	20.52	28.47
4.	30	42.73	41.84	41.83
5.	45	74.43	77.91	78.18
6.	60	81.57	88.72	94.69

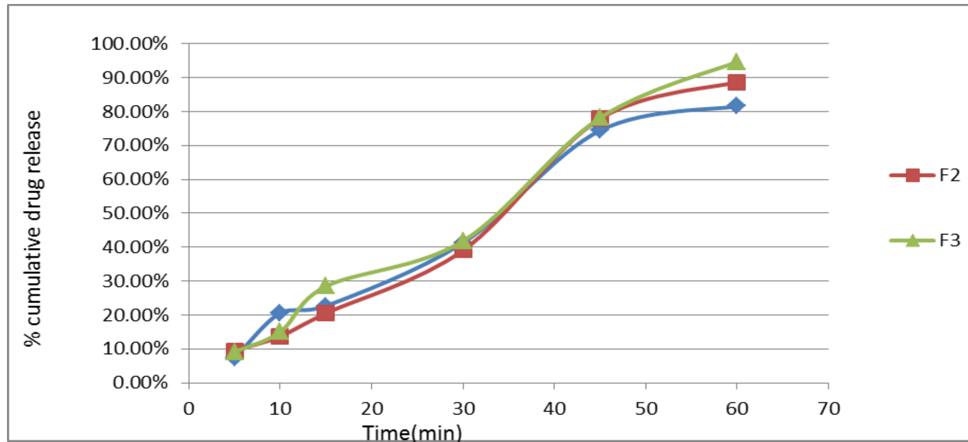


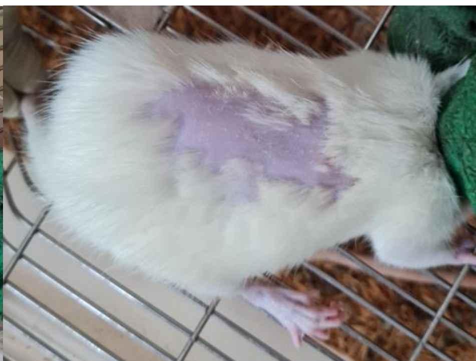
Fig. 10: Graphical representation of % CDR vs Time.

7) Skin irritation test

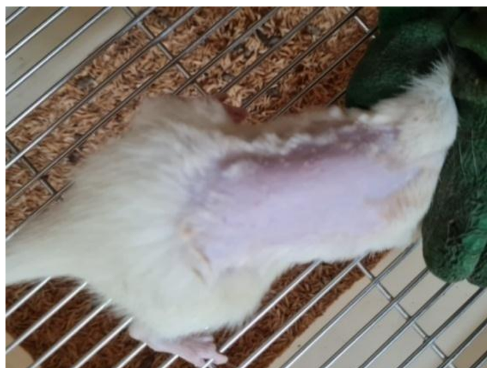
Skin irritation study was performed on albino Wister rat. but there was no erythema, edema or reddening of skin.

Control

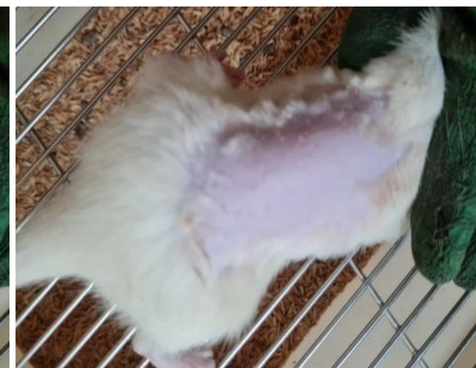
Formulated gel F1



Marketed gel F1



F2



F2

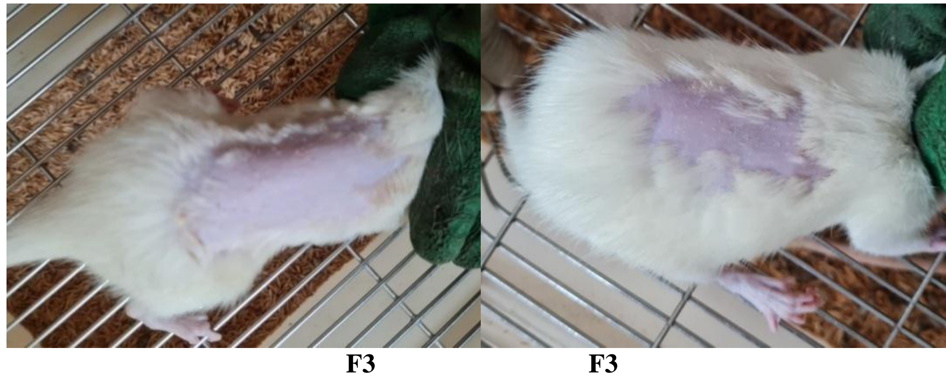


Fig. 11: Skin irritation test.

Table 19: Determination of skin irritation test.

Formulation code	Skin irritation
F1	No irritation
F2	No irritation
F3	No irritation

8) *In vitro* anti –fungal test

In vitro anti-fungal activity of optimized gel F2, marketed gel M, blank gel B, control c was determined by cup plate method using candida albicans as test organism and zone of inhibition was measured and compared

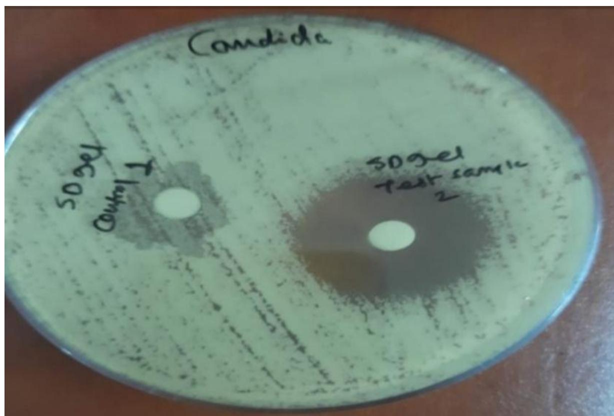


Fig. 12: *In vitro* anti-fungal test

Table 20: Zone of Inhibition for Luliconazole Gel control and test sample.

Sample Name	Result
SD Gel test sample	27mm
Control	13mm
Nystatin	21mm

CONCLUSION

Solid dispersion incorporated Luliconazole gel are thermodynamically stable. The solid dispersions are prepared by kneading method followed by being incorporated into carbopol 940 based gel matrix to form solid dispersion incorporated Luliconazole solid dispersion incorporated topical gel. In the present study, an attempt was made to increase the *In-vitro* dissolution rate of Luliconazole by solid dispersion technique. Solid dispersions were prepared in various ratios using each carrier. Solubility study and dissolution study showed that as the concentration of the carrier increase, the solubility and dissolution rate of Luliconazole increases. FT-IR spectra of all the polymers and excipients used were compatible with the drug. The particle size and surface morphology of solid dispersion were studied by SEM. The study shows that F3 batch having highest drug release of solid dispersion and Gels.

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