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Formulation and Evaluation of Transdermal Patches for Nanosized Itraconazole Delivery

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Abstract:
The main objective of this work was to create and analyses nanoparticles of Itraconazole using solvent displacement or nano precipitation methods. The Preformulation research assessed the organoleptic characteristics, solubility, melting point, partition coefficient, and identification using FT-IR spectroscopy and UV spectroscopy. Itraconazole exhibited the properties of a finely textured, odorless, and white to yellow powder. It shown limited solubility in aqueous solvents, but significant solubility in alcohol and methylene glycol. The melting point of the substance was confirmed to be 162.2°C, consistent with the values documented in the literature. The purity of the drug powder was confirmed using FT-IR spectroscopy, while a calibration curve for quantification was constructed by UV spectroscopy. Subsequently, Itraconazole nanoparticles were synthesized and characterised for their drug content, zeta potential, polydispersity index (PDI), and particle size. The formulations displayed particle sizes appropriate for transdermal administration, with entrapment efficiencies often above 62% and particle sizes ranging from 194 to 584 nm. Further research focused on the fabrication of transdermal patches containing Itraconazole nanoparticles. The drug concentration, thickness, tensile strength, folding durability, moisture absorption, and in vitro drug release kinetics were assessed. The polymer ratios used in the development were altered. The findings suggest that these formulations have the capacity to be used in transdermal treatments for regulated and prolonged drug administration purposes.

Keywords:nanoparticles, Itraconazole, FT-IR spectroscopy and UV spectroscop

1.**Introduction:** Delivery of drug devices through topical drug delivery systems; also called as "patches," transfer a therapeutically effective and regulated dosage of medication to a patient's skin in a controlled way. Owing to its unique advantagesincluding its ability to prevent first-pass metabolism, prolong therapeutic efficacy, and facilitate drug discontinuation TDDS has garnered deliberate attention for use in systemic or local administration of API. Rate-controlling membranes, API, release liners, permeation enhancers, backing laminates, adhesives, etc. are some of the essential parts of above drug delivery system. This drug delivery system is separated into micro reservoir systems,reservoir and matrix, as a result of architectural modifications [1].

For thousands of years, people have used topical medications to treat localized medical conditions. In the current era, a plethora of topical formulations have been developed to meet these needs [2] easy pharmaceutical therapy discontinuation is just a few of its advantages. The three primary mechanisms by which pharmaceuticals enter the body are the appendageal,transcellular, and intercellular pathways. When administering medication by this method, it's crucial to take the following into account: environmental factors, physicochemical traits, age, and state of the skin [3]. any pharmaceutical formulation applied topically to release the active ingredient into the bloodstream is referred to as a "transdermal delivery system" in general. Systems for transdermal therapy were developed to provide continuous and regulated medication delivery to systemic circulation through the skin [4].

In addition, technique is used to give both hydrophilic and hydrophobic medicines. With TDDS, medications may be efficiently distributed throughout the body. Modern drug delivery techniques like transdermal patches are used topically to produce a systematic effect. The transdermal system offers a number of medical benefits over other deliveries[5].

Itraconazole, often known as ITZ, is an antifungal drug that is used to treat various fungal infections. Aspergillosis, blastomycosis, paracoccidioidomycosis, coccidioidomycosis, and histoplasmosis are among them. It can be administered intravenously or orally.Spectrumantifungal drug, itraconazol ehasan active metabolite called hydroxyl Itraconazol e. ITZ prevents the generation of ergosterol, which helpsfungusmaintain their cell membrane. Ergosterol is produced when lanosterol undergoes a 14 alpha-methylation process,which is catalyzed by a fungus termed as fungal 14 alpha-demethylase.By interfering with the substrate binding region of the fungus 14 alpha-demethylase, ITZ inhibits this reaction to occur. Anomalies in the fungal membrane cause permeability to increase, the integrity of the fungal cell membrane to be damaged, and the function of enzymes that are membrane-bound to change as a result of the decreased synthesis of ergosterol [6].

Itraconazole is a CYP3A4 substrate, and the CYP 450 system significantly metabolises the medi cation. Its half-life is between 34and42hours. Between 3and18%of the medication is eliminated in the faeces and35%in the urine.

2. Partition Coefficient: By means of the flask shake method, the partition coefficient of the drug sample is computed. The equal amount of water or phosphate buffer with a pH of 7.4 was added to aglass stoppered flask.This flask was filled with the medication (10mg), and the resultin g combination was shaken briskly. The drug is divided into two phases and separated by a separating funnel. Subtracting the overall drug quantity from the drug concentration in the aqueous phase yields the amount of API in the n-octanol phase [7].

Log P = Conc. of drug in organic phase/Conc. of drug in aqueous phase

3. DeterminationofMelting Point: Thiel’s melting point device was used to record the melting temperature of the powder after a small amount of the medication was placed into a capillary tube with one end closed to ascertain the medications' melting points. Three readings were taken, and the average was noted.

4. Fourier Transform Infrared Spectroscopy (FT-IR): The test drug was identified and the compatibility between the drug and the used polymer was evaluated using the FTIR spectrum as an analytical approach. Only the drug sample's individual peaks were compared to those of polymer and a physical drug: polymer (1:1) combination. For FTIR analysis, you can employ the potassium bromide (KBr) dispersion technique. To do this, mix floating esomeprazole polymeric microspheres with KBr and compress (hydrostatically) to form a homogeneous pellet examine the pellet with a resolution of 4 cm3 and in the 400–4000 cm^3 range [8].

5. Development of standard curve of Itraconazole

4.1 Preparation of Stock Solution: A flask, specifically a 100 ml volumetric flask, is filled with 100 milligrams of the drug. Thevolumetric flask's capacity was expanded to 100ml by adding methanol to it, which was already100mlinsize.

5.2 Preparationofsecondarystocksolution(50µgm/ml): A 100 ml volumetric flask was pipetted with 6 ml of the previously described stock solution, and the remaining methanol was used to bring the volume up to 100 ml.

5.3 Preparation of working standard solution: Aseries of diluted solutions made from the abo ve mentioned secondary stock solution were prepared in a 10-ml volumetric flask, and the remaining volume was filled with methanol. Pipette 4g/ml, 6g/ml, 8g/ml, 10g/ml, 12g/ml and 14g/ml concentrations from standard stock solution into six 10ml volumetric flasks. The volume in each flask was making up with methanol. At 261 nm, the absorbance of the aforementioned standard solution was measured, and a graph was created with the concentration and absorbance on the X and Y axes, respectively.

6. Preparationofnanosuspension

6.1 SolventDisplacementMethod: Eudragit RL100 was used in conjunction with the solvent displacement approach to manufacture Itraconazole polymeric nanoparticles. The polymer (100 mg) and Itraconazole (100 mg) were dissolved in 20 ml of acetone and methanol (3:1) to generate the organic phase. At atmospheric pressure and with moderate magnetic stirring (1000 rpm), this organic phase was added to a 40 ml aqueous medium that contained 1% polyvinyl alcohol (PVA), a hydrophilic surfactant, as a stabilizing agent. The rate of incorporation was 1 ml/min. Stirring was continued at the same pace for an additional hour after the inclusion of the organic phase. After an hour, it was sonicated for two minutes to get the required particle size.The solvents, acetone and methanol, were subsequently extracted from the colloidal dispersion by heating it to 580° under reduced pressure. The solvent to non-solvent ratio determines the concentration of the resulting mixture [9]

Table1:FormulationofItraconazolenanosuspension

INGREDIENTS	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
API(ITZ)	150	150	150	150	150	150	150	150	150
EudragitRL (100mg)	150	150	150	250	250	250	300	300	300
Acetone: Methanol(ml)	1:4	1:4	1:4	1:4	1:4	1:4	1:4	1:4	1:4
(PVA) Poly Vinyl alcohol (%)	1	2	3	1	2	3	1	2	3
Water(ml)	50	50	50	50	50	50	50	50	50

6.2 Preparation of transdermal patch with prepared nano suspension: To make transdermal patches, varying amounts of Polyvinylpyrrolidone (PVP) and HPMC were dissolved in hot water. A homogenous solution was made using a magnetic stirrer and magnetic bead. To make a

uniform suspension, the aforementioned solution was mixed with the required amount of dried Itraconazole nanoparticles and stirred for 20 minutes. Then plasticizers were added, like polyethylene glycol (PEG) in concentrations of0.5, 1%, and 2%. The concentrations of plasticizer that were used varied from 1 to 5%. In every movie, there were one percent of narcotics. The solvent casting method was used to create the patches.A specially built stainless-steel spherical assembly consisting of two plates with an interior diameter of 7.9 cm (an area of 48.99 cm^2) was treated with the solution mixture.The solvent was allowed to evaporate at 370.5° and 405% relative humidity. On top of the metallic structure, an inverted funnel was placed to prevent the solvent from evaporating too quickly. All of the patches were removed from the casting assembly using a sharp knife, and they were then put in the desiccator to dry until they were needed [10].

Table 2: CompositionforItraconazolenanosuspensionloadedtransdermalpatch

Ingredients	**1**	**2**	**3**	**4**	**5**	**6**
ITZ Nanosuspension (mg)	100	100	100	100	100	100
HPMC	75	150	300	50	100	200
PVP	75	150	300	50	100	200
PEG 400 (%)	0.5	1	2	0.5	1	2
Methanol: Water (2:1)	10	10	10	10	10	10

7. EvaluationofpreparedItraconazolenanosuspensionloadedtransdermalpatch

7.1 Scanning electron microscopy (SEM): Under as canning electron microscope, the manufa ctured, optimised Trans dermal patch with Itraconazole nanoparticles was examined for morphol ogy. Double-sided adhesive tape was used to fix the sample to the slab surface, and various magnifications of scanning electron photomicrographs were taken [11].

7.2 Particle size and polydispersibility index: The particle size analyzer Photon Correlation Spectroscopy (PCS) Delsa Nano C (Beckman CoulterCounter, USA) was employed to determine particle size and polydispersibility index. For the measurements; samples were suitably diluted with the aqueous phase of the formulation. Polystyrene cuvettes were used to store the samples and observations and were carried out at a fixed angle of165° [12].

7.3 Drug content: In 100 ml of Phosphate Buffered Saline (PBS) 7.4 buffer, 50 mg of drug-equivalent nanoparticles was distributed, and the mixture was agitated for two hours. Samples were appropriately diluted before beingexaminedat265nmina UV spectrophotometer [13].

7.4 Entrapment efficiency: Itraconazole-loaded nanoparticles' free drug concentration in the aqueous phase was assessed. The created suspension of nanoparticles was centrifuged for 45 minutes at 10,000 rpm in a high-speed cooling centrifuge. After appropriate dilutions, the supernatant was collected and subjected to UV-Visible spectrophotometer analysis at265 nm. The following equation was used to determine the drugentrapmentefficiency(EE) [14]

7.5 Thickness: Using a micrometer, the resultant films' thickness was determined. Five different spots on each film have been utilised to measure its thickness, and the mean values were determined.

7.6 Tensile strength: Using a tensiometer, the patch's tensile strength was determined. There are two load cell grips in it. The upper on ecouldbemoved, but the lower one was fixed. Betweenthes ecellgrips, 2x2cm2film strips were fastened, and force was gradually applied until the film snapped. The dial reading in kilo grammes was used to find the tensilestrength [15].

7.7 Folding endurance: This test was run to determine how brittle the prepared films were. The films were folded repeatedly in the same spot until they completely broke down. The amount of folds necessary to rupture the films was calculated [16].

7.8 Moisture uptake: The films were stored for a full day in a desiccator filled with silica gel before being weighted (Wi) using a digital balance. After that, the films were transferred to another desiccator and placed in a saturated sodium chloride solution at 25° with a 75% relative humidity until they reached a constant weight. After reaching equilibrium, the patches were weighed (Wf) [17].

7.9: MoistureContent: The patch composition was measured (Wi) and maintained at 25° in a silica gel-filled desiccator until their weight (Wd) remained constant. The moisture content was determined by using the given formula [18]:

$$\textbf{Moisture content}\% = \frac{\boldsymbol{Ws - Ed}}{\boldsymbol{Ws}} \times \mathbf{100}$$

7.10 In-vitrodissolutionstudiesandreleasekinetics: A U.S.P. dissolution test apparatus (paddle over disc type method) warmed to 37°C and agitated at a speed of 50 rpm was used to measure the drug release. The study was conducted in a washbasin environment. Using cyanoacrylate adhesive, each film was attached to a glass slide so that the medication could only be discharged from the upper face. A 7.4 pH phosphate buffer solution (900 ml) was submerged in the slide [19]. Every hour for a maximum of twenty-four hours, 5 ml aliquots of the sample were taken out using a graduated pipette and replaced with an equivalent volume of phosphate buffer. The sample was measured at 261 nm using spectrophotometry to determine the total amount of medication released throughout the course of several time intervals. Three duplicates of each sample were tested [20].

7. RESULTANDDISCUSSION

Itraconazole nanoparticles are generated using solvent displacement or Nano precipitation methods. Before the drug could be successfully included in a nano solution, several technical challenges had to be overcome.

7.1 **Preformulation study conducted on Itraconazole powder**

7.1.1 **Organoleptic properties:**The drug sample's organoleptic characteristics were noted and are displayed in the table. It was observed that the organoleptic properties of the drug comply with standards. This can be used as a preliminary identification tool for drugs.

Table 3:Organoleptic Properties of Drug

S.No.	OrganolepticProperties	Standard	Observed
1.	Appearance	Fine powder	Fine powder
2.	Odour	Odorless	Odorless
3.	Colour	Whitetoyellow	White

7.1.2 Solubility studies: ITZ's solubility in different solvents. ITZ is not particularly soluble in water. This is due to the medication molecules' predominant nonpolarity. ITZ is unable to penetrate the crystalline structure of water; hence Table below solubility data for the medication in deionized water is only 2.8 g/ml.

Table 4:SolubilityAnalysis

Sr.No.	Solvent	ExtentofSolubility
1.	Water	1µg/mlorless(insoluble)
2.	Alcohol	300µg/ml(slightlysoluble)
3.	MethyleneGlycol	239 µg/ml(wellsoluble)

7.1.3 Melting Point: Using the capillary tube method, the melting point of Itraconazole was discovered to be 162.2°C. The value in the literature citation and this value are identical.

7.1.4 Partition coefficient: Water and n-octanol were used in the partition coefficient of Itraconazole determination investigation. At pH 8.1, it was discovered that the logarithmic value of the partition coefficient (log pKa) for Itraconazole was 5.66. This suggests that the drug Itraconazole is very lipophilic.

7.1.5 Identification of drugs using FT-IR: The acquired FT-IR of the medication demonstrates the identification of distinct functional groups that were compared with the reference spectra and no significant difference was seen, confirming the purity of the powder of Itraconazole.

7.1.6 EstimationofItraconazoleasAPIbyUVSpectroscopy: Drugexhibitedabsorbancemaximaat201nm asshownbelow:

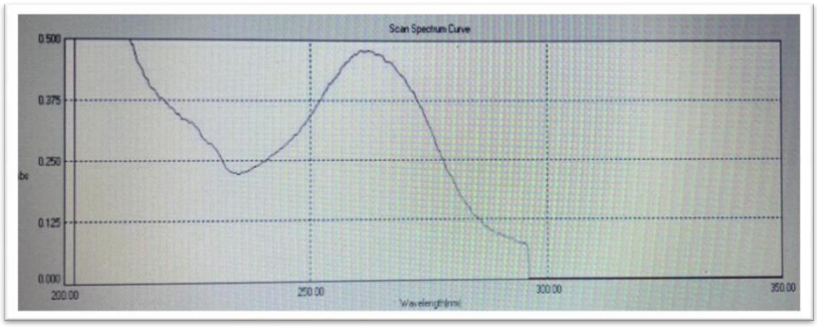


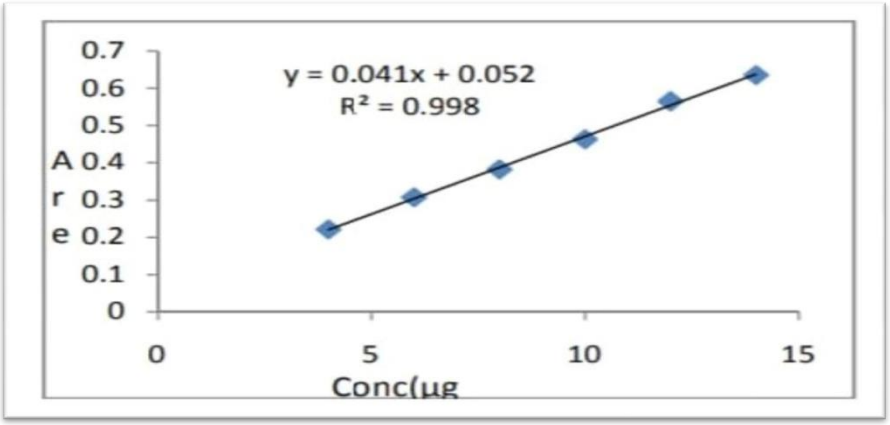
Figure1:WavelengthEstimation

7.1.7 Standard curve of Itraconazole at 261 nm: The standard curve of the drug was prepared in methanol. Beer's Lambert Law was in the concentration range of 5-20 µg/ml at 261 nm as shown below in the table. A straight line indicates compliance with Beer's Law within the working range.

Table 5:StandardcurveofItraconazole

Sr.No.	Concentration(µg/ml)	AbsorbanceMeanS.D(n=5)	PercentageC.V
1	4	0.211±0.0018	0.85
2	6	0.307±0.0022	0.74
3	8	0.382±0.0014	0.39
4	10	0.465±0.0027	0.57
5	12	0.563±0.0042	0.74
6	14	0.630±0.0058	0.92

Figure 2:CalibrationCurveofItraconazole



7.2 Characterization of nanosuspension

7.2.1 Particle size and size distribution: Table 8 and Fig. 8 display the particle size, size distribution, and entrapment effectiveness of the produced formulations, which range from F1 to F9. Each formulation had a modest mean size, making them appropriate for transdermal delivery. The poly-dispersibility index ranges from 0.227 to 0.807, while the particle size ranges from 194 to 584 nm.All of the produced formulations had drug content values in the range of 90% or above**.**

In more than half of the formulations, more than 62% of the drug was entrapped. On the other hand, in terms of drug entrapment efficiency, formulation F5 fared better than any other formulation (84.07%). The statistics appear to be consistent across all formulation batches when the drug content and drug entrapment efficiency have low standard deviation values.

Table 6: EvaluationParametersforPreparedNanoparticles

Formulation	**Average Size Particle(nm)**	**PolyDispersibilityIndex(PDI)**	**ZetaPotential (mVs)**	**Entrapment Efficiency of Drug(%)**	**Content of Drug(%)**
FTP1	351.1±0.50	0.786±0.09	19.1±1.44	70.19±4.15	95.675±0.32
FTP2	491.4±0.70	0.367±0.04	16.8±4.21	78.17±2.93	99.987±0.11
FTP3	514.3±0.22	0.745±0.01	12.3±1.33	66.12±6.12	98.546±0.45
FTP4	232.5±0.84	0.624±0.04	17.4±3.88	60.13±2.86	92.677±1.23
FTP5	184.1±0.33	0.213±0.07	16.6±3.11	89.07±3.67	98.628±0.80
FTP6	441.1±0.76	0.395±0.08	13.3±2.22	75.18±1.27	95.562±1.23
FTP7	393.6±0.66	0.501±0.05	18.0±2.67	71.13±1.81	99.774±0.44
FTP8	224.8±0.45	0.544±0.04	15.4±1.50	72.65±3.50	96.521±0.56
FTP9	302.9±0.43	0.807±0.05	15.6±2.22	69.77±4.44	84.422±0.77

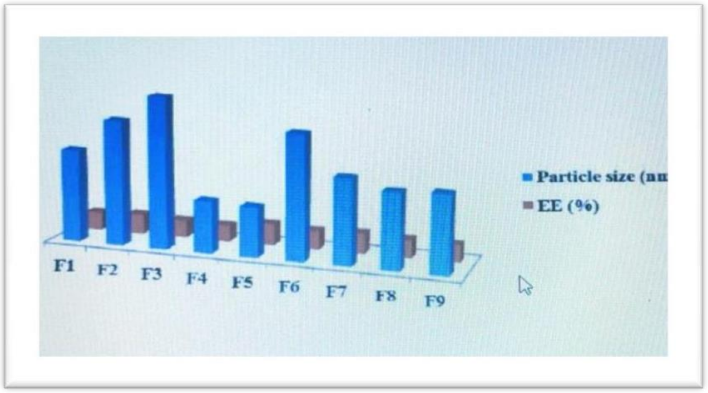


Figure 3: A graph shows the synthesized Itraconazole nanoparticles' particle size and entrapment efficiency.

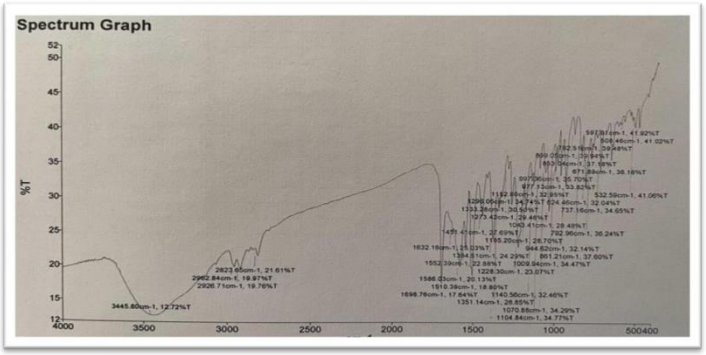
Table 9: Polydispersibility index

Sr.NO.	(PDI)VALUERANGE	INDICATION
1.	0-0.5	Monodisperse
2.	Lessthan0.7	Nearlymonodisperse
3.	Morethan 0.7	Highlypolydisperse

The drug: polymer ratio in the F5 formulation is 1:2 and includes 2% PVA. To use them in the making of a transdermal patch filled with nanoparticles, to create dry nanoparticles, the F5 nano suspension was further lyophilized. Itraconazole nanoparticle-containing transdermal patches were made by varying the ratios of HPMC and PVP.

7.2.2 Fourier-Transform Infrared Spectroscopy (FT-IR) and Differential Scanning Calorimetry (DSC).

1. Itraconazole



1.EudragitRL100+Itraconazol

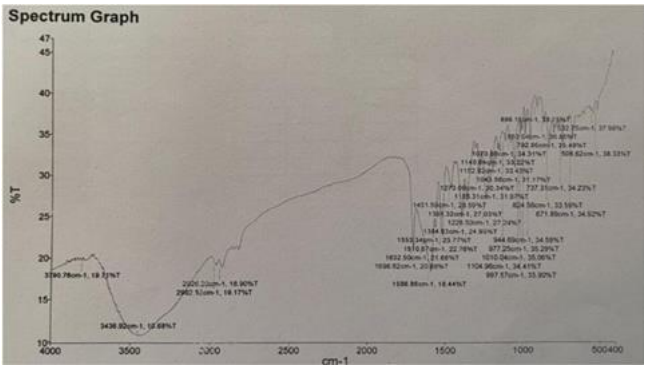


Figure 4: FT-IR Spectroscopy Studies of 1. Itraconazole 2. Eudragit RL100 + Itraconazole.

7.2.3 Differential Scanning Calorimetry (DSC): Thevalues of permeation plot regression coefficient for the best-fit equation are in the range of 0.9833 to 0.9981.

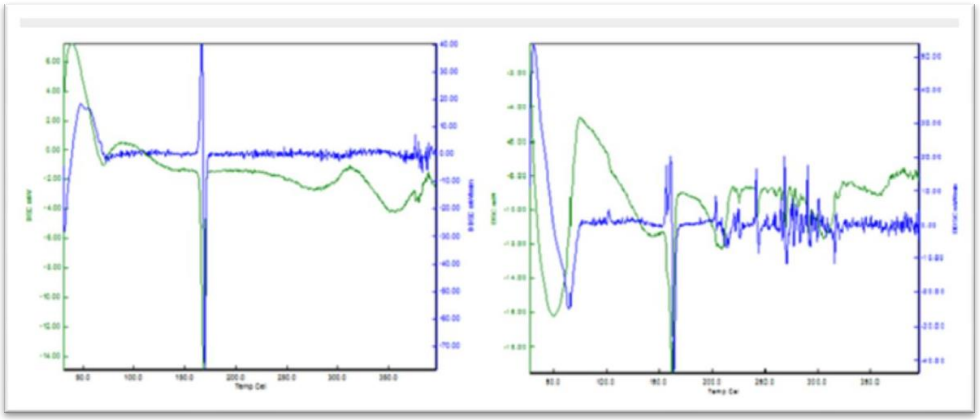


Figure 5: DSC Studies of Pure Drugs and Optimized Formulations.

7.2.4: Shape and Surface Morphology (Scanning Electron Microscopy, SEM): EM image, re vealed that in the nanoparticles embed dedtrans dermal patch, there is no effect in size or shape o f nanoparticles, indicating the acceptability of this formulation.

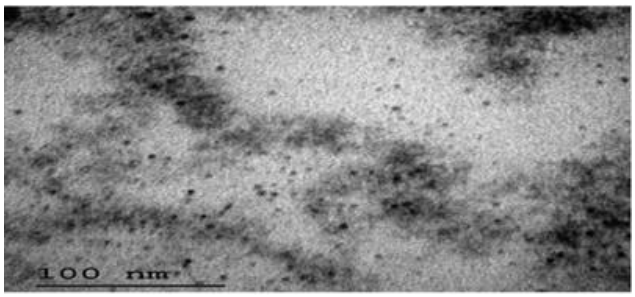


Figure 6:SEM picture of the FTP2 transdermal patch integrated with a nanoparticle loaded with Itraconazole

7.2.5 In-vitro Drug Release Study: For 12 hours, the medication was delivered biphasically and gradually from F1 to F3 when the drug to polymer ratio was 1:1 (fig. 2). It was demonstrated that as the polymer concentration around the medication rose, the percentage of drug release did not. The outcome implies that higher concentrations of polymers either have the capacity to slow down medication release or do so already. All drug release profiles showed evidence of a biphasic release, with a high release rate in the first two hours and a gradual, progressive release

rate over the course of the following twelve hours. The entrapped drug that has been adsorbed to the polymer is most likely the cause of the drug's rapid release in the first two hours. The drug: polymer ratio in the F5 formulation is 1:2 and includes 2% PVA. To use them in the creation of a transdermal patch filled with nanoparticles, to create dry nanoparticles, the F5 nanosuspension that was created was further lyophilized. Itraconazole nanoparticle-containing transdermal patches were created by varying the ratios of HPMC and PVP.

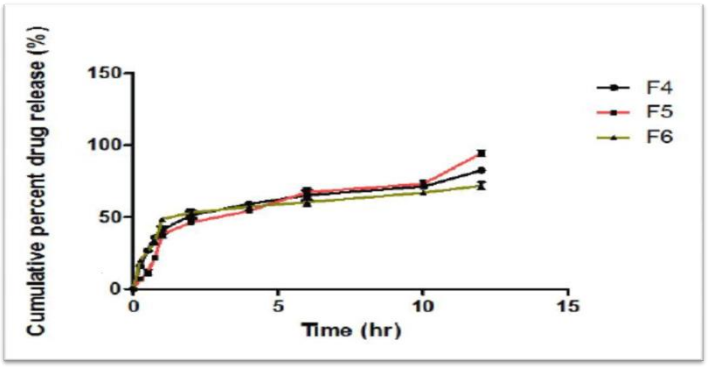


Figure7:DrugReleaseProfileofPreparedItraconazoleNanoparticles

7.3 Evaluation of prepared transdermal patches

7.3.1 Drug content: The readings for the drug content range from 93.74% to 97.22%.

Table10: DrugContent of Patches

Sr.No.	Formulationcode	Observation
1.	FTP1	**93.745±0.62**
2.	FTP2	**98.228±0.55**
3.	FTP3	**96.063±0.34**
4.	FTP4	**90.934±1.64**
5.	FTP5	**97.628±0.78**
6.	FTP6	**89.562±1.01**

7.3.2 Thickness: According to the findings, the thickness of the patch increased as the amount of polymer grew likewise. In general, the patches were uniform in thickness, ranging from 0.2140.467 to 0.2760.914 mm.

Table11: Thickness of Patches

Sr No.	Formulationcode	Observation (mm)
1.	FTP1	0.214±0.03
2.	FTP2	0.227±0.02
3.	FTP3	0.276±0.02
4.	FTP4	0.215±0.03
5.	FTP5	0.269±0.02
6.	FTP6	0.273±0.02

7.3.3 Tensile strength: Tensile strength of a patch composed of HPMC and PVP ranges from 0.932 to 1.952 kg/cm2. It was discovered that as PVP concentration and HPMC grew, the patch's tensile strength improved gradually.

Table 12: Tensile Strength of Patches

Sr.No.	Formulationcode	Observation(kg/cm$^{3)}$
1.	FTP1	0.932±0.02
2.	FTP2	1.023±0.06
3.	FTP3	1.825±0.01
4.	FTP4	1.432±0.07
5.	FTP5	1.654±0.16
6.	FTP6	1.952±0.12

7.3.4 Folding endurance: The folding endurance test is crucial for determining how well the sample can resist folding. Brittleness is indicated by this. The study's folding endurance ranged from 193 to 251 folds, which is regarded as satisfactory and indicates positive qualities in the picture.

Table13: Folding Enduranceof Patches

Sr.No.	Formulationcode	Observation
1.	FTP1	193±1.23
2.	FTP2	251±2.14
3.	FTP3	209±3.21
4.	FTP4	219±2.29
5.	FTP5	198±3.56
6.	FTP6	220±2.43

Table14: Moisture content of Patches

Sr.No.	FormulationCode	Observation
1.	FTP1	7.9±0.42
2.	FTP2	6.5±0.53
3.	FTP3	7.6±0.24
4.	FTP4	6.8±0.76
5.	FTP5	8.2±0.34
6.	FTP6	8.5±0.98

7.3.4 In-vitro drug release study: Throughout the entire FTP series (FTP1 to FTP6), the drug release was gradual, biphasic, and sluggish. The maximum amount of drug from the FTP2 batch was nevertheless released, and the drug release lasted for 12 hours. Zero-order, first-order, Higuchi, and Peppa's equation models were used to analyze the release data.

7.3.5 Moisture uptake: We measured moisture uptake values for the patches from 9.170.08 to 16.750.63%. The material is kept safe from microbial contamination and bulkiness by low moisture uptake.

Table15:Moistureabsorbance/uptake(%)of Patches

Sr.No.	Formulationcode	Observation(%)
1.	FTP1	9.17±0.08
2.	FTP2	11.22±0.98
3.	FTP3	14.21±0.24
4.	FTP4	14.25±0.08
5.	FTP5	15.34±0.45

6.	FTP6	16.75±0.63

7.3.6 Moisture content: The range of moisture content is 6.5±0.53 to 8.5±0.98%. The formulations' moisture content rose with increasing PVP concentration and HPMC grade. The compositions' reduced moisture content aids in their stability and helps them solidify into a fully dry, brittle coating.

Table 16: Values of the Correlation Coefficient (r) according to the Higuchi, Peppa's Equation Models, First Order, Zero Order, and Analysis of Release Data

KineticModels	Parameters	FTP1	FTP2	FTP3	FTP4	FTP5	FTP6
Zero Order Kinetics	**K_0**	6.98	7.884	6.787	8.98	6.432	7.256
	T_{50}	6.890	4.782	8.991	7.984	7.112	7.786
	T_{90}	11.645	12.278	17.798	13.886	13.237	12.945
	R	0.8000	0.9124	0.9769	0.9543	0.9547	0.93234
First Order Kinetics	**K_1**	0.256	0.378	0.167	0.143	0.141	0.180
	T_{50}	3.456	1.870	7.457	5.532	6.781	5.189
	T_{90}	13.56	8.208	20.450	13.900	19.176	15.765
	r	0.989	0.9666	0.9786	0.9488	0.9544	0.9322
Higuchi	**K_H**	22.404	26.732	19.032	23.232	21.734	22.567
	R	0.9234	0.9654	0.9679	0.9407	0.9612	0.9762
Korsmeyer	**K_{KP}**	36.546	36.890	35.923	31.976	32.550	30.772
Peppas	**N**	0.124	0.256	0.489	0.467	0.390	0.427
	R	0.9976	0.9832	0.9956	0.9947	0.9978	0.9932

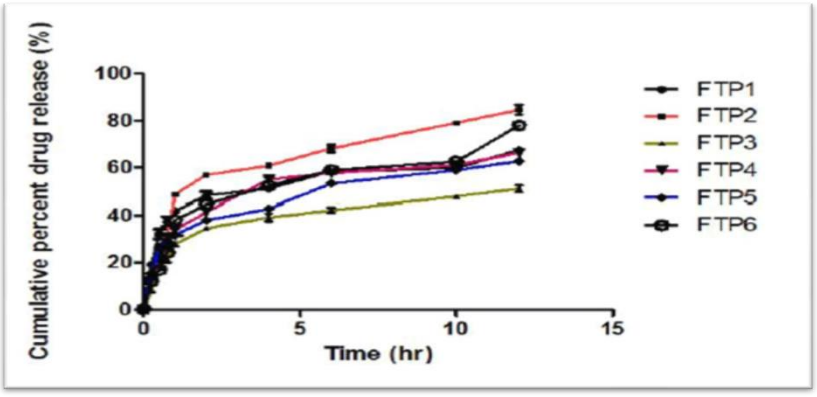


Figure 8: Drug release profiles of a nanoparticle-loaded Itraconazole transdermal patch.

CONCLUSION

Based on the findings of this study, Itraconazole is effectively incorporated into a transdermal patch loaded with nanoparticles and made up of Eudragit, HPMC, and PVP, which meet the requirements for transdermal applications, with nanoparticles and a suitable release profile that are suitable for transdermal applications. For transdermal distribution, the produced patches were sturdy and secure. As a result of this system, medication can be released in a consistent rhythm, which can reduce medication administration frequency and increase patient compliance.

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