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PAMAM DENDRIMER-BASED LULICONAZOLE GEL FORMULATION AND EFFICIENCY EVALUATIONS

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Abstract - This research is aimed at developing the PAMAM dendrimer mediated transdermal formulation of Luliconazole and explore the potential of PAMAM dendrimer as noval drug delivery to enhance the skin permeation and to avoid the serious toxic effects caused by oral and other topical formulation available.Solubility, Identification and characterization of drug of drug were carried out using various parameters like Organoleptic properties, Solubility Study of Drug, Melting Point, Partition Coefficient (Kp), Fourier Transform Infrared Spectroscopy of Drug and Drug Release Kinetics. Optimized formulation was further assessed by evaluation of gel studies along with accelerated stability study. FTIR spectrum of luliconazole confirms the presence of different groups and matched with the values as reported in official Pharmacopoeia. The melting point determined of luliconazole found to be 150-152 °C. Luliconazole was found to be soluble in methanol, Methanol, DMSO, Di-methyl formamide and Chloroform.In the solubilization studies, the effect of dendrimer concentration, pH of the solution of Luliconazole was investigated. Luliconazole with a pKa of 4.15 exhibits pH dependent solubility.It has been concluded that luliconazole was distributed with the PAMAM dendrimer and that PAMAM dendrimer may be used as a potential medication to enhance skin permeation and avoid severe toxic effects caused by the oral or other existing wording.

Keywords: Dendrimers; Formulation; Development; Luliconazole Gel; Partition Coefficient (Kp)

INTRODUCTION

In the dendrimer band, which is primarily studied in drug delivery, the PAMAM dendrimers are used to regulate functional groups in specified size, type and position. Polyamidoamines (PAMAM) are special dendritic polymers which play an essential, efficient and effective role in the provision of pharmaceutical products and increase the biopharmaceutical and pharmacokinetic effects of drugs [1, 2]. The PAMAM dendrimer is usually structurated by three basic components: a multifunctional central core in which other molecules can be trapped, central core branched units and external capping groups [3]. Drug molecules can be connected by hydrogen bonds, electrostatic interaction and hydrophobic interactions in the PAMAM cavity to peripheral groups through covalent and non-covalent connections [3, 4].

The high water solubilities, special architecture, and the high number of chemically versatile surface groups of PAMAM dendrimers are some of the benefits of supplying therapeutic agents and of increasing the bioavailability of poorly soluble products [5, 6].

The imadazole family of antifungal drugs contains luliconezole. It prevents the lanosterol demethylase enzyme in the fungal cell synthesis of ergosterol. A wide variety of trucks, including solid, semi-solid and liquid preparation are available for skin care and topical treatment of dermatological diseases. The use of clear emulgel in both cosmetics and medicinal products has grown in the main classes of semisolide preparations. For hydrophobic or water insoluble drugs, emulsion or gellified emulsion is stable and most

suited as luliconazole [7]. Emulgel is therefore particularly appropriate to patients and both emulsions and gels have their benefits. They have therefore been used recently as vehicles for different bioactivities in the skin [7, 8].

There are some drawbacks to the clinical trials testing the potency of luliconazole. The effectiveness of luliconazole was contrasted by at least one other drug, such as bifonazole, terbinafine, sertaconazole or amorolfin, explicitly in four first trials [9]. In three trials, the number of subjects involved is too limited for any conclusions to be drawn. Second, some of the experiments compared various doses (once a day luliconazole was administered with sertaconazole twice a day and application durations (a two weeks long luliconazole was applied compared to bifonazole applied for 4 weeks) [10].

The pharmaceutical industry has revolutionised transdermal pharmaceutical supply (TDD). In contrast with traditional injection and oral processes, TDDS has several benefits. It decreases strain that is usually exerted on the digestive tract and liver by an oral route and offers a regulated and constant administration of the medication [11]. It increases patient conformity and minimises the detrimental impacts of a medication induced by a temporary overdose. It is realistic, especially in patches which only take once a week.

Dendrimers have a modern impact in the development of transdermal and topical systems that offer many advantages, such as solubilization of water-insoluble drugs, prolonged and controlled release, and have been confirmed to be valuable for the delivery of a variety of drugs by transdermal and topical system [12, 13]. The best solution for resolving side-effects and increasing its effectiveness remains luliconazole with dendrimer dependent gel system.

In recent years, considerable attention has been paid to the development of PAMAM dendrimer-based effective drug delivery systems. Some experiments have examined the efficiency of dendrimers of poly (amidamine) (PAMAM) as drug carriers and the safety of transdermal drug delivery tests [14, 15]. In the present study, our goal was to develop the PAMAM dendrimer-based gel system as a suitable drug delivery system to carry luliconazole (Figure 1) and to investigate the solubility of luliconazole along with improving the therapeutic efficacy at a lower dose by reducing its undesired effect.

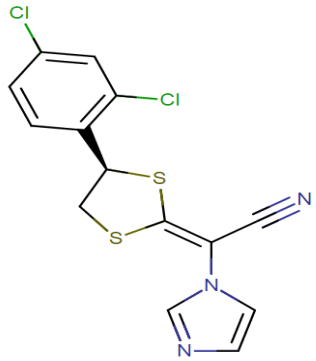


Fig. 1: Structure of Luliconazole

MATERIAL AND METHODS

Luliconazole was obtained as a gift sample from Pure Chem Pvt. Ltd, Ankleshwar, Gujarat. Carbopol 940,ethanol Liquid paraffin, Methyl parabene, propylene glycolfrom Pure Chem Pvt. Ltd. Analytical grades of the other chemical materials used were used without further chemical modifications.

Method of gel base

Dispersion processes used in varying amounts for the preparation of gels are HPMCK4M and Carbopol 940. Gels is created to distil distilled water by dispersing gelling agent. Then the blend could swell overnight. By falling wise triethanolamine, the mixture was neutralised. Then to control the viscosity, gel was applied to glycerol. Added and combined the dendrimer dispersion appropriately to this gel solution.

When a clear gel appeared, mixing proceeded. Gel were prepared and processed at 4-8°C and filled in glass bottles.

PREFORMULATION STUDIES:

Identification,Solubilityand characterization of drug sample:

Organoleptic properties
Color, smell and taste recording of the new drug using descriptive terms include organoléptic properties. Early batches colour record very useful to determine acceptable later-producing requirements. Drugs typically have traditional smells and tastes. Disagreeable masked during the synthesis later.

Solubility Study of Drug
Solubility tests of the medicinal substance were performed in various solvent forms used for further analysis. The solvent was saturated by the addition of the excess drug to the vehicles and shaking of the shaker for 48 hours at a steady vibration of 25 ± 0.5°C (REMI DGS-2). After this time, UV spectrophotometers at 295 nm have been purified, diluted and analysed. For each sample the solubility of the substance was calculated in three ways.

Melting Point
The open capillary system used to render the luliconazole melting point. Melting point determination gives idea regarding purity of the provided sample, M.P. was found to be higher or lower than the reported value then there are chances of impurity in test sample. M.P. was obtained to matching with that of official reported (At IP / BP / USP).

Partition Coefficient (Kp)
By shaking the same amount of oil and the water step in a separation funnel, the drug's partition coefficient was calculated. A 1 mg/ml solution of purified water was taken and 50 ml of this solution in a separating funnel and treated with equivalent quantities of octanol for 10 minutes and allowed 24 hours with occasional shaking. The solution was taken with a separating funnel. In order to obtain the partition coefficient values, the aqueous stage was then measured before and after division using the UV spectrophotometer.

Fourier Transform Infrared Spectroscopy of Drug
Shimadzu FT-IR spectrometer registered the infrarot spectra of pure drug. Samples were prepared and tested in the transmitting mode using the KBr disc system 2 mg assay in 100 mg of KBr). A frequency range of 4000-400 cm^{-1} was measured per wavelength. the sample IR spectra is interpreted and combined with the IR spectra comparison.

Evaluation of Luliconazole gel

Spreadability
The spreadability of the LF1-LF6 was assessed by spreading 0,5 g of gel over a 2 cm circle, which was pre-screened on a glass plate. The upper glass plate was allowed to sit on half a kilogramme of the weight for 5 minutes. The circle diameter was determined after the gel spread.

Percentage yield:
Dividing the weights of prepared dendrimer gel by the dry drug overall weight, and excipients that were applied to the individual formulation, the percentage yield was determined. Particulate size was measured using the Beckman Coulter LS 13 320 analyzer using a dynamic laser dispersion system for the optical model in the USA. Drop-in the sample cell inside the instrument the suspension was applied. The addition of suspension of sample was continued up to the obscuration rate of 3%. The graph was obtained between volume (%) versus particle diameter (μm) and calculation was done from 0.375 to 2000 μm. The data obtained was used to determine the size distribution.

Percentage yield = Practical yield × 100 / Theoretical yield

Percent entrapment efficiency:
The dendrimer gel was carefully measured and 10 mg of powder was spread into 5 ml of methanol and then the substance was removed by whirlwinds. Centrifugated (R-4C, Remi Centre, Vasai, India) for 10 minutes at 2000 to 1 minute and spectrophotomerically analysed filtrate. By following equations, percentage prescription quality and percent implantation efficacy have been estimated:

$$\% \text{ Entrapment efficiency} = (\text{Drug loading} / \text{Theoretical drug loading}) \times 100.$$

Viscosity:
Viscosity has significant role in the performance of topical products. Viscosity of formulation closely linked to the product characteristics, such as spreadability, ease of application, drug release and stability. The Brookfield viscosity (Ametek Brookfield) was calculated and the angular velocity of 5, 10, 25, 50, 100 rpm was increased and values were recorded.

The patches have been checked for the skin discomfort they can cause. Although the skin (Goat) is a critical organ by which medicine is transmitted, a primary skin irritation test was carried out. On the skin is the safest formulation (LF6). The gel was administered for 24 hours and a skin reaction was measured according to table 4 in relation to the control.

Drug Release Kinetics:
Locally modified diffusion cell is tested in vitro for the release of luciconazole loaded dendrimer gels. Dendrimer gel in vitro diffusion was carried out through one end of the 17 mm hollow tube (2.011cm^2). This was the compartment of donors. In a beaker used as a receptor compartment, 50 mL of Phosphate Buffer saline 7.4 is taken. The membrane had a known amount distributed evenly. In interaction with the receptor cabinet the donor cabinet was preserved and the temperature stayed at 37±0.5 ºC. The receptor side solutions were stirred by a thin magnetic bead and rotated continuously. The samples have been removed and replaced by 5ml of PBS at fixed intervals. Drug levels in the aliquot were measured at 427 nm with sufficient blanks for drug levels using a UV spectrometer (Lab India UV-3000+).

Diverse cinematic structures including the Korsmeyer-peppas, Higuchi plot, first order and zero order plot have been researched in the kinetics of drug release. Data from in-vitro drug release experiments have been collected in a variety of kinetic models to study releases: zero-order as the total amount of drog released versus time, first order as a cumulative percentage of medicine left versus time and Higuchi's model as the cumulative percentage of medicine released versus time as a square root.

The value of the correlation coefficient almost 1. The best fit model was verified. For the most fitting model, the data were presented.

Zero Order: The graph indicates total sum of medication released compared with time.

$$C = K0\ t \qquad \text{Eqn (1)}$$

Where K0 is the zero-order constant in concentration/time units, and t is time in hours. A graph of concentration vs. time would create a clear direction equal to K0 and the root of the axis would be intercepted.

First Order: The table indicates the total percentage of drugs left between log and time.

$$\text{Log } C = \text{Log } C0 - kt/2.303 \qquad \text{Eqn (2)}$$

Where C0 is the first drug substance, k is the first order and t is the time.

Higuchi's Model: The graph was related to the square root of time between the total percentage of drugs released.

$$Q = Kt1/2 \qquad \text{Eqn (3)}$$

Where K represents the system's configuration variables and t is the time in hours. The release rate of medicines is thus proportional to the mutual root of time.

Korsmeyer-Peppas: Dissolution data also were used to explain the drug release behaviour in polymeric systems (as a cumulative percentage of a drug released versus a log time) and exponent N was determined via the slope of the straight connection.

$$Mt / M\infty = Ktn \text{ Or } \log Mt / M\infty = \log K + n \log t \qquad \text{Eqn (4)}$$

Where, Mt /M∞ is a fractional solvent release while Mt is the amount of medication released at time t, Master is the amount of pharmaceutical products released in an infinite amount of time, t is the release time; K is a kinetically released constant property of the drug / polymer system.

If exponent n = 0.45, the Fickian Distribution Drug Releasing Process is then 0.45 < n < 0.89, the non-Fickian or pathological Dissemination is then. An exponent value of 0.89 shows the transportation Case-II or the usual zero order release.

Stability Studies

Stability tests are the collection of tests aimed at collecting knowledge about pharmaceutical stability to determine its service life and application under the unique conditions of packaging and storage.

RESULTS AND DISCUSSION:

Preformulation Study:

Identification of the Drug:

Table 1: Comparison of the Result of Organoleptic Characters of Drug Sample with the Reported Standards

S. No.	Identification test	Observed Result	Standard
1	Appearance	Powder	White to Orange to Green powder to crystal
2	Colour	Yellowish white	White solid crystal
3	Odour	Odourless	Odourless
4	Taste	Slightly acidic	Slightly acidic

Solubility Study of Drug:

The solubility test becomes a purity test only when in the individual monograph a special quantitative test is given and is an official requirement. According to USP 2009, Luliconazole is slightly soluble in ethanol and very slightly soluble in water, in dil. acids and most organic solvents. Solubility study of drug sample was studied in different types of solvent and data shows that drug was very sparingly soluble in methanol, soluble in phosphate buffer (pH-7.4) and freely soluble in rest of another solvent and insoluble in water which is shown in Table 2.

Table 2: Solubility of Drug in a Different Solvent

S. No.	Solvent	Solubility (mg/ml)
1	Methanol	10
2	DMSO	20
3	Di-methyl formamide	33
4	Chloroform	07

Melting Point: According to Indian Pharmacopoeia, a substance's melting range/time is defined as those points at which the substance coalesces and is fully melted except as otherwise defined for such substances. The melting range is defined. The drug's melting point meets the literature values published. The melting point of the drug was observed to be in the range of 150 ºC- 152 ºC with decomposition, i.e. the substance characterize as it starts to melt which is shown in Table 3.

Table 3: Comparison of the Result of the Melting Point of Drug Sample with the Reported Standards

S. No.	Identification test	Observed Result	Standard
1	Melting Point	150-152	150-154

Partition Coefficient (Kp): The permeability coefficient was found to be 3.09 which indicate that drug sample is lipophilic and come under high (value 3-4) class and results were shown in Table 4. The log P=0 implies that the compound is also water soluble and the partitioning solvent. It is worth remembering. When the compound has a log P=5, the compound in the partition solvent is 100,000 times more soluble. A logP=-2 is 100 times more hydrophilic, indicating that the compound is water soluble. Therefore, from obtained result drug have 1000 times more soluble in the partitioning solvent (octanol).

Table 4: Comparison of the Result of Partition Coefficient (Kp) Drug Sample with the Reported Standards

S. No.	Observed Value	Standard Value
1	6.22	6.34

Fourier Transform Infrared Spectroscopy of Drug:

As we know, the infrared spectroscopy mostly used for the identification of organic compound whose spectra are complex and provides numerous maxima and minima that are useful for comparison purpose. A sampler registered the powdered medication-KBr-Mixture and the spectrum by scanning with the FTIR spectrophotometer in the 4000-400 cm^{-1} wavelength region. The FTIR spectra of luliconazole were taken which is shown in Figure 2. The principal peak for IR of drug sample matched with the standard spectrum for luliconazole which is shown in Table 5.

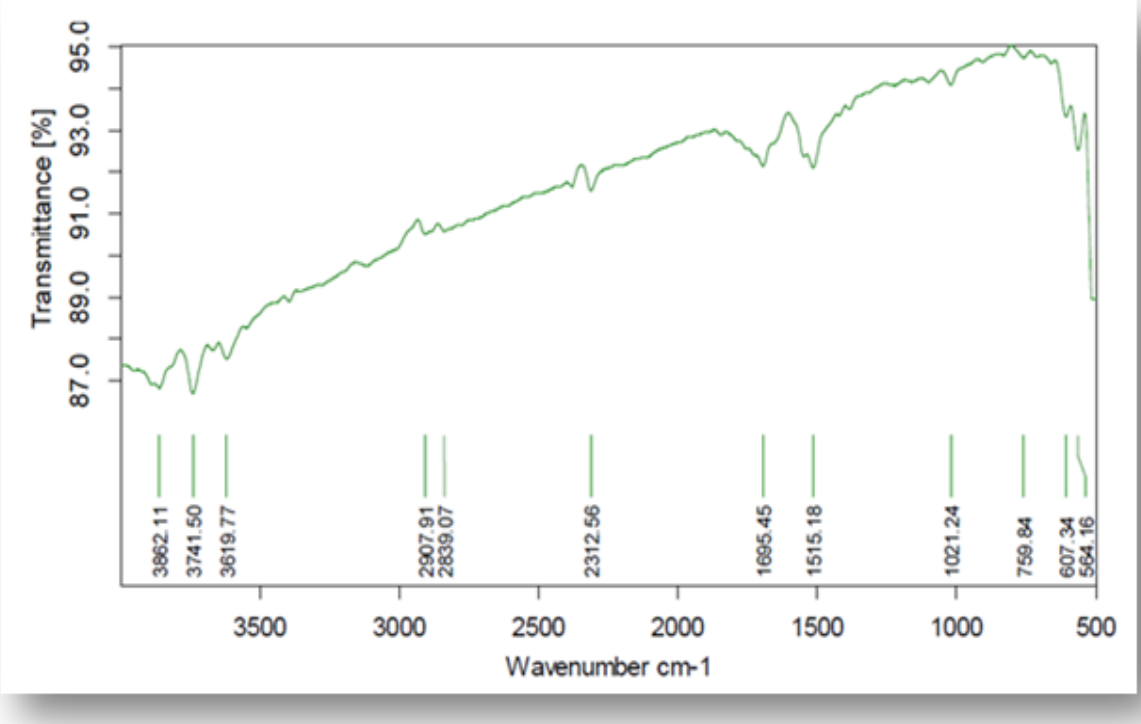


Fig. 2: FTIR Spectra of pure Luliconazole

Table 5: Interpretation of IR spectra of Drug

S. No.	Characteristic functional group	Standard Range (cm^{-1})	Observed peaks (cm^{-1})
1	-OH and –NH stretching	3650-3300	3619.77
2	Aromatic –C=C-H	3300-2700	2907.9057, 2839.0710
3	C=O stretching	1850-1680	1695.4498
4	Aromatic –C=C-	1680-1450	1515.1774
5	Aromatic-NH	1360-1250	1326
6	N-CH_3 stretching	1220-1050	1021.2430

FTIR spectrum of Luliconazole was showing characteristics peaks at 3619.77, 2907.9057, 2839.0710, 1695.4498, 1515.1774, 1326 and 1021.2430 cm^{-1} which are indicating, O-H and N-H stretching, Aromatic -C=C-H, C=O stretching, Aromatic -C=C, Aromatic NH, N-CH_3 stretching, respectively.

Formulation development and characterization

Preparation of gel:

A beaker was taken with Carbopol 940 and filtered water and allowed to swim for 24 hours. The amount of triethanolamine was neutralised with the carbopol 940. Glycerin as a damping agent and Tween 80 as an enhancer in penetration and benzyl alcohol as a conservative have been added to it with constant stirring until the same gel has been formed.

Table 6: Formulation of Gel Base

S. No.	Ingredients	Quantity
1	Carbopol 934	10 gm
2	Benzyl Alcohal	2.5 ml
3	Tween 80	3 ml
4	Glycerine	20 ml
5	Triethanolamine	5 ml
6	Water	Upto 100 ml

Table 7: Formulation Design for dendrigel

S. No.	Formulation code	Dendrimer (ml)	Drug polymer (mg)	Gel base (gm)
1	LF1	1	10	10
2	LF2	2	15	10
3	LF3	3	10	10
4	LF4	4	15	10
5	LF5	5	10	10
6	LF6	6	15	10

Evaluation of Luliconazole gel

Percentage Yield: After studying and performing the gel formulation, percentage yield was found to be 93.569%, 96.024%, 89.91%, 95.003%, 97.003% and 99.011% for formulation LF1, LF2, LF3, LF4, LF5 and LF6 respectively.

Table 8: Percentage Yield of Gel Formulations

S. No.	Formulation	Percentage yield %
1.	LF1	93.569
2.	LF2	96.024
3.	LF3	89.91
4.	LF4	95.003

5.	LF5	97.003
6.	LF6	99.011

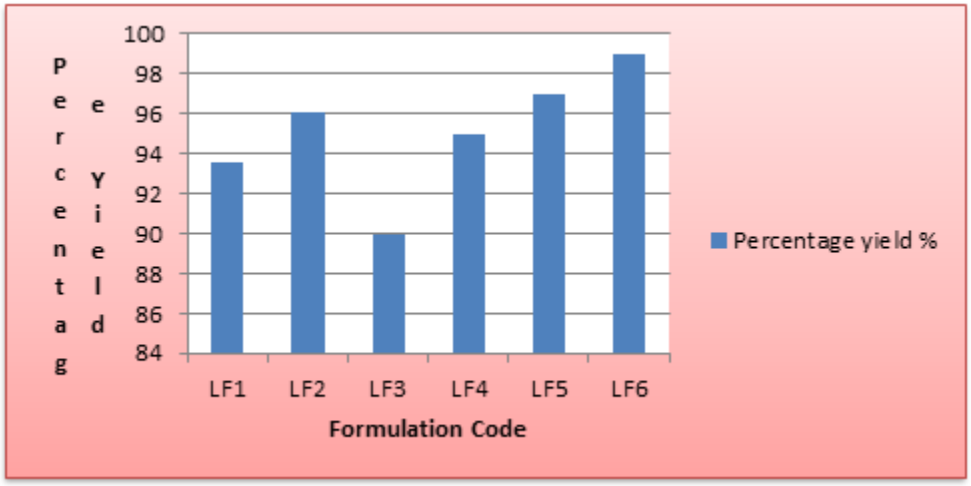


Fig. 3: Percentage Yield of Gel Formulations

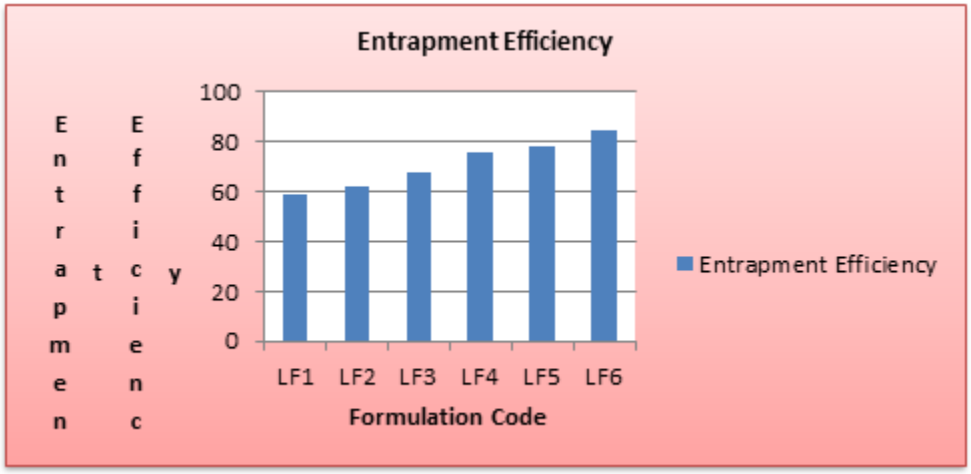
Entrapment Efficiency

In context to the experimental design, the entrapment efficiency of dendrimer gel on varying EC can be correlated to in vitro adsorption study results. An increase in entrapment efficiency was observed with increase in concentration of EC, which indicated adsorption of luliconazole on the adsorption sites on the polymeric fragments used for fabrication of dendrimer. In addition to surface adsorption, the entrapment of drug within the matrix of dendrimer gel to drug entrapment in the range of 58.9±3.4 to 84.6 ±2.3% (Table 9). The entrapment efficiency was also dependent on PVA concentration.

Table 9: Entrapment Efficiency of Gel Formulations

S. No.	Formulation	Entrapment Efficiency
1.	LF1	58.9±34
2.	LF2	62.4±13
3.	LF3	68.1±34
4.	LF4	75.9±52
5.	LF5	78.4±87
6.	LF6	84.6±2.33

Fig. 4: Entrapment Efficiency of Gel Formulations



Spreadability: Spreadability was found to be 10.45, 11.81, 10.94, 11.19, 11.04 and 11.20 for formulation LF1, LF2, LF3, LF4, LF5 and LF6 respectively. The spreadability tests performed for all formulations, with increased polymer concentration, decreased the spreadability of the gel formulations. Stretching is very significant as it shows the actions of gel in the tube.

Table 10: Spreadability Test of Gel Formulations

S. No.	Formulation	Spreadability(gm.cm^2)
1.	LF1	10.45
2.	LF2	11.81
3.	LF3	10.94
4.	LF4	11.19
5.	LF5	11.04
6.	LF6	11.20

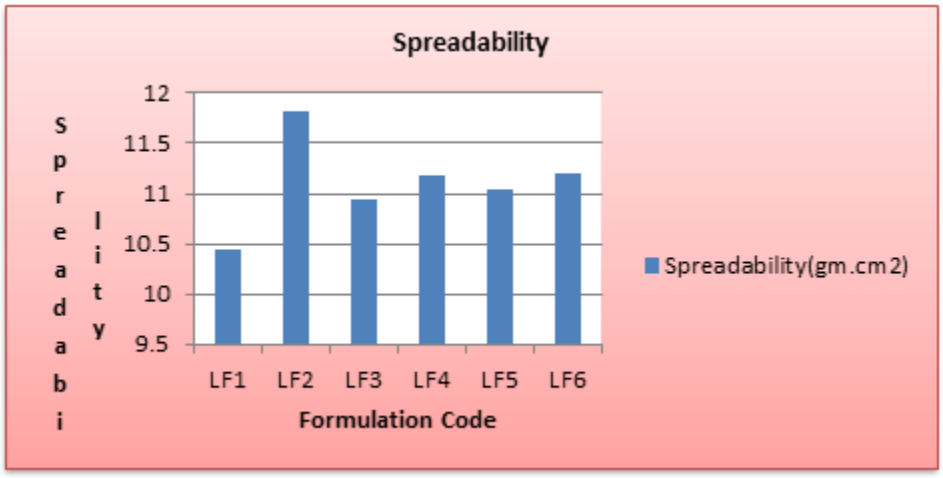


Fig. 5: Spreadability Test of Gel Formulations

Viscosity Estimation:

Viscosity plays a major role in stability of gel. For all 6 formulations viscosity is determined by Brookfield viscometer. F6 is having more viscosity compare to all formulations LF4 is having ideal viscosity was shown in Table 11.

Table 11: Measurement of the Viscosity for Formulations

S. No.	Formulation	Spreadability (gm.cm^2)
1.	LF1	24500 ± 10
2.	LF2	25120 ± 10
3.	LF3	26700 ± 10
4.	LF4	31000 ± 10
5.	LF5	34700 ± 10
6.	LF6	36100 ± 10

Skin irritation test:

The skin irritation studies showed no presence of erythema and edema after application of gel (Table 12). Thus dendrimer gel is free from significant skin irritation.

Table 12: Possible Score for Skin Irritation

Test	Skin Reaction	Score
Erythema	Very slight erythema	0
	Well defined erythema	0
	Moderate to severe erythema	0

	Severe erythema	0
Total possible erythema score		**0**
Edema	Very slight edema	0
	Well defined edema	0
	Moderate to severe edema	0
	Severe edema	0
Total possible edema score		**0**
Total score for primary skin irritation		**0**

***In-vitro* drug release**

For 12 hours, diffusion experiments were performed in the 7.4 phosphate buffer solution for the entire gel formulation. Due to the diffusion experiments, drug diffusion from formula LF6 was observed at the end of 12th hours, presented in Tables 13. The kinetics of drug diffusion profiles were found out by plotting different graphical models. Kinetic data is presented in the respective Table 14.

Table 13: *In-vitro* drug release

Time in hours		% drug permeated (µg/cm^2)*				
	LF-1	**LF-2**	**LF-3**	**LF-4**	**LF-5**	**LF-6**
0	0	0	0	0	0	0
1	5.15±0.17	5.75±0.21	5.89±0.25	6.05±0.31	5.12±0.34	6.67±0.25
2	11.34±0.34	12.03±0.93	11.94±0.45	11.42±0.78	12.06±0.34	13.23±0.56
4	19.76±0.45	19.72±0.76	20.06±0.19	19.45±1.02	20.06±0.34	21.07±0.67
6	29.56±1.15	29.89±1.45	30.67±1.98	29.89 ±1.67	29.45±1.56	31.05±0.45
7	40.78±1.56	39.87±1.56	40.56±1.34	41.89±1.21	41.10±1.98	42.75±1.76
8	51.92±1.25	50.45±1.25	48.98±1.27	50.45±1.26	51.89±1.28	52.13±1.57
9	61.34±1.24	61.67±1.25	60.12±1.25	59.47±1.25	60.98±1.28	61.95±1.28
10	70.67±1.21	70.87±1.25	70.67±1.20	69.13±1.21	70.01±1.26	72.98±1.28
11	79.45±1.27	79.97±1.25	78.87±1.21	79.14±1.24	80.54±1.26	81.41±1.27
12	87.90±1.45	86.97±1.35	88.90±1.21	88.59±1.23	89.66±1.26	90.61±1.27

*Values are mean±SD, n=3

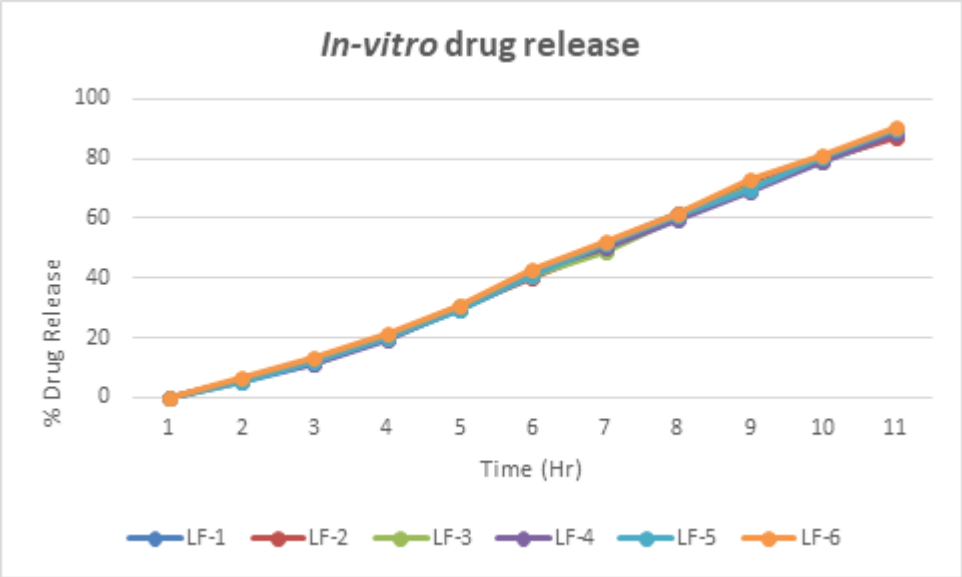


Fig. 6: *In-vitro* drug release

The *in-vitro* releases were handled with kinetic models to understand the mechanisms of drug release, and the linearity of higuchi equations was observed. The coefficient of correspondence achieved from the plot

of Higuchi was 0.9896. This shows that the drug release process was of type diffusion. The release of drugs from all formulations follows first order release and Higuchi model, as shown by higher R2 values. The diffusion mechanism was swelling and diffusion regulated after it was verified as a Higuchi model.

The Peppas model is used commonly to validate whether ficky diffusion, non-fickia diffusion or zero order is the release mechanism. The value 'n' can be used for characterising various release mechanisms. The 'n' values were found to be over 0.50 for both formulations. This then shows that diffusion leads to the mechanism for Fickian diffusion.

Table 14: Drug Release Kinetic Profile of Luliconazole Formulation LF 6 (2.5 mg/cm^2)

Time (hrs)	√ T	Log T	%Cumulative Drug Release	Log %Cum Drug Released	% Cum. Drug Retained	Log % Cum Drug Retained
0	0	0	0	0	0	0
1	1.001	0.000	12.34	1.056	89.66	1.920
2	1.294	0.094	15.15	1.160	86.58	1.920
3	1.532	0.222	19.86	1.287	83.14	1.913
4	1.930	0.288	25.32	1.440	76.38	1.857
6	2.129	0.390	32.12	1.550	68.88	1.975
8	2.718	0. 444	39.82	1.630	60.18	1.782
10	3.162	0.495	45.54	1.677	54.47	1.738
12	3.464	0.528	52.12	1.785	48.88	1.650

Table 15: Results of Model Fitting of Luliconazole dendrimer Gel

Formulation	Zero order	First order	Higuchi Matrix	Peppas plot	'n' values
LF6	0.9664	0.9986	0.9896	0.9968	0.6111

Fig. 7: Zero order

Fig. 8: First order

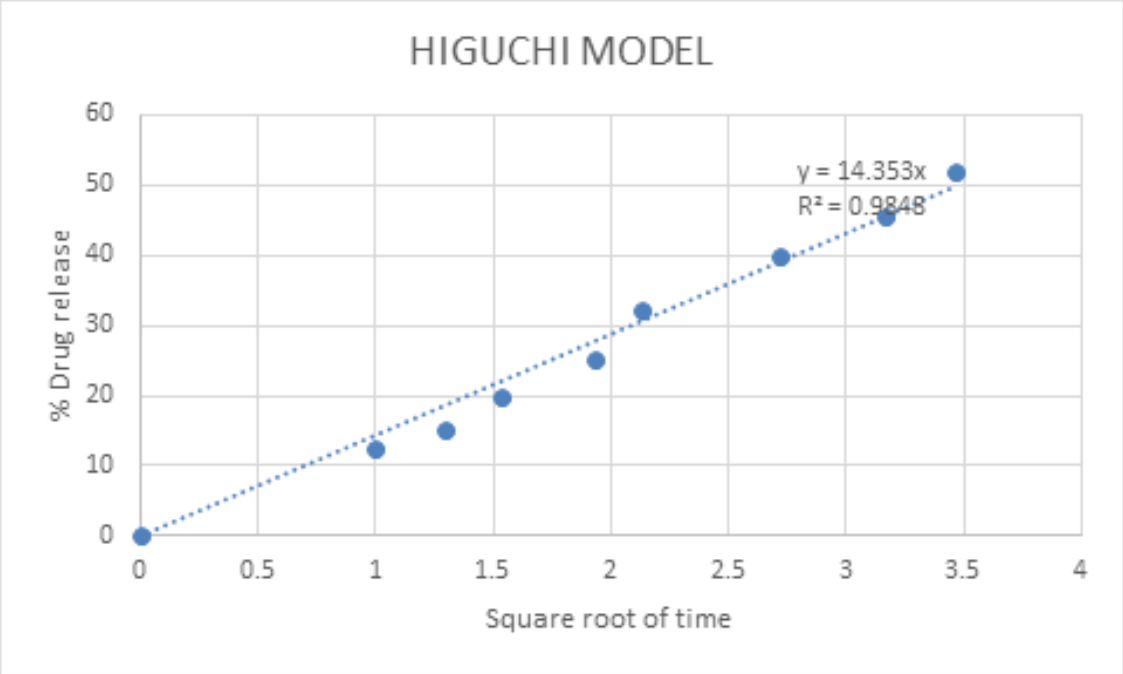


Fig. 9: Higuchi model

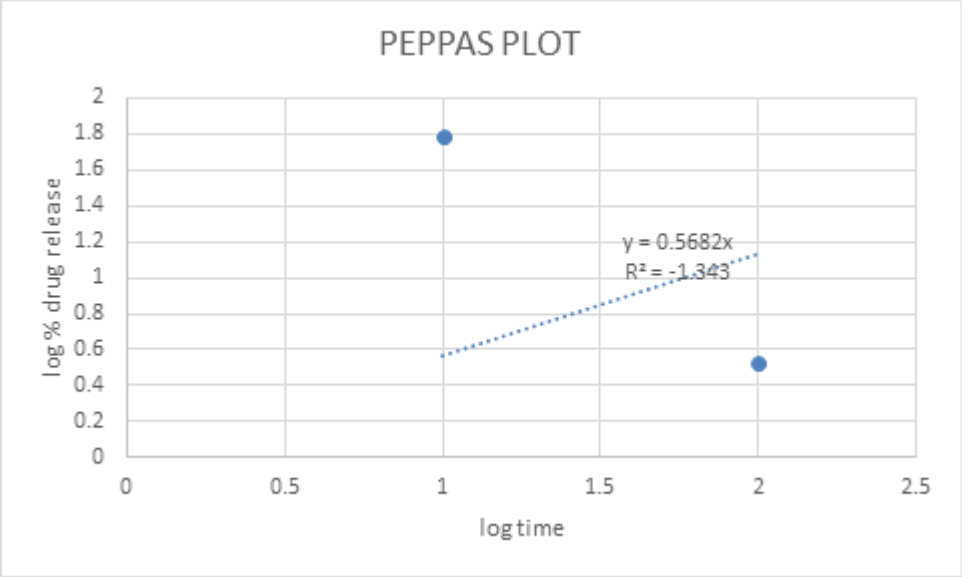


Fig. 10: Peppas plot

Stability Study:

In order to determine the amount of drug content presented in Table 16, Stability Tests for Luliconazole Loaded Dendrimer Gel were carried out. At the end of 60 days, stability tests and an approximate drug content were conducted on optimised formulation LF6. However the drug quality of the formulation LF6 did not improve significantly.

Table 16: Stability studies of Optimized LF6 formulation

Sampling Intervals in Days	Drug content 25^0C/60 % RH	Drug content 30^0C/65 % RH	Drug content 40^0C/75 % RH
0	97.67	97.67	97.67
15	98.19	98.27	98.31
45	98.16	98.12	98.49
60	98.32	98.39	98.41

CONCLUSION

It has been concluded that Luliconazole was distributed with the PAMAM dendrimer and that PAMAM dendrimer may be used as a potential medication to enhance skin permeation and avoid severe toxic effects caused by the oral or other existing wording. Dendrimers are used in the drug delivery as they have hydrophilic and hydrophilic center such that they are ideal for all forms of pharmaceuticals and display greater absorption in the medium of both hydrophils and lipophils. It induces continuous release for the low plasma half-life drug. By increasing its effectiveness, the bioavailability of the drug is improved. Cyclodextrin and micellulose are more likely to solve dendrimers as high as 5 to 10^{-7} mol / litre, while SLS and michelle will solve a concentration of8.1 to 10^{-3} mol / litre.

FTIR spectrum of Luliconazole confirms the presence of different groups and matched with the values as reported in official pharmacopoeia.

The melting point determined of Luliconazole found to be 150-152 °C. Luliconazole was found to be soluble in methanol, Methanol, DMSO, Di-methyl formamide and Chloroform.

From the above study, it can be also concluded that formulation containing more amount of dendrimer concentration provides higher flux than formulation containing lower amount of dendrimer. This may be due to an increased thermodynamics activity of the drugin dendrimic formulation at lower concentration of dendrimer.

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