WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Formulation and Evaluation of Luliconazole Emulgel

Sahil Hasan*, Saloni Bhandari, Anshu Sharma

M.Pharm. Pharmaceutics Scholar, Bhupal Nobles' College of Pharmacy, BN University, Udaipur (Raj.), 313001
Email: sahilhasan44@gmail.com

ABSTRACT

The present study was undertaken with an intention to develop a stable and effective topical formulation containing luliconazole. Luliconazole belongs to a class of drugs called Antifungals. Luliconazole exhibits highest antifungal activity against *Trichophyton spp. Candida albicans*, *Malassezia spp*., and *Aspergillus fumigatu*, which are major causative agents of dermatophytosis. However, luliconazole suffers from drawbacks such as lesser skin retention, low aqueous solubility and poor skin penetration because it comes under BCS Class II. Materials and methods: Luliconazole emulgel was prepared by hot melt emulsification technique. The formulation of emulgel includes three steps; first step is to prepare O/W emulsions in which the API is included, and then in second step the preparation of the gel base using carbopol 934 and eventually in the third step emulsion is added to the gel by constant stirring to produce an emulgel. The presence of a gelatinizing agent in the water phase converts a classical emulsion into an emulgel. This strategy is suitable to enhance the permeability of luliconazole and deliver to the target site in a controlled release system. The luliconazole emulgel was evaluated for the physical appearance, pH, spreadability, viscosity, extrudability and drug content. Result and discussions: the drug content was found to be maximum in formulation F3 with 72.21%. The results of the various evaluation tests performed for all the four formulations were close to the standard values, indicating that this method for formulating luliconazole emulgel is apt.

Key words: Luliconazole, antifungal, emulgel, BCS class II, controlled release system.

INTRODUCTION

Emulgels are the combination of gel and emulsion. Both oil-in-water (o/w) and water- in-oil (w/o) type of emulsion are used as a vehicle to deliver various drugs to the skin. Emulgels represents the dosage form having high skin permeability. The presence of the gelling agent in water phase converts a classical emulsion into an emulgel. Emulgel for dermatological use has several advantages such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, water- soluble, longer shelf life, bio-friendly, transparent and pleasing appearance. [1-3]

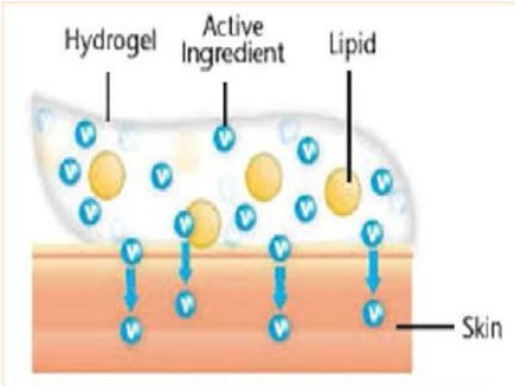

Figure 1: Emulgel Structure [4]

Formulation of Emulgel

For the preparation of emulgel some constituents are used:

- Vehicle- Comply with the ideal characteristics given in the Pharmacopeias.
- Aqueous material- The aqueous phases used is water, alcohol, etc.
- Oil- Oils used for preparation of emulsion includes mineral oils and paraffin, either alone or in combination. [5]
- Emulsifiers- Emulsifiers are used for preparation of emulsion. Classical examples are span 80, tween 80, stearic acid, sodium stearate.
- Gelling agents- Gelling agents are used to prepare gels, which enhances consistency and provides thickness to the preparation.
- Penetration enhancers- Penetration enhancers help to absorb drug to the skin. [6]

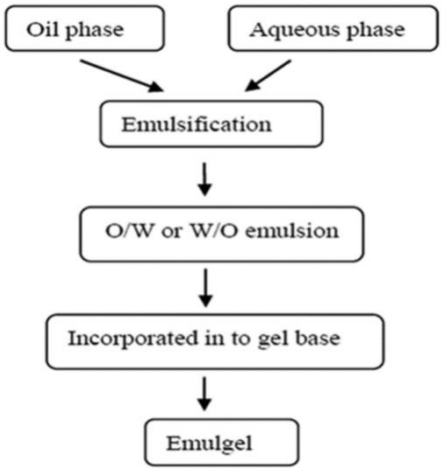

Figure 2: Preparation of Emulgel [7]

LULICONAZOLE

Luliconazole is an antifungal medication belonging to the azole class of drugs. It is used to treat *Tinea corporis* (ringworm) and *Tinea pedis* (athlete's foot). Although the exact mechanism of action against dermatophytes is unknown, but it appears to act by inhibiting synthesis of fungal enzyme cytochrome P450 'lanosterol 14-demethylase' there by preventing ergosterol synthesis leading to cell abnormalities like lack of a cell membrane. [8, 9]

MATERIALS AND METHODS

Luliconazole, methyl paraben, liquid paraffin, ethanol, carbopol 934, tween 20, propylene glycol and span 20 were obtained from the laboratory of Bhupal Nobles College of Pharmacy, Udaipur. All chemical solvents were of analytical grade and used without further purifications.

PREFORMULATION STUDIES

Melting point determination:

The melting point of the sample is done to check the purity of the sample. Melting point is defined as the temperature at which a solid substance transits its state from solid to liquid. [10]

Melting point of luliconazole was found by using the digital melting point apparatus from Remi Instrument.

Solubility analysis:

Solubility is defined as the ability of a solute to dissolve in a liquid (solvent) to form a homogeneous solution. Factors affecting solubility are; type of solvent used, temperature and pressure. [11]

Solubility analysis was primarily performed in order to find out a suitable solvent to dissolve the API, lipid and excipients used for formulation preparation.

Partition Coefficient of the Drug:

Partition coefficient is the measure of the lipophilic and hydrophilic nature of a drug substance. It is defined as the extent to which a substance is distributed between two liquid phases, one being the aqueous phase and other being the oily phase. The majorly used phases are water and n-octanol (oil phase) in the ratio 1:1. [12]

$$\mathbf{P}_{o/w} = \frac{\mathbf{C\,(n-octanol)}}{\mathbf{C\,(water)}}$$

Determination of λ_{max} of luliconazole in ethanol:

Stock solution of 100µg/ml was prepared by dissolving accurately weighed 100mg luliconazole in 100ml of ethanol. The dilution was scanned from 400–200 nm with UV spectrophotometer using the blank solution as ethanol. The spectrum of absorbance versus wavelength was recorded on UV-spectroscopy and analyzed for absorbance maximum and the highest absorbance was noted.

Calibration curve of λ_{max} of luliconazole in ethanol:

Luliconazole (100mg) was dissolved in 100ml of ethanol solution in a volumetric flask. This solution of 100µg/ml was used to prepare aliquots of varying concentration of 2-20 µg/ml respectively. Absorbance of each of the solution was measured at 296 nm in UV-spectrophotometer using ethanol solution as blank and graph of concentration versus absorbance was plotted. The slope, straight line equation and correlation coefficient were obtained from the calibration curve intercept.

PREPARATION OF LULICONAZOLE EMULGEL

Preparation of emulsion:

In this o/w emulsion, the oily phase was prepared by dissolving Span 20 in light liquid paraffin while the aqueous phase was prepared by dissolving Tween 20 in purified water. Methyl paraben was dissolved in propylene glycol whereas drug was dissolved in methanol and both solutions were mixed with the aqueous phase. Both the phases were heated separately to 70° to 80°C; then the oily phase was added to the aqueous phase with continuous

stirring until cooled to room temperature.

Preparation of gel:

The gel was prepared by dispersing Carbopol 940 in purified water with constant stirring at a moderate speed and then the pH was adjusted approximately to 6 using tri-ethanol amine. Finally, the emulgel was prepared by mixing both the gel and emulsion in 1:1 ratio.

The composition of different formulations has been discussed in Table 1:

Table1: Composition of Different Formulation Batches (%w/w)

Ingredients	F1	F2	F3	F4
Luliconazole	0.5	0.5	0.5	0.5
Carbopol 934	0.5	0.5	0.5	0.5
Liquid Paraffin	12.5	12.5	18.75	18.75
Tween 20	2.5	5	2.5	5
Span 20	2.5	3.75	2.5	3.75
Propylene Glycol	12.5	12.5	12.5	12.5
Methanol	6.25	6.25	6.25	6.25
Methyl Paraben	0.075	0.075	0.075	0.075
Purified Water	q.s.	q.s.	q.s.	q.s.

Figure 3: Prepared Carbopol Gel

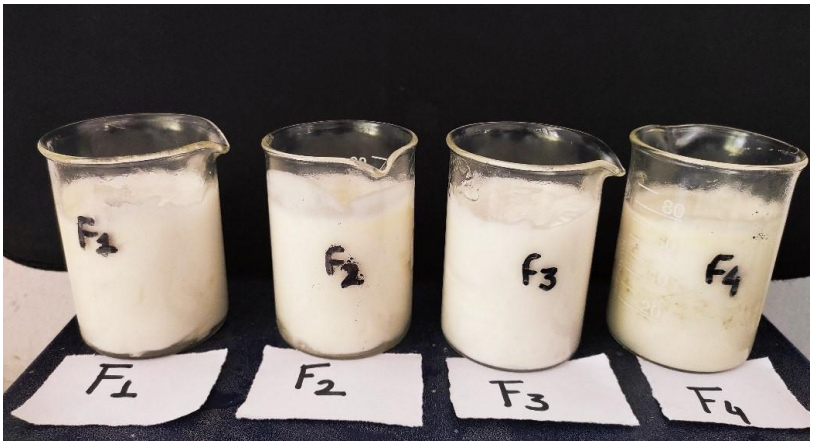

Figure 4: Prepared Luliconazole Emulgel

EVALUATION OF PREPARED LULICONAZOLE EMULGEL

Physical appearance:

The prepared gel was examined for clarity, colour, homogeneity, odour, feel upon application (greasiness, grittiness) and texture.

pH:

For pH measurements, freshly prepared solutions were kept at 25±2°C for a period of 30 min. After pH measurement, each solution was placed in a water bath and heated gradually up to 60 °C. The pH was determined using digital pH meter.

Drug Solubility: [13]

The shake-flask method was employed for the drug solubility experiment. The drug was solubilized in each solvent by stirring at room temperature. The sample solutions were filtered (0.45µm, Millipore, MA) before they attained the maximum solubility of Luliconazole in varying solvents.

Viscosity:

The viscosity of the prepared gel was carried out using a Brookfield viscometer using T-bar spindle (spindle-L4). The speed of 6 rpm was maintained for spindle rotation and the values were measured when the gel level was stabilized.

Viscosity (mPa.S) = Dial Reading x Factor

Spreadability: [14]

The spreadability of the prepared gel was determined using the following technique: 5 g emulgel was placed within a circle of 1 cm diameter pre-marked on a glass plate over which a second glass plate was placed. A weight of 500 gm was allowed to rest on the upper glass plate for 5 minutes. The increase in the diameter due to spreading of the emulgel was noted from the formula:

$$S = M. L / T$$

Where, S is the spreadability (gm.cm/sec), M is the mass placed on the pan, L is the length of the slide (cm), and T is the time (in seconds) required to move the upper slide.

Extrudability: [15]

The test was performed using a clean aluminum collapsible tube (20 g capacity) with a tip opening diameter of 1 cm. The extrudability was evaluated in by measuring the weight of gel sample ejected from the tube opening upon pressing with fingers, while holding the tube in hands.

Drug content: [16]

The drug content of the prepared emulgels was conducted by dissolving accurately weighed quantity of 1g gel in 10 ml volumetric flask and volume was made up to 10 ml with solvent. The mixture was filtered through Whatman paper No. 41. From the above solution, 5ml of the solution was further diluted into a 10 ml volumetric flask and volume was made up to mark with solvent. The drug content was estimated spectrophotometrically on a UV-VIS spectrophotometer.

RESULTS AND DISCUSSION

Identification of pure drug

Melting point determination:

Luliconazole melting point was observed to be 152^0C.

Melting point falls line with standard, thus confirms that the drug is free from impurities.

Solubility profile:

The solubility of the drug in different solution was studied and it was found that Luliconazole is very soluble in methanol, chloroform and acetone.

Table 2: Solubility of Luliconazole in Different Solution

S.No.	Solution	Solubility in (µg/ml)
1	Water	0.006
2	Phosphate Buffer	0.018
3	Ethanol	13.547
4	Acetone	15.984
5	Chloroform	19.578
6	Methanol	21.562

Partition coefficient:

The Log P of Luliconazole was found to be around 2.80, indicating that the drug is highly lipophilic in nature.

Determination of λ_{max}:

A double beam UV spectrophotometer in the range 400nm-200nm was used for quantitative elucidation of luliconazole. A plot of absorbance verses wavelength is made. The outcome is shown in Figure 5.

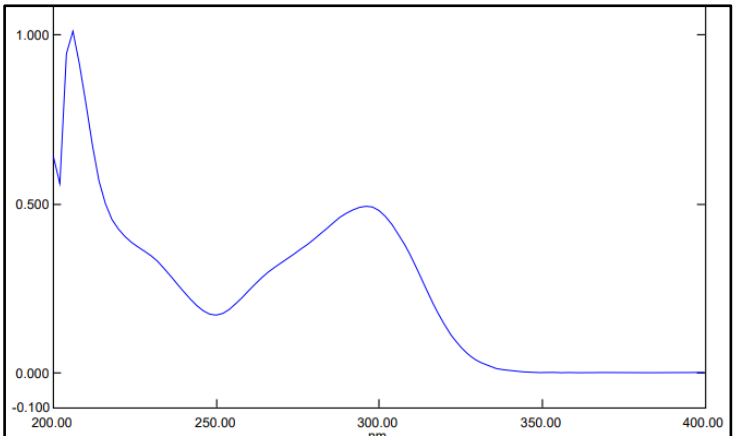

Figure 5: UV spectrum of Luliconazole

Preparation of Luliconazole UV calibration curve:

The calibration curve of luliconazole was obtained by using the 2 to 20µg/ml concentration of luliconazole in ethanol.

The absorbance was measured at 296nm. The calibration curve of luliconazole as shows in graph indicated the regression equation.

Table 3: Preparation of Luliconazole UV calibration curve (λ_{max}= 296nm)

Concentration (µg/ml)	Absorbance
2	0.120
4	0.170
6	0.249
8	0.330
10	0.380
12	0.410
14	0.514
16	0.622
18	0.746
20	0.869

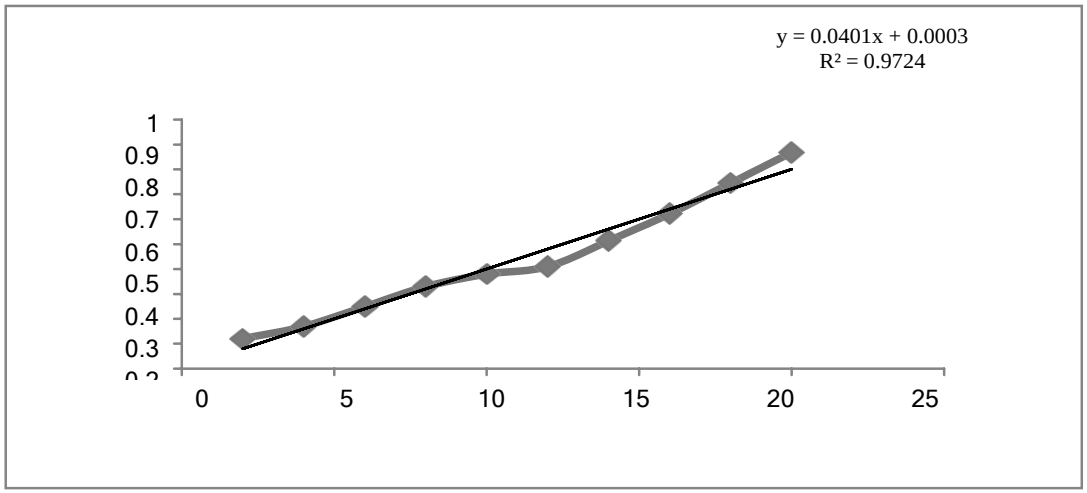

Figure 6: Calibration Curve for Luliconazole

Table 4: Result of Regression Analysis of UV Method

Statistical parameters	Results
λ_{max}	296
Regression equation (y = mx + c)	0.0401x+0.0003
Slope (m)	0.0401
Intercept (c)	0.0003
Correlation coefficient (r^2)	0.9724

EVALUATION OF LULICONZOLE EMULGEL

Physical appearance, pH, viscosity, spreadability and extrudability of the prepared gel:

All the prepared formulations were homogenous in appearance and smooth in texture and none of the formulation displayed any sort of phase separation. The pH of all was found to be in range of 5.5-6.5, which suit the skin pH indicating the skin compatibility.

Table 5: Physical Appearance, pH, Viscosity, Spreadability and Extrudability of the Prepared Emulgel

Formulation	Appearance	Phase Separation	pH	Viscosity (mPa.S)	Extrudability (gm)	Spreadability (gm.cm/sec)
F1	White, Homogenous	None	5.9±0.5	32000±0.54	5.4 ± 0.11	20.01±2
F2	White, Homogenous	None	6.1±0.5	25000±0.98	6.8 ± 0.21	22.40±2
F3	White, Homogenous	None	6.3±0.5	39000±0.65	9.0 ± 0.15	28.31±2
F4	White, Homogenous	None	5.8±0.5	26000±0.75	4.4 ± 0.3	23.26±2

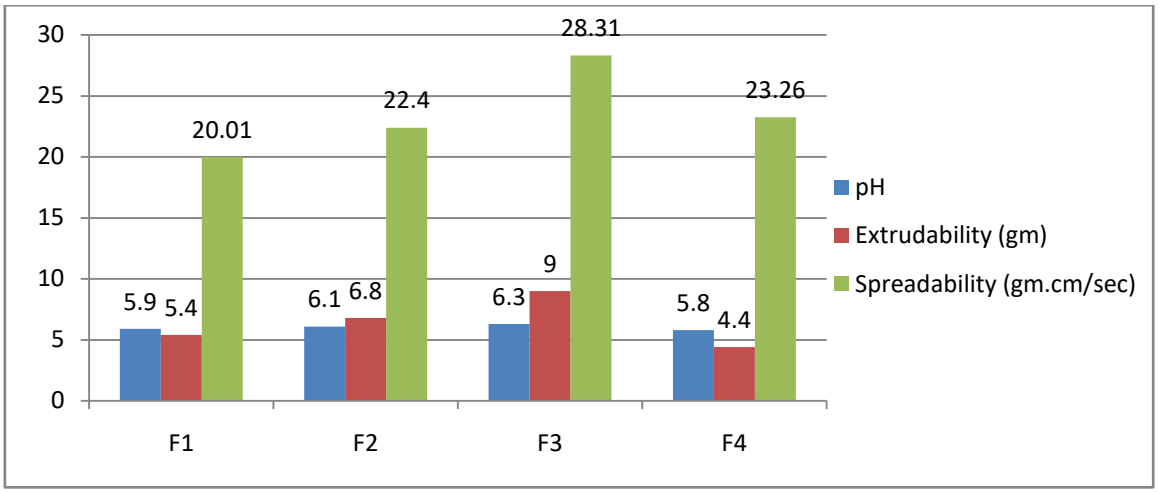

Figure 7: pH, Extrudability and Spreadability of the Prepared Emulgel

Drug Content:

The drug content of different emulgel formulations (F1, F2, F3, and F4) was estimated by using UV Spectrophotometer. The release of drug through prepared formulation was found to be 60.82%, 62.55%, 72.21% and 67.98% respectively and the result were F3>F4>F2>F1 respectively. The % drug content of all the formulations was found to be satisfactory. Therefore, the method adopted for emulgel formulations was found to be suitable. Results have been discussed in Table 6.

Table 6: %Drug content of Luliconazole Topical Emulgel

S. No.	Formulation Code	Drug Content (%)
1.	F1	60.82
2.	F2	62.55
3.	F3	72.21
4.	F4	67.98

SUMMARY AND CONCLUSION

The main goal of the study was to formulate an antifungal luliconazole emulgel for topical route of administration to treat patients suffering from Candida albicans, Malassezia spp., and Aspergillus Luliconazole has been concluded to be a drug of BCS Class II (low soluble and high permeable drug).

The present work focused on preparing luliconazole emulgel by employing varied concentrations of methanol, propylene glycol, liquid paraffin, span and tween to form an appropriate formulation. The prepared emulsions were loaded into the hydrogel made up of Carbopol 934 in order to get the required emulgel.

As resulted all the preparations, F1-F4 was found to be suitable in all preparations and formulation F3 was most stable. All the formulations were stored at room temperature 25-35°C and then observed for 1 month. Stored formulations were observed for phase separation and related substances (bacterial growth). None of the formulation showed phase separation and bacterial growth.

The % drug release studies revealed that formulation F3 showed the maximum amount of drug release within five hours. Hence, from all the preparations prepared, F3 was chosen to be the best one.

According to the findings, it can be concluded that that luliconazole emulgel can prove to be an effective and more efficient system for topical fungal treatment as compared to the traditional luliconazole systems that are commercially available.

ACKNOWLEDGEMENT

The authors would like to sincerely thank to Dr. Kamal Singh Rathore, BN College of Pharmacy, Udaipur, and all the staff of the college for their valuable support.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ABBREVATIONS

API: Active Pharmaceutical Ingredient; BCS: Biopharmaceutical Classification System; USFDA: United States Food and Drug Administration.

REFERENCES

1. Kullar R, Saini S, Steth N, Rana AC. Emulgel a surrogate approach for topical used hydrophobic drugs. Int J Pharm Biol Sci 2011; 1:117-28.
2. Single V, Saini S, Joshi B, Rana AC. Emulgel: a new platform for topical drug delivery. Int J Pharm Biol Sci 2012; 3:485-98.
3. Hasan S, Bhandari S, Sharma A, Garg P. Emulgel: A Review. Asian Journal of Pharmaceutical Research. 2021; 11(4): 263-268. Doi: 10.52711/2231-5691.2021.00047
4. K.P. Mohammade Haneef, Sherry Easo, P.V. Hafsa, Guru Prasad Mohanta, Chandini Nayar. Emulgel: An Advanced Review. Journal of Pharmaceutical Science and Research, 2013; 5(12), 254-258.
5. Pant S, Badola A, Baluni S, Pant W. A review on emulgel novel approach for topical drug delivery system. World Journal of Pharmacy and Pharmaceutical Sciences, 2015; 4: 1728-1743.
6. Mortazavi SA, Aboofazeli R. An Investigation into the Effect of Various Penetration Enhancers on Percutaneous Absorption of Piroxicam. Iranian Journal of Pharmaceutical Research, 2003; 135-140.
7. Shingade GM. Review on: recent trend on transdermal drug delivery system. Journal of drug delivery and therapeutics. 2012; 2(1).
8. Luliconazole - Drug Summary PDR. https://www.pdr.net/drug-summary/Luzu- luliconazole-3401
9. Luliconazole FDA label [File] https://s3-us-west-2.amazonaws.com/drugbank/cite_this/attachments/files/000/001/441/original/Luliconazole_F DA_label.pdf?1536357038
10. Giani S, Towers NM. Compliance with amended General Chapter USP<741> Melting Range or Temperature.
11. Savjani KT, Gajjar AK, Savjani JK. Drug Solubility: Importance and Enhancement Techniques. International Scholarly Research Notices. 2012.
12. Bodor N, Gabanyi Z, Wong CK. A New Method for the Estimation of Partition Coefficient. Journal of the American Chemical Society. 1989 May; 111(11):3783-6.
13. Savjani KT, Gajjar AK, Savjani JK. Drug solubility: importance and enhancement techniques. International Scholarly Research Notices. 2012.
14. Howard CA, Loyd V, Allen JR, Nicholns GP. In: Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems 8th Ed. Lippincott Williams and Wilkins; 2005.
15. Shahin S, Hamed S, Hatim S. Alkhatib HS. Effect of Formulation Variables on the Physical Properties and Stability of Dead Sea Mud Masks. Journal of Cosmetic Science. 2015.
16. Monica R, Girish S, Sheetal A, Manmeet K. Optimization of Metronidazole Emulgel: A Conceptual framework. Journal of pharmaceutics; 2012.