FORMULATION AND EVALUATION OF TOPICAL ANTIFUNGAL GEL OF LULICONAZOLE

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ABSTRACT

The goal of this study was to create a luliconazole antifungal gel utilizing neem oil, tulsi oil, cinnamon oil and aloevera gel to treat fungal infections. Essential oils are utilized as an antifungal and antibacterial agent, and aloevera is used as a gelling agent . Prior to the formation of a gel, medication preformulation tests were conducted. " Cold Mechanical Method '' were performed to obtained a desire antifungal gel created by different polymer ratio and using essential oils.By altering the polymer ratio, gel were created. F1, F2, F3, F4, F5 and F6 were among the gel compositions created. Then, several evaluation characteristics such as spreadability, viscosity, pH,swelling index, percentage yield, and drug content were used to determine the gel. The topical antifungal gel of luliconazole was successfully prepared utilizing neem oil, tulsi oil, cinnamon oil, and aloe vera as the gelling agent. As a result, it was established that essential oils and aloe vera gel were employed in the formulation, and excipients were chosen to ensure that the gel was compatible with luliconazole and could be used to treat a variety of conditions. By enhancing its activity as it shows synergistic effect and reduces the side effects of the drugs. The best-fitting formulation (F3) was chosen among the six batches since it meets all the requirements .

Keywords – Luliconazole, materials and methods, evaluation parameters, limitations, discussion, conclusion.

INTRODUCTION

Topical drugs are administered to the skin for effects on the surface, localized, or systemic. Fungus is responsible for a variety of skin illnesses. Nowadays, fungus infection is one of the most common skin concerns. For the topical treatment of skin disease, a variety of solid, semisolid, and liquid preparations are available. A wide range of products are used to apply to the skin. Topical and dermatological products are two types of medicinal products [3]. The aim of the study is to formulate and evaluate a antifungal gel of luliconazole containing Aloevera gel as a gelling agent, Neem oil, Cinnamon oil and Tulsi oil are also used . These essential oils possess antifungal properties. Cinnamon oil is extracted from the Cinnamomum zeylanicum Blume plant's bark (Lauraceae). The oil has carminative, stimulating, aromatic, germicidal, and fungicidal properties . Neem oil is used to cure skin and scalp infections caused by fungus or bacteria. It's used to heal wounds and reduce the appearance of warts and moles. Tulsi oil is used to treat wound healing, fungal infections .Various evaluation parameters of the gel are also studied .

Luliconazole

Luliconazole belongs to the azole class of antifungal medicines. It acts by inhibiting the growth of infection-causing fungus.

Luliconazole is used to treat tinea pedis (athlete's foot; a fungal infection of the skin on the feet and between the toes) and tinea corporis (ringworm; a fungal skin infection caused by dermatophytes such as Trichophyton rubrum

and Epidermophyton floccosum that causes a red scaly rash on various parts of the body)[8].

It is a topical antifungal medication that was first introduced in Japan in 2005. They have antifungal action against dermatophytes across a broad spectrum [9].

MATERIALS AND METHODS

MATERIALS: The ingredients for the mixture were purchased from commercial sources. All of the compounds were analytical grade and were utilized without being purified or modified in any way.

TABLE 1: CHEMICALS NAME USED

S.NO	CHEMICALS	ROLE	MANUFACTURER
1	Luliconazole	As an antifungal drug	NASANT Pharma , Dehradun
2	Hydroxy Propyl Methyl Cellulose (HPMC)	Hydrophilic polymer	LOBA CHEME Pvt. Ltd, India
3	Carbopol	As a gelling agent	LOBA CHEME Pvt. Ltd, India
4	Triethanolamine	As a pH buffer	LOBA CHEME Pvt. Ltd, India
5	Glycerine	Moistening agent	LOBA CHEME Pvt.Ltd, India
6	Methyl Paraben	As a preservative	RFCL Ltd
7	Aloe vera	As a gelling agent	
8	Tulsi oil	Antifungal agent	BIOSUR PHARMA
9	Neem oil	Antifungal & antibacterial agent	BIOSUR PHARMA
10	Cinnamon oil	Antibacterial agent	BIOSUR PHARMA
11	Alcohol		LOBA CHEME Pvt.Ltd, India

METHOD OF PREPARATION OF ALOE VERA GEL FROM ALOE VERA PLANT

Aloe vera leaves were collected from a nearby farm. Aloe vera leaves were harvested from the plants. The leaves were then washed in distilled water before being surface sterilized with 70 percent ethanol. The gel was drained out when the parenchymatous coating of the leaves was peeled away. The gel was then placed in a tightly sealed container.

METHOD OF PREPARATION OF GEL

Gel formulation were prepared by a cold mechanical method. 0.1gm of luliconazole drug was dissolved in 15ml of glycerin with the aid of mild heat (phase A) . Weighed quantity of HPMC and Carbopol was dissolved in 50ml of distilled water with constant stirring by using lab stirrer so that there was no formulation of lumps in the dispersion then add methyl paraben , aloe vera gel , ethanol in it (phase B).

Then phase A solution was added into the phase B solution and mixed thoroughly with constant stirring and homogenous dispersion was obtained. Drop wise triethanolamine solution was added in it up to gel get formed. Finally the required quanitity of Neem Oil, Tulsi Oil and Cinnamon Oil was added at room temperature.

Luliconazole gel were prepared by using different essential oils.

TABLE 2: FORMULATION CODE FOR GEL PREPARATION:

Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Luliconazole	2	2	2	2	2	2
Carbopol	0.2	-	0.3	0.5	0.5	-
HPMC	0.3	0.3	-	0.5	-	0.7
Methyl paraben	0.3	0.3	0.3	0.3	0.3	0.3
Glycerine	15	15	15	15	15	15
Alcohol	3	3	3	3	3	3
Triethanolamine	4	4	4	4	4	4
Aloe vera gel	5	5	5	5	5	5
Neem oil	0.5	-	-	1.0	1.0	1.0
Tulsi oil	-	0.5	-	1.0	-	1.0
Cinnamon oil	-	-	0.5	1.0	1.0	-
Water	50	50	50	50	50	50

RESULTS

1. MORPHOLOGY: The drug sample of luliconazole was determined by organolepticproperties.

TABLE 1.1 : ORGANOLEPTIC PROPERTIES

S.No	**Organoleptic property**	**Observed Result**
1	**Colour**	**Slightly yellow**

2	**Odour**	**Odourless**
3	**Taste**	**Tasteless**

2. SOLUBILITY PROFILE OF LULICONAZOLE

TABLE 2.1: SOLUBILITY PROFILE

S.NO	**SOLVENTS**	**SOLUBILITY**
1	Distilled water	Very slightly soluble
2	Ethanol	Slightly soluble
3	Methanol	Very springly soluble

Report : From the solubility study we observed that luliconazole is slightly soluble in ethanol and very springle soluble in methanol and distilled water.

3. MELTING POINT:

TABLE 3.1: MELTING POINT

S.NO	**MELTING POINT (°C)**	**AVERAGE**
1	150°C	150.3°C
2	151°C	
3	150°C	

Report : The observed melting point of the API was recorded at 150.3ºC . The observed range of melting point of luliconazole drug was 150°- 151°C .

4. PARTITION COEFFFICIENT

TABLE 4.1 : PARTITION COEFFICIENT

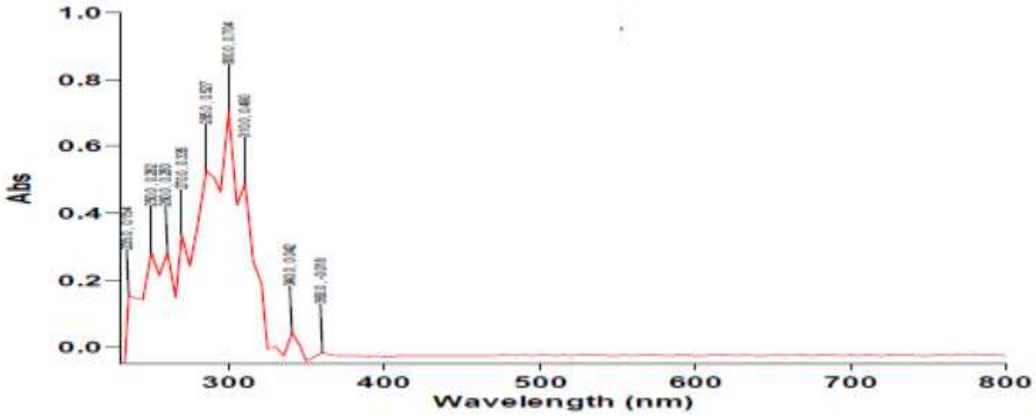
S.No.	**Observed Value**	**Standard Value**
1	3.12	6.22

Report : The partition coefficient was found to be 3.1 which represented the drug sample was lipophilic because it come across near 3 -4 class results was shown in the Table 4.1 .

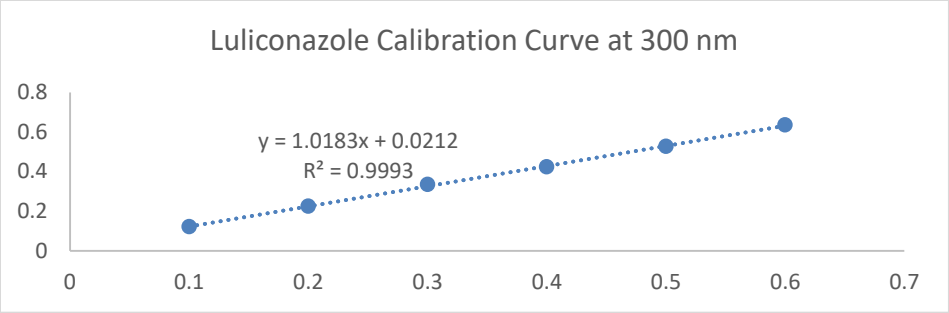
5. UV ANALYSIS:

TABLE 5.1: UV CURVE

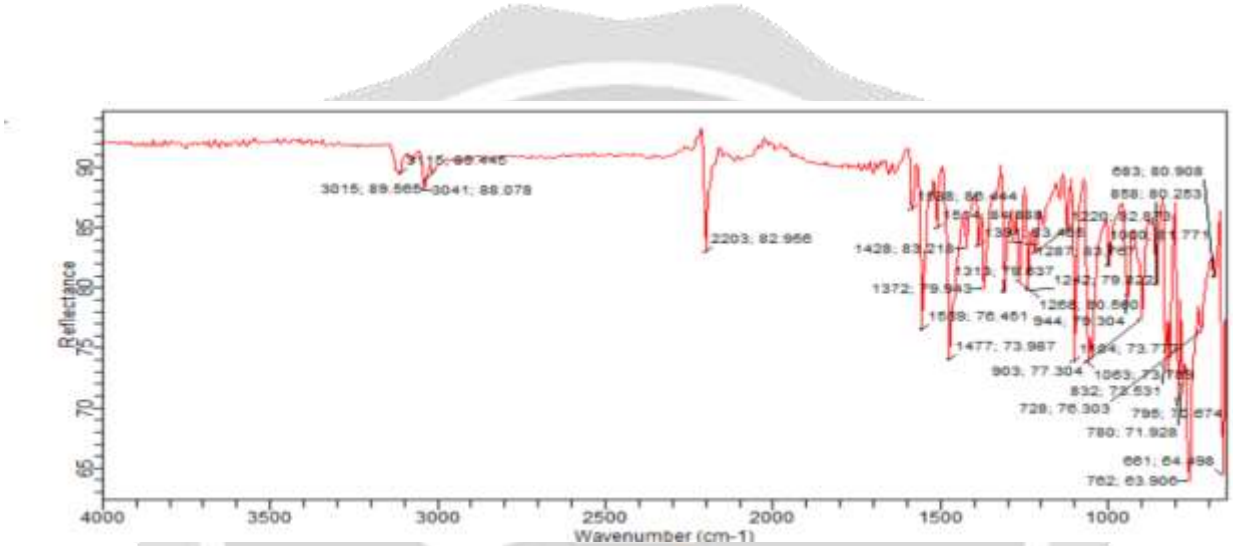
S.NO	**CONCENTRATION (µg/ml)**	**ABSORBANCE (Λ_{max} 300)**
1	0.1	0.1214
2	0.2	0.2243
3	0.3	0.3348
4	0.4	0.4234
5	0.5	0.5265



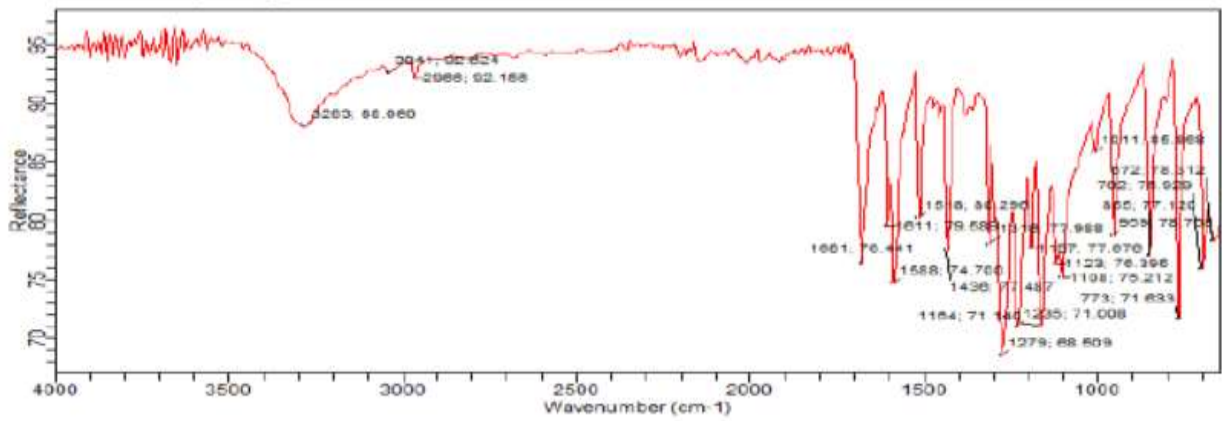
Absorption curve of luliconazole



6. FT –IR SPECTRA



FT- IR spectra of luliconazole



FT-IR spectra of physical mixture of luliconazole, HPMC, Carbopol and methyl paraben.

6. pH OF GEL FORMULATION

TABLE 6.1 : pH OF GEL FORMULATIONS

Formulation	**pH**
F1	4.43
F2	4.44
F3	4.49
F4	4.62
F5	6.71
F6	4.41

Report: Various formulation of gel were prepared and determined their pH . F5 have highest pH value in comparison to other formulations. Mainly the pH range of all the formulations are near 4.62. So it was considered non- irritant and best for application.

7 . VISCOSITY OF GEL FORMULATIONS

TABLE 7.1 : VISCOSITY OF GEL FORMULATIONS

Formulation Code	**Spindle No.**	**RPM**	**Viscosity Centipose**
F1	64	10	3675
F2	64	10	2807
F3	64	10	3715
F4	64	10	3845
F5	64	10	3766
F6	64	10	4475

Report : All 6 formulations (F1, F2, F3, F4, F5,F6) viscosity were determined by Brookfield Viscometer .The values of viscosity ranged from 2807 to 4475. F2 has lower viscosity i.e 2807 in compare to other formulations. F6 have highest viscosity compare to other formulations. Viscosity of gel increase with increasing the concentration of polymers.F3 having ideal viscosity shown in table.

8. SPREADABILITY OF GEL FORMULATIONS

TABLE 8.1 : SPREADABILITY OF GEL FORMULATIONS

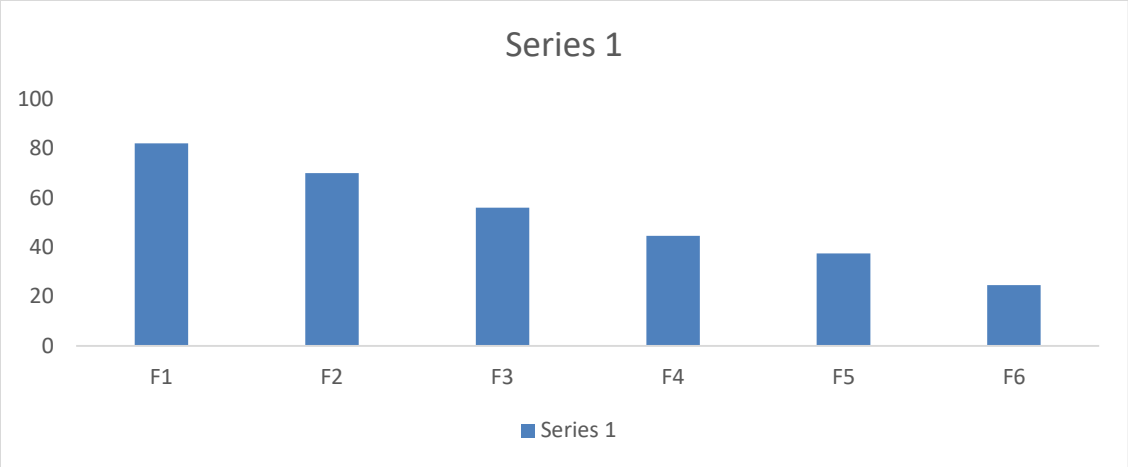
Formulation	**R1**	**R2**
F1	1	3
F2	1.2	4
F3	1.4	4.2
F4	1	4.3
F5	1.6	3.5
F6	2	4.6

Report : Spreadability of various formulations (F1, F2, F3, F4, F5, F6) were determined i.e. 3, 4, 4.2, 4.3, 3.5 and 4.6 . The Spreadability test were performed for all formulations with increase in polymer concentration then increased the spreadability value of the gel formulations. F6 have greater Spreadability in compare to other formulations.

9. SWELLING INDEX OF GEL FORMULATIONS

TABLE 9.1 : SWELLING INDEX OF GEL FORMULATIONS

Formulation Code	**Initial volume**	**Final volume**	**Result**
F1	10	18	82
F2	20	30	70
F3	30	44	56
F4	40	55.4	44.6
F5	50	62.5	37.5
F6	60	75.4	24.6



Swelling index of Gel formulation

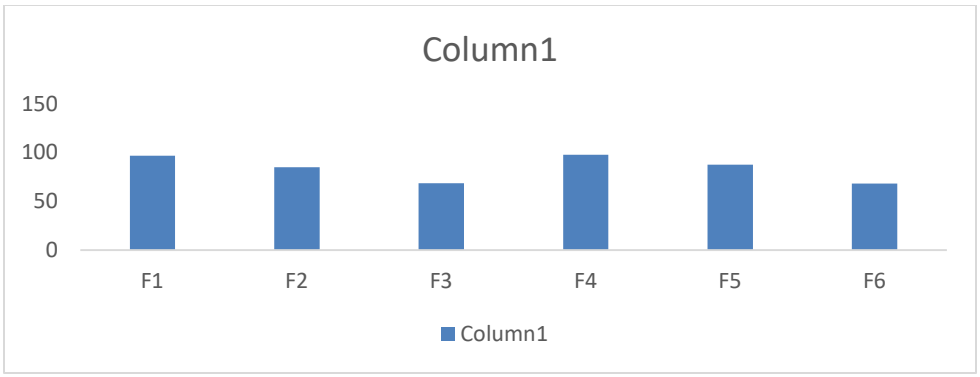
Report : After performing all formulation of gel . The swelling index of a gel was found to be 82, 70, 56, 44.6, 37.5, 24.6 of all formulations F1, F2, F3, F4, F5, F6. Hence decreasing the swelling index of a gel from F1 to F6 formulations. F6 have low swelling index in comparison to others formulation.

10. PERCENTAGE YIELD OF GEL FORMULATIONS

TABLE 10.1 : PERCENTAGE YILED OF GEL FORMULATIONS

Formulation Code	**Percentage yield**
F1	97%
F2	85.1%
F3	68.5%
F4	97.7%
F5	87.5%
F6	68.4%

Report : After preparation of the various formulation of gel (F1, F2, F3, F4, F5, F6) . The percentage yield found to be 97 %, 85.1% , 68.5% , 97.7% , 87.5% and 68.4% . The F4 have higher percentage yield in comparison to other formulations and F6 have least percentage yield i.e. 68.4.

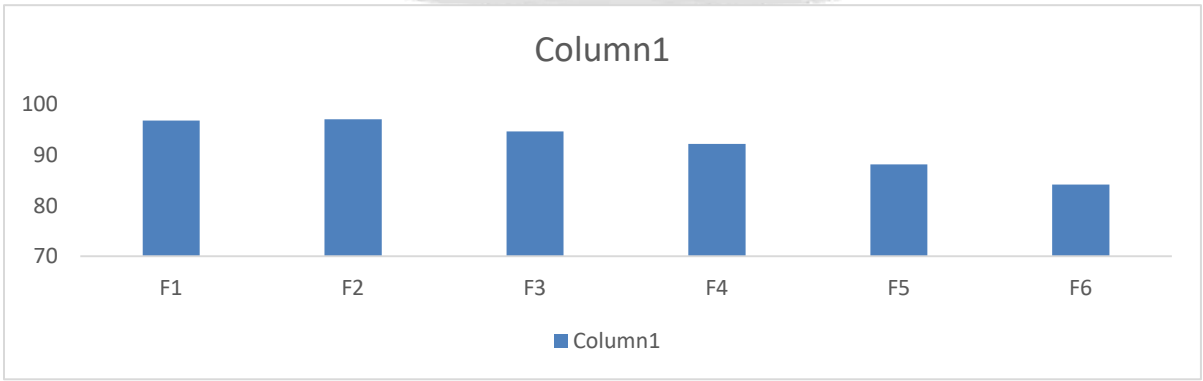


Percentage yield of the formulations

11. DRUG CONTENT OF GEL FORMULATIONS

TABLE 11.1 : DRUG CONTENT OF GEL FORMULATIONS

Formulation Code	**Drug content**
F1	96.7
F2	97
F3	94.6
F4	92.1
F5	88.1
F6	84.1



Drug Content of Gel Formulation

Report: The drug content of various gel formulation is found to be 96.7, 97 , 94.6, 92.1, 88.1 and 84.1 of all formulation i.e F1, F2, F3, F4, F5 and F6 . F2 have higher drug content i.e. 97. It was shown that when the concentration of gelling agent increase then the drug content found to be lowest.

DISCUSSION

The goal of this study is to develop and test a luliconazole topical antifungal gel using neem oil, tulsi oil, cinnamon oil, and natural aloe vera gel as a gelling agent. Compared to oral medication delivery systems, topical drug administration systems have various advantages.

Gel, cream, ointment, and lotion are examples of these delivery systems. Based on the results obtained after the gel formulation, the luliconazole medication was discovered to be a somewhat yellowish powder with an acidic taste and no odour.

The drug's solubility in ethanol revealed that it was very minimally soluble. In both water and methanol, the medication dissolves quickly. The drug's melting point was also determined. and found to be 150.3ºC .The calibration curve also obtained by using ethanol as a medium.

Then, using an Aligent FT-IR spectrometer, an FT-IR research of a drug and polymer was performed, and the luliconazole drug peak was acquired and displayed in the FT-IR spectra.

The polymer's FT-IR spectra investigation was then confirmed by the peaks found in the spectra. The medication and polymer compatibility investigation was confirmed by FT-IR spectra.

The viscosity, pH, spreadability, drug content, swelling index, percentage yield, and sensitivity test were used to evaluate the topical antifungal gel of luliconazole made with neem oil, tulsi oil, cinnamon oil, and natural aloe vera as the gelling agent.

F5 have highest pH value in comparison to other formulations. Mainly the pH range of all the formulations are near 4.62. So it was considered non- irritant and best for application.

F2 has lower viscosity i.e 2807 in compare to other formulations. F6 have highest viscosity compare to other formulations. Viscosity of gel increase with increasing the concentration of polymers. F3 having ideal viscosity shown in table.

The Spreadability test were performed for all formulations with increase in polymer concentration then increased the spreadability value of the gel formulations. F6 have greater Spreadability in compare to other formulations.

The swelling index of a gel was found to be 82, 70, 56, 44.6, 37.5, 24.6 of all formulations F1, F2, F3, F4, F5, F6. Hence decreasing the swelling index of a gel from F1 to F6 formulations. F6 have low swelling index in comparison to others formulation .

F2 have higher drug content i.e. 97. It was shown that when the concentration of gelling agent increase then the drug content found to be lowest.

From all the evaluation parameters, it was found that F3 was the best formulation that satisfied all the parameters.

CONCLUSION

The topical antifungal gel of luliconazole was successfully prepared utilizing neem oil, tulsi oil, cinnamon oil, and aloe vera as the gelling agent.

Various formulation preparations (F1, F2, F3, F4, F5, and F6) were created utilizing appropriate polymers (Carbopol and HPMC) and aloe vera gel as a gelling agent.

Different preformulation research and compatibility investigations were used to determine the study of API. The presence of various groups can be seen in the FTIR spectrum of Luliconazole. The melting point of luliconazole was discovered to be between 150 - 151°C. In ethanol, luliconazole was just weakly soluble.

Different factors such as viscosity, spreadability, percentage yield, swelling index, drug concentration, and pH were used to determine the formulation of luliconazole.

Viscosity studies of all formulations were conducted, and it was discovered that F3 performed better than the others. In comparison to other formulas, F2 has a reduced viscosity.

The gel that had been created was put to the test. In comparison to other formulations, the full batch of F3 delivered the best conceivable outcome.

As a result, it was established that essential oils and aloe vera gel were employed in the formulation, and excipients were chosen to ensure that the gel was compatible with luliconazole and could be used to treat a variety of conditions. By enhancing its activity as it shows synergistic effect and reduces the side effects of the drugs.

LIMITATIONS

Preparing an antifungal gel of luliconazole with essential oils was a novel notion, and because the drug isn't very old, it isn't listed in the Indian Pharmacopoeia, making it difficult to discover information about it.

Because of their consistency and viscosity, blending the various polymer ratios and oils was difficult. Sometimes the chances of recurrence of the infection are more .

The process of determining the viscosity of the gel makes it more viscous, and determining the pH was a difficult operation.

It was fascinating to mix aloevera gel into the mixture, and adequate precautions must be observed during the process. Essential oils such as tulsi, neem, and cinnamon are used in many products.

FUTURE PROSPECTS

Luliconazole was an antifungal medication with a broad spectrum of activity. Antifungal and antibacterial activities are also found in aloe vera leaves.

It also had a synergistic impact in this study when coupled with neem, tulsi, and cinnamon oils, which have antifungal and antibacterial characteristics.

Luliconazole was used to treat a variety of skin conditions, including ringworm, tinea corporis, and tinea pedesis.

There are just a few luliconazole lotions and creams on the market, and when mixed with natural sources, they provide synergistic benefits.

Luliconazole has a few side effects, such as redness and itching, but having no toxicity.

When used in conjunction with natural sources, the side effects gel's adverse effects have also decreased, making it ideal for treating fungal infections .

REFERENCES

1.Parashar B, Kabra A, Chandel A. Formulation and evaluation of gel containing miconazole nitrate an antifungal agent. Int J Pharm Res Rev. 2013 Jun; 2(6):18-28.

2.Hugar S, Patel PM, Nagmoti J, Uppin C, Mistry L, Dhariwal N. An invitro comparative evaluation of efficacy of disinfecting ability of garlic oil, neem oil, clove oil, and tusli oil with autoclaving on endodontics K files tested against Enterococcus faecalis. International journal of clinical pediatric dentistry. 2017 Jul; 10 (3): 283.

3.Borse VA, Gangude AB, Deore AB. Formulation and Evaluation of Antibacterial Topical Gel of Doxycycline Hyclate, Neem Oil and Tea Tree Oil. INDIAN JOURNAL OF PHARMACEUTICAL EDUCATION AND RESEARCH. 2020 Jan 1;54(1):206-12.

4.Gupta S, Tiwari S, Prajapati RN, Yadav RD, Chanchal DK, Mansoori MF. PAMAM DENDRIMER-BASED LULICONAZOLE GEL FORMULATION AND EFFICIENCY EVALUATIONS. European Journal of Molecular & Clinical Medicine. 2021 Jan 30;7(8):4881-94.

5. Dandagi PM, Pandey P, Gadad AP, Mastiholimath V. Formulation and Evaluation of Microemulsion Based Luliconazole Gel for Topical Delivery. Indian Journal of Pharmaceutical Education and Research. 2020 Apr 1;54(2):293-301.

6. Kaur M, Singh K, Jain SK. Luliconazole vesicular based gel formulations for its enhanced topical delivery. Journal of liposome research. 2020 Oct 1;30(4):388-406.

7. Preparation of luliconazole nanocrystals loaded hydrogel for improvement of dissolution and antifungal activity. Heliyon. 2019 May 1;5(5):e01688.

8. Kansagra H, Mallick S. Microemulsion-based antifungal gel of luliconazole for dermatophyte infections: formulation, characterization and efficacy studies. Journal of Pharmaceutical Investigation. 2016 Feb 1;46(1):21-8.

9. Garg AK, Maddiboyina B, Alqarni MH, Alam A, Aldawsari HM, Rawat P, Singh S, Kesharwani P. Solubility enhancement, formulation development and antifungal activity of luliconazole niosomal gel-based system. Journal of Biomaterials Science, Polymer Edition. 2021 May 28;32(8):1009-23.

10. Helal DA, El-Rhman DA, Abdel-Halim SA, El-Nabarawi MA. Formulation and evaluation of fluconazole topical gel. Int J Pharm Pharm Sci. 2012;4(5):176-83.

11. Parashar B, Kabra A, Chandel A. Formulation and evaluation of gel containing miconazole Chaurasia G. A review on pharmaceutical preformulation studies in formulation and development of new drug molecules. International Journal of Pharmaceutical Sciences and Research. 2016 Jun 1;7(6):2313.

12. Bansod S, Rai M. Antifungal activity of essential oils from Indian medicinal plants against human pathogenic Aspergillus fumigatus and A. niger. World Journal of Medical Sciences. 2008 Jan;3(2):81-8.