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Formulation And Evaluation Of Curcumin Based Lotion For Treating Fungal Infection

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Abstract

The formulation is applied directly to the skin to treat skin conditions using a topical medication delivery method. The delivery of hydrophobic medications is a drawback of the gel formulation. Lotion, a unique medicine delivery system, can help overcome this. Lotion is a combination of two formulations: emulsion and gel. Psoriasis, acne, and fungal infections are among the skin conditions that the Lotion is used to treat. In-vitro drug release, comparative in-vitro drug release studies, SEM studies, FTIR studies, pH analysis, spredability, swelling index, drug content, globule size, and in-vitro drug release kinetics using zero order, first order, highchair model, and Korsmeyer papas model were studied and characterized for the lotion. Curcumene and the excipients used did not appear to interact chemically, according to FTIR tests. The pH of the compositions was within a range that was appropriate for skin. The swelling index and spredability were at their peak for better patient compliance.

Keywords: emulgel, hydrophobic, emulsion, gel, topical

Introduction

Mucocutaneous, subcutaneous, systemic, superficial, and cutaneous are the terms used to describe fungal infections of the skin. People all over the world are afflicted by superficial skin infections. According to estimates, they affect 20% to 25% of the world's population, and their frequency is still rising.Age, sex, race, and sociocultural norms all influence these infections differently. The top layer of skin, hair, nails, and mucous membranes in specific body regions are all impacted by superficial mycosis.Mycoses are dermatophytes that are frequently brought on by Malassezia species, such as Pityriasis versicolor (seborrheic dermatitis) and Candida albicans (candidiasis).

In comparison to oral administration, topical application of antifungal advantages is restricted to the infected skin for the treatment of these illnesses. This includes things like antibiotic exposure and restricted medication entrance into the bloodstream.Topical drug delivery can be advantageous over other methods for a variety of reasons, including avoiding the need for prescription drugs and potential risks.Another is the ability of the medications to reach the affected area of the skin or eyes directly. Miconazole, ketoconazole, voriconazole, sertaconazole, and fluconazole are examples of topical antifungal drugs that are commonly used to assess systemic adverse responses. These drugs are also more convenient for patients to use than those that are administered through other routes.

Topical treatments are more effective in eliminating fungal infections, but their effectiveness is restricted because the stratum corneum acts as a skin barrier, resulting in lengthy treatment durations and low patient compliance when applied as a standard gel or emulsion.One of the best droplet sizes for distribution is lotion. The lotion is often translucent or semi-transparent and has a high stability rating. A clear lotion that is thermodynamically safe and stabilized by an interfacial surface of surfactants and surfactant molecules with droplet sizes smaller than 100 nm.

A topical drug delivery system is a technique that involves applying a formulation containing an API directly to the skin in order to treat local cutaneous symptoms [1,2]. when local skin diseases, including tine capitals and tine padi (fungal infections), are the main treatment for parenteral, sublingual, and rectal administration routes, or when these methods are inadequate. The avoidance of presystolic metabolism, patient discomfort, and the risks associated with intravenous

therapy and different absorption conditions, such as the presence of enzymes and pH fluctuations, are among the main advantages of topical drug delivery [3]. Topical drugs come in a wide variety of formulations and are administered directly to the skin. Although they are available in liquid or powder form, semisolid is the most widely used formulation. Although gels release medications more quickly than creams and ointments, one of their main drawbacks is that they cannot deliver hydrophobic pharmaceuticals. Therefore, lotion is created to get over this restriction. The ocular, rectal, vaginal, and cutaneous are the possible routes for topical medication administration. Lotion has qualities such being thixotropic, greaseless, readily spreadable, and bio-friendly, which improves patient acceptance. The Zingiberaceae family includes the commonly used and well-liked Indian medicinal herb turmeric (Curcuma longa). Curcumin is a polyphenolic substance that has a lipophilic character. Curcuma longa is the source of this active ingredient, which gives turmeric its color. Curcumene has been utilized historically for its many therapeutic benefits, including its anti-inflammatory, anti-oxidant, antibacterial, and anticancer effects. Different methane, a curcumene chemical, is what gives turmeric its yellow hue.

Only negligible amounts of the chemical show up in the blood when taken orally (up to 8 g daily), and it is poorly absorbed. Because of its significant first-pass metabolism, it becomes a good choice for topical gel formulation. [4]

Materials and methodology

Sample collection and preparation

- The rhizomes of Turmeric were collected from the local market of Bareilly, U.P.
- The collected samples were washed and dried in an oven at 100 - 110˚C for 3-4 hours.
- Then dried rhizome samples were crushed by using mortar & pestle.
- The crushed samples were screened through a sieve no 80 so as to obtain uniform powder.
- The Turmeric powder were collected in a sterilized polybags and kept into refrigerator to prevent moisture.

Rhizome Turmeric **Dried Turmeric** **Powdered Turmeric**

Figure 1:Turmeric

Curcuminion using Soxhlet apparatus: Soxhlet method for curcuminion of curcumin (Tian Jiang et al., 2021).
The 15 gram of Turmeric powder was weighed and packed into the Whatman No.1 filter paper, and then the paper packet was placed in a thimble part of Soxhlet apparatus

- Then 250 ml of acetone as curcuminion solvent was added to the boiling flask of Soxhlet apparatus and boiling flask was placed over heating element.
- The curcuminion procedure was carried out at 60˚C for 8hr.

- Once the curcuminion process completed. The acetone was separated out from the curcumin using rotary evaporator under vacuum at 35˚C. The residue was dried.

Figure 2: Turmeric residue

Curcuminion of Curcumin from turmeric residue

- In 250ml beaker add 5 gram of Turmeric was taken and 150 ml of 95% ethanol was added to it.
- Then the sample was allowed to mix well & kept it dark at room temperature for 48hrs.
- Precipitated curcuminoids crystals was found in the bottom of flasks and then it was purified by washing several times with 95% ethanol

Physicochemical characterization of curcumin

The curcumin was characterized for pH, total ash, total yield, and moisture.

pH: The pH meter was calibrated using buffers with pH values of 3, 7, and 10, and the electrode was then dipped directly into the curcumin solution until the pH remained constant.

Ash: Weighing one gram of semi-solid crude medication in a tared silica dish, burning it at a temperature of no more than 400°C until it was carbon-free, cooling it in a desiccator, and measuring the amount of ash was how we calculated the total ash. Until the weight was constant, the procedure was repeated.

TLC: Utilizing pre-coated TLC plates made of silica gel G that had been cut into strips and had a straight line marking the origin, thin layer chromatography was carried out. After being identified on the origin line of the TLC plate, Convolvulus cneorum ethanol curcumin was put in a development chamber with a solvent system (ethyl acetate: n-hexane; 9:1) [5-7].

Preformulation studies

Physical properties:

The physical description of the compound was analyzed.

Melting Point Determination:

The United States Pharmacy (USP) procedure was used to determine the melting point. A tiny quantity of medication was placed in a capillary tube that was sealed. The tube was inserted using the melting point apparatus. The device's temperature was dramatically raised, and both the point at which the entire drug dissolved and the point at which the medication started to melt were noted.

Solubility:

The solubility of drugs were tested in various solvents such as distilled Water, ethanol 95%, Dimethyl Formamide, Isopropyl alcohol and DMSO.

UV Spectrophotometric study:

To make a standard stock solution, the drug was dissolved in 60:40 ethanol:phosphate buffer pH 7.4 at a final concentration of 1 mg/ml. Different aliquots were taken from the stock solution and diluted with ethanol:phosphate buffer pH 7.4 to produce a range of concentrations from 2 to 20 µg/ml. The absorbance λmax was measured between

200 and 400 nm. **Table 1: Ingradients**

Ingradient	Percentage %				
	F1	F2	F3	F4	F5
Curcumin	5	4	4	6	7
Lavender	2	2	2	2	2
Cethyl alcohol	2	1	1.5	2.5	0.5
Zinc oxide	12	11	10	9	8
Stearic acid	4	3	2	3	4
Glycerin	2	2	2	2	2
Vitamin E	1	1.5	1.5	2	2.5
Triethanolamine	1	1	1.5	1.3	1.4
HPMC	10	15	10	15	10
Propylparaben	0.5	o.5	1	1	1
Distilled Water	50.50	75.50	80.50	50.50	80.50

Calibration curve:

The calibration curve was created using a 1 mg/ml solution made by dissolving 10 mg of precisely weighed medicine in 10 ml of ethanol:phosphate buffer pH 7.4 at 60:40. Pipetting 10 milliliters of this solution into a 100 milliliter volumetric flask and diluting it with 100 milliliters of ethanol:phosphate buffer (pH 7.4) produced a 100 µg/ml solution. Volume make-up was done up to 10 ml using ethanol:phosphate buffer pH 7.4 after 0.2, 0.4, 0.6, 0.8, and 1.0 ml of medication were pipetted out into a series of 10 ml volumetric flasks to obtain 2, 4, 6, 8, and 10 µg/ml of medication, respectively. The resultant solution's absorbance was measured at 363 nm and recorded in the table [8,9].

FTIR analysis:

The Fourier transform infrared spectrum were obtained using the Agilent Technologies ATR FTIR Spectrophotometer (Model: CARY 630). The spectra, which were obtained in the 4000-650 cm-1 region, were used to examine interactions between excipients and active components by detecting notable shifts in peaks.

Preparation and formulation of lotion

The amounts of glycerin, cetyl alcohol, stearic acid, and hydroxypropyl methylcellulose (HPMC), among other essential ingredients, were weighed and are shown in the table below. Water was mixed with 2.0 g of triethanolamine while being constantly agitated. After that, the water sample was heated to 90°C. Following that, a tiny amount of melted cetyl alcohol, zinc oxide, stearic acid, glycerin, hydroxypropyl methylcellulose mixture, and propylparaben should be added to the water solution at a time, stirring constantly, until the sample reaches the appropriate temperature. Stirring continuously will result in a uniformly smooth paste. The lotion that was created was then let to cool. Convolvulus cneorum ethanolic curcumin, as weighed out,then added, and everything is well combined until.

Physico-chemical characterization of lotion

A Brookfield viscometer was used to measure the gel's physical characteristics, and a digital pH meter was used to measure its viscosity.

a. Physical appearance: Visual inspection was done on physical characteristics including color and appearance.

b. Viscosity: Using spindles 3 and 4, the Brookfield viscometer (Acutek A220B) was used to measure the gel's viscosity.

c. pH: pH of the gel was measured by using a digital pH meter after calibrating with buffer pH 3, 7, 10.

d. Spreadability: In order to determine the spreadability, 0.5 g of lotion was poured on a glass plate in a circle that had

been marked with a diameter of 1 cm. After that, 50 g of weight was allowed to rest on the upper glass plate for five minutes while a second glass plate was set on top of it. As the lotion spread, the diameter of the circle grew; this increase was measured in centimeters. These results were viewed as comparative spreadability values.

e. Extrudability: We loaded and transported the formulation into aluminum tubes that could be folded up. The lotion was left in the jar to solidify. A pressure of 1 kg/cm2 was then applied using the Monsanto hardness tester to ascertain the formulation's extrudability.

f. Homogeneity: Following gel setting in the container, ocular inspection was used to verify the homogeneity of all generated lotions. Their appearance and the existence of aggregates were examined [10-12].

Antifungal study

The well diffusion method was used to test the lotion's antifungal properties against fungus. The fungal suspension was prepared using a 48-hour-old fungus culture cultivated in potato dextrose broth (PDB). After being autoclaved at 121°C for 15 minutes, the PDA solution was transferred onto sterile petri dishes. After streaking the entire surface of the plates with a sterile spreader, 50 µl of fungal suspension was added to the agar plates to inoculate them. In the solidified media, 8 mm wells were cut with a sterile borer, and lotion was then added to each well. A 72-hour incubation period at 25°C was followed by the measurement of the diameter (mm) of the inhibitory zone surrounding the well Itraconazole (Itromed 1%, Leeford Healthcare Ltd.) [13,14].

Stability studies

The meticulously selected and refined F1 formulation underwent three months of accelerated stability testing at 40 2°C and 75 5% relative humidity. To perform stability tests, the lotion was kept in aluminum tubes for around three months. Using the previously described techniques for evaluating produced lotions, the lotion's physicochemical characteristics, physical attributes, and antifungal activity were evaluated.

Statical analysis

Calibration curve data was subjected to linear regression analysis to study linearity and various optical characteristics were calculated.

Results and Discussion

Pre-formulation studies

In order to avoid selecting further tests for uneven formulations with hazy and phase separation, mixing is done methodically and under observation.Finding the optimal formula at each stage of the formulation is the aim of the optimization.The results of the studies of ethanol and tween 80 (smix) mixes containing lavender oil are shown in Table 1. The lotion formula was developed using the optimal ratio of ethanol to tween 80 (smix), which is 1:4. When the ketoconazole lotion is made, the mixture to oil ratio is 9:1, as shown in Table 3.

The formulation of lotions F1 and F2 was already hazy and precipitating after stirring, therefore the excipient concentration was inadequate to stabilize the mixture.The solution in Formula F3 was initially smooth and stable, but after a while it became somewhat hazy and precipitated because the excipient concentration was insufficient to keep the lotion in place. Although formulas F1 through F3 cannot be maintained due to their lack of stability, formulas F4 and F5 are consistent and clearly can be continued for further research.

Melting point

Table 2: Analysis of melting point

Drug	*Tm (□C)	Casual range (□C)
Ketoconazole	138.50 ± 0.246	137-1380

Study solubility of Ketoconazole

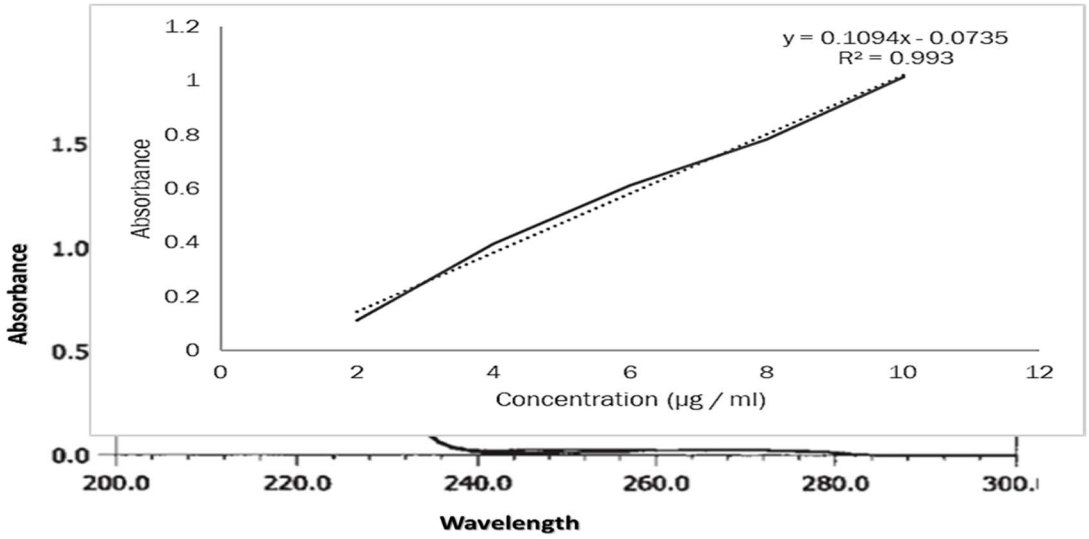
Ketoconazole's solubility in surfactant, oil, and co-surfactant is shown in Table. According to the results in Table, ethanol (co-surfactant), lavender oil (oil), and Tween 80 (surfactant) have the best solubility of ketoconazole.

Table 3: Solubility Profile of Ketoconazole

S no.	Excipients	Solubility (mg / ml)
1.	Tween 20	Soluble
2.	Tween 80	Dissolve in Moderate Amounts
3.	Isopropyl myristate	Soluble
4.	Lavender oil	Soluble
5	Propylene glycol	Soluble
6	Polyethylene glycol 400	Soluble
7	Ethanol	Dissolve in Moderate Amounts

λ_{max} determination of Ketoconazole

In this experiment, the Ketoconazole was scanned in the 200 nm – 400 nm range. The maximum absorbance value was



obtained at 235 nm.

Figure 3: Graph 1: λ_{max} of Ketoconazole

Standard curve of Ketoconazole

Table 4: Tabular representation of Ketoconazole standard curve

S no.	Conc. (µg / ml)	OD
1	**2**	**0.112**
2	**4**	**0.395**
3	**6**	**0.612**
4	**8**	**0.782**
5	**10**	**1.012**

Figure 4: Graph Standard curve

Study of components by FTIR analysis

The report spectrum demonstrating the drug purity is paired with the IR spectrum analysis for the few elements or components needed for the formulation.

FTIR of Ketoconazole:

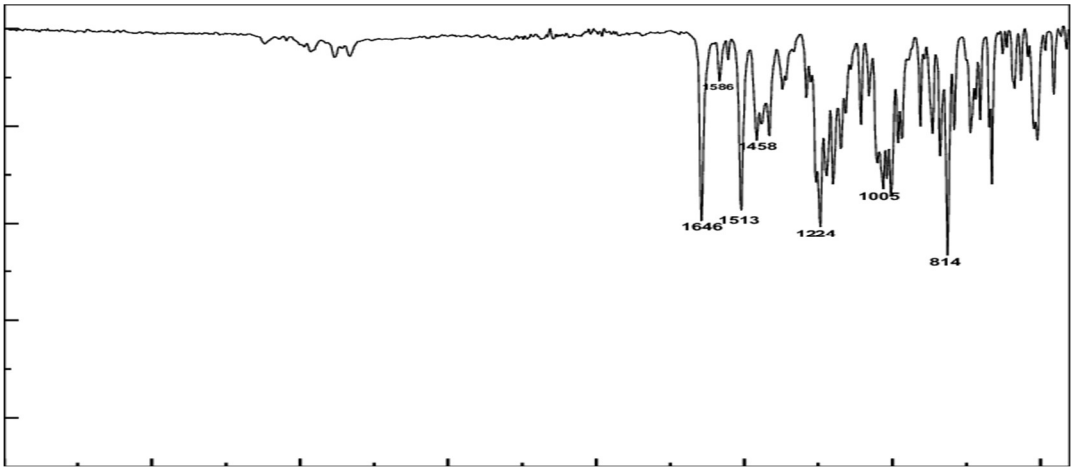


Figure 5: FTIR spectrum of pure drug Ketoconazole.

Optimization and Formulation of lotion

Optimized formulas were used to create the lotions. Figure displayed the lotions that were created.

Table 5: Optimization of drug with lotion

S no.	Formulation	Composition (%)			
		Ketoconazole	Lavender oil	Methanol	Tween 80
1	F1	3	0.6	1.0	3.7
2	F2	3	1.2	2.0	7.4
3	F3	3	1.8	3.0	11.1
4	F4	3	2.4	4.0	14.8
5	F5	3	3.0	5.0	18.5

Figure 6: Five formulated lotions

Evaluation of lotion

The findings of the lotion evaluation during the first week were shown in Table 4.

Organoleptic:

Soft golden, slightly viscous, translucent, uniform, and devoid of phase differentiation are the characteristics of formulas F1 through F5. This indicates that the 96 percent ethanol (co-surfactant) and lavender oil (oil) concentrations utilized are enough. When the composition is applied to the skin, it dissolves swiftly and leaves a little greasy hint. This is a result of the extremely high Tween 80 content.

pH:

The formulation's ideal pH falls between the skin's pH range of 4.5 and 6.5. Not only should the pH not be too alkaline,

which can irritate the skin and result in scaly skin, but it should also not be too acidic [14]. Every formulation created has a pH that is still within the range of the skin.

Viscosity:

With a Brookfield viscometer, the viscosity was determined. Five distinct viscosity formulations are available for this emulsion. Depending on the desired effects of the formulation's increased oil content, the amount of twenty-eight as a surfactant would also grow in order to affect its fluidity.The larger the number of 80, the smaller the globule will be. The system's attempt to maintain a constant density is proportional to the number of particles, which is increased by the globule's reduced size. By increasing the quantity of small globules, the viscosity of globule contact might be enhanced. [16]

.

Table 6: Evaluation of lotion in the 1st week

Formula	Colour	Odor	Clarity	pH	Viscosity
F1	Soft yellow	Specific	Translucent	6.21	518.245
F2	Soft yellow	Specific	Translucent	6.09	526.025
F3	Soft yellow	Specific	Translucent	6.15	565.214
F4	Soft yellow	Specific	Translucent	5.63	569.210
F5	Soft yellow	Specific	Translucent	5.21	589.325

Figure 7: pH studies of the formulated lotions

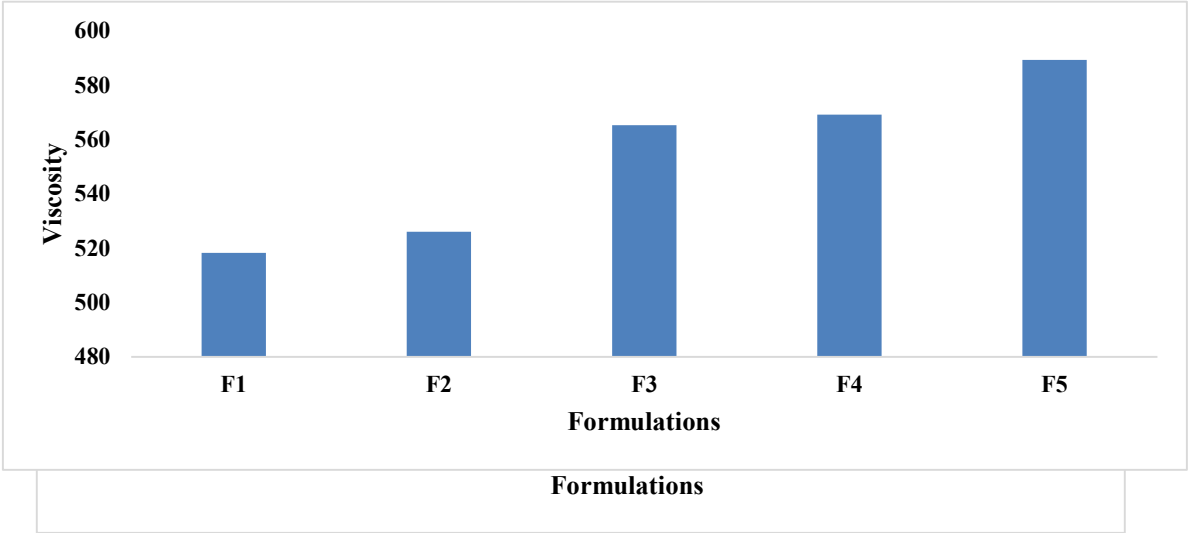
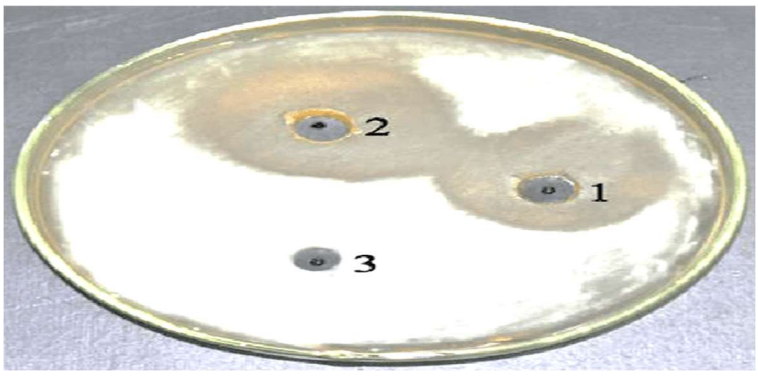


Figure 8: pH studies of the formulated lotions

Antifungal activity

While analyzing the antifungal activities of the formulated lotions it was found that the F4 and F4 show maximum



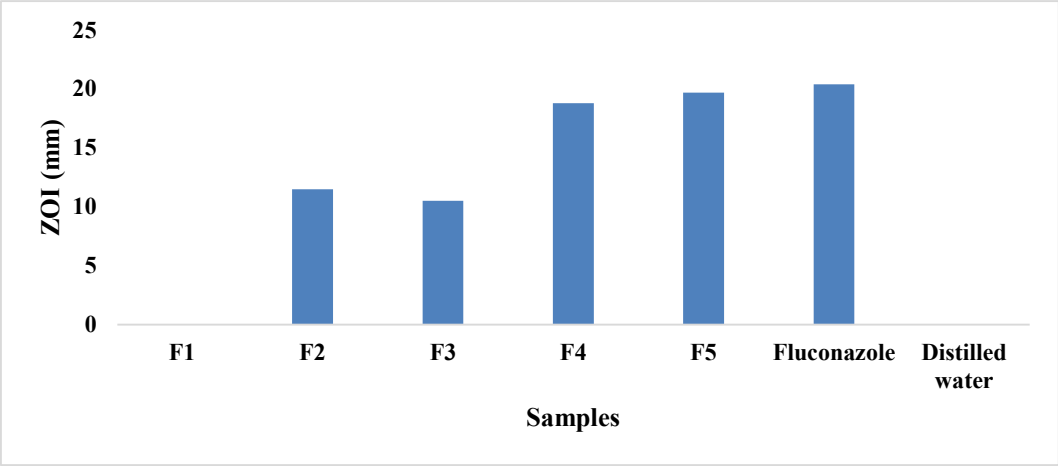
inhibitory effect against the *Candida albicans[15].*

Figure 9: Antifungal analysis of the lotion

Figure 10: Antibiogram analysis of formulated lotions.

Table 7: Antibiogram analysis of formulated lotions.

Formulations	ZOI (mm)
F1	0
F2	11.5
F3	10.5
F4	18.8
F5	19.7
Fluconazole	20.4
Distilled water	0



Conclusion

Sodium carboxymethyl cellulose was used to create a lotion formulation of hydro-methanolic curcumins of leaf combination (1:1), which produced a gel with acceptable physicochemical properties. The results of the lotion formulation stability tests were excellent. Research on the lotion's effects on Candida albicans revealed that both medications, either by itself or in combination, increased antifungal activity. These samples' phenol, lignan, and alkaloid may be the cause of their antifungal qualities. The impact of each of these phytoconstituents on antifungal activity has to be confirmed by more research. Therefore, developing a polyherbal lotion is superior to formulating a single herb, as demonstrated by F5. Accordingly, our research shows that both leaf curcumins are effective antifungals; their methanolic hydro curcumins may be made into lotion with acceptable physicochemical characteristics.

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