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FORMULATION AND EVALUATION OF ANTI-FUNGAL HAIR GEL CONTAINING KETOCONAZOLE

RAHUL JODH*, MUKUND TAWAR, GAURAV MUDE, HITESH KHODASKAR, KARISHMA KINEKAR

Department of Pharmacology, P.R. Pote Patil College of Pharmacy, Amravati-444602

ABSTRACT

Ketoconazole is used to treat fungal infection in immune compromised individuals. Because it reduces the generation of adrenal sex hormone, it has recently been used as a therapy for advanced prostatic cancer. Despite the fact that oral ketoconazole was already subjected to labelling changes and market removal due to major harmful effects (AEs), applied ketoconazole is universally considered to be effective as well as safe for the lowest priority fungal infections. Some of the novel dermatitis indications of external ketoconazole use include hair loss, blepharitis, and onychomycosis. Ketoconazole is an antifungal medication made from synthetic imidazoles that is used to treat chronic mucocutaneous candidosis, genital candidosis, and superficial fungal infections. Unlike older imidazole antifungals such as miconazole and clotrimazole, ketoconazole is really an artificial imidazole compound that is efficacious after oral administration. It's effective against skin fungal diseases, including dermatophytosis, as well as genital candidiasis. It has been the treatment of choice for chronic mucocutaneous candidosis.

The prepared antifungal hair gel of ketoconazole was shown the pH range 6.9 to 7.5, viscosity 3256 to 5126 cps, extrudability range 68.50 to 90.65, spreadability range 6 to 9.3gm/sec. zone of inhibition range 25 to 30 mm, drug content ranges 93.78% to 96.56 %.

The drug content, viscosity, in vitro drug release, spreadability, washability, & antifungal effectiveness of ketoconazole hair gel were all examined.F4 outperformed all other formulae. As a result, the formulation and evaluation of ketoconazole hair gel met their objectives.

***KEYWORDS**: Ketoconazole, Hair Gel, Antifungal, Dandruff, Pityriasis*

INTRODUCTION

Fungi discovered in human hair are known as "dandruff." The medical word for it is pityriasis simplex capitis. Either it will be dry or greasy. Dry dandruff is silvery and white, whereas greasy falkas are light yellowish and smell terrible. Dandruff is a non-contagious hair condition that occurs with aging. [(1)] It's a common embarrassing disorder that affects about 5% of the world's population. A wide range of antifungal medicines are available to treat dandruff. 2-hydroxybenzoic acid, acid, steroids, sulphur, imidazole derivatives, zinc pyrithione and tar compounds are now available as treatment alternatives for dandruff control. For dandruff treatment, many antifungal chemicals are widely utilised in hair shampoos.[(2)]

Any of the roughly 144,000 different fungus species. This kingdom includes microbes, yeasts, smuts, moulds, rusts, and mushrooms. Spore moulds or oomycetes (water moulds) are examples of fungal creatures which do not belong to such fungus kingdoms and were acquired. The domain chromista includes a wide range of species, including fungi. Some fungi may survive both in water and in soil. Plants and animals host parasitic or symbiotic organisms. Fungi are eukaryotic organisms that have membrane-bound organelles and nuclei that are well-defined. (3) Fungi-caused infections are common all throughout the world. And if an extensive fungus takes over a part of the body that the immune system can't regulate, it's called a fungal infection. [(4)] Ketoconazole (KTZ) was licenced by the US Food & Drug Administration (FDA) in 1981 as an expansive azole antifungal for treating systemic fungal infections. When alternative antifungal drugs are unavailable or inadequate, oral KTZ is the only option for treating endemic mycoses. 2% shampoo, 1% shampoo, 2% cream, 2% gel, seborrheic dermatitis, and 2% aerosol foam All 2-percentage shampoos require treatment, but 1% shampoo can be purchased over-the-counter. Generic equivalents are available for everything except the 1 percent shampoo and 2 percent gel. [(5)]

ANTIFUNGAL ACTIVITY

The therapeutic effectiveness of antifungal medications might be established by reducing fungal growth in a controlled environment. The gels were studied microbiologically using the cup-plate method, which depends on the drug diffusing through a layer of hard agar in the petri dish, resulting in increased growth. In a zone, microorganisms are completely destroyed well all the way around the cup. Increased medication release from either the body base or the brain is a sign of a larger inhibition zone, which is a positive thing. [(6)]

Medium used: Sabouraud's dextrose broth

Candida albicans species was used as a test organism.

Because of the medium's low pH and high sugar content, it's very fungi-selective. It's also antibacterial and antifungal. Adjust to pH 5.4 Autoclave at 1210 C for 2 hours after dissolving the contents with heat and filtering through cotton gauze.

MATERIALS AND METHODS

Chemicals-

Ketoconazole, ethanol, Triethanolamine, glycerin, carbapol 940, and polyethylene glycol are some of the medications used. All of the excipients were laboratory-grade reagents.

Preparation of calibration curve of ketoconazole: -

1) At various sample dilutions at 2, 4, 6, 8, & 10 g per ml of medication in methanol, the absorbance of every solution was measured on 226 nm in comparison to a methanol blank.
2) By plotting the concentration vs, the absorbance values, a standard graph was produced.[8]

Preparation of gel containing ketoconazole:

1) Polyethylene glycol, glycerin, and methylparabens were measured and dissolved in 35 ml of water in a beaker, then stirred at high-speed using a mechanical stirrer.
2) Then, while stirring, Carbopol 940 was slowly added to the beaker containing the above liquid.
3) Ketoconazole medication was dissolved in ethanol in a separate beaker and stirred into the above solution.
4) Triethanolamine solution was carefully added to the solution and stirred continuously until the gel was formed. [9]

Table 1: Formulation Chart

Ingredients	F1	F2	F3	F4	F5	F6
Ketoconazole(gm)	0.1	0.1	0.1	0.1	0.1	0.1
Carbopol 940(gm)	0.1	0.2	0.3	0.4	0.5	0.6
Polyethylene Glycol 400(gm)	4	4	4	4	4	4
Methylparaben(gm)	0.1	0.1	0.1	0.1	0.1	0.1
Triethanolamine(ml)	0.3	0.3	0.3	0.3	0.3	0.3
Glycerine(ml)	0.5	0.5	0.5	0.5	0.5	0.5
Propylene glycol(ml)	3	3	3	3	3	3
Distilled water (ml) (Q.S)	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S

EVALUATION PARAMETERS

1] Psychorheological characteristic: The psychorheological characteristics (color, homogeneity, texture, and clogging) were examined for hair gel formulations.

2] Washability:The ease &extent of washing using water was personally verified after formulations are applied to the skin. (10)

3] Spreadability: Each formula's 0.5 g sample was squished between two slides and left for 5 minutes without any expectation of further spreading. The diameters of spread circles in centimetres were used to measure spreadability. The final findings were obtained by averaging three different determinations. (11)

4] Extrudability Study: -For extrusion testing, hair gel formulations are put in collapsible metal tubes with collapsible aluminum tubes. The material was extruded and passed through tubes, and the formulation's extrudability was evaluated.

5] PH determination: -The pH of hair products was measured using a digital pH meter. The electrode was then submerged as in solution for 30 minutes to get a consistent reading after one gram of both the gel was dissolved in 25 ml**.** There was a lot of processing to do as well. The pH values of each formulation were double-checked. (12)

6] Viscosity: -A Brookfield digital viscometer was used to determine the viscosity of the produced gel. At 10 rpm and 25°C, the viscosity was tested with spindle no. 6. An adequate amount of the gel was dispensed into a wide-mouthed container. The sample was placed inside the large-mouth container so that it could be dipped into the spindle of the viscometer. All gel samples are given 30 min. to settle at a constant temperature of (25 + 1°C) before the measurements.(13)

7] In vitro drug release study: -Ketoconazole was in vitro released as hair gel by using dialysis test tube approach. A donor medium phosphate buffer (pH 7.4) be gathered and placed in a 250 ml beaker. The egg membrane or even a sample of 5 ml was taken as from donor medium every 5 min so maintain proper sink condition. The donor medium has also been spun on even a magnetic stirrer with 50 rpm at around 37o 0.5 oC whereas its hair gel solution was retained in a test tube. After that, the samples were examined using UV visible spectroscopy at 226 nm while utilizing phosphate buffer pH 7.4 as both a control. (14)

8] Drug content: -The drug concentration was evaluated by diluting 1 g of sample gel in such a 10 ml volumetric flask & measuring this at 226 nm2 with both a UV-Visible Spectrophotometer.

RESULT AND DISCUSSION

Evaluations of gel formulation

Evaluation Parameters: - All formulations, with the exception of F5 and F6, exhibit acceptable psychological characteristics. Carbopol amounts to more than 4.5gm and impacts two psychorheological characteristics: clogging and homogeneity. With the exception of F5 and F6, every one of the formulas could be washed.Excellent :(+++) Good :(++) Average :(+) Poor :(-)

Table 2: Evaluation Parameters

Form	Colour	Clogging	Homogeneity	Texture	Washability
F1	Turbid	Absent	++	Smooth	++
F2	Off white	Absent	++	Smooth	++
F3	white	Absent	++	Smooth	++
F4	Off white	Absent	++	Smooth	++
F5	Off white	Present	+	Smooth	+
F6	white	Present	+	Smooth	+

Extrudability: -Extrudability was good to satisfactory in all formulations. The ejection of the gel from either tube is critical for patient compliance and administration. Gel compositions using lower gelling agent concentrations extruded well, whereas gel formulations having higher gelling agent concentrations extruded well.

Table 3: Extrudability

Formulation	Extrudability
F1	90.65
F2	85.21
F3	80.14
F4	68.50
F5	75.62
F6	70.86

Spreadability: -Spreadability is critical to patient comfort and aids in the universal application of gel to such skin. An excellent gel has such a large spreadability range and spreads swiftly. The spreadability of both the generated gels decreased when the concentration of the gelling agent was increased.

Table 4: Spreadability

Formulation	Spreadability(gm/sec)
F1	9.3
F2	8.5
F3	7.2
F4	7
F5	6.8
F6	6

5] Determination of pH: The pH of all gel prepared formulations is between 6.9 and 7.5, which is within the normal pH range of the skin.

Table 5: Determination of pH

Formulation	pH
F1	6.9
F2	7.1
F3	7
F4	7.1
F5	7.3
F6	7.2

Viscosity: -Because it impacts the Extrudability, spreadability and release of drug, viscosity is an important property for defining gels. The viscosity of all generated gels increased when the amount of the gel forming ingredient was increased.

Table 5: Determination of Viscosity

Formulation	Viscosity(cps)
F1	3256
F2	3470
F3	3864
F4	4255
F5	4786
F6	5126

Drug content: -The drug content in all of the created gel formulations was constant and within acceptable limits, indicating that the gels had homogeneous drug dispersion.

Table 6: Drug Content

Formulation	Drug content
F1	93.78%
F2	96.34%
F3	96.02%
F4	96.56%
F5	96.14%
F6	95.57%

Anti-fungal Activity:

In both the release and inhibition zones, F4 exceeded another formulation. As a consequence, the best hair gel composition F4 has been chosen.

Table 7: Fungal Activities

Sample number	Zone of inhibition
Negative control	No zone
Positive control	25mm
Standard	26mm
Test	30mm

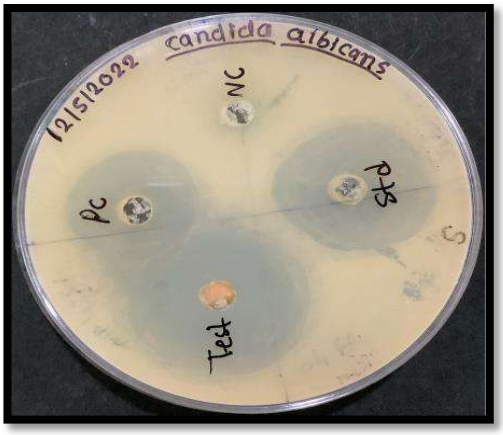

Figure 1: Zone of Inhibition of Prepared Hair Gel

Drug Release:

Some in vitro release of drug from gel was lowered even when the gelling agent concentration was raised. The higher viscosity of such gels might be the cause of the reduced in vitro drug release.

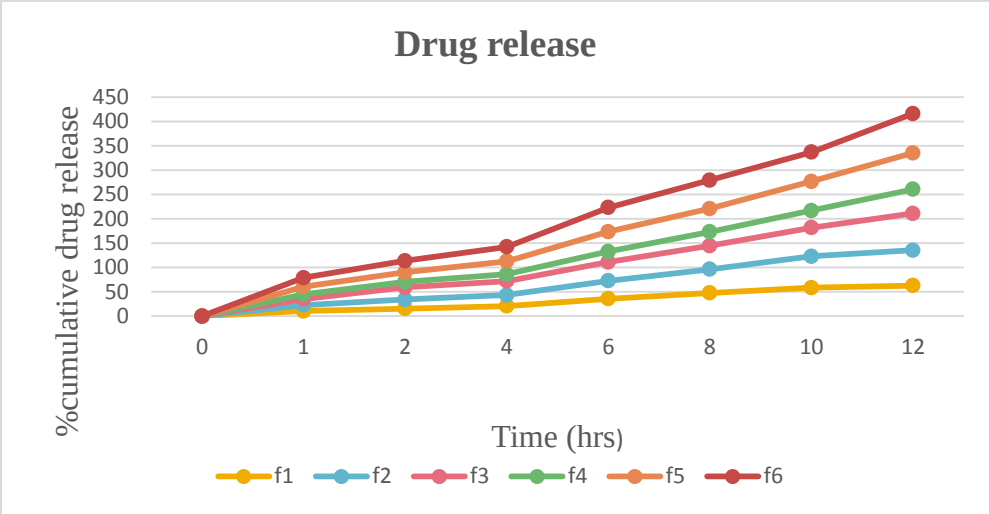

Figure 2: Cumulative Drug Release of Prepared Hair Gels

FTIR (Fourier transform infrared) spectroscopy:

FTIR spectroscopy research could be performed such as determine if medications and excipients interact. IR spectra of just a clear drug (ketoconazole) and then a drug combination preparation that contains the medication as well as all excipients.

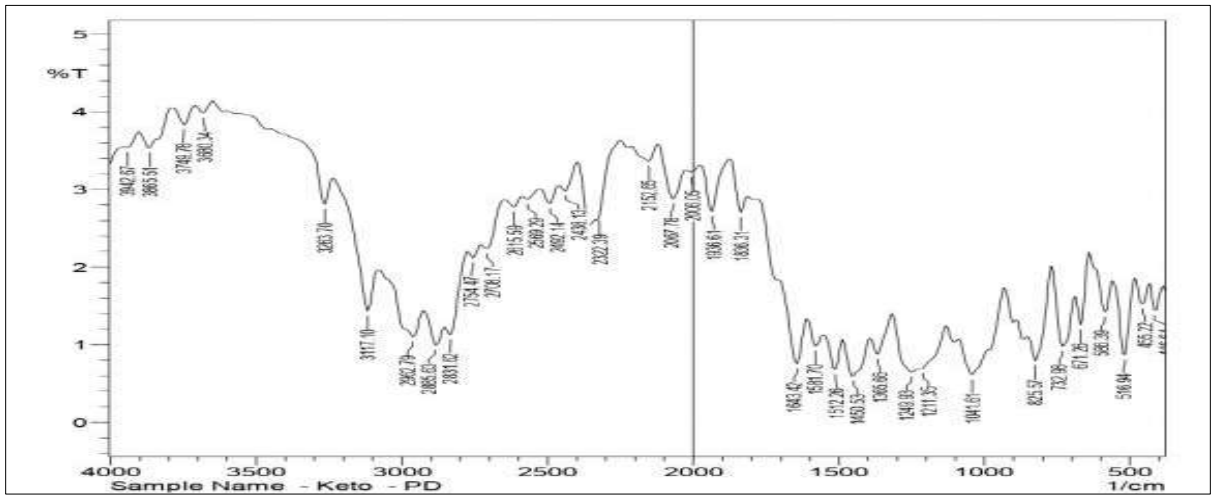

Figure 3: FTIR Pure Ketoconazole

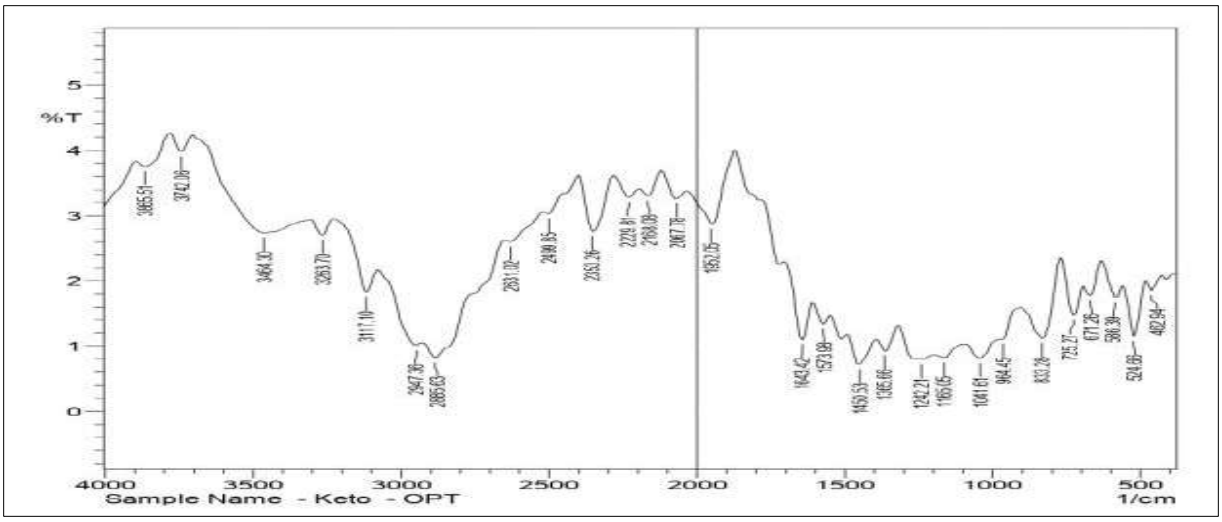

Figure 4: FTIR Ketoconazole Hair Gel Optimized

Differential Scanning Calorimetry (DSC):

Figure 5 and 6 illustrates the results of DSC studies, which demonstrate that pure ketoconazole has a significant exothermic peak of about 152.860C. This corresponds towards its melting point. The enhanced formulation's peaks have been determined to be 150.330C and 66.570C, and have low intensity and wide exothermic peaks when compared with pure drug.

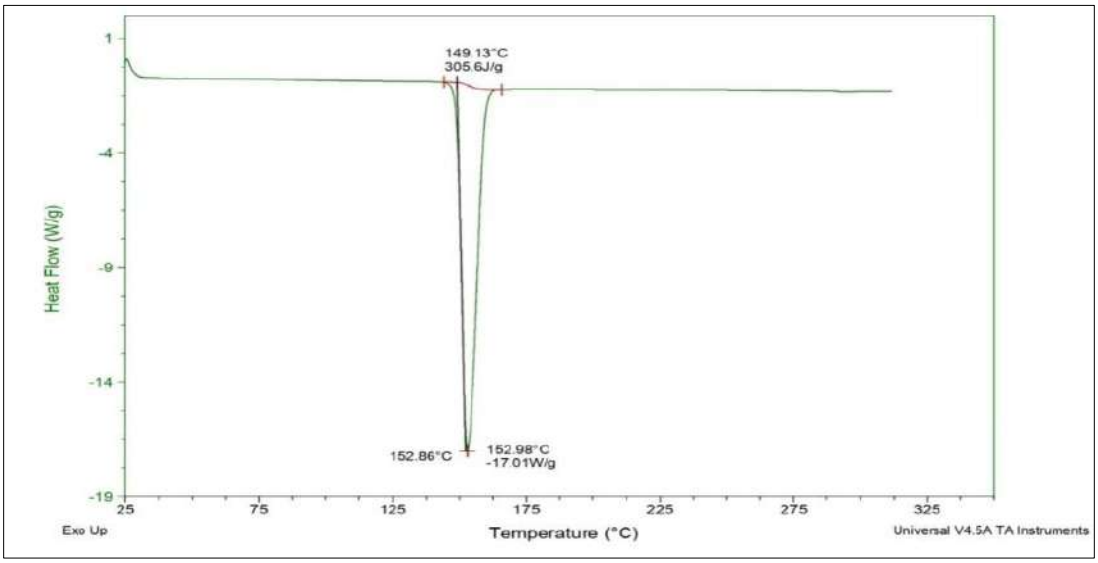

Figure 5: DSC Pure Ketoconazole

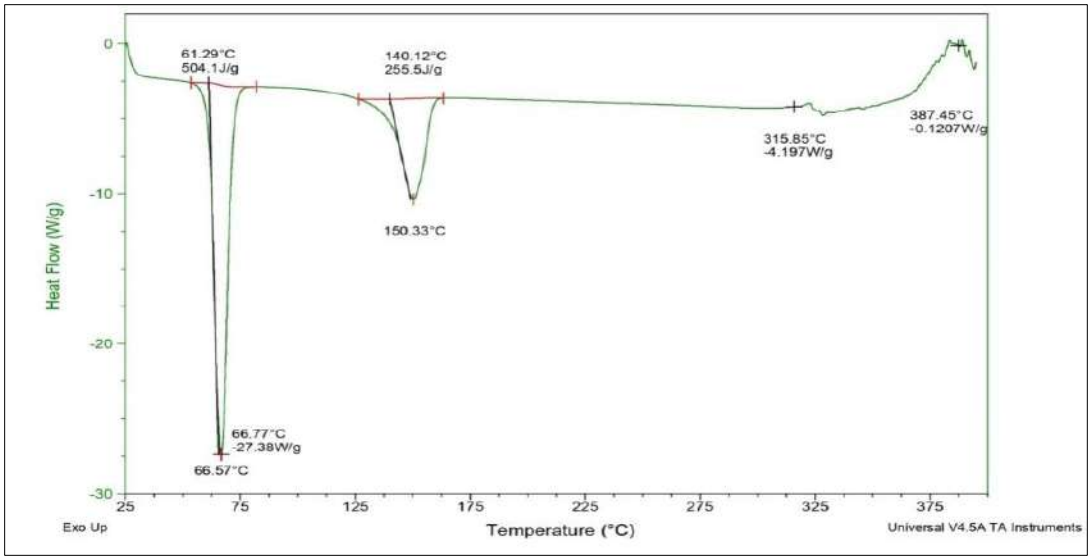

Figure 6: DSC Optimized Ketoconazole

CONCLUSION

Ketoconazole hair gel was examined for its drug content, in vitro drug release, spreadability, washability, viscosity &antifungal activity. When compared to many other formulas, F4 outperformed them all. As a result, the formulation and assessment of ketoconazole hair gel achieved its objectives.

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