

FORMULATION AND EVALUATION OF HERBAL OIL-BASED ITRACONAZOLE CREAM FOR FUNGAL INFECTION

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ABSTRACT

Objective: The current study was to formulate and to evaluate itraconazole herbal oil-based cream for fungal infection.

Methods: Six herbal oils were used for the formulation of itraconazole creams, namely, mustard oil (MO), olive oil (OO), wheat germ oil (WGO), jojoba oil (JO), tea tree oil (TTO), and combined oil (CO). Creams were formulated by the trituration method. Each herbal oils containing three different formulations of different concentrations of oils.

Results: All the prepared formulation was evaluated successfully. Out of all the formulations from each herbal oils the best two formulations were finalized, that is, MO₂ and CO₂ which show the greater *in vitro* diffusion rate among all. Formulation MO₂ shows 55.45±0.10% and CO₂ showed 59.43±1.18% within 480 min, respectively. Optimized formulations were also compared with the marketed formulation, which results in formulation CO₂ as the best formulation among all.

Conclusion: It can be concluded that herbal oil-based cream proved better alternate than oral preparation and improve patient compliance, ease of administration, local bioavailability, and better proves for fungal infected patients.

Keywords: Itraconazole, Creams, Mustard oil, Olive oil, Mycoses.

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INTRODUCTION

Mycoses, a fungal infection of the skin caused by fungi, which are common and commonly minor. Two important types of infections, namely, superficial and subcutaneous fungal infection have been widely reported. Superficial fungal infections affect the superficial layer of the skin such as hair, nails, and especially in mucous membranes whereas subcutaneous infections involve a deeper layer of the skin. Numbers of disease caused by fungus are *Aspergillus*, blast mycosis, candidacies, and histoplasmosis [1,2]. In modern years, the incidence of these infections has increased steadily, mainly because of the rising number of immunocompromised patients and the growing status of health clubs and public swimming pools, which simplify the spread of infection [3,4]. The causes of fungal infection are generally accidental. Fungi often develop both virulence mechanisms and morphologic form, namely, yeasts and hyphae that simplify their reproduction within the host [5]. Tinea pedis, or athlete's foot, is a common condition and also is a disease that frequently is self-treated with over-the-counter preparations, often at the risk for recurrence and chronicity. Causal agents are dermatophyte species of the *Trichophyton*, *Epidermophyton*, and *Microsporum* genera [6]. Fungal infections occur progressively more in older adults. In general, tinea corporis and tinea cruris infection require once to twice-daily treatment for 2 weeks. Tinea pedis require treatment for 4 weeks. Several antifungal agents can be effectively used against these fungal infections, namely, fluconazole, miconazole, itraconazole, and sertaconazole [7-10].

The itraconazole is one of the effective antifungal agents against fungal infections which are used for the treatment of fungal infection in both HIV and non-HIV infected individuals. It is highly lipophilic as compared to the fluconazole and miconazole or practically insoluble in water [11]. Itraconazole is active against fungal infections such as aspergillosis, blastomycosis, histoplasmosis, as well as fungal infection restricted to the toenails and fingernails. The absorption of itraconazole from the gut is incomplete [12-15].

In the present study, the herbal oil-based herbal cream of itraconazole investigated for topical fungal infections. The herbal cream of itraconazole for fungal infection was prepared by using six different oils, namely, mustard oil (MO), olive oil (OO), wheat germ oil (WGO), jojoba oil (JO), tea tree oil (TTO), and combined oil (CO). The different ingredients such as soft paraffin, cetyl alcohol, stearic acid, tween 80, and isopropyl myristate with different ratios and concentration were used to formulate the creams.

MATERIALS AND METHODS

Itraconazole drug was procured as a gift sample of Cipla Pvt Ltd., and all herbal oils; MO, OO, WGO, JO, and TTO were purchased from LobaChemicals Pvt Ltd. All other chemicals and solvents were used of Central Drug House Ltd. All chemicals were used of analytical grades.

Preformulation studies

Preformulation studies include physical appearance, melting point, partition coefficient, solubility, identification of drug by UV spectroscopy, and Fourier transformed infrared (FTIR) spectroscopy. All the physical characterization was observed and compared with the standard monograph in official pharmacopoeia.

Characterization of itraconazole by UV spectroscopy

Characterization of itraconazole was performed in methanol by scanning the standard concentration of known drug solution in a range of 200–400 nm to find out the absorption maxima (λ_{max}) of itraconazole.

Preparation of the stock solution

10 mg of itraconazole was accurately weighed and dissolved in 10 ml of methanol to obtain a concentration of 1000 µg/ml. Subsequently, 5 ml was withdrawn from the above solution, and volume was made up to 100 ml with methanol to get a 50 µg/ml solution.

Preparation of working standard

A series of dilution of a standard solution containing 4–14 µg/ml itraconazole were prepared in methanol using a stock solution. The absorbance was measured at 262 nm against similarly treated blank using a UV spectrophotometer. The procedure was repeated 3 times and the average value of absorbance was calculated.

FTIR study of itraconazole

FTIR spectra of the pure drug were observed and analyzed by the potassium bromide (KBr) press pellet method. Pure drug itraconazole was uniformly mixed with dry powdered KBr in the ratio of 1:100 and the mixture was then compressed into the transparent disk under high pressure using special dies. The disk was placed in the FTIR spectrophotometer and the spectrum was recorded. Spectrum was analyzing for the identification of the pure drug.

Formulation of cream

Creams were prepared using the trituration method, as the trituration method is the easiest method for the formulation of cream.

Preparation of aqueous phase

Glycerine, tween 80, EDTA, and isopropyl myristate were weighed properly and melted in a beaker. The temperature of the water phase is maintained between 65 and 70°C.

Development of cream formulation

The water portion was then slowly incorporated into the oil phase at 65–70°C and mixed for 10–15 min. with continuous stirring. Then, the dispersion part was added into the above part slowly when the temperature reaches 40°C. The pH of cream was kept between 5.8 and 6.8.

Optimization of oil for cream

The various oils, namely, MOs, TTO, JO, WGO, OO, and CO are used to prepare the different formulation of itraconazole cream. In CO formulation, 10ml of stock solution of CO is prepared by using 2 ml of each oil and different formulations were prepared (Tables 1 and 2).

Evaluation of creams

Physical appearance

Color, homogeneity, consistency, appearance, and texture were observed visually.

pH of creams

Creams pH was evaluated using a digital pH meter.

Determination of the type of emulsion

The determination of creams was done using the dye test. A minute amount of creams were used and a drop of dye was added to the cream. The creams were directly observed under the microscope at higher magnification to determine the type of emulsion [16].

Content of uniformity

1 g of each formulation was taken in 100 ml of volumetric flask and diluted with methanol. The sample was shaken properly until the whole sample was dissolved and finally makes up the solution with methanol. The solution was filtered and the filtrate was pipette out and diluted to 10 ml with methanol. The sample was analyzed spectrophotometrically against a similarly treated blank at λ_{\max} 262 nm [17].

Viscosity

The viscosity of cream was determined by Brookfield viscometer. The prepared formulation was poured into the adaptor of the viscometer and determined the viscosity of the test sample as per the standard operating procedure of viscometer. The spindle was rotated at speeds of 0.5, 1, 5, 10, and 20 rpm. At each speed, the corresponding dial reading on the viscometer was noted. The spindle speed was consecutively lowered and the corresponding dial reading was noted [18].

Spreadability

The spreadability of cream was determined by the apparatus, which consists of a wooden block, which was provided by a pulley at one end. By this method, spreadability was measured based on slip and drug characteristics of cream.

About 2 g cream was placed on the ground slide. Another slide was placed on that slide which has a dimension of a fixed ground slide and provided with the hook. 1 kg weighted was placed on the top of the two slides to provide a uniform film of the cream between the slides. The top plate was then subjected to a pull of 30 gm. With the help of string attached to the hook and the time (in seconds) required by the top slide to cover a distance of 7.5 cm be noted. A shorter interval indicates better spreadability [19,20].

Spreadability was measured using the equation:

$$S = M \times L/T$$

Where, M = Weight (gm) taken, L = Length of the slide, T = Time (s) taken.

Determination of tube extrudability

Creams were filled in a clean lacquered aluminum collapsible tube and pressed firmly at the crimped end. When the cap was removed, cream extruded until pressure dissipated. Weight in grams required to extrude a 0.5 cm ribbon of cream in 10 s was determined [21].

In vitro diffusion study

In vitro diffusion studies were carried out in a modified Franz diffusion cell. The receptor compartment was filled with saline phosphate buffer (pH 7.4). The whole assembly was maintained at $37.0 \pm 1.0^\circ\text{C}$ temperature and the receptor solution was stirred with a magnetic stirrer at 100 rpm throughout the experiment. 1 ml sample was withdrawn at regular intervals for 480 min and the withdrawn sample was replaced with an equal volume of fresh medium. The entire sample was suitably diluted with methanol and analyzed using a UV spectrophotometer at 264 nm. After analyzing all the study of all formulations from different oils, the best-optimized formulation was evaluated based on *in vitro* diffusion studies. Optimized formulations were then compared with the marketed formulation [22,23].

RESULTS

Preformulation studies

Preformulation studies for pure itraconazole were carried out to assess the physicochemical characters and compatibility of the drug.

Characterization of itraconazole by UV spectroscopy

Absorption maxima (λ_{\max}) of itraconazole was determined in methanol in a UV spectrophotometer by scanning in a wavelength range of 400–200 nm. λ_{\max} of itraconazole was found to be 264 nm (Figs. 1 and 2 and Table 3).

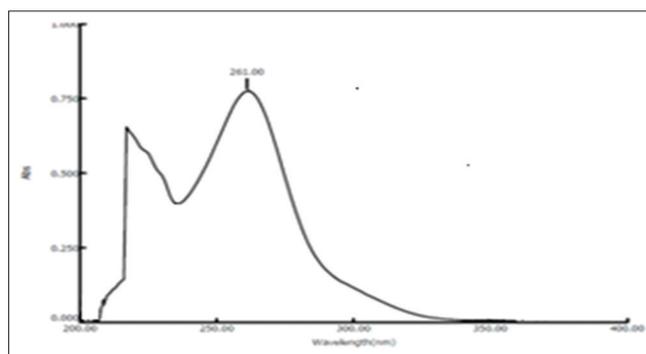


Fig. 1: Absorption maximum (λ_{\max}) of itraconazole

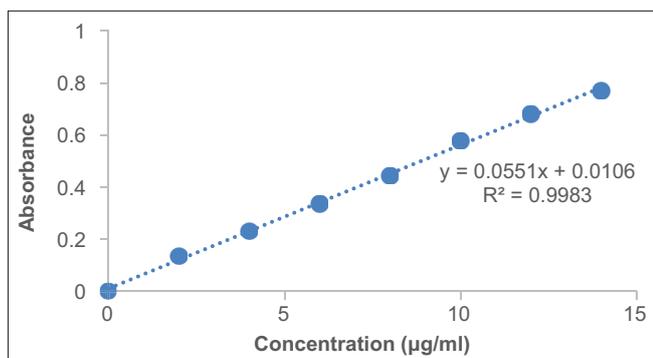


Fig. 2: Standard calibration curve of itraconazole

FTIR study of itraconazole

The FTIR spectrum of itraconazole discovered the presence of a peak at 783 cm^{-1} due to C-Cl stretching; while peaks at 1627.92 cm^{-1} due to aromatic C=C and C=N stretching. A peak at 1274.94 cm^{-1} due to C-O while peaks at 1699.29 cm^{-1} due to C=O and peak at 1334.74 cm^{-1} due to C-N. As per the literature reported peaks, which further supports the purity of the drug (Fig. 3).

Formulation of cream

Cream of itraconazole was prepared by the trituration method and optimized for various parameters.

Optimization of oils concentration

The oil concentration was optimized in the range of 4–6%. It was observed that as the concentration of oil was increased, viscosity of

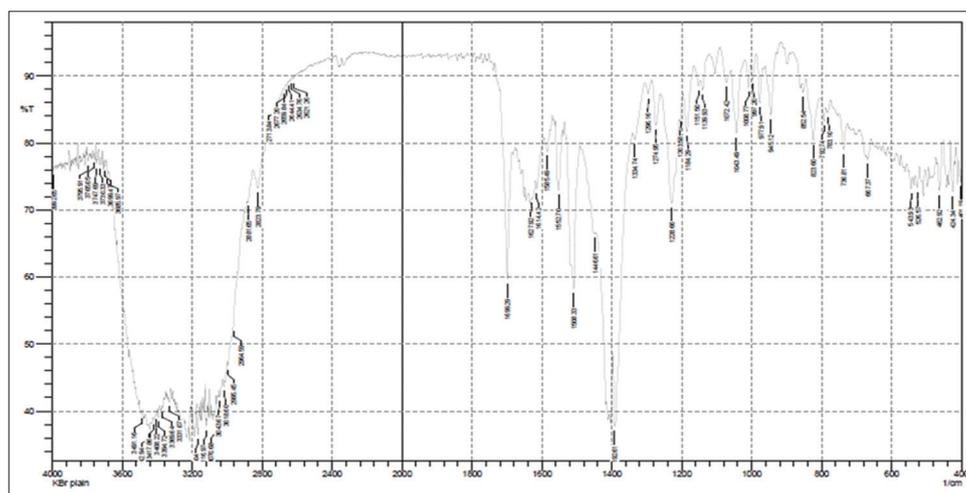


Fig. 3: FTIR spectra of itraconazole

Table 1: Optimized formulae of itraconazole herbal oil-based cream

Formulation code	MO1	MO2	MO3	TTO 1	TTO 2	TTO 3	OO1	OO2	OO3
Itraconazole	10	10	10	10	10	10	10	10	10
Soft paraffin	5	5	5	5	5	5	5	5	5
Cetyl alcohol	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Stearic acid	20	20	20	20	20	20	20	20	20
Herbal oil	4	5	6	4	5	6	4	5	6
Glycerine	45	45	45	45	45	45	45	45	45
Tween 80	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
EDTA	2	2	2	2	2	2	2	2	2
Isopropyl Myristate	4	4	4	4	4	4	4	4	4
Methyl Paraben	5	5	5	5	5	5	5	5	5
Triethanolamine	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

*MO: Mustard oil, TTO: Tea tree oil, OO: Olive oil, q.s: Quantity sufficient

Table 2: Optimized formulae of itraconazole herbal oil-based cream

Formulation code	JO1	JO2	JO3	WGO1	WGO2	WGO3	CO1	CO2	CO3
Itraconazole	10	10	10	10	10	10	10	10	10
Soft paraffin	5	5	5	5	5	5	5	5	5
Cetyl alcohol	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Stearic acid	20	20	20	20	20	20	20	20	20
Herbal oil	4	5	6	4	5	6	4	5	6
Glycerine	45	45	45	45	45	45	45	45	45
Tween 80	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
EDTA	2	2	2	2	2	2	2	2	2
Isopropyl Myristate	4	4	4	4	4	4	4	4	4
Methyl Paraben	5	5	5	5	5	5	5	5	5
Triethanolamine	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

*JO: Jojoba oil, WGO: Wheat germ oil, CO: Combined oil, q.s: Quantity sufficient

cream was improved. The prepared cream was evaluated for various parameters, namely, physical appearance, pH, drug content, viscosity, and spreadability. The physical appearance of all prepared cream is good and pH was found in the range of 6.14 ± 0.02 – 7.4 ± 0.04 . The type of emulsion of cream was found to w/o. The drug content of prepared cream was found to be $85.32 \pm 0.12\%$ – $96.42 \pm 0.12\%$. The viscosities of different formulations were found to be in the range of 5498 ± 42.21 – 8829 ± 23.02 cp. Data are tabulated in Tables 4 and 5.

In vitro diffusion study

In vitro release studies of the prepared cream formulations (MO1-MO3, TTO1-TTO3, OO1-OO3, JO1-JO3, WGO1-WGO3, and CO1-CO3) were done by Franz diffusion cell. Cumulative percent drug release of all formulations was between $42.11 \pm 1.21\%$ and $59.43 \pm 1.18\%$,

respectively. Through, all the formulations MO2 and CO2 show the best *in vitro* drug release, that is, $55.45 \pm 1.10\%$ and $59.43 \pm 1.18\%$ within 480 min (Fig. 4). These two final formulations were further subjected to the comparison of the marketed formulation. Data are tabulated in Tables 6 and 7.

In vitro diffusion study for final formulation

The optimized final formulation (MO2 and CO2) was subjected to *in vitro* diffusion studies with the marketed formulation. The cumulative percent drug release of MO2 was $55.45 \pm 0.10\%$, CO2 was $61.98 \pm 0.10\%$, and the marketed formulation was $57.72 \pm 0.14\%$ respectively. Therefore, from the data, formulation CO2 shows better results while comparing to the MO2 formulation as well as the marketed formulation. The results are shown in Table 8.

DISCUSSION

Itraconazole herbal oil-based creams were prepared using different oils with their different optimized concentrations (4-6%). Preformulation studies show purity and identification of the drug and all the data were with the specific limits. Different optimized formulations were prepared using different concentrations of oils. All the formulation exhibits good consistency and good tube extrudability [18,19]. The drug content of all the formulations was within the standard limits. The spreadability of all the formulation was between 6.11 ± 0.13 and 9.76 ± 0.31 cm (Tables 4 and 5). Formulation JO₂ shows the highest spreadability; 9.76 ± 0.31 cm and formulation CO₂ shows the highest

Table 3: Calibration curve of itraconazole

Conc. ($\mu\text{g/ml}$)	Absorbance (mean \pm SD, n=3)
0	0
2	0.135 ± 0.004
4	0.231 ± 0.002
6	0.335 ± 0.004
8	0.444 ± 0.001
10	0.578 ± 0.002
12	0.68 ± 0.003
14	0.77 ± 0.001

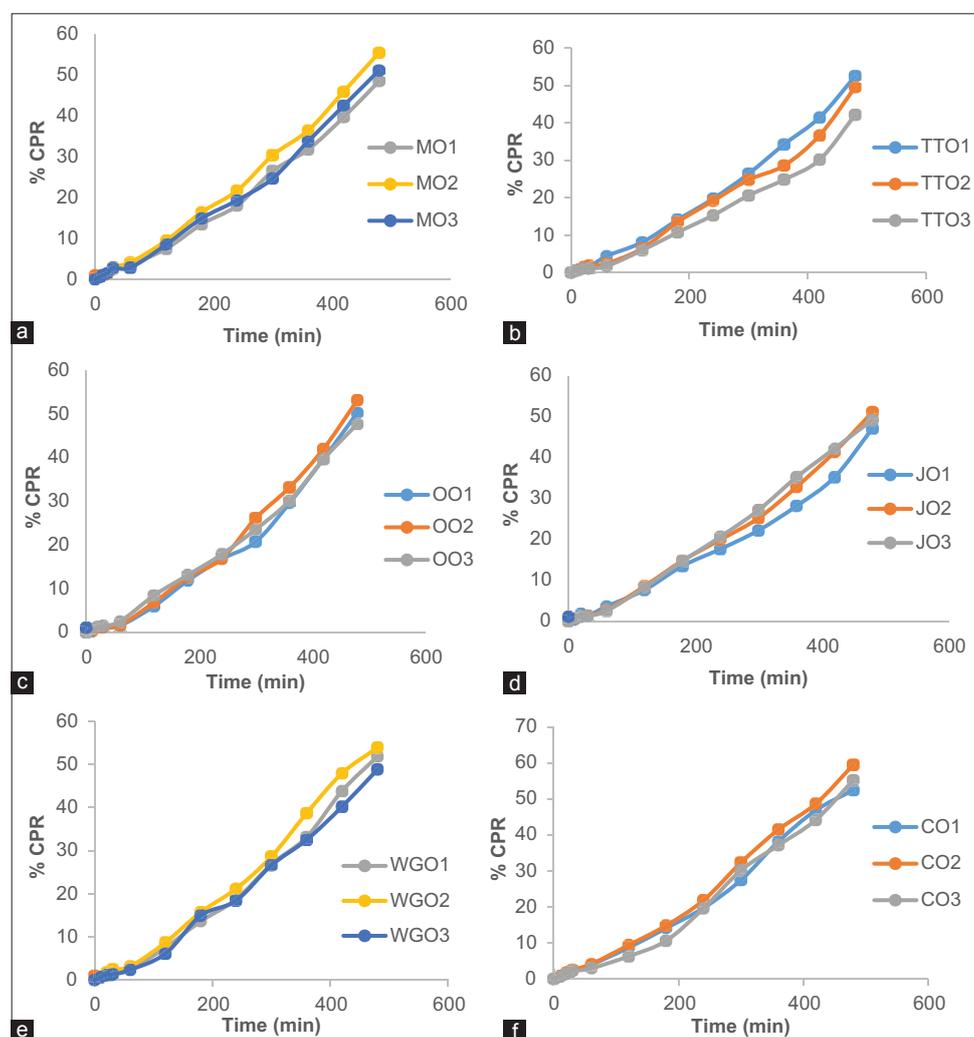


Fig. 4: *In vitro* diffusion study of different formulations (a) mustard oil, (b) tea tree oil, (c) olive oil, (d) jojoba oil, (e) wheat germ oil, (f) combined oil

Table 4: Evaluation parameter for optimized formulation

Parameters	MO1	MO2	MO3	TT01	TT02	TT03	OO1	OO2	OO3
Color	Light yellow	White	White	White					
Feel	Not smooth	Smooth	Smooth	Not smooth	Smooth	Smooth	Smooth	Smooth	Smooth
Consistency	Not good	Good	Good	Not good	Good	Good	Not good	Good	Good
pH	6.27±0.03	6.50±0.01	6.29±0.04	6.31±0.04	6.58±0.01	6.41±0.01	6.25±0.02	6.61±0.01	6.14±0.02
% Drug content	92.32±0.14	91.32±0.11	86.34±0.10	89.52±0.13	91.14±0.13	85.32±0.12	88.34±0.14	92.23±0.12	89.44±0.09
Spreadability (cm)	6.45±0.13	9.17±0.12	7.15±0.18	6.48±0.10	8.49±0.11	7.24±0.24	7.16±0.21	8.43±0.13	7.11±0.04
Tube extrudability	Good	Excellent	Good	Good	Good	Good	Good	Excellent	Good
Viscosity (cp)	5498±42.21	8542±12.45	7432±15.45	6469±33.65	7845±32.78	7065±32.14	8045±12.54	7965±32.11	6678±21.65

*mean±SD, n=3, SD: Standard deviation, cp: Centipoise, cm: Centimeter, MO: Mustard oil, TTO: Tea tree oil, OO: Olive oil

Table 5: Evaluation parameter for optimized formulation

Parameters	JO1	JO2	JO3	WGO1	WGO2	WGO3	CO1	CO2	CO3
Color	White	White	White	White	White	White	Light yellow	Light yellow	Light yellow
Feel	Smooth	Smooth	Smooth	Not smooth	Smooth	Smooth	Smooth	Smooth	Smooth
Consistency	Good	Good	Good	Not good	Good	Good	Good	Good	Good
pH	6.5±0.02	6.8±0.02	7.4±0.04	7.2±0.03	6.5±0.01	7.4±0.02	7.4±0.03	6.7±0.01	7.2±0.04
Drug content	91.41±0.01	95.44±0.14	89.53±0.12	88.52±0.11	94.72±0.23	91.42±0.12	91.41±0.30	96.42±0.12	89.42±0.22
Spreadability (cm)	6.11±0.13	9.76±0.31	8.43±0.53	7.54±0.11	8.71±0.21	8.32±0.14	7.16±0.13	9.23±0.23	8.19±0.11
Tube extrudability	Good	Excellent	Good						
Viscosity (cp)	8147±11.45	6836±21.65	7951±31.21	7894±25.14	7568±14.65	7987±32.24	8519±42.61	8829±23.02	7532±12.35

*mean±SD, n=3, SD: Standard deviation, cp: Centipoise, cm: Centimeter, JO: Jojoba oil, WGO: Wheat germ oil, CO: Combined oil

Table 6: In vitro diffusion study of optimized formulations

Time (min)	MO1	MO2	MO3	TT01	TT02	TT03	OO1	OO2	OO3
% cumulative drug release									
0	0	0	0	0	0	0	0	0	0
10	0.69±1.12	0.98±1.16	0.78±1.23	0.82±1.11	0.73±1.12	0.56±1.12	0.24±1.23	0.39±1.16	0.77±1.20
20	1.16±1.18	1.29±1.17	1.45±1.12	1.19±1.14	1.42±1.14	1.2±1.24	1.19±1.25	1.06±1.18	1.27±1.19
30	2.38±1.11	2.95±1.12	2.82±1.14	1.42±1.15	1.89±1.11	1.19±1.21	1.14±1.14	1.24±1.18	1.49±1.12
60	3.65±1.14	4.17±1.10	2.85±1.12	4.45±1.15	2.49±1.12	1.77±1.12	1.52±1.9	1.62±1.20	2.45±1.18
120	7.45±1.15	9.45±1.14	8.48±1.11	8.12±1.16	6.45±1.15	5.98±1.12	5.98±1.20	6.86±1.25	8.43±1.15
180	13.49±1.12	16.42±1.17	14.89±1.17	14.11±1.12	13.51±1.14	10.79±1.18	11.86±1.11	12.64±1.19	13.11±1.14
240	18.04±1.12	21.67±1.11	19.32±1.15	19.76±1.10	19.18±1.18	15.35±1.18	16.78±1.18	16.85±1.28	17.84±1.21
300	26.45±1.10	30.34±1.10	24.65±1.10	26.42±1.09	24.81±1.19	20.61±1.17	20.71±1.25	26.11±1.24	23.56±1.24
360	31.75±1.15	36.41±1.09	33.75±1.12	34.26±1.09	28.61±1.21	24.85±1.19	29.61±1.27	33.17±1.21	30.14±1.22
420	39.65±1.14	45.91±0.21	42.44±1.14	41.45±1.13	36.68±1.25	30.17±1.19	39.68±1.11	41.98±1.22	39.61±1.16
480	48.49±1.16	55.45±0.10	51.11±1.15	52.43±1.11	49.51±1.21	42.11±1.21	50.24±1.16	53.11±1.17	47.73±1.10

*mean±SD, n=3, SD: Standard deviation, MO: Mustard oil, TTO: Tea tree oil, OO: Olive oil

Table 7: In vitro diffusion study of optimized formulations

Time (min)	JO1	JO2	JO3	WGO1	WGO2	WGO3	CO1	CO2	CO3
% cumulative drug release									
0	0	0	0	0	0	0	0	0	0
10	0.43±1.21	0.69±1.25	0.71±1.17	0.65±1.21	0.79±1.11	0.68±1.23	0.77±1.15	0.88±1.12	0.69±1.28
20	1.75±1.12	1.18±1.24	1.15±1.18	1.13±1.22	1.78±1.10	1.18±1.15	1.62±1.15	1.79±1.18	1.58±1.14
30	1.26±1.20	1.42±1.18	1.26±1.19	1.37±1.10	2.52±1.18	1.33±1.10	2.33±1.15	2.62±1.13	2.21±1.11
60	3.58±1.10	2.76±1.14	2.48±1.20	2.41±1.18	3.16±1.15	2.39±1.14	3.98±1.24	4.15±1.21	2.98±1.19
120	7.63±1.18	8.52±1.15	8.21±1.11	7.54±1.16	8.72±1.21	6.14±1.18	8.72±1.18	9.42±1.11	6.33±1.14
180	13.48±1.16	14.78±1.12	14.65±1.15	13.65±1.14	15.74±1.26	14.94±1.10	14.12±1.11	14.85±1.18	10.62±1.13
240	17.63±1.14	19.92±1.11	20.63±1.11	18.72±1.22	21.18±1.15	18.43±1.19	19.75±1.17	21.86±1.19	19.63±1.20
300	22.18±2.02	25.17±1.10	27.12±1.12	26.85±1.19	28.65±1.28	26.62±1.15	27.47±1.14	32.32±1.20	30.17±1.24
360	28.14±1.14	32.81±1.14	35.17±1.15	33.18±1.14	38.71±1.10	32.53±1.20	38.16±1.20	41.46±1.24	37.13±1.22
420	35.16±1.11	41.32±1.11	42.18±1.22	43.85±1.17	47.95±1.14	40.21±1.17	46.83±1.22	48.65±1.17	44.18±1.10
480	47.11±1.19	51.09±1.17	49.21±1.28	51.85±1.15	53.89±1.27	48.81±1.13	52.45±1.19	59.43±1.18	55.16±1.17

*mean±SD, n=3, SD: Standard deviation, JO: Jojoba oil, WGO: Wheat germ oil, CO: Combined oil

viscosity of 8829±23.02 cp. *In vitro* diffusion studies were performed using a modified Franz diffusion cell. All the data are shown in Tables 6 and 7. Formulation MO₂ and CO₂ shows the highest percent drug release rest of all. MO₂ shows 55.45±0.10% and CO₂ shows 59.43±1.18% drug

release [23]. Both the final formulations were subject further diffusion study with the marketed formulation and found that formulation CO₂ was the best formulation among two and shows a percent drug release of 61.98±1.10% (Table 8 and Fig. 5).

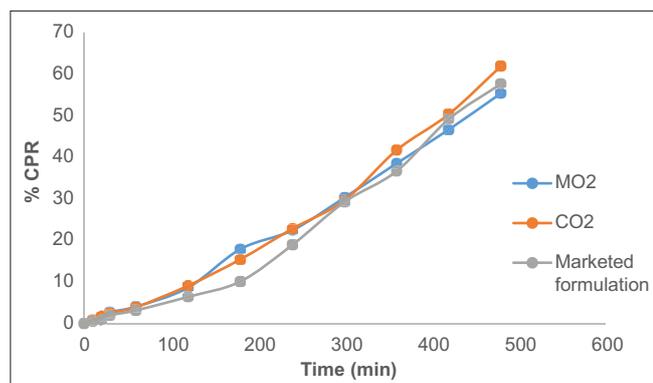


Fig. 5: Comparison of drug release profile of final formulations (MO2 and CO2) with marketed formulation

Table 8: *In vitro* diffusion study for final formulations (MO2 and CO2) with marketed formulation

Time (min)	MO ₂	CO ₂	Marketed formulation
	% cumulative drug release		
0	0	0	0
10	0.88±1.12	0.84±1.15	0.55±1.13
20	1.49±1.13	1.81±1.14	0.97±1.09
30	2.75±1.16	2.52±1.10	1.99±1.10
60	4.07±1.12	3.95±1.09	3.18±1.18
120	8.65±1.12	9.12±1.06	6.44±1.14
180	17.92±1.14	15.45±1.08	10.13±1.14
240	22.47±1.13	22.84±1.10	18.96±1.12
300	30.34±1.11	29.69±1.12	29.29±1.13
360	38.58±1.10	41.76±1.11	36.71±1.15
420	46.72±1.08	50.41±1.10	49.22±1.16
480	55.45±1.10	61.98±1.10	57.72±1.14

*mean±SD, n=3, SD: Standard deviation, MO: Mustard oil, CO: Combined oil

CONCLUSION

The herbal oil-based creams were prepared by the trituration method. Six herbal oils were used, namely, MO, OO, JO, TTO, WGO, and CO. Each oil was formulated different formulations with different ratio of oils. Preformulation data were within the specified limits. From the complete discussion, it was concluded that CO₂ is the best formulation among all. The various parameters of CO₂ formulation were found, namely, drug content was 95.55±0.12%, viscosity was 8419±42.61 cps, spreadability was 8.23±0.13 cm excellent tube extrudability, and percent drug release was 59.43±1.18% within 480 min which was greater than rest of the formulations. Hence, herbal oil-based cream of itraconazole improves patient compliance, ease of administration, local bioavailability, and better prove for fungal infected patients.

AUTHORS' CONTRIBUTIONS

All the author have contributed equally.

CONFLICTS OF INTEREST

None.

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