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Original Research Article

Comparative Clinical Effectiveness and Safety of Super-Bioavailable Itraconazole and Conventional Itraconazole Capsules in the Management of Recalcitrant, Recurrent and Relapsing Superficial Dermatophytosis: An Analytical Interventional Study

Deepak Kumar[1], Prem Prakash Pravakar[2], Md. Mobarak Hussain[3], Shikha Kumari[4]

[1]Senior Resident, Department of Skin & V.D., Anugrah Narayan Magadh Medical College & Hospital, Gaya Ji

[2]Associate Professor, Department of Skin & V.D., Anugrah Narayan Magadh Medical College & Hospital, Gaya Ji

[3]Senior Resident, Department of Skin & V.D., Anugrah Narayan Magadh Medical College & Hospital, Gaya Ji

[4]Junior Resident, Department of Skin & V.D., Anugrah Narayan Magadh Medical College & Hospital, Gaya Ji

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Corresponding Author: Dr. Md Mobarak Hussain

Conflict of interest: Nil

Abstract

Background: The rising prevalence of chronic, recurrent and relapsing dermatophytosis in India has become a major therapeutic challenge. Conventional itraconazole remains a commonly prescribed systemic antifungal agent; however, its variable absorption and bioavailability may affect treatment outcomes. Super-bioavailable itraconazole has been developed to overcome these pharmacokinetic limitations.

Objectives: To compare the clinical effectiveness and safety of super-bioavailable itraconazole and conventional itraconazole in the treatment of recalcitrant, recurrent and relapsing superficial dermatophytosis.

Methods: A prospective analytical interventional study was conducted among 100 adult patients with KOH-confirmed superficial dermatophytosis. Patients received either conventional itraconazole 200 mg once daily or super-bioavailable itraconazole 130 mg once daily for four weeks. Clinical effectiveness was assessed using Total Symptom Score (TSS) and Extent of Lesion Score. Safety was evaluated by recording adverse events. Patients achieving significant cure were followed for recurrence over an additional four weeks.

Results: Ninety patients completed the treatment phase. At week 4, significant clinical cure was observed in 58% of patients receiving super-bioavailable itraconazole compared with 36% receiving conventional itraconazole ($p=0.03$). Mean reduction in TSS was greater in the super-bioavailable itraconazole group ($\Delta TSS=5.23$) than in the conventional itraconazole group ($\Delta TSS=4.38$). Both treatments were well tolerated, with only mild gastrointestinal adverse events reported. Recurrence was observed in both groups without a statistically significant difference.

Conclusion: Super-bioavailable itraconazole demonstrated superior clinical effectiveness compared with conventional itraconazole while maintaining a comparable safety profile.

Keywords: Dermatophytosis, Tinea, Itraconazole, Super-Bioavailable Itraconazole, Antifungal Therapy.

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Introduction

Dermatophytosis comprises a group of superficial fungal infections caused by keratinophilic fungi belonging to the genera Trichophyton, Microsporum and Epidermophyton. These organisms invade keratinized tissues including the stratum corneum, hair and nails, resulting in a variety of clinical presentations such as tinea corporis, tinea cruris, tinea faciei, tinea pedis and onychomycosis. Dermatophytosis represents one of the most common infectious dermatoses worldwide and contributes substantially to outpatient dermatology visits, particularly in tropical and subtropical regions where warm and humid climatic conditions favour fungal growth and transmission.[1] Over the last decade, India has witnessed a remarkable epidemiological shift in the pattern of dermatophytic infections. Previously regarded as a relatively straightforward condition with predictable therapeutic outcomes, dermatophytosis has increasingly manifested as chronic, recurrent,

recalcitrant and relapsing disease. Numerous investigators have described this phenomenon as the "Indian epidemic of dermatophytosis," characterized by extensive body surface involvement, prolonged disease duration, frequent recurrence and reduced responsiveness to conventional antifungal therapy.[2-5] This changing clinical profile has emerged as a major public health concern because of its adverse effects on quality of life, occupational productivity and healthcare expenditure.

Several factors have been implicated in the emergence of chronic and recurrent dermatophytosis. The widespread availability and irrational use of fixed-dose topical corticosteroid combinations is considered one of the most important contributors. Inappropriate corticosteroid use suppresses local immune responses, alters clinical morphology and may facilitate persistence of fungal infection. Additional factors including poor treatment adherence, reinfection from infected family members, environmental contamination, host susceptibility and emerging antifungal resistance have also been proposed.[2-5] Molecular studies have demonstrated a predominance of Trichophyton mentagrophytes genotype VIII and increasing reports of terbinafine resistance among dermatophyte isolates in India, further complicating disease management.[5-7]

Systemic antifungal therapy remains the cornerstone of treatment for extensive, recurrent and recalcitrant dermatophytosis. Among currently available oral antifungal agents, itraconazole has emerged as one of the most frequently prescribed drugs because of its broad antifungal spectrum, favourable pharmacodynamic profile and ability to achieve high concentrations within keratinized tissues. Itraconazole acts by inhibiting fungal cytochrome P450-dependent 14α-demethylase, thereby interfering with ergosterol synthesis and disrupting fungal cell membrane integrity.[8] Despite its widespread use, conventional itraconazole capsules exhibit several pharmacokinetic limitations that may influence therapeutic efficacy. Absorption of the drug is highly dependent upon gastric acidity and food intake. Consequently, co-administration with proton pump inhibitors, H_2 receptor antagonists or conditions associated with reduced gastric acidity may significantly decrease systemic drug exposure. Furthermore, conventional formulations demonstrate considerable intra-patient and inter-patient variability in absorption, resulting in unpredictable serum and tissue concentrations.[9] These limitations may contribute to inconsistent clinical outcomes and treatment failure in patients with difficult-to-treat dermatophytosis. To address these shortcomings, a novel formulation known as superbioavailable itraconazole (SBITZ) has been developed. The formulation employs a pH-dependent polymeric matrix technology that improves dissolution characteristics and enhances intestinal absorption. Pharmacokinetic studies have demonstrated improved bioavailability, greater systemic exposure and reduced variability compared with conventional itraconazole formulations. In addition, absorption of superbioavailable itraconazole is less affected by food intake and concomitant acid-suppressive therapy, potentially providing more consistent therapeutic drug levels.[9-11] Although pharmacokinetic advantages of superbioavailable itraconazole have been established, there remains a relative paucity of clinical studies directly comparing its effectiveness with conventional itraconazole in patients with chronic, recurrent and relapsing dermatophytosis. Given the growing burden of difficult-to-treat dermatophytic infections in India and the need for more effective therapeutic strategies, the present study was undertaken to compare the clinical effectiveness and safety of superbioavailable itraconazole and conventional itraconazole in the management of recalcitrant, recurrent and relapsing superficial dermatophytosis.

Materials and Methods

Study Design and Setting: This prospective analytical interventional study was conducted in the Department of Dermatology at a tertiary care centre in Bihar from June 2025 to May 2026.

Ethical Considerations: Approval was obtained from the Institutional Ethics Committee before the conduct of the research. Written informed consent was obtained from all participants before enrolment.

Study Population: A total of 100 consecutive patients fulfilling the inclusion criteria were enrolled.

Inclusion Criteria

- Adults aged ≥18 years
- Recalcitrant, recurrent or relapsing dermatophytosis

Exclusion Criteria

- Significant systemic illness
- Diabetes mellitus
- Cardiac disease
- Liver disease
- Immunocompromised state
- Pregnancy and lactation

Study Procedure: Diagnosis was confirmed by direct microscopic examination of skin scrapings after 10% potassium hydroxide preparation.

Patients were allocated into two treatment groups:

Group A: Conventional itraconazole 200 mg once daily

Group B: Superbioavailable itraconazole 130 mg once daily

Both groups received a standard emollient preparation containing light liquid paraffin and white soft paraffin.

No additional systemic or topical antifungal agents were prescribed during the study period.

Clinical Evaluation: The following parameters were recorded at baseline, week 2 and week 4:

1. Erythema
2. Pruritus
3. Scaling
4. Extent of lesion involvement

Each parameter was scored from 0 to 3.

Total Symptom Score (TSS) was calculated by summing individual symptom scores.

Primary Outcome: Proportion of patients achieving significant clinical cure at week 4.

Secondary Outcomes

- Change in Total Symptom Score (ΔTSS)
- Recurrence rate at week 8
- Safety profile

Safety Assessment: All adverse events were documented and graded according to severity.

Statistical Analysis: Data were analysed using SPSS version 24. Quantitative variables were expressed as mean ± standard deviation. Categorical variables were analysed using Chi-square test or Fisher's exact test. A p-value <0.05 was considered statistically significant.

Results

Patient Disposition

A total of 100 patients were enrolled.

SBITZ group:

50 patients enrolled
46 completed treatment
27 completed recurrence assessment

CITZ group:

50 patients enrolled
44 completed treatment
16 completed recurrence assessment

Baseline Characteristics

The two groups were comparable regarding age, gender distribution, disease pattern and baseline severity.

Table 1: Baseline demographic and clinical characteristics of study participants

Parameter	Superbioavailable Itraconazole (n=46)	Conventional Itraconazole (n=44)	P value
Age (years), mean ± SD	35.10 ± 11.25	33.25 ± 10.15	0.541
Male, n (%)	26 (57.25)	25 (58.70)	0.574
Female, n (%)	20 (42.47)	19 (41.14)	0.512
Tinea cruris et corporis, n (%)	20 (43.47)	19 (43.18)	0.467
Tinea corporis, n (%)	13 (28.26)	12 (27.27)	0.537
Tinea cruris, n (%)	8 (17.12)	9 (20.45)	0.564
Tinea corporis et faciei, n (%)	3 (6.50)	2 (4.54)	0.348
Tinea faciei, n (%)	2 (4.12)	2 (4.54)	0.984
Mild BSA involvement, n (%)	8 (17.39)	7 (15.90)	0.431
Moderate BSA involvement, n (%)	17 (36.95)	16 (36.36)	0.364
Severe BSA involvement, n (%)	21 (45.65)	21 (47.72)	0.613
Baseline TSS, mean ± SD	6.13 ± 1.23	6.08 ± 1.65	0.480

SD = Standard deviation; TSS = Total Symptom Score.

Clinical Effectiveness

At week 4, significant clinical cure was achieved in:

SBITZ Group: 58% (27/46)

CITZ Group: 36% (16/44)

The difference was statistically significant (p=0.03).

Table 2: Clinical effectiveness outcomes at week 4

	Superbioavailable Itraconazole (n=46)	Conventional Itraconazole (n=44)	P value
Significant clinical cure, n (%)	27 (58.7)	16 (36.4)	0.03
No significant cure, n (%)	19 (41.3)	28 (63.6)	
Mean reduction in TSS (ΔTSS)	5.23	4.38	0.08

TSS = Total Symptom Score.

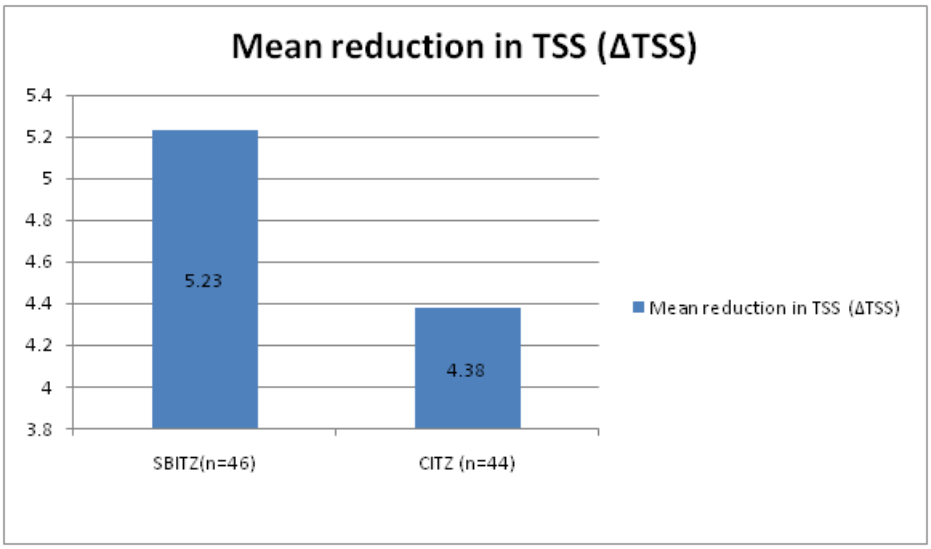


Figure 1:

Improvement in Symptoms

Mean reduction in Total Symptom Score was:

SBITZ Group: 5.23

CITZ Group: 4.38

Although numerically greater in the SBITZ group, statistical significance was not achieved (p=0.08).

Safety Outcomes

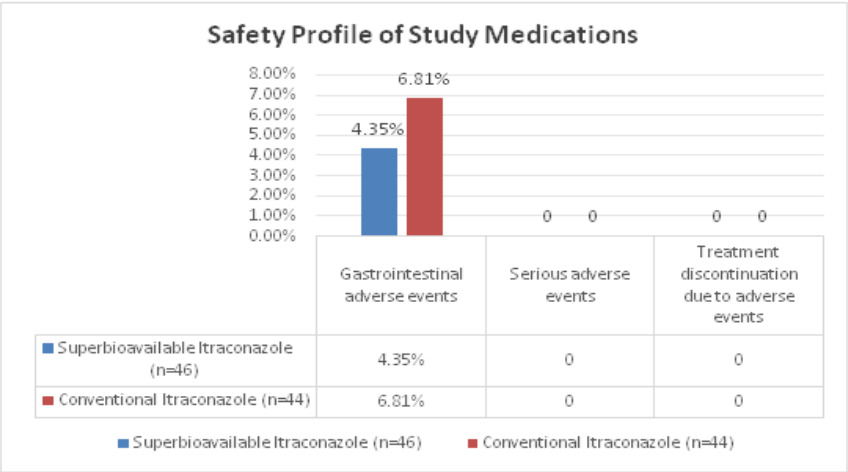


Figure 2:

Both formulations were generally well tolerated.

Only five patients reported mild gastrointestinal adverse events:

SBITZ: 2 patients

CITZ: 3 patients

No serious adverse events were observed.

Table 3: Safety profile of study medications

Adverse Event	Superbioavailable Itraconazole (n=46)	Conventional Itraconazole (n=44)
Gastrointestinal adverse events	2 (4.35%)	3 (6.81%)
Serious adverse events	0	0
Treatment discontinuation due to adverse events	0	0

Values expressed as n (%).

Recurrence Analysis

Table 4: Recurrence analysis at Week 8 (for teaching purposes only)

Outcome	Superbioavailable Itraconazole (n=27)	Conventional Itraconazole (n=16)	P value*
Recurrence present, n (%)	6 (22.2)	5 (31.3)	0.52
Recurrence absent, n (%)	21 (77.8)	11 (68.7)	
Total	27	16	

*Fisher's exact test.

Discussion

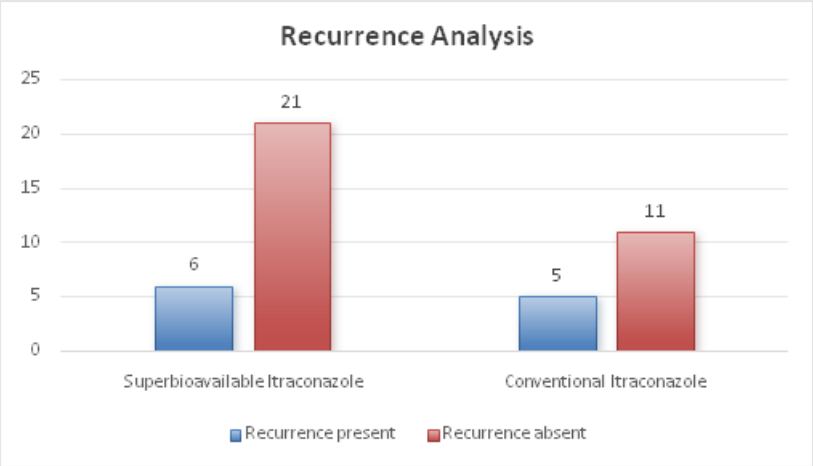


Figure 3:

Recurrence was observed in both treatment groups. Although recurrence was numerically lower in the superbioavailable itraconazole group (22.2%) compared with the conventional itraconazole group (31.3%), the difference was not statistically significant (p=0.52).

The management of superficial dermatophytosis has become increasingly challenging in contemporary dermatological practice, particularly in the Indian subcontinent where chronic and recurrent disease has emerged as a significant therapeutic concern. Several studies have documented increasing rates of treatment failure, prolonged disease duration and recurrence despite the availability of multiple systemic antifungal agents.[2-5] Against this backdrop, optimization of antifungal drug delivery and bioavailability has assumed considerable clinical importance.

In the present study, patients treated with superbioavailable itraconazole demonstrated significantly higher clinical cure rates compared with those receiving conventional itraconazole. Approximately 58% of patients in the superbioavailable itraconazole group achieved significant clinical cure after four weeks of treatment compared with 36% in the conventional itraconazole group. These findings suggest that enhanced bioavailability may confer a meaningful therapeutic advantage in patients with difficult-to-treat dermatophytosis.

The observed superiority of superbioavailable itraconazole is biologically plausible and can be explained by its improved pharmacokinetic characteristics. Conventional itraconazole capsules depend upon gastric acidity for dissolution and subsequent absorption. Consequently, factors such

as food intake, gastric pH variations and concomitant proton pump inhibitor therapy can significantly influence systemic drug exposure.[9] In contrast, superbioavailable itraconazole utilizes a polymer matrix technology designed to improve dissolution and facilitate more predictable absorption. Pharmacokinetic investigations conducted by Abuhelwa et al. demonstrated superior systemic exposure and reduced variability with SUBA-itraconazole compared with conventional formulations.[10] Likewise, Lindsay et al. reported minimal effects of food and omeprazole administration on drug absorption, highlighting the relative independence of the formulation from gastric pH alterations.[11]

An additional finding of the present study was the greater reduction in Total Symptom Score observed among patients receiving superbioavailable itraconazole. Although the difference did not reach statistical significance, the trend toward superior symptomatic improvement supports the primary effectiveness findings. The absence of statistical significance may be attributable to the relatively modest sample size rather than a true absence of clinical benefit. Larger multicentric studies may help clarify whether this observed difference is reproducible and clinically relevant.

The findings of the present study are consistent with the growing body of evidence emphasizing the importance of achieving adequate tissue drug concentrations in dermatophytosis. Because dermatophytes colonize keratinized tissues, successful treatment depends not only on intrinsic antifungal activity but also on sufficient drug penetration into the stratum corneum. Inadequate tissue concentrations may permit persistence of viable fungal elements and contribute to recurrence. Improved bioavailability may therefore translate into superior therapeutic outcomes through enhanced tissue drug delivery.

The safety profile observed in the present study was favourable and comparable between treatment groups. Only five patients experienced mild gastrointestinal adverse effects, and no serious adverse events were reported. These findings are in agreement with previous studies evaluating itraconazole formulations and suggest that enhanced bioavailability does not result in a clinically significant increase in treatment-related toxicity. The low incidence of adverse effects may also contribute to improved treatment adherence and overall patient satisfaction.

Recurrence continues to represent one of the most important unresolved challenges in dermatophytosis management. Although recurrence was observed in both treatment groups, no statistically significant difference was identified. This observation highlights the multifactorial nature of recurrent dermatophytosis. Reinfection from household contacts, contaminated fomites, environmental reservoirs, host immune factors and treatment adherence all influence long-term outcomes. Consequently, optimization of antifungal therapy alone may not completely eliminate recurrence risk. Comprehensive management strategies incorporating patient education, treatment of affected family members and maintenance of personal hygiene remain essential components of care.

The present study possesses several strengths. Diagnosis was confirmed using direct microscopy, thereby improving diagnostic accuracy. The study directly compared two clinically relevant itraconazole formulations and evaluated both effectiveness and safety outcomes. Furthermore, the inclusion of patients with recalcitrant, recurrent and relapsing disease reflects real-world clinical practice and enhances the external validity of the findings.

Nevertheless, certain limitations merit consideration. The study was conducted at a single center and included a relatively small number of participants. Fungal culture and species identification were not performed, precluding analysis of species-specific treatment responses. Therapeutic drug monitoring was not undertaken and serum itraconazole concentrations were therefore unavailable. Additionally, the follow-up period was relatively short and may not fully capture long-term recurrence patterns.

Future multicentric randomized controlled trials incorporating fungal culture, molecular identification, antifungal susceptibility testing and therapeutic drug monitoring would provide a more comprehensive assessment of the comparative efficacy of itraconazole formulations. Long-term follow-up studies are also required to determine whether improved initial cure rates ultimately translate into sustained disease remission. In conclusion, the present study demonstrated that superbioavailable itraconazole was associated with significantly higher clinical cure rates than conventional itraconazole while maintaining a comparable safety profile. These findings suggest that superbioavailable itraconazole may represent an effective therapeutic option for the management of recalcitrant, recurrent and relapsing superficial dermatophytosis in the Indian setting. Given the growing burden of chronic dermatophytosis and the therapeutic challenges associated with conventional treatment approaches, optimization of itraconazole bioavailability may play an important role in improving clinical outcomes.

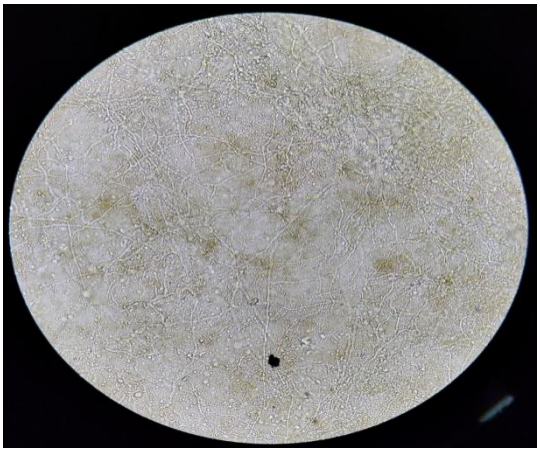
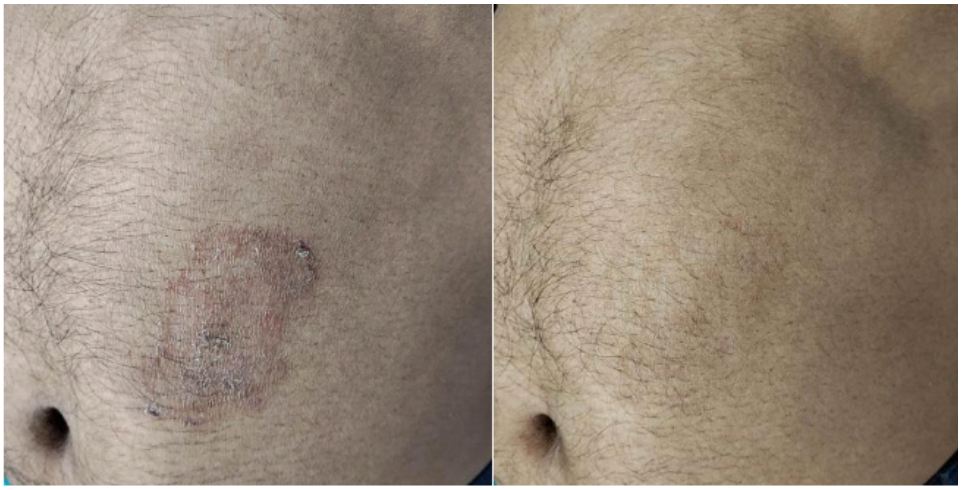
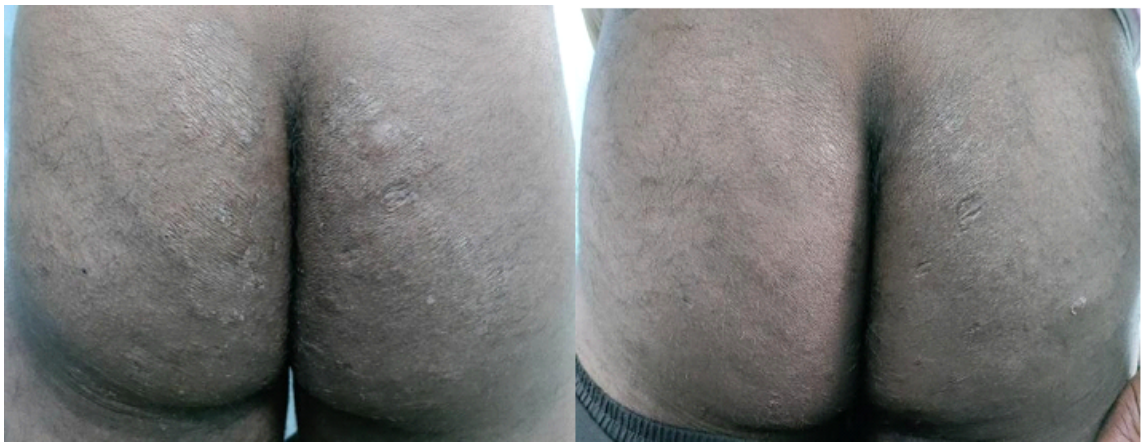


Figure 4: 40x Microscopic Examination of Scrapping After 10% KOH Wet Mount



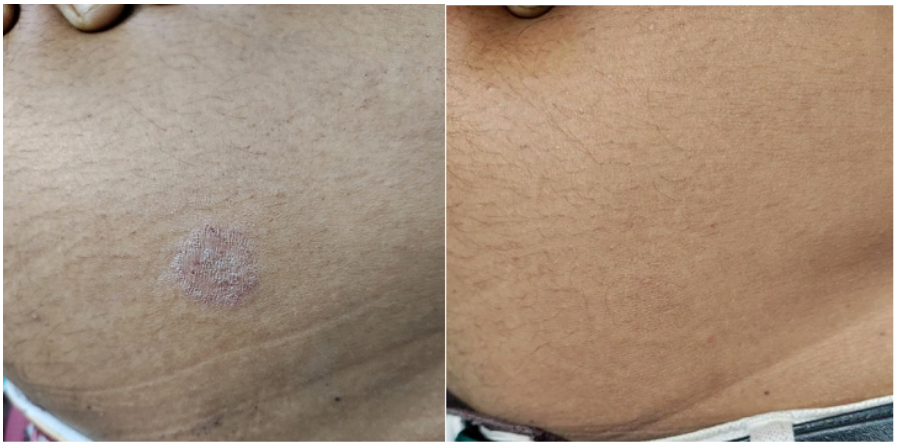
Initial lesion **After 4 weeks of SBITZ Treatment**

Figure 5:



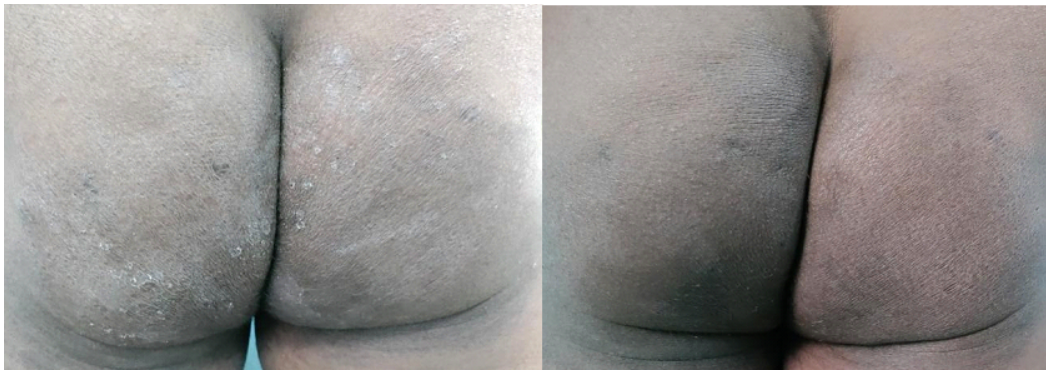
Initial Lesion **After 4 Week of SBITZ Treatment**

Figure 6:



Initial Lesion After 4 Week of SBITZ Treatment

Figure 7:



Initial Lesion After 4 Week of SBITZ Treatment

Figure 8:

Conclusion

Superbioavailable itraconazole demonstrated significantly better clinical cure rates than conventional itraconazole in patients with recalcitrant, recurrent and relapsing superficial dermatophytosis. Both formulations exhibited comparable safety profiles. Superbioavailable itraconazole may therefore represent a valuable therapeutic option for the management of difficult-to-treat dermatophytosis in routine clinical practice.

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Conflicts of Interest: The authors declare no conflicts of interest.

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