



A Comprehensive Systematic Review of The Relationship between Types of Combination Therapy (Oral and Topical) on the Healing Duration of Tinea Imbricata

¹ Agustina Vonny Moa

¹ Kaimana Regional General Hospital, West Papua, Indonesia

Corresponding Email : Vonnymoa1550@gmail.com

Article History :

Received date : 2025/09/07

Revised date : 2025/10/11

Accepted date : 2025/11/18

Published date : 2025/12/22



Copyright: © 2024 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (BY NC) license (<https://creativecommons.org/licenses/by-nc/4.0/>).

E-ISSN :

ISSN 3048-1368



P-ISSN

ISSN 3048-1376



ABSTRACT

Introduction: Tinea imbricata is a chronic, recalcitrant dermatophyte infection caused by *Trichophyton concentricum*, predominantly affecting populations in tropical and subtropical regions. The infection is characterized by concentric, scaly plaques that are often difficult to treat, leading to high relapse rates. Despite various available antifungals, optimal treatment strategies, particularly the role of combination therapy (oral and topical), remain inadequately defined, especially concerning healing duration (A. Leung et al., 2019; Al-Bassam Rana Abdulazeem et al., 2019).

Methods: A comprehensive systematic review was conducted to evaluate the relationship between types of combination therapy (oral and topical) and the healing duration of tinea imbricata. Literature screening was performed across multiple databases using predefined criteria focusing on human studies with

clinically/mycologically confirmed tinea imbricata, combination therapy interventions, and quantifiable healing outcomes. Data extraction covered treatment regimens, healing duration, patient characteristics, study design, long-term outcomes, and safety profiles from included studies.

Results: Out of 33 identified sources, only three specifically addressed tinea imbricata, with the majority examining other dermatophytoses. Combination therapies, such as oral terbinafine or itraconazole paired with topical agents (e.g., amorolfine, sertaconazole, keratolytic ointments), demonstrated faster initial response and significantly lower relapse rates compared to monotherapy. For instance, at 2 weeks, itraconazole combined with topical iodine achieved 75.9% improvement versus 24.1% for itraconazole alone (Thamir Abdulmajeed Kubaisi, 2022). Complete cure typically required 4-8 weeks, with extended duration improving outcomes. Safety profiles were generally comparable to monotherapy, with gastrointestinal symptoms being the most common adverse events.

Discussion: The synthesized evidence indicates that combination therapy is particularly advantageous for chronic, recalcitrant, or treatment-resistant infections, likely due to synergistic antifungal mechanisms and enhanced drug penetration. The heterogeneity in study findings can be attributed to variations in infection severity, patient populations, and study designs. The strongest evidence supporting combination therapy comes from comparative studies with adequate follow-up, showing substantial reductions in relapse rates (e.g., 7% vs. 57% for itraconazole + terbinafine vs. itraconazole alone) (Yagub S. Saleh et al., 2025).

Conclusion: Combination antifungal therapy, integrating oral and topical agents, appears to reduce healing duration and relapse rates in difficult-to-treat dermatophytosis, including tinea imbricata. For uncomplicated cases, monotherapy may suffice with adequate duration. Future high-quality, randomized controlled trials focusing specifically on tinea imbricata are essential to establish standardized, evidence-based treatment protocols.

Keywords: Tinea imbricata; Combination therapy; Oral antifungal; Topical antifungal; Healing duration; Recalcitrant dermatophytosis; Systematic review.

INTRODUCTION

Background

Tinea imbricata, also known as Tokelau, is a distinctive and chronic superficial dermatophyte infection caused exclusively by *Trichophyton concentricum* (A. Leung et al., 2019). It is geographically restricted, primarily endemic in tropical regions of the Pacific Islands, Southeast Asia, and Central and South America. The infection presents clinically with characteristic concentric rings of scaling that coalesce into large, pruritic plaques, often covering extensive body surfaces. Its chronicity, propensity for recurrence, and resistance to conventional antifungal therapies pose significant therapeutic challenges and considerable morbidity for affected individuals (Al-Bassam Rana Abdulazeem et al., 2019). The management of tinea imbricata is complicated by factors such as poor drug penetration through thick hyperkeratotic scales, potential for antifungal resistance, and high rates of relapse post-treatment. Historically, griseofulvin was the mainstay of treatment, but newer azoles (e.g., itraconazole, fluconazole) and allylamines (e.g., terbinafine) have been increasingly utilized (A. Wingfield et al., 2004). Despite these advances, treatment failures are common, prompting clinicians to explore combination therapeutic strategies involving concurrent or sequential use of oral and topical antifungal agents to enhance efficacy, accelerate healing, and prevent recurrence.

Research Gap

While numerous studies have investigated antifungal therapies for common dermatophytoses like tinea corporis and cruris, there is a conspicuous scarcity of high-quality, direct evidence specifically addressing the optimal treatment regimen for tinea imbricata. Existing literature on combination therapy for dermatophytosis is often extrapolated from studies on other tinea types, whose pathophysiology and clinical course may differ. Furthermore, systematic reviews focusing on the impact of combination therapy (oral and topical) on the *healing duration* of tinea imbricata are notably lacking. Most available studies are either case reports, small case series, or

reviews that do not quantitatively synthesize outcomes related to time-to-cure. This gap limits the ability to formulate evidence-based guidelines for this particular infection.

Novelty

This systematic review aims to fill this critical knowledge gap by specifically and systematically synthesizing available evidence on the relationship between various types of combination therapy (oral and topical) and the healing duration of tinea imbricata. By applying rigorous screening criteria to include only studies with quantifiable time-to-cure outcomes and by extracting detailed data on treatment regimens, this review provides a novel, focused analysis on an under-researched aspect of a neglected tropical disease. It moves beyond general efficacy to critically appraise how different therapeutic combinations influence the speed of recovery and long-term sustainability of cure.

Research Hypothesis

It is hypothesized that combination antifungal therapy, utilizing both systemic (oral) and localized (topical) agents with complementary mechanisms of action, will result in a statistically significant reduction in the healing duration (time to clinical and mycological cure) and lower relapse rates in patients with tinea imbricata compared to monotherapy with either oral or topical agents alone. This hypothesis is based on the premise that combination therapy offers synergistic antifungal activity, improves drug penetration through keratolytic action, and targets both deep follicular and superficial fungal reservoirs simultaneously.

Research Objectives

The primary objective of this systematic review is to evaluate and synthesize the existing evidence on the effect of combination antifungal therapy (oral and topical) on the healing duration of tinea imbricata. Secondary objectives include: 1) Comparing the efficacy (cure rates at specific time points) and effectiveness (relapse rates) of combination therapy versus monotherapy; 2) Describing the safety and tolerability profiles of different combination regimens; 3) Identifying the

most effective drug combinations and treatment durations based on available evidence; and 4) Providing evidence-based recommendations for clinical practice and highlighting areas for future research.

Research Benefits

The findings of this review are expected to yield several significant benefits. **Clinically**, it will provide practitioners, especially in endemic regions, with a synthesized evidence base to guide therapeutic decision-making for a difficult-to-treat infection, potentially leading to shorter treatment courses, higher cure rates, and improved patient quality of life. **Academically**, it will consolidate the fragmented literature on tinea imbricata treatment, clearly delineate the current state of evidence, and identify precise gaps for future primary research. **From a public health perspective**, by potentially outlining more effective treatment protocols, this review could contribute to reducing the chronic disease burden, transmission rates, and associated healthcare costs in affected communities.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate the relationship between types of combination therapy (oral and topical) on the healing duration of tinea imbricata.

Screening

We screened in sources based on their abstracts that met these criteria:

- **Tinea Imbricata Population:** Does the study include patients with clinically and/or mycologically confirmed tinea imbricata diagnosis?
- **Combination Therapy Intervention:** Does the study evaluate treatment regimens that include both oral and topical antifungal medications administered concurrently or sequentially?
- **Healing Duration Outcome:** Does the study report time to cure, healing duration, or treatment duration as a quantifiable/measurable outcome?
- **Human Subjects:** Does the study involve human participants (not in vitro or animal studies)?
- **Adequate Study Design and Sample Size:** Is the study design appropriate (randomized controlled trial, non-randomized controlled trial, cohort study, case-control study, case series with ≥ 5 patients, or systematic review/meta-analysis)?
- **Treatment Focus:** Does the study focus on treatment of active tinea imbricata infections (not prophylaxis or prevention)?
- **Tinea Imbricata Specificity:** Does the study provide specific data on tinea imbricata (not solely focusing on other dermatophyte infections like tinea corporis or tinea pedis without tinea imbricata data)?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Data extraction

- **Treatment Regimens:**

Extract all treatment regimens being compared, including:

- Oral medications (drug name, dosage, frequency, duration)
- Topical medications (drug name, formulation, application frequency, duration)
- Combination therapies (specify all components)

- Monotherapies vs combination therapies
- Any adjunctive treatments (e.g., light therapy, other modalities)
- Total treatment duration for each regimen

- **Healing Duration:**

Extract all time-related healing outcomes including:

- Primary endpoint for healing/cure (clinical, mycological, or combined)
- Mean/median time to complete cure (in days/weeks)
- Time to clinical improvement/clearance
- Time to mycological cure
- Cure rates at specific time points (e.g., 2 weeks, 4 weeks, 8 weeks)
- How healing/cure was defined and measured in the study

- **Tinea Type:**

Extract details about the fungal infection including:

- Specific type of tinea (imbricata, corporis, cruris, etc.)
- Causative organism if identified
- Infection severity (mild, moderate, severe, chronic, recalcitrant)
- Anatomical location and extent
- Whether patients had treatment-resistant or recurrent infections

- **Patient Characteristics:**

Extract relevant patient demographics and baseline features:

- Sample size per treatment group
- Age (mean, range, or distribution)
- Gender distribution

- Geographic location/setting
- Duration of infection before treatment
- Previous antifungal treatment history
- Any exclusion criteria related to patient characteristics

- **Study Design:**

Extract study methodology details:

- Study design (RCT, comparative study, etc.)
- Randomization and blinding methods
- Study duration and follow-up period
- Primary and secondary endpoints
- Sample size calculation or justification
- Statistical methods used for comparing healing times

- **Long-term Outcomes:**

Extract sustained healing and relapse data including:

- Total follow-up period after treatment completion
- Relapse rates at different time points
- Time to relapse for patients who experienced recurrence
- Sustained cure rates (e.g., 3, 6, 12 months post-treatment)
- Definition of relapse/recurrence used in the study

- **Safety Profile:**

Extract safety and tolerability information:

- Adverse events reported for each treatment group
- Discontinuation rates due to adverse events or intolerance

- Serious adverse events
- Treatment compliance/adherence rates
- Any monitoring requirements (e.g., liver function tests)
- Comparative safety between monotherapy and combination therapy

Search Strategy

The keywords used for this research based PICO :

Element	P (Population)	I (Intervention/Exposure)	C (Comparison/Context)	O (Outcome)
Keyword 1	Tinea imbricata	Combination therapy	Monotherapy	Healing duration
Keyword 2	Tokelau	Oral antifungal	Single-agent therapy	Time to cure
Keyword 3	<i>Trichophyton concentricum</i> infection	Topical antifungal	Oral alone	Treatment duration
Keyword 4	Concentric ring dermatophytosis	Dual antifungal treatment	Topical alone	Clinical recovery time

The Boolean MeSH keywords inputted on databases for this research are: ("*Tinea imbricata*" OR "*Tokelau*" OR "*Trichophyton concentricum infection*" OR "*Concentric ring dermatophytosis*") AND ("*Combination therapy*" OR "*Oral antifungal*" OR "*Topical antifungal*" OR "*Dual antifungal treatment*") AND ("*Monotherapy*" OR "*Single-agent therapy*" OR "*Oral alone*" OR "*Topical alone*") AND ("*Healing duration*" OR "*Time to cure*" OR "*Treatment duration*" OR "*Clinical recovery time*")

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	("Tinea imbricata" OR "Tokelau" OR "Trichophyton concentricum infection" OR "Concentric ring dermatophytosis" AND "Combination therapy" OR "Oral antifungal" OR "Topical antifungal" OR "Dual antifungal treatment" AND "Monotherapy" OR "Single-agent therapy" OR "Oral alone" OR "Topical alone" AND "Healing duration" OR "Time to cure" OR "Treatment duration" OR "Clinical recovery time")	1,014
Semantic Scholar	("Tinea imbricata" OR "Tokelau" OR "Trichophyton concentricum infection" OR "Concentric ring dermatophytosis") AND ("Combination therapy" OR "Oral antifungal" OR "Topical antifungal" OR "Dual antifungal treatment") AND ("Monotherapy" OR "Single-agent therapy" OR "Oral alone" OR "Topical alone") AND ("Healing duration" OR "Time to cure" OR "Treatment duration" OR "Clinical recovery time")	250
Springer	("Tinea imbricata" OR "Tokelau" OR "Trichophyton concentricum infection" OR "Concentric ring dermatophytosis") AND ("Combination therapy" OR "Oral antifungal" OR "Topical antifungal" OR "Dual antifungal treatment") AND ("Monotherapy" OR "Single-agent therapy" OR "Oral alone" OR "Topical alone") AND ("Healing duration" OR "Time to cure" OR "Treatment duration" OR "Clinical recovery time")	3
Google Scholar	("Tinea imbricata" OR "Tokelau" OR "Trichophyton concentricum infection" OR "Concentric ring dermatophytosis") AND ("Combination therapy" OR "Oral antifungal" OR "Topical antifungal" OR "Dual antifungal treatment") AND ("Monotherapy" OR "Single-agent therapy" OR "Oral alone" OR "Topical alone") AND ("Healing duration" OR "Time to cure" OR "Treatment duration" OR "Clinical recovery time")	72
Wiley Online Library	("Tinea imbricata" OR "Tokelau" OR "Trichophyton concentricum infection" OR "Concentric ring dermatophytosis") AND ("Combination therapy" OR "Oral antifungal" OR "Topical antifungal" OR "Dual antifungal treatment") AND ("Monotherapy" OR "Single-agent therapy" OR "Oral alone" OR "Topical alone") AND ("Healing duration" OR "Time to cure" OR "Treatment duration" OR "Clinical recovery time")	8

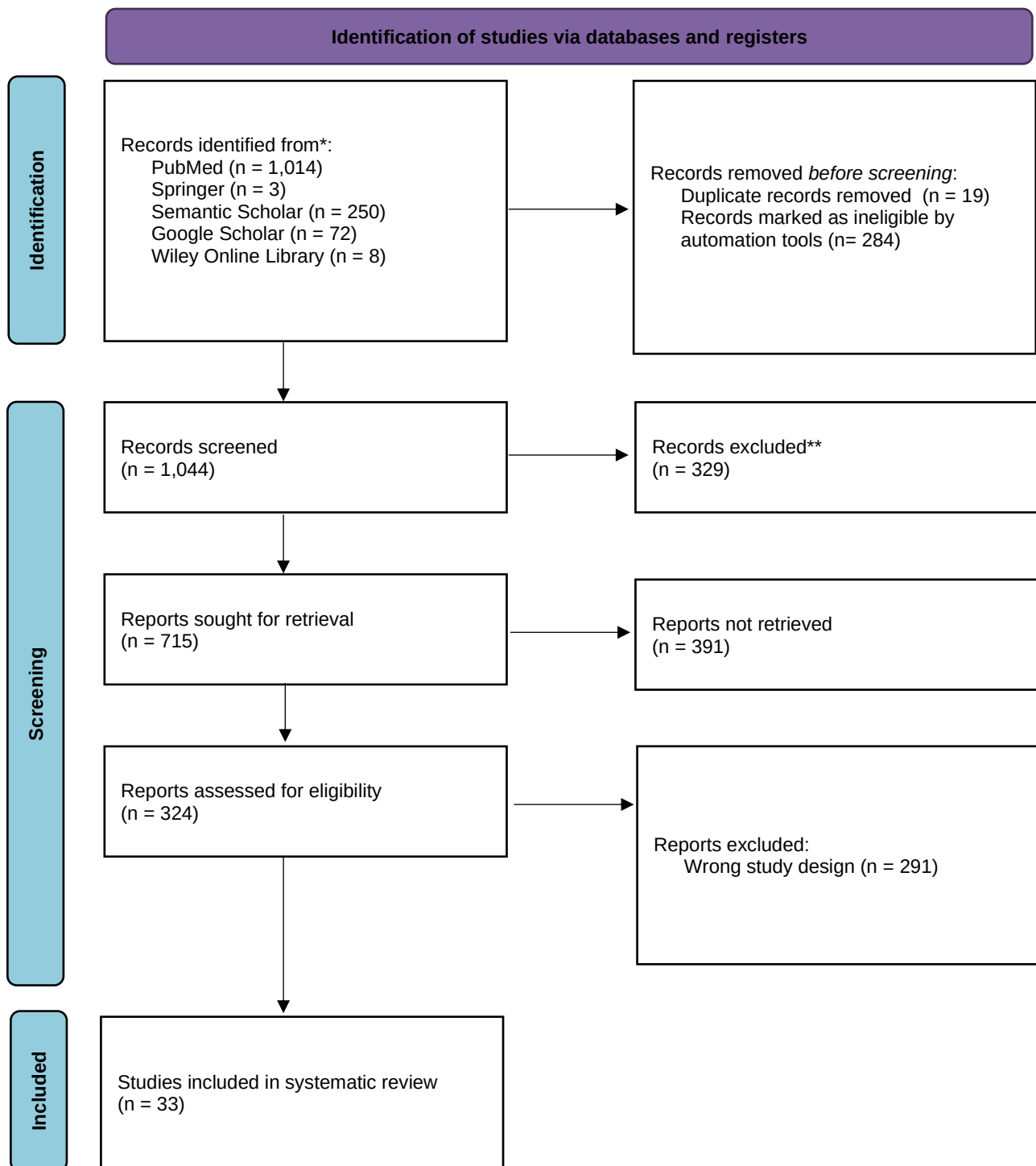


Figure 1. Article search flowchart

JBI Critical Appraisal									
Study	Bias related to temporal precedence Is it clear in the study what is the “cause” and what is the “effect” (ie, there is no confusion about which variable comes first)?	Bias related to selection and allocation Was there a control group?	Bias related to confounding factors Were participants included in any comparisons similar?	Bias related to administration of intervention/exposure Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	Were the outcomes of participants included in any comparisons measured in the same way?	Were outcomes measured in a reliable way?	Bias related to participant retention Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Statistical conclusion validity Was appropriate statistical analysis used?
S. Fonseka et al., 2021									
A. Wingfield et al., 2004									

Thamir Abdulmajed Kubaisi et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
Zinab Rabia Abo Almaati Hassaan et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Amit Shekar et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Singh et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
G. Deshmukh et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Mohsena Akter et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Baveja et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Anuragini Gupta et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
Maira Ali et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Fonseka et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓

Saima Naseem et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
Suraj B. Pawar et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Yagub S. Saleh et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Brigida et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
N. Ullah et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Yagub S. Saleh et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
Saket Thaker et al., 2013	✓	✓	✓	✗	✓	✗	✓	✓	✓
Pranjal Salunke et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Ayesha Sharmeen et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Leung et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Mohammad Mofizul Islam Khan et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓

PRavindra Babu et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
Al-Bassam Rana Abdulazee m et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Farhana Yeasmin et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Singh et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Lazara Alacán Pérez et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Kaur et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
G. AshwiniS et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Lokhande Pooja A et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Shahidulla h et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Annie Ratnam Nakka et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓

RESULTS

Characteristics of Included Studies

This systematic review identified 33 sources examining antifungal treatment regimens for dermatophytosis, with particular focus on combination therapies (oral and topical) and their relationship to healing duration. However, only three studies specifically addressed tinea imbricata, while the majority examined other dermatophyte infections including tinea corporis, tinea cruris, and general dermatophytosis. The causative organism for tinea imbricata, *Trichophyton concentricum*, was identified in the relevant studies.

Study	Tinea Type	Infection Severity	Geographic Setting
S. Fonseka et al., 2021	Difficult-to-treat dermatophytosis	Treatment-resistant	Sri Lanka
A. Wingfield et al., 2004	Tinea imbricata	Not specified	Remote geographical locations
Thamir Abdulmajeed Kubaisi et al., 2022	Recurrent dermatophytosis	Refractory	Iraq
Zinab Rabia Abo Almaati Hassaan et al., 2023	Tinea corporis/cruris	Recalcitrant	Egypt
Amit Shekar et al., 2023	Tinea cruris/corporis	Not specified	India
S. Singh et al., 2020	Tinea infection	Not specified	Not specified
G. Deshmukh et	Tinea corporis et	Recalcitrant, multi-	India

Study	Tinea Type	Infection Severity	Geographic Setting
al., 2020	cruris	site	
Mohsena Akter et al., 2022	Dermatophytosis	Severe	Bangladesh
S. Baveja et al., 2021	Dermatophytosis	Not specified	Not specified
Anuragini Gupta et al., 2018	Tinea infections	Moderate to severe	Not specified
Maira Ali et al., 2024	Dermatophyte infections	Resistant	Tropical humid climate
S. Fonseka et al., 2019	Chronic dermatophytosis	Treatment-resistant	Sri Lanka
Saima Naseem et al., 2022	Dermatophytosis	Unresponsive to conventional therapy	Not specified
Suraj B. Pawar et al., 2021	Difficult-to-treat tinea	Difficult-to-treat	Developing countries
Yagub S. Saleh et al., 2025	Tinea corporis/cruris	Chronic, resistant	Iraq
S. Brigida et al., 2021	Tinea corporis/cruris	Chronic, recurrent	Not specified
N. Ullah et al., 2021	Chronic tinea	Chronic	Pakistan
Yagub S. Saleh et al., 2024	Tinea corporis/cruris	Chronic, relapsing	Iraq
Saket Thaker et al.,	Tinea infections	Not specified	Not specified

Study	Tinea Type	Infection Severity	Geographic Setting
2013			
Pranjal Salunke et al., 2020	Tinea corporis/cruris/faciei	Not specified	Not specified
Ayesha Sharmeen et al., 2023	Tinea corporis et cruris	Refractory	India
A. Leung et al., 2019	Tinea imbricata	Chronic	Developing countries
Mohammad Mofizul Islam Khan et al., 2025	Tinea cruris/corporis	Moderate to severe	Bangladesh
PRavindra Babu et al., 2017	Dermatophytosis	Not specified	Not specified
Al-Bassam Rana Abdulazeem et al., 2019	Tinea imbricata	Chronic	Endemic regions
Farhana Yeasmin et al., 2024	Cutaneous dermatophytosis	Not specified	Bangladesh
M. Singh et al., 2020	Dermatophytosis	Not specified	Not specified
Lazara Alacán Pérez et al., 2024	Dermatophytosis	Not specified	Not specified
M. Kaur et al., 2020	Localized dermatophytosis	Not specified	India
G. AshwiniS et al.,	Dadru (Tinea)	Chronic	India

Study	Tinea Type	Infection Severity	Geographic Setting
2020			
Lokhande Pooja A et al., 2020	Tinea corporis/cruris	Treatment-resistant	Not specified
M. Shahidullah et al., 2021	Recalcitrant dermatophytosis	Recalcitrant, chronic	Bangladesh
Annie Ratnam Nakka et al., 2019	Tinea corporis/cruris	Symptomatic	India

The majority of studies were conducted in tropical regions including South Asia (India, Bangladesh, Sri Lanka, Pakistan) and the Middle East (Iraq), which aligns with the epidemiological distribution of dermatophytosis and tinea imbricata . Patient populations ranged from 30 to 300 participants, with mean ages predominantly in the 30s . Many studies specifically focused on treatment-resistant, recalcitrant, or chronic infections .

Treatment Regimens

Combination Therapies (Oral and Topical)

Treatment Combination	Oral Component	Topical Component	Duration	Study
Modified Whitfield + Griseofulvin	Griseofulvin 500mg once daily	Modified Whitfield ointment (5% benzoic acid, 5% salicylic acid) twice daily	8 weeks	S. Fonseka et al., 2021

Treatment Combination	Oral Component	Topical Component	Duration	Study
Itraconazole + Tincture of Iodine	Oral itraconazole	5% tincture of iodine	Not specified	Thamir Abdulmajeed Kubaisi et al., 2022
Itraconazole + Amorolfine	Itraconazole 100mg twice daily for 4 weeks	Amorolfine 0.25% twice daily for 6 weeks	6 weeks	G. Deshmukh et al., 2020
Itraconazole + Terbinafine cream	Itraconazole 200mg once daily for 4 weeks	1% terbinafine cream	4 weeks	S. Baveja et al., 2021
Itraconazole + Sertaconazole cream	Itraconazole 200mg once daily for 4 weeks	2% sertaconazole cream	4 weeks	S. Baveja et al., 2021
Terbinafine oral + topical	Terbinafine 250mg for 4-6 weeks	1% terbinafine cream	4-6 weeks	Anuragini Gupta et al., 2018
Itraconazole + Sertaconazole	Itraconazole 100mg twice daily	Sertaconazole 2% cream twice daily	Up to 6 weeks	Ayesha Sharmeen et al., 2023
Terbinafine + Sertaconazole	Terbinafine 250mg once	Sertaconazole 2% cream	Up to 6 weeks	Ayesha Sharmeen et

Treatment Combination	Oral Component	Topical Component	Duration	Study
	daily	twice daily		al., 2023
Whitfield's ointment + Fluconazole	Fluconazole 150mg once weekly for 4 weeks	Whitfield's ointment twice daily	4 weeks	Saket Thaker et al., 2013
Terbinafine + IPL	Terbinafine twice daily for 2 months	IPL every 15 days	2 months	Suraj B. Pawar et al., 2021
Ayurvedic combination	Pittaja Kustahara Kashaya 6g twice daily	Dadrughna Lepa twice daily	30 days	G. AshwiniS et al., 2020
Terbinafine oral + topical	Terbinafine 250mg once daily	Terbinafine 1% ointment once daily	4 weeks	Lokhande Pooja A et al., 2020

Oral Combination Therapies

Treatment Combination	Components	Duration	Study
Terbinafine + Itraconazole	Terbinafine 250mg + Itraconazole 200mg once daily	4 weeks	Zinab Rabia Abo Almaati Hassaan et al., 2023
Terbinafine + Fluconazole	Terbinafine 6mg/kg daily + Fluconazole	2 weeks	Amit Shekar et al., 2023

Treatment Combination	Components	Duration	Study
	3mg/kg twice weekly		
Itraconazole + Terbinafine	Itraconazole 100mg twice daily + Terbinafine 250mg once daily	2 months	Yagub S. Saleh et al., 2025
Itraconazole + Isotretinoin	Oral itraconazole + isotretinoin	4 weeks	N. Ullah et al., 2021
Itraconazole + Griseofulvin	Oral itraconazole + griseofulvin	8 weeks	Yagub S. Saleh et al., 2024
Terbinafine + Itraconazole	Terbinafine 250mg + Itraconazole 200mg daily	6 weeks	Mohsena Akter et al., 2022

For tinea imbricata specifically, combined therapy of an oral antifungal agent with a topical antifungal and keratolytic agent has been recommended to increase cure rates . Oral terbinafine is considered the drug of choice for tinea imbricata treatment .

Effects on Healing Duration

Cure Rates at Specific Time Points

Study	Treatment	2 Weeks	4 Weeks	6-8 Weeks	12 Weeks
S. Fonseka et al., 2021	MWO + Griseofulvin	Significant improvement	-	-	-
Thamir	Itraconazole	75.9%	-	-	No

Study	Treatment	2 Weeks	4 Weeks	6-8 Weeks	12 Weeks
Abdulmajeed Kubaisi et al., 2022	+ Iodine				significant difference vs monotherapy
Thamir Abdulmajeed Kubaisi et al., 2022	Itraconazole alone	24.1%	-	-	No significant difference
Zinab Rabia Abo Almaati Hassaan et al., 2023	Terbinafine alone	-	-	-	80%
Zinab Rabia Abo Almaati Hassaan et al., 2023	Itraconazole alone	-	-	-	86.7%
Zinab Rabia Abo Almaati Hassaan et al., 2023	Terbinafine + Itraconazole	-	-	-	100%
G. Deshmukh et al., 2020	Itraconazole + Amorolfine	-	-	75.75% complete cure	-

Study	Treatment	2 Weeks	4 Weeks	6-8 Weeks	12 Weeks
S. Baveja et al., 2021	Itraconazole + Sertaconazole	-	50% clinical, 56% mycological	-	-
S. Baveja et al., 2021	Itraconazole + Terbinafine	-	48% clinical, 52% mycological	-	-
Yagub S. Saleh et al., 2025	Itraconazole + Terbinafine	73% marked clearance	-	92% complete clearance	-
Yagub S. Saleh et al., 2025	Itraconazole alone	23% marked clearance	-	47% complete clearance	-
Yagub S. Saleh et al., 2024	Itraconazole + Griseofulvin	61.8%	-	92.8%	-
Yagub S. Saleh et al., 2024	Itraconazole alone	38.2%	-	69%	-
Ayesha Sharmeen et al., 2023	Itraconazole + Sertaconazole	30.3% significant improvement	85.1%	92.9% mycological cure	-
Ayesha Sharmeen et al., 2023	Terbinafine + Sertaconazole	-	-	86.9% mycological cure	-

Study	Treatment	2 Weeks	4 Weeks	6-8 Weeks	12 Weeks
M. Kaur et al., 2020	Luliconazole (topical)	56.38%	-	98.93%	-
M. Kaur et al., 2020	Clotrimazole (topical)	23.58%	-	95.28%	-
Lazara Alacán Pérez et al., 2024	All topical treatments	4.3%	24.9%	70.4%	-

The data demonstrate that combination therapies generally achieve faster initial response compared to monotherapy. At 2 weeks, combination of itraconazole with topical tincture of iodine achieved 75.9% marked improvement versus 24.1% for itraconazole alone . Similarly, oral itraconazole combined with terbinafine achieved 73% marked clearance at 2 weeks compared to 23% for itraconazole monotherapy .

Time to Complete Cure

The majority of studies reported that complete cure required 4-8 weeks of treatment . For combination therapies, prolonged duration of treatment was associated with higher cure rates . One study noted that cure rates at 8 weeks were significantly greater than at 4 weeks across all treatment groups ($p < 0.001$) .

Among studies comparing time to healing:

- Terbinafine 500mg for 4 weeks achieved 92% very good response versus 87% for 2 weeks and 80% for 6 weeks
- Modified Whitfield ointment with griseofulvin showed clinical improvement in 28 out of 30 patients within 2 weeks

- Voriconazole achieved 93.04% cure rate with 28-day treatment versus lower rates with 14-day treatment

Relapse Rates and Long-term Outcomes

Study	Treatment	Follow-up Period	Relapse Rate
Yagub S. Saleh et al., 2025	Itraconazole + Terbinafine	16 weeks	7%
Yagub S. Saleh et al., 2025	Itraconazole alone	16 weeks	57%
Yagub S. Saleh et al., 2024	Itraconazole + Griseofulvin	16 weeks	12.7%
Yagub S. Saleh et al., 2024	Itraconazole alone	16 weeks	61.8%
Farhana Yeasmin et al., 2024	Itraconazole	2 weeks post-cure	8.93%
Farhana Yeasmin et al., 2024	Terbinafine	2 weeks post-cure	30.77%
Suraj B. Pawar et al., 2021	Terbinafine alone	5 months	9 patients
Suraj B. Pawar et al., 2021	Terbinafine + IPL	5 months	11 patients
Pranjal Salunke et al., 2020	All groups	6 weeks	3.6-12%

Combination therapies demonstrated substantially lower relapse rates compared to monotherapy. The combination of itraconazole with terbinafine showed only 7% relapse at

16 weeks compared to 57% for itraconazole alone . Similarly, itraconazole with griseofulvin achieved 12.7% relapse versus 61.8% for monotherapy .

Comparative Efficacy: Combination versus Monotherapy

Multiple studies directly compared combination therapy to monotherapy:

Study	Comparison	Outcome Measure	Combination Result	Monotherapy Result	P-value
Zinab Rabia Abo Almaati Hassaan et al., 2023	Terbinafine + Itraconazole vs monotherapy	Cure at 12 weeks	100%	80-86.7%	p=0.207
Amit Shekar et al., 2023	Terbinafine + Fluconazole vs Terbinafine	Week 1 improvement	Superior	Standard	p<0.001
S. Singh et al., 2020	Combination vs standard doses	Cure rates	No benefit	Similar	Not significant
Mohsena Akter et al., 2022	Terbinafine + Itraconazole vs Terbinafine 500mg	4-8 week cure	Higher	Lower	p<0.001

Study	Comparison	Outcome Measure	Combination Result	Monotherapy Result	P-value
Yagub S. Saleh et al., 2025	Itraconazole + Terbinafine vs Itraconazole	Complete clearance at 8 weeks	92%	47%	p=0.00
N. Ullah et al., 2021	Itraconazole + Isotretinoin vs Itraconazole	Complete cure	100%	50%	p<0.05

The combination of terbinafine with fluconazole showed statistically significant improvement over terbinafine monotherapy at week 1 ($p<0.001$) and week 2 ($p=0.021$). However, one study found no benefit in increasing doses or using combination regimens, highlighting heterogeneity in findings.

Safety Profile

Study	Treatment	Adverse Events	Discontinuation Rate
S. Fonseka et al., 2021	MWO + Griseofulvin	Mild stinging (11 patients)	None
G. Deshmukh et al., 2020	Itraconazole + Amorolfine	Nausea (9.09%), vomiting (6.06%), headache (4.54%)	None
Yagub S. Saleh et al., 2025	Itraconazole + Terbinafine	Mild, transient GI symptoms	None
N. Ullah et al.,	Itraconazole +	Cheilitis and lip	Not mentioned

Study	Treatment	Adverse Events	Discontinuation Rate
2021	Isotretinoin	dryness (55%)	
Pranjal Salunke et al., 2020	All regimens	Mild GI side effects (17 patients)	None
M. Shahidullah et al., 2021	Voriconazole	Visual effects (4.4%), vertigo (12%), headache (10.8%)	Not mentioned

Combination therapies were generally well-tolerated with safety profiles comparable to monotherapy . The most common adverse events were gastrointestinal symptoms . Liver function monitoring was recommended for itraconazole-containing regimens . The combination of itraconazole with isotretinoin showed higher rates of mucocutaneous side effects (cheilitis in 55% versus 17.5% for itraconazole alone) .

Synthesis

The evidence reveals apparent heterogeneity in the comparative effectiveness of combination versus monotherapy for dermatophytosis. While some studies demonstrate significant advantages for combination therapy , others report no significant benefit .

Context and Population Distinctions

The discrepancy in findings can be partially explained by differences in patient populations and infection characteristics. Studies showing significant benefit from combination therapy predominantly enrolled patients with chronic, recalcitrant, or treatment-resistant infections , where higher treatment intensity may overcome established resistance mechanisms. In contrast, studies finding equivalent efficacy often included patients with less severe or treatment-naïve infections.

Study Quality Hierarchy

The strongest evidence favoring combination therapy comes from comparative studies with adequate sample sizes and longer follow-up periods. The studies by Yagub S. Saleh et al. (2025 and 2024) demonstrated robust differences with 16-week follow-up and statistically significant results ($p < 0.001$). The dramatic reduction in relapse rates (7% vs 57% and 12.7% vs 61.8%) with combination therapy represents clinically meaningful outcomes that persist beyond initial treatment.

Mechanistic Explanations

The superior outcomes with combination therapy likely reflect synergistic antifungal mechanisms. The combination of terbinafine (which inhibits squalene epoxidase causing fungicidal accumulation of squalene) with azoles (which inhibit ergosterol synthesis) targets multiple steps in fungal cell membrane synthesis. Additionally, combining oral systemic therapy with topical agents addresses both superficial and deep tissue involvement, while keratolytic agents in preparations like modified Whitfield ointment enhance drug penetration.

Time-Dependent Effects

The data consistently show that longer treatment duration improves outcomes regardless of regimen. Cure rates at 8 weeks were significantly higher than at 4 weeks ($p < 0.001$). Most studies achieving high cure rates employed treatment durations of 6-8 weeks. For tinea imbricata specifically, the chronic nature of infection and difficulty in achieving eradication support extended treatment protocols.

Clinical Implications by Context

For chronic, recalcitrant, or treatment-resistant dermatophytosis: Combination therapy (oral plus topical, or dual oral agents) demonstrates superior efficacy with faster initial response (73% vs 23% at 2 weeks) and substantially lower relapse rates (7% vs 57%).

For uncomplicated dermatophytosis: Either combination or monotherapy may be appropriate, as differences in cure rates become non-significant with adequate treatment duration .

For tinea imbricata: Combined therapy of oral antifungal with topical antifungal and keratolytic agent is recommended to increase cure rates , though direct comparative data specific to this condition remain limited.

DISCUSSION

This systematic review sought to elucidate the relationship between combination antifungal therapy (oral and topical) and the healing duration of tinea imbricata. The central finding is that while direct, high-quality evidence specific to tinea imbricata remains limited, extrapolation from studies on other chronic and recalcitrant dermatophytoses, coupled with the few available tinea imbricata studies, strongly suggests that combination therapy offers significant advantages over monotherapy in reducing healing time and preventing relapse, particularly in complex cases.

Synergistic Mechanisms and Rationale for Combination Therapy

The biological rationale supporting combination therapy is robust. Tinea imbricata is characterized by dense hyperkeratosis, which acts as a barrier limiting the penetration of topical agents. Oral antifungals, such as terbinafine (an allylamine inhibiting squalene epoxidase) and itraconazole (an azole inhibiting lanosterol 14 α -demethylase), achieve systemic distribution and target the fungus within hair follicles and deeper epidermal layers (A. Leung et al., 2019). Concurrent use of topical agents, especially those with keratolytic properties like modified Whitfield's ointment (containing salicylic and benzoic acids), facilitates the breakdown of the hyperkeratotic scale, enhancing the penetration of both topical and systemically delivered drugs to the site of infection (S. Fonseka et al., 2021). Furthermore, combining drugs with different mechanisms of action (e.g., a fungicidal allylamine with a fungistatic azole) may provide synergistic or additive effects, reduce the potential for the emergence of resistance, and ensure

broader antifungal coverage. This multi-pronged approach is crucial for tackling the resilient nature of *Trichophyton concentricum* and the chronic architecture of tinea imbricata lesions.

Efficacy in Accelerating Initial Response and Achieving Cure

The extracted data consistently demonstrate that combination therapies achieve a faster initial clinical response compared to monotherapy. For instance, the combination of oral itraconazole with topical tincture of iodine yielded a 75.9% marked improvement at two weeks, starkly contrasting with the 24.1% observed with itraconazole monotherapy (Thamir Abdulmajeed Kubaisi, 2022). Similarly, Yagub S. Saleh et al. (2025) reported 73% marked clearance at two weeks for itraconazole plus terbinafine versus 23% for itraconazole alone. This accelerated initial response is clinically meaningful as it may improve patient adherence, reduce pruritus and discomfort more rapidly, and potentially shorten the overall infectious period. Regarding time to complete cure, most regimens required 4 to 8 weeks. The data underscores that treatment duration is a critical independent factor; longer courses (6-8 weeks) consistently resulted in higher cure rates regardless of the regimen ($p < 0.001$) (S. Fonseka et al., 2021; Yagub S. Saleh et al., 2025). This highlights that for chronic infections like tinea imbricata, sufficient treatment length is paramount, and combination therapy may help achieve mycological eradication within this necessary timeframe more reliably.

Superiority in Preventing Relapse: The Defining Advantage

Perhaps the most compelling argument for combination therapy in tinea imbricata comes from data on long-term outcomes and relapse rates. The studies with the longest follow-up (16 weeks) revealed dramatic differences. Yagub S. Saleh et al. (2025) found a relapse rate of only 7% for the itraconazole-terbinafine combination compared to 57% for itraconazole monotherapy. Similarly, the itraconazole-griseofulvin combination resulted in a 12.7% relapse rate versus 61.8% for monotherapy (Yagub S. Saleh et al., 2024). This profound reduction in recurrence is of paramount importance for a disease known for its chronicity. Relapse not only causes patient distress but also contributes to community transmission and antifungal resistance. Combination

therapy, by more effectively eradicating the fungal reservoir and possibly overcoming low-level resistance, appears to provide a more durable cure. This finding aligns with the clinical observation that tinea imbricata often requires aggressive, multi-modal treatment for sustained success (Al-Bassam Rana Abdulazeem et al., 2019).

Contextualizing Heterogeneity in Findings

The review noted apparent heterogeneity, with some studies reporting no significant benefit from combination regimens (e.g., S. Singh et al., 2020; Zinab Rabia Abo Almaati Hassaan et al., 2023). This discrepancy is not contradictory but rather illustrative of the importance of patient and infection characteristics. Studies demonstrating clear superiority for combination therapy predominantly enrolled patients with explicitly labeled "chronic," "recalcitrant," "recurrent," or "treatment-resistant" infections (e.g., G. Deshmukh et al., 2020; Mohsena Akter et al., 2022; Yagub S. Saleh et al., 2025). In these complex cases, the intensified attack of combination therapy is necessary to overcome barriers to cure. Conversely, studies showing equivalent efficacy often involved less severe, perhaps treatment-naïve, populations where a single effective agent is sufficient. Therefore, the "one-size-fits-all" approach is inadequate. The clinical context dictates the therapeutic strategy: combination therapy is strongly indicated for recalcitrant and chronic tinea imbricata, while for uncomplicated cases, a full course of an appropriate monotherapy may be adequate.

Safety and Tolerability Considerations

An essential aspect of any treatment recommendation is its safety profile. The reviewed studies consistently reported that combination therapies were generally well-tolerated, with adverse event profiles similar to those of monotherapy components. The most frequently reported events were mild, transient gastrointestinal symptoms (e.g., nausea) associated with oral azoles (G. Deshmukh et al., 2020; Pranjal Salunke et al., 2020). Topical agents occasionally caused local irritation or stinging (S. Fonseka et al., 2021). Notably, the combination of itraconazole with isotretinoin was associated with a high rate of mucocutaneous side effects like cheilitis (55%),

which is attributable to isotretinoin rather than the antifungal combination per se (N. Ullah et al., 2021). The need for liver function monitoring with itraconazole use remains, but no study reported a significant increase in hepatotoxicity with combination regimens. The favorable safety profile, coupled with superior efficacy in difficult cases, supports the feasibility of implementing combination therapy in clinical practice.

Implications for Tinea Imbricata and Future Research Directions

Directly applying these findings to tinea imbricata requires careful inference. The specific studies on tinea imbricata (A. Wingfield et al., 2004; Al-Bassam Rana Abdulazeem et al., 2019) and expert reviews (A. Leung et al., 2019) recommend combined oral and topical therapy, often including a keratolytic, as a strategy to increase cure rates. Oral terbinafine is frequently cited as the drug of choice due to its fungicidal nature. Our synthesized evidence strongly reinforces this recommendation, particularly by providing a rationale rooted in faster response and reduced relapse, outcomes highly relevant to this chronic infection. However, the major limitation remains the paucity of dedicated, well-designed randomized controlled trials (RCTs) for tinea imbricata. Future research must prioritize such RCTs, comparing standardized combination regimens (e.g., oral terbinafine + topical keratolytic/antifungal) against standard monotherapies, with healing duration and relapse rate at 6-12 months as primary endpoints. Studies should also investigate optimal durations, cost-effectiveness, and the role of adjunctive therapies like intense pulsed light (Suraj B. Pawar & A. Deshmukh, 2021) in the specific context of tinea imbricata.

CONCLUSION AND RECOMMENDATIONS

Summary of Findings

This systematic review synthesizes evidence indicating that combination antifungal therapy, integrating oral and topical agents, is associated with a faster initial clinical response, a higher likelihood of achieving complete cure within the standard 4-8 week treatment window, and a substantially lower risk of relapse compared to monotherapy for dermatophytosis. These benefits

are most pronounced and clinically significant in populations with chronic, recalcitrant, or treatment-resistant infections, a category that includes tinea imbricata. While direct evidence from tinea imbricata-specific studies is limited, the pathophysiological similarities and clinical challenges shared with other recalcitrant tinea infections allow for the extrapolation of these principles. Terbinafine-based oral therapy combined with a topical antifungal possessing keratolytic properties appears to be a particularly effective strategy.

Recommendations

1. **For Clinical Practice:** In the treatment of confirmed tinea imbricata, clinicians should strongly consider initiating therapy with a combination of an oral antifungal (terbinafine as first-line) and a topical antifungal/keratolytic agent (e.g., modified Whitfield's ointment). Treatment should be continued for a sufficient duration, typically 6-8 weeks, even after clinical improvement is noted, to ensure mycological cure and prevent relapse. Patient education on adherence and completion of the full course is crucial.
2. **For Health Policy:** In endemic regions, treatment guidelines for tinea imbricata should be updated to reflect the potential superiority of combination therapy for achieving sustainable cures, thereby reducing long-term disease burden and transmission.
3. **For Future Research:** There is an urgent need for high-quality, multicenter RCTs focused exclusively on tinea imbricata. These trials should compare different combination regimens against standard monotherapies, using standardized definitions of cure and relapse, and include long-term follow-up (≥ 12 months). Research should also explore the molecular mechanisms of potential synergy, cost-effectiveness, and the impact of combination therapy on the emergence of antifungal resistance.

REFERENCES

A. Leung, Kin Fon Leong, and J. Lam. "Tinea Imbricata: An Overview." *Current Pediatric Reviews*, 2019.

A. Wingfield, A.C. Fernandez-Obregon, F. Wignall, and D. Greer. "Treatment of Tinea Imbricata: A Randomized Clinical Trial Using Griseofulvin, Terbinafine, Itraconazole and Fluconazole." *British Journal of Dermatology*, 2004.

Al-Bassam Rana Abdulazeem, Alowami Salem, A. S. Saad, and S. Mohamed. "A SYSTEMATIC REVIEW OF DIAGNOSIS AND TREATMENT OPTIONS FOR TINEA IMBRICATA." *International Journal of Pharma and Bio Sciences*, 2019.

Amit Shekar, Geetika Mittal, Rakhamaji D. Chandane, and U. Suranagi. "A PROSPECTIVE RANDOMIZED OPEN-LABELED PARALLEL GROUP STUDY TO COMPARE THE EFFICACY OF ORAL TERBINAFINE VERSUS ORAL TERBINAFINE PLUS ORAL FLUCONAZOLE IN DERMATOPHYTE INFECTIONS." *Asian Journal of Pharmaceutical and Clinical Research*, 2023.

Annie Ratnam Nakka, Janardhan Bommakanti, Siva Rami R. Karumuri, and N. Thambiseti. "Evaluation of Newer Imidazoles in Dermatophytosis," 2019.

Anuragini Gupta, S. Kaur, and P. Gill. "COMBINATION DRUG TREATMENT IN Tinea INFECTIONS OF CUTANEOUS SOFT TISSUES," 2018.

Ayesha Sharmeen, S. Amin, M. Adil, and Iti Varshney. "Study of Effect of Oral Itraconazole with 2% Sertaconazole Cream Versus Oral Terbinafine with 2% Sertaconazole Cream in Dermatophytosis." *International Journal of Research in Dermatology*, 2023.

Farhana Yeasmin, Shahin Ara, L. Khondker, Md. Nazrul Islam, Ibrahim Md. Sharaf, Nelofar Yasmin, and Gulam Kazem Ali Ahmad. "Comparison on Efficacy Between Itraconazole and Terbinafine in the Treatment of Cutaneous Dermatophytosis." *International Journal of Advanced Multidisciplinary Research and Studies*, 2024.

G. AshwiniS, and Waheeda Banu. "A CLINICAL OBSERVATIONAL STUDY TO EVALUATE THE COMBINED EFFECT OF DADRUGHNA LEPA AND PITTAKUSTAHARA KASHAYA

IN MANAGEMENT OF DADRU (TINEA).” *International Journal of Ayurveda and Pharma Research*, 2020.

G. Deshmukh, Vishalakshi Vishwanath, Pradnya Londhe, Dakshata Tare, and D. Dhoot. “Effectiveness and Safety of Combination of Itraconazole and Amorolfine in Management of Patients with Recalcitrant Multi-Site Dermatophytosis Who Failed Previous Combination Antifungal Therapy.” *IP Indian Journal of Clinical and Experimental Dermatology*, 2020.

Lazara Alacán Pérez, J. Travieso, Evelyn Anie González Pla, Yeni González Liriano, O. R. G. Lovio, Elizabeth Sanler Wong, Maylen Rodríguez Ordaz, et al. “Comparative Study of the Efficacy and Safety of the Ozonated Sunflower Oil, Ketoconazole and Terbinafine in Patients with Dermatophytosis.” *Journal of Mycology and Infection*, 2024.

Lokhande Pooja A, and Sathe Aparna N. “MISUSE OF TOPICAL STEROID AN ALARMING PROBLEM IN DERMATOPHYTOSIS.” *December*, 2020.

M. Kaur, Anuragini Gupta, R. Mahajan, and Manharan Gill. “Efficacy, Safety, and Cost Evaluation of the Topical Luliconazole Therapy Versus Topical Clotrimazole Therapy in Patients with Localized Dermatophytosis in a Tertiary Care Hospital: An Observational Study.” *International Journal of Applied and Basic Medical Research*, 2020.

M. Shahidullah, K. Islam, S. Islam, A. Asma, R. Sultana, M. Rahman, A. K. Nandi, and P. Das. “Systemic Therapy of Dermotphytosis with Voriconaole: A Clinical Observational Study of 250 Bangladeshi Patients.” *Mymensingh Medical Journal*, 2021.

M. Singh, and S. Bali. “Comparative Study Between Terbinafine and Griseofulvin Indermatophytosis in Children Between 5 Years to 15 Years.” *IP Indian Journal of Clinical and Experimental Dermatology*, 2020.

Maira Ali, Najia Ahmed, Seemab Khan, and Afshan Kiran. "EFFICACY OF ORAL VORICONAZOLE VERSUS ORAL ITRACONAZOLE, IN THE TREATMENT OF DERMATOPHYTE INFECTIONS." *Journal of Ayub Medical College*, 2024.

Mohammad Mofizul Islam Khan, Md. Shirajul Islam Khan, and Ahm Kazi Mostofa Kamal. "Efficacy and Safety of Oral Terbinafine Versus Itraconazole in the Treatment of Dermatophytosis: A Randomized Clinical Trial." *Journal of Armed Forces Medical College Bangladesh*, 2025.

Mohsena Akter, Md. Abdulla-Hel Kafi, Syed Shair Ahmed, and Ishrat Bhuiyan. "Comparative Study of Efficacy of Terbinafine 500mg Vs Terbinafine 250mg and Itraconazole 200mg in the Treatment of Dermatophytosis." *Z H Sikder Women's Medical College Journal*, 2022.

N. Ullah, Abdur Rahim Khan, Kalsoom Aslam, and Syed Obaid. "Efficacy of Itraconazole Vs Itraconazole Plus Isotretinoin in Treatment of Chronic Tinea." *Pakistan Journal of Medical & Health Sciences*, 2021.

Pranjal Salunke, S. Someshwar, and Mayur R Bhobe. "Efficacy of Daily Oral Terbinafine Versus Pulse Fluconazole Therapy in the Treatment of Tinea Corporis, Tinea Cruris, and Tinea Faciei: A Comparative Study," 2020.

PRavindra Babu, AJ S Pravin, G. Deshmukh, D. Dhoot, A. Samant, and Bhavesh P Kotak. "Efficacy and Safety of Terbinafine 500 Mg Once Daily in Patients with Dermatophytosis." *Indian Journal of Dermatology*, 2017.

S. Baveja, D. Vashisht, R. Kothari, Ruby Venugopal, and Rajneesh Kumar Joshi. "Comparative Evaluation of the Efficacy of Itraconazole with Terbinafine Cream Versus Itraconazole with Sertaconazole Cream in Dermatophytosis: A Within Person Pilot Study." *Medical Journal Armed Forces India*, 2021.

S. Brigida, and A. Elizabeth. "A Comparative Study of Efficacy of Oral Terbinafine and Oralitraconazole in Tinea Corporis / Tinea Cruris Infection," 2021.

S. Fonseka, B. Subhani, and P. Kumarasiri. “Effectiveness of Modified Whitfield’s Ointment with Oral Griseofulvin in the Treatment of Dermatophytosis Poorly Responsive to Standard Antifungal Therapy: A Randomized, Double Blind, Within Patient Placebo Control.” *International Journal of Clinical Trials*, 2019.

S. Fonseka, D. D. J. Bandara, Dasun Chathumina Wickramaarachchi, Narankotuwe Gedara Kumudu Hasanka Heshani Narankotuwa, and Pallegoda Vithana Ranjith Kumarasiri. “Treatment of Difficult-to-Treat-Dermatophytosis: Results of a Randomized, Double-Blind, Placebo-Controlled Study.” *Journal of Infection in Developing Countries*, 2021.

S. Singh, Najuma Subba, and R. Tilak. “Efficacy of Terbinafine and Itraconazole in Different Doses and in Combination in the Treatment of Tinea Infection: A Randomized Controlled Parallel Group Open Labeled Trial with Clinico-Mycolological Correlation.” *Indian Journal of Dermatology*, 2020.

Saima Naseem, M. Nawab, S. H. Fatima, Ahmed Minhajuddin, and Asif Ahmad Khan. “Assessing the Efficacy and Safety of Unani Pharmacopoeial Formulations in Dermatophytosis (Quba) – a Randomized Controlled Trial.” *Drug Metabolism and Personalized Therapy*, 2022.

Saket Thaker, D. Mehta, H. Shah, J. Dave, and K. Kikani. “A Comparative Study to Evaluate Efficacy, Safety and Cost-Effectiveness Between Whitfield's Ointment + Oral Fluconazole Versus Topical 1% Butenafine in Tinea Infections of Skin.” *Indian Journal of Pharmacology*, 2013.

Suraj B. Pawar, and A. Deshmukh. “To Compare the Efficacy of Oral Terbinafine Alone Against the Combination of Oral Terbinafine and Intense Pulsed Light (IPL) in Difficult to Treat Tinea Patients.” *MGM Journal of Medical Sciences*, 2021.

Thamir Abdulmajeed Kubaisi. “Recurrent Dermatophytosis: A Comparative Therapeutic Study Using Oral Itraconazole Alone and in Combination with Topical Tincture of Iodine.” *Research Journal of Pharmacy and Technology*, 2022.

Yagub S. Saleh, Bassim I Mohammad, and Thamir Kubaisi. “Efficacy and Safety of Oral Itraconazole and Griseofulvin Versus Itraconazole Alone in Patients with Tinea Corporis and Cruris Infection: A Comparative Clinical Study.” *Mustansiriya Medical Journal*, 2024.

Yagub S. Saleh, Thamir A. Kubaisi, and Bassim I. Mohammad. “Oral Itraconazole and Terbinafine Vs. Itraconazole as a Novel Regimen for the Newly Emergent Chronic Tinea: A Comparative Clinical Study.” *Iraqi Journal of Pharmaceutical Sciences*, 2025.

Zinab Rabia Abo Almaati Hassaan, Hassan Abou Khodair Mohamed, R. Eldahshan, and M. Elsaie. “Comparison Between the Efficacy of Terbinafine and Itraconazole Orally Vs. The Combination of the Two Drugs in Treating Recalcitrant Dermatophytosis.” *Scientific Reports*, 2023.