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## A Review on Comparative Study of Topical Antifungal Agents Amorolfine versus Ciclopirox in the Treatment of Onychomycosis



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### ABSTRACT

Onychomycosis, the most frequent cause of nail disease, and its prevalence ranges from 2-13%. It is an important disorder which affect both health and quality of life of patients. So the patient requires prompt and effective treatment.<sup>1,2</sup> Standard treatments include topical medications, systemic therapies, laser therapy, and combination of both systemic and topical therapies. It will affect on both toenails and fingernails and the most affected is toenails because the growth is slower and exposure is more<sup>3,4</sup> Various studies have been conducted to clearly understand the effectiveness of topical antifungal agents like amorolfine and ciclopirox in onychomycosis. Amorolfine 5% and ciclopirox 8% nail lacquers are commonly used for the treatment of onychomycosis. These formulations may be used alone or in combination with oral antifungal agents. Amorolfine and ciclopirox are valuable therapeutic options, however, their usage in monotherapy should be limited. Proper amorolfine and ciclopirox penetration through the nail plate is provided by transungual drug delivery systems. Although amorolfine and ciclopirox have a different mode of action, they both exhibit a broad antifungal activity. The use of antifungal nail lacquers in combination with oral agents, such as terbinafine and itraconazole, improves efficacy of antifungal therapy. The main focus of this review article is to understand the efficacy of topical antifungal amorolfine over topical antifungal ciclopirox.<sup>8,9</sup>



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## INTRODUCTION

Onychomycosis is a fungal infection of nails in which dermatophytes yeast, and non dermatophyte molds as the etiological agents. It is mostly affected on finger nails and toe nails. Although onychomycosis is life threatening, and its high prevalence rate and associated morbidity such as psychosocial effects, occupational discomfort, permanent damage to the nail, spread of the infection to other persons, and high treatment cost have made it an important public health problem.<sup>5,6</sup> Onychomycosis can have significant negative effects on patients' emotional, social, and occupational functioning and can, in addition, consume a sizable proportion of health care dollars. Affected patients may experience embarrassment in social and work situations, where they feel blighted or unclean, unwilling to allow their hands or feet to be seen. Patients may fear that they will transmit their infection to family members, friends, or coworkers, fears that can lead to diminished self-esteem and the avoidance of close relationships.<sup>7</sup>

The main different types of onychomycosis include Distal subungual infection, White superficial infection, Proximal subungual infection, Candidial infection. The treatment is based on the severity of the disease using the SCIO index and the type of the disease.<sup>8</sup>

There are four approved classes of antifungal drugs for the treatment of onychomycosis: the allylamines, azoles, morpholines and hydroxypyridinones. The three main pharmacological strategies are oral treatment, topical treatment and combination therapy.<sup>11,14</sup>

Normally topical agents have generally been as ineffective, mainly because of poor penetration power into the nail plate. However, newer topical agents, such as ciclopirox and amorolfine, have been formulated to provide effective delivery into the nail unit. White superficial will respond best to the topical therapy because of the superficial infection.<sup>10,12</sup>

The anatomy of the nail unit and the process of nail growth may be helpful in understanding the pathogenesis of dermatophytic fungi in the nail unit. It consists of the following structures: proximal and lateral folds, cuticle, matrix, nail plate, nail bed, and hyponychium. Fingernails grow at a rate of 2 to 3 mm per month, and toenails grow at a rate of 1 mm per month. Therefore, it takes about 6 months to replace a fingernail and between 12 and 18 months to replace a toenail. This rate of growth is often decreased in the presence of peripheral vascular disease and onychomycosis and in the elderly. Although the use of topical agents alone or in combination with oral therapies has been disappointing, topical agents may be useful in

preventing the relapse of chronic tinea pedis, which often accompanies onychomycosis. Concomitant use of topical therapy with the newer oral antifungal agents may result in a more rapid cure, a possibility that will be evaluated in clinical trials.

#### **Risk factors for onychomycosis**

Predisposing factor, Increasing age, Family history, Poor general state of health, Frequent nail trauma

Environmental contact with pathogens, Climate conditions, Sports activities, Shared bathing facilities

Occlusive clothing and footwear, Immunosuppressed persons, Prevalence of tinea pedis

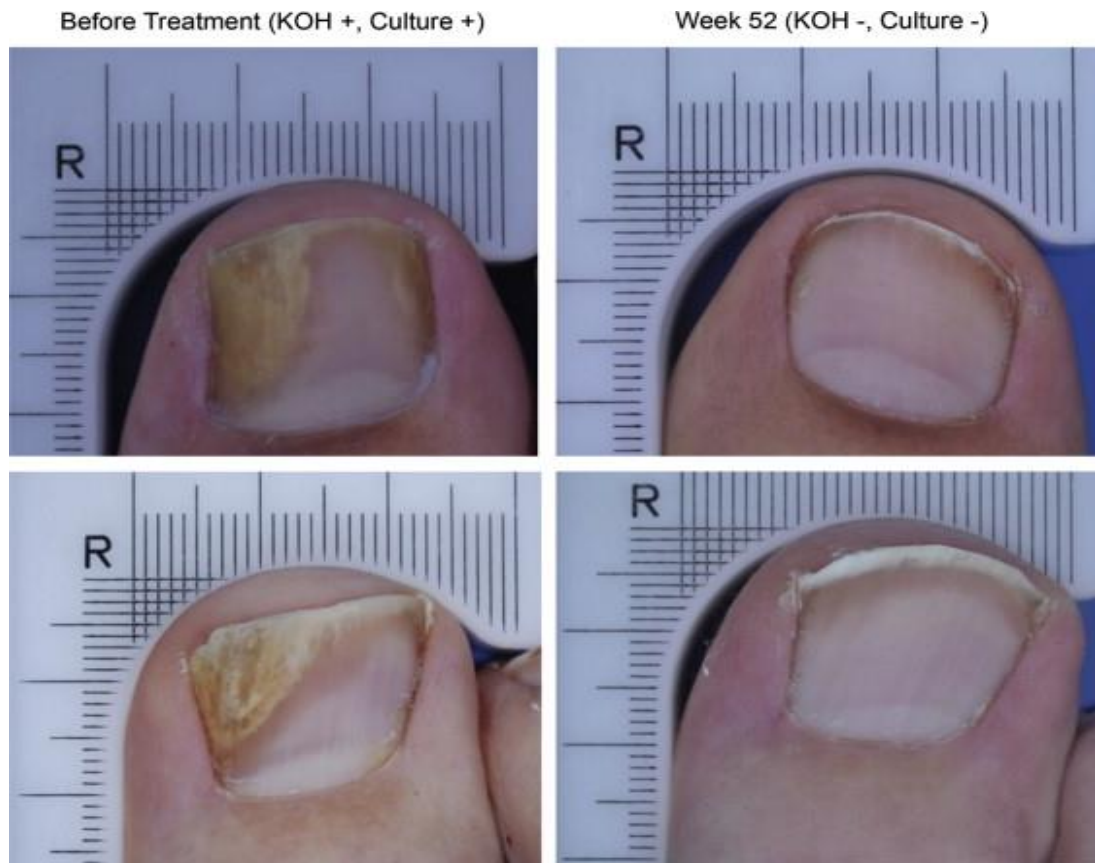
Trauma, Infections

Diabetes

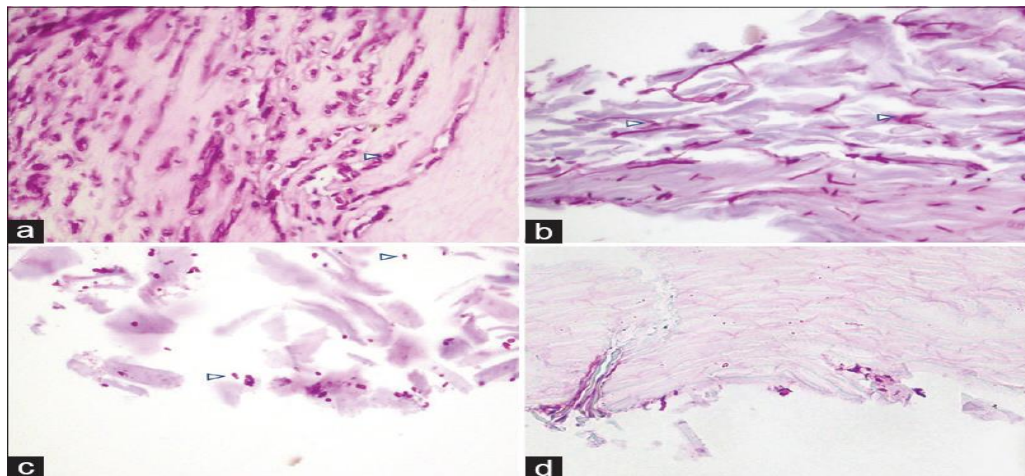
#### **DIAGNOSIS**

The onychomycosis mainly based on clinical manifestations and confirmed through KOH wet-mount and mycological culture. The efficacy criteria were defined by the following five clinical categories:

1. Cured: The nail plate was completely covered by healthy new nail
2. Markedly improved: healthy new nail covered over 70% of the affected nail plate
3. Improved: healthy new nail covered 40-70% of the affected nail plate
4. Slightly improved: healthy new nail covered no more than 40% of the affected nail plate
5. No change: worsened condition, or treatment discontinued due to adverse effects



➤ Mycological cure was defined by having negative results on KOH wet-mount and on fungus culture after treatment.<sup>13,15</sup>



**Fig: 1-** culture method which shows a) *Fusarium* with large chlamydospores (arrow). (b) *Aspergillus* with acute angle branching hyphae (arrow). (c) *Candida* Species with budding spores (arrow). (d) Fungal elements in *Scedosporium apiospermum* not diagnostic for species. (Periodic acid–Schiff stain, a-d, ×400)

## TREATMENT

Amorolfine is a morpholine derivative with antifungal activity, introduced in 1981.<sup>16</sup> Amorolfine is effective against dermatophytes, some molds and other pathogenic fungi, but not against bacteria except *Actinomyces*. Pharmacokinetic properties enable good penetration through the nail to the nail bed and absorption of the active substance into circulation is very low.<sup>17</sup>

Amorolfine can be identified in the nail for about 2 weeks. Treatment with amorolfine should continue until clinical and mycological cure achieved. Time of treatment depends on severity and infection site as well as the growth of nail plate, usually 6 months. Assessment of the treatment efficacy is recommended for every 3 months.<sup>18,19</sup>

The amorolfine lacquer is applied once or twice a week on a cleaned nail plate and left for 3–5 min until dry.<sup>22</sup>

Adverse effects such as erythema, burning sensation, nail discoloration and onycholysis.<sup>20</sup>

Ciclopirox is a hydroxy-pyridone derivative investigated since 1973 but used in the form of lacquer since the 1990s. Ciclopirox is marketed in various forms including cream, suspension, shampoo, gel, solution, powder and globules and used for treatment of skin, scalp and onychomycosis. Ciclopirox demonstrates a broad antifungal activity.<sup>21,23</sup>

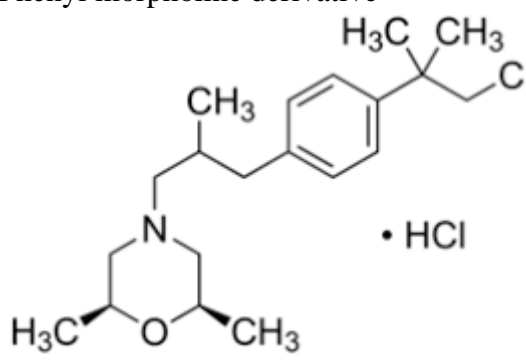
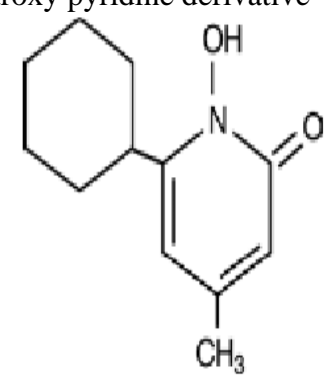
Parameter	Amorolfine	Ciclopirox
Chemical structure	Phenyl morpholine derivative 	Hydroxy pyridine derivative 
Drug delivery system used	Water-insoluble polymers	Water-insoluble polymers, hydroxypropyl-chitosan
Mechanism of action	Inhibits sterol synthesis in fungal cell wall, depletion of ergosterol and accumulation of non-typical spherical sterols	Decrease in activity of metal-dependent enzymes which affects ion transport through cytoplasmic membranes
Antifungal activity	Dermatophytes, Yeasts, Molds, other Pathogenic fungi.	Dermatophytes, Yeasts, Molds
Antibacterial activity	Only <i>Actinomyces</i>	Gram-positive bacteria ( <i>Staphylococcus</i> spp., <i>Streptococcus</i> spp.), Gram-negative bacteria ( <i>Escherichia</i> spp., <i>Proteus</i> spp., <i>Klebsiella</i> spp., <i>Salmonella</i> spp., <i>Shigella</i> spp., <i>Bacillus</i> spp., <i>Pseudomonas</i> spp.), <i>Mycoplasma</i>
Anti inflammatory effects	Absent	Present

Table reference <sup>25</sup>

## CONCLUSION

From all the studies that has been conducted on comparative study of amorolfine and ciclopirox in onychomycosis. Overall, results from these *in vitro* and *in vivo* studies indicate that, amorolfine and ciclopirox can effectively penetrate nail tissue. Although majority of topical agents can be prescribed as monotherapy for mild to moderate onychomycosis, amorolfine and ciclopirox nail lacquers are generally considered the most convenient one. However, from current monotherapy recommendations suggest applying ciclopirox to all nails, once daily,



amorolfine nail lacquer has an advantage in that only once-weekly applications to affected nails are required.

Recent investigations shown that the combination of oral therapies with a topical agent, such as amorolfine or ciclopirox, have considerable advantages over mono- therapy with either drug type co-administration of amorolfine with an oral antifungal drug can result in dose-sparing effects and can increasing the number of patients cured from onychomycosis compared with systemic therapy alone. In addition, to this cost effectiveness can be made by using oral and topical agents together.

We can conclude that amorolfine is more effective than ciclopirox. Further studies are being conducted which will define the role of various agents which will upcoming in the paths of treatment. The improved effectiveness and economic advantages of combined topical/oral therapies benefit both patients and health providers; these treatment regimens have an important role to play in the modest treatment for onychomycosis.

In addition to specific drug therapies, some patients may benefit from several hygiene measures that may prevent relapse. Patients should wear thong sandals in public showers and slippers in hotel rooms and should rest shoes periodically to limit exposure to infectious fungi. The importance of instilling realistic expectations in patients with onychomycosis can hardly be overemphasized. Patients should be told that, just as onychomycosis developed gradually over several months or years, a cure is not likely to be achieved overnight. In fact, particularly for toenail infections, treatment may require several months. The positive aspect of modern treatments is that a cure is probable and side effects are rare. Immunocompromised patients face a particularly difficult situation with respect to compliance, because cure may take even longer in their cases.

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