

Home Treatments for Fungal Nails – Are they really any good?

Topical treatment of fungal nail infection is a popular way to treat onychomycosis in the toenails. Local application of a chemical or a medicine is appealing to many as a safe and convenient way to treat nail infections avoiding the risks of side effects and complications of their systemic counterparts. As a podiatrist, the choice of topical drugs available to treat the infection is limited. The latest guidelines from the Clinical Knowledge Summaries at the National Institute for Health and Care Excellence, suggest amorolfine 5% as the drug of choice. To reinforce this a recent review has shown amorolfine to be effective [1] but what about other topical treatments with substances that are not drugs or medicines?

For patients seeking topical treatments from the pharmacist, they can be confronted with an array of various products off-the-shelf making various claims to be able to treat unsightly toenails and banish stubborn fungal nail infections. Most of these products are not drugs (as they have no direct pharmacological action on the fungal infection) but are classed as medical devices. Their mode of action broadly falls into two categories. Firstly, acidifying agents that exert their effects by lowering the local pH of the nail to a level which can be fungistatic or fungicidal. These include organic acids such as acetic, lactic and citric acid or ethyl lactate. The second group may utilise a cosmetic ingredient which has some anti-fungal properties (such as Norway spruce resin). Often added into these formulations is a penetration enhancer such as urea (which may help to soften nail keratin acting as a keratolytic) or dimethyl isosorbide which improves chemical delivery through the nail. Patients often come into the clinic and they say they have used such a product – (successfully or unsuccessfully) but what do we really know about their efficacy?

Is there much evidence that they actually work?

A recent paper, published in *Mycoses*[2], earlier this year caught my eye as it was a rare publication which evaluated a range of these products to assess their inhibitory ability against one of the common nail dermatophytes, *T. mentagrophytes*. The study compared Excilor[®], Naloc/Nalox[®] (marketed as Emtrix[®] in the UK), Nailner[®], Mycosan, Scholl Nail Treatment, Kruidvat fungal nail pen[®] and Boots fungal nail treatment pen[®]. The antifungal activities of all these products were measured against the medicine, amorolfine (marketed as Loceryl[®] and Curanail[®] in the UK) using cow hoof as the test medium. Slices of the hoof were bathed daily in the antifungal products and then after 7 days were placed in an agar culture of *T. mentagrophytes* still applying the treatment for a further 7 days and following incubation, the size of the area of inhibition was calculated for each product tested.

Whilst amorolfine showed a strong inhibitory effect, interestingly only Excilor[®] and Nailner[®] only modestly inhibited some fungal growth in the petri-dish. The remaining products in this experiment showed no activity against *T. mentagrophytes* at all. The authors suggest that the antifungal properties seen in these two products were due to the effects of the organic acids contained within them.

Another study published this year has generally concurred with these results[3]. Once again, the medicine amorolfine was compared in a lab study this time to Excilor[®], Scholl Fungal Nail Treatment[®] and Nailner. Using six human cadaver nails, a similar process was adopted but this time against the

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more common foot dermatophyte - *T. rubrum*. The results showed the amorolfine, once again, was the only product that showed inhibition against this dermatophyte with the other three showing no inhibition of fungal growth at all. The authors suggest that the three products although acidifying, could not reach a pH low enough in the nail model to inhibit fungal growth. So data from these lab studies does not seem to demonstrate any significant antifungal ability. But....

Is there any other evidence for these products?

A quick look at the National Library of Medicine Database (PubMed) pulls up a few studies which have investigated Emtrix® (also marketed as Nalox® and Naloc®). The product containing propylene glycol, urea and lactic acid, appears in a paper published in the respected journal "Mycoses" but this time demonstrates anti-fungal activity against *T. rubrum* in the laboratory[4].

But what about in real patients? Only two clinical studies of this product could be found. In 1989, Faergemann and Swanbeck [5] treated 23 patients with the solution and demonstrated improvement (according to patient reported measures) whilst using the treatment Emtrix®. Latterly, Emtestam and colleagues [6] conducted a double blind, placebo controlled study of Emtrix® on 346 patients with confirmed distal, sub-ungual onychomycosis. The results demonstrated the treatment was more than twice as effective as placebo after 26 weeks of treatment. Those with less than 50% nail involvement showed a 27% mycological cure rate versus 10.4% for placebo. Of those with greater than 50% of the nail involved, 19% showed improvement versus 7% for those treated with placebo.

Canespro® is a treatment marketed for onychomycosis in the UK. The formulation contains a 40% urea compound with beeswax and lanolin. Interestingly, the treatment itself contains no natural anti-fungal agent but is said to work by removing the diseased part of the nail, leaving the unaffected nail intact. If a nail has the commonest form of onychomycosis (sub-ungual infection), it would be hard to see how the treatment could be effective. However, 40% urea has been shown to soften nail. Studies have shown regular application of 40% urea prior to drug therapy to improve outcomes [7, 8], but results of urea treatment alone on a mycotic nails are lacking in the medical literature.

Abicin® (Espere) is a relatively new product introduced into the UK market this year and will probably be making its way into pharmacies shortly. The active ingredient of the product is 30% Resin from the Norwegian spruce [*Picea sp.*] (see earlier post on my blog) and it is combined with propylene glycol in a topical nail solution. So is there any evidence of effectiveness? In a laboratory study, the product has been shown to be effective [9] at this concentration against three dermatophytes – *rubrum*, *tonsurans* and *mentagrophytes*. In its first small clinical study, running for nine months on 14 patients, it showed 60% of dermatophyte proven nail infection were culture negative at the end of the study with clinical improvement in 40% of patients over the study period. In a larger randomised controlled (investigator blind) trial [10] a daily regime for nine months of abicin®, was compared with 9 months of weekly applied amorolfine applications with a three-month course of oral terbinafine. At 10 months, complete mycological cure rates were 13% (abicin), 8% (amorolfine) and 56% (terbinafine). The authors suggesting the abicin® treatment was as effective as amorolfine.

So what does this mean clinically?

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1. The action of many of these consumer products on specific fungi species has not been fully explored.
2. Laboratory based work in vitro has shown the effectiveness of amorolfine as an anti-fungal drug superior to most of the medical device products. Some of these products showing no effect at all in the laboratory studies mentioned above.
3. Clinical evidence of consumer nail treatments is in very short supply but studies using a randomized controlled trial design have shown the effectiveness of amorolfine and abicin[®] (Resin from the Norwegian Spruce) in onychomycosis. Whilst Emtrix[®] (a combination of propylene glycol, urea and lactic acid) has been shown to be better than placebo through a randomized controlled trial.
4. The use of urea based ointments (similar to Canespro[®]) has been shown to improve outcomes in treatment but only when used in combination an antifungal drug.

It is important to add, that the podiatrist has an important role for any patient presenting with fungal nails. If they are to be treated with topical agents, then it is important to remember:

1. It is worth establishing a positive diagnosis of onychomycosis as 50% of presenting nail dystrophies are due to causes other than fungal infection. An incorrect diagnosis is a waste of time and money for the podiatrist and the patient.
2. Skin should be treated adequately as this is the commonest route of fungal infection back into the nail. Skin re-infection can cause nail infection relapse or reinfection. Patients should be advised how to recognise if their fungal skin infection on their foot has returned and treat it promptly.
3. Debridement of the nail may improve the outcome when used alongside topical and systemic drug therapies [8, 11].
4. Finally, if any fungal nail treatment is successful, it cannot always restore the nail back to its pristine condition as fungal nails are frequently damaged long before the infection sets in. So patients should be advised that although a treatment may work, the nails may not look significantly better (in some cases).

Common Nail Treatments in Pharmacies in the UK

Product	Active Ingredient	Penetration Enhancer
Abicin Nail Resin®	Picea Resin Propylene Glycol	-----
Boots Advanced Fungal Nail Treatment Pen®	Olive leaf Extract Pentylene Glycol	Dimethyl Isosorbide
Canespro Nail Treatment®	Urea (40%)	-----
Emtrix®	Propylene Glycol Lactic Acid	Urea
Excilor®	Acetic acid Ethyl lactate	Dimethyl Isosorbide
Nailner Antifungal Pen®	Ethyl Lactate Lactic Acid Citric Acid	-----
Scholl Fungal Nail Treatment®	Citric Acid	Urea

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