

**MedChem & CADD 2015: Terbinafine based nail lacquer for treatment of nail fungal infections****Barbara Susana Gregori Valdes***Universidade de Lisboa, Portugal*

This study focused on the synthesis and characterization of polyurethanes to prepare a nail lacquer formulation with terbinafine hydrochloride in order to obtain a topical nail release system. The synthesis of polymer was carried out by the reaction of IPDI, PPG and isosorbide with 6:1:5 ratio, under a dry nitrogen atmosphere using 0.5 mL of DABCO as catalyst. The polymer was characterized by FTIR, NMR, DSC PALS and the biocompatibility with keratinocytes cell was studied. The in vitro release profile of terbinafine from different nail lacquer formulations was investigated using Franz Cells. The FTIR spectrum showed a band of 1695  $\text{cm}^{-1}$  attributed to the stretching vibration of the C=O carbonyl of urethane. The PU melting temperature was around 60 °C. The presence of protons of -NH- between 5.2 and 7.5 ppm in the  $^1\text{H}$  NMR spectrum in DMSO confirm the reaction between the isosorbide hydroxyl groups and the pre-polymer isocyanate groups. The PU presents cell viability measured by the MTT reduction. The release profile, demonstrated that the formulation had the ability to release the drug. In this research, new polyurethane was synthesized and characterized. The polyurethane synthesized presented biocompatibility. The results so far obtained are promising for a novel terbinafine based nail lacquer for the treatment of fungal infections.

**Nail Fungal Infection**

Fungal nail infections are the most common nail diseases, accounting for about 50% of nail abnormalities. The fungus is normally present on the body, but if it proliferates it can become a problem. They are also known as onychomycosis and ringworm unguis. Nails and toes are susceptible to infection, which usually manifests as discoloration and thickening of the nail and

crumbling edges. The condition most commonly occurs in the toenails.

**Treatment**

OTC creams and ointments are available, but they have not been found to be very effective. Oral nail fungus medications include: terbinafine (Lamisil); itraconazole (Sporanox) and fluconazole (Diflucan).

**Causes**

Microscopic organisms called fungi cause fungal nail infections; they do not need sunlight to survive and can therefore thrive in these regions. The pathogens that cause fungal nail infection usually enter the skin through small cuts or small separations between the nail and the nail bed. Fungi develop when the nail provides a sufficiently warm and humid environment.

**Symptoms**

Nails infected with fungi are usually: thickened, brittle, brittle, tattered, deformed, dull and darker or yellowish. Fungal nail infections can cause pain in the toes or fingertips, and can even emit a foul odor. Another symptom associated with nail fungus is fungus-free skin lesions called dermatophytides. These can appear as rashes or itching in an area of the body that is not infected with the fungus - much like an allergic reaction.

When fungi infect a nail, they usually start at its free edge, then spread from the side of the nail to the base of the cuticle. Ultimately, the entire nail may be involved. The infected areas turn white or yellowish and become thickened and brittle. Less commonly, there may be white areas on the surface of the nail. The nails most commonly affected by fungal infections are those of the big and small toes. Sometimes, especially

in those who do regular wet work like housewives or cleaners, the skin around the nail becomes red and swollen. This is called paronychia and can allow the infection to reach the nail.

### **Diagnosis**

In order to diagnose fungal nail infections, a doctor will usually examine the debris that is scraped under the nail. Nail scraping will be used in tests, such as a potassium hydroxide (KOH) smear or a fungal culture. The KOH test can be done quickly, while the fungal culture can take weeks. Doctors should be careful when diagnosing fungal infections of the nail, as several other conditions can cause similar symptoms.

Terbinafine causes nail fungus to resolve 76% of the time. It is taken once a day for 6 to 12 weeks. There is no effect of food on absorption. As it is a fat-soluble drug, it accumulates in the skin, adipose tissue and also the nails. It persists in the nails for long periods after the end of treatment. It is metabolized by the liver with a half-life of 17 hours.