EMTRIX® Fungal Nail Treatment

Summary of published clinical studies supporting the efficacy of Emtrix®

Emtrix (K101) is an effective and clinically proven topical treatment for nails affected by fungal nail infection or psoriasis. Efficacy and safety in patients with nail fungus has been demonstrated in several studies including more than 500 patients. This summary covers mode of action and three published studies supporting the efficacy and safety of Emtrix. For full publications see www.emtrix.com.

Mode of Action

Propylene glycol has humectant properties and is used similarly to glycerol in topical moisturising preparations[1]. Urea promotes hydration and is mainly applied topically in the treatment of ichthyosis and hyperkeratotic skin disorders[1]. Lactic acid is used in topical formulations, particularly cosmetics, for its softening and conditioning effect on the skin[2]. Lactate and urea are natural humectants and constituents of the "natural moisturising factor" within the stratum corneum[3]. The principal intended action of *K101 Nail Solution* exploits the keratolytic properties of the combination of ingredients to facilitate gentle sloughing of damaged and unsightly nail tissue and to increase hydration, thereby promoting normal healing of unguinal surface lesions.

Low pH in skin and nails is important for antimicrobial protection against both pathogenic fungi and bacteria[4]. The action of the relatively acidic pH of *K101 Nail Solution* (approximately pH 4) contributes to its efficacy. The pH of the formulation is controlled in the product specification with acceptance criteria of pH 3.5 to 5.0 for a 50% aqueous solution.

In vitro studies have characterised the physical antifungal action of K101 Nail Solution; establishing that there is a purely physical basis to such action[5]. Observed structural changes (physical degradation of the cell wall and cell membrane leads to increased permeability thus giving rise to osmotic changes and collapse) following treatment with K101 Nail Solution imply an unspecific physical mode of action.

1. Martindale: The Complete Drug Reference; 37th Edition; 2011
2. Handbook of Pharmaceutical Excipients; 5th Edition; 2006
3. Bikowski J; Cutis; 68(5 Suppl): 3-11; December 2001
4. Schmid-Wendtner MH, Korting HC; The pH of the Skin Surface and its Impact on the Barrier Function; *Skin Pharmacol Physiol* 2000; 19: 296-302.
5. Hultenby K, Chryssanthou E, Klingspor L, Rensfeldt K, Strömbeck L and Faergemann J; The effect of K101 Nail Solution on *Trichophyton rubrum* and *Candida albicans* growth and ultrastructure; *Mycoses* 2014 doi: 10.1111/myc.12211.

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Early and Visible Improvements after Application of K101 in the Appearance of Nails Discoloured and Deformed by Onychomycosis

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ABSTRACT

Onychomycosis is a fungal infection of the nails of the fingers and toes and is difficult to cure. A previous 24-week, placebo-controlled study demonstrated that a solution containing propylene glycol, urea and lactic acid (K101) was well-tolerated and effective in the treatment of onychomycosis. Patients who received K101 judged that their condition had improved from Week 2 of treatment onwards. The aim of the current study was to further evaluate and document early visible effects on nail appearance after application of topical K101 in an 8-week baseline-controlled study in 75 patients. Patients graded the appearance of their nail compared with baseline using a four-point scale. Compared with baseline, 91.8% (67/73; 95% confidence interval (CI): 83.0%, 96.9%) of the patients experienced at least some improvement in their target nail after 8 weeks of treatment. At Week 2, the proportion showing some improvement was 76.7% (56/73; 95% CI: 65.4%, 85.8%) with this number increasing to 87.7% (64/73; 95% CI: 77.9%, 94.2%) at Week 4. Proportions of patients reporting less thickened, less discoloured, less brittle and softer nails increased over the course of the study. No safety issues were identified. In conclusion, K101 provided early visible improvements in nails affected by onychomycosis.


BEFORE TREATMENT


2 WEEKS


4 WEEKS


8 WEEKS

Mycoses, 2012, 55, 532-540

Treatment of distal subungual onychomycosis with a topical preparation of urea, propylene glycol and lactic acid: results of a 24-week, double-blind, placebo-controlled study

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ABSTRACT

Onychomycosis is difficult to cure as this requires eradication of the primary infection and protection of new areas of growth from reinfection. A new topical treatment (K101) has been developed. The aim of this study was to assess the efficacy, safety and tolerability of K101 treatment of distal subungual onychomycosis. This was a 24-week (plus 2-week washout), multicentre, randomised, double-blind, placebo-controlled study in 493 patients with distal subungual onychomycosis (K101, n = 346; placebo, n = 147), stratified according to degree of nail involvement. More patients with 50% nail involvement achieved the primary endpoint (mycological cure after 26 weeks) in the K101 group (27.2%) than placebo (10.4%; P = 0.0012). Proportions for patients with 51–75% involvement were 19.1% for K101 and 7.0% for placebo (not significant). More patients applying K101 than placebo judged that their condition had improved from week 2 (P = 0.0148) to week 24 (P = 0.0004). No safety issues were identified. K101 provides early visible improvements in nail appearance and a clinically meaningful antifungal activity.

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The effect of K101 Nail Solution on *Trichophyton rubrum* and *Candida albicans* growth and ultrastructure

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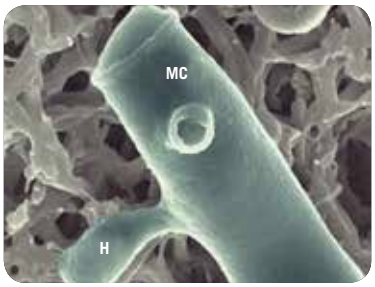
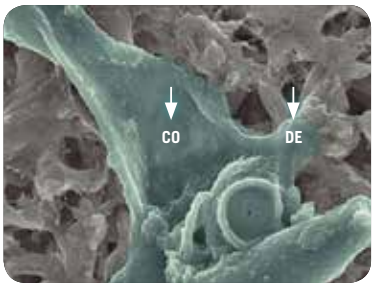
ABSTRACT

K101 Nail Solution (trademarks Emtrix®, Nalox™, Naloc™) is a combination of propylene glycol, urea and lactic acid in a topical formulation for the treatment of nails affected by onychomycosis. The aim of this study was to investigate the Minimal Cidal Concentration (MCC) of K101 Nail Solution against *Trichophyton rubrum* and *Candida albicans* as well as the effect of K101 Nail Solution on the micromorphology of these fungi. The MCC of K101 Nail Solution against *T. rubrum* and *C. albicans* was 50% after 60-min exposure time. A MCC of 50% for K101 Nail Solution means that K101 Nail Solution diluted with e.g. water to 50% will totally kill the fungi tested. In the scanning electron microscope *C. albicans* cells, treated with 50% K101 Nail Solution, showed a shrunken surface. *T. rubrum* cells were severely damaged shown as collapse and degradation of the cells. In the transmission electron microscope most *C. albicans* cells, treated with 50% K101 Nail Solution exhibited destroyed organelles and many necrotic cells were found. The cell wall was clearly degraded and the contact between the cell wall and the inner membrane was punctured. In *T. rubrum* most cells were necrotic. Some cells were clearly collapsed and the content in the cytoplasm was degraded shown as small membrane vesicles and many big vacuoles. The cell wall was clearly degraded and the membrane was punctured. In conclusion, this *in vitro* study documents the efficacy of K101 Nail Solution against *T. rubrum* and *C. albicans*.

SCANNING ELECTRON MICROSCOPY:



T. RUBRUM UNTREATED CONTROL
(BAR=500NM, MC=MICROCONIDIAE, H=HYPHAE)



T. RUBRUM TREATED WITH 50% K101
(CO=COLLAPSED, DE=DEGRADED)

Moberg PHARMA

EMTRIX®
www.emtrix.com