pretreatment by mefenamic acid, ibuprofen, verapamil, cyclosporine, and verapamil + ibuprofen in individual groups. Ibuprofen presented positive effect on intestinal permeation of PCT. C(max) and area under the serum concentration versus time curve (AUC) after pretreatment by ibuprofen was decreased when the oral dose of PCT was decreased to 50 and 25 mg/kg, while dose-blood concentration relationship was nonlinear. Rise in oral bioavailability of PCT after pretreatment by cyclosporine was lower than ibuprofen. It seems that by using ibuprofen in concomitant with potent Pgp inhibitors before PCT solution, oral delivery of PCT could be promising.

Monti, D. et al. (2014). "Ciclopirox vs amorolfine: In vitro penetration into and permeation through human healthy nails of commercial nail lacquers." *J Drugs Dermatol* 13(2):143–147.

One of the prerequisite for a successful topical antifungal drug indicated for onychomycosis is its bioavailability into the nail unit for achieving fungal eradication and clinical benefit. The aim of this study was to compare in vitro permeation/penetration through and into human nails of amorolfine (MRF) from a 5% anhydrous commercial formulation (Loceryl® and ciclopirox (CPX) from the 8% aqueous formulation in hydroxypropyl chitosan (HPCH) technology (Onytec®. The ability of the active ingredient to reach efficacious concentrations to inhibit nail pathogens was also evaluated. The amounts of drug permeated and retained in human healthy nails were determined using a suitably modified diffusion apparatus. HPLC analysis of the samples was performed. The HPCH-based CPX formulation demonstrated an efficient penetration into and permeation through the nail plates. Conversely, Loceryl(R) produced an amount of MRF permeated through and penetrated into the human toenails significantly lower than CPX. The evaluation of the efficacy index showed a higher potential efficacy of Onytec(R) with respect to Loceryl(R) on nail pathogens. The present work not only reinforced the previous results on different experimental substrates, but pointed out the superiority of HPCH-based Onytec(R) formulation containing CPX with respect to Loceryl(R) commercial product with MRF, both in terms of higher permeation through and penetration into the human nail, and for the efficacy towards the most common ungual pathogens.

Nayak, A. et al. (2016). "Lidocaine carboxymethylcellulose with gelatine co-polymer hydrogel delivery by combined microneedle and ultrasound." *Drug Deliv* 23(2):658–669.

A study that combines microneedles (MNs) and sonophoresis pretreatment was explored to determine their combined effects on percutaneous delivery of lidocaine from a polymeric hydrogel formulation. Varying ratios of carboxymethylcellulose and gelatine (NaCMC/gel ranges 1:1.60–1:2.66) loaded with lidocaine were prepared and characterized for zeta potential and particle size. Additionally, variations in the formulation drying techniques were explored during the formulation stage. Ex vivo permeation studies using Franz diffusion cells measured lidocaine permeation through porcine skin after pretreatment with stainless steel MNs and 20 kHz sonophoresis for 5- and 10-minutes durations. A stable formulation was related to a lower gelatine mass ratio because of smaller mean particle sizes and high zeta potential. Lidocaine permeability in skin revealed some increases in permeability from combined MN and ultrasound pretreatment studies. Furthermore, up to 4.8-fold increase in the combined application was observed compared with separate pretreatments after 30 minutes. Sonophoresis pretreatment alone showed insignificant enhancement in lidocaine