# Nail Drug Permeation of Topical Formulations Including Fluconazole and Ibuprofen (EctoSeal P2G)

Topical formulations are ideal to treat fungal infections of the nails but drug permeation is limited which leads to poor treatment efficacy. In this study, the drug uptake (permeation) of topical formulations including fluconazole and ibuprofen was evaluated. Fluconazole showed greater drug uptake from the EctoSeal nail hydrogels than the DMSO nail solution, which suggests that PCCA EctoSeal P2G is a potential compounding base for the delivery of topical nail formulations.

## Introduction:

Disorders of the nail are a common occurrence, particularly fungal infections (onychomycosis) which are often characterized by nail brittleness, discoloration and thickening (Figure 1). Topical treatments are ideal because the active pharmaceutical ingredients (APIs) are concentrated externally at the site of infection, thus avoiding the systemic effects and drug interactions of the oral treatments. However, topical formulations have low efficacy due to the poor permeation of drugs through the nails.[1] As such, there is a lot of research being conducted to enhance nail drug permeation.[2] The purpose of this study is to evaluate the transungual (through the nails) drug uptake (permeation) of topical formulations including fluconazole and ibuprofen in PCCA EctoSeal P2G.[3] These APIs are commonly indicated in the treatment of onychomycosis, and the associated inflammation and pain that can be presented in these infections. Fluconazole has antifungal properties and ibuprofen has anti-inflammatory and analgesic effects, which provides a synergistic approach to the topical treatment.


***Figure 1.*** *Illustration of toe nail fungal infection. Stock vector ID 1474800791.*

## Methodology:

The transungual drug uptake experiment consisted of collecting nail clippings from volunteers, exposing the nail clippings to the test formulations, then analyzing the samples to quantitatively determine the amount of fluconazole and ibuprofen that penetrated the nails.

Materials (test formulations):

1. Fluconazole 2%/Ibuprofen 2% Topical Nail Hydrogel (EctoSeal P2G™) (PCCA Formula 15341) (Table 1).

| Rx | |
|---|---|
| Fluconazole | 2 g |
| Ibuprofen | 2 g |
| Benzyl Alcohol | 1.5 g |
| DMSO | 2 g |
| Base C | 5 g |
| Base, PCCA EctoSeal P2G™ Powder | 15 g |
| Purified Water | q.s. 100 g |

***Table 1.*** *Fluconazole 2%/Ibuprofen 2% Topical Nail Hydrogel (EctoSeal P2G™): PCCA Formula 15341.*

2. Fluconazole 2%Topical Nail Hydrogel (EctoSeal P2G™) (PCCA Formula 15340).

3. Fluconazole 2%/Ibuprofen 2%/Dimethyl Sulfoxide (DMSO) Nail Solution (PCCA Formula 12663).

Informed consent was obtained from 5 volunteers who met the eligibility criteria and were willing to participate in this study. All volunteers were female, Asian and Caucasian, aged between 28 and 55 years old. The collected nail clippings were cleaned and immersed in Di water for 1 hr. After drying out with Kimwipes®, the test formulations were applied onto the nail clippings and put into moisturized box to avoid drying. After 48 hrs, the nail clippings were washed with water and methanol to remove any of the remaining fluconazole and ibuprofen. The clippings were immersed in liquid nitrogen and then struck with a hammer to reduce the nails to a fine powder. The pulverized nail powder was suspended in methanol overnight to extract fluconazole and ibuprofen from the nails. Followed by filtration with PVDF filter, fluconazole and ibuprofen concentrations were measured using Ultra-Performance Liquid Chromatography (UPLC). The amount of fluconazole and ibuprofen retained in the nail plate were presented as mass (µg) per mg of nails.

***Figure 2.*** *Nail without EctoSeal Preparation.*

***Figure 3.*** *Nail with EctoSeal Preparation.*

## Results and Discussion:

The transungual drug uptake experiment showed that fluconazole penetrated well into the nail plate across the three test formulations. As shown in Figure 1, fluconazole displayed similar nail drug permeation in both topical hydrogels formulated with PCCA EctoSeal P2G which means that ibuprofen did not interfere with the drug uptake. When the topical nail hydrogel is compared with the nail solution, it is concluded that EctoSeal P2G facilitated greater transungual drug uptake than DMSO. Although preliminary, results from this study indicate that PCCA EctoSeal P2G is a potential compounding base for the delivery of topical nail formulations.

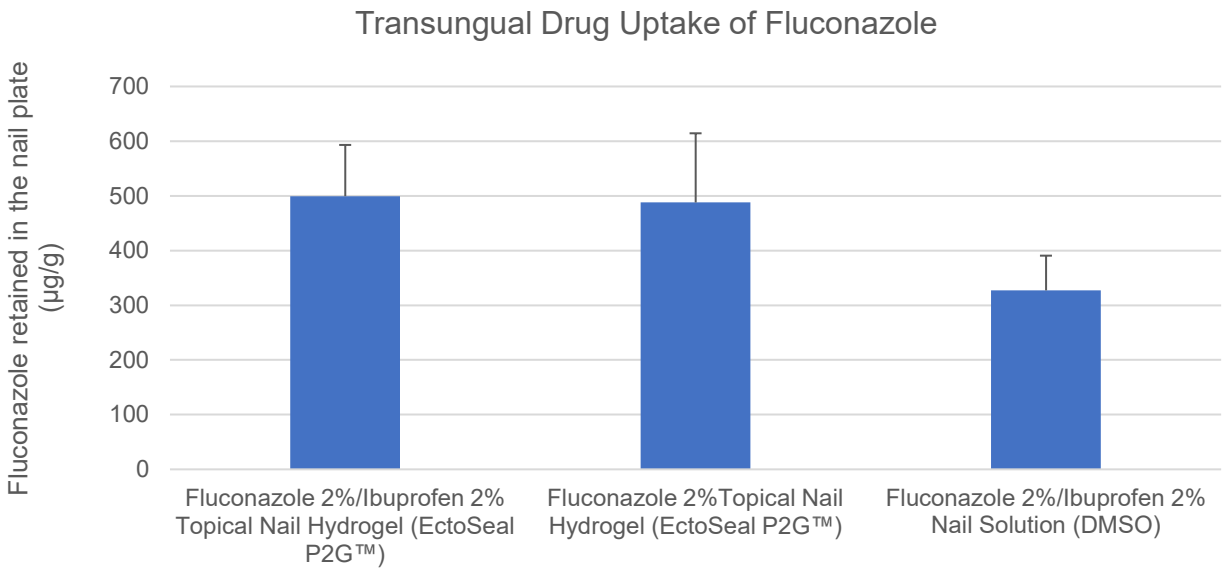


***Figure 1.***
*Transungual drug uptake of fluconazole across the three test formulations (PCCA Formulas 15341, 15340 and 12663).*

## References:


1. Pollard TD, Bonetti M, Day A, et al. Printing Drugs onto Nails for Effective Treatment of Onychomycosis. Pharmaceutics. 2022;14(2):448. Published 2022 Feb 19.
2. Kerai LV, Bardés J, Hilton S, Murdan S. Two strategies to enhance ungual drug permeation from UV-cured films: Incomplete polymerisation to increase drug release and incorporation of chemical enhancers. Eur J Pharm Sci. 2018;123:217-227.
3. PCCA (2023) PCCA EctoSeal P2G™ Powder (30-5217). Available at: https://www.pccarx.com/products/PCCAECTOSEALP2G%E2%84%A2POWDER/30-5217/PROPRIETARYBASES