W1230-01-02

Nail Drug Permeation of Fluconazole and Ibuprofen Topical Compounded Formulations

Guiyun Song, Kendice Ip, Gabriel Banov, Christine Vu, Maria Carvalho
Professional Compounding Centers of America (PCCA)

gsong@pccarx.com

aaps National Biotechnology CONFERENCE

PURPOSE

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 therapy is a preferred treatment option because it delivers active pharmaceutical ingredients (APIs) directly to the site of infection while avoiding systemic adverse effects and drug–drug interactions associated with oral antifungals. 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 fluconazole and ibuprofen formulations using a topical compounding base (EctoSeal P2G™), and to compare the drug uptake using a conventional dimethyl sulfoxide (DMSO) nail solution. The APIs chosen are commonly used to treat onychomycosis and its associated inflammation and pain, with fluconazole providing antifungal activity and ibuprofen offering anti-inflammatory and analgesic effects for a synergistic topical approach. EctoSeal P2G is a proprietary powder-to-hydrogel, film-forming polymer complex base with tissue-protective and microbiome-supportive properties (3).

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

METHODS

The transungual drug uptake study 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 (Figure 2). The materials (test formulations) were as follows: fluconazole 2% and Ibuprofen 2% topical nail hydrogel (EctoSeal P2G) (see Prescription); fluconazole 2% topical nail hydrogel (EctoSeal P2G); fluconazole 2% and ibuprofen 2% Dimethyl Sulfoxide (DMSO) nail solution.

Informed consent was obtained from five 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 clippings without test formulation (top) and with test formulation (bottom).*

RESULTS

Fluconazole permeated the nail plate in all tested formulations, as shown in Figure 3. Quantitative analysis demonstrated higher fluconazole concentrations in nail samples treated with the powder-to-hydrogel formulations (499.34 ug/g and 487.90 ug/g) compared with those treated with the DMSO nail solution (327.18 ug/g). Similar levels of fluconazole uptake were observed between the fluconazole-only hydrogel and the fluconazole/ibuprofen hydrogel, indicating that the presence of ibuprofen did not interfere with fluconazole permeation through the nail. These findings suggest that the powder-to-gel hydrogel base facilitated enhanced transungual drug delivery relative to the solvent-based comparator.

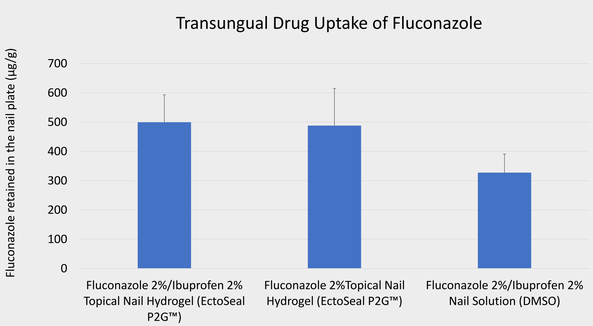
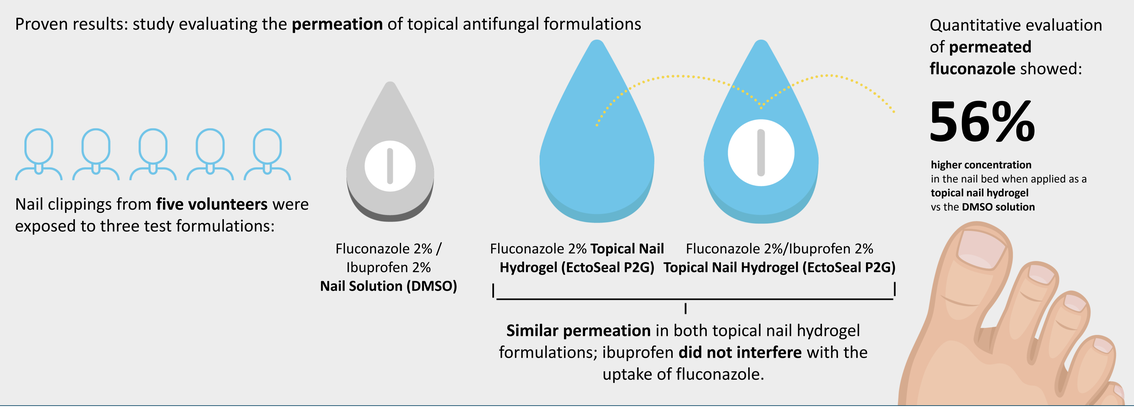
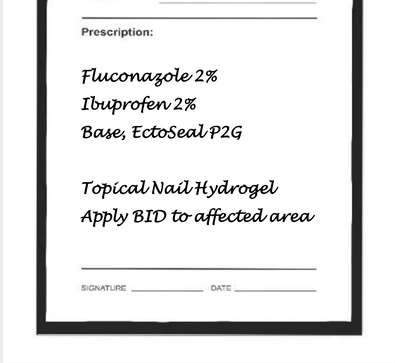


Figure 3. *Transungual drug uptake of fluconazole across the three test formulations.*



CONCLUSION

This study demonstrates that the powder-to-hydrogel compounding base can enhance transungual delivery of fluconazole compared with a conventional DMSO nail solution. The addition of ibuprofen did not adversely affect fluconazole uptake, supporting the feasibility of combination topical formulations targeting both fungal infection and associated inflammation or pain. Although preliminary, these results suggest that the compounding base may be a suitable alternative for compounded topical nail formulations intended to enhance drug delivery in the management of onychomycosis.



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. Banov, D.; Song, G.; Foraida, Z.; Tkachova, O.; Zdoryk, O.; Carvalho, M. Integrated In Vivo and In Vitro Evaluation of a Powder-to-Hydrogel, Film-Forming Polymer Complex Base with Tissue-Protective and Microbiome-Supportive Properties. *Gels* 2024, 10, 447. https://doi.org/10.3390/gels10070447.