A Novel Method to Selectively Differentiate Between the Loss of Water and Other Volatiles from Topical Semisolid Products

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Introduction

The loss of water and other volatile components from a topical semisolid product can impact the solubility and diffusion of the drug in the dosage form, and the partitioning of soluble drug into the skin. In some cases, the loss of volatile ingredients may lead to supersaturation and a greater availability of the drug for partitioning and skin permeation. In other cases, the loss of water may lead to product drying, recrystallization and a decrease in the amount of soluble drug available for diffusion and partitioning. A routine gravimetric analysis of weight loss cannot discriminate between the loss of volatiles and water from a semisolid formulation. Therefore, a novel, sensitive and specific evaporimeter-based method was developed to measure the loss of water during drying of a topical semisolid product.

Methodology

Water loss over time was measured for different formulations of metronidazole applied on a flat surface at room temperature in vitro. A closed chamber evaporimeter (Biox AquaFlux) apparatus was slightly modified to measure the loss of water, specifically. The total weight loss (measured gravimetrically) and the specific loss of water (measured by the modified evaporimeter) were compared at similar time points. Two (reference and generic) creams, two (reference and generic) gels, and one lotion were studied to compare results among formulations that contained varying amounts of water and other volatile components.

Results

The loss of water from the cream products (Fig1a) appeared to account for all the weight loss measured gravimetrically (within error). However, for the gels (Fig1b) and the lotion (Fig 1c), the loss of water accounted for a significantly smaller fraction of the total loss of volatiles measured gravimetrically.

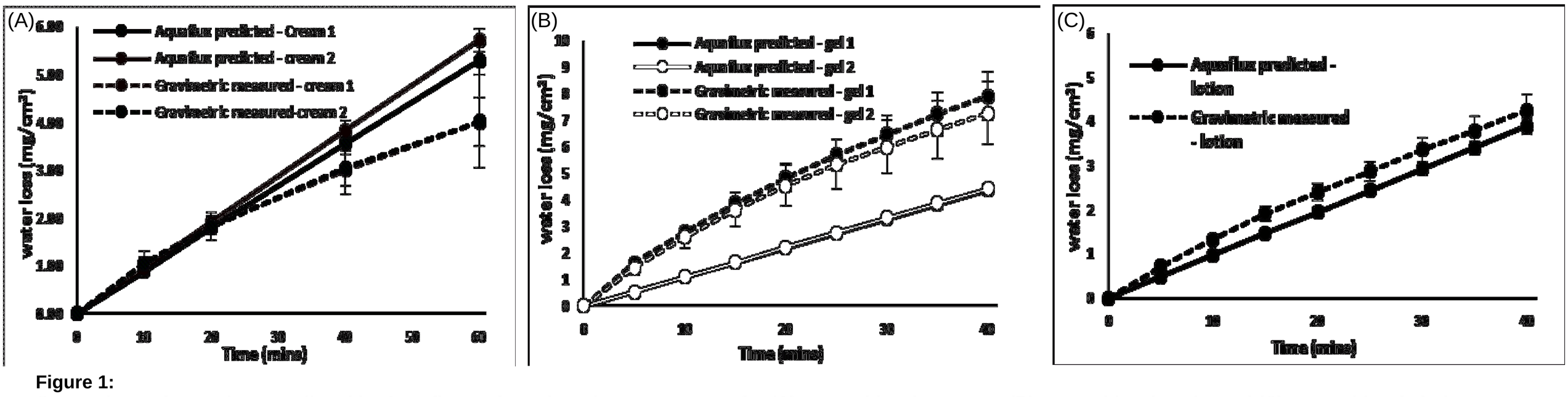

Figure 1:
Comparison of water loss predicted by Aquaflux and gravimetric measurement for (A) metronidazole creams, (B) metronidazole gels, and (C) metronidazole lotion.

Conclusion

The novel methodology developed here for characterizing the compositional metamorphosis of a topical semisolid drug product can differentiate between the loss of water and the loss of other volatiles. This technique can be used to differentiate dosage forms that contain varying amounts of water and other volatiles (e.g., creams, gels and lotions) or to compare the influence of changes in product composition/manufacturing on the relative rate of loss of water, which may have mechanistic implications for drug solubility, diffusion and partitioning.

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