

# Evaluation of the *in vitro* percutaneous absorption of progesterone, testosterone, estriol and estradiol topical compounded formulations



Guiyun Song<sup>1\*</sup>, Kendice Ip<sup>1</sup>, Ashley Shan<sup>1</sup>, Daniel Banov<sup>1</sup>, Hui Song<sup>2</sup>, August S. Bassani<sup>1</sup>, Maria Carvalho<sup>1</sup> and A.J. Day<sup>1</sup>

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**Introduction:** The safety, effectiveness and use of compounded bioidentical hormone replacement therapy has been questioned by the US Food and Drug Administration in the light of the recently published study report by The National Academies of Sciences, Engineering and Medicine. Compounded hormones are customized to meet the specific patient’s needs and have been used successfully in the USA and worldwide for decades. Transdermal compounded hormones, in particular, are delivered through the skin and into the general circulation for systemic effects with the advantage of avoiding gastrointestinal drug absorption difficulties and the first pass metabolism.

**Materials and Methods:** An *in vitro* study was conducted to evaluate the human skin percutaneous absorption of commonly prescribed bioidentical hormones using the Franz Skin Finite Dose Model<sup>1</sup>. A topical compounded cream (VersaBase® Cream) and gel (VersaBase® Anhydrous HRT) were prepared for progesterone 100 mg/g, testosterone 1 mg/g, and estriol/estradiol [50%/50%] 2 mg/g. The 6 formulations were applied to the outer surface of *ex vivo* skin mounted in Franz diffusion chambers (9 tissues/formulation) to evaluate the total absorption, rate of absorption and skin content of the bioidentical hormones.

**Results and Discussion:** The topical creams and gels for progesterone and testosterone exhibited similar mean flux profiles, characterized by a rise in skin percutaneous absorption to a peak at approximately 7 hrs (progesterone) and 5 hrs (testosterone) after dose application, followed by a slow decline in flux over time (24 hrs) (Figures 1-2). The estrogens did not show a peak rise but instead a steady mean flux that increased slightly over the study time (Figures 3-4). Overall, the total absorption of the bioidentical hormones was higher for the topical gels in comparison to the creams. The total recovery (receptor medium, skin content and surface wash) of the bioidentical hormones varied from 87-97%.

Versabase Cream and Versabase Anhydrous HRT are a proprietary topical bases developed for the delivery of female hormones into and through the skin. The anhydrous base (water activity below 0.6) offers extended stability and thus compounded preparations with longer default beyond-use-dates<sup>2</sup>. The two bases facilitated the percutaneous absorption of all hormones *in vitro* using the dermatomed human skin model. As such, the two bases may be used in pharmaceutical compounding for the preparation of permeation-enhancing topical creams and gels.

**Conclusions:** This study demonstrates that the bioidentical hormones penetrate through the skin (stratum corneum, epidermis and dermis) upon application of the topical compounded creams and gels. These results are important evidence to support the effectiveness of compounded bioidentical hormone replacement therapy since the *in vitro* model used has proven to accurately predict *in vivo* permeation kinetics.

## References:

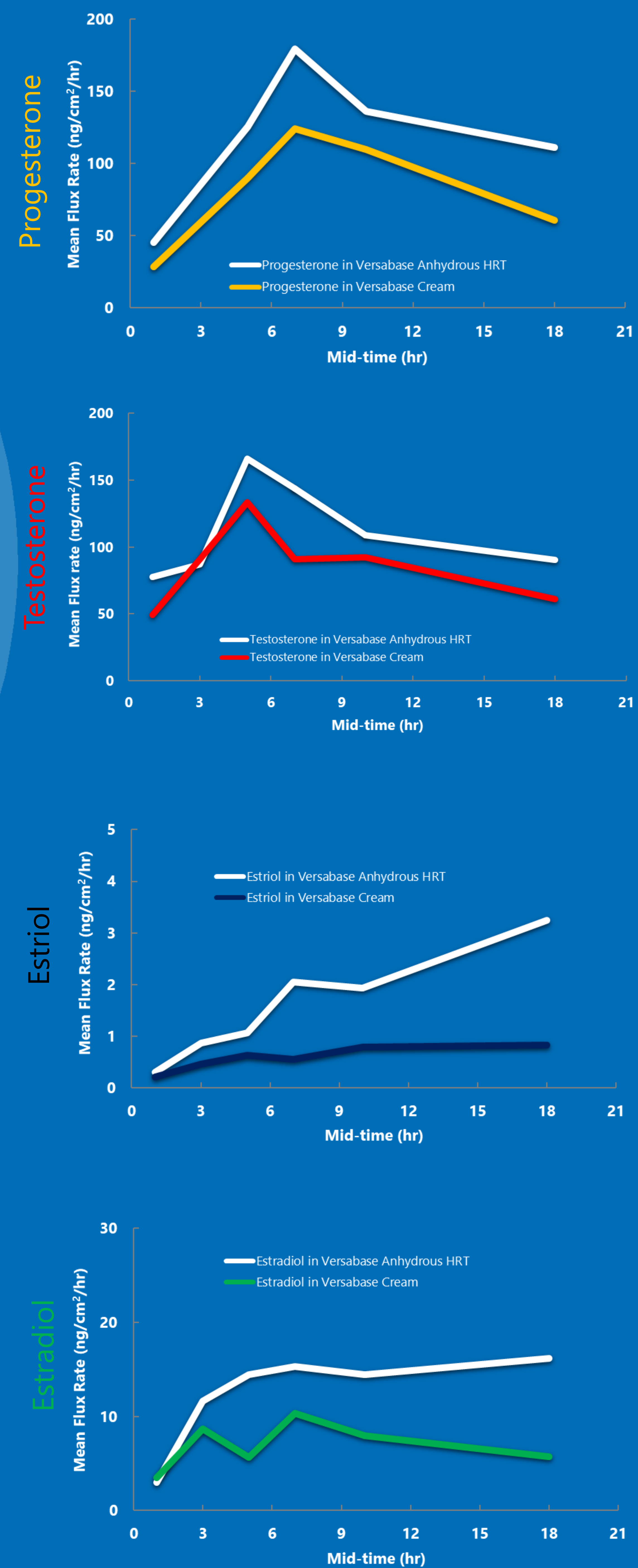
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\* gsong@pccarx.com

1. PCCA, Houston (TX) USA

2. University of Houston



Figures 1-4. Percutaneous absorption of progesterone, testosterone, estriol and estradiol: mean flux across donors over time for the two Versabase formulations.