PCCA Cream Bases Now Proven to Transport Progesterone Into and Through Human Skin

Performance Better Than Vanicream®

Study:

EVALUATION OF THE PERCUTANEOUS ABSORPTION OF PROGESTERONE, *IN VITRO*, USING THE HUMAN CADAVER SKIN MODEL

(Study performed by PRACS Institute, Ltd., an independent contract research facility.)

Summary

The study was designed to evaluate the percutaneous absorption pharmacokinetics of progesterone. Absorption was measured in human cadaver skin, *in vitro*, using the finite dose technique and Franz Diffusion Cells.

Important Note: This study should not be used as a means of determining dosing of progesterone topically. It is a study intended to evaluate the ability of certain cream vehicles to transport progesterone across a human skin sample, *in vitro*. It is not a substitute for *in vivo* pharmacokinetic studies. It also is important to note the formulations in this study are NOT rubbed into the skin, but simply applied to the skin via a pipette and left to diffuse.

Bases Tested

The bases used in the testing were: **VersaBase® Cream, Cosmetic HRT™,** a mixture of **VersaBase® Cream** and **VersaBase® Gel** (95% Cream/5% Gel) and the commercial cream **Vanicream®*.** The progesterone used was **Progesterone USP, PCCA Special Micronized**. Pentylene glycol was used as a wetting agent at a concentration of 10%. The concentration of progesterone in each preparation was 50 mg/gm.

Study Skin Preparation

Percutaneous absorption was measured using the *in vitro* cadaver skin finite dose technique. Human cadaver trunk skin without obvious signs of skin disease, obtained within ~24 – 48 hours of death, was used in this study. It was dermatomed, prepared for cryo-preservation, sealed in a water impermeable plastic bag, and stored at ≤ -70° C until the day of the experiment. Prior to use it was thawed in ~37° C water, then rinsed in tap water to remove any adherent blood or other material from the surface.

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DONOR DEMOGRAPHICS

DONOR ID	AGE	RACE	SEX	INTEGRITY TEST RESULT[1]
DA100405	34	Caucasian	Male	0.24 ± 0.05
MM011907	48	Caucasian	Male	0.72 ± 0.22
BS120705	53	Caucasian	Male	0.54 ± 0.24

[1] *Results are reported as µL-equ 3H2O; Acceptance ≤ 1.56 µl-equ/cm2*

** Vanicream® is a registered trademark of Pharmaceutical Specialties, Inc., Rochester, Minn.*

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Results

The data indicate that progesterone does penetrate into and through human skin, *in vitro,* from the test formulations evaluated in this study.

In general the penetration profile from all formulations is characterized by a rise in absorption to a peak at approximately 7 hours after dose application followed by a slow decline in flux over time. A transient lower secondary peak of penetration is observed at approximately 28 hours after dose application at approximately half the flux than seen at the maximum.

When comparing the bases' abilities to transport progesterone deep into the dermis, VersaBase® Cream out-performed all bases, and delivered more than 4 times as much progesterone as the commercial base Vanicream®.

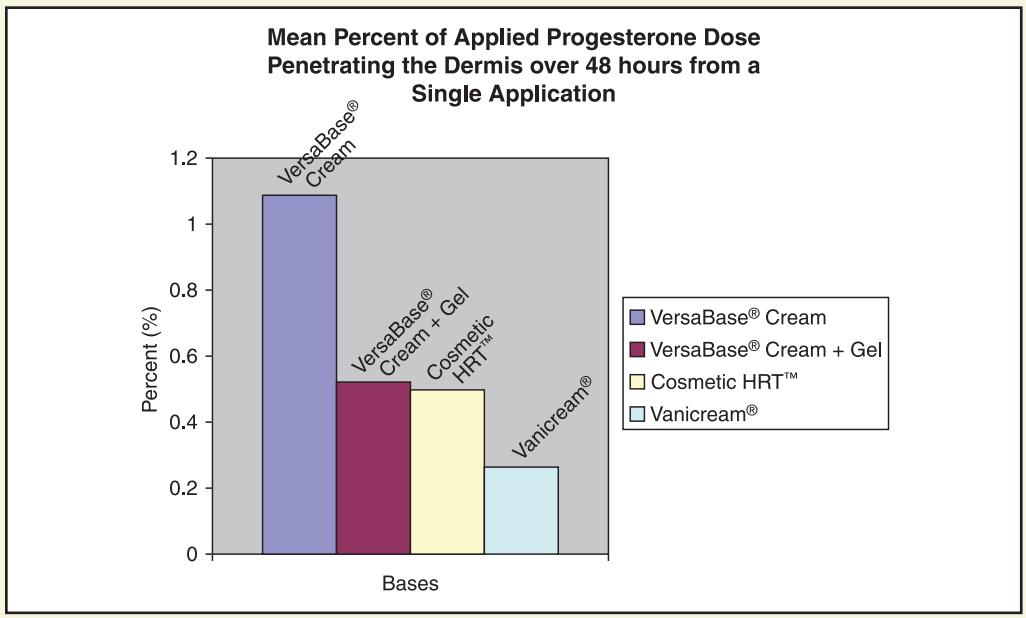
PCCA PRODUCT INFORMATION

VersaBase® Cream . . . **PCCA #30-3641**

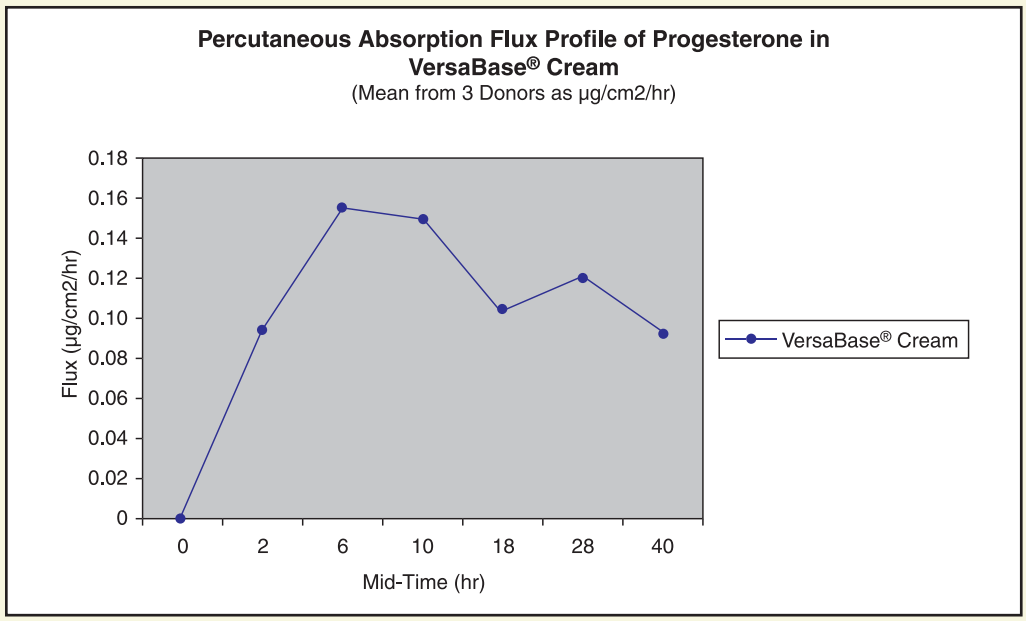
VersaBase® Gel. . . . . **PCCA #30-3656**

Cosmetic HRT™ Base. . . . . **PCCA #30-3337**

Progesterone USP, PCCA Special Micronized . . . . . **PCCA #30-3530**



VersaBase® Cream delivered 4.07 times as much progesterone to the dermis as Vanicream®.



Peak flux of progesterone into receptor compartment at approximately 7 hours post application.

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PCCA Special Micronized Progesterone

Don't Settle For Anything But The Best For Your Patients

PCCA #30-3530

Because of PCCA's commitment to quality, we search the globe for the finest chemicals. In doing so, we have found that not all hormone powders are alike. Pharmacists understand the importance of working with pharmacopoeial grade hormone powders that consistently meet potency standards. PCCA's Special Micronized Progesterone meets these high standards but also excels in an additional category: particle size. **PCCA's Special Micronized Progesterone is 99% less than 5 microns.** Particle size is very important in drug delivery, regardless if it is transdermal, oral, buccal, vaginal or rectal.

Progesterone USP, PCCA Special Micronized
PCCA #30-3530

Consider this quote from the text *Pharmaceutical Dosage Forms and Drug Delivery Systems* by Howard Ansel and Nicholas Popovich –

YOU BE THE JUDGE...

PCCA Progesterone:

- White Crystalline Powder – Micronized
- Particle Size (100% <10 microns and 95-99% <5 microns) – Independently Tested
- Above and Beyond USP Standards
- Tested with PCCA Formulations
- Consistent Source – FDA-Registered Facilities and GMP Compliant

Other Progesterone Sources:

- Larger Particle Size (approximately 20 microns)
- Black Specks in the Product
- Yellowish Color, Distinctive Odor
- Inconsistent Sources
- Potency Inconsistency
- GMP Non-Compliance

"When a drug particle is reduced to a larger number of smaller particles, the total surface area created is increased….this generally results in an increase in the rate of dissolution. Increased therapeutic response to orally administered drugs due to smaller particle size has been reported for a number of drugs. To achieve increased surface area pharmaceutical manufacturers frequently use micronized powders. The use of micronized powders are not confined to oral preparations. For example, ophthalmic ointments and topical ointments utilize micronized drugs for their preferred release characteristics. Due to different rates and degrees of absorption obtainable from drugs of various particle size, it is conceivable that products of the same drug substance prepared by two or more reliable pharmaceutical manufacturers may result in different degrees of therapeutic response in the same individual."

PCCA