

The background features a woman's face on the right side, looking through a magnifying glass. The magnifying glass is focused on a circular inset showing a cross-section of skin with various colored cells (blue, yellow, purple) and a network of lines, representing a biological or medical process. The overall design includes abstract, flowing lines in shades of red, green, and white.

**American Society of
Plastic Surgeons (ASPS)**

**The Benchmark for Skin Care in the
21st Century: Permeation**

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Required Disclosure Statement

- **Dr. Kung has no relationships that require disclosure**

- **No matter where you go these days, whether you see a plastic surgeon or a dermatologist, everyone is doing the same type of skin care – ablative skin care.**
- **Examples of ablative skin treatments include laser resurfacing, chemical peels, and dermabrasion. It is debatable what the long term affects of ablative treatments are to facial skin. However, ablative skin treatments generally result in longer recovery, greater downtime, slower recovery and more discomfort for patients.**

- **Ablative Skin Care**
 - Laser Resurfacing
 - Chemical Peeling
 - Mechanical Dermabrasion



Is there Anything Else?

- **Yes – there is an entire of segment of non-ablative skin treatment which I advocate.**
- **The essence of non-ablative skin treatment is the concept of feeding the skin instead of breaking it down.**
- **The greatest factor in feeding the skin is the ability to penetrate it in a non-ablative fashion.**

The Gold Standard of Skin Care = Permeation

Before 1980: Cosmetics

- **Relating to beauty, especially of the complexion**
 - Drawback: Only enhancement and concealment, no long term result

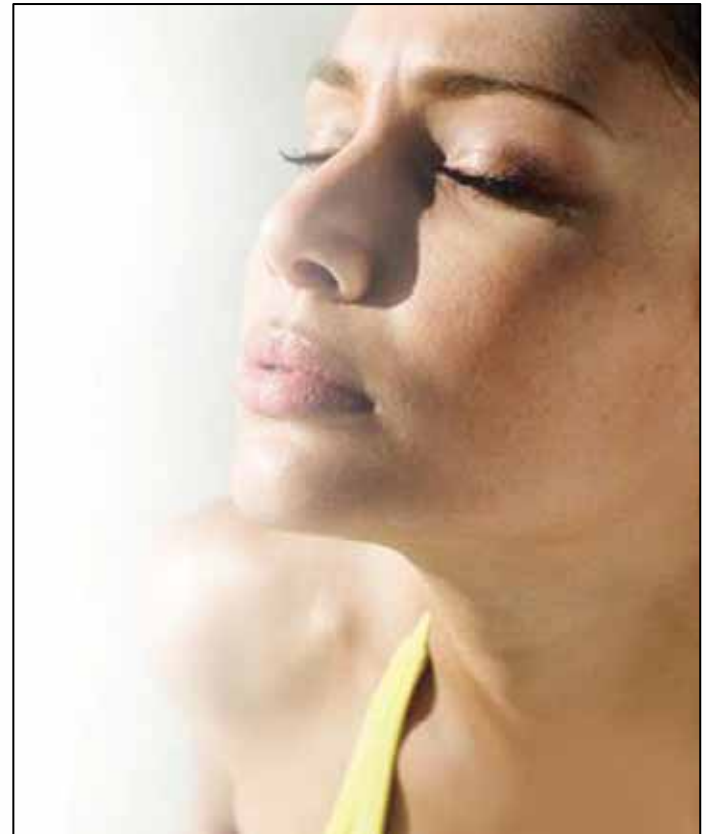


1980 – 1997: Cosmaceutical

- **Cosmetic + Pharmaceutical**
- **AHA, Chemical Peel, Retinol, etc.**
- **Stimulate skin turnover rate**
 - Drawback: Irritation, redness, pigmentation problems

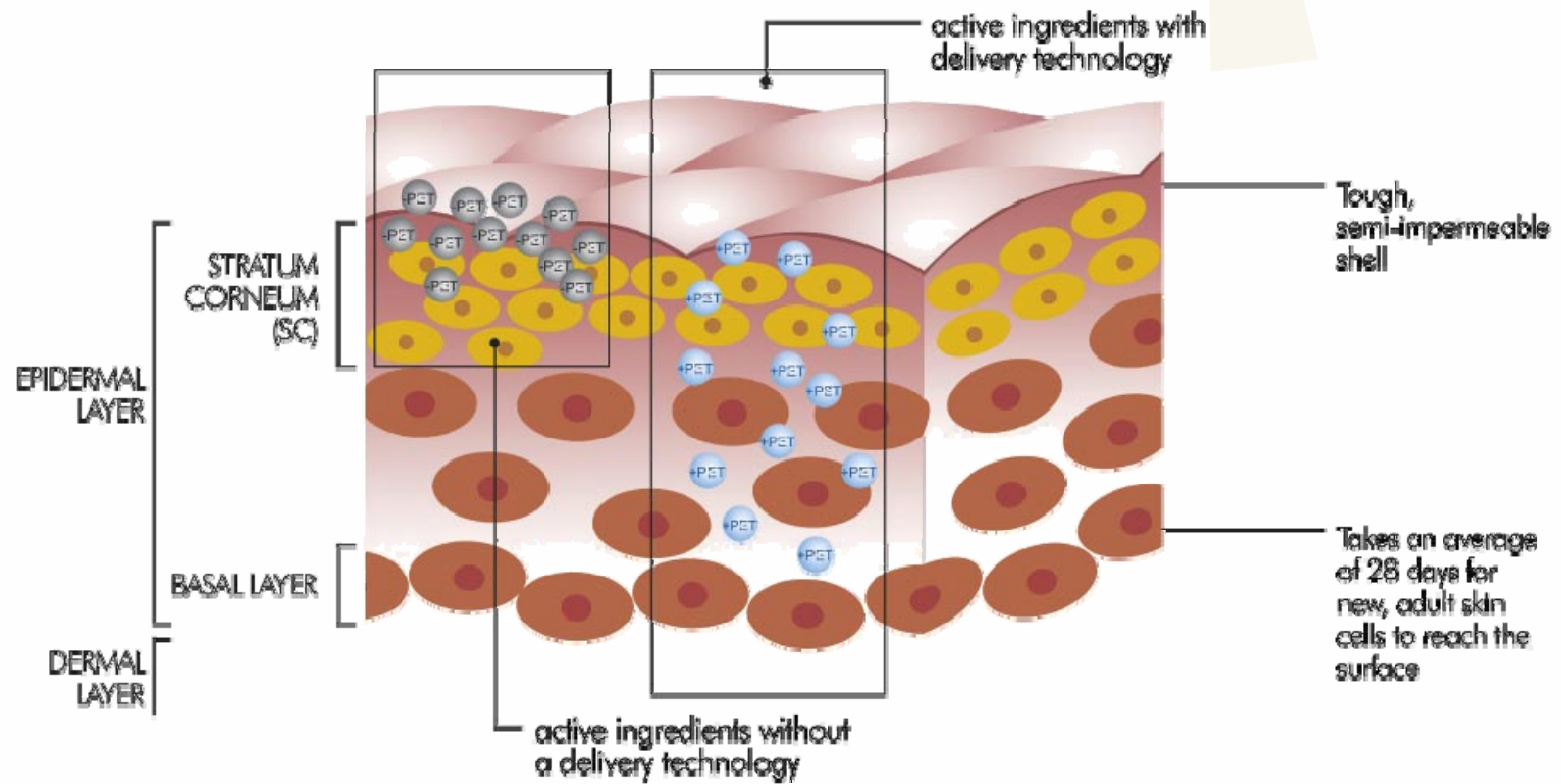
1997 – Present: Nutra-Cosmaceutical Skin Care

- **Nutrients + Cosmaceutical**
- **Delivery System**
- **Antioxidants, Botanic Extracts, Enzymes, Growth Factors, Peptides**
- **Nourish skin from cellular level**
 - Drawback: Big molecules, difficult to penetrate through skin



Skin Anatomy & Physiology

- Permeation Evaluation



Epidermis – Barrier to the Outside

- **Corneum**
 - Nonviable protective barrier to penetration,
~ 20 cell layers thick
- **Lucidum**
- **Granulosum**
- **Germinativum**
 - Spinosum
 - Basale

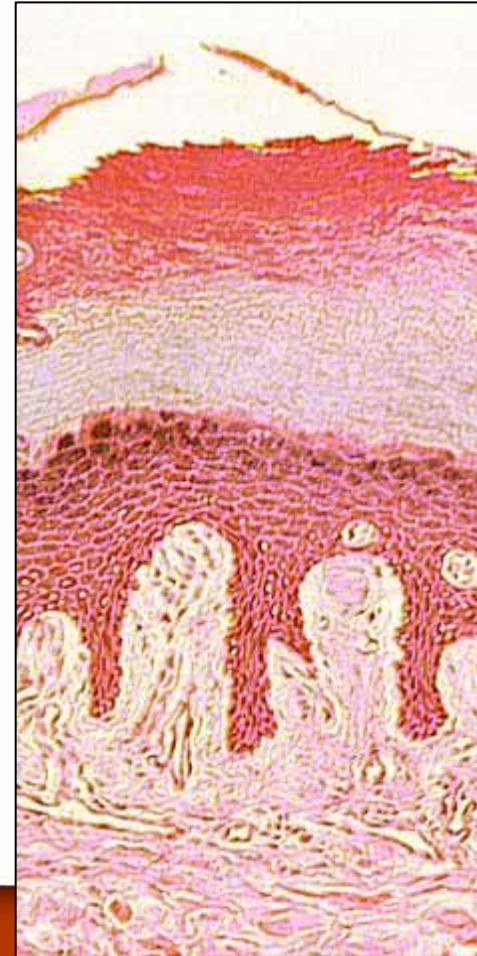
Stratum corneum

Stratum lucidum

Stratum granulosum

Stratum spinosum

Stratum basale

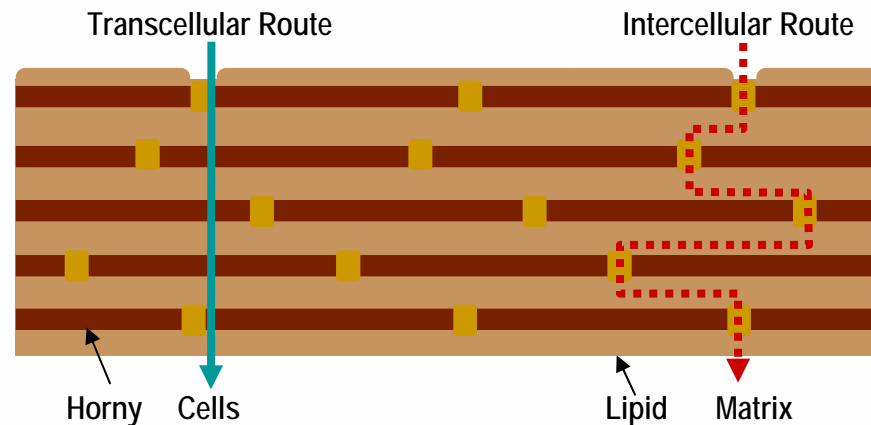


Why Penetration Enhancement?

- It is not enough to understand the nutra-cosmeceutical ingredients in a formulation: we should also assess whether those ingredients actually get to their target site.
- Penetration enhancement enables delivery of active ingredients to their target site.

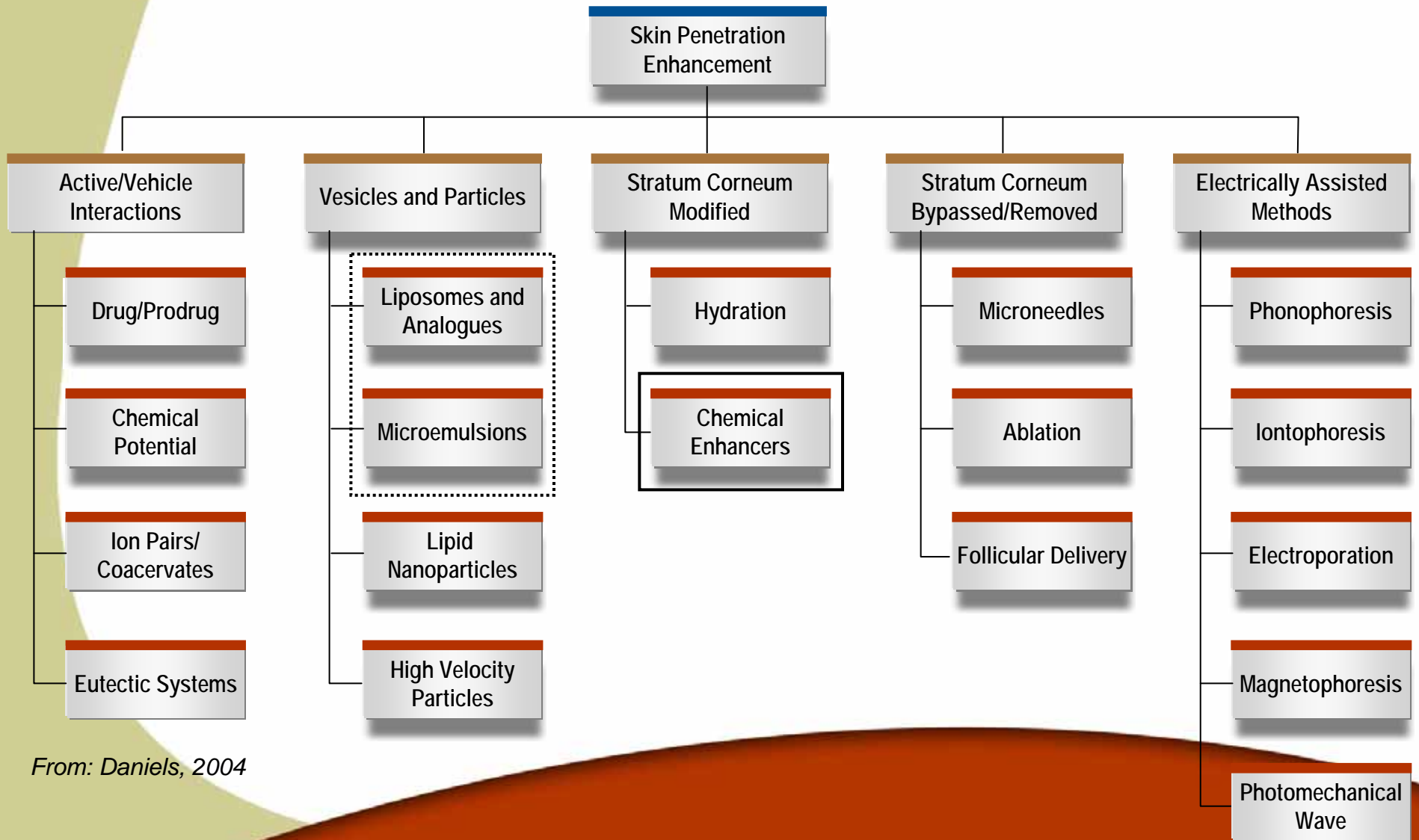
3 Routes to Penetrate the Skin Barrier

1. **Transcellular** – into and through the stratum corneum cell barrier
2. **Intercellular** – around and through the overlapping stratum corneum cells



3. **Trans-appendageal** (through other pathways in the skin) – via the hair follicles, sebaceous glands and sweat glands

Skin Barrier Penetration Strategies



From: Daniels, 2004

What are some Desirable Features for a Chemical Penetration Enhancer?

- **Controllable**
 - Able to balance enhancement of skin vs. systemic penetration of actives
 - Penetration enhanced selectively only for desired formulation ingredients
- **Safe and Well Tolerated**
 - Membrane compatibility
 - Produces only a temporary change to the skin barrier in order to facilitate penetration
 - Well tolerated for long term topical use
 - No local irritation, or risk from systemic exposure to penetration agent

Chemical Penetration Enhancers

Table 2. Chemical Classes of Penetration Enhancers

Chemical class	Example(s)
Fatty acids	Oleic acid, Undecanoic acid
Fatty alcohols	Octanol, Nonanol
Terpenes	Menthol, Thymol, limonene
Sulfoxides	Dimethyl sulfoxide, Dodecyl methyl sulfoxide
Anionic-surfactants	Sodium lauryl sulfate
Cationic-surfactants	N,N-bis (2 hydroxy ethyl) octylamine
Non ionic-surfactants	Polyoxyethylene (20) sorbitan mono oleate
Zwitterionic-surfactants	Dodecyl dimethyl ammonio propane sulfate
Polyols	Propylene glycol, Polyethylene glycol
Amides	n,n-dimethyl-n-toluamide
Ureas	Urea
Lactam	Laurocapram (Azones)
Sugars	Cyclodextrins

From: Kanikkannan *et al*, 1999

- Example:
- Lipophilic
- Membrane compatible
- Rapidly deactivated in blood/plasma
- Found naturally in Angelica Plant (omega-angelica lactone)

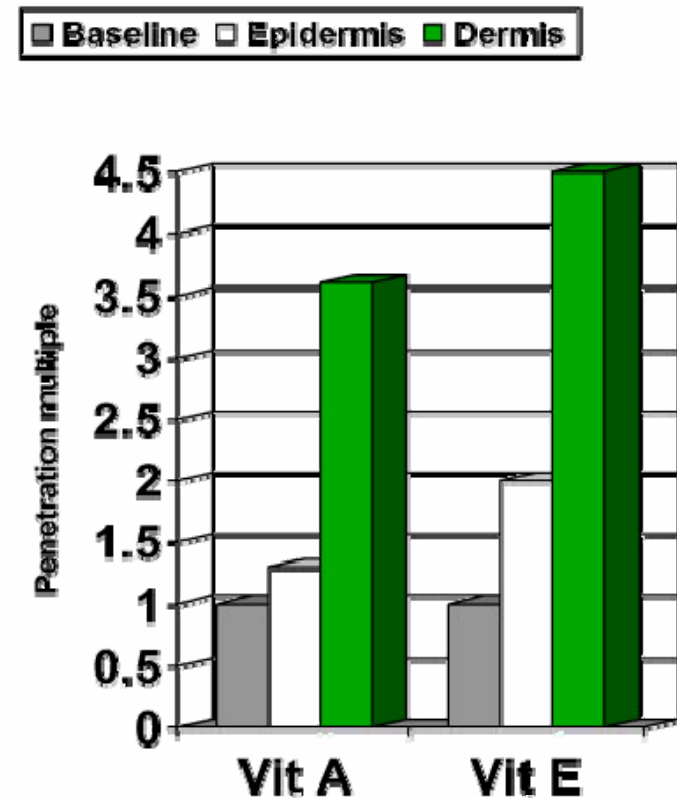
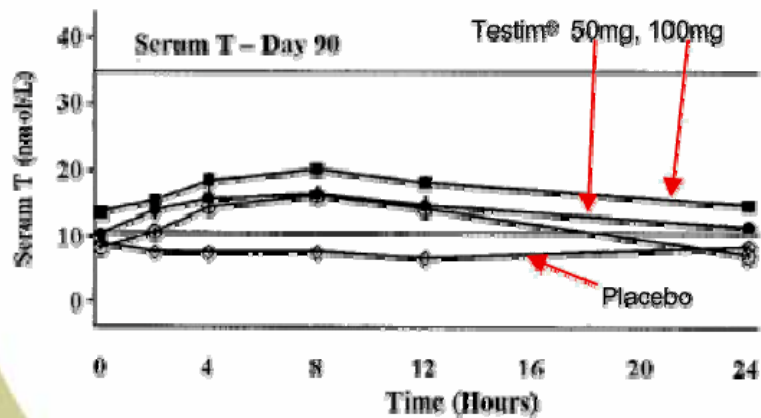
About Angelica Archangelica

- **Common Name:** Angelica;
Latin Binomial: *Angelica archangelica* L.; **Family:** Apiaceae (Umbelliferae)
- **Part Used:** Root (An oil is also distilled from the seed)
- **Countries of Origin:** considered to be native to Europe, although it was possibly introduced from Syria. It is cultivated in Belgium, Holland, France, Germany, Hungary, India, the United States and Canada.



Objectives of Penetration Enhancement

- **Transdermal** – actives through the skin to the blood.
- **Local** – actives into the skin for nutritive, prophylactic or regenerative benefits.

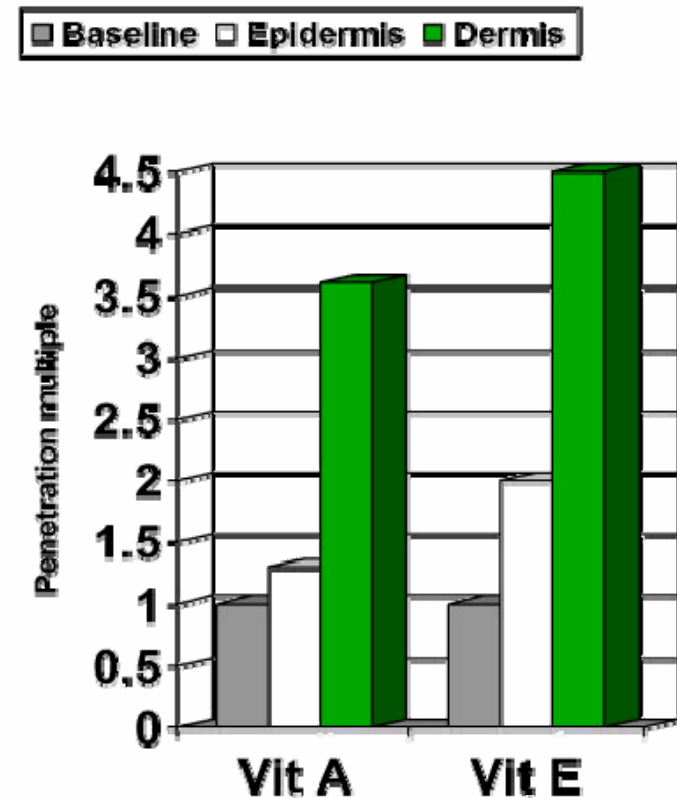


Objective Evaluation of Efficacy of Penetration Enhancement in Product Formulations

- **What data should we look for?**
 - In vitro skin cell data (e.g. Franz Cell): concentrations in/through skin layers is increased vs. those without penetration technology
 - Histology (animal or human skin biopsy): slides of epidermal thickness changes over time –e.g. 120 days treatment
 - Patient outcome data (NOT before & after photos): unbiased measurement e.g. silastic casting of wrinkles; skin tension; skin color

In Vitro Data: Vitamin A&E in Skin

- **Baseline** = tissue vitamin concentration for formulation without a penetration agent
- **Epidermis** and **Dermis** = formulations containing penetration enhancer

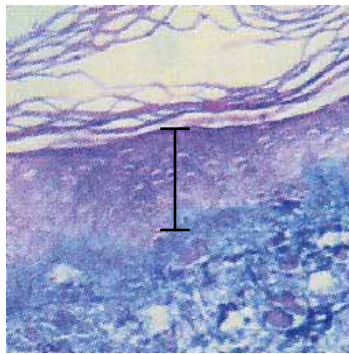


Franz Cell *in vitro* Human Skin Penetration

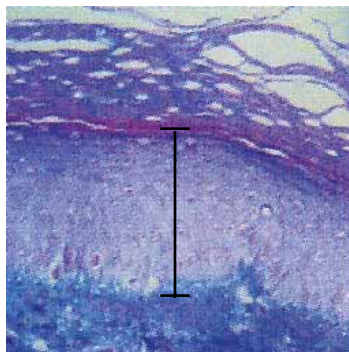
Histology Data: Clinical Study Data

- Increased Thickening of the Epidermis to Day 180

Day 1

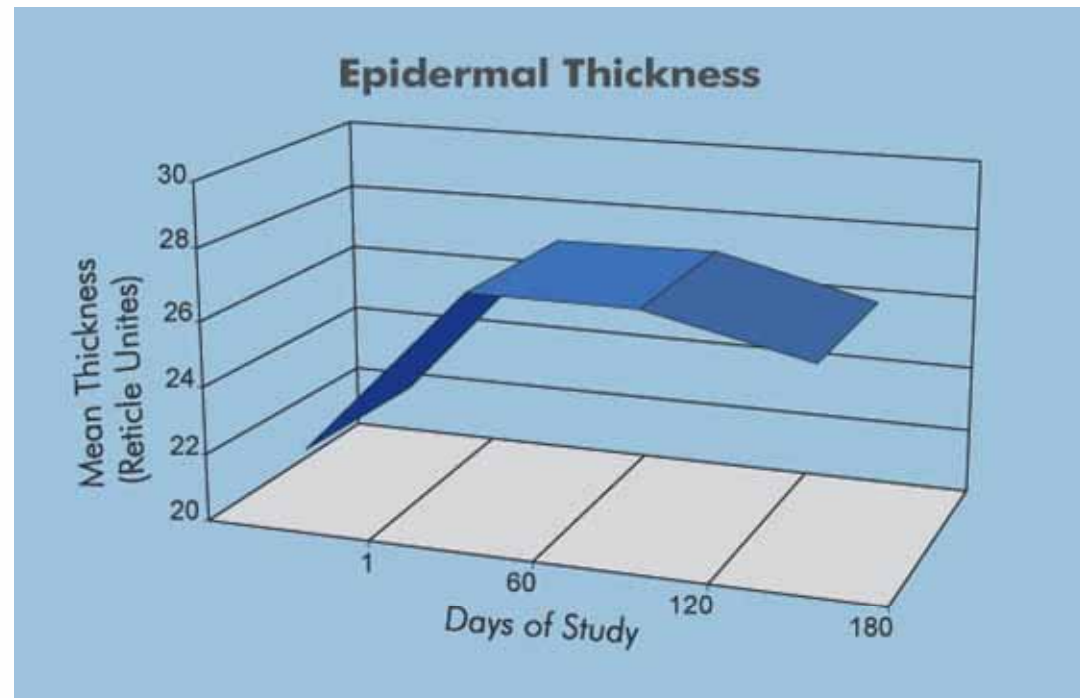


Day 180



Shown 400x

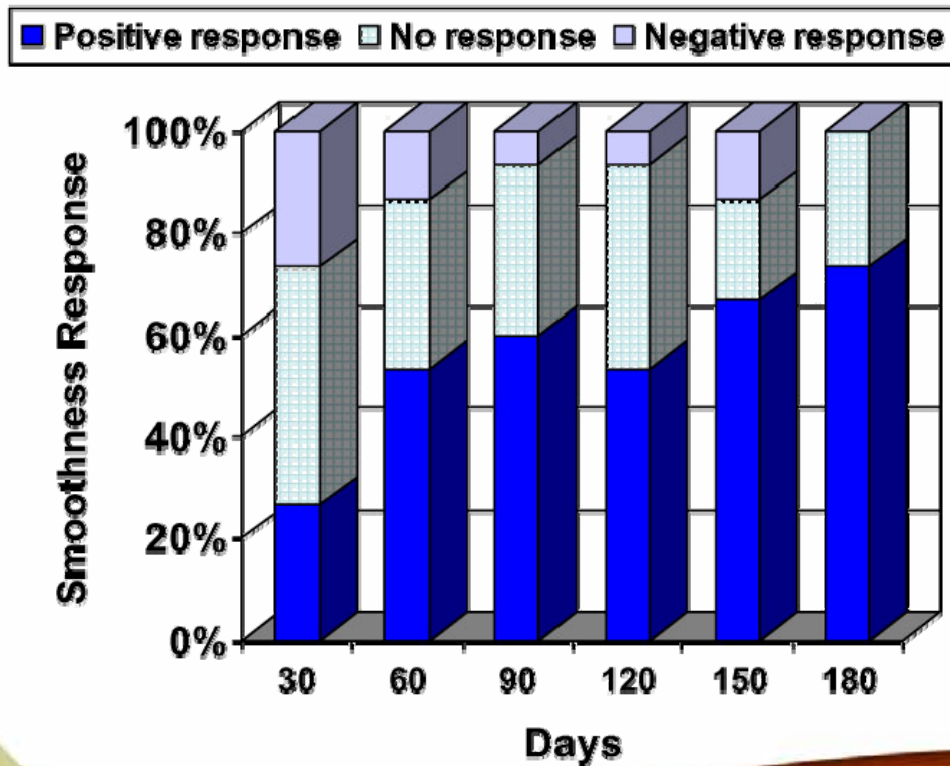
Ultrasound Average of Thickness



N=15 subjects >50 yrs of age, daily application of Vit ACE formulation containing penetration enhancer

Patient Outcome Data: Clinical Study Non-invasive Silastic Casting

- Silastic Casting of lines and wrinkles showed smoothing of skin surface with long term treatment



References and Additional Reading on: Penetration Enhancement

- C. Steidle, S. Schwartz, K. Jacoby, T. Sebree, T. Smith, R. Bachand, and The North American AA2500 T Gel Study Group. AA2500 Testosterone Gel Normalizes Androgen Levels in Aging Males with Improvements in Body Composition and Sexual Function. *J Clin Endocrinol Metab* 88: 2673–2681, 2003.
- Daniels, R. Strategies for Skin Penetration Enhancement. *SkinCare Forum* (an online journal) Issue 37 Aug 2004.
- Hsieh, D.S. In: *Drug Permeation Enhancement*, Hsieh, D.S. Ed.: Marcel Dekker; New York, 1994: 3-17.
- Kannikannan, M.S., Kandimalla K., Lamba, S.S. and Singh, M. Structure-activity relationship of chemical penetration enhancers in transdermal drug delivery. *Current Medicinal Chemistry*, 1999. 6, 593-608.

A woman's face is shown in profile on the right side of the image, looking through a magnifying glass. The magnifying glass shows a microscopic view of several cells, some with blue nuclei and others with yellow nuclei. The background is a dark red color with several thin, curved lines in shades of green and blue. The text "Thank You!" is written in a large, bold, italicized, brown font in the center of the image.

Thank You!