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# Assessing Active Ingredients in Skincare

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# Agenda

**1**

## **What are actives?**

- Overview of Actives
- Actives for Different Concerns
- Active Delivery

**2**

## **Active Evaluation: Critically Assessing the Evidence**

- Study Types and Design
- Formula Considerations
- New Actives/Special Topics




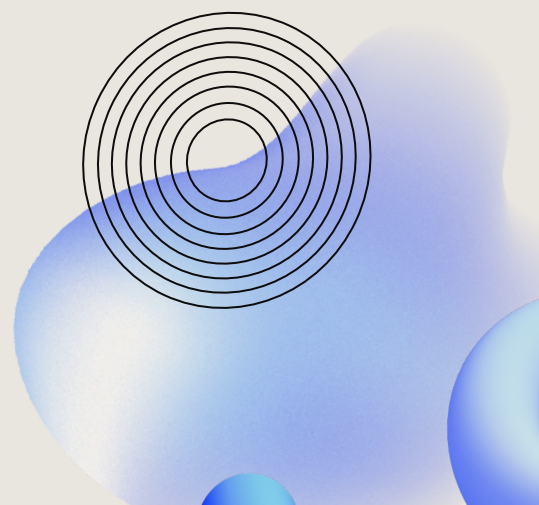

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# What Are Actives?

Actives are ingredients that impart some sort of benefit to the skin or help to address a skin concern.



# Before We Dive In...

## Drug

- ❑ Used to diagnose, cure, treat, or prevent disease
- ❑ Affect structure and biological function
- ❑ OTC monograph, NDA

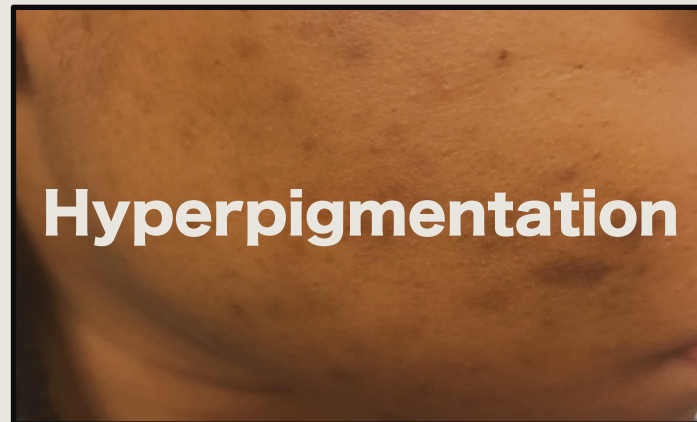
VS

## Cosmetic

- ❑ Cannot claim to treat or cure disease
- ❑ Cleanse, beautify, promote attractiveness, alter appearance
- ❑ Not subject to premarket approval

**Cosmetics can still contain ingredients that impart skin benefits.**

# Skin Concerns





# Well Studied Actives for Different Skin Concerns

## ❑ Acne



- ❑ **Anti-acne actives:** Benzoyl Peroxide, Sulfur, Adapalene, Salicylic Acid
  - ❑ All OTC drugs
- ❑ **Keratolytics:** Retinoids (retinol, retinal), Hydroxy Acids, Azelaic Acid
  - ❑ Retinyl ester derivatives have variable efficacy

## ❑ Hyperpigmentation

- ❑ Increase skin turnover
  - ❑ Retinoids, Hydroxy Acids
- ❑ Inhibit melanocyte activity
  - ❑ Niacinamide, Retinoids, Kojic Acid, Vitamin C, Alpha Arbutin, Azelaic Acid
- ❑ Prevent UV stimulation of melanocyte activity
  - ❑ Sunscreen/UV filters - OTC

## ❑ Anti-Aging

- ❑ Protect against extrinsic aging
  - ❑ Sunscreen/UV filters
- ❑ **Antioxidants:** Vitamin C, Retinoids
  - ❑ Protect against free radical & ROS damage
- ❑ Hydroxy Acids
- ❑ Niacinamide

## ❑ Dryness/Hydration

- ❑ **Humectants:** Glycerin, Panthenol, Sodium PCA
- ❑ **Occlusives:** Petrolatum, Lanolin
- ❑ **Barrier repairing:** Ceramides, Cholesterol, Niacinamide

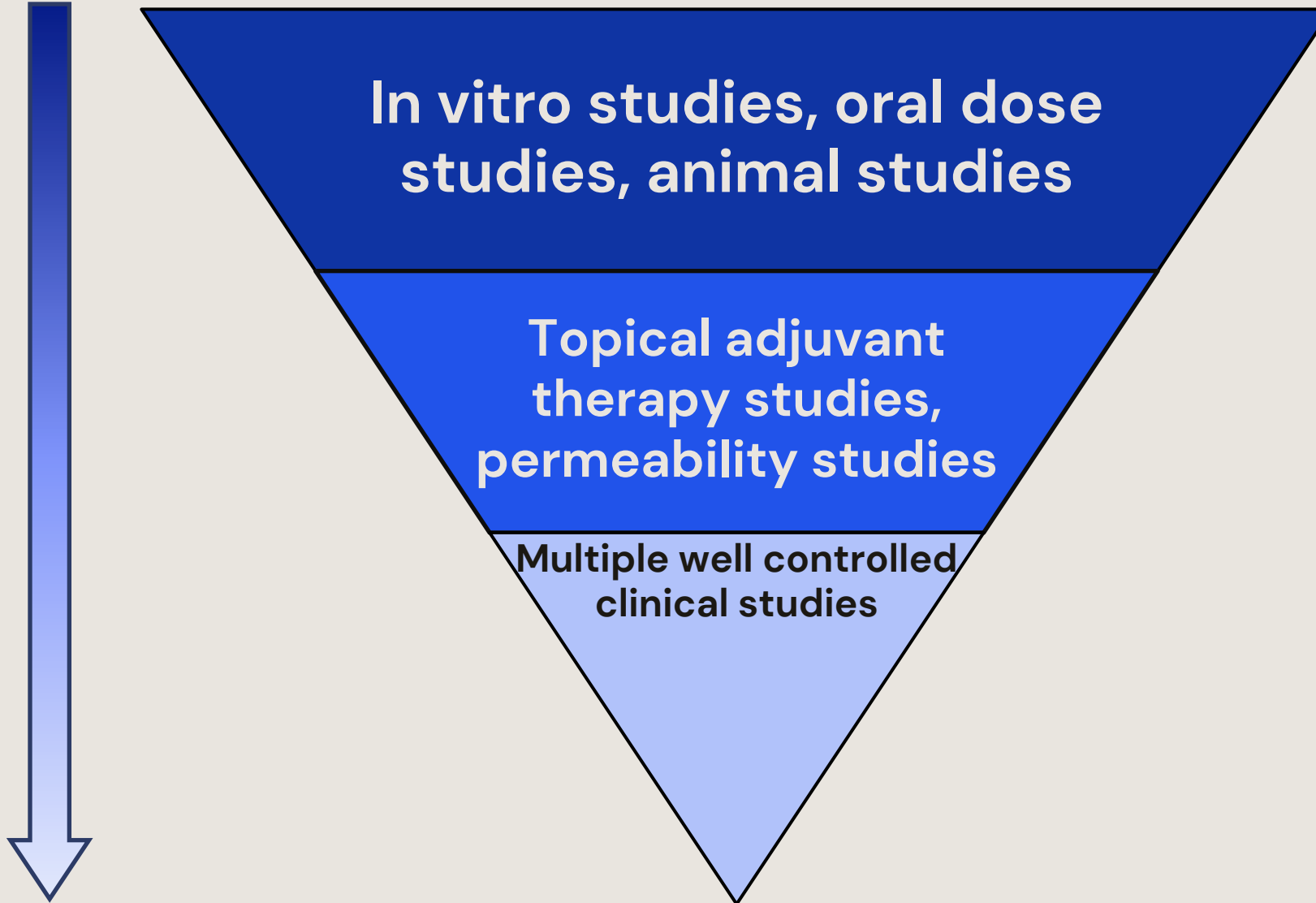
## ❑ Redness

- ❑ **Soothing/Anti-Irritant:** Colloidal Oatmeal, Aloe Vera




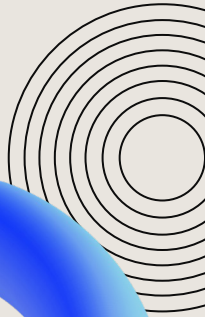




# Hierarchy of Evidence

Increasing  
Evidence



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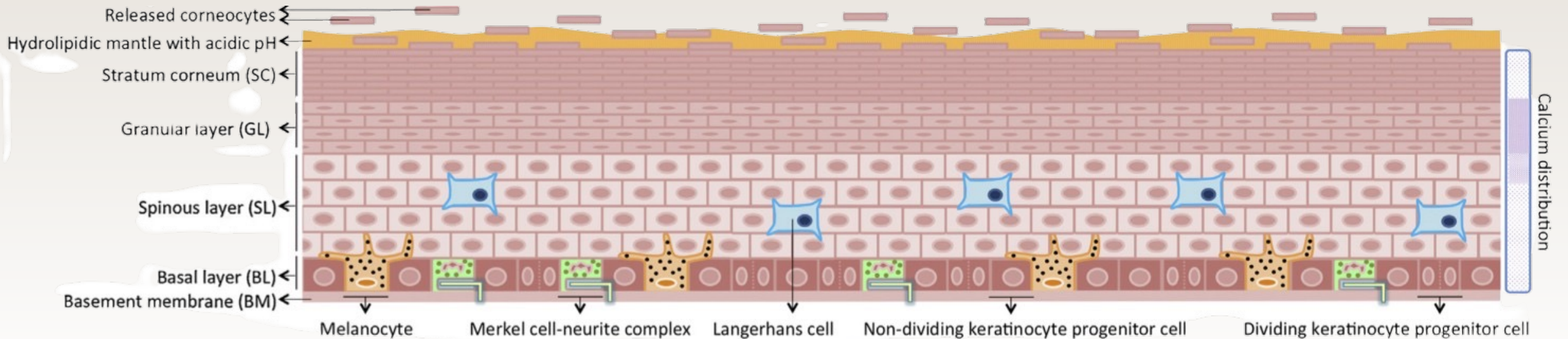
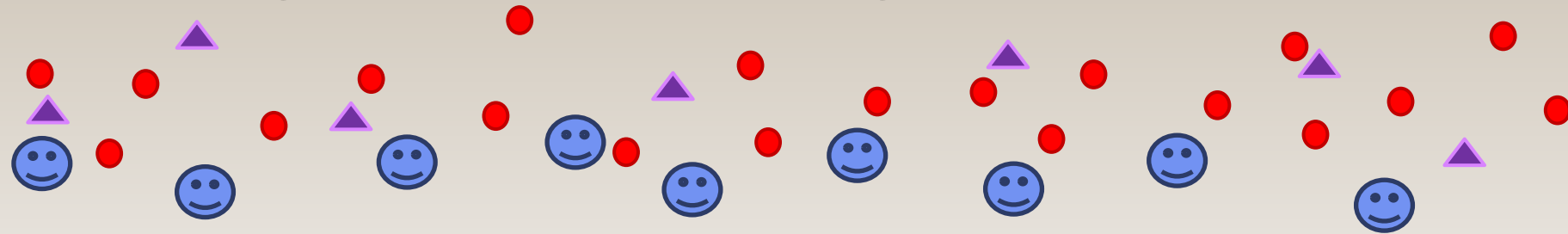
**Having an active does not  
guarantee that the active  
will work as intended!**

**Cosmetics are not drugs! They do not have to prove safety or efficacy to be sold.**



There is a misconception that it is easy for the skin to absorb substances that are applied to it...

**You have to get the right active to the right place in the right form at the right amount.**



There are a many important characteristics of actives that influence their delivery...

Size,  $MW \leq 500$  Da  
 Hydrophobicity, log P  
 Ionization Constants, pka  
 Solubility  
 Stability

It taps into the power of pure, water-based hydration from hyaluronic acid. At the right molecular weight, this humectant ingredient helps attract water to the skin and then locks it in to provide long-lasting comfort and hydration. It sinks in quickly to quench dryness and soften the appearance of fine lines, helping to restore the visible plumpness of youthful skin. Perfect for ALL skin types to deliver a lightweight layer of moisture.

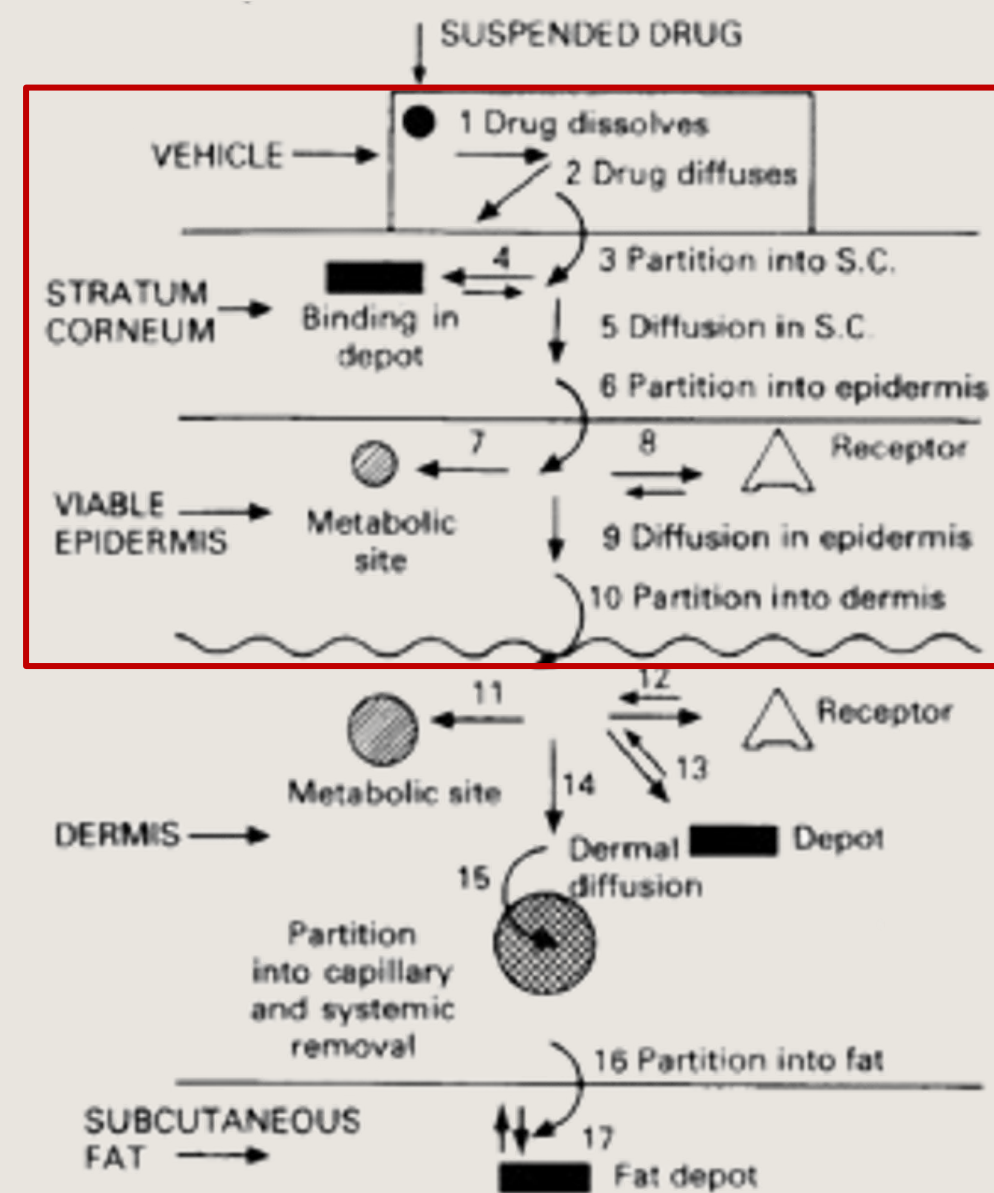


Fig. 22.4 Some stages in percutaneous absorption from a suspension ointment. Emulsion vehicles may also include dissolution and partitioning processes in the internal phase. (Source: Barry 1983. Reproduced with permission of the copyright owner)

# Remember: A salesperson's job is to sell you things.

## Absorption efficacy of collagen peptides with different molecular weights

From the data, the oligopeptides composed of 2-10 amino acids have a molecular weight between **600-1000DA**. They have excellent performance in the repair of damaged skin and the improvement of ordinary skin. They can take into account the characteristics of high permeability and high biological activity at the same time. After taking two hours, they can enter the systemic circulation in the body, and the absorption rate in the human body is even higher. more than 90 percent.

Chemical test				
Test Result(s):				
Test Item(s)	Unit	Test Method(s)	Test Result(s)	LOQ
Proportion of protein hydrolysates with relative molecular weight <1000u	%	GB/T 22729-2008 appendix A GPC/UV	72.81	-
Total average molecular weight (Mn)	-	GB/T 22729-2008 appendix A GPC/UV	807	-

Molecular weight distribution			
Molecular weight range	Percentage of peak area (%) ( $\lambda$ 220nm)	Number-average molecular weight (Mn)	Weight-average molecular weight (Mw)
>5000	0.35	6001	6147
5000-3000	2.42	3545	3607
3000-2000	4.94	2398	2431
2000-1000	19.47	1326	1382
1000-500	33.07	653	678
500-189	35.24	292	315
<189	4.50	-	-

Combined with the skin test of the test

population, it can be determined that this value of collagen peptides can be well absorbed and utilized by the human body and skin tissues, and can precisely act on the stratum corneum, epidermis and dermis of the skin, supplementing collagen and promoting its own collagen. protein synthesis.

1. Size  $\geq 500$  Da

2. This data says nothing about absorption or systematic circulation.

3. Data presented does not support assertions or conclusions.




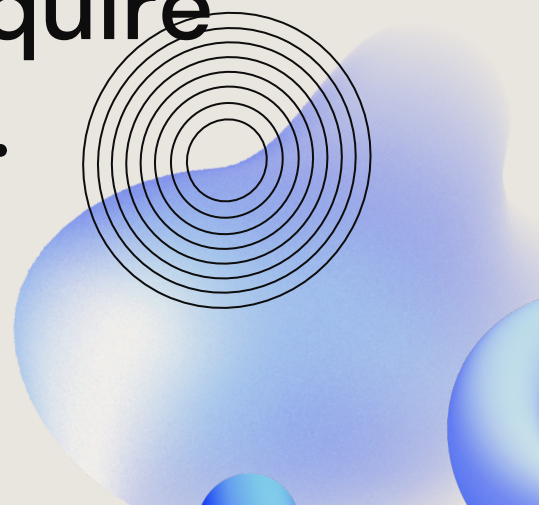

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# Active Evaluation

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Never take what is said about an active at face value whether that be a company, supplier, or the literature. Actives require special attention and evaluation.



# Looking at the Evidence

1

## Clinical Study

- Evidence of efficacy
- Route / dosage form
- Concentration
- Effects
- Adverse reactions

2

## Supplier/Company Data

- Suppliers usually do some testing on active ingredients
- Ingredient pamphlets and brochures

3

## Chemical Characterization

- Characteristics of compound/mixture
- Solubility
- Molecular weight
- Hydrophobicity
- pKa

# Critical Evaluation of Literature

Not every study is a good one. Does this study **adequately** measure what it claims to?

- Study Design
  - Study Size?
  - Length of Study?
  - Study Type?
    - In vitro
    - In vivo
  - Model?
    - Cell – cell type
    - Animal – species

- Methods
  - Inclusion/exclusion criteria?
  - Delivery route?
  - Adequate controls?
  - Influence of other actives?
  - Blinding and randomization?
  - Measurements?
  - Analysis?



# Everyone is looking for the next “new” active ingredient.

Newer actives may be used to make **outlandish claims based off little evidence**



## Derivatives

- Derivatives are **not the same** as the original active
- Changes in structure can influence delivery and activity, **need to be separately evaluated**
- Either show activity at the **same target** or are **biologically converted** to active

## Naturals/ Botanical Extracts

- Complex mixtures** with many different components, used at low amounts
- Batch to batch, regional, and seasonal **variations in composition**
- Must ensure that **extract contains active** compound

# Example: Two Clinical Studies on Tranexamic Acid

## Topical 5% tranexamic acid for the treatment of melasma in Asians: a double-blind randomized controlled clinical trial

Pinyapat Kanechorn Na Ayuthaya<sup>1</sup>, Nucha Niumphradit, Aranya Manosroi, Artit Nakakes

Affiliations + expand

PMID: 22506692 DOI: [10.3109/14764172.2012.685478](https://doi.org/10.3109/14764172.2012.685478)

[Full text links](#)

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### Abstract

**Background:** Topical tranexamic acid has been claimed to lighten melasma without serious adverse effects. However, controlled studies assessing the efficacy and safety of topical tranexamic acid (TA) for the treatment of melasma is limited.

**Objective:** To assess in a double blind, randomized, prospective study, the efficacy of topical 5% tranexamic acid versus vehicle for treatment of melasma.

**Methods:** Twenty-three women with bilateral epidermal melasma enrolled in a split-face trial lasting 12 weeks. Patients blindly applied topical 5% tranexamic acid and its vehicle, to the designated sides of the face twice daily in addition to the assigned sunscreen each morning. Pigmentation and erythema were measured objectively using a mexameter and Melasma Area and Severity Index (MASI), in addition to physician and patient global assessments.

**Results:** Twenty-one patients completed the study. Eighteen out of twenty-three patients (78.2%) showed decrease in the melanin index on either or both sides of the face by the end of 12 weeks compared to baseline. The MASI scores were also significantly reduced on both tested sides. However, lightening of pigmentation induced by TA gel was neither superior nor different ( $p > 0.05$ ) compared to its vehicle although erythema was significant on the TA-applied site ( $p < 0.05$ ).

**Conclusions:** Although lightening of pigmentation was obtained, the results were not significant between the two regimens. However, topical TA produced erythema.

## Effect of tranexamic acid on melasma: a clinical trial with histological evaluation

J I Na<sup>1</sup>, S Y Choi, S H Yang, H R Choi, H Y Kang, K-C Park

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PMID: 22329442 DOI: [10.1111/j.1468-3083.2012.04464.x](https://doi.org/10.1111/j.1468-3083.2012.04464.x)

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### Abstract

**Background:** Melasma is associated with epidermal hyperpigmentation, weak basement membrane, vascular proliferation and increased numbers of mast cell. Tranexamic acid (TXA), a plasmin inhibitor, is reported to improve melasma when injected locally. However, the effects of oral and topical TXA on melasma have not been well studied and the underlying mechanism remains unclear.

**Objectives:** To elucidate the effects of oral and topical TXA on melasma.

**Methods:** A clinical study was conducted with 25 women for 8 weeks from March to July 2010. Volunteers were instructed to take two TXA tablets three times a day and apply a TXA topical agent twice a day for 8 weeks. Skin pigmentation and erythema was measured using a Mexameter® during each visit and skin biopsies were collected from eight subjects before and 8 weeks after treatment. Fontana-Masson, anti-CD31, antitryptase and antitype IV collagen staining was performed.

**Results:** Twenty-two subjects completed the study and no serious adverse events occurred during the study period. The mean lesional melanin index (MI) scores decreased significantly. Interestingly, the MI scores for the perilesional skin increased. The erythema index scores of lesional and perilesional skin also showed a similar pattern. Histological analysis showed significant reduction of epidermal pigmentation, vessel numbers and mast cell counts. Type IV collagen staining was not observed in all specimens.

**Conclusion:** TXA decreased epidermal pigmentation associated with melasma and also reversed melasma-related dermal changes, such as vessel number and increased numbers of mast cells.



# Chemical Characteristics

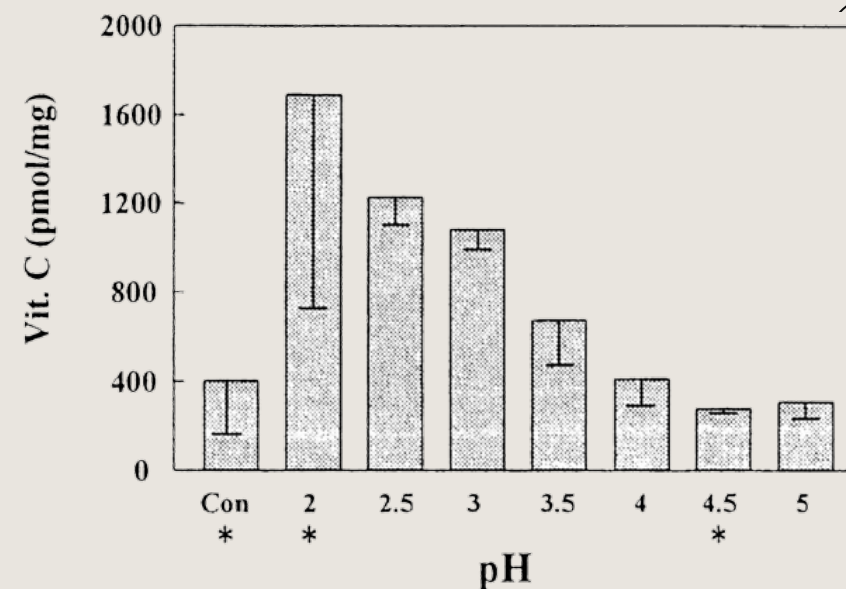
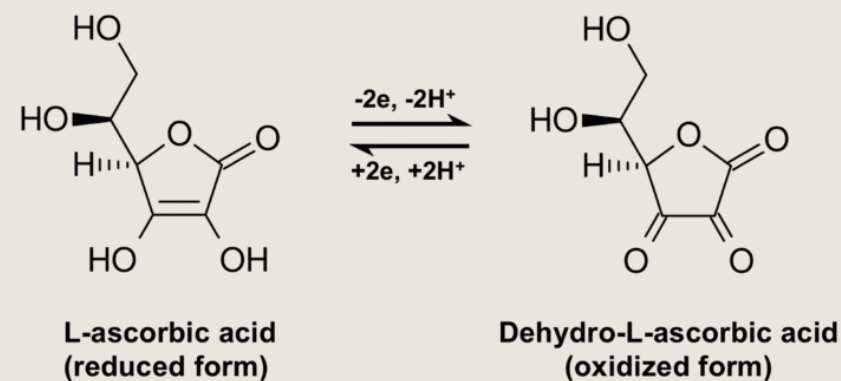
Understanding chemistry of your active is important to:


## ❑ Prevent degradation of the active

- ❑ Oxidation
- ❑ Photo instability

## ❑ Ensure correct form of active and formula compatibility

- ❑ Acids must be in unionized form
- ❑ Some actives have pH dependent activity
- ❑ Solubilize active in product

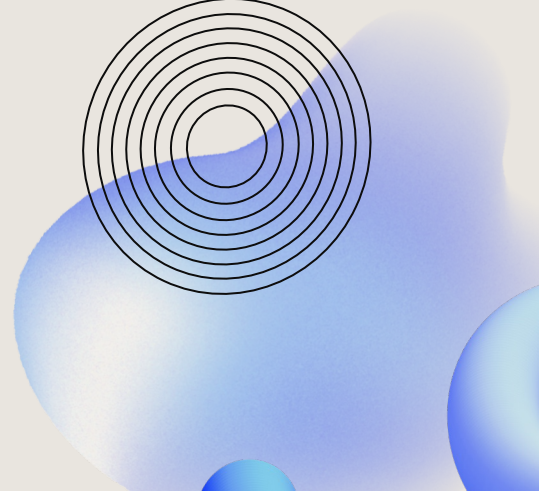


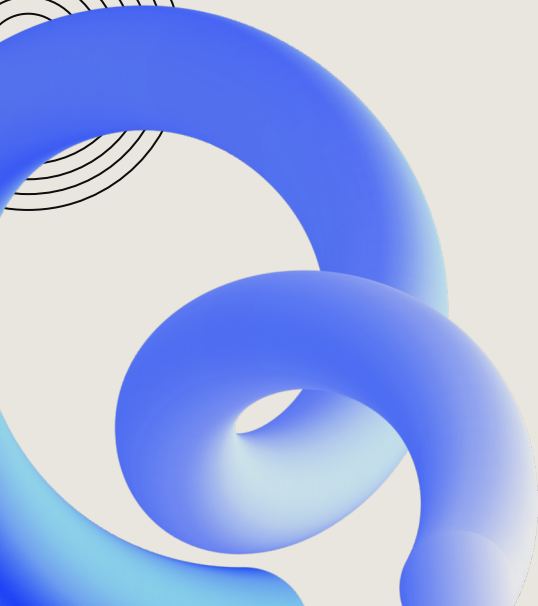




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Now, I've done all this research to learn about my active, does it guarantee that my product will work?



No





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# Importance of Formulation

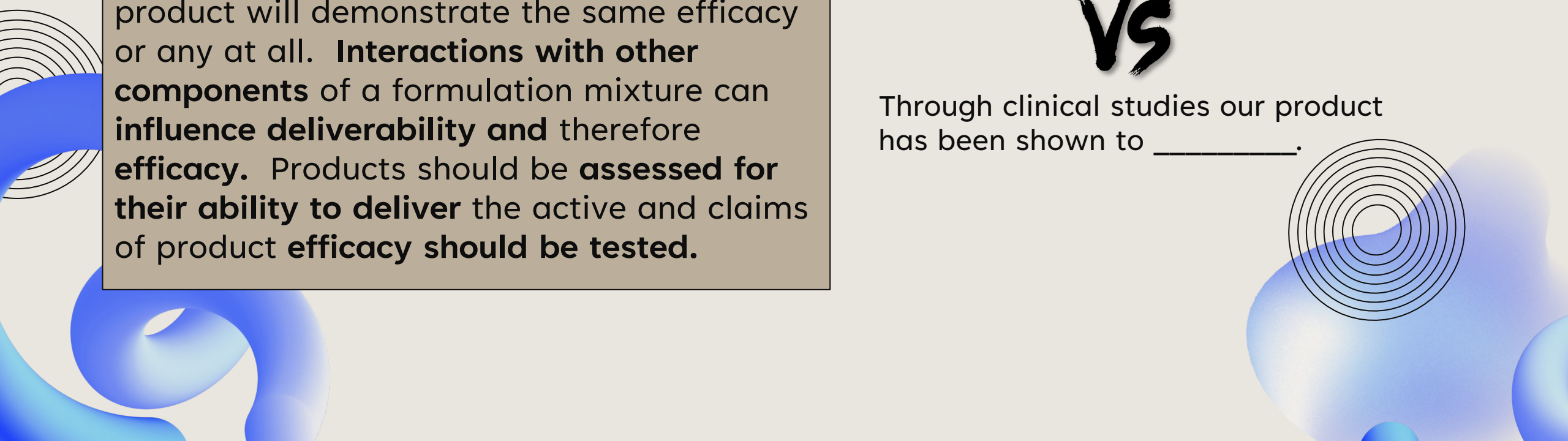
+ Clinical results are great but the other ingredients in a **formulation matter too!** Just because a clinical study observed a particular result doesn't mean that your product will demonstrate the same efficacy or any at all. **Interactions with other components** of a formulation mixture can **influence deliverability and therefore efficacy.** Products should be **assessed for their ability to deliver** the active and claims of product **efficacy should be tested.**

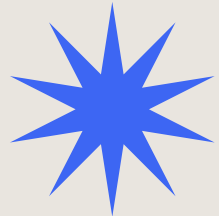
For consumers important claims language:

Our product contains \_\_\_\_\_ which has been clinically shown to \_\_\_\_\_.

**VS**

Through clinical studies our product has been shown to \_\_\_\_\_.





# Thanks!

Do you have any questions?

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 <https://shorturl.at/pQW27>

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