

ANTI-AGING COSMETICS

*New Technologies Replace
“Hope in a Jar” with
a “Dermatologist in a Jar”*

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“HOPE IN A JAR” OR “THE FOUNTAIN OF YOUTH?”

As any consumer who visits a cosmetic counter knows, there are hundreds of cosmetics for sale that should put plastic surgeons out of business! These products, say the product labels loudly, can “dramatically reduce the appearance of wrinkles, fine lines, and just about any skin imperfection that would prevent any women from looking like Christie Brinkley, Gillian Anderson (my favorite), or whomever you consider to have perfect-looking skin. And, for most of these products, these youth-renewing effects will work in several days, and for some, in only one day!

Well, what happened? When I walk in town, only few women look vaguely like Gillian Anderson, and many look like everyone’s’ grandmothers! Could it be that these products exaggerate?

IS VASELINE™ THE BEST ANTI-AGING PRODUCT ?

The truth is, with few exceptions, most “anti-aging” cosmetics work only as elegant moisturizers that allow the skin to trap water which acts to plump-up the skin’s outer layer, the stratum corneum. In fact, perhaps the most potent product of this type is the old standby, Vaseline™-brand petrolatum, that greasy, sticky, but highly effective moisturizer that forms a water-tight barrier on the skin that prevents water from evaporating. Essentially, all present cosmetic moisturizers, and most “anti-aging” cosmetics attempt to mimic the water-trapping and hydrating activity of petrolatum while minimizing its undesirable aesthetic properties. A good moisturizer will actually visibly reduce fine lines for the several hours while it remains on the skin.

COSMETICS YOU CAN EAT AND MAKE YOU LOOK YOUNGER ?

Another effective trick of the cosmetic industry that really works (at least for a few hours) is to add various proteins to the cosmetic mix. Yes, these are the same proteins that make up all living creatures and the food we eat. These proteins are frequently hydrolyzed (cooked and broken up) and include keratin (hair), collagen, elastin, fibonectin and gelatin (from skin), egg, soy, wheat, milk, oats, peas, sweet almond, fish, silk, and generally, proteins from anything that walks, crawls, flies, slimes or is simply alive. What all these proteins have in common is their ability

to hold water and change shape as they dry. In a cosmetic jar, proteins become saturated with water and frequently assume an elongated shape. After they are applied to the skin in a cosmetic, water evaporates and the proteins contract and curl up, causing the skin underneath to contract and viola, fine lines and wrinkles are reduced.

IN COME THE VITAMINS

We all know that we should eat our fruits and vegetables and take our vitamins – Mom always told us that. It turns out that she was more correct than she realized! In fact, some vitamins, especially those related to vitamins A and C, can indeed have anti-aging properties, either by protecting the skin against sun-induced aging, or by actually acting as a hormone that turns on some of the skin's anti-aging reparative processes. Vitamin A acid (also called retinoic acid or tretinoin) is available as the prescription drugs, Retin-A™ for acne treatment and Renova™ for treating aged skin. The tretinoin in Renova™ which has been formulated to reduce skin dryness has been shown to actually reduce some of the sun-induced skin damage (fine lines and wrinkles and “liver spots”, actually called solar lentigos or freckles) that is the most important cause of the visible signs of aged skin (that's why sunscreens are so important, chronic sun exposure is the major reason our skin looks older than it should). In some people, the effects of tretinoin can be dramatic. Unfortunately, in all people, tretinoin causes the skin to become very sensitive to sunlight, and causes many otherwise non-irritating chemicals, including those found in cosmetics and pharmaceuticals that cause stinging, burning and redness. In time, these symptoms can subside but for many they are too intense to tolerate.

True Vitamin A, retinol, is also sold for its reputed anti-aging properties. While retinol itself does not have anti-aging activity, the idea is that retinol is converted by skin enzymes into tretinoin in small quantities thus producing a Renova™-like effect. Unfortunately for consumers, when retinol is used at the concentration necessary to produce a mild anti-aging benefit, Renova™-like irritation frequently occurs, although with much less intensity. Retinol is also highly unstable to destruction by oxygen and must be formulated in oxygen-free systems that encapsulate retinol or otherwise preserve it. For these reasons, many of the cosmetics that advertise retinol have only a tiny amount so that they can have an acceptable level of irritation or simply because much of it was destroyed during storage and use.

Vitamin C (ascorbic acid), the vitamin made famous by the Nobel Prize-winning chemist, Linus Pauling, is another vitamin touted as an anti-aging ingredient. When formulated properly, it can actually protect the skin against some of the oxidative damage from sun exposure – the leading cause of aging skin. Some recent studies in fact show that high concentrations of vitamin C can stimulate collagen synthesis when applied topically and can reduce fine lines and wrinkles. Like retinol, vitamin C is also highly unstable in typical cosmetic formulations and must be specially formulated, either at a very acidic, and potentially irritating pH

(around 2.5) or in formulations that physically shield it from oxygen and water. The acidic formulations can be irritating, especially in sensitive skin. A number of vitamin C derivatives such as ascorbyl glucosamine and magnesium ascorbyl phosphate that much more stable, but according to recent research, may not be converted into vitamin C in human skin.

ALPHA-HYDROXY ACIDS (AHAS)

For over 25 years, physicians have used AHAs, typically lactic acid and glycolic acid, in the form of chemical peels and moisturizers for home use to treat the visible signs of aged skin. Compared to all other “anti-aging” ingredients used in cosmetics today, AHAs have the most substantial body of scientific and medical data that demonstrate their ability to reduce fine lines and wrinkles and to generally “rejuvenate” aged skin. During the early 1990s, major cosmetic companies introduced a flurry of AHA cosmetics, all promising to produce the same medical benefits as the much more potent AHA products used by physicians. Within a short time, it became clear that these mass-marketed AHA products did not come close to living up to their promise. It turned out that in order to have high anti-aging potency, AHA products also had a substantial ability to irritate the skin, causing stinging, burning, itching and redness. The challenge for industry was to try to preserve the clinical benefits of AHAs while reducing the risk of irritation and inflammation. In response, cosmetic companies, in essence, “watered down” their AHA products to the point where irritation was acceptably low, but unfortunately that also greatly reduced anti-aging potency.

THE “SECRET” OF AHAS’ ANTI-AGING POTENCY

As physicians had determined from their own clinical experience, the “secret” of how to maximize the anti-aging benefits of AHAs was quite simple and logical. AHA products need to have two properties:

1) A high concentration

AND

2) A low pH (the same as high acidity)

Two questions naturally arise from these facts: (1) How high does the concentration need to be to achieve true anti-aging activity (as opposed to only a temporary anti-wrinkle effect from a moisturizer), and (2) How low a pH must the formulation be to allow the AHAs to work their best?

Unfortunately, the answer is not simple. The presence of acid actually “activates” an AHA molecule and enables it to stimulate skin to rejuvenate itself. So at any given AHA concentration, a portion of the total AHA in the product will be in the “inactive” form, and part will be in the “active” form, also called the “free acid” form.

Sounds complicated? Well, it really isn't once you can visualize what's really going on. Let's define some terms that will help our understanding. First, What do we mean by acid?

As I described in my earlier article in *Les Nouvelles Esthetiques*, acidity or pH measures the concentration of the positively charged hydrogen ion (H^+) in water. Also known as a proton, this tiny atomic particle carries with it remarkable properties that act to rejuvenate the skin. In its simplest sense, an acid is any molecule that carries a proton that can be released into its environment. When the proton is released into the skin, for example, it stimulates the skin to renew new skin cells faster, therefore younger-looking skin is produced faster. Think of protons, in a sense, as fertilizer for your skin! When an acid has its proton "on board" and ready to be released, the acid is called "free acid", since it is "free" to release its acidic proton.

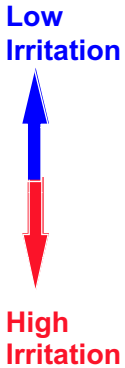
The amount of acid is measured in units of "pH", each unit representing a tenfold difference in acid concentration. The pH scale ranges from 0 (highest acidity – e.g. battery acid) to 14 (lowest acidity or the most alkaline or basic, e.g. lye). When the pH is less than 7, the solution is termed acidic. The skin, for example, typically has a pH of 5.3 to 6.1 and is therefore slightly acidic. At a pH greater than 7, the solution is basic or alkaline, such as blood with a pH of 7.4 or a solution of sodium hydroxide, (NaOH), frequently found in drain cleaners which may have a pH of 13-14. Since each unit of pH is tenfold different from the next unit, a small change in pH means a large change in acidity. For example, a solution with pH 4 has 1000 times more acid than one with pH 7.

Since the concentration of acid, measured by pH, is based on powers of ten, a single unit pH difference is equivalent to a 10-fold difference in acid concentration. For this reason, the amount of the "free acid" form of an AHA is very sensitive to small changes of pH. As **Figure 1** demonstrates, when the pH of a 10% lactic acid solution is changed from 4 to 5, the concentration of free acid is reduced by 83%. Similarly, when the pH is raised from 3.5 to 4, the free acid level is reduced by 40%¹.

FIGURE 1

Effect of pH on AHA Free Acid (Data for 10% Lactic Acid)

<u>pH</u>	<u>Free Acid</u>	<u>Irritation Potential</u>
5.0	0.7 %	None
4.0	4.2 %	Low
IRRITATION BARRIER		
3.5	7.0 %	Moderate
3.0	8.8 %	High
2.0	10.0 %	Very High



Unfortunately, as the free acid level in products rises, so does the irritation potential of the product. For this reason, AHA products sold by the major cosmetic companies are limited to approximately 8% AHA at pH 3.8, equivalent to 4% free acid. Above this level, sensory irritation in the form of stinging, burning and itching and potentially redness greatly increases, essentially producing an “irritation barrier” that prevents the use of more effective AHA formulations. For this reason, the Cosmetic Ingredient Review Expert Panel (CIR) of the Cosmetic, Toiletry and Fragrance Association (CTFA) recommended that no AHA product should be sold without physician supervision with an AHA concentration higher than 10% and a pH of less than 3.5, equivalent to 7% free acid ².

When the overall clinical “anti-aging” efficacy of AHA-containing products is measured, the free acid concentration of the AHA appears to be the most important factor in determining the overall ability of an AHA to reduce the appearance of fine lines, wrinkles and other signs of aging skin ^{3,4}. In his review of the medical literature related on AHAs, Michael Dorman, M.D. summarized the effect of AHA free acid and their “anti-aging” effects on the skin in **Figure 2**.

FIGURE 2

EFFECT OF FREE ACID ON AHA “ANTI-AGING” EFFICACY (Adapted from Michael Dorman, M.D. - <i>Dermatology Times</i> , Jan. 97)		
	<u>FREE ACID</u>	<u>EFFECTS ON SKIN</u>
↑ Low Irritation	0 - 2%	Increased Moisturization
	2 - 4%	Smoother, Softer Skin Moderate Increase in Glycosaminoglycans
<hr/>		
↓ High Irritation	4 - 8%	Moderate Increase in Squamous Cell Turnover Significant Increase in Glycosaminoglycans
	8 - 12%	Significant Increase in Squamous Cell Turnover Moderate Increase in Collagen Deposition
	12 - 15%	Significant Increase in Collagen Deposition Thicker, Less Fragmented Elastic Fibers
	15 - 20%	Reversal in Basal Cell Atypia More Uniform Melanin Pattern

According to Dr. Dorman’s review, when the AHA free acid concentration is between 0 and 2% (2 % free acid is equivalent to 4% AHA at pH 3.8), the AHA formulation acts essentially as only a moisturizer. Most AHA products sold in the mass market have AHA concentrations and free acid levels in this range. When the free acid concentration reaches 4% (e.g. 8% AHA at pH 3.8), the skin’s smoothness increases and biochemical changes associated with younger-looking skin start to occur. For example, glycosaminoglycans (GAGs) that act as molecular sponges and can hold 1000 times their weight in water are synthesized at moderately increased rates that act to “plump up” the skin from within. As the free acid concentration increases from 4 to 8%, the rate of synthesis of new skin cells is moderately increased (increase in squamous cell turnover) and GAGs are significantly increased. Above 8% free acid, the biochemical changes in the skin become significant and “medical-strength” skin changes occur ⁵.

HOW COSMETIC COMPANIES MAY MISLEAD CONSUMERS

Since high concentration, low pH AHA products have the most anti-aging activity, but are also the most irritating, considerable efforts have been expended to reduce product irritation. Unfortunately for consumers, many times manufacturers hide

critical information about their products or, in some cases, deliberately mislead consumers about their products' AHA content. Some existing practices include:

1. **Not providing the AHA concentration on the product label.** To not provide this critical information is like not telling you what your salary will be when you start a new job. And like homeopathy, the quackish pseudoscience that says that the amount of a drug given a patient does not make any difference is no more valid than the idea that the amount of your salary doesn't make any difference – any amount will do the same for you!
2. **Not providing the pH of the formulation.** As I discussed, the pH is required to estimate the total AHA free acid concentration in the product. Without it, it is impossible to assess the product's anti-aging potency.
3. **Using deliberately misleading AHA concentration information.**
An example of this practice is to label the product "10% AHA" with an " * " after the 10%. The careful reader will note that somewhere on the label, usually in small print, the " * " explains something like: "of a 70% AHA complex solution". This means that to calculate the actual AHA concentration, the consumer has to multiple the listed AHA concentration (10%) by the concentration of the AHA solution that was used to formulate the product (60%) to arrive a at the actual AHA concentration in the product (10% * 70% = 7%).
4. **Using exotic AHA derivatives for which clinical data is not available.**
There is substantial data, in the form of publications in peer-reviewed medical journals, that demonstrate the anti-aging activity of lactic and glycolic acids. In many instances, there are no publications available to support the activity of exotic AHA-like products not available for independent scientific evaluation.
5. **Non-Peer-reviewed clinical data**
"Clinical data" purporting to show that a product has specific anti-aging benefits that is "unpublished" or has been published in non-peer reviewed journals does not prove that a product works as advertised.

The most stringent test for whether a clinical study has been conducted properly and its conclusions are warranted by the data is to provide the study to an independent expert in the field for critique. In science and medicine, this process is known as "peer-review". To publish in a peer-reviewed journal, the author sends the manuscript to the journal editor, who sends it anonymously to several experts in the field. A typical journal may have 25 to 50 or more experts who have agreed to review papers. These "referees" then send the journal their candid critique of the paper, including whether they think that the study, its methods and data adequately support the authors' conclusions. In many instances, these critiques require the author to perform additional studies, or may require the author to alter the paper's conclusions if they are not supported by the data. As hundreds of years of scientific progress has demonstrated, the

peer-review publication process is the best one yet devised to separate medical and scientific “fact” from speculation or fiction.

Ask any company who makes unusual claims for their products to provide copies of their peer-reviewed publications – it can be rather funny to hear the excuses for why they don’t have them!:

“It’s too expensive to conduct studies”; “everyone knows it works, why spend money to prove it?”; “The medical industry won’t let it be published, otherwise doctors would be out of a job”, “My dog ate the data”, etc.

ARE HIGHLY POTENT AHA ANTI-AGING PRODUCTS POSSIBLE?

Since high concentration, low pH AHA products have the most anti-aging activity, but are also very irritating, are consumers doomed to have only comfortable AHA products that have low potency? Fortunately the answer is “NO”. Recent research, published in peer-reviewed medical journals has demonstrated that a simple, natural element found in seawater, in the foods we eat and in our bodies can protect the skin from high potency AHA irritation while allowing AHAs to provide their maximum anti-aging potency possible^{6,7,8}. This element is the trace metal element, strontium, element 38 in the periodic table. Strontium, which closely resembles calcium, is unique in its ability to “turn down the volume control” of the skin’s irritant sensors, called type C nociceptors, thus reducing AHA irritation and their potential to cause skin damage while allowing AHAs to produce maximum anti-aging effects.

STOPPING THE SKIN FROM DAMAGING ITSELF

As I described in my two previous articles in *Les Nouvelles Esthétiques*, strontium formulated with many irritating ingredients, including AHAs, stops the stinging, burning, itching and redness caused by type C nociceptors and their release into the skin of inflammation-producing chemicals. Because we eat more strontium every day in green-leafy vegetables than can be absorbed by strontium-containing products, it is safe as well.

An example of strontium’s use to produce an anti-aging AHA product that has the highest concentration of AHA, and lowest pH recommended for use outside of a doctor’s office is presented below.

The level of stinging, burning and itching was quantified every minute for 10 minutes according to the following scale:

Sensory Irritation Scores (Stinging, Burning & Itching)

Commercially Acceptable

0 = none

1 = slight----- transient irritation, noticeable but “doesn’t bother” them

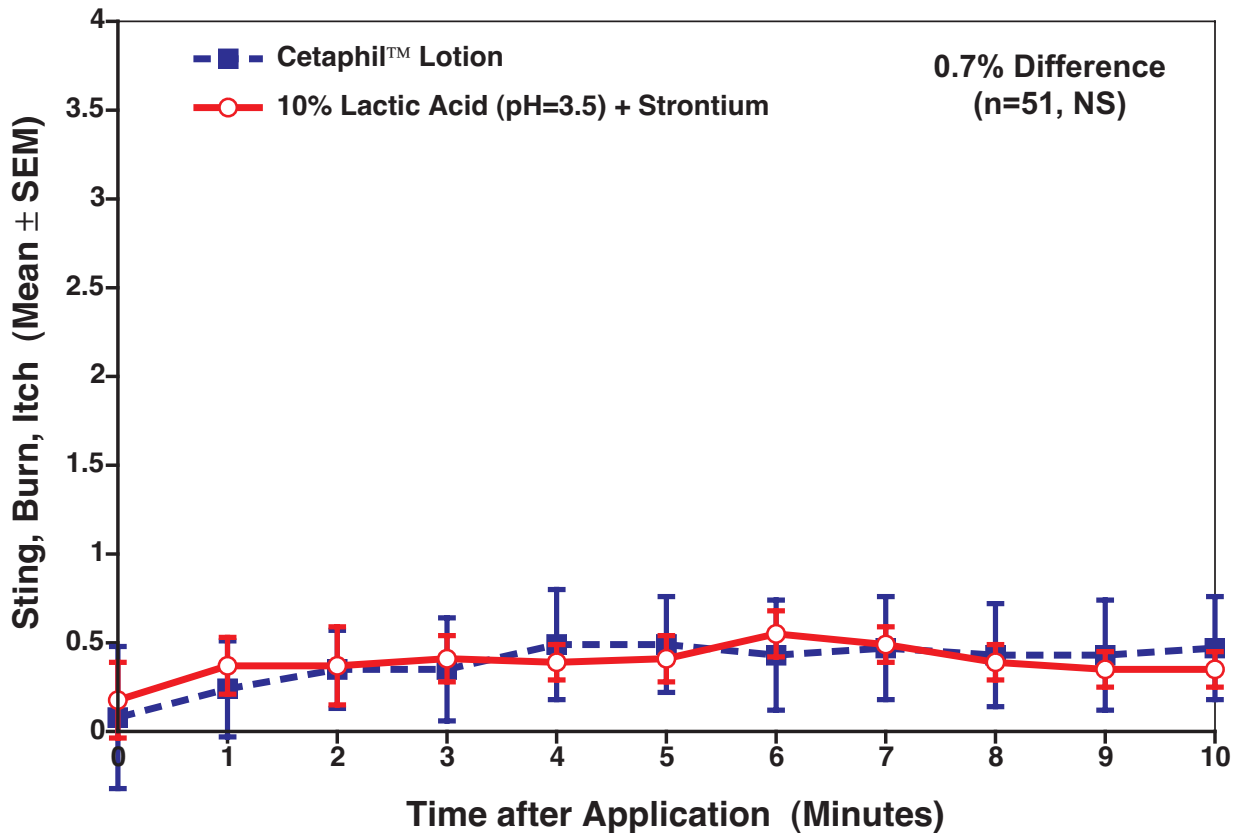
Commercially Unacceptable

2 = mild ----- continuous irritation, “bothers them”

3 = moderate----- “bothers them” & interferes with concentration

4 = severe----- intolerable irritation, redness and swelling possible

GRAPH 1: Time Course of Sensory Irritation



Graph 1 presents the level of stinging, burning and itching over 10 minutes for Cetaphil™ lotion and a 10% lactic acid (pH 3.5) lotion containing strontium in 51 subjects with sensitive skin. Each point represents the mean \pm standard error of the mean (SEM) for all 20 subjects. As is evident, the two products had negligible, and essentially identical irritation which differed by only 0.7% over the entire 10 minute period.

The results of this clinical study are remarkable since the 10% (pH 3.5) lotion is the strongest AHA product recommended without the supervision of a physician, since according to the Cosmetic Ingredient Review Expert Panel, such products can produce substantial irritation. In fact, no major cosmetic company sells an AHA this powerful to the general public because of irritation concerns. Such data demonstrates that strontium, added to high potency AHA products, can “break through the irritation barrier” that has previously limited AHA potency.

FROM “HOPE IN A JAR’ TO A “DERMATOLOGIST IN A JAR”

Cosmetics have come a long way since “Hope in a Jar” accurately described the anti-aging activities of these products. Recent research has shown that the skin can be biochemically altered by potentially powerful chemical ingredients that are capable of “turning back the aging clock”. Through an increased understanding of how the skin can be protected from irritation that has previously limited anti-aging cosmetic potency, future cosmetics can truly be labeled a “dermatologist in a jar”.

About the Author

Gary S. Hahn, M.D., is a graduate of Stanford University (BS, Biology) and the University of California, San Diego School of Medicine, is a licensed physician in California and serves as an Assistant Clinical Professor, Immunology and Allergy Division, Department of Pediatrics at UCSD. Dr. Hahn previously founded Immunetech Pharmaceuticals (now Dura Pharmaceuticals) where he served as Senior Vice President for Research and Scientific Director and Cosmederm Technologies. He is a member of the American Academy of Dermatology, Society of Investigative Dermatology and is an author of numerous publications, medical book chapters and pharmaceutical patents. He discovered and patented a technology, called COSMEDERM-7™, derived from the natural element strontium that has the unique ability to selectively reduce the sensitivity of type C nociceptors to chemical irritants and histamine without affecting pain or other tactile sensations. For this reason, products formulated with COSMEDERM-7™ can contain the highest “anti-aging” potency of active ingredients, including AHAs, while protecting the skin against irritation. For more information about products containing COSMEDERM-7™, please e-mail Cosmederm7@cosmederm.com, or call toll free 1(866) 550-7070.

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