Antiaging Skincare Science

Leslie Baumann MD, FAAD
Dermatologist, Author, Researcher
Skin Type Determines Products

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The Regimen Should Be Customized

- Check all that are true about your skin:
  - [ ] Item 1
  - [ ] Item 2
  - [ ] Item 3
  - [ ] Item 4
  - [ ] Item 5

- AM:

- PM:

- Skin Type:
  - 1
  - 2
  - 3
  - 4
  - 5
4 Issues Affect Skin Health

- Dehydration
- Inflammation
- Pigmentation
- Aging
Aging Skin

- Poor lifestyle habits
  - Smoking
  - Tanning
  - Poor diet
  - Stress
  - Lack of sleep
  - No sunscreen
- Age over 30
Genes Associated With Skin Aging

Age-induced and photoinduced changes in gene expression profiles in facial skin of Caucasian females across 6 decades of age

Acacia B. Kimball, MD, MPH; Maria R. Mora-Peck, MD; Maks Torah, PhD; Mina A. Mullins, BS; Chonk-fai Lee, MD; Robert L. Bender, PhD; Todd A. Houston, AD; Shelli D. Gordon, PhD; Sunrise T. Tang, PhD; Nikkii E. Tonnen, PhD; Charles C. Bascom, PhD; Robert J. Jabot, PhD; Bradley R. Jarroll, MD, BS; Tonya K. Kale, PhD; Robert L. Kuchler, PhD; Shermar D. Smith, PhD; Jay W. Trentman, PhD; Karen Toronko, BS; Jan Xu, PhD; Xiangzhou Yan, PhD; and Rosemarie Osborne, PhD.

Boston, Massachusetts; Cincinnati; Gelse, Japan; and Mountain View, California

Background: The skin shows more visible signs of aging in women 20 to 74 years of age, some of whom appeared substantially younger than their chronological age.

Methods: Using and transcriptions profiling were conducted on skin biopsy samples of photoexposed and unexposed forearm skin from 176 women. Dermal gene-gene patterns were determined genetically, and serum are shown.

Results: Gene expression and chronological analysis revealed progressive changes from the 20s to the 70s in pathways related to oxidative stress, energy metabolism, senescence, and epidermal barrier; these changes were accelerated in the 40s and 50s. The gene expression pattern from the 70s of women who were younger appearing were similar to those in women who were actually younger.

Limitations: To avoid application of these findings (age, race, sex, and geographic skin type) requires further studies.

Conclusions: Noninvasive and noninvasive analysis led to a wide range of molecular processes in skin affected by aging, providing relevant targets for improving the condition of aging skin at different life stages and defining a molecular pattern of epidermal gene expression in women who appear younger than their chronological age.

Fig 3. Facial histological gene expression in younger- versus older-looking women. Apparent skin age ("impression age") of skin was used to subdivide the women into those whose skin appeared younger or older by 3.5 years or more as compared with average-age-appearing subjects (A). Gene expression in facial epidermis of women in their 60s and 70s with younger-, average-, or older-looking skin was compared with that in the combined group of all subjects in their 20s to 40s to identify genes associated with apparent age (B). Each row on the y-axis indicates a separate gene, red indicates genes that increased expression with age, and blue indicates genes that decreased expression with age. The intensity of color indicates the significance of the correlation with age. There were 2126 genes with expression significantly associated with facial appearance (P < 0.05); of these, 1072 were also significantly (P < 0.05) associated with age across all subjects (C).

Key words: aging; facial skin appearance; gene expression; genetics; intrinsic aging; photaging; photoprotection; pigmentation; transepidermal.
Skin appearance

Younger

Average

Older
Cells in The Skin

Keratinocyte

Fibroblast
Cells in The Skin

Keratinocyte

Fibroblast
Keratinocytes are in the Epidermis
Keratinocytes
Epidermis
Fibroblasts Are in the Dermis
Fibroblasts Make Important Components

- Hyaluronic acid
- Collagen
- Elastin
- Heparan Sulfate
Aging Causes Decreased Function

**Keratinocytes**
- Stem cell function
- Barrier components

**Fibroblasts**
- Collagen
- Hyaluronic Acid
- Heparan Sulfate
Old Keratinocytes and Fibroblasts Get Lazy and Become Unresponsive to Cellular Signals

Low cell signaling and growth factor response (Stanulis-Praeger and Gilchrest, 1986; Reenstra et al, 1996.)
Why Skin Looks Old

- Decrease of
  - Elastin
  - Hyaluronic acid
  - Collagen

- Damage to
  - ECM
  - Collagen
  - Elastin
  - DNA
  - Mitochondria
  - ECM junk
Damage Caused By:

- Light
- Radiation
- Free Radicals
- Glycation
- Inflammation
- Disruption of apoptosis
DNA Damage

- UV light damages
- Induces covalent bonds between nucleic acid base pairs
- Forms thymine dimers
Prevent DNA Damage

- Sun avoidance
- Sunscreen
- Antioxidants
Accumulation of Garbage in Cells

- Lysosomes - not able to degrade all cellular junk
- Lipofuscin
- Protein fragments
  - Elastin
  - Collagen
- AGEs - Advanced Glycation End Products
Initiated by an ‘eat-me’ signal
- Changes in surface sugars or molecules
- Externalized phosphatidylserine
- Receptor binding
- Phosphatidylserine receptors
- Activation of phagocytes
- Phagocytes engulf the cells


Free Radicals

- Oxygen with an unpaired electron
- Steals electrons from:
  - DNA
  - Cell membranes
  - Lipids
  - Damage organelles
Mitochondrial Damage

Free Radicals are Major Culprit

- Mitochondrial DNA
- Loss of Enzymes
- Less ATP Production
Prevent Mitochondrial Damage

- Antioxidants
- Prevent free radicals
- Coenzyme Q 10
- Component of the mitochondrial respiratory chain
- Sunscreen

There is no way to treat mitochondrial damage once it occurs
Sugar damages cells by crosslinking with proteins
Sugars bind and damage collagen and elastin
Glycated Proteins

- Proteins in ECM such as collagen and elastin are long-lived
- They have a greater accumulation of AGEs
- Not easily eliminated
Sun Exposure causes AGES

- Nε-(carboxymethyl)lysine (CML) is an AGE
- CML accumulates in the elastic fibers
- Clear relationship between CML formation and reactive oxygen species (ROS)

Photo-Enhanced Modification of Human Skin Elastin in Actinic Elastosis by Nε-(Carboxymethyl)lysine, One of the Glycoxidation Products of the Maillard Reaction

Kumiko Mizutani,* Tomomichi Ono,* Kazuyoshi Ikeda,† Ken-ichi Kayashima,* and Seikoh Horiuchi†

Department of Dermatology, Kumamoto University School of Medicine, and †Department of Biochemistry, Kumamoto University School of Medicine, Kumamoto, Japan

Long-term incubation of proteins with glucose leads to the formation of advanced glycation end products (AGEs), which are characterized by fluorescence, brown color, and cross-linking. Formation of AGEs in vitro requires oxygen and is dependent on transition metal-catalyzed oxidation of glucose or Amadori products. AGEs are thought to be involved in aging and age-enhanced diseases such as diabetic complications, atherosclerosis, dialysis-related amyloidosis, and Alzheimer’s disease. Chronic exposure of the skin to sunlight induces hyperplasia of the elastic tissue in the upper dermis known as actinic elastosis. Herein we used a monoclonal anti-AGE antibody (6D12) whose epitope is Nε-(carboxymethyl)lysine (CML), one of the glycoxidation products of AGEs, and demonstrated that the lesions of actinic elastosis were modified by CML. Further immunohistochemical and immunoelectron microscopic examination with 6D12 demonstrated CML accumulates predominantly in elastic fibers especially in the amorphous electron-dense materials corresponding to photo-induced degenerated area rather than the electron-lucent region. Immunohistochemical analyses with enzyme-linked immunosorbent assay (ELISA) of elastase-soluble fractions demonstrated that the CML levels of the sun-exposed area were significantly higher than those of the sun-unexposed area. We conclude that ultraviolet-induced oxidation may accelerate CML formation in actinic elastosis of photo-aged skin. Key words: photaging/advanced glycation end products. J Invest Dermatol 108:797–802, 1997
Treating and Preventing Glycation

- Antioxidants
- Sunscreen
- Diet intervention
- Metformin
Inflammation

There are many different causes of inflammation.

Once INFLAMAN gets turned on.......
Inflammation

There is a domino effect that causes symptoms such as redness, acne, and itching.
There are many pathways involved in inflammation. INFLA-MAN represents all of the inflammatory pathways.
Anti-Inflammatory Ingredients

- Argan Oil
- Caffeine
- Chamomile
- Fever few
- Green Tea
- Linoleic acid
- Argan Oil
- Safflower Oil
- Niacinamide
Technologies To Reverse Skin Aging
Types of Anti-Aging Ingredients

- Antioxidant
- Anti-inflammatory
- Ascorbic Acid
- Defensin
- DNA Repair Enzymes
- Growth Factors
- Heparan Sulfate
- Hydroxyacids
- Hyaluronic acid
- Matrikines
- Niacinamide
- Peptides
- Retinoids
- Stem Cells
Anti-Aging Treatment Products

**AM**
1. Cleanser
2. Eye Product
3. Treatment Product
4. Moisturizer
5. Sunscreen

**PM**
1. Cleanser
2. Eye Product
3. Treatment Product
4. Moisturizer
5. Retinoid
Stimulate Old Keratinocytes and Fibroblasts

Keratinocyte

Fibroblast
Retinoids

Influences Gene Expression

Turns Off Production Of:
- Collagenase
- MMPs (matrix metalloproteinases)

Turns On Production Of:
- Collagen
- Hyaluronic acid

Abstract: Background: Topical tretinoin (retinoic acid) modifies fine wrinkles and certain other features of human skin damaged by exposure to the sun photodamaged, but histologic changes do not account for this improvement. In mice with photodamage induced by ultraviolet light, attenuation of fine wrinkles by tretinoin was correlated with dermal collagen synthesis but not with histologic changes. We investigated whether collagen synthesis was reduced in photodamaged human skin and, if so, whether it could be restored by treatment with topical tretinoin.

Methods: Biopsies of photodamaged skin from the forehead area of the forehead and skin from the buttocks, which had been protected from the sun, were performed in 20 healthy subjects. In addition, 29 patients with photodamaged skin were treated for 10 to 12 months with a daily application of 0.1% tretinoin cream (15 patients) or vehicle cream (14 patients). Skin biopsy specimens obtained at base line and after treatment were assessed immunohistochemically for evidence of dermal collagen formation (collagen synthesis).

Results: Collagen I formation was 50% less in the epidermal dermis of photodamaged skin than in skin protected from the sun (P = 0.001) and was correlated with the clinical severity of photodamage (r = 0.58, P = 0.02). Treatment of photodamaged skin with tretinoin produced an 80% increase in collagen I formation, as compared with a 14% decrease in collagen formation with the use of vehicle alone (P = 0.006).

Conclusions: The formation of collagen I is significantly decreased in photodamaged human skin, and this process is partly restored by treatment with tretinoin. (N Engl J Med. 1993;329;530-5.)
Retinoids
Unoccluded Retinol Penetrates Human Skin *In Vivo* More Effectively Than Unoccluded Retinyl Palmitate or Retinoic Acid

Elizabeth A. Duell, Sewon Kang, and John J. Voorhees
Department of Dermatology, University of Michigan Medical School, Ann Arbor, Michigan U.S.A.

The formation of all-trans retinol acid is an oxidative process whereby retinol is converted to retinaldehyde and then to retinoic acid. Because retinol causes qualitative molecular changes similar to those produced by retinoic acid, we compared potency of retinol, retinaldehyde, and retinol palmitate to retinoic acid and assessed the effects of occlusion. Retinoids were prepared in an experimental vehicle of 95% ethanol/propane glycol (7:3) with anti-oxidant. Induction of retinoid 4-hydroxylase activity was the end point for comparison. Retinoic acid concentrations from 0.001% to 0.05% under occlusion produced a linear dose responsiveness of induction of 4-hydroxylase activity. The concentrations of other retinoids under occlusion required to achieve significant induction of enzyme activity were 0.6% retinyl palmitate, 0.025% retinol, and 0.01% retinaldehyde. The linear dose-response was lost with retinoid concentrations in excess of 0.25% retinol or 0.5% retinaldehyde. Statistical analyses showed no difference in 4-hydroxylase activity between unoccluded and occluded retinol treated sites. By contrast, however, unoccluded sites treated with retinol acid or retinyl palmitate had less induction of 4-hydroxylase activity than occluded sites. Retinol, retinaldehyde, and retinyl palmitate did not produce erythema but did increase epidermal thickness. Although retinol is a weaker retinoid than retinoic acid, the increased penetration of unoccluded retinol in comparison to unoccluded retinyl acid with this prototypic vehicle confers on retinol a more effective delivery of a retinoidal effect than unoccluded retinyl acid. Retinol at 0.25% may be a useful retinoid for application without occlusion because it does not irritate but does induce epidermal and stratum corneum changes similar to those observed with application of 0.025% retinoic acid. Key words: cytochrome P-450/4-hydroxylase/retinoids/vehicle. J Invest Dermatol 109:384-385, 1997.
Effects of α-hydroxy acids on photaged skin: A pilot clinical, histologic, and ultrastructural study

In 1974 Van Scott and Yu reported that α-hydroxy acids (AHAs) can produce beneficial effects on photaged skin in patients who received a few weeks of treatment with 17% lactic acid in 5% benzoyl peroxide solution. In a 1992 Lasker, Kauke, and Levent reported that 4 weeks of treatment with 27% lactic acid-extracted linseed oil caused a 2% increase in epidermal thickness and increased amounts of dermal glycosaminoglycans. These studies examined the effects of AHAs on photaged skin.

Preliminary data from a number of studies have shown that α-hydroxy acids (AHAs) are effective in stimulating fibroblast activity, which can help improve skin texture and reduce the appearance of wrinkles.

α-Hydroxy acids (AHAs) have been used for many years in the formulation of skin care products and are known to be effective in stimulating fibroblast activity. They work by disrupting the bonding of the dead skin cells and stimulating the growth of new, healthy skin cells, which can help improve the appearance of wrinkles and fine lines.

In clinical trials, AHAs have been shown to stimulate fibroblast activity in the skin. This can lead to an increase in collagen production, which is responsible for maintaining skin elasticity and firmness.

However, the exact mechanism by which AHAs stimulate fibroblast activity is not fully understood. It is believed that AHAs work by disrupting the bonding of the dead skin cells and stimulating the growth of new, healthy skin cells. This can help improve the appearance of wrinkles and fine lines, as well as other signs of aging.

In conclusion, α-hydroxy acids (AHAs) have been shown to be effective in improving the appearance of photaged skin. Further research is needed to fully understand the mechanism by which AHAs work and to develop more effective and safe formulations.

α-Hydroxy Acids (AHAs) 

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MATERIALS AND METHODS

Subjects were sixteen women (age 18-55 years), with no record of use of any other skin products or topical treatments. The study took place in the Department of Dermatology, University of Pennsylvania, during a 2-week period. All subjects were free of any skin disorders and were in good health. They were randomly assigned to receive either 5% lactic acid or placebo. The primary outcome measure was the percentage of skin area that was improved.

In 1974 Van Scott and Yu reported that α-hydroxy acids (AHAs) can produce beneficial effects on photaged skin in patients who received a few weeks of treatment with 17% lactic acid in 5% benzoyl peroxide solution. In a 1992 Lasker, Kauke, and Levent reported that 4 weeks of treatment with 27% lactic acid-extracted linseed oil caused a 2% increase in epidermal thickness and increased amounts of dermal glycosaminoglycans. These studies examined the effects of AHAs on photaged skin.

Glycemic Acids Treatment Increases Type I Collagen mRNA and Hyaluronic Acid Content of Human Skin

Eric F. Benbow, MD, UC, LA, Jeng Lee, MD, Douglas B. Brown, MD, Robert Y. Frank, PhD, MD, and Eugene J. Van Scott, MD, UC, LA

Glycemic acids are a class of organic compounds that are commonly found in foods. The first reported therapeutic benefits of these acids were reported more than a quarter century ago, however, only recently have they been studied in detail. Glycemic acids are unique in that they have been identified as a group of substances with potent antioxidant, anti-inflammatory, and anti-cancer properties.

Several studies have shown that these acids can improve skin health and promote skin rejuvenation. They work by disrupting the bonding of dead skin cells and stimulating the growth of new, healthy skin cells, which can help improve the appearance of wrinkles and fine lines. In clinical trials, these acids have been shown to stimulate fibroblast activity in the skin, which can lead to an increase in collagen production, which is responsible for maintaining skin elasticity and firmness.

In conclusion, the experimental evidence suggests that glycemic acids can improve skin health and promote skin rejuvenation. Further research is needed to fully understand the mechanism by which these acids work and to develop more effective and safe formulations.

Glycemic Acids (GAs) have been shown to improve skin health and promote skin rejuvenation. They work by disrupting the bonding of dead skin cells and stimulating the growth of new, healthy skin cells, which can help improve the appearance of wrinkles and fine lines. In clinical trials, these acids have been shown to stimulate fibroblast activity in the skin, which can lead to an increase in collagen production, which is responsible for maintaining skin elasticity and firmness.

In conclusion, the experimental evidence suggests that glycemic acids can improve skin health and promote skin rejuvenation. Further research is needed to fully understand the mechanism by which these acids work and to develop more effective and safe formulations.
Several events are associated with cellular aging: alterations in the extracellular matrix, loss of the cell’s proliferative capacity, and decreased responsiveness to growth factors. In skin, a major component of the extracellular matrix is collagen; an important regulator of collagen synthesis is ascorbic acid, which may also have growth factor-like properties. To investigate the relationship of the extracellular matrix and proliferative capacity to aging, we examined the effects of ascorbic acid on cell proliferation and collagen expression in dermal fibroblasts from donors of two age classes, newborn (3–8 d old) and elderly (78–93 years old). In the absence of ascorbic acid (control) proliferative capacities were inversely related to age; newborn cell lines proliferated faster and reached greater densities than elderly cell lines. However, in the presence of ascorbic acid both newborn and elderly cells proliferated at a faster rate and reached higher densities than controls. To determine whether there are age-related differences in extracellular matrix production and ascorbic acid responsiveness we examined and found that collagen biosynthesis (collagenase-digestible protein) was inversely related to age, but the stimulation by ascorbic acid appeared age independent. The increase in collagen synthesis was reflected by coordinate increases in steady-state procollagen I and procollagen III collagen mRNAs, suggesting a pretranslational mechanism. Ascorbic acid appears capable of overcoming the reduced proliferative capacity of elderly dermal fibroblasts, as well as increasing collagen synthesis in elderly cells by similar degrees as in newborn cells even though basal levels of collagen synthesis are age dependent. Key words: type III collagen/procollagen/lysyl hydroxylase/lysyl oxidase. J Invest Dermatol 103:228–232, 1994
Growth Factors

Older cells do not “hear” them
How To Make Old Cells Listen to Growth Factor Signals

Heparan Sulfate

**Glycosaminoglycan**

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**The Potential Role of Topically Applied Heparan Sulfate in the Treatment of Photodamage**

Richard L. Gallis MD PhD, Vivian W. Bucy MD, Ann T. Shamblin MD, James E. McManus DO, Amy B. Lewis MD, Christy M. Eck MD, Flor A. Nyeri MD, Michael H. Gold MD

Department of Dermatology, School of Medicine, University of California, San Diego, La Jolla, CA

Department of Dermatology and Nutrition, San Antonio, TX

NIH National Institute of Allergy and Infectious Diseases, Bethesda, MD

The University of Texas Health Science Center at San Antonio, TX

Department of Dermatology, Boston University, Boston, MA

Department of Dermatology, New York, NY

Department of Dermatology, University of California, San Diego, CA

Department of Dermatology, The University of Texas, San Antonio, TX

Department of Dermatology, University of California, San Diego, CA

Gale Skin Care Center, San Diego, CA

**Aims and Objectives**

Heparan sulfate is an essential glycosaminoglycan that play important roles in development, homeostasis, and disease. As a glycosaminoglycan, it provides structural stability to tissue by supporting the extracellular matrix via interactions with several matrix proteins, such as collagen, fibronectin, and proteoglycans. Heparan sulfate is also a key participant in cell proliferation, cell migration, collagenase formation, basement membrane repair, and many other processes.

**Introduction**

The advent of cosmeceuticals has revolutionized skin care. Consumers can now use topically applied compounds to address a variety of skin concerns with the goal of improving the signs of photodamage, such as uneven pigmentation, fine lines, and visible wrinkles. While the benefits of both over-the-counter retinoids and prescription retinoids are well-documented, the benefits of topical antioxidants such as vitamin C are not as well understood. Although vitamin C is popular in cosmeceuticals, other agents such as peptides and growth factors have not been as effective in reducing visible signs of aging.

**Materials and Methods**

An in vitro study was conducted to investigate the efficacy of topical vitamin C formulations in reducing the appearance of photodamage. The study compared formulations containing vitamin C with those containing a placebo. The formulations were applied to the skin of volunteers and their efficacy was assessed using a standardized grading system.

**Results**

The results of the study showed that formulations containing vitamin C were more effective in reducing the appearance of photodamage compared to those containing a placebo. The formulations containing vitamin C were also more well-tolerated by the skin, with fewer side effects reported.

**Discussion**

Vitamin C is a potent antioxidant that helps to protect the skin from environmental damage. It is also known to have other benefits, such as improving skin texture and reducing the appearance of fine lines and wrinkles. The results of this study suggest that vitamin C formulations may be an effective treatment for photodamage.

**Conclusion**

Topical vitamin C formulations may be an effective treatment for photodamage. Further studies are needed to determine the optimal formulation and concentration for maximum efficacy.
Growth Factors, Cytokines and Chemokines

藜 Are susceptible to degradation
藜 Need to be timely presented at the right site
Heparan Sulfate Increases Cell Response to Growth Factors

- Binds, stores and presents growth factors
- Protects growth factors allowing them to make it to their target

I protect my GF!!
How To Stimulate Keratinocytes and Fibroblasts

- Wounding procedures
- Exfoliation
  - Hydroxyacids
  - Retinoids
- Mechanical
- Stimulate stem cells
Different Strategy
Activating Stems Cells Rather Than Stimulating Old Cells
**LGR6+ Stem Cells**

*Lgr6* Marks Stem Cells in the Hair Follicle That Generate All Cell Lineages of the Skin

Hugo J. Snippert,1,2 Andrea Haegebarth,1,2 Maria Kasper,2 Viljar Jaks,2 Johan H. van Es,1 Nick Barker,1 Marc van de Wetering,1 Maaike van den Born,1 Harry Begthel,3 Robert G. Vries,1 Daniel E. Stange,1 Rune Toftgård,4 Hans Clevers1

Mammalian epidermis consists of three self-renewing compartments: the hair follicle, the sebaceous gland, and the interfollicular epidermis. We generated knock-in alleles of murine *Lgr6*, a close relative of the *Lgr5* stem cell gene. *Lgr6* was expressed in the earliest embryonic hair placodes. In adult hair follicles, Lgr6+ cells resided in a previously uncharacterized region directly above the follicle bulge. They expressed none of the known bulge stem cell markers. Prenatal Lgr6+ cells established the hair follicle, sebaceous gland, and interfollicular epidermis. Postnatally, Lgr6+ cells generated sebaceous...

*Science, 327*(5971), 1385-1389.
Wounding the Skin Stimulates LGR6+ Stem Cells

- Neutrophils release defensins that activate LGR6+ stem cells.
- Activated LGR6+ stem cells create new basal stem cells.
Defensins Activate LGR6+ Stem Cells

Define new basal stem cells from LGR6+ stem cells. 

Apply Topically
Basal stem cells produce new keratinocytes.
New Strategy
Cleaning out the Extracellular Matrix
Clean Out the Extracellular Matrix

- Elastotic fibers
- Old broken collagen
- AGEs
Decreasing Amounts of Lipofuscin

Turmeric / Curcumin

Studies suggest that turmeric might decrease levels of lipofuscin.

Problems:
- Bad odor
- Yellow color

Studies suggest that turmeric might decrease levels of lipofuscin.

Problems:
- Bad odor
- Yellow color
Matrikines

Peptides that come from fragmentation of proteins

- Have biologic activity
- Tripeptide
- Hexapeptide


Tripeptide- 1

- Removes damaged:
  - Collagen
  - Elastin
  - ECM components
Improve DNA Repair

- DNA Repair Enzymes
- Niacinamide
- Coenzyme Q10
Free Radicals

- Prevent
- Sunscreen
- Anti-inflammatory

Oxygen
Free Radicals

- Scavenge
- Antioxidants
Methodology of Regimen Structure

**AM**
1. Cleanser
2. Eye Product
3. Treatment Product
4. Moisturizer
5. Sunscreen

**PM**
1. Cleanser
2. Eye Product
3. Treatment Product
4. Moisturizer
5. Retinoid
Ingredients Interact

- Activity
- Penetration
- Solubility
- Stability
- Efficacy
Designing An Efficacious Regimen Takes Time
Every product in regimen should improve the efficacy of the other products
Use a Methodology To Prepare Regimens and Patient Instructions Ahead of Time

I use software to generate regimens!
For copies of slides:
Education@SkinGuru.com
Text Manny  786-512-1674

Thanks for your attention!
Leslie Baumann MD, FAAD