

Aging

اللهم افتح لي قديمي يدهلي
انساعة وانظر هزال بشرتي بكرم
يخجلني امرتقاعة وانر بصيرتي بالذسباب
والحكمة ما يعلو شي قناعة وارضي وارضا عني
رضاً لك اشقر بعدك ابدآ.
اللهم آمين

And Its Modulation Part II

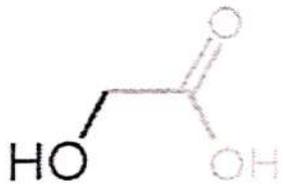
Hydroxy acids

- Organic carboxylic acids: *اسمها اعادة فواكه لانه يصنعها من*
مكوناتها مصدره من الفاكهة لاني
منه كالليمون
- AHAs: lactic acid, glycolic acid, malic acid, tartaric acid, citric acid, mandelic acid
- BHA: salicylic acid
- Polyhydroxy acids (PHAs): gluconolactone

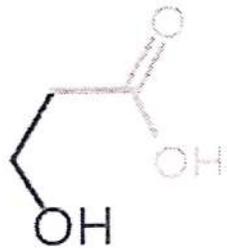
FutureDerm

FOUR TYPES OF HA'S

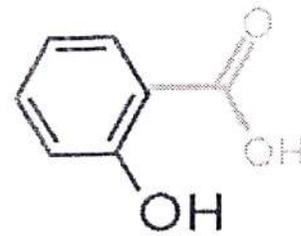
AHA



BHA



SA
(salicylic acid)



PHA
(gluconolactone)



↑ mw

Saja Hamed, Ph.D

Numerous skin effects for HAs

Numerous skin effects for HAs

- Exfoliation ⇒ تقشير
- Moisturization ⇒ humectant رطب من عدمه
proparites
- Anti-inflammatory properties ⇒ like salicylic acid (SA)
- Antioxidative effects

Exfoliants: AHAs and BHAs

- *Exfoliatio*: in *latin* meaning falling off in scales or layers
- Cosmetic benefits attributed to skin exfoliation has been long known since the time of ancient Egyptians → *كانوا يستخدمونها بدون ما يعرفوا فائدتها فكانوا يستخدموا الحليب ويستفيدوا منه بسبب ان lactic acid التي فيه*
- AHA and BHA are naturally occurring organic acids that help induce exfoliation and speed the cell cycle

الفترة التي تحتها | كناية عنها تقسم
بالـ *basal layer* لتوصل للـ SC
وبعد من سير لها *shedding*.

Hydroxy acids → different conc. gives different preparation

- Low conc (4-10%) in nonprescription creams → promoted for skin aging
- High concentration (>20%) can be used as chemical peels to treat calluses, acne, photo-aging

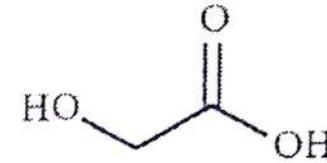
for wrinkles

AHAs

- A group of compounds that contain the hydroxy group in the alpha position

deep in the skin α penetration more irritant
رأته بعد رطل دة
دنة ال سائل انها أقل

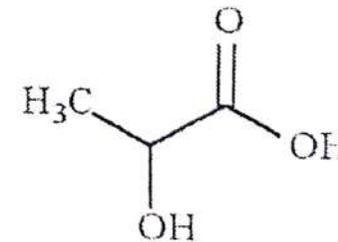
- Glycolic acid (sugar cane), lactic acid (sour milk), citric acid (citrus fruits), and phytic acid (rice)
لما يفتتوا ماء الارز
ممكن يستفيدوا منه



Glycolic acid
(2-Hydroxyethanoic acid)

Figure 20-3.

Chemical structure of glycolic acid. The OH group is in the alpha position; therefore, this is in the α-hydroxy acid family.



Lactic acid
(2-Hydroxypropanoic acid)

Alpha- hydroxy acids (AHA):

■ The effect of AHA depends on their concentration. The higher the concentration the more effective the treatment:

1. Low concentrations- up to 10% \Rightarrow for customer use
2. Moderate to high concentrations up to 70% \Rightarrow need professional for use.

سائل، ليعطى صورا *uncharged* من ال *salt* و *more acidic* و *قاعدة* و *مركبات* ال *pH* ال *irritation* و *مركبات*

Alpha- hydroxy acids (AHA):

1. Low concentrations- up to 10%:

- These preparations can be bought freely over the counter at cosmetics departments
- AHA are safe to use in cosmetic preparations in concentrations up to 10% provided that the pH of the preparation is not less than 3.5. من ال *FDA* عشان الناس *لعاديين* *irritation* من ال *pH* ال *اصلا* *تزيد* ال *OTC* *تستخدمها* *ك*

2. Moderate to high concentrations – up to 70%:

- They require physician supervision
- Are used for superficial chemical peeling

Effects of low concentrations of AHA- up to 10%:

1. Exfoliation: They weaken the bond between dead cells of the outer layers of the skin and enhance desquamation of the outer layer of the skin → the replacement of the dry outer layer by a new layer gives the skin a smooth appearance

2. Humectants (absorb water)

. HA جليسيرين جليسيرين

Effects of moderate to high concentrations of AHA- up to 70%:

- Their use require medical supervision
- They are used to achieve superficial chemical peeling of the skin → by dissolving the outer layer of the epidermis *completely*
- It usually takes at least four superficial peels before patients can begin to see improvement of photodamage, sun spots, and melasma
- Higher concentrations of AHA have a high acidity level → can burn the skin

higher activity ⇒ higher irritation so can burn the skin.

- Higher concentrations at low pH values cause epidermolysis to produce varying degrees of exfoliation
- when they are applied in lower concentrations they reduce intercorneocyte cohesion directly above the granular layer which enhance desquamation and thinning of the SC
- This leads to quickening of the cell cycle and smoothing of the stratum corneum

لذلك تنزل الطبقة العليا وتطبع الطبقة

التي تحدها التي هي still smooth

وما تعرضت لتسوس وال environment

AHAs:

- AHAs are useful in the management of dry skin, ^{⇒ humectant and exfoliating Activity} acne, scarring, actinic keratoses, as well as photodamaged skin
- At least 1 billion US dollars in sales, maybe more
- Long known as skin conditioners, on the market only since 1993 as 'anti-aging' products.
- Moderate effects on skin hydration.

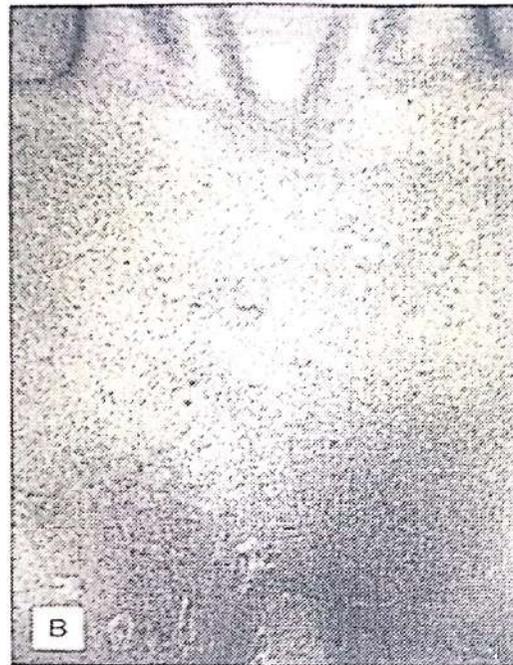
مع اد هجى رى - slowing down of cell cycle و تزد التصبغات

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لا تستخدمها الا اذا كنت حابه - photo damaged skin , acne scar

الها رعى عندك - irritation and post inflammatory hyperpigmentation

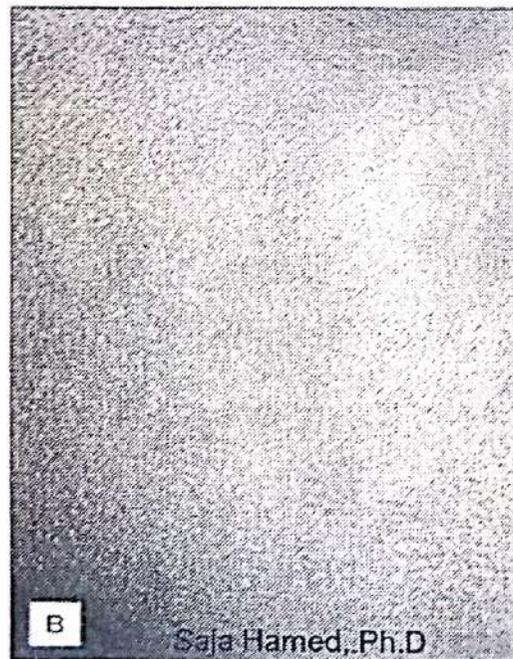
لا تستخدم moisturizer - humectant , occlusive and emollient.



مثال كحل تستخدمها ال peeling
تبع الحامض الفواكه وهو
professional peeling
لد acne scar وكيفية تحسين
ال skin texture

Fig. 16.4 Alpha hydroxy acid peels can be used on the chest to improve acne and skin texture. (A) Before. (B) After

اذا انت مسن



جاءتهم روح تحل irritation
postinflammatory hyperpigment
Skin sun sensitivity وتزيد ال
minimal erythema ال تقل ال
(تسير الجلد يتأثر بالشمس) dose
د dose بسيطة جدا
مقارنة بال dose ال
كانت تحمله بالوضع الطبيعي

Fig. 16.5 Improvement in skin texture following an alpha hydroxy acid peel is demonstrated. (A) Before. (B) After

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AHAs:

- Glycolic acid is the simplest molecule with the lowest Mwt and a pK_a of 3.83:
 - Water soluble
 - It is used in its partially neutralized form for topical home care products and in a free acid form in peeling products *عن طريق اضافة Alkaline Compound .*
- Combination with other antiaging agents

Formulation الجاهزة الـ pK_a
Active form هو الـ Acid (unchanged) form
at which half of the molecule is salt form and the other half is unchanged form (Acid form)
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exfoliation هو الـ neutralization
exfoliation هو الـ Na carbonate solution
هو الـ exfoliation

- AHAs and BHA are classified as superficial chemical peeling agents
- Superficial and medium-depth peels do not significantly enhance deep wrinkles or sagging skin *يعتبر على الطبقة العليا من الـ epidermis*
- But can improve color and texture of the skin
- Authors have reported success using such products in the treatment of photoaging by improving mottled pigmentation, fine lines, surface roughness, freckles, and lentigines

من بين الامثلة واذكرها

→ Trichloroacetic acid peel

- Chemical peels are categorized based on the depth of the procedure: superficial, medium, or deep
- Superficial peels induce necrosis of all or parts of the epidermis ⇒ *base layer* وطالغ
- Medium-depth peels create necrosis of the epidermis and part or all of the papillary dermis in the treatment area ⇒ *مع اول جزء من ال dermis (ال papillary)*
- Deep peels create necrosis deep in the reticular dermis ⇒ *كثير deep*

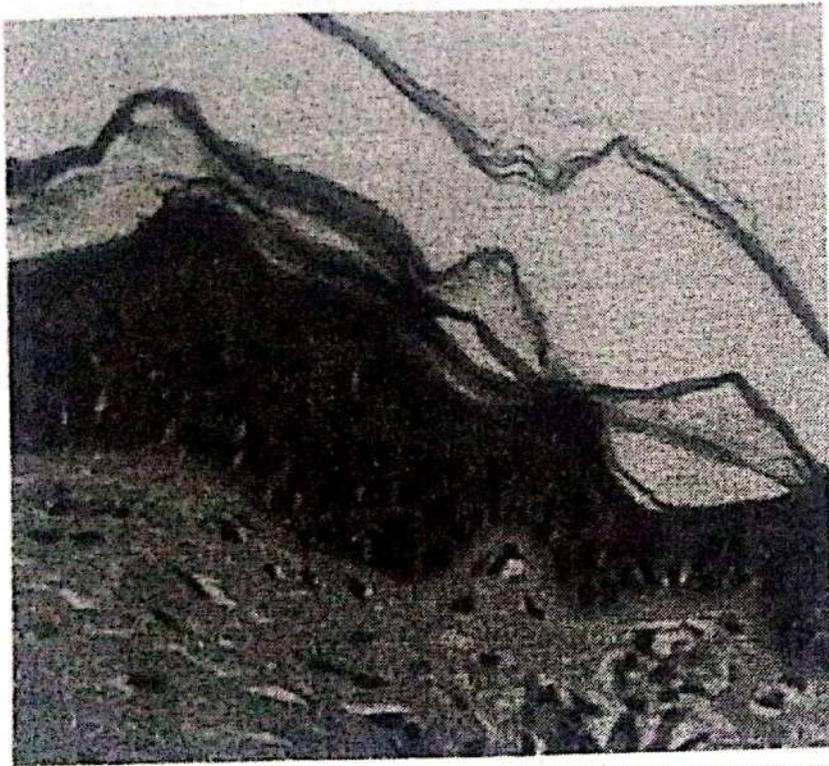
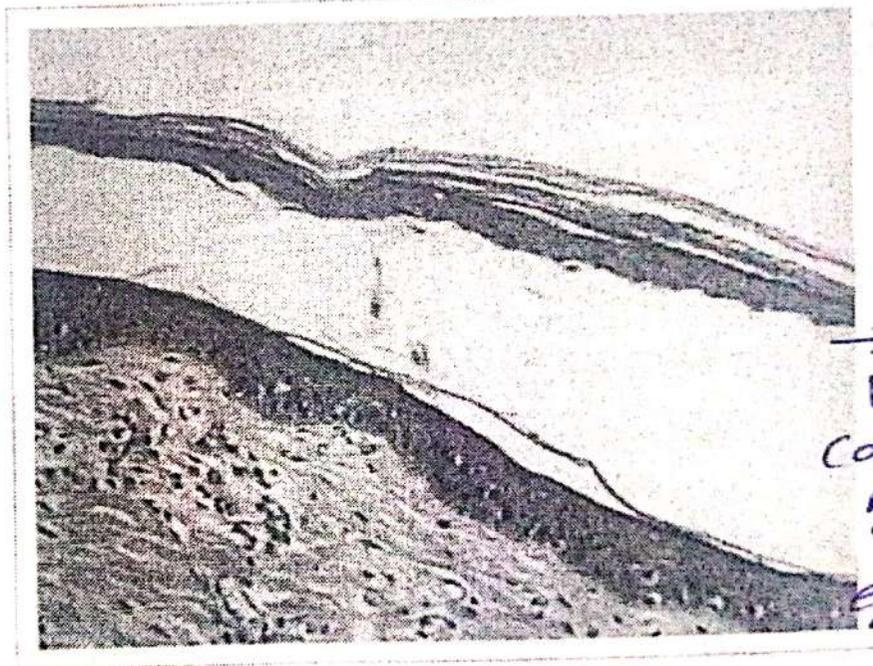


Figure 20-1. *normal*
 A hematoxylin and eosin (H&E) stain of untreated normal bovine skin.



الغشاء
 → peel
 طبقات
 Complete
 lysis
 ن
 epidermis

Figure 20-2.
 A hematoxylin and eosin (H&E) stain of bovine skin treated with a superficial chemical peel (two coats of the Pigment Peel Plus. This biopsy demonstrates a split in the spinous layer of the epidermis.

- GA and LA might work on pigmentary lesions not only by accelerating the turnover of the epidermis but also by directly inhibiting melanin formation in melanocytes
- GA and LA in doses of 300 or 500 $\mu\text{g/ml}$ suppressed melanin formation by directly inhibiting tyrosinase activity

ameliorating skin pigmentation

** تعيد الـ skin pigmentation بطريقة طبيعية **

1- exfoliate the upper layer of skin (remove the excess pigment in the upper layer).

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2- by themselves are able to inhibit tyrosinase which is the rate limiting enzyme of melanine synthesis.

ALPHA-HYDROXY ACIDS

(19)

Cherie et.al investigated the effects of alpha-hydroxy acids (AHAs) on photo-aged skin.

■ 17 white subjects with moderate photo-aged skin were selected.

■ Subjects were randomly assigned 25% of AHA lotion, (5 each were given lactic acid and glycolic acid and 7 were given citric acid).

- دراسة نُجِّلَتْ على الـ *photoaged skin* ، وهي دراسة
عسائر تلتب ففاعة المستحضرات ما ينفع فيجب *Volunteer* شباب
لذاتة لو استخدموها على شباب مارج يكون *Chemical improvement*
لذاتة ما عندهم مشاكل .
(J. Amer. Acad. Dermatol 34: 187-195,1996)

- صحاح الدراسة انجلى على ناس عندهم *photoaged skin*
جلوتهم ستخدموا الماخذ الفواكة بتركيز 1.5% على الـ *forearm* واحدة فقط والاخرى
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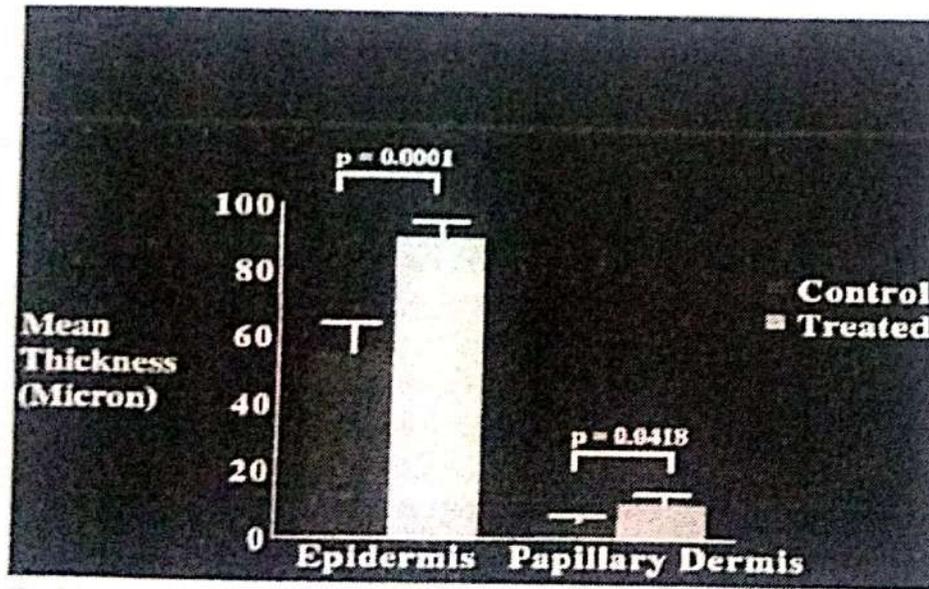
(20)

ALPHA-HYDROXY ACIDS

- Subjects were instructed to apply the given lotion to one forearm and the placebo lotion to the other forearm.
- Subjects were observed monthly for 6 months.
- 4mm punch biopsy specimens were obtained at the end of the study period.

- امتدوا فترة بعد 6 أشهر وبتأقوا
الـ improvement اللـ حصلت .

ALPHA-HYDROXY ACIDS

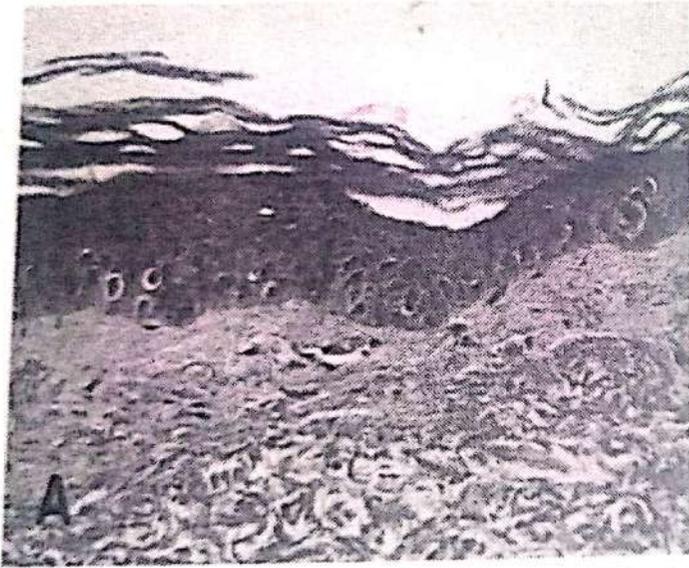


د. م. دوا انچه ديد 6 ايشهر فولا
Thickness increase
Dermis and epidermis
كان في
رابع ال

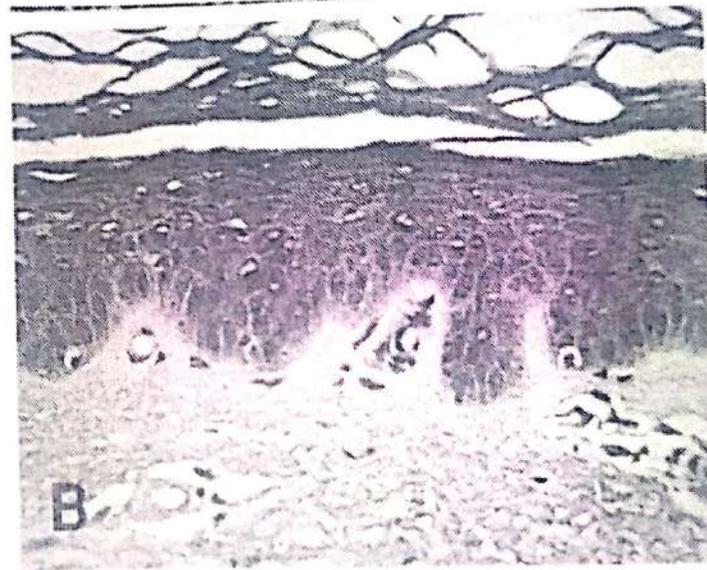
Quantitative histometric analysis of mean thickness of epidermis and papillary dermis.

- There was an increase in the epidermis and papillary dermis thickness in AHA treated specimens than in the control specimens.

ALPHA-HYDROXY ACIDS



A = control arm



B = treated arm

تحسين موجي
ال rete ridge
بعد ما كانت
flattened
سبب ال
aging
صغار وفتحها
أحسن بال (B)

- There was a return to more undulating rete pattern in AHA treated specimen.

ALPHA-HYDROXY ACIDS



A = control arm



B = treated arm

لا يظهروا حتى
الميكروسكوب
حتى يار elastin
fiber في ال (B)

- The elastic fibers tended to be longer, thicker and less fragmented in AHA treated specimens compared with the control.

ALPHA-HYDROXY ACIDS

CONCLUSIONS

- Topically applied AHAs cause significant improvements in both epidermal and dermal components.
- Clinical and histological findings suggest that AHAs reverse photo-aging.

- لو علناها على متطوعين اصحاء مارح يكون
عنا effect .
نحن اذا عندهم اصلا مشاكل رح يبين ان effect .

BHA:

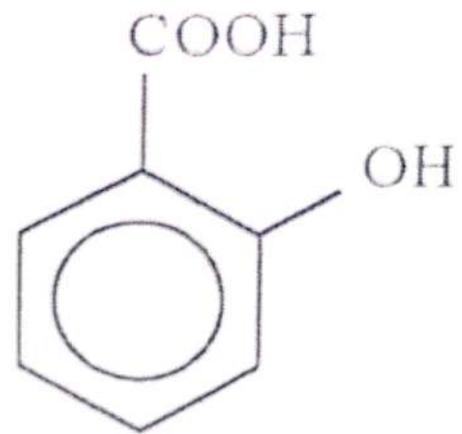
Salicylic acid

يفضل في حالة acne

- SA is fat soluble ⇒ sebum التي فيها pores ال يدخل داخل ال pores وتنقل comedolysis
- 2%-12% causes keratolysis of SC
- Found in the OTC home products usually at 2% concentration ترسيز ال washes
بجدة ال acne
وصي صير ممتازة
- Most physicians use preparations of 20% or 30% for the in-office peels يستخدم لسامير الملح تعمل Ikeratolysis كامل للنتيجة
- Such peels have been shown to fade pigment spots, to decrease surface roughness, and to reduce fine lines
- SA, unlike AHAs, exhibits anti-inflammatory capabilities by affecting arachidonic acid
- The anti-inflammatory effects of BHA make it a useful peel in patients with acne and rosacea ⇒ inflammatory skin

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يكون عدم مسكلة بال blood vessel Condition
sensitive كثير ورسولم
Dilation (توسع ذك وعية)،
انهم



Salicylic Acid

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BHA:

Salicylic acid

- There is no published data examining BHA's effect on collagen production
- There have been case reports of children with multiple excoriations and elderly patients with ichthyosis that were treated with topicals containing SA who developed salicylism ← *لازم نتجته انة ما يذبط على area كبيرة عند ا Children لانه يسهل الامتصاص excessive absorption*
- Therefore, large body surfaces should be treated with care and the physician should watch for the signs of salicylism that include nausea, disorientation, and tinnitus
- BHA is contraindicated in patients who are pregnant, breast-feeding, or allergic to aspirin
- Home-care products that contain SA (typically labeled as "acne washes") should also be avoided in patients who are pregnant, breast-feeding, or allergic to aspirin

BHA
 Table 20-1. *Table 20-1. AHA و BHA کے درمیان فرق In office peel* *بھیا رٹا*

Comparison of AHAs and BHA

	AHAs	BHA
Useful in photoaging	Yes	Yes
Useful in acne	Yes	Yes
Useful in melasma	Yes	Yes
Useful for dry skin	Yes	Yes
Speeds cell cycle	Yes	Yes
Enhances exfoliation	Yes	Yes
Lipophilic	No	Yes
Inhibits arachidonic acid	No	Yes
Anesthetic properties	No	Yes
Anti-inflammatory properties	Maybe	Yes
Must be neutralized	Yes	No
Visible frost	No	Yes
Risk of salicylism	No	Yes
Variety of available concentrations	Yes	Minimal
FDA approved for home use	No	Yes (dry skin)
Shown to increase collagen synthesis	Yes	No
Use in pregnancy/breast feeding	Unknown	No

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AHA کے لئے ضروری ہے کہ اسے
 BHA کے لئے ضروری ہے کہ اسے

Disadvantages:

Irritation and skin dryness can result from AHA and BHA products

Patient should alternate between hydroxy acid containing products and regular moisturizers that do not contain hydroxy acids

It usually takes at least four superficial peels before patients can begin to see improvement of photodamage, solar lentigo, and melasma

Superficial peels are unable to correct moderate to severe wrinkles and scars

Many cosmetic companies noted an increase of sunburn cells in patients treated with AHA preparations → should be used in combination with a sunscreen

Some experts suggest that continued use of hydroxy acids might show a decrease in efficacy with continued use as a result of accommodation by the skin. Thus, it may be beneficial to have patients stop their AHA preparations periodically to enhance the efficacy of these products when used for long-term

dryness - ممكنة بجل damage in the barrier فتره ال TEW loss وهذا يزيد ال

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للجل اذا بدك بجل superficial peeling لازم بجل اكثر من جلبة جستان يبيني تأثيرها

- مع الوقت بجل مع ال وقت بجل تأثيرها نلازم سركوها فترة بعد من ترجع سكونها مرة تالية
عشان يرجع ال effect

- Smith 1995 found that while skin thickness, firmness and improvement in wrinkle characteristics continued to improve beyond a 26-week treatment period, after 20 weeks of use both glycolic and lactic acids are 60% less effective at increasing cell renewal as they were during the initial period of use

- وجدوا انه بعد 20 اسبوع من الاستخدام ، اداءه وفاعليته اضعف ،
cell renewal rate (تقل وتضعف تقريبا) (أقل فاعلية)
السبب انه الجلو صار يعمل buffering and neutralization لها في النهاية

The accommodation effect with AHAs

Test Material (3.0%), pH 3	Renewal Rate*, Start	Renewal rate after 10 Weeks Treatment	Renewal rate after 20 Weeks treatment
Control	4.7	4.9	4.8
Lactic Acid	28.6	17.3	10.3
Glycolic Acid	29.3	16.8	11.6
Salicylic Acid	33.2	26.7	17.2

التي ما عالجوها
 ضمت ضمن الـ range الطبيعي.

* Rates are expressed as % increase from pretreatment values.

مع الاستخدام وكذلك الـ Renewal rate يقل
 وكذلك الـ salicylic acid مع الوقت في يقل الـ effect
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Evaluating and comparing hydroxy acid preparations

ما نقدر نقارها فقط اعتماداً على التركيز
وما نقدر نحكي اية الة تركيزه أعلى هو احسن

■ The amount of available free acid:

مثلاً: 10% glycolic acid ويكون
بال neutralized او ال pH

- Concentration of hydroxy acid

الها مستو Acidic او slightly أعلى يكون

- pKa of acid preparation

تأثيره اضعف من لو صطين 5% glycolic acid
على pH تكون acidic.

- pH of the solution

- Whether or not the preparation is buffered

أكثر ال preparations
اللي فيها ترايز عاليتين

■ Because of too many factors, it is difficult to compare one brand of chemical peel to another

الفاضل لفاوكة
تكون buffered

■ Differences in vehicle can affect the clinical response

↓
رحين اضا فو لها
Alkaline agent

■ Urea may affect the efficacy of these products because it increases their penetration

عشان يقل ال free acid
وكذلك ال irritation
وتقل الفاعلية لانه يقل
ال Active form

عن لو ما هطينا
ختلف الوضع لو هطينا penetration enhancer

more Active = more irritative

Evaluating and comparing hydroxy acid preparations

- pKa is the pH at which the level of free acid is the same as the level of the salt form of the acid
- When pH is less than the pKa the free acid form predominates
- Acid form is the "active form"
- It is necessary to have the proper balance of the salt and acid form to have an efficacious peel with minimal irritation
- pKa for SA= 2.97
- pKa for AHAs= 3.83
- It is difficult to formulate a combination product that reaches an optimal pH
- AHA-BHA combination product with a pH of 3.5??

- إذا كان pH للمستحضر أقل من pKa المادة الحرة هي التي تسيطر عليها
 free acid
 salt form

المسحوق هو الـ FDA

Not good combination
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في pH أقل من 3.5
 من AHA في شكل Acid Form
 في BHA في شكل Active Form
 في BHA في شكل salt form
 في AHA في شكل salt form
 في BHA في شكل Active Form
 في AHA في شكل Acid Form

موضوع: ارزیابی و مقایسه اسیدهای هیدروکسی

Evaluating and comparing hydroxy acid preparations

۳۵

- Lower pH= increased irritation and efficacy
- Buffered solutions:
 - When a base such as sodium bicarbonate is added to the solution
 - This produces an increased amount of the salt form
 - Less free acid and a higher pH: decrease side effects and decrease efficacy
 - They are resistant to pH changes

نفس التركيز : pH مختلف يؤثر على ال irritation potential
 الفواكه فقط

Cumulative
 irritation
 scores for
 AHA
 formulations
 and products

AHA	%	pH	N	Score
GA	8.0	4.40	21	1/882
GA	8.0	3.80	21	49/882
GA	8.0	3.25	21	119/882
LA	12.0	4.40	21	30/882
GA	13.0	4.40	21	33/882
GA	10.0	3.80	21	21/882
GA	9.0	3.80	21	7/882
GA	10.0	4.40	23	18/966
GA	10.0	3.80	23	38/966
GA	10.0	3.25	23	404/966
GA	10.0	3.00	23	631/966
GA	10.0	2.50	23	746/966
GA	10.0	2.00	23	768/966
GA**	5.0	2.40	23	770/966
GA**	9.0	3.25	23	481/966
GA**	8.0	3.60	23	258/966
GA	8.0	3.60	23	148/966
GA	15.0	3.80	23	14/966
GA	20.0	3.80	23	37/966

→ irritations
 قتل
 مع pH أقل صار
 ال irritation أعلى

ع بالنهاية اتماما
 نقدر نقارن بناء آ
 على ال Conc. فقط
 الفواكه فقط
 اتمنا يهتوا نعرف
 ال pH عشان نعرف
 كم عينا Free Acid

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** Commercial products

-
- In 1997, the Cosmetic Ingredient Review Panel (CIR) concluded that AHAs (glycolic acid, lactic acid, and their related chemical compounds) are safe for use in products intended for cosmetic use when:
 - The AHA conc. is 10% or less
 - The final product has a pH of 3.5 or greater
 - The final product is formulated in such a way that it protects the skin from increased sun sensitivity or its package directions tell consumers to use sunscreen products

- FDA is cautioning persons using AHA products to avoid sun exposure when possible and or to use adequate sun protection as these products increase skin sensitivity to sun

Careless about sun protection ⇒ post-inflammatory pigmentation and other sun related problems.

Remarks about HA

- When to use → إذا كانت عندك مشاكل بالبشرة غير صحت ما تفتي داعي .
- Conc
- Frequency → don't use as a daily bases , use them twice weekly *مرتين*
- Do I really need them
- AHA vs BHA vs PHA
- What about physical exfoliation! → مثل السكراب أو ستونجوا *مزشاة ميكانيكية*

BHA ⇒ إذا البشرة دهنية أو فيها acne او مزجة لا ACne
 PHA ⇒ for sensitive skin
 لينة ال ساه أكبر
 غير ذلك تستخدم AHA

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إذا شديداً على بشرتك
 irritation
 they are not gentle
 to skin .
 ممكن تستخدمها لكن
 dryness *اللي فيها*
 لكن للوجه لازم تكون
 very gentle in
 exfoliation
 أي صغف بسيط زيادة
 ممكن يعجل irritation

Antioxidants:

Antioxidants:

- The free radical theory of aging, proposed in 1956, is one of the most widely accepted theories to explain the cause of aging
- ROS take electrons from vital components (DNA, proteins, and membranes) leaving them damaged
- ROS are involved in the aging process and are believed to be involved cutaneously in causing photoaging, carcinogenesis, and inflammation
- UV-induced skin damage is partly mediated by ROS
(Black HS: Potential involvement of free radical reactions in ultraviolet light-mediated cutaneous damage. *Photochem Photobiol*, 46: 213, 1987)

Antioxidants:

تستغل طاعا

reactive oxygen species

ضعفنا قدرته لكي
زيادتها من ال

bad life habit,

smoking, sun exposure

رج تبطل قدر

تستغل عليها

Natural antioxidants in the skin: superoxide dismutase, catalase, α -tocopherol (vitamin E), ascorbic acid (vitamin C), ubiquinone, and glutathione

UV light exposure:

Inhibit many of these defense mechanisms (*Fuchs et al.: Acute effects of near ultraviolet and visible light on the cutaneous antioxidant defense system. Photochem Photobiol, 50: 739, 1989 & Fuchs et al.: Impairment of enzymic and nonenzymic antioxidants in skin by UVB irradiation. J Invest Dermatol, 93: 769, 1989*)

Cause an increase in free radical formation (*Dreher F & Maibach H: Protective effects of topical antioxidants in humans. Curr Probl Dermatol, 29: 157, 2001*)

Antioxidants:

٤٣

- Topical antioxidants are currently marketed for:

التي أكثر من Claim

- Prevention of aging and photoaging

- Treatment of wrinkles مسخيل يعالج الـ
wrinkles

- and treatment of erythema caused by inflammation مسخيل ازالة يعالج الـ

- the free radical theory of aging explains why antioxidants are thought to prevent wrinkles but it does not justify the use of antioxidants to treat wrinkles that are already present

help لكن مسخيل يعالج الـ Total prevention life style الـ
باستخدام عدة مع تعديل

Network antioxidants:

- Most of antioxidants used in the cosmetic industry are “network antioxidants”. → انة مثل سقندم ال Vit C وال Vit E مع بعض
- They work synergistically to “enhance the power” of each other
- After an antioxidant “disarms” a free radical it is unable to function further as antioxidant unless it is recycled
- Five known network antioxidants: vitamins C & E, glutathione, lipoic acid, and coenzyme Q₁₀ (CoQ₁₀)
- Vitamin C or CoQ₁₀ can recycle vitamin E
- Lipoic acid can recycle vitamin C or glutathione

Fat-Soluble Antioxidants:

Vitamin E

- موجود في حمض دهني
مقاوم للتأكسد مع
وال (ROS)
oxidative stress

- vitamin E is the primary lipid soluble antioxidants in skin that protect cells from oxidative stress
- ROS induce changes in the biosynthesis of collagen and GAGs in cultured human dermal fibroblasts. This alteration was prevented with the addition of α -tocopherol to the fibroblasts
(Tanaka et al.: the effect of reactive oxygen species on the biosynthesis of collagen and glycosaminoglycans in cultured human dermal fibroblasts. Arch Dermatol Res, 285: 352, 1993)
- vitamin E lowers prostaglandin E2 production and raises IL-2 production leading to anti-inflammatory and immunostimulatory activity

Fat-Soluble Antioxidants:

Vitamin E

- Topical D- α -tocopherol acetate diminish erythema caused by sunburn, edema, and skin sensitivity in mice when applied after exposure to UVB (*Trevithick et al.: Topical tocopherol acetate reduces post-UVB, sunburn-associated erythema, edema, and skin sensitivity in hairless mice. Arch Biochem Biophys, 296: 575, 1992*)
- 5% tocopherol applied to mice prior UVB exposure lead to 75% decrease in skin wrinkling and reduction in cutaneous tumors (*Bissett et al.: Photoprotective effect of superoxide-scavenging antioxidants against ultraviolet radiation-induced chronic skin damage in the hairless mouse. Photodermatol Photoimmunol Photomed, 7: 56, 1990*)

vit E ← يساعد الجسم في
تقليل الضرر الناتج عن
UV exposure

Saja Hamed, Ph.D

• الناتج عن UV exposure

Fat-Soluble Antioxidants: Vitamin E

- A double-blind, placebo-controlled study examined the protective effects of orally administered vitamin E (400 IU per day) against UV-induced epidermal damage in humans for a 6 months period. There was no significant difference between the placebo group and those treated with vitamin E in MED and histologic response (Werninghaus et al.:

Evaluation of the photoprotective effect of oral vitamin E supplementation. Arch Dermatol, 130: 1257, 1994)

Minimal erythema dose

Fat-Soluble Antioxidants:

Vitamin E

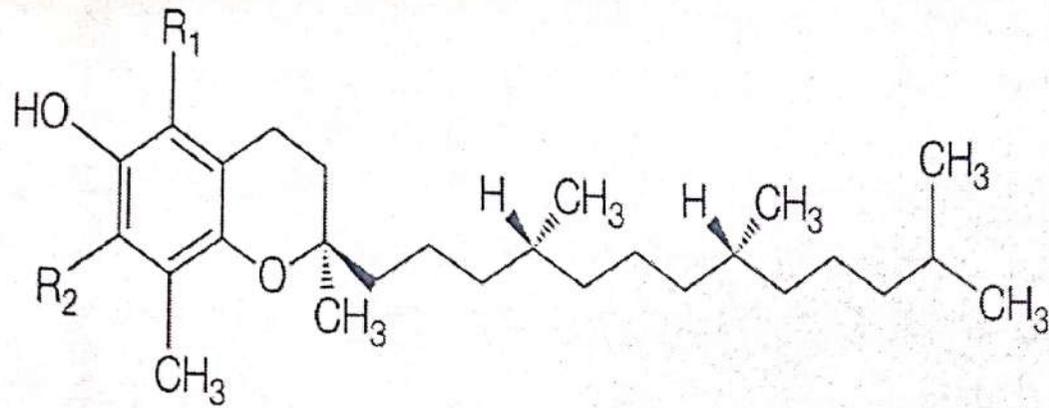
- It is suggested that vitamin E may require to interact with other antioxidants such as vitamin C to provide photoprotection (*Chan AC: Partners in defense, vitamin E and vitamin C. Can J Physiol Pharmacol, 71: 725, 1993*)
- In a study that assessed the cosmetic benefit resulting from the use of topically applied vitamin E to a surgical scars patient applied 320 IU of D- α -tocopheryl per gram of Aquaphor to one side of the scar and Aquaphor alone to the other side of the scar for 6 months. Vitamin E preparation failed to improve the cosmetic appearance of surgical scars (*Baumann & Spencer: The effects of topical vitamin E o the cosmetic appearance of scars. Dermatol Surg, 25: 311, 1999*)

عملوا دراسة استخدموا Vit E
بإضافة كريم Cream وخطوا على جزء من Scar
والجزء الثاني منها خطوا عليه
Saja Hamed, Ph.D
Cream بدون Vit E لمدة 6 أشهر
لم يكن أي improvement of scar في المنطقة
التي خطوا عليها Vit E

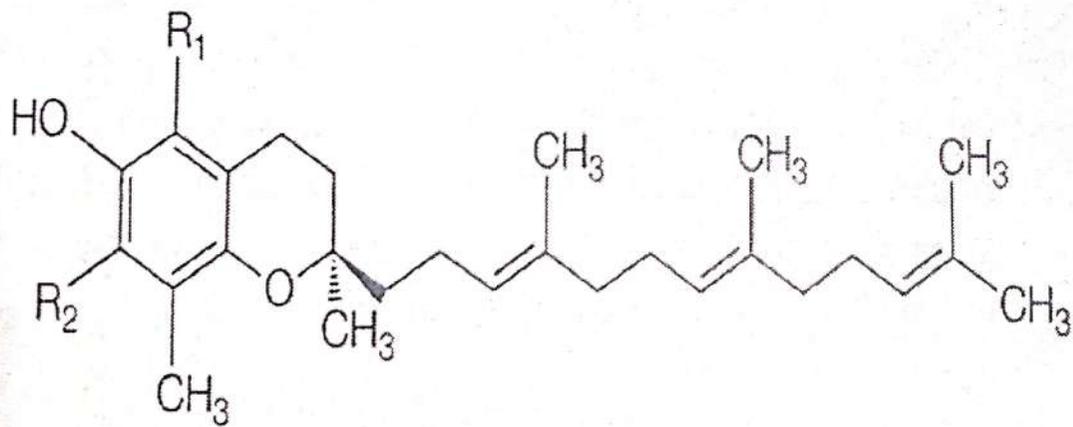
Forms of vitamin E

- Vitamin E is a family of compounds called tocopherols (α , β , γ -, and δ - tocopherol)
- α -tocopherol is the most active form and is the form that the recommended daily allowance (RDA) is based on
- The names of all types of vitamin E begin with either D or DL \Rightarrow synthetic
- The natural form (D-) is more active and better absorbed
- Synthetic supplements contain α -tocopherol
- Food sources contain several different tocopherols

natural



Tocopherols



Tocotrienols

Fig. 7.1 Chemical structure of tocopherols and tocotrienols.

Tocopherols (α : $R_1 = R_2 = \text{CH}_3$, 430.7 g/mol; β : $R_1 = \text{CH}_3$, $R_2 = \text{H}$, 416.7 g/mol; γ : $R_1 = \text{H}$, $R_2 = \text{CH}_3$, 416.7 g/mol; δ : $R_1 = R_2 = \text{H}$, 402.7 g/mol); **Tocotrienols** (α : $R_1 = R_2 = \text{CH}_3$, 424.7 g/mol; β : $R_1 = \text{CH}_3$, $R_2 = \text{H}$, 410.6 g/mol; γ : $R_1 = \text{H}$, $R_2 = \text{CH}_3$, 410.6 g/mol; δ : $R_1 = R_2 = \text{H}$, 396.6 g/mol)

Forms of vitamin E

Tocopherol is not stable like ascorbic acid

01

- The vitamin E forms typically used in cosmetics are α -tocopheryl acetate and α -tocopheryl linoleate
- Tocopheryl esters are more poorly absorbed by the skin than the tocopherol forms
- α -tocopheryl acetate and α -tocopheryl succinate failed to prevent photocarcinogenesis in a study (Gensler et al.: Importance of the form of topical vitamin E for prevention of photocarcinogenesis. Nutr Cancer, 26: 183, 1996)

Tocopheryl linoleate دافيتا ال
stability حاولوا يستخرجوهم بالاصطناع عن طريق ال

more studies * كذا ال
عشان يثبتوا كفا ل
photo damaged skin

02

Vitamin E

■ A study demonstrated that even the use of rinse-off products containing α -tocopherol in concentrations of less than 0.5% leads to significantly increased levels of vitamin E in the SC of human skin

في الـ cleanser

■ Therefore, topical formulations with α -tocopherol (but not vitamin E ester) at concentrations ranging from 0.1 to 1% are very likely to be efficient in improving antioxidant protection of the skin barrier.

(Ekhanayake-Mudiyanselage et al.: Vitamin E delivery to human skin by a rinse-off product: penetration of alpha-tocopherol versus wash-out effects of skin surface lipids. *Skin Pharmacol Physiol.* 2005 Jan-Feb;18(1):20-6)

حتى لو استخدمت بتركيز قليل
كانت آلية ألة فعالية وصورة
مستأن بغير posting لقدرة الجلد
على الـ detoxification الـ ROS

Saja Hamed, Ph.D

Reactive oxygen
species

Vitamin E

- A clinical placebo controlled study on 96 atopic dermatitis patients were treated with either placebo or oral vitamin E (400IU/day) for 8 months
- دراسة عن استخدام oral vit E لمدة ٨ أشهر على ٩٦ مريضين مع Atopic Dermatitis (immune system) وبيد أن يكون لها علاقة بالمناعة.

- An improvement and near remission of atopic dermatitis and a 62% decrease in serum IgE levels in the vitamin E treated group

(Tsourelis-Nikita et al.: Evaluation of dietary intake of vitamin E in the treatment of atopic dermatitis: a study of the clinical course and evaluation of the immunoglobulin E serum levels. International Journal of Dermatology, 41: 146-150, 2002)

Vitamin E: Side effects

- The incidence of contact dermatitis due to vitamin E topical application may be relatively high (*Jenkins et al.: Failure of topical steroids and vitamin E to reduce postoperative scar formation following reconstructive surgery. J Burn Care Rehabil, 7: 309, 1986*)
- In 1992, Swiss researchers evaluated 1000 cases of an atypical contact dermatitis provoked by vitamin E linoleate that was an additive to cosmetics and found that oxidize vitamin E derivatives can operate *in vivo* as haptens or irritants (*Perrenoudet al.: An epidemic outbreak of papular and follicular contact dermatitis to tocopheryl linoleate in cosmetics. Swiss Contact Dermatitis Research Group. Dermatology, 189: 225, 1994*)

١- د زعم تعرف على سو كيتوي ار supplement اللى اناج
تقوية

٢- نوع ار exceptient وادنا ممكن ييجل irritation

٣- بعضه ار vit E اللى كتر
Saja Hamed, Ph.D

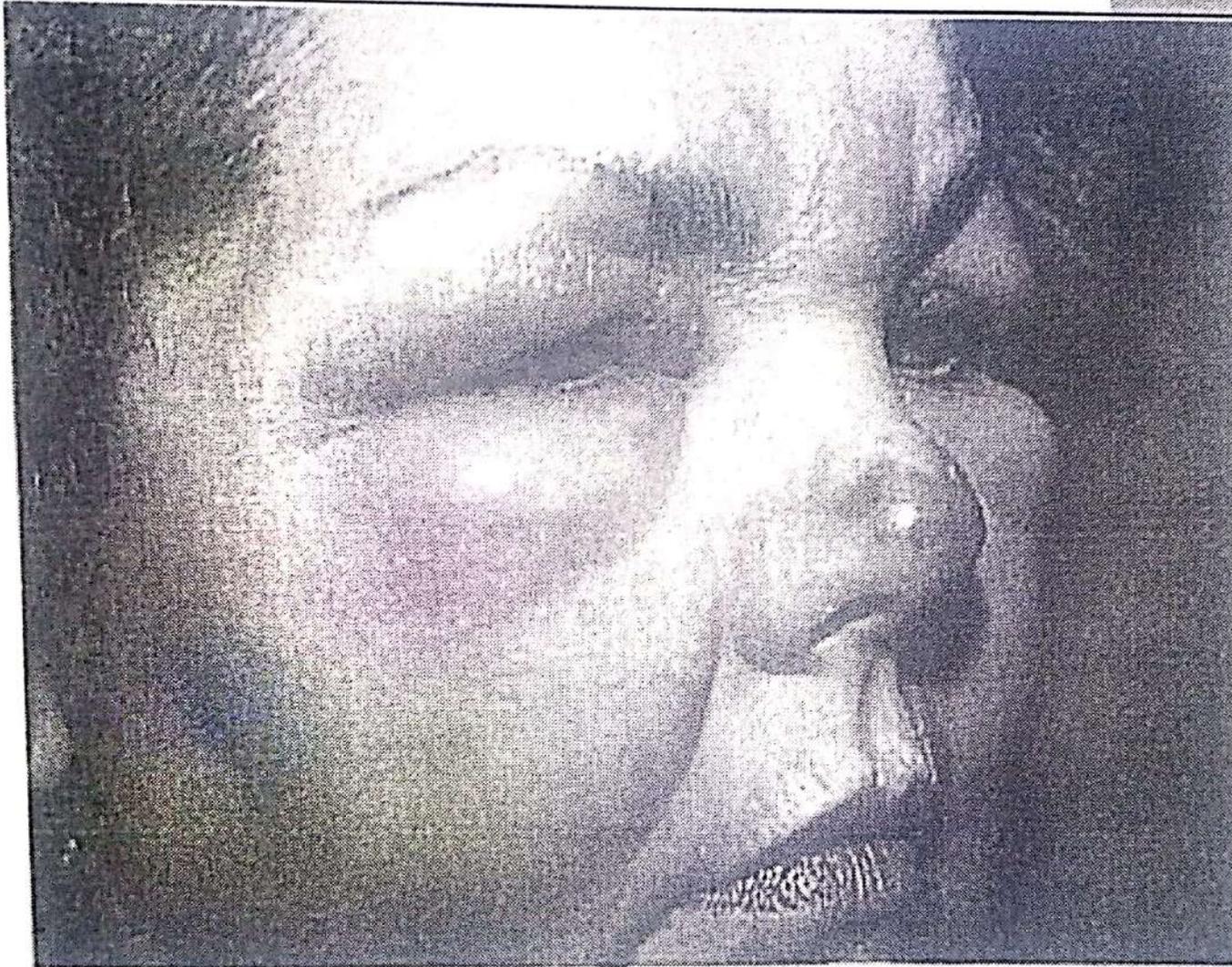
ناس عندهم irritation و ممكن ييجل dermatites

* د زعم ييجل اختبار ل vit E containing serum
or preparations

عنه منطقة من جسمه بالجسم عنان
تتاكد اذا عندك allergy اول
قبل اللى ستخدمه

Vitamin E

00



Saja Hamed, Ph.D

VITAMIN E

Cause allergic reaction

07

Vitamin E:

Conclusion

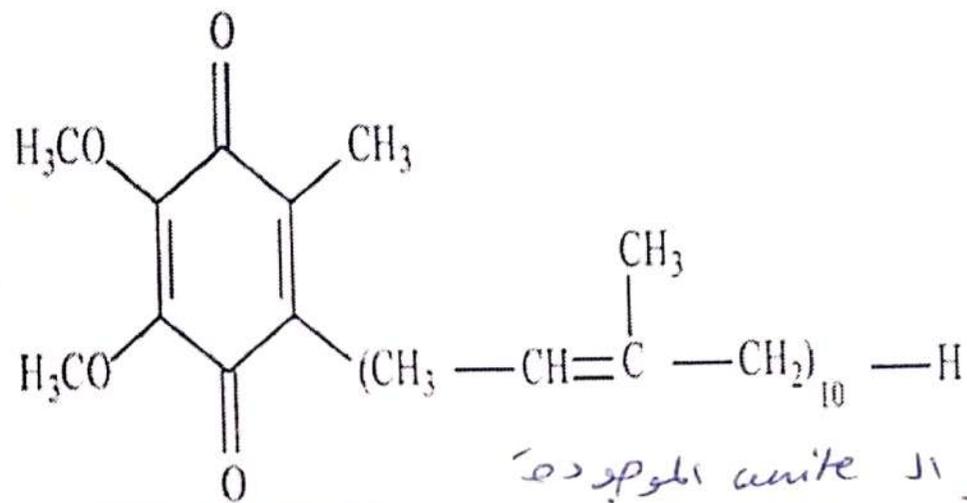
- Vitamin E has been used to protect against a variety of dermatologic conditions
- Research results have varied just as widely as the range of diseases treated
- The most promising reason for research into the dermatologic use of vitamin E appears to be its antioxidant activity *mainly*
- This antioxidant potency can be increased through combination with other antioxidants *شبكة الستيروئيد network Antioxidant*

Saja Hamed, Ph.D

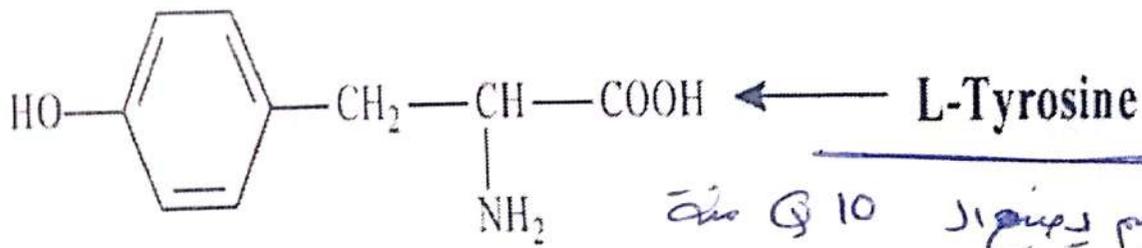
*atopic dermatitis orally ستيروئيد -
Can help in photo damaged skin -*

Coenzyme Q₁₀ or Ubiquinone:

- Is a naturally occurring nutrients
- Fish and shelfish
- It is a fat-soluble compound found in all cells as part of the electron transfer chain responsible for energy production
- It is also an antioxidants
- The “Q” = member in quinone family
- The “10” identifies the number of isoprenoid units on its side chain



د ۱۰ ایسوپرنوئیک یونٹوں کے ساتھ
 structure ہے



Coenzyme Q10 کے لیے

Figure 15-1.
 The chemical structure of coenzyme Q₁₀. It has 10 isoprenoid units side units and requires tyrosine for biosynthesis.

Coenzyme Q₁₀ or Ubiquinone:

٥٦

تقل مع العمر

- Age-related decline of CoQ₁₀ levels in animals and humans
- Hoppe et al. demonstrated that CoQ₁₀ penetrated into the viable layers of the skin and significantly suppressed the expression of collagenase in human dermal fibroblasts following UVA irradiation (Hoppe et al.: *Coenzyme Q10, a cutaneous antioxidant and energizer. Biofactors 9: 371, 1999*)
- ✓ ■ There is a need for more research to examine the long-term preventive effects of these products to see if they are truly able to prevent signs of aging seen in the skin

قدر شديداً
تأثير الـ
Radiation
بإزالة يزيد
الـ MMR

Coenzyme Q₁₀ or Ubiquinone: Side effects

- Oral Q₁₀ supplementation is associated with a caffeine-like side effect and may cause a nervousness
- It is recommended that CoQ₁₀ not to be taken at night
- No side effects have been reported with topical application →

• *insomnia*
• *عصبية ليلية*

help
not treat

Water-Soluble Antioxidants: Vitamin C

عليه كثير دراسات
و استوفت مع
other topical
preparations
تفيد

74

Topical vitamin C has been used as a topical antioxidant to:

Prevent sun damage (*Darr et al.: Topical vitamin C protects porcine skin from ultraviolet radiation-induced damage. Br J Dermatol, 127: 247, 1992*)

Treat melasma (*Kameyama et al.: Inhibitory effect of magnesium L-ascorbyl-2-phosphate (VC-PMG) on melanogenesis in vitro and in vivo. J Am Acad Dermatol, 34: 29, 1996*)

تستعمل

Treat striae alba (*Ash et al.: Comparison of topical therapy for striae alba (20% glycolic acid/0.05% tretinoin versus 20% glycolic acid/10% L-ascorbic acid). Dermatol Surg, 24: 849, 1998*)

To treat postoperative erythema in laser patients (*Alster et al.: Effect of topical vitamin C on postoperative carbon dioxide laser resurfacing erythema. Dermatol Surg, 24: 31, 1998*)

■ Topical vitamin C was first studied as a photoprotectant by using a porcine skin model (*Darr et al.: Topical vitamin C protects porcine skin from ultraviolet radiation-induced damage. Br J Dermatol, 127: 247, 1992*)

Saja Hamed, Ph.D
درستوه على الحيوانات
روبو و انة خفيف ال (ROS)

75

Water-Soluble Antioxidants:

Vitamin C ⇒ ما يتصنع بالجسم، يتقبل عليه
مما ذكره رسول

- Oral supplementation with vitamin C produces only a limited increase in skin concentration
- Because even with ingestion of massive doses, the absorption of vitamin C is limited by active transport mechanisms in the gut

إذا أخذنا كمية أكبر من ال receptor
لجملها ما رح تستخدمه بالتالي احسرها
لذلك انك تزيد في الأكل لا يعني انك
رح تزيد في جسمك .

Water-Soluble Antioxidants:

Vitamin C

72

- 3 forms are found in cosmeceuticals:
 - L-ascorbic acid (active form, least stable):
formulations turned yellow due to oxidation by air
 - Ascorbyl-6-palmitate
 - Magnesium ascorbyl phosphate

stability
↓

Stability studies demonstrated that magnesium ascorbyl phosphate is the most stable in solution and emulsion followed by ascorbyl-6-palmitate

Water-Soluble Antioxidants: Vitamin C

- لازم هتة تقطى تأثيره
الجلد اهنا عنده مشاكل او
كانوا ضعيفين في موضوع
نقذ يتهم لكونا اذا ما حنت حاجة مارح يعطى effect
effect

- Topically applied vitamin C has been shown to enhance collagen production in human skin
- Skin biopsies taken from postmenopausal women who applied 5% L-ascorbic acid to one forearm and vehicle to the other showed an increase in mRNA levels of collagen I and III

(Nusgens et al.: Topically applied vitamin C enhances the mRNA level of collagens I and III, their processing enzymes and tissue inhibitor of matrix metalloproteinase 1 in the human dermis. *J Invest Dermatol.* 2001 Jun;116(6):853-9)

vit C ⇒ is water soluble ⇒ ^{Saja Hamed, Ph.D} ذلك اذا طبقته Topically
غير مؤثر على الـ fibroblast او deep in dermis deep
صتة يوصل ويؤثر على (collagen synthesis)

Water-Soluble Antioxidants: Vitamin C

- Sunscreens even when applied properly block only 55% of free radicals produced by UVA exposure (*Haywood et al.: Sunscreens inadequately protect against ultraviolet-A-induced free radicals in skin: implications for skin aging and melanoma? J Invest Dermatol. 2003 Oct;121(4):862-8*)
- These data suggest that in order to optimize UV protection, sunscreens should be used in conjunction with topical antioxidants

UV Light
oxidative stress
photo protection
vit C
Saja Hamed, Ph.D
Reactive oxygen species
vit E
sunscreen
protection
vit C
Reactive oxygen species

- The purpose of this study was to see if a combination of topical vitamins C and E is better for UV protection to skin than an equivalent concentration of topical vitamin C or E alone.

الدراسة تفضل
مع بعض
كل واحد لحال

- Vitamin C and E were applied alone or in combination for 4 days to pig skin and then irradiated with a solar simulator.

- Either 15% L-ascorbic acid or 1% alpha-tocopherol alone also was protective but the combination was superior

Water-Soluble Antioxidants: Vitamin C

- Histological examination revealed that animals treated with topical ascorbic acid exhibited fewer sunburn cells than did those animals treated with vehicle alone when exposed to both UVA and UVB irradiation
- Sunburn cells are basal keratinocytes undergoing programmed cell death as a result of irreparable DNA damage and represent a method to quantifying the damaging effects of UV irradiation

Water-Soluble Antioxidants: Vitamin C

- In addition, they observed a decrease in erythema in areas treated with vitamin C ^{ملاحظة ان erythema post operative بعد الليزر}
- Darr et al. found that topical vitamin C combined with either a UVA or UVB sunscreen improved sun-protection as compared to sunscreen alone (Darr et al.: *Effectiveness of antioxidants (vitamin C and E) with and without sunscreens as topical photoprotectants. Acta Dermatol Venereol, 766: 264, 1996*)
- Vitamin C also reduced oxidized vitamin E back into its active form so it amplifies the antioxidant capabilities of vitamin E (Chan AC: *Partners in defense, vitamin E and vitamin C. Can J Physiol Pharmacol, 71: 725, 1993*)

- Vitamin C may help in lightening hyperpigmentation
- Magnesium-L-ascorbyl-2-phosphate suppressed melanin formation by tyrosinase and melanoma cells
- Topically applied 10% magnesium-L-ascorbyl-2-phosphate cream caused a significant lightening of melasma and lentigenes when applied to the face

عند قدرة تقليل
من تصنيع
الميلانين
في الميلانوسايت

(Kameyama et al.: Inhibitory effect of magnesium L-ascorbyl-2-phosphate (VC-PMG) on melanogenesis in vitro and in vivo. J Am Acad Dermatol. 1996 Jan;34(1):29-33)

Water-Soluble Antioxidants:

Vitamin C

- There are no studies that demonstrate that ingestion of oral vitamin C increases the levels of vitamin C in the skin

* صافٹی سے، یعنی اللہ اذا اظن
ع تاں اکثر رح بزرگ
نسبتہ کی الجلد

- Unfortunately:

- many of the currently available topical preparations are unable to penetrate the stratum corneum

- Most preparations of topical vitamin C do not come in airtight containers that are protected from UV radiation

و ممکن ما علو الاسباب الطلویہ
صح ان ینحوا ان oxidation اللہ

Water-Soluble Antioxidants: Vitamin C

- A small number of patients may experience minimal discomfort (stinging and mild irritation) from the topically applied formulations
- Major disadvantages of the various formulations include:
 - High cost
 - Questionable efficacy
- When it might help?

دواء water soluble
ممكن انه يصل
ويعمل
dermis

Water-Soluble Antioxidants:

Vitamin C

Summary:

- Vitamin C preparations are useful in preventing or lessening the harmful effects of UV radiation, and for ameliorating disorders of hyperpigmentation, striae, and post-laser erythema

vit A سیدو سیدو سیدو
derivative

- Until an affordable, stable, and absorbable topical product is developed, the oral supplements are superior

تفضل في الـ Topical
بأنه يصل إلى Dermis من خلال الجلد.

The Fat- and Water- Soluble Antioxidants: α - Lipoic Acid

٢٢

- Synthesized in the mitochondria of plants and animals, including human
- It is a good candidate for topical application:
 - A small, stable molecule
 - A potent antioxidant
 - Soluble in both aqueous and lipid environment
- A split face study was done on 33 women. Topical application twice daily of 5% lipoic acid cream for 12 weeks decreased skin roughness by 50.8% when compared with the placebo. In addition, reduction in lentigenes and fine wrinkles were noted (*Beitner H: Randomized, placebo-controlled, double blind study on the clinical efficacy of a cream containing 5% alpha-lipoic acid related to photoaging of facial skin. Br J Dermatol, 149: 841-849, 2003*)

* الـ لاسك ٢٠٠٠ جزيء
بـ لاسك ٢٠٠٠ جزيء
• Topically

٢٣

Botanical extracts

- Antioxidation: coffee and pomegranate تبع الرواح
- Photoprotection: black tea and olive
- Smoothing, calming, anti-inflammatory effects: chamomile and various mushrooms
- Skin lightening: blueberry and ginseng
- Skin tightening: peppermint and witch hazel
- Emolliating effect: jojoba and coconut extract

Botanical extracts:

٧٥

■ Keep in your mind:

- Herbal extracts exhibit more variation than synthetic products regarding content
- The constituents depend on growing conditions, climate, harvesting methods and extraction methods
- They are often used in very small amounts in cosmetic products (far below therapeutic range)
- Limited number of clinical studies performed with topical formulations containing such extracts
- So the real usefulness is still questionable

تختلف حسب الموسم

وطريقة الاستخلاص

وشكله كثيرة جداً

Active ingredients

ingredients

٧٦ * بالعادة هي اد extract تنمو بكميات قليلة جداً تكون عرسية من ال preservative
* عن limited studies لذلك نركز على الأشياء التي عليها دراسات ومثبتة أفضل