THE TRICKY TEAR TROUGH:
PERIORBITAL SKIN REJUVENATION

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• Patients are often seeking advice about which topical products are most effective in treating periorbital rhytides
SEPHORA SKINCARE
Periorbital hyperpigmentation is a result of thinning of the skin, atrophy of the malar fat pad with age, and enlargement of the orbital bony space leading to a hyperpigmented concavity at the medial border of the eyelid and cheek.
• Epidermal thickness: 0.2-0.4 mm

• Caution: due to thin skin and close proximity to the eye
Classically, treatment options are divided into 3 groups:

- **Surgical**
- Non-Surgical (fillers, neuromodulators, laser and light therapy)
- Adjunctive (topicals and peels)
Klingman: three golden rules of cosmeceuticals

1) Can the active ingredient penetrate the stratum corneum and be delivered in sufficient concentrations to its intended target in the skin over a time course consistent with its mechanism of action?

2) Does the active ingredient have a specific biochemical mechanism of action in the target cell or tissue in human skin?

3) Are there published peer-reviewed, double-blinded, placebo controlled statistically significant clinical trials to substantiate the efficacy claims?
Effects of retinoids on fine lines and rhytides are well known.

Retinol, retinyl esters and retinaldehyde are all converted to trans-retinoic acid.

Caution: retinoids have been shown to cause conjunctival irritation.

Due to retinoids ability to induce irritation, there is hesitation to use these products near the eye with the potential to damage to the eye or cause unappealing periorbital erythema.
• Efficient water soluble antioxidant

• Neutralizes free radicals (intracellularly and extracellularly)

• Protected porcine skin from UVA phototoxic injury & UVB induced erythema & sunburn cell formation

• Essential in collagen biosynthesis; cofactor for both lysyl & prolyl hydroxylase

• Provides lightening benefits via inhibition of tyrosinase

• 3 month double blind vehicle controlled study- 84.2% preferred side treated with vitamin C and optical profilometry demonstrated 73.7% improvement of crows feet
• Greatest challenge: product stability and adequate penetration

• Water soluble $\Rightarrow$ prone to oxidation $\Rightarrow$ byproduct dehydroascorbic acid

• Thus, must be formulated at pH < 3.5 to enter the skin

• Maximal concentration for optimal percutaneous absorption is 20%

• Beneficial combination of anhydrous ascorbic acid + lipid soluble terahexyldecyl (THD) ascorbate
• Lipophilic antioxidant: protective for cell membrane & stratum corneum lipid bilayer
  
  • Neutralizes free radicals & promotes healing process

• Decreases UVB- induced photodamage, inhibits human metalloproteinases that degrade elastin & inhibits UV- induced tumor formation

• 4 month facial study with 5% topical vitamin E showed improvement in periorbital rhytides post-UV inflammation

• 15% L-ascorbic acid & 1% α-tocopherol ➔ 4-fold photoprotection against erythema & sunburn cell formation

• Synergistic photoprotection: d/t combining the hydrophilic & lipophilic antioxidants ➔ stabilized formulation
Antioxidant effects, reduces skin yellowing, hyperpigmentation, erythema & blotchiness, improves the epidermal barrier & reduces fine lines & wrinkles

- Inhibits melanosome transfer from melanocytes to keratinocytes

- Increases collagen production as shown in fibroblast cultures & reduces excess dermal glycosaminoglycans (GAGs) which are characteristic of photodamaged skin

- Increases lipid and protein components of the stratum corneum \( \Rightarrow \) reduces transepidermal water loss (TEWL) & increases the skin’s barrier properties

- One of the best studied cosmeceutical ingredients for antiaging
• Epigallocatechin-3-gallate (EGCG): most abundant & physiologically active polyphenol

• EGCG is a powerful free-radical scavenger that has been shown to reduce UVA-induced sun damage and UVB-induced lipid peroxide, to downregulate UV-induced expression of AP-1 and NF-kB, to inhibit expression of collagenase in cultured human fibroblasts, and to prevent collagen crosslinking in hairless mice

• Histologic exam: green tea application protected epidermal Langerhans cells from UV damage and reduced the number of sunburn cells
GREEN TEA CHALLENGES

• Lack of stability and epidermal penetration

• EGCG is a highly reactive compound that is easily oxidized

• Oil-in-water emulsion = most effective percutaneous penetration

• Glycosalated form: more efficacious for targeting keratinocytes & max. antioxidant activity

• Skepticism: the only randomized, double-blind, controlled clinical study found no statistically significant clinical improvement

• If stability & penetration can be addressed, the benefits of green tea for the human skin could become a powerful adjunct in our cosmeceutical armamentarium
Lysine-threonine-threonine-lysine-serine (KTTKS) is a fragment of procollagen I, which has been shown to stimulate dermal matrix production in fibroblast cultures.

Palmitoyl, a fatty acid fragment, added to this hydrophilic peptide improves cutaneous penetration.

12 wk, double-blind, placebo controlled, split face study, topical 3 parts/million pal-KTTKS → significant improvement in the appearance of facial rhytids.

Indefinite modifications can be made to the amino acid sequences comprising peptide molecules.

As the amino acid residues increase, so does the cost and difficulty of skin penetration.

This technology will continue to evolve in the future and will play an integral role in the cosmeceutical industry.
Integral role in the repair and remodeling of dermal infrastructure

Topical application promotes growth of keratinocytes, dermal fibroblasts & other cells with decreased proliferative capacity due to aging

Two studies utilizing GF & cytokines obtained from cultured human fetal fibroblasts ➔ 17% improvement of periorbital wrinkles after 2 months of BID application & 33% improvement after 6 months of BID usage

On histology: 37% increase in grenz-zone collagen & 30% increase in epidermal thickness after 60 days of BID application
Alternative to human growth factors ➔ topical product containing secretions of the snail Cryptomphalus aspersa (SCA)

Shown to provide significant improvement of periorbital rhytides after 12 wks of use

Large molecular size of growth factors: effective skin penetration?

Penetrate via a vertical pathway such as hair follicles, sweat glands or microlesions in the inter-follicular stratum corneum

Growth factors & cytokines will likely continue to be an emerging area of study for periorbital rejuvenation
Glycolic acid, lactic acid, mandelic acid & benzilic acid

- Decreases corneocyte cohesion above the stratum granulosum, promoting exfoliation of the outer layers of stratum corneum

- Topical AHAs for 6 months resulted in 25% increase in epidermal thickness with improved synthesis of glycosaminoglycans, collagen & possibly elastic fibers

- Also reversed basal cell atypia, dispersal of melanin pigmentation & return to a more normal rete pattern
• Formulated in daily skin care regimens

• Higher concentrations may be used for chemical peels

• Address the crucial issues of periorbital rejuvenation including photoaging & hyperpigmentation
• Naturally occurring glycosaminoglycan; major component of ECM

• Humectant: attracts moisture; binds 1,000 X its volume in water

• Helps maintain tissue elasticity, turgor, and hydration
HYALURONIC ACID CHALLENGES

• Challenge: the ability to penetrate the dermis to achieve maximal deposition

• Most OTC hyaluronic molecules are 3,000 nm in diameter, whereas the intercellular space is only 15 to 50 nm

• Recent study: efficacy of a nanoproduct of 5nm in reducing the depth of wrinkles, increasing moisture and elasticity of the face and periorbital region found a statistically significant change
• Essential component of the stratum corneum

• Integral role in skin barrier function & maintenance of homeostasis

• Improves skin hydration, reduces TEWL & increases tretinoin tolerability

• Addition of ceramides to any periorbital rejuvenation regimen will provide improvement in overall skin hydration
In vitro studies indicate caffeine exerts antioxidant properties

Exhibits anti-inflammatory properties

Caffeine stimulates lipolysis by autonomic neural mechanisms ➔ improves lower eyelid sagging and puffiness

Although caffeine is used in many cosmeceutical products, there is still caution for its anti-aging use, as it has been shown to reduce collagen synthesis in human cultured skin fibroblasts.
• Moderate anti-oxidant activities

• Potent anti-inflammatory action

• Further studies need to be performed to clearly demonstrate the role of chamomile in reducing puffiness and irritation of periorbital skin
• Glycyrrhetinic acid: pharmacologically active compound in licorice root with anti-inflammatory properties

• Licorice root contains liquiritin and isoliquertin which disperse melanin and glabridin which inhibits tyrosinase

• Licorice root is effective in treating the hyperpigmentation associated with photoaging

• More studies are needed to examine its role specifically in periorbital hyperpigmentaiton
TOPICAL BLEACHING AGENTS

- Accelerate skin turnover ➔ Hydroxy acid, retinoic acid
- Premelanin synthesis ➔ Tretinoin
- Tyrosinase inhibition ➔ Hydroquinone, azelaic acid, kojic, arbutin, soy, mushroom, peptides
- Post melanin synthesis tyrosinase degradation ➔ Linoleic acid
- Postmelanin synthesis melanosome transfer inhibition ➔ Soy, niacinamide
- Interacts with copper ions to reduce dopaquinone ➔ Vitamin C
Noninvasive polymer emulsion which can be applied to the under eye area ➔ resultant in-situ crosslinking functionality & formation of an invisible film

A randomized, split face study identified a one grade improvement in lower lid bag protrusion & increased epidermal thickness
CONCLUSION

• Periorbital region is a critical aspect of facial rejuvenation

• Periorbital treatment options have exponentially grown from extensively studied retinoids, to recent technology, such as growth factors and peptides

• Future scientific advances will continue to expand our treatment armamentarium for periorbital rejuvenation
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