Cosmeceuticals: focus on topical retinoids in photoaging

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Abstract Evidence from a randomized clinical trial showed that, in spite of the many surgical procedures effective in ameliorating the clinical appearance of photoaged skin, the only medical therapy with proven benefits in photoaged skin are topical retinoids, in particular tretinoin, isotretinoin, and tazarotene. The application of retinoids might not only clinically and biochemically repair photoaged skin, but their use might also prevent photoaging. Furthermore, new evidence suggests a beneficial role of topical retinoids in the treatment of intrinsically aged skin.

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Introduction

Vitamin A and its derivatives, both natural and synthetic, have been popular additives in topicals for years and are recognized as the gold standard for the prevention and treatment of photoaging.

The following topical retinoids are recognized as being useful:

- **Natural retinoids**
  - Retinol (vitamin A alcohol)
  - Retinyl-palmitate (vitamin A ester)
  - Retinyl-acetate (vitamin A ester)
  - Retinaldehyde (vitamin A aldehyde)
  - Tretinoin (all-trans-retinoic acid)
  - Isotretinoin (13-cis-retinoic acid)
  - Alitretinoin (9-cis-retinoic acid)

- **Synthetic retinoids**
  - Tazarotene
  - Adapalene

Tretinoin, isotretinoin, alitretinoin, tazarotene, and adapalene are registered as drugs; the others are cosmeceuticals (medicinally active cosmetics).

Vitamin A and its derivatives exert their action by binding to specific nuclear receptors. The ligand-receptor complex modulates the expression of the genes involved in cellular differentiation and proliferation, normalizing cell keratinization.

Retinoids might also act independently from the binding to nuclear receptors. Each of them exerts its own activity, offering a further choice to the dermatologists who deal with topical retinoids.

Although there are several studies proving the efficacy of tretinoin as topical treatment of photoaging, few studies are available for the other retinoids.

Tretinoin

Kligman and Willis\textsuperscript{1} first introduced retinoids for use as photoaging agents. After its application, the author noticed improvement of skin depigmentation and rejuvenation.\textsuperscript{2,3}

When used on photodamaged skin, tretinoin’s clinical effects include improvement of wrinkles, roughness, mottled pigmentation, and skin appearance as a whole.
The histologic changes observed are decreased corneocyte adhesion (loss of desmosomes, decreased tonofilaments, increased autolysis of keratinocytes, intracellular glycogen deposition), epidermal hyperplasia, increased number of Langerhans cells, increased synthesis of collagen and elastin, and angiogenesis. Tretinoin enhances epidermal cell turnover, decreasing contact time between keratinocytes and melanocytes and promoting a rapid loss of pigment through epidermopoiesis.

Tretinoin is available in different concentrations (0.01%, 0.25%, 0.5%, and 0.1%) and as different formulations (cream, gel, solution). Creams are generally prescribed for sensitive skins, whereas gels are prescribed for oily skins.

Continuous once-daily application is mandatory to achieve maximum results, in any case not occurring before a 3-month period. The only clinical improvement that appears after only 1 month is skin smoothness. To maintain the results, long-term treatment is necessary. There are no limits to the duration of tretinoin topical use.

Moderate cutaneous side effects, especially erythema and desquamation, are observed in most patients even if after 2 to 4 weeks these side effects decrease without discontinuing the treatment. It may be necessary to interrupt the treatment for 2 to 3 days, to apply a calming and moisturizing cream, and then to restart treatment once every 2 days.

Whenever tretinoin is prescribed, the use of sunscreen is very important to avoid sunburns (the treated skin is thinner) and worsening of photodamage (UV radiations decrease the expression of retinoid receptors in skin cells, thus limiting the effects of retinoids).

### Retinol

There are no studies comparing its effectiveness with that of tretinoin, although retinol does not appear to be as effective. In photoaging, it is used as a cream in different concentrations, ranging from 0.075% to 1%. It can be considered a “light” alternative to tretinoin in case of sensitive skins.\(^5\)

### Retinyl-palmitate and retinyl-acetate

Esters are not considered effective against photoaging if used alone.\(^6^,^7\) Most of the products available are, in fact, a combination of esters and hydroxy acids.

### Retinaldehyde

Retinaldehyde is formulated as cream or gel and in concentrations varying from 0.015% to 0.1%. Its efficacy is similar to that of tretinoin, but it is much less irritating.\(^8^,^9\)

### Isotretinoin

Topical isotretinoin is available as a 0.05% cream or gel. It appears to be less irritating, yet less effective, than tretinoin.\(^10\)

### Alitretinoin

The theoretic benefit of alitretinoin 0.1% gel in the treatment of photoaging originates from the binding and activation of all nuclear retinoid receptors, but larger, blind, and controlled trials are necessary to better investigate its role.\(^11\)

### Tazarotene

Tazarotene is an analogue of tretinoin that belongs to the family of acetylenic retinoids. It has a specific binding profile for beta and gamma retinoid receptors. Tazarotene improves skin roughness, fine wrinkling, and epidermal atrophy.\(^12\) It is available at 0.05% and 0.1% gel and cream.

### Adapalene

Even if usually indicated for acne, adapalene has also been tested for the treatment of photoaging.\(^13\) Once-daily application of adapalene 0.1% gel for 4 weeks, followed by a twice-daily application for up to 9 months, significantly reduced actinic keratoses and lentigines.

### References


