

A review of the efficacy of popular eye cream ingredients

Hanin Hamie, BS^a, Reem Yassine, BS^a, Rajaa Shoukfeh, BS^{b,*}, Dilara Turk, MD^c, Farhan Huq, MD^c, Meena Moossavi, MD, MPH^c

ABSTRACT

Background: Due to the periorbital region's high susceptibility to damage from external factors, along with its tendency to demonstrate early signs of aging, periorbital skin is a common target for antiaging therapy.

Objective: This review aims to evaluate the efficacy of active ingredients commonly found in eye creams, particularly focusing on their impact on periorbital skin concerns.

Methods: A comprehensive review of the literature on active ingredients in eye creams, including retinoids, vitamins C and E, peptides, ceramides, hyaluronic acid, caffeine, and niacinamide, was conducted. Clinical studies assessing the efficacy of these ingredients in addressing periorbital concerns were examined.

Results: Studies demonstrate the potential of these ingredients to improve various aspects of periorbital skin, including hydration, elasticity, collagen synthesis, and reduction of inflammatory mediators. Ingredients such as retinoids, vitamin C, and caffeine show promise in addressing wrinkles and hyperpigmentation, while peptides and hyaluronic acid aid in collagen production and hydration. Niacinamide and ceramides offer benefits in reducing wrinkles and enhancing the skin barrier function.

Limitations: The lack of clinical trials specifically targeting eye cream formulations and periorbital skin is a notable limitation. Furthermore, the variability in study designs, sample sizes, and concentrations of active ingredients across studies complicates direct comparisons.

Conclusion: The reviewed studies highlight the potential of active ingredients in eye creams to address various periorbital concerns. Further research, particularly large-scale clinical trials focusing on eye cream formulations and their efficacy on periorbital skin, is warranted to establish their significance and comparability with other dermatologic products.

Keywords: eye cream, periorbital skin

Introduction

Periorbital skin has a unique physiology, as it is the thinnest and most dynamic of the entire body. In some patients, the thickness of this skin measures as little as 0.2 mm.¹ The orbicularis oculi muscle is intimately intertwined with the eyelid dermis, and there is minimal subcutaneous fat present between the muscle and skin layers.¹ Periocular skin is especially susceptible to damage from sun exposure and other extrinsic factors including smoking, pollution, contact dermatitis, and chronic rubbing due to seasonal allergies.¹

Eye cream is a topical product that is targeted to address skin concerns unique to this region, including moisturizing

and reducing fine lines and wrinkles.² Due to the periocular skin's predilection towards irritation, wrinkles, hyperpigmentation and puffiness, eye cream formulations tend to be thicker

What is known about this subject in regard to women and their families?

- It is known that the periorbital region is highly susceptible to damage from external factors and is a common target for antiaging products.
- Many of the ingredients found in topical eye creams have been studied with respect to their efficacy and mechanism of action on facial skin as a whole.

What is new from this article as messages for women and their families?

- We present a review evaluating the efficacy of popular topical ingredients found in eye creams, including retinoids, vitamin C, vitamin E, peptides, ceramides, hyaluronic acid, caffeine, and niacinamide.
- This manuscript is unique because it offers a comprehensive review of the efficacy of these ingredients on periorbital skin in particular.
- We also detail any adverse reactions associated with these topical ingredients.
- This review sheds light on the need for further clinical trials to investigate the comparability of the efficacy and combination of ingredients within eye cream specifically.

^a College of Osteopathic Medicine, Michigan State University, East Lansing, Michigan

^b School of Medicine, Wayne State University, Detroit, Michigan

^c Department of Dermatology, Wayne State University, Detroit, Michigan

* Corresponding author.

E-mail address: rajaa.shoukfeh@med.wayne.edu (R. Shoukfeh).

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and contain more oil than regular facial creams.² Additionally, eye creams tend to have a greater amount of active ingredients to target specific complications of the periocular skin, and may reduce concerns such as dark circles, puffiness, and wrinkles.²⁻⁵

Dark eye circles are a major periocular skin concern among people of all ages. Hypervascularity, aging, and tear trough depression are all causes of dark undereye circles.^{6,7} Eye creams that contain niacinamide,⁸ caffeine,⁹ and vitamin E¹⁰ have been shown to decrease periocular hyperpigmentation. In addition, eye creams that contain vitamin C have been shown to increase under eye brightness.¹¹

Another common periocular skin concern is undereye puffiness. There are multiple causes of puffiness including photodamage, fluid accumulation, hollow tear troughs, and cheek descent.¹ Eye creams containing active ingredients, such as caffeine, reduce fluid retention, strengthen vasculature, and increase skin laxity, which all contribute to decreased puffiness.^{1,9}

Wrinkles are caused by photodamage, squinting, constant movement of the eyes, aging, and chronic rubbing due to seasonal allergies. Popular eye creams including active ingredients like caffeine,⁴ retinol,¹⁰ vitamin C,¹¹ peptides,¹² hyaluronic acid (HA),¹³ and niacinamide¹⁴ are designed to prevent and reduce wrinkle formation.

Retinoids

Retinoids refer to a class of chemical compounds that are composed of vitamin A, derived from vitamin A, or that have similar structural and functional characteristics to the vitamin.^{10,15,16} When bound to receptors, retinoids act as important transcription factors that function in the normal maintenance of epidermal differentiation.¹⁰ Vitamin A derivatives, retinol, retinol esters, and retinaldehyde are abundantly found within over-the-counter cosmetic products, including eye creams.¹² These compounds are not biologically active until enzymatic conversion to trans-retinoic acid, the principal active ingredient.¹² Tretinoin comprises 50% of the active cellular form, therefore isotretinoin, adapalene, and tazarotene may be applied in their active form.

Photoaging is characterized by fine and coarse wrinkles, laxity, sallowness, drying, and telangiectasias.¹⁷ Studies suggest, cutaneous aging results from the interplay of extrinsic damage by ultraviolet (UV) radiation, intrinsic increases in collagen-degrading matrix metalloproteinases, and decreased collagen synthesis.¹⁰ Retinoids increase collagen content in the upper papillary dermis by inhibiting collagen degradation and increasing collagen synthesis.¹⁶ Topical tretinoin increases the production of type I collagen by 80% in photoaged skin, normalizes the elastic tissue organization, epidermal hyperplasia, and compaction of the stratum corneum (SC), which increases the smoothness of the skin and wrinkle effacement.¹⁶

Multiple studies have been conducted to test the clinical efficacy of topical retinoids in dermatologic products. A study utilizing human skin samples showed that topical 1% retinol inhibits the increase of metalloproteinases and stimulates collagen synthesis in aged, sun-protected, and photoaged skin.¹⁰ Chiu and Kimbal¹⁰ demonstrated that retinol may be able to restimulate fibroblast growth potential, which is found to decrease with age. Furthermore, Chiu and Kimbal¹⁰ presented evidence of retinaldehyde cutaneous penetration and encouraged the application of retinaldehyde and retinol to decrease fine lines and wrinkles. A study utilizing 0.05% tretinoin cream applied nightly showed epidermal thickening and improvement in fine wrinkles in 3 months. After 6 months of the treatment protocol, further improvement in fine and coarse wrinkles, sallowness, dyschromia, laxity, and roughness.¹⁶ The studies address the efficacy of topical retinoids on facial skin, rather than periocular skin specifically. There is a lack of clinical trials particularly

reviewing the efficacy of retinoids contained within an eye cream formulation and used on periorbital skin.

Overall, topical retinoids are well tolerated by patients however mild complaints of erythema, peeling, and dryness have been reported.¹⁷ The severity of the reaction is decreased with time and can be avoided with the use of decreased concentrations of topical tretinoin overtime.¹⁶

Vitamin C

Vitamin C is the most abundant antioxidant available in human skin and is involved in the formation of the skin barrier and collagen in the dermis.^{18,19} Ascorbyl palmitate, magnesium ascorbyl phosphate, and L-ascorbic acid are 3 forms that are commonly available in cosmetics.²⁰ L-ascorbic acid is the most biologically active and well-studied form of vitamin C which has been well-established as a cofactor for collagen synthesis.^{10,19} Vitamin C has been utilized in a myriad of under eye creams for its antioxidant, antiaging, photoprotective and anti-pigmentary effects.^{12,19}

Oxidative stress derived from environmental factors such as pollution, UV radiation, and smoking can accelerate skin damage.^{11,19} UV radiation causes skin aging through the production of free radicals and reactive oxygen species that interfere with collagen biosynthesis, degrade collagen and elastic fibers, and damage cell membranes leading to ceramide and arachidonic acid release which leads to inflammation.¹¹ Vitamin C is a potent antioxidant that neutralizes this oxidative stress.^{19,21}

Vitamin C is essential for collagen biosynthesis, it directly functions as a cofactor in the hydroxylation of procollagen as well as plays a role in the activation of transcription and stabilization of procollagen mRNA that regulates type I and III collagen synthesis.^{12,19} Vitamin C is also known to augment the effects of other commonly used active ingredients, such as vitamin E and retinol.^{12,19} A clinical study demonstrated that the topical use of daily 3% vitamin C led to significant increases in dermal papillae.¹⁹ A double-blind randomized trial was conducted to evaluate the clinical effects of 5% vitamin C on photoaged skin over a 6-month period. Compared with placebo, vitamin C led to a clinically apparent improvement in the overall appearance of photodamaged skin as well as a decrease in deep furrows.²² Another study found that using 20% vitamin C, vitamin E, and raspberry leaf extract led to an improvement in most signs of skin aging, including the periorbital region, namely darkening, smoothness, and wrinkles.¹¹

Vitamin E

Vitamin E is a lipid-soluble antioxidant that protects cellular membranes from damage by free radical lipid peroxidation.¹⁰ Topical vitamin E has become a popular treatment for many skin disorders.²³ Vitamin E cannot be synthesized by humans, therefore levels of cutaneous tocopherol is dependent on oral intake and topical delivery.²⁴ Many over-the-counter antiaging creams consist of 0.5 to 1% vitamin E due to its effective reduction in dark eye circles.²³

A study concluded that the depletion of vitamin E in the human epidermis is a sensitive indicator of environmental oxidative damage.¹⁰ Free radicals cause the disruption of lipids, proteins, nucleic acids, and deplete the stores of endogenous antioxidants.¹⁰ Reactive oxygen species also have the ability to alter the biosynthesis of collagen and glycosaminoglycans in the skin.²³ Vitamin E modulates the damage by acting as a scavenger for these free radicals and lipid peroxyl radicals.¹⁰

Dark undereye circles are due to excessive pigmentation, vascular stasis, thin and translucent lower eyelid skin, and shadowing due to skin laxity and tear trough.²⁵ As the skin ages, the skin appears darker due to sagging and bulging of the lipid layer in the periorbital region that creates shadows.²⁵ Tocopherol is

thought to decrease levels of matrix metalloproteinases through suppressive effects on AP-1 DNA binding, suppress melanogenesis, and inhibit nitric oxide production.²⁶ This leads to decreased pigmentation, inflammation, and collagen breakdown, counteracting the common physical manifestations of periorbital aging. In a human hemiface trial, 5% vitamin E demonstrated reduced skin roughness, length of facial lines, and depth of wrinkles in comparison to vehicle control.¹⁰ Aparecida Sales de Oliveira Pinto et al.²⁷ proved topical application of vitamin E resulted in increased SC hydration and water binding capacity. Another study found that periorbital rhytides were decreased by 14.07% after 4 weeks of applying an eye cream that included vitamin E.²⁸

Peptides

Peptides are short sequences of amino acids that compose the building blocks for proteins. When applied topically, peptides assist in the reversal of the dermal and epidermal signs of aging.^{29,30} This is through the support of dermal fibroblast functions and the stimulation of collagen, elastin, and glycosaminoglycan production.³¹ Collagen is the main structural protein in the skin.³² With age, the skin is exposed to various factors that decrease metabolic activities related to collagen content.³² Increases in dermal collagen are thought to improve signs of aging.³³ Peptides upregulate *in vitro* collagen production and topical formulations have shown clinical improvement when applied to photodamaged skin.¹²

A topical pentapeptide, containing the sequence lysine-threonine-threonine-lysine-serine (KTTKS) is a fragment of procollagen I.³⁴ This synthetic peptide stimulates collagen production, which provides structure and support to the skin.³⁴ A 12-week double-blind, placebo-controlled, split-face study with moisturizer containing 3 parts/million palmitoyl-KTTKS showed a significant reduction in fine lines and wrinkles.³⁴ Another study utilizing 3 peptide derivatives, in a mixed form, resulted in increases in dermal collagen and epidermal protein expression, leading to significant improvement in crow's feet and other wrinkles.³¹

Cosmetic manufacturers also offer topical cell culture extracts with natural enzymes and growth factor proteins that have shown improvement in periorbital wrinkles, roughness, and pigmentation when tested.¹² Idebenone is an organic compound that acts as a synthetic analog of coenzyme Q₁₀. A study conducted over 6 weeks, demonstrated immunohistochemical evidence of decreased interleukins and matrix metalloproteinases, in addition to an increase in collagen after topical application of 0.5% and 1% idebenone.²⁹ However, the use of idebenone is limited by the risk of allergic contact dermatitis.²⁹

Ceramides

The SC, the outermost layer of the epidermis, is composed of 3 lipid components including ceramides, cholesterol, and fatty acids.^{35,36} The ceramide component of the SC functions to connect corneocytes, forming a waterproof barrier that protects the skin from dehydration. Ceramides also act as repair agents for the SC.^{35,37} The SC is oriented in parallel stacks of water-repellent lamellar bilayers which serve 2 main functions including protection from inward absorption of harmful substances and restriction of outward loss of water and electrolytes.³⁸ Ceramides also have anti-inflammatory properties. Ceramides that are biosynthesized from genetically modified yeast have been shown to significantly inhibit nitric oxide production and suppress the expression of pro-inflammatory proteins including cyclooxygenase-2 and tumor necrosis factor- α .^{39,40}

Decreased levels of ceramides often manifests as dry and itchy skin.⁴⁰⁻⁴² Topical formulations containing ceramides and

pseudoceramide-dominant emulsions are widely used for the treatment of skin conditions that involve pruritus and transepidermal water loss.⁴³

Ceramide-containing cream has been demonstrated to significantly increase the water content of eyelid skin.⁵ Ophthalmologic testing showed no adverse reactions to ceramide application to the eyes and related eye areas.^{5,44} Additional appealing aspects of ceramide use include their ability to relieve dryness without having an undesirable adhesive quality and that they are safe to use in both adult and pediatric populations.⁵

Hyaluronic acid

HA is a large nonsulfated glycosaminoglycan found in the extracellular matrix of epithelial and connective tissue. Due to its unique helical coil conformation, HA can trap up to 1000-fold of its weight in water and is essential for maintaining tissue structure and volume.⁴⁵ It has an essential role in maintaining the skin's water reserve, turgor, and moisture.⁴⁶

Due to its variety in molecular weights, HA may be incorporated into different formulations to meet consumer needs including fillers, creams, gels, and drops. Additionally, changing the molecular weight impacts the therapeutic effect of HA. For example, the smaller the molecular weight of HA, the greater the skin penetration and hydration in wrinkle efficacy treatment.⁴⁵ High molecular weight-HA suppresses inflammation and angiogenesis. Large polymers of HA generally have anti-angiogenic and immunosuppressive functions.⁴⁷ Low-molecular weight-HA, on the other hand, scavenges for antioxidants and promotes wound healing.^{48,49}

HA has been proven to reduce periocular wrinkles.¹³ In a study of 76 female subjects (ages 30–60 years) with periocular wrinkles, HA cream was applied twice daily for 60 days. Compared to the placebo group, there was a significant improvement in skin hydration and elasticity in subjects treated with the low-molecular-weight-HA-based cream. Additionally, there was a significant improvement in the roughness index of subjects treated with the HA-based cream.¹³ Another study compared popular topical cream formulations containing HA tested on 20 women with periorbital wrinkles for 3 months.⁵⁰ Significant improvement in skin elasticity and tightness by 13 to 30%, reductions of wrinkle depth by 10 to 20%, and improved hydration levels were observed in all 20 subjects.⁵⁰

Caffeine

Caffeine is a naturally occurring purine alkaloid with antioxidant and anti-inflammatory properties.⁵¹ Due to caffeine's function as a phosphodiesterase inhibitor, it can raise intracellular cyclic adenosine monophosphate levels and ultimately suppress various inflammatory pathways. Furthermore, an increase in cyclic adenosine monophosphate stimulates the breakdown of triglycerides into free fatty acids, which leads to inhibition of fat accumulation.⁵²

Caffeine has also been proven to promote apoptosis of damaged cells. Caffeine's metabolites have antioxidant effects against reactive oxygen species.⁵³ These properties may help reduce wrinkles and protect the skin against free radical damage.⁵³ A 2018 study showed that caffeine has protective effects from oxidative stress-induced senescence by activation of A2AR/SIRT3/AMPK-mediated autophagy.⁵⁴

Recent studies have demonstrated that caffeine decreases periorbital hyperpigmentation. Periorbital hyperpigmentation is a common dermatologic condition that presents as darkness beneath the lower eyelids. In a study of 11 healthy women, treatment with a 3% w/w caffeine pad for 1 month resulted in significantly reduced periorbital pigmentation, improved blood circulation and skin luminescence in the periorbital region.³

Table 1
List of active ingredients commonly found in eye creams: composition and mechanism of action

Active ingredient	What are they?	How do they work?
Retinoids	A class of chemical compounds that are composed of, derived from, or structurally or functionally similar to vitamin A	Increase collagen content
Retinols		Normalizes elastic tissue organization
Retinol esters		Stimulate fibroblast growth potential
Retinaldehyde	Most abundant antioxidant available in human skin	Neutralizes oxidative stress
Vitamin C		Cofactor for collagen synthesis
Ascorbyl palmitate Magnesium ascorbyl-phosphate	Lipid-soluble antioxidant (not synthesized by humans, dependent on external intake)	Regeneration of oxidized forms of vitamin E
L-ascorbic acid		Acts as scavenger for free radicals and lipid peroxy radicals
Vitamine E		
a-tocopherol	Short sequences of amino acids that compose the building blocks for proteins	Support dermal fibroblasts
Peptides		Stimulate collagen, elastin, and glycosaminoglycan production
Palmitoyl-KTTKS	Lipid component of the stratum corneum	Connect the corneocytes of the stratum corneum, essential for forming a waterproof barrier and repair. Prohibit water-bound molecules from freezing or evaporating
Idebenone		
Ceramides		
Hyaluronic acid	Nonsulfated glycosaminoglycan found in extracellular matrix	Maintains water reserve, turgor and gaps within extracellular matrix
Caffeine	Purine alkaloid found naturally in many beverages, such as tea and coffee	Acts as an antioxidant and an anti-inflammatory agent. Promotes apoptosis of damaged cells. Increases skin elasticity and enhances skin barrier function by decreasing TEWL
Niacinamide	Water-soluble amide isotype of vitamin B3	Inhibits IL-1, PARP-1, and TNF- α . Antioxidant effects through polyadenosine diphosphate-ribose polymerase inhibition and melanosome transfer inhibition. Improves facial elasticity and decreases wrinkles

TNF- α , tumor necrosis factor- α .

Additionally, in people who have periorbital puffiness, caffeine has been shown to stimulate lipolysis and significantly improve lower eyelid puffiness.^{47,55} Caffeine also has been proven to have antiwrinkle effects by increasing skin elasticity and improving skin barrier function.⁵⁶ Caffeine improves the function of the epidermal barrier by decreasing the amount of transepidermal water loss.⁴ Topical caffeine in concentrations up to 3% is considered safe and easily absorbed into human skin.⁴

Niacinamide

Niacinamide (nicotinamide) is a water-soluble amide isotype of vitamin B3.⁵⁷ Niacinamide is converted into several essential coenzymes, including nicotinamide adenine dinucleotide and nicotinamide adenine dinucleotide phosphate which are both essential for healthy metabolism.⁵⁷ It has also been proposed that niacinamide acts as an antioxidant through polyadenosine diphosphate-ribose polymerase inhibition and melanosome transfer inhibition.^{57,58}

Niacinamide is currently used in many different cosmetic formulations including treatments for melasma,⁵⁹ hyperpigmentation,⁸ rosacea,⁶⁰ wrinkles,⁶¹ and acne vulgaris.⁶² In a study of 50 female subjects with clinical signs of fine lines, wrinkles, poor texture, and hyperpigmented spots, 5% niacinamide was applied to half of the face while a vehicle control was applied to the other half twice daily for 12 weeks. Overall, this study showed that 5% niacinamide had a significant effect on improving facial elasticity and decreasing wrinkles.¹⁴ Furthermore, in a randomized controlled comparative study evaluating the efficacy of cosmetic eye cream formulation containing niacinamide with a prescription 0.02% tretinoin regimen, it was found that the former significantly improved wrinkle appearance after 8 weeks and was better tolerated than tretinoin.⁶³

Discussion

Eye cream is an increasingly popular category of antiwrinkle treatments. The food and drug administration (FDA) defines

products as either a cosmetic or drugs, based solely on the product's intended use. A cosmetic is used to increase attractiveness, cleanse, and beautify while a drug is used to affect the structure or function of a body part. This distinction can determine the degree of FDA regulation and make clinical trials essential for determining efficacy. Eye creams are marketed towards beautification, categorizing them as a cosmetic and therefore not requiring FDA regulation or mandating of clinical trial conduction. This may be responsible for the lack of numerous clinical trials specifically targeted towards eye cream effectiveness. Most trials demonstrate the molecular improvements of topical ingredients to facial skin, rather than the changes explicitly observed in the periorbital region.

Eye cream is commonly a safe and effective addition to one's daily skincare routine, however, due to the inherent structure of the periocular skin, it can be easily irritated by various topical ingredients. An adverse effect of using topical products, such as eye cream, on the periorbital region is contact dermatitis. Some individuals are genetically more susceptible to more intense and frequent reactions to topical products, colloquially termed as having sensitive skin.⁶⁴ The dosing of the products reviewed is commonly limited by this reaction. The thinner skin of the eyelid predisposes it to greater allergen absorption, and it is therefore more prone to contact dermatitis than facial skin.^{65,66}

The periorbital area is often a target for the reversal of cutaneous aging. Drying, laxity, wrinkles, and hyperpigmentation

Table 2
Summary of eye cream active ingredients and the periorbital skin concern they address

Periorbital skin concern	Eye cream ingredients to utilize
Hyperpigmentation	Niacinamide, caffeine, vitamin E, vitamin C
Puffiness	Caffeine
Wrinkles	Caffeine, retinol, vitamin C, peptides, hyaluronic acid, niacinamide

in this region promote the aged appearance of the skin. Of the ingredients reviewed in clinical trials, they were all found to cause a significant change in the skin. Table 1 summarizes the composition and mechanism of action of active ingredients commonly found in periocular topicals. Table 2 provides a summary of eye cream active ingredients and the periorbital concern that they address.

Through the improvement of hydration, elasticity, increases in collagen, and decreases in inflammatory mediators, these ingredients have been proven to affect aspects of the skin. The degree to which these changes lead to improvement in the physical appearance of the skin is not universally proven. While the mechanisms of these topicals on the skin have been tested, large clinical trials are needed to further investigate the comparability of efficacy and the combinations of ingredients within eye cream specifically. This is necessary to clearly establish the efficacy of various eye creams and determine their significance in comparison to other dermatologic products such as facial creams and serums.

Conflicts of interest

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HH, RY, DT, and FH: Participated in research design, writing of the manuscript, and approval of the version of the manuscript to be published. RS: Participated writing of the manuscript, and approval of the version of the manuscript to be published. MM: Participated in research design, and approval of the version of the manuscript to be published.

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