Dermocosmetics in the management of acne vulgaris. Recommendations of the Polish Dermatological Society. Part II

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ABSTRACT

Acne vulgaris is the most common dermatosis among adolescents, but it can also affect adults. Acne lesions located on the face cause discomfort and lead to impaired quality of life for many patients. Acne is a dermatological condition with multiple causes and clinical manifestations, as well as varying degrees of severity. Dermatological treatment alone does not always bring good therapeutic effects, and occasionally it may result in symptoms of skin irritation. Therefore, using appropriate dermocosmetics is crucial in managing the condition. Dermocosmetics play a potentially important role in minimizing the adverse effects of acne medications, providing a synergistic effect by addressing other acne-causing factors and/or enhancing the efficacy of other treatment modalities, and protecting the skin against the adverse impacts of the exposome. In cases of mild acne, dermocosmetics can be used in monotherapy as an alternative to acne medications or for maintenance therapy. It is also advisable to combine dermocosmetics with topical or systemic therapies to achieve a synergistic effect or to prevent and reduce drug-induced adverse reactions. Dermocosmetics have keratolytic and anti-inflammatory properties, regulate sebum production, and help maintain the balance of the skin's natural microbiome.

Key words: acne vulgaris, microbiome, dermocosmetics, active substances.

INTRODUCTION

Acne vulgaris is a skin condition with multiple causes and is the most common dermatosis during adolescence. Acne occurs in 80% of adolescents, with roughly 9% of the global population, totaling about 5 million individuals, affected by the disorder [1]. In recent years, acne vulgaris has also been increasingly seen in adults, especially women [2, 3]. A systematic analysis conducted in the Global Burden of Disease Study 2010 found the prevalence of acne vulgaris to be 9.81% in women and 8.96% in men [4, 5].

Acne lesions encompass a wide spectrum of presentations, ranging from isolated microcomedones, open or closed comedones, papules, and pustules, to nodules, scars, and skin discolorations. The severity of acne lesions may be mild, moderate or severe [4]. Acne lesions located on the face cause discomfort in many patients, potentially leading to impaired quality of life and depression [6]. Hence, effective therapeutic management coupled with appropriate skin care and lifestyle adjustments are very important for addressing this condition. Even though most young individuals do not need dermatological intervention, the widespread presence of acne can also be viewed as a social concern [6]. Effective skin care stands as one of the key elements in the management of acne vulgaris. It varies depending on whether it is the sole therapy aimed at maintaining skin condition (e.g. after dermatological treatment or in patients with minor lesions) or whether it complements the main therapy used. Skin care products continue to advance, which emphasizes the necessity to educate patients about the significance of dermocosmetics in managing acne vulgaris. Dermocosmetics are used to reduce the adverse effects of treatment, or as maintenance or adjunctive therapy. Various formulations can be employed for this purpose, including creams, gels or serums. Active ingredients used in some dermocosmetics are designed to target various pathways associated with acne, which makes them a viable option for maintenance therapy. This approach helps sustain the achieved level of improvement and prevent the emergence of new lesions [1, 7]. Dermocosmetics are also used to reduce acne lesions, particularly post-inflammatory hyperpigmentation [7].

Young individuals with acne typically have seborrheic or combination skin types. Adult acne presents a more complex challenge, as the skin tends to be dry, with early signs of aging, while simultaneously displaying typical inflammatory acne lesions. Skin care regimens should involve cleansing the skin, minimizing irritation, addressing skin imperfections, applying moisturizers and agents regulating the epidermal barrier, and ensuring adequate photoprotection [1, 7, 8].

IMPORTANCE OF CLEANSING SUBSTANCES FOR THE CARE OF SKIN WITH ACNE VULGARIS

Individuals affected by acne vulgaris are advised to cleanse the face twice daily to remove exfoliated epidermis and unblock sebaceous gland openings. Recommended skin cleansers include syndets with a physiological pH formulated with a surfactant, characterized by good tolerability and effective skin cleansing properties. The type of formulation should be chosen according to the patient's skin needs and personal preferences (foam, gel, cleansing cream). Products of this type help cleanse the skin in the morning by removing residues of the previous night's skin care routine, and in the evening by effectively washing off make-up, other cosmetics, and impurities. Skin cleansers contain a diverse range of active substances aimed at managing sebum production, providing a keratolytic effect, and protecting the lipid barrier and skin microbiome [1, 7, 9].

ACTIVE SUBSTANCES USED IN DERMOCOSMETICS

A major role in dermocosmetics for acne skin care is played by active substances contained in both cleansing and daily care formulations. They may exhibit keratolytic, sebostatic, anti-inflammatory, antibacterial, and skin-lightening effects, and improve the epidermal barrier and microbiome. Some of these substances target multiple mechanisms involved in the development of acne vulgaris simultaneously [1, 8, 9].

The common substances used in dermocosmetics encompass salicylic acid, glycolic acid, lipohydroxy acid (LHA), linoleic acid, alpha hydroxy acids (AHAs), hydroxyethylpiperazineethanesulfonic acid (HEPES), retinol derivatives, bakuchiol (BAK), *Bixa orellana* seed extract as well as substances that enhance the microbiome and epidermal barrier while reducing skin discolorations.

BETA HYDROXY ACIDS (BHAS)

The BHA group includes salicylic acid. It is a metabolite of acetylsalicylic acid known for its comedolytic, bactericidal, and skin exfoliating properties. The hydroxyl and carboxyl groups in salicylic acid have the ability to attach to calcium ions within the corneodesmosome, causing disruption of cellular connections and removal of hyperkeratinized cells. Salicylic acid has keratoplastic properties up to a concentration of 10%. Beyond this level, it dissolves the intercellular cement, demonstrating a keratolytic effect. BHA are most widely used in daily anti-acne sk-

incare formulations at concentrations of 1–2% [9–11]. The exfoliating action of salicylic acid promotes skin cell renewal and enhances the penetration of moisturizing substances [9, 10]. In turn, the antimicrobial effect occurs as the acid penetrates bacterial cell walls, where it binds to the lipid layer, ultimately resulting in bacterial elimination. Being lipophilic, BHA easily enters pilosebaceous units and can be used in all stages of acne. It is non-toxic and self-neutralizing at shallow skin penetration. Adverse effects of salicylic acid, including dry skin and erythema, are mild and transient. They are caused by an excessive salicylic acid concentration and/or repeated use of the acid within a short period of time. Occasionally, salicylic acid can lead to skin irritation and dryness [7, 12, 13].

It is important to note, though, that in a portion of patients, salicylic acid can trigger contact allergies. If inflammation spreads beyond the application site or if there are severe subjective symptoms like itching or burning, discontinuation of the product is advised [12, 13].

ALPHA HYDROXY ACIDS

AHAs are organic acids with one hydroxyl group attached at the α position of the organic acid. The category comprises glycolic acid (GA), lactic acid (LA), malic acid (MA), tartaric acid (TA), and citric acid (CA), which are commonly utilized in cosmetic formulations. AHAs are primarily used in dermatology and cosmetology for skin exfoliation. They are generally safe for all skin types, posing a minimal risk of adverse effects. AHAs at different concentrations offer both therapeutic and cosmetic benefits, forming an integrated system that acts as a physical and immunological defense barrier against harmful external factors. AHAs reduce the integrity of corneocytes directly above the stratum granulosum by separating and exfoliating the stratum corneum. Because of their acidic character, AHAs decrease the pH of the skin, inhibit transferases and kinases, and interfere with the formation of ionic bonds, which subsequently contributes to the separation of desmosomes and promotes skin exfoliation. AHAs may also enhance epidermal barrier function by controlling hyperkeratosis and normalizing epidermal thickness and microbiome composition. They exhibit immunomodulatory properties and help regulate skin inflammation [11, 14]. Adverse effects associated with the use of AHAs, particularly at high concentrations, include red skin, edema, burning and itching sensations, post-inflammatory hyperpigmentation, changes in skin markings, and scars [15–17].

Glycolic acid (GA) is the most frequently used acid. Depending on the concentration, pH, time of application, applied amount, and carrier type, it can be employed in daily skin care routines and in-office procedures such as chemical peels [17]. In 2009, Fabbrocini classified chemical peels into three types depending on GA concentration [18].

- GA at concentrations between 5% and 15% is used in home skin care products, causes microscopic (invisible to the naked eye) exfoliation of the stratum corneum, hydrates the skin, and accelerates the processes of regeneration and renewal of the dermis.
- GA at concentrations between 20% and 35% is used in superficial peels. It effectively cleanses and moisturizes the skin, making it suitable for individuals with abnormal keratinization and oily skin types.
- GA at concentrations between 50% and 70% is used in potent deep peels performed by dermatologists. It may cause skin irritation and redness, with exfoliation of dead epidermal cells visible after 2 to 3 days. By inducing inflammation, the treatment enhances regenerative processes within the dermis, stimulating the production of collagen and elastin. In addition to reducing wrinkles, it lightens post-inflammatory hyperpigmentation and solar lentigines.

GA works by loosening the bonds between keratinocytes, causing exfoliation of stratum corneum cells, corneocytes and keratinocytes damaged by higher GA concentrations, which leads to the exfoliation of microcomedones and comedones, thus contributing to a smoother skin texture [1, 16, 19]. GA increases the penetration of other active ingredients contained in cosmetics, improves skin hydration, diminishes acne scars, and helps lighten post-inflammatory hyperpigmentation and solar lentigines. These characteristics of glycolic acid are used for the care and treatment of acne vulgaris [1, 8, 18, 20]. GA is frequently combined with other active ingredients, which amplifies its positive effects on the skin [21, 22].

LIPOHYDROXY ACID (LHA)

LHA is a salicylic acid derivative with unique skin effects. The chemical structure of LHA leads to reduced skin penetration when compared to salicylic acid. In terms of skin penetration, it has a profile similar to glycolic acid. Moreover, the highly lipophilic properties of LHA slow down its penetration and cause cell-by-cell exfoliation which more closely mimics physiological exfoliation. As a result, LHA is better tolerated by patients than AHA and BHA [1, 23]. Research has shown that it stimulates fibroblasts into producing glycosaminoglycans, collagen, and elastin, leading to improvements in skin quality. These properties make it a common ingredient in anti-aging formulations. The lipophilic nature of LHA results in high affinity for pilosebaceous units, showing an effective comedolytic action. LHA is widely used for both the treatment and care of acne-prone skin [24–27].

RETINOIDS

Retinoids are a class of vitamin A-derived compounds which are extensively used in skin treatment and care. Based on their molecular structure and receptor selectivity, retinoids are classified into four generations [26, 27]. They have a wide range of applications not only in the treatment of acne, also in the care of acne-prone skin. Their impact on reducing seborrhea is moderate, but they exhibit a more pronounced comedolytic effect, while also normalizing keratinocyte differentiation and proliferation [28, 29]. These properties of retinoids induce the exfoliation and unblocking of follicular ostia from accumulated sebum, thereby removing and preventing the formation of comedones [30].

Retinoids also possess anti-inflammatory effects by inhibiting bacterial-induced pro-inflammatory pathways, reducing the activity of Toll-like receptors (TCR), and suppressing the release of cytokines. They enhance the skin's barrier function, which protects the skin against the negative effects of the exposome. In addition, retinoids hinder tyrosinase activity and melanosome transfer to keratinocytes, thereby decreasing melanin production and inhibiting hyperpigmentation [1, 27, 30–32]. Very good skin care and therapeutic effects are achieved by combining retinoids with other active substances exhibiting multifaceted mechanisms of action. By using a conjugate consisting of induced retinoid, AHA, and BHA, a formulation targeting several mechanisms involved in the formation of acne lesions has been created. Retinoids regulate cell differentiation, while AHAs promote exfoliation in hydrophilic regions and BHAs facilitate exfoliation in lipophilic areas [33].

BAKUCHIOL

Bakuchiol (BAK) is a meroterpene phenol commonly found in the seeds and leaves of *Psoralea corylifolia* plants. It is often included in skin care products not just for acne treatment, but also as an ingredient slowing down skin aging processes [34]. It has comparable efficacy to retinoids but without inducing the adverse effects typically associated with retinoid use. Even though BAK shares no structural similarities with retinoids, it may act as a retinol analogue by regulating gene expression similarly to retinol. In addition, it reduces and modulates the secretion of 5α-reductase [34, 35]. BAK has antifungal and antibacterial properties, especially against *Streptococci* and *Cutibacterium acnes* [36]. It shows antioxidant effects by inhibiting the release of reactive oxygen species (ROS) particularly singlet oxygen and superoxide radicals, and suppresses lipid peroxidation. It reduces symptoms of inflammation by blocking PGE 2, inhibits the release of metalloproteinases (MMPs), stimulates the tissue inhibitors of MMPs (TIMPs), and prevents the formation of post-inflammatory hyperpigmentation and solar lentigines by suppressing melanin secretion [37–39]. Bakuchiol salicylate (Bakusylan) is a bipartite compound obtained by merging two components: bakuchiol and salicylic acid. These two active substances with complementary bioactive profiles also have a better potential to penetrate the stratum corneum, which enhances their anti-acne effects [33, 39].

HEPES

HEPES (4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid) is a derivative of aminosulfonic acid. It is a synthetic compound capable of activating enzymes in the skin, thereby enhancing the exfoliation of keratinocytes in the stratum corneum. HEPES has buffering properties that help stabilize the pH of dermocosmetics. It is often combined with glycolic acid and lactic acid to sustain consistent skin pH throughout the chemical reaction. Thanks to its properties, HEPES also improves the penetration of other active ingredients used in cosmetics into the skin. HEPES is most commonly used in peels, creams, toners and sera for the treatment of oily and acne-prone skin [40].

BIXA ORELLANA

Bixa orellana (achiote) is a fast-growing tropical tree found in South America. The seeds of achiote tree are used in the production of annatto, one of the most sought-after natural colorants with a range of applications in lipsticks and color cosmetics, and as a UV protectant. The primary active ingredient in achiote is bixin, classified within the carotenoid family. Bixin is a potent antioxidant with anti-inflammatory properties. An alcoholic solution of *Bixa orellana* leaves and seeds shows robust antibacterial, antifungal, and astringent effects. These characteristics make achiote a suitable ingredient for treating skin affected by acne vulgaris [41].

MICROBIOME PROTECTION

Preserving the skin microbiome is seen as another crucial mode of action of dermocosmetics. Alterations in skin barrier function lead to changes in the microbiome and activation of innate immunity through the penetration of antigens as pathogens. The role of the skin microbiome combined with the epidermal barrier function makes a strong argument for optimizing skin care. Study findings show that dysbiosis in acne is not related to the *C. acnes* count, but rather to the proliferation of a specific phylotype of this bacterial species (IA1). In addi-

tion, the loss of microbial diversity triggers the activation of innate immunity, resulting in the secretion of pro-inflammatory cytokines. Thus, it is important to maintain a healthy microbiome [9, 42–46].

A novel ingredient implicated in skin microbiome regulation is Phylobioma. This natural substance extracted from the pericarp of unripe pomegranates is biologically effective owing to its complex mixture of polyphenols. Polyphenols alleviate acne symptoms through the properties of Phylobioma that target the four primary components of acne pathophysiology: regulating sebaceous gland activity, addressing hyperkeratosis, modulating the microbiota, and reducing inflammation. It also acts by inhibiting the proliferation of the IA1 phylotype of *C. acnes*, a key factor in the pathogenesis of acne. Furthermore, polyphenols contained in the formulation exhibit robust antioxidant activity [47–49].

LYSATES

Vitreoscilla filiformis (VF) bacteria, cultivated in a medium enriched with La Roche-Posay thermal spring water, acquire distinctive properties and transform into what is known as Super VF. Selenium and strontium present in thermal water act as catalysts for bacterial enzymes, enhancing the activity of bacteria of the genus *Vitreoscilla*. In turn, high-temperature inactivation and VF bacterial fragmentation result in a bacterial lysate devoid of pathogenic potential. The resultant non-pathogenic VF, known as Aqua Posay Filiformis, modulates the inflammatory response, reduces substance P-induced inflammation, and strengthens the epidermal barrier [50].

Patients with mild to moderate acne show higher TEWL compared to the control group. The skin of these patients might also have lower ceramide levels, which inversely correlates with the functionality of the epidermal barrier. Active ingredients, including panthenol, ceramides, glycerin, niacinamide, thermal water, and mannose, play a role in enhancing the epidermal barrier, which helps reduce irritation and other undesired effects associated with acne treatment. Preserving the integrity of the skin barrier stands as an important mechanism through which dermocosmetics can contribute to acne treatment. Epidermal barrier dysfunction can be inherent to the condition itself or result from acne treatment with over-the-counter (OTC) products, prescribed therapies, improper skin care, and procedures such as peels or laser therapy [1, 51–54].

PANTHENOL, DEXPANTHENOL, VITAMIN B_5

The first formulation containing dexpanthenol for topical use (Bepanthen™ ointment) was developed over 70 years ago [55]. Pantothenic acid is essential for the proper functioning of the epithelium. The compound is part of coenzyme A which acts as a cofactor in numerous enzyme-catalyzed reactions crucial for the metabolism of carbohydrates, fatty acids, proteins, sterols, steroid hormones, and porphyrins, and in the process of gluconeogenesis [55, 56]. Topical applications of dexpanthenol, a stable alcoholic analogue of pantothenic acid, rely on its good penetrability into the dermis. Used topically, dexpanthenol acts as a moisturizer, improving the hydration of the stratum corneum, decreasing transepidermal water loss, and keeping the skin soft and supple. In addition, it contributes to the activation of genes involved in wound healing. It helps prevent and alleviate symptoms of skin irritation, such as dryness, roughness, flakiness, itching, or erythema [56, 57].

NIACINAMIDE

Niacinamide has a range of properties that prove beneficial in managing oily and acne-prone skin. It exhibits anti-inflammatory, anti-seborrheic, antimicrobial, antioxidant, and antipruritic effects [58, 59]. The antimicrobial activity of niacinamide is comparable to that induced by clindamycin, but the former compound does not cause drug resistance. Formulations (gels, creams) containing 2–4% nicotinamide are very well tolerated, with no adverse effects [60]. Erythematous changes may arise when using formulations with nicotinamide at concentrations exceeding 4%. Nicotinamide inhibits UVA-induced melanocytic proliferation and disrupts the transfer of melanosomes from melanocytes to keratinocytes, thereby preventing the development of post-inflammatory hyperpigmentation and solar lentigines. The use of niacinamide, irrespective of the skin type, improves skin hydration and reduces the feeling of dry skin, tightness and burning commonly experienced during isotretinoin therapy [57–60].

NEW PLANT EXTRACTS

Emerging prospects for acne therapy and care of acne-prone skin are associated with an extract of milk thistle (*Sylibum marianum*). The extract has demonstrated its impact on the LRIG1+ sebaceous stem cells within the pilosebaceous duct isthmus by suppressing the process of microcomedone formation. In addition to inhibiting the development of primary acne lesions and their progression, this mechanism of action helps alleviate the course of acne by reducing both inflammatory and non-inflammatory lesions. It also has a potential for preventing acne recurrence, as corroborated by findings of clinical studies. Moreover, operating through an entirely different mecha-

nism compared to other formulations, it can be used in monotherapy or in conjunction with other topical preparations [61, 62].

SUBSTANCES REDUCING POST-INFLAMMATORY HYPERPIGMENTATION

Active substances reducing post-inflammatory hyperpigmentation and solar lentigines include ingredients with skin-lightening properties (azelaic acid, kojic acid, α-arbutin, vitamin C, mandelic acid, lactic acid), antioxidants (vitamin C and E, phytic acid, ferulic acid, and phloretin) or exfoliating agents (glycolic acid, salicylic acid, and gluconolactone) [13, 15, 27, 31]. The gold standard in the treatment of hyperpigmentation continues to be hydroquinone, but the use of the substance as an ingredient in cosmetics was banned in the EU in 2001 because of adverse effects [63]. A relatively new molecule is isobutylamido thiazolyl resorcinol (thiamidol), a tyrosinase inhibitor. It shows a high binding capacity with tyrosinase, consequently inhibiting its activity. It is typically well-tolerated, rarely leading to adverse effects, and its activity and achieved outcomes are comparable to those of hydroquinone [64, 65].

Multiple active substances show diverse properties (sebostatic, keratolytic, anti-inflammatory, etc.). These can be used in the treatment of acne of varying severity, including monotherapy, maintenance therapy, or synergistic therapeutic approaches. Based on

Table 1. Active ingredients in dermocosmetic formulations used for skin care in acne vulgaris

Variable	Mild	Moderate	Severe
Cleansing	Keratolytic Sebum control	Keratolytic Sebum control	
Properties of the main ingredients	Skin barrier and microbiome protection pH between 4.7 and 5.75 + soap-free	Skin barrier and microbiome protection pH between 4.7 and 5.75 + soap-free	
Monotherapy Properties of the main ingredients	Keratolytic: Phylobioma, salicylic acid, glycolic acid, LHA, linoleic acid, AHAs, HEPES, retinol derivatives, maltodextrin/Bixa orellana seed extract, Phylobioma Anti-inflammatory: Phyllobioma, niacinamide, zinc, decanediol, soy isoflavones, bakuchiol, panthenol, Procerad, 5-ALA + peptide, willow bark, licochalcone A, lactoferrin, vitamin B_3, Sylibum marianum Sebum control: Phylobioma, niacinamide, zinc, ECGC, 5-ALA + peptide, L-carnitine, lactoferrin, bakuchiol, fullerene, Sylibum marianum, maltodextrin/Bixa orellana seed extract Antibacterial: Zinc, mannose, Aqua Posae Filiformis, decanediol, tea tree oil, bakuchiol, Octopirox, BPO, 5-ALA + peptide, willow bark, pirocton olamine, lactoferrin, Sylibum marianum Skin barrier and microbiome protection: Phylobioma, niacinamide, zinc, Aqua Posae Filiformis, Procerad, glycerin, shea butter, ceramides, panthenol, HEPES, mannose Blocking comedogenesis: extract Sylibium Marianum		
Adjunct treatment Properties of the main ingredients		Skin barrier and microbiome protection: Phylobioma, niacinamide, zinc, panthenol, glycerin, shea butter, ceramides, HEPES, mannose, Procerad, Aqua Posae Filiformis Anti-inflammatory, reducing pigmentation disorders: Phylobioma, niacinamide, zinc, willow bark, decanediol, soy isoflavones, lactoferrin, panthenol, Procerad, Sylibum marianum Sebum control: Phylobioma, niacinamide, zinc, willow bark, decanediol, soy isoflavones, lactoferrin, bakuchiol, ECGC, L-carnitine, fullerene, licochalcone A, Sylibum marianum Blocking comedogenesis: extract Sylibium Marianum	
Maintenance treatment Properties of the main ingredients	Blocking comedogenesis: extract Sylibium Marianum Keratolytic: Phylobioma, salicylic acid, glycolic acid, LHA, linoleic acid, AHAs, HEPES, retinol derivatives, maltodextrin/Bixa orellana seed extract Anti-inflammatory: Phylobioma, niacinamide, zinc, decanediol, soy isoflavones, bakuchiol, panthenol, Procerad, 5-ALA + peptide, willow bark, licochalcone A, lactoferrin, vitamin B_3, Sylibum marianum Sebum control: Phylobioma, niacinamide, zinc, ECGC, 5-ALA + peptide, L-carnitine, lactoferrin, bakuchiol, fullerene, maltodextrin/Bixa orellana seed extract, Sylibum marianum Antibacterial: Zinc, mannose, Aqua Posae Filiformis, decanediol, tea tree oil, bakuchiol, Octopirox, BPO, 5-ALA + peptide, willow bark, pirocton olamine, lactoferrin Skin barrier and microbiome protection: Phylobioma, niacinamide, zinc, Aqua Posae Filiformis, Procerad, glycerin, shea butter, ceramides, panthenol, HEPES, mannose Blocking comedogenesis: extract Sylibium Marianum		

a literature review, the active ingredients of dermocosmetics used in acne skin care and treatment are listed in table 1 along with respective rationales for their use [1, 7, 27, 28, 44, 49, 66, 67].

CONCLUSIONS

Dermocosmetics play a distinct role in the care and treatment of acne-prone skin. Series of complementary dermocosmetics are available, comprising products with cleansing, active, soothing, and moisturizing properties. Dermocosmetics formulated with active substances can be used in acne monotherapy based on the effectiveness of specific active ingredients in alleviating symptoms of acne without any adverse effects reported so far. Effective skin care not only serves as a preventative measure by addressing the underlying causes of acne but also helps mitigate the adverse effects of pharmacological therapy and helps in the management of complications such as scarring and post-inflammatory hyperpigmentation.

CONFLICT OF INTEREST

The authors are lecturers and/or members of the Advisory Boards for companies including L'Oreal, Dermedic, Avene, Eucerin, NAOS, Emolium, Urgo, Cerko.

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