Azeco
Cosmeceuticals

Azepur99®

Azelaic acid - cosmetic grade

Essential Guide

When **quality and reliability** come first

1.Introduction

1.1 About Azeco Cosmeceuticals

Azeco Cosmeceuticals is a specialized supplier of Azelaic acid for cosmetic applications. With satisfied customers all over the world, a long experience and a passion for quality, Azeco Cosmeceuticals BV is at your service for your Azelaic acid business.

Main characteristics Azepur99® en Certifications

- 100% Bio-based
- 100% Renewable, derived from vegetable biomass
- ISO 16128-1:2016 compliant as a naturally derived ingredient
- In compliance with Halal and Kosher standards
- Non-GMO origin
- Not tested on animals
- TSE/BSE free
- No animal-derived ingredients
- COSMOS approved
- In compliance with vegan standards

Regulatory file is available upon request

Global delivery via:

- Courier
- Road Transport
- Airfreight
- Seafreight

Lead time

Product available from stock for immediate delivery.

Technical support

For technical questions or assistance, Azeco Cosmeceuticals' technical support team is available at service@azeco-cosmeceuticals.com

Azeco Cosmeceuticals B.V.

Phone: +31 475 20 60 70
Mail: service@azeco-cosmeceuticals.com
Website: www.azeco-cosmeceuticals.com

Disclaimer

Azeco Cosmeceuticals has compiled the information contained to be best of its knowledge and capabilities, respecting the rights of third parties. However, Azeco Cosmeceuticals accepts no responsibility or liability for any consequences arising from the use of this information. Azeco Cosmeceuticals will not be liable if the use of this information by third parties infringes a patent or any other right belonging to a third party.

Table of content

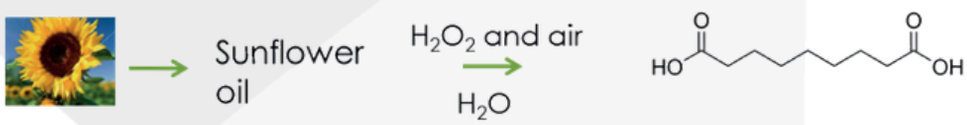
2. Azepur99® Azelaic acid

Azelaic acid has been marketed for over 50 years for various applications not only as an active ingredient in skin and haircare products, but also as a plasticizer, a lubricant ingredient for greases, and a monomer for polyesters and polyamides.

Until a few years ago, it was produced industrially by oxidizing oleic acid with ozone to obtain the dicarboxylic acid (Azelaic acid) and the monocarboxylic acid (pelargonic acid). Over time, an alternative synthesis method was developed to reduce energy consumption and provide a greener, safer process using different input chemicals and techniques. As a result, a new process for producing a green, sustainable, and multi-functional active ingredient for cosmetic applications has been developed in Europe. Azelaic acid is well-known to dermatologists for its strong safety profile and proven efficacy. In addition to its skin lightening properties, it offers antibacterial, antioxidant, and soothing (lenitive) actions making it a multitasking agent that promotes healthier skin.

Today, it is possible to formulate skin and haircare products using this multi-action active ingredient, now obtained through a sustainable process that avoids ozone and utilizes raw materials sourced from European agriculture, in compliance with the European framework for Safe and Sustainable by Design (SSbD) criteria for chemicals and materials.

The figure below illustrates the chemical process steps used to obtain sustainable Azelaic acid without ozone.



In particular, the double bond present in the oleic chain of sunflower oil triglycerides undergoes a series of transformations. Due to the oxidative action derived from hydrogen peroxide (H_2O_2) and compressed air, and in the presence of a catalyst, the double bond is first epoxidized, then hydroxylated, and finally cleaved to produce triazelain and pelargonic acid. The resulting triazelain is hydrolyzed into glycerine and Azelaic acid. The Azelaic acid obtained through this oxidative cleavage process is then distilled and crystallized from water multiple times until a highly pure substance (≥99%, the highest purity available on the market) is achieved. Thanks to this optimized purification process, the final Azelaic acid features an exceptionally low content—below the limit of detection (LOD) of even the most sensitive analytical methods—of heavy metals, residual solvents, residual pesticides, and any other potential contaminants from raw materials or processing. This grade of Azelaic acid, commercialized by Azeco Cosmeceuticals under the trade name Azepur99®, is produced using a new proprietary chemical process aligned with green chemistry principles (EPA Green Chemistry). It is of 100% natural origin, GMO-free, and its sustainability is further enhanced by the European origin of the sunflower used for oil extraction. Moreover, the sunflower seeds are not sourced from lands with high biodiversity value, high carbon stock, or peatland—compliant with the EU Directive 2018/2001 (RED II) on promoting the use of energy from renewable sources. According to ISO 16128 (Guidelines on technical definitions and criteria for natural and organic cosmetic ingredients), Azepur99® qualifies as a naturally derived ingredient with 100% bio-based carbon content. Azepur99® differentiates itself from other naturally derived Azelaic acids on the market through its exceptional purity: ≥99%.

3. Background of Azelaic acid

3.1. The History of Azelaic acid

Azelaic acid has been used since ancient times for its medicinal properties. It was first mentioned in 16th-century Europe, when a German physician named Valerius Cordus noted its effectiveness in treating skin disorders. In the 19th century, Azelaic acid was used to treat acne and other skin conditions, and it would remain a popular topical treatment until more powerful antibiotics became available in the early 20th century. Some of these were initially discovered by Drs. Marcella Nazzaro-Porro and Siro Passi of the S. Gallicano Dermatological Institute, Rome, and applied clinically with benefit to some cutaneous hyperpigmentary disorders.

Subsequent collaborative laboratory and clinical studies in Rome, Turin, and London and later at other centers have established that Azelaic acid is an inhibitor of tyrosinase, mitochondrial enzymes of the respiratory chain, and DNA synthesis. It exhibits antiproliferative and cytotoxic effects on various tumor cells in culture, while normal cells remain largely unaffected. Azelaic acid also acts as a scavenger of harmful free radicals, inhibits the generation of reactive oxygen species by neutrophils, and demonstrates broad-spectrum bactericidal activity against a range of microorganisms.

Controlled clinical trials have established topical Azelaic acid as an effective treatment for acne and chloasma, and it may also benefit selected cases of melanoma in situ. Its potential role as an adjuvant therapy for primary invasive melanoma, as well as a palliative treatment for disseminated melanoma and possibly other tumors, remains under investigation. Due to its anti-free radical and antibacterial properties, Azelaic acid may also be useful in treating a variety of infectious and inflammatory conditions. Given the positive outcomes in pharmaceutical applications and its excellent safety profile, Azelaic acid has increasingly been incorporated into a wide range of cosmetic products for both skin and haircare. Today, many Azelaic acid-based cosmetic products are available on the market.

3.2. The characteristics

Azelaic acid has several unique properties that make it an ideal ingredient in skincare formulations. It has anti-inflammatory effects that help reduce redness, swelling and irritation on the skin. Additionally, Azelaic acid has antimicrobial activity which can help to kill certain bacteria associated with acne breakouts. Furthermore, Azelaic acid also acts as a tyrosinase inhibitor, meaning it helps to reduce hyperpigmentation caused by sun damage or acne scars. Finally, Azelaic acid functions as a keratolytic, which helps to improve the skin's texture and reduce the appearance of enlarged pores.

3.3. Side effects of Azelaic acid

Although uncommon, Azelaic acid products can sometimes cause mild and temporary skin irritation. The following are some potential side effects:

- A temporary burning or tingling sensation on the skin
- Mild dryness, redness, or peeling at the application site
- Mild eye irritation if the product comes into contact with the eyes
- Respiratory tract irritation if inhaled
- Less common adverse effects may include fever, difficulty breathing, blisters, hives, joint pain, loss of appetite, constipation, changes in taste, nausea, and diarrhea

Compared to other personal care ingredients, the side effects of Azelaic acid are often mild and limited to a temporary reaction after application.

3.4. pH considerations

Azelaic acid performs optimally in formulations with a pH between 3.5 and 5.5. Although less pH-dependent than AHAs or BHAs, an environment that is too acidic or too alkaline can still reduce its stability, efficacy, and absorption.

As a diacid with two pKa values (4.5 and 5.3), Azelaic acid is most effective in formulations around pH 4.5 to 5.0. At this range the molecule remains sufficiently in its acidic form while maintaining favorable solubility, which supports both stability and skin penetration.

A clinical study (DOI: 10.3109/03639045.2011.63537) demonstrated this clearly: a formulation at pH 4.9 showed significantly higher retention in the epidermis and dermis compared to pH 3.9. The measured flux at pH 4.9 was approximately five times greater, indicating that ionization and solubility strongly influence bioavailability. While the non-ionized form penetrates more easily, the ionized species dissolves better in water. The higher solubility compensates for lower permeability, making a pH close to 5 the ideal balance for skin delivery. pH also affects the biological activity of Azelaic acid. At lower pH levels, its antibacterial and anti-keratinizing effects are enhanced. By reducing skin pH, Azelaic acid creates an environment less favorable for Propionibacterium acnes while also supporting gentle exfoliation by loosening the bonds between corneocytes.
In practice, maintaining the correct pH ensures that Azelaic acid reaches its full potential: stable in formulation, effectively absorbed, and biologically active against key skin concerns.

3.5 Recommended cosmetic use levels of Azelaic acid

Azelaic acid is a highly versatile active ingredient that can be incorporated into a wide range of cosmetic and dermo-cosmetic formulations. While general use levels typically range between 3% and 20%, the optimal concentration depends strongly on the targeted skin or scalp concern, the formulation type, and the desired balance between efficacy and tolerance.
For daily use skincare products, Azelaic acid is most commonly applied at concentrations between 8% and 10%. This range is well suited for long-term maintenance, offering visible benefits for skin clarity and tone while remaining well tolerated for regular use.
For skin prone to acne, slightly higher concentrations are often preferred. Levels between 10% and 12% are widely used in leave-on products designed to reduce blemishes, normalize keratinization, and support a clearer complexion. This concentration range is frequently selected for consumers seeking noticeable improvement while maintaining good skin compatibility.
For hyperpigmentation and uneven skin tone, higher use levels are typically required. Concentrations around 15% are commonly applied in targeted brightening treatments, where Azelaic acid supports a more even complexion through its tyrosinase-inhibiting properties and its ability to reduce post-inflammatory pigmentation. In haircare and scalp formulations, Azelaic acid is usually incorporated at lower concentrations. Typical use levels range from 3% to 5%, supporting scalp balance and hair follicle health while minimizing the risk of irritation in rinse-off or leave-on scalp applications. Although concentration is an important factor, performance is also strongly influenced by formulation design. Solubility, dispersion quality, delivery system, and pH all contribute significantly to the final efficacy and user experience. For this reason, the recommended concentration should always be selected in combination with a formulation strategy that ensures stability and optimal bioavailability.

Typical concentration guidelines:

- Daily use skincare: 8–10%
- Skin prone to acne: 10–12%
- Hyperpigmentation: 15%
- Haircare and scalp care: 3–5%

Please note that maximum permitted concentrations of Azelaic acid may be subject to specific cosmetic regulations depending on the country or region where the product is marketed. Formulators are advised to verify local regulatory requirements before finalizing the product composition.

4. Applications of Azelaic acid

Skincare applications of Azelaic acid cover several key areas that represent highly significant segments of the cosmetic market:

- Skin prone to acne
- Skin prone to rosacea
- Skin lightening

In addition to its skincare benefits, Azelaic acid is also used in haircare products to support hair growth and regrowth.

4.1 Azelaic acid and skin prone to acne products

When used in cosmetic formulations, Azelaic acid, due to its unique easy to be dispersed and solubilized characteristics, penetrates the skin effectively and stimulates cellular activity. It is able to assist in normalisation of the microflora on the skin. Organisms that have become opportunistic are normalised to their normal level, including P.acnes, and it thus assists in many cases in clearing and preventing acne. Azelaic acid displays three main beneficial properties on impure skin:

1. It normalizes the disturbed follicular keratinization that leads to the formation of comedones. The reduction in the count of comedones has subsequently been demonstrated in various clinical studies.
2. It has also a significant antibacterial effect on the follicular Propionibacterium acnes and Staphylococcus epidermidis (in vitro). This effect is primarily bactericidal but may in vivo be modified to a bacteriostatic one.
3. In addition, Azelaic acid, also reveals direct anti-inflammatory activities by reducing the production and release of reactive oxygen species.
4. Azelaic acid is also an effective inhibitor of tyrosinase, the enzyme involved in the conversion of tyrosine to melanin.

Products used for the treatment of acne vulgaris

Next to ordinary acne (acne vulgaris) several other forms of acne are known, such as acne conglobata (a severe form of acne, mainly with males) and acne keloidalis. Acne ectopica (hidradenitis suppurativa, caused Staphylococcus epidermidis) is a form of acne that shows up in unusual places, such as the armpits, groin and on the buttocks. It can be serious and painful. Recurrent infections and abscesses are highly inconvenient for the patient. This form of acne usually occurs after the age of 20, especially with smokers. Acnelike anomalies may also be caused by mechanical influences such as acne under a chin strap or head band (helmet), or because of contact with comedogenic products such as tar, oil, chlorine, steroids (oral contraceptives) and particular cosmetics. Mallorca acne may occur upon (over)exposure to direct sun light. It shows up as a large ensemble of white spots on the skin, and has little to do with the opportunistic behaviour of Propionibacterium acnes. Medications for acne include benzoyl peroxide, salicylic acid, α-hydroxy acids, retinoids, antibiotics (doxycycline, clindamycin), nicotinamide (vitamin B3) and keratolytic preparations. Especially benzoyl peroxide and salicylic acid are under scrutiny; the FDA recommends a careful approach using these products. The use of topically or orally applied antibiotics is frequently identified as “healing is worse than the disease”. The same can be said from the oral use of retinoids, that eventually may lead to birth defects. These side effects are absent when using Azelaic acid. Azelaic acid is believed to function on the basis of its antimicrobial activity and normalization of keratinization, the process by which epithelial cells mature as they move towards the skin surface and then desquamated. The limitation for the use of Azelaic acid is its solubility; nonetheless significant progress has been made by improving the solubility characteristics. The European Union considers Azelaic acid as a cosmetic ingredient that can be applied without concentration restrictions. In the USA Azelaic acid is FDA approved for the treatment of acne (and rosacea). A variety of commercial products containing 10-25% Azelaic acid are available.

The results indicate that the antibacterial activity of Azelaic acid is associated with the perturbation of intracellular pH of the organisms. The use of Azelaic acid as anti-acne ingredient is highly favourable compared to the traditional anti-acne ingredients, as the side effects are minimal and can easily be controlled by adjustment of the concentration Azelaic acid in the cream or gel.

APPLICABILITY

PRODUCTS FOR TREATMENT OF ACNE VULGARIS	COSMETIC USE	MEDICAL DEVICE USE	PHARMACEUTICAL USE
Azelaic acid	++	++	++
BENZOYL PEROXIDE	-	-	+
RETINOIDS	+/-	+/-	+
A-HYDROXY ACIDS	++	++	++
ADAPALENE	-	-	++
TAZAROTENE	-	-	++
SALICYLIC ACID	+	+	+
SULPHUR	+	+	+
ANTIBIOTICS	-	-	+

TABLE 2: Legend: (++ Strongly recommended / Very suitable) (+ Limited recommended / Suitable) (+/- Limited allowed / Limited suitable) (- Forbidden)

FUNCTIONALITY

PRODUCTS FOR TREATMENT OF ACNE VULGARIS	COSMETIC USE	MEDICAL DEVICE USE	PHARMACEUTICAL USE
Azelaic acid	+	+	++
BENZOYL PEROXIDE	-	+/-	+/-
RETINOIDS	+/-	+/-	+
A-HYDROXY ACIDS	-	-	-
ADAPALENE	-	-	++
TAZAROTENE	-	-	++
SALICYLIC ACID	+/-	+/-	+
SULPHUR	+	+/-	+/-
ANTIBIOTICS	-	-	+

TABLE 3: Legend: (++ Strongly recommended / Very suitable) (+ Limited recommended / Suitable) (+/- Limited allowed / Limited suitable) (- Forbidden)

APPLICABILITY

PRODUCTS FOR TREATMENT OF ACNE VULGARIS	CMR PROPERTIES	SKIN IRRITATION	SIDE EFFECTS	EXFOLIATION	PHOTO ACTIVITY	CYTOTOXICITY
Azelaic acid	-	-	-	-	-	-
BENZOYL PEROXIDE	++	++	++	++	++	++
RETINOIDS	+	++	+	++	+	++
A-HYDROXY ACIDS	-	+	-	++	+/-	-
ADAPALENE	++	+	++	-	+	++
TAZAROTENE	++	+	++	-	++	++
SALICYLIC ACID	++	++	+	+	-	+
SULPHUR	+	+/-	-	+	+/-	+
ANTIBIOTICS	++	-	++	-	+/-	++

TABLE 4: Legend: (++ Very strong effects) (+ Noticeable effects) (+/- Hardly noticeable) (- Not noticeable)

General ingredient characteristics

Azelaic acid

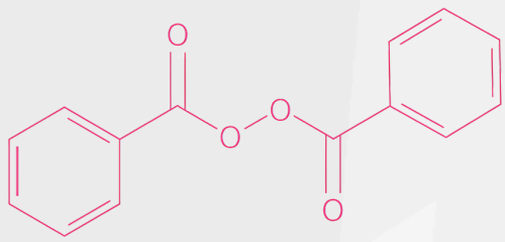
Azelaic acid is considered as the rising star for anti-acne over-the-counter (OTC) products. Azelaic acid may be used in personal care and cosmetic products, in medical devices and in pharmaceutical products without concentration limitations in most countries. It shows no significant side effects, it has no cytotoxic properties and does not exhibit carcinogenic, mutagenic, reprotoxic (CMR) properties.

The major constraint for the use of Azelaic acid is its solubility. However, the solubility problem of Azelaic acid can be solved using particular solvent systems or using smart formulation techniques. Because of the poor solubility the bio-availability is also limited, but that problem may simultaneously be solved while tuning the solubility.

The mode of action of Azelaic acid is not well-known, although it is considered likely that Azelaic acid is detrimental for Propionibacterium (P.) acnes but will not affect most other micro-organisms. P.acnes is an aerotolerant anaerobe gram-positive organism, identified as a commensal. The selectivity for P.acnes enables to normalise the P.acnes population while leaving the other native micro-organisms in peace. The absence of adverse effects, compared to other products used for fighting acne, makes Azelaic acid a preferred ingredient for anti-acne products.

Benzoyl peroxide

Probably the most frequently used anti-acne ingredient is benzoyl peroxide. It has outspoken anti-bacterial properties, but the disadvantage is its total lack of selectivity. Bacteria present on the skin and in the hair follicle are completely eliminated. This includes also P.acnes, the organism that is held responsible for the development of acne. Thus, it prevents acne from progressing.



Commercially available products may contain up to 10% benzoyl peroxide, while a minimum concentration required to combat acne is generally considered to be approximately 2.5%. The absolute amount of benzoyl peroxide applied depends on the severity of the acne outbreak and on the degree of skin irritation induced by the substance.
Skin irritation is observed more frequently in certain skin types. Classification based on racial or ethnic background, however, is not a reliable approach. A functional skin type classification provides a more accurate description of skin behaviour. Prof. Proserpio distinguished five different skin types, which better reflect the actual situation:

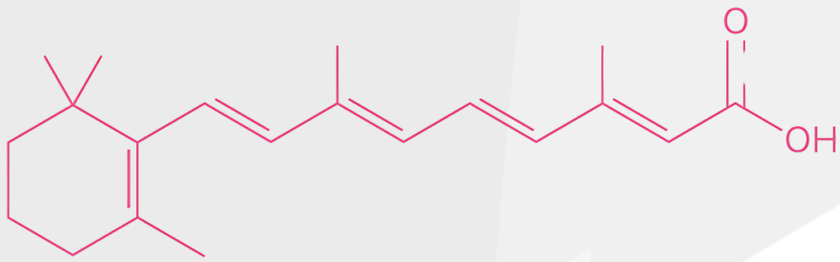
- Dry skin
- Sensitive skin
- Mature skin with wrinkles
- Oily skin
- Oily skin with enlarged pores

Benzoyl peroxide, like all organic peroxides, is chemically unstable. The bond energy of the –O–O bond is relatively low (approximately 29 kcal per mole). Thermal bond cleavage occurs readily, leading to the formation of two benzoyl radicals. A multitude of subsequent reactions may occur as a result.
These benzoyl radicals are highly reactive and act without selectivity. They can react directly with the cell walls of bacteria, moulds and yeasts, but also affect the commensal micro-organisms living on the skin in symbiosis with the human host. Due to their high reactivity, interactions with skin tissue and accessible subcutaneous tissue may also occur. The damage caused by these radical reactions can be significant and is associated with irritation, sensitisation and cytotoxic effects.
In addition, benzoyl radicals may undergo decarboxylation, resulting in the formation of phenyl radicals. These phenyl radicals may abstract hydrogen atoms from suitable substrates, leading to the formation of benzene. Benzene is classified as a substance of concern due to its carcinogenic, mutagenic and reprotoxic properties and is therefore undesirable in personal care applications.

Within the European Union, benzoyl peroxide is subject to strict regulatory control. Under Regulation (EC) No 1223/2009, its use in cosmetic products is restricted and permitted only under defined conditions following a safety assessment. As a consequence, products containing benzoyl peroxide intended for the treatment of acne are often regulated as medicinal products rather than cosmetic products. In contrast, the legal situation in the United States differs. Benzoyl peroxide is currently permitted in over-the-counter anti-acne products, although its safety profile continues to be evaluated by regulatory authorities.

Retinoids

Retinoids are defined as C20-terpenoids. The most important representatives are retinoic acid/tretinoin and retinol (vitamin A). Retinol and its esters may be used in personal care cosmetic products.



Retinoic acid plays an important role in growth and development. It is required in all chordate animals and is important during early embryonic development. Vitamin A (retinol) plays a role in the maintenance of the immune system and is, as retinaldehyde, indispensable in the chemistry of vision. A variety of cis-trans isomers of retinoic acid are known. Retinoic acid (tretinoin; Renova®/Johnson and Johnson) identified as all-trans, and its salts exhibit anti-acne activity. It was developed by Kligman and is considered to be one of the most powerful anti-aging agents. Isotretinoin (13-cis-retinoic acid; Roaccutane®/Roche) is more powerful than tretinoin, but the side effects are also more pronounced. Alitretinoin (9-cis-retinoic acid) is used as an anti-neoplastic ingredient and is also used for chronic hand eczema.

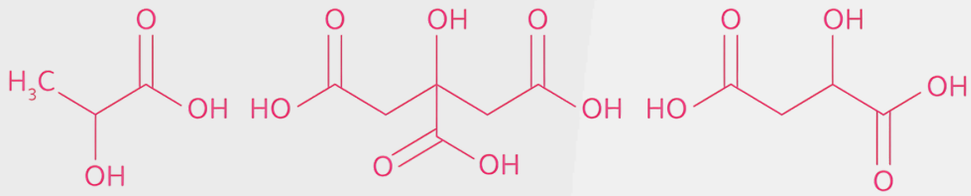
All these first-generation retinoids exhibit significant side effects such as dry lips, skin and mucous membrane irritation or sensitisation, reduced tear fluid production resulting in eye irritation, disturbed liver function, thinning of the skin, increased sensitivity to sunlight, hair loss (usually reversible) or hirsutism, joint and muscle pain, and an increased cholesterol level. Diabetic patients shall be careful because of potential hyperglycaemia. For males, gynaecomastia and disturbed potency have been reported. Many retinoids exhibit significant phototoxicity and cytotoxicity. These retinoids shall never be used during pregnancy or planned pregnancy, as retinoids are considered severely teratogenic. This restriction creates a strong demand for effective alternatives with a safer toxicological profile. Azelaic acid is considered suitable for use during pregnancy, as it shows minimal side effects and does not exhibit carcinogenic, mutagenic or reprotoxic properties. For this reason, Azelaic acid is increasingly preferred in acne and redness focused skincare concepts for pregnant consumers.

The mechanism for the activity of retinoids in the treatment of acne is unknown. On a cellular level, there is evidence that it decreases the ability of epithelial cells in hair follicles to stick together, leading to fewer blackheads. It also seems to make the epithelial cells divide faster, causing the blackheads to be pushed out.

α-Hydroxycarboxylic Acids

α-Hydroxycarboxylic acids, usually abbreviated as α-hydroxy acids or AHAs, and frequently named fruit acids, are characterised as carboxylic acids where the carbon atom in the 2-position carries a hydroxyl group. Well-known members of this group are glycolic acid, lactic acid, pyruvic acid, malic acid, tartaric acid, citric acid, and others. These are usually relatively strong acids that are also effective solvents for the cement between the cells of the epidermis. This cement is composed of ceramides, triglycerides, and some sterols, mostly cholesterol. Elimination of the cement between the dead skin cells of the stratum corneum enables easy exfoliation.

α-Hydroxycarboxylic acids are not true anti-acne products. Because of their exfoliating qualities, the tallow glands are opened up to enable the sebum to flow out and distribute on the skin. This is best identified as the keratolytic activity of α-hydroxycarboxylic acids, but there is no activity against Propionibacterium acnes, the organism that is considered the main culprit.

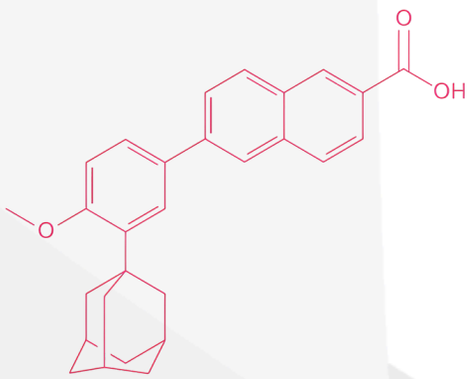


α-Hydroxy carboxylic acids, usually applied as a combination of the free acids and their conjugated bases, are suitable for both personal care and cosmetic application, for medical devices and pharmaceutical preparations. Many of these products are body-own products or occur in nature, without CMR properties, no serious side effects (except when used in extreme concentration), inducing only limited phototoxic properties and no cytotoxicity.

Adapalene

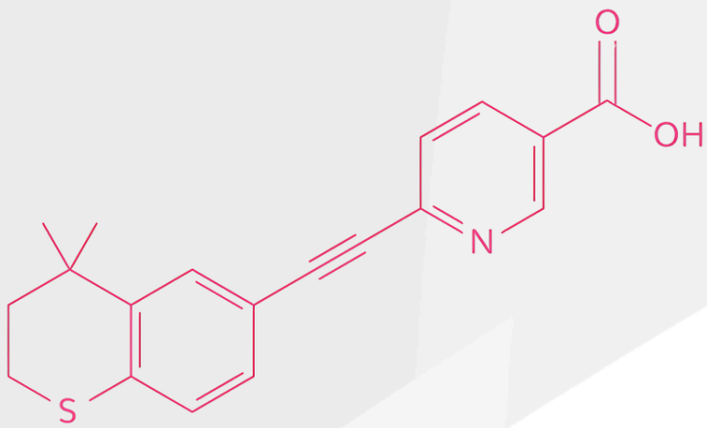
Adapalene is frequently identified as a third-generation retinoid. However, the structure of adapalene does not at all compare to retinoids such as vitamin A (retinoic acid; vitamin A), retinaldehyde, or retinol. The structure of adapalene compares more to quinine, which is also used for the treatment of malaria and similar protozoal infections. Adapalene is a pharmaceutical ingredient that shall not be used in personal care and cosmetic products or medical devices.

Commercially available as Differin® Gel (0.1-1.0% adapalene), it is used for the treatment of acne vulgaris by shedding dead skin cells and promoting the formation of new skin cells. It also helps to unclog pores and reduces inflammation. When using an acne treatment with the active ingredient of adapalene, acne may worsen temporarily at first but should eventually improve. Side effects can include skin irritation, stinging and burning sensations, and sensitivity to UV light.



The functionality of adapalene is improved when using the product in conjunction with clindamycin, an antibiotic used for the treatment of bacterial infections. Clindamycin is also used for the treatment of otitis media, pneumonia, and endocarditis, and is sometimes used to handle MRSA (Methicillin-Resistant Staphylococcus Aureus). Major side effects of adapalene include skin irritation (or burning or stinging sensation), dryness and peeling of the skin, itching, and redness of the skin. Adapalene shall not be used if the patients suffer from eczema, sunburn, or pregnancy. It may take considerable time before the functionality of adapalene becomes obvious (8-10 weeks).

Another pharmaceutical anti-acne ingredient is taratozene, also defined as a third generation retinoid.

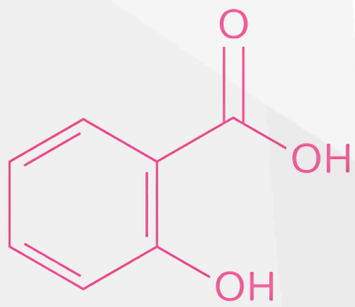


It is used for the treatment of acne, psoriasis, and photo-damaged skin. The mechanism of action is still unknown. Common side effects include worsening of acne, increased sensitivity to sunlight, dry skin, itchiness, redness, and in some cases, extreme drying and cracking of the skin. For most patients, these side effects are uncomfortable but mild and decrease markedly after the first 2–4 weeks of use, except for increased sensitivity to sunlight.

Tazarotene is not allowed in personal care and cosmetic products and medical devices and must be prescribed by a medical professional. Despite the undesired side effects of tazarotene, it is frequently preferred over tretinoin, which has even more serious side effects.

Salicylic Acid

Salicylic acid is chemically described as 2-hydroxybenzoic acid. It is also considered to be an α-hydroxy acid. Salicylic acid is used as a preservative in personal care and cosmetic products with a maximum concentration of 0.5%, and it is not to be used in products for children younger than three years of age. Salicylic acid may be used in excess of 0.5% for purposes other than inhibiting the development of microorganisms in the product. This purpose must be apparent from the presentation of the product. Salicylic acid is poorly soluble in water (2.5 g/l; 25°C). The sodium salt is easily soluble in water but is subject to decarboxylation, with phenol being the primary reaction product.



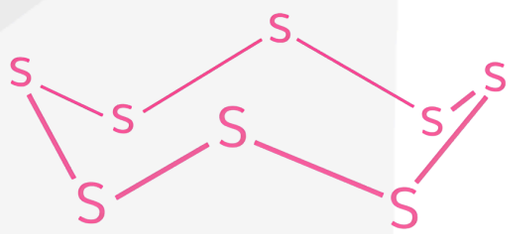
Salicylic acid is frequently used in personal care and cosmetic products as an exfoliant to shed off dead skin cells (keratolytic) and to avoid the dead cells from blocking the pores, allowing the sebum to pass through. EU Regulation allows a maximum of 2% in stay-on products.

Salicylic acid may exhibit multiple side effects: skin irritation (which can eventually be quite serious), dry skin, itching and stinging, unusually warm skin, and swelling of the face, lips, and tongue (potentially leading to suffocation). Possible suffocation may also be induced by salicylic acid derivatives, such as some fragrance compounds (e.g., benzyl salicylate, methyl salicylate), and salicylic-based UV filters. Furthermore, salicylic acid may exhibit side effects that are potentially life-threatening.

The FDA is currently evaluating the status of salicylic acid, as the product may eventually not be safe to use in personal care and cosmetic products and medical devices.

Sulphur

Sulphur is probably one of the oldest anti-acne ingredients. At present, it is rarely used, and if it is used, it is always in combination with other anti-acne ingredients. Sulphur is a bright yellow crystalline solid found in free form in nature and is mostly from volcanic origin. It melts at 115°C and has a typical, unpleasant smell. Sulphur occurs as an eight-membered ring structure.



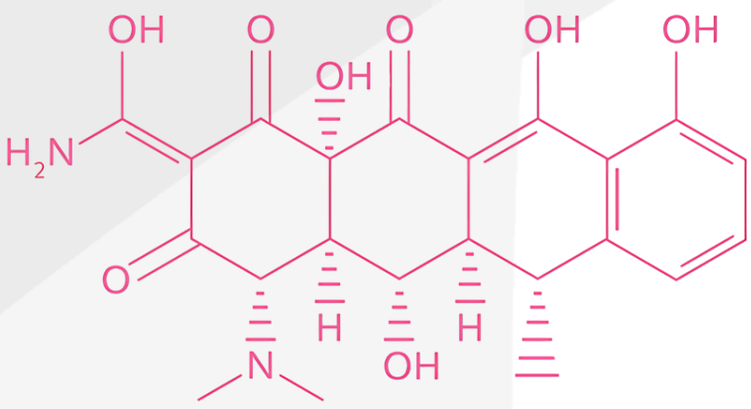
Sulphur is able to remove dead skin cells and eliminate excess oil from the skin's surface. This property may help in the prevention of acne, but sulphur is also known to exhibit adverse side effects. Redness is a common side effect when using products containing sulphur. Acne may begin to subside at first, but the skin quality can become worse if sensitive to sulphur. Soreness is also attributed to the use of acne products containing sulphur.

Sulphur has germicidal, fungicidal, parasitical, and keratolytic properties. The germicidal activity may be the result of its conversion to pentathionic acid ($H_2S_5O_6$) by particular microorganisms. Also, the formation of hydrogen sulphide and polysulphides, as well as (di)methyl (poly)sulphides, will occur. Polysulphides generally have the formulae RSnR. These substances have a particular odor: hydrogen sulphide (H_2S) smells like rotten eggs, methylmercaptan (CH_3SH) has a distinctive putrid odor, while the odor of dimethyl sulphide is commonly described as cabbage-like. Dimethyl disulphide has the characteristic odor of onions. The odor threshold value for these products is low, usually < 1 ppm. Creams and ointments containing elementary sulphur always have the typical odor of these sulphides and are usually impossible to fragrance. Apart from the poor odor, sulphides are usually toxic. The LD50-value of hydrogen sulphide is 800 ppm; H_2S acts in a similar fashion as carbon monoxide and is considered to be a sincere CMR (Carcinogenic, Mutagenic, or Reproductive toxic) ingredient.

Antibiotics

The application of antibiotics for the treatment of acne is exclusively reserved for medical professionals. Antibiotics are not allowed in personal care and cosmetic products or medical devices. Antibiotics can be taken orally or administered via the skin using a cream. Frequently, the use of antibiotics is combined with benzoyl peroxide to avoid antibiotic resistance. Topically applied antibiotics include clindamycin and erythromycin. Orally taken antibiotics include doxycycline and minocycline (tetracyclines), as well as erythromycin.

The side effects of these antibiotics are numerous: skin rash, upset stomach and intestines, and fungal infections. Sometimes, the side effects can be quite serious, including severe allergic reactions (such as difficulty breathing and facial swelling), destruction of intestinal flora (leading to bloody diarrhea), vaginal candidiasis, and mouth sores. Combined with the potential for antibiotic resistance, the use of antibiotics for the treatment of (juvenile) acne should only be considered if no other options are available.



Virtually all antibiotics used for the severe cases of acne also have cytotoxic properties and have distinct CMR and hormone disrupting properties. Antibiotics also should not be used during pregnancy, unless unavoidable.

4.2 Azelaic acid and anti-rosacea products

Azelaic acid has been demonstrated to be effective for the treatment of rosacea. It helps reduce inflammatory lesions and erythema in rosacea patients. A major advantage of Azelaic acid is that it lacks the common side effects often associated with pharmaceutical treatments. Azelaic acid works by reducing inflammation, decreasing the number of bacteria on the skin, and lowering the production of keratin—a protein that can block pores and cause acne. These combined effects help alleviate redness, flushing, and other symptoms related to rosacea. It is available in various forms, including creams, gels, and lotions. Azelaic acid is considered an effective and well-tolerated treatment for rosacea.

Products used for the treatment of rosacea

Rosacea is a common, chronic, and incurable skin condition that often resembles acne. It primarily affects the central part of the face, especially the nose. Outbreaks of rosacea can, to some extent, be predicted based on certain triggers. Typical symptoms include persistent facial redness, tiny red pimples, and fine red lines known as telangiectasia (commonly referred to as spider veins). These spider veins are small, dilated blood vessels located near the surface of the skin and may also appear on other parts of the body, such as the arms and legs. A more severe manifestation of rosacea is rhinophyma, which presents as an enlarged, bulbous, and red nose. Treatment options for rosacea are limited. Aside from Azelaic acid and certain flavonoids, most available treatments are pharmaceutical in nature.

APPLICABILITY

PRODUCTS FOR TREATMENT OF ROSACEA	COSMETIC USE	MEDICAL DEVICE USE	PHARMACEUTICAL USE
Azelaic acid	++	++	+
BRIMONIDINE	–	–	++
METRONIDAZOLE	–	–	+
A-HYDROXY ACIDS (AHAS)	+	+/-	+/-
ORAL ANTIBIOTICS	–	–	+
ISOTRETINOIN	–	–	++
ALTERNATIVE THERAPIES	+/-	+/-	+

TABLE 5: Legend: (++ Strongly recommended / Very suitable) (+ Limited recommended / Suitable) (+/- Limited allowed / Limited suitable) (- Forbidden)

FUNCTIONALITY

PRODUCTS FOR TREATMENT OF ROSACEA	COSMETIC USE	MEDICAL DEVICE USE	PHARMACEUTICAL USE
Azelaic acid	++	++	+
BRIMONIDINE	-	-	+
METRONIDAZOLE	-	-	+
ALPHA-HYDROXY ACIDS	+	+	+/-
ORAL ANTIBIOTICS	-	-	+/-
ISOTRETINOIN	-	-	++
ALTERNATIVE THERAPIES	+	+/-	-

TABLE 6: Legend: (++ Strongly recommended / Very suitable) (+ Limited recommended / Suitable) (+/- Limited allowed / Limited suitable) (- Forbidden)

ADVERSE EFFECTS

PRODUCTS FOR TREATMENT OF ROSACEA	CMR PROPERTIES	SKIN IRRITATION	SIDE EFFECTS	EXFOLIATION	PHOTO ACTIVITY	CYTOTOXI-CITY
Azelaic acid	-	+	-	+	-	-
BRIMONIDINE	+	+	+	-	-	+
METRONIDAZOLE	+	+	+	-	-	+
ALPHA-HYDROXY ACIDS	-	+	-	++	+	-
ORAL ANTIBIOTICS	++	++	++	-	+	++
ISOTRETINOIN	++	++	++	-	++	++
ALTERNATIVE THERAPIES	+/-	+/-	+/-	+/-	-	+/-

TABLE 7: Legend: (++ Very strong effects) (+ Noticable effects) (+/- Hardly noticable) (- Not noticable)

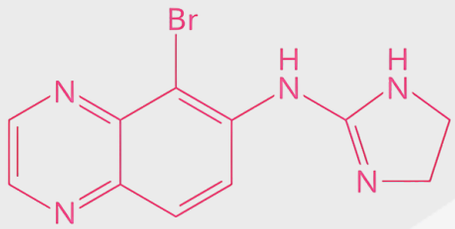
General anti-rosacea ingredient characteristics

Azelaic acid

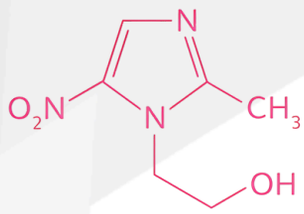
Azelaic acid has been considered effective for the treatment of rosacea. It is available as a 20% cream or a 15% hydrogel. Azelaic acid reduces inflammatory lesions and erythema in rosacea patients and also inhibits neutrophilic Reactive Oxygen Species (ROS). In the neutrophil system, Azelaic acid inhibits ROS formation in a dose-dependent manner, significantly decreasing the number of free radicals. In the xanthine–xanthine oxidase system, none of the generated ROS was decreased by any dose of Azelaic acid. This indicates that Azelaic acid does not scavenge ROS after they are formed but instead inhibits cell metabolism—possibly by reducing enzymatic activity within the cell membrane. Azelaic acid is likely the only non-pharmaceutical ingredient that has demonstrated substantial efficacy in treating rosacea, with minimal or no side effects.

Brimondine & Metronidazole

These pharmaceutical ingredients are not allowed to be used in personal care and cosmetic products as well as in medical devices. Brimonidine, applied as a gel or as a stick, is reasonably effective for redness reduction in mild cases of rosacea. It functions by vasoconstriction of the small blood vessels. Brimonidine binds to the cellular α-2-adrenergic receptors receptors of the small veins, leading to vasoconstriction. Consequently the transport of blood through these small blood vessels is reduced resulting in a reduced facial redness. The effects become visible after 6-12 hours and are fully reversible. Brimonidine is not a cure for rosacea, and that is also the case metronidazole. Brimonidine is also used to lower the intraocular pressure.



Brimonidine



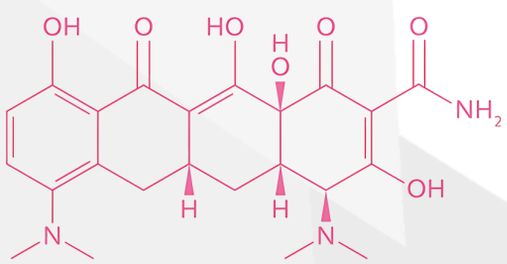
Metronidazole

Metronidazole is considered an antibiotic, which is also used for the treatment of bacterial infections. It is ineffective for yeast infections, such as vaginal yeast infections caused by, e.g., Candida albicans.

Oral Antibiotics

The application of antibiotics, mostly tetracyclines, for the treatment of rosacea is exclusively reserved for medical professionals. Antibiotics are not allowed in personal care and cosmetic products and medical devices. Antibiotics for the treatment of rosacea are mostly taken orally. Orally taken antibiotics are doxycycline and minocycline (tetracyclines).

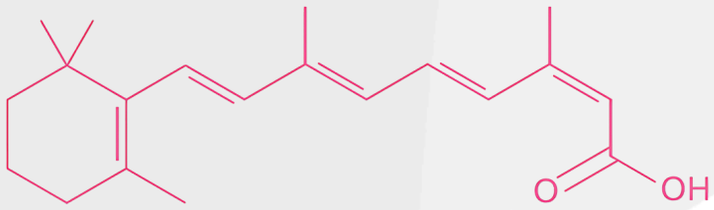
The side effects of these antibiotics are numerous: skin rash, upset stomach and intestine, and fungal infections. Sometimes, the side effects can be quite serious, such as severe allergic reactions (difficult breathing, facial swelling), destruction of the intestinal flora (bloody diarrhea), vaginal candidiasis, and mouth sores. Combined with potential antibiotic resistance, the use of antibiotics for the treatment of rosacea should only be considered if there are no other options left. Having said that, the efficacy of antibiotics for the treatment of rosacea is not well proven.



Virtually all antibiotics have cytotoxic properties and have distinct CMR and hormone disrupting properties. Antibiotics should not be used during pregnancy, unless unavoidable. In actual fact, the use of antibiotics for the treatment of rosacea is sincerely discouraged.

Isotretinoin

In case of severe rosacea that does not respond to antibiotics, isotretinoin may be helpful. Isotretinoin is also a powerful oral acne drug that also helps to clear up acne-like lesions of rosacea. Isotretinoin has severe side effects and should not be used during pregnancy or planned pregnancy as it causes serious birth defects (teratogenic activity).



Isotretinoin is not compatible with oral antibiotics, oral contraceptives and particular botanicals such as St. John's Wort. This botanical product has been reported to deactivate oral contraceptives.

Alternative therapies

A number of alternative therapies have been proposed for the treatment of rosacea. Examples are colloidal silver, emu oil and oregano oil. No conclusive evidence supports the idea that any of these substances are effective.

Chrysanthellum indicum contains phenylpropenoic acids and flavonoids, and has a well-documented effect on vascular wall permeability and increase of the mechanical resistance of capillaries. Particular flavonoids such as apigenin, rutin, silymarin and naringenin have been reported to strengthen the capillaries. The combination of flavonoids with Azelaic acid is considered challenging because of the absence of side reactions, but much more information must be gathered on the functionality of flavonoids.

4.3 Azelaic acid and skin lightening/brightening products

Azelaic acid is advantageously used for skin lightening processes. It can be used both for integral skin brightening to obtain a more radiant complexion, but also to fight "old-age spots". One of the major advantages of using Azelaic acid for skin lightening is the fact that it does not interfere with any of the bodily processes. This is contrary to virtually all other skin lightening products that exhibit sincerely side reactions that are detrimental for human health, or are insufficiently selective.

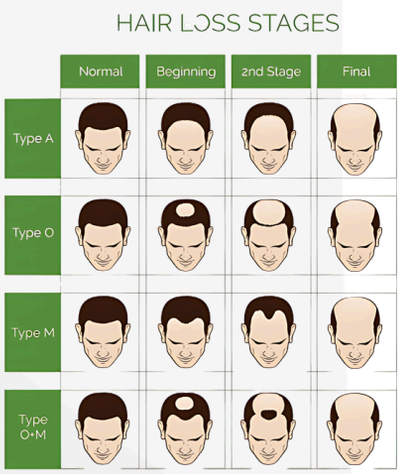
General ingredient characteristics

Azelaic acid is an effective inhibitor of tyrosinase, the enzyme involved in the conversion of tyrosine to melanin, then the enzyme behind the tan. Azelaic acid is also used for the treatment of melasma, lentigo maligna and other disorders of hyperpigmentation. Azelaic acid has been reported to be effective for hypermelanosis caused by physical or photochemical agents. It is also used for the treatment of lentigo maligna melanoma and other disorders characterized by abnormal proliferation of melanocytes.

The mechanism of action of Azelaic acid is inhibition of DNA synthesis and mitochondrial enzymes, thereby inducing direct cytotoxic effects toward the melanocyte. Acne lesions are frequently darker coloured compared to the surrounding skin. Azelaic acid can effectively be used for this postinflammatory hyperpigmentation, believed to be caused by reactive oxygen species. Free radicals are believed to contribute to hyperpigmentation, and Azelaic acid acts by reduction of the free radical production. Azelaic acid 20% is currently available in the US and is only indicated for the treatment of acne, although it has off-label use for hyperpigmentation.

4.4 Azelaic acid and hair-growth and regrowth products

Azelaic acid is a potent 5-α-reductase inhibitor (type 1), the enzyme that converts testosterone into 5-α-dihydrotestosterone, a major cause for alopecia areata and hair loss. Due to the relative absence of dihydrotestosterone, regression of the hair follicle will take place (the catagen stage) and subsequently hair generation will take place (the anagen stage). This enables the use of Azelaic acid for hair regrowth. Significant research is available to demonstrate the ability of Azelaic acid to suppress the scalp's production of dihydrotestosterone, the hormone generally accepted as the primary cause of male pattern balding, and as a frequent factor in female hair loss. According to the published studies, 5-α-reductase inhibition is already detectable at an Azelaic acid concentration as low as 0,2 mMol/l. Inhibition is complete at a concentration of 3 mMol/l, equivalent to ~0,6 mg/l.
Hair grows everywhere on our body except on the palms of our hands and the soles of our feet. An average human adult is the proud owner of approximately 150,000 hairs on her/his head, but also loses up to 100 of them per day. A lot of people, however, own a rather broad hair line, that even may spread over the complete skull. Virtually all individuals will face sooner or later involutional alopecia (old age hair loss) and that can only be delayed by providing the hair follicles with a frequent shot of essential nutrients (B vitamins and some metal ions). A low-protein diet or severely calorie-restricted diet frequently causes temporary hair loss. Alopecia areata (spot baldness) and alopecia universalis (total body hair fall-out, including eyebrows and eye lashes) are auto-immune disorders for which no general treatment is available. Azelaic acid is a well-known inhibitor for 5-α-reductase, and is therefore able to inhibit the conversion of testosterone into dihydrotestosterone. Inhibition of the formation of dihydrotestosterone enables to wake up the dormant hair follicle, and if the follicle has not been completely destroyed, hair growth/regrowth is possible. The most frequently observed cause of hair loss is genetic: androgenetic alopecia. Common types of hair loss may furthermore be caused by hair diseases such as alopecia diffusa (effluvium) whereby the scalp becomes visible due to hair loss, shortage of iron, malfunctioning of thyroid gland, cancer or the use of particular medicines (some oral contraceptives or chemotherapeutic agents), and also psychological artefacts such as trichotillomania, also known as "hair pulling disorder".



Azelaic acid is an ideal ingredient to use in a variety of personal care products for hair, providing important benefits that consumers desire. Here's a brief overview:

- Anti-hair-thinning agent
- Stimulating the life cycle of the hair
- Promoting the reactivation of silent follicles, stimulating hair growth, promoting root regeneration & preventing hair loss
- Antioxidant & anti-inflammatory properties
- Keeping scalp and hair follicles calm and functioning normally
- Combatting oxidative stress, which can contribute to both balding and the premature aging of hair follicles
- Controlling hair loss & promoting new hair regrowth

Products used for hair-growth & regrowth

APPLICABILITY

PRODUCTS FOR REACTIVATE HAIR GROWTH	COSMETIC USE	MEDICAL DEVICE USE	PHARMACEUTICAL USE
Azelaic acid	++	++	+
ANTHRALIN	-	-	+
FINASTERIDE	-	-	++
DUTASTERIDE	-	-	++
MINOXIDIL	-	-	++
SPIRONOLACTON	-	-	+
CAFEINE	++	++	+
BOTANICAL PRODUCTS	+	+	-

TABLE 8: Legend: (++ Strongly recommended / Very suitable) (+ Limited recommended / Suitable) (+/- Limited allowed / Limited suitable) (- Forbidden)

FUNCTIONALITY

PRODUCTS FOR REACTIVATE HAIR GROWTH	COSMETIC USE	MEDICAL DEVICE USE	PHARMACEUTICAL USE
Azelaic acid	++	++	++
ANTHRALIN	-	-	+
FINASTERIDE	-	-	++
DUTASTERIDE	-	-	++
MINOXIDIL	-	-	++
SPIRONOLACTON	-	-	+
CAFEINE	+	+	+
BOTANICAL PRODUCTS	+	+	-

TABLE 9: Legend: (++ Strongly recommended / Very suitable) (+ Limited recommended / Suitable) (+/- Limited allowed / Limited suitable) (- Forbidden)

ADVERSE EFFECTS

PRODUCTS FOR REACTIVATE HAIR GROWTH	CMR PROPERTIES	SKIN IRRITATION	SIDE EFFECTS	EXFOLIATION	PHOTO ACTIVITY	CYTOTOXICITY
Azelaic acid	-	+/-	-	+	-	-
ANTHRALIN	++	+	+	-	+	+
FINASTERIDE	++	+/-	+	-	-	+
DUTASTERIDE	++	+/-	++	-	-	+
MINOXIDIL	+	+	++	-	+/-	++
SPIRONOLACTON	++	-	+	-	+/-	+
CAFFEINE	-	-	-	-	+/-	-
BOTANICAL PRODUCTS	+/-	-	+/-	-	+/-	-

TABLE 10: Legend: (++ Very strong effects) (+ Noticable effects) (+/- Hardly noticable) (- Not noticable)

General ingredient characteristics

Azelaic acid

Azelaic acid is a potent 5-α-reductase inhibitor, type 1. According to Stamatiadis 5-α-reductase inhibition is already detectable at an Azelaic acid concentration as low as 0,2 mMol/l. Inhibition is complete at a concentration of 3 mMol/l, equivalent to ~0,6 mg/l. Stamatiadis also studied the inhibitory effects of zinc sulphate (3-9 mMol/l) using an in vitro assay with 1,2[3H]-testosterone as substrate; also zinc sulphate showed to be a potent 5-α-reductase inhibitor. An additive effect of these two inhibitors was observed. Pyridoxine (vitamin B6) potentiated the inhibitory effect of zinc sulphate, but not of Azelaic acid. This observation suggests that different mechanisms are involved. Simultaneous use of the three products showed to be already effective for the treatment of androgenic alopecia, indicative for a powerful synergy.

The powerful combination {Azelaic acid + zinc sulphate + vitamin B6} for the treatment of androgenic alopecia is cosmetically suitable, contrary to the steroidal and non-steroidal pharmaceutical preparations. In addition, Azelaic acid has a superior toxicological profile. Side effects of Azelaic acid boil down to the particular cosmetic properties: skin lightening at the site of application, a slight risk of hypertrichosis, and [seldom] slight skin irritation.

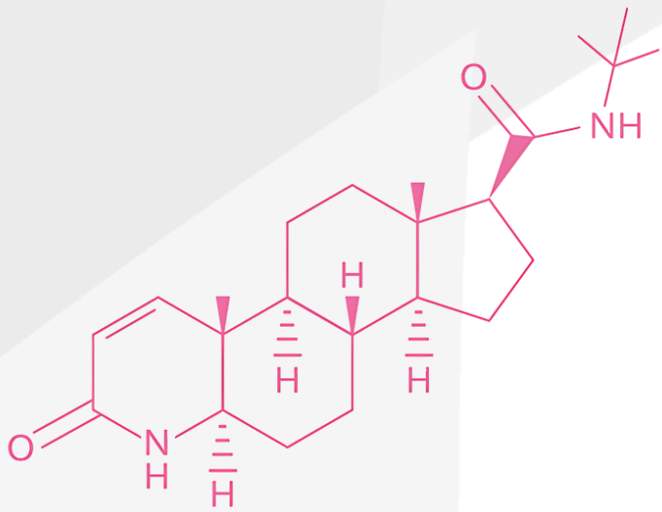
Combinations of minoxidil and Azelaic acid are commercially available, despite the unwanted side effects of minoxidil. Both products work on the basis of different mechanisms of action in preventing baldness. The combination of the two would work more effectively than either alone. Commercial products contain up to 15% Azelaic acid and 5% minoxidil. These high concentrations are explained because of the poor bioavailability of especially minoxidil. Lower but equally effective preparations can be made using transdermal preparations based on phosphatidylcholine-based organogels, to be mentioned organogels containing Azelaic acid and caffeine.

Anthralin

Anthralin is used for the treatment of long-term psoriasis. It is chemically described as 1,8-dihydroxyanthron and is found in goa powder. Goa powder, also named Bahia powder, comes from the araroba tree (Andira araroba). At present anthralin is produced artificially. Anthralin is also used to promote hair growth, but there are sincere concerns on the safety of the product. Insufficient toxicological information is available, both for application against psoriasis and for hair growth stimulation.

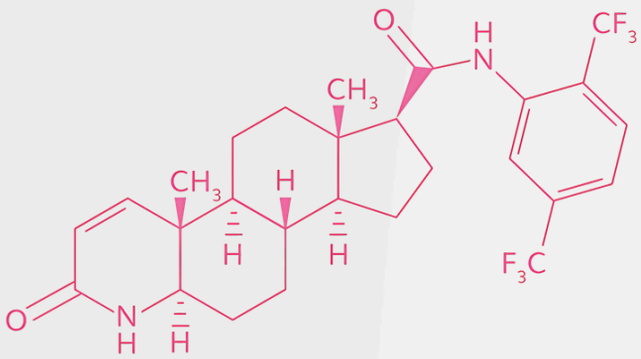
Finasteride & Dutasteride

Finasteride is regarded as the most effective medication proven for the treatment of androgenic alopecia. It is prescribed for males with a genetic predisposition of male-pattern baldness. Finasteride is a 5-α-reductase type II inhibitor, approved by the FDA, for the treatment of enlarged prostate glands.



A side effect of the medication with finasteride was decreased hair loss and often also hair regrowth. In 1998 finasteride was also approved for anti-baldness treatment. Finasteride is marketed by Merck as Proscar for prostate treatment and Propecia for hair loss treatment. The enzyme 5-α-reductase is responsible for the conversion of testosterone into dihydrotestosterone (DHT). For males that are subject to genetic predisposition for hair loss DHT assumes responsibility for the hair follicle to enter the telogen state. Finasteride inhibits 5-α-reductase, so many of the follicles that would have quit instead continue to produce new hairs. The limitation is that the treatment must be continued to be used; if treatment is discontinued baldness returns, although this may take considerable time. Finasteride is exclusively approved for males only; it is not suitable for (pregnant) females and may cause male foetus to develop ambiguous genitals; female foetuses are not affected. Finasteride may lead to multiple sexual disorders, eventually impotence.

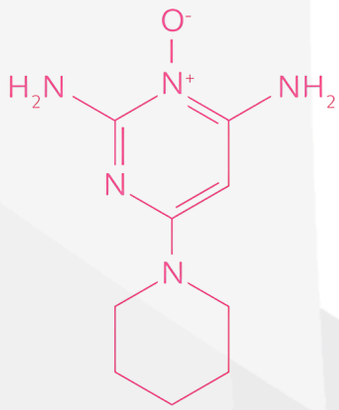
As an extension of finasteride, dutasteride has been developed. Like finasteride it is also an anti-androgen and is also used to treat an enlarged prostate; it also inhibits 5-α-reductase. Dutasteride is expected to be effective for the treatment of androgenic alopecia. However, the side effects are more sincere than in the case of finasteride.



Both finasteride and dutasteride are pharmaceutical products and shall by no means be used in personal care and cosmetic products and medical devices.

Minoxidil

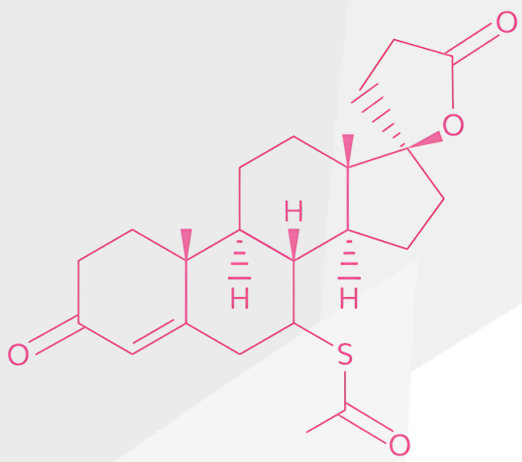
Minoxidil was originally developed for the treatment of high blood pressure, but it was also observed that it affected hair growth. Contrary to finasteride and dutasteride minoxidil has no hormonal activity. However, the medication is not allowed in personal care and cosmetic preparations as well as in medical devices, mainly because it is a pharmaceutical product. A disadvantage of minoxidil is the fact that newly formed hairs frequently stay in the "vellus" phase, underpinning short and fine, soft and usually not pigmented hairs. On the other hand, Minoxidil is a medication that is used to treat hair loss and promote hair growth. It is a topical solution that is applied directly to the scalp. It is available in both a liquid and foam form. The drug works by increasing the blood flow to the scalp, which helps to stimulate hair growth. It also helps to prolong the growth phase of the hair cycle, which helps to increase the number of hairs that are in the growing phase. Additionally, it helps to reduce the amount of time that hairs spend in the resting phase, which helps to reduce the amount of hair loss.



Minoxidil has a number of side effects: acne, headache/migraine, heart palpitations and irregular heart beat and (unwanted) blood pressure lowering. Minoxidil shall not be used by lactating females. The mode of action of minoxidil is yet unknown.

Spironolactone

Spironolactone is a potassium-sparing diuretic that prevents from absorbing too much salt and keeps the potassium levels from getting too low. It is also used for the treatment of acne, hirsutism and androgenic alopecia. Spironolactone is for females what finasteride is for males.

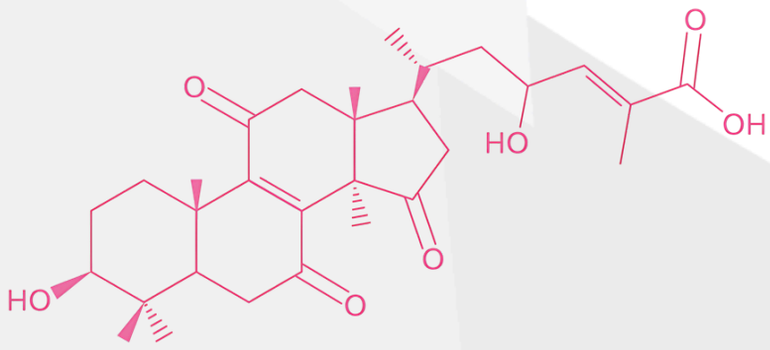


The efficacy of spironolactone is rather limited indeed, and hair regrowth is merely a side effect of the diuretic activity. The side effects may be quite sincere indeed. The product shall by no means be part of personal care and cosmetic products and medical devices. Spironolactone is also used to treat certain types of acne, hirsutism (excessive hair growth), and polycystic ovary syndrome (PCOS). In these cases, it works by blocking the action of androgens, hormones that can cause acne and excessive hair growth. By blocking the action of androgens, spironolactone can help to reduce acne and hair growth.

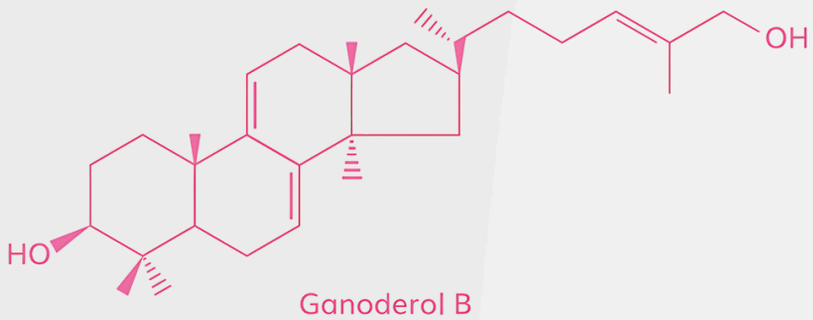
Botanical products

There are not too many cosmetically allowed products that inhibit 5-α-reductase; saw palmetto (INCI: Sabal Serrulata/Serenoa Repens) is an example. The applicable part of saw palmetto is the ripe fruit. The lipid fraction of the volatile oil and fatty oils contains constituents active in treating benign prostatic hyperplasia (BPH), for which saw palmetto is recommended. Saw palmetto has a proven positive track record for hair (re)growth preparations because of its potential to inhibit 5-α-reductase. Saw palmetto also hides a significant content of phytosterols (ß-sitosterol, stigmasterol, lupeol, lupenone and cycloartenol).

Some other botanical products are also claimed to inhibit 5-α-reductase, but there is insufficient proof of their activity. Examples are Ganoderma lucidum (reishi mushroom), that lives on the oil palm (Elaeis guineensis); ganoderic acid and ganoderol B are believed to be the active species.



Ganoderic Acid



Ganoderol B

Ganoderol B has been described as a potent anti-androgen. Ganoderol B has recently also received quite a bit of attention for the treatment of diabetes mellitus type II. It is a α-glucosidase inhibitor that prevents digestion of carbohydrates.

In addition, alfalfa (Medicago sativa), the Japanese pagoda tree (Sophora japonica), red clover (Trifolium pratense) and the often praised Indian mulberry (noni fruit, Morinda citrifolia) have been reported to exhibit 5-α-reductase inhibition properties. Although the inhibitory effect has been clearly demonstrated its efficacy is quite variable indeed due to seasonal variation and frequently a high degree of adulteration of the extracts. Furthermore, many of those extracts also contain isoflavones (genistein, daidzein, biochanin, formonometin, etc., either as the glycosides or the aglycons) that exhibit estrogenic properties.

5.4.3. Androgenetic alopecia

Androgenetic alopecia is hereditary and androgen-dependent. Currently only oral finasteride and topical minoxidil are approved for pharmaceutical treatment of androgenetic alopecia. Recently caffeine has also been shown to have beneficial effects in patients suffering from androgenetic alopecia. The proposed mechanism includes phosphodiesterase inhibition rather than inhibition of 5-α-reductase thereby increasing cAMP levels in cells and promoting cell proliferation by stimulating cell metabolism (T.W.Fischer, U.C.Hipler, P.Elsner, Effect of caffeine and testosterone on the proliferation of human hair follicles in vitro. Int.J.Dermatol., 46,27, (2007)).

The combination of caffeine with Azelaic acid shall be mentioned as a powerful method to treat androgenic alopecia, with the advantage that both caffeine and Azelaic acid are recognised personal care and cosmetic ingredients that also may be used in medical devices.

4.5 Azelaic acid and scalp care

The scalp is an extension of the skin and contains the roots of hair follicles. It is constantly exposed to external stressors such as sun, pollution, and harsh chemical treatments, making it prone to conditions like dandruff, dryness, and irritation that negatively affect hair health and growth. Inflammation or flaking of the scalp can disrupt follicle stability, leading to hair loss. Similarly, clogged follicles can obstruct healthy hair growth. For this reason, scalp imbalances, whether from excess oil, dryness, or dandruff, often contribute to noticeable hair fall.
Addressing scalp health at its root is therefore essential in effectively managing hair loss.

Growing Awareness of Scalp Care
Awareness of scalp care is increasing globally, particularly in Asia, where hot and humid climates heighten the need for scalp maintenance. Consumers are beginning to recognize that a healthy scalp is key to achieving thick, healthy hair.
Dermatologists and trichologists emphasize that scalp care is just as important as skincare, particularly for preventing hair loss, dandruff, itchiness, and excessive oiliness. This has driven interest in specialized scalp products such as exfoliating scrubs, clarifying shampoos, and moisturizing serums.
Like facial skin, the scalp must be cleansed, exfoliated, and moisturized regularly to remain balanced. Without proper care, scalp disorders including dandruff, seborrheic dermatitis, or psoriasis can interfere with follicle function and hinder new growth. Chronic inflammation has been linked to thinning conditions such as telogen effluvium and androgenetic alopecia. Antioxidant-enriched serums further help protect follicles from environmental stressors.

The role of exfoliation
Scalp exfoliation removes dead skin cells and excess oil that clog pores, enhancing microcirculation and oxygen delivery to the follicles. It prevents dandruff, regulates oil production, and reduces buildup from styling products. A clean scalp also allows deeper penetration of topical treatments, reduces redness and bacterial activity, and lowers the risk of infections that can trigger hair loss.

Common scalp disorders
Several conditions can impair scalp health and hair growth, including dandruff, psoriasis, folliculitis, seborrhea, atopic dermatitis (scalp eczema), alopecia areata, and product buildup. Dandruff is often caused by oil overproduction and yeast imbalance, leading to flaky scales and itching. While it does not directly cause hair loss, scratching can damage follicles, and related conditions such as seborrheic dermatitis may result in temporary shedding. Psoriasis, an autoimmune disorder, produces red, scaly plaques on the scalp and can affect follicle health. Folliculitis is a bacterial or fungal infection that causes red pimples and localized hair loss. Seborrhea results from overactive sebaceous glands that produce excess oil, causing greasy hair and irritation. Atopic dermatitis leads to dryness, itching, and inflammation, which are often made worse by harsh products or allergens. Alopecia areata is another autoimmune condition in which the immune system attacks hair follicles, causing patchy hair loss. Finally, product buildup from styling products or dead skin cells can obstruct follicle function and reduce scalp health.
Taking early action against these conditions helps prevent long-term hair damage.

Azelaic acid in scalp care
While Azelaic acid is well known in skincare for its benefits against acne and hyperpigmentation, it also offers promising applications in hair and scalp health. Its anti-inflammatory and antimicrobial properties help create a healthier scalp environment, which is fundamental for optimal hair growth. By reducing inflammation and limiting microbial activity, Azelaic acid contributes to favorable conditions for hair follicles.

Research indicates that Azelaic acid, particularly when formulated with synergistic compounds such as zinc salts and vitamin B6, may support scalp health and stimulate hair growth. These formulations are believed to help manage thinning hair and alopecia. Azelaic acid assists in unclogging follicles, potentially improving hair density and scalp balance. As a result, its use in haircare formulations is becoming an area of interest for both consumers and manufacturers.
When incorporating Azelaic acid into formulations, it is important to source a high-purity, cosmetic-grade ingredient. Azeco Cosmeceuticals offers Azelaic acid with a purity greater than 99%, providing formulators with a reliable solution for scalp treatments and haircare applications.

Clinical Study Results

A proprietary clinical study was conducted using a hair serum containing 10% Azepur99®. The trial involved 50 male and female participants who applied the product once daily for 90 days.
After 90 days, hair density increased by an average of 3% compared to baseline, with 74% of participants showing measurable improvement. The scalp's barrier function improved by an average of 14%, with 57% of participants experiencing stronger scalp resilience. Sensitivity decreased by an average of 16%, and 63.64% of participants reported no sensitivity at all following regular use.
Subjective evaluations supported these findings. After 90 days, 91.3% of participants reported reduced hair fall during washing and combing, while 95.65% reported less overall hair loss and lower scalp sensitivity. Additionally, 65.22% noticed reduced scalp irritation and redness, and 69.57% experienced less itching. In terms of product perception, 65.22% had a positive impression of the serum, 60.87% indicated they would purchase it, and 73.91% expressed overall satisfaction.

Application Potential

The tested serum, containing 10% Azepur99®, demonstrated the ability to improve hair density and scalp comfort in both men and women. According to both objective measurements and participant feedback, the formulation provided meaningful improvements in scalp health and hair density, while reducing sensitivity and discomfort. After 90 days of continuous use, more than 80 % of participants expressed satisfaction with the product.
Azepur99® is therefore well suited for inclusion in shampoos, lotions, hair masks, and other scalp and haircare formulations. It provides significant benefits such as preventing hair thinning, stimulating the hair growth cycle, reactivating dormant follicles, protecting against oxidative stress, and maintaining calm, balanced follicle function. By promoting both scalp health and follicle vitality, Azelaic acid represents a powerful solution for advanced scalp care and hair growth treatments.

5. Solubility of Azelaic acid

Azelaic acid is only sparingly soluble in water: 2,1 g/l (20°C). The solubility markedly increases with increasing temperature: at 50°C 22 g/l Azepur99® will dissolve. Saturated solutions of Azelaic acid are slightly acidic: Azelaic acid is a diprotic acid with dissociation constants (pKA values) of 4,55 & 5,50. The solubility of saturated linear α,ω-dicarboxylic acid (table 11) decreases quite significantly with increasing chain length while the dissociation constants do not show much variation (with the exception of oxalic and malonic acid).

DICARBOXYLIC ACID	FORMULA	SOLUBILITY
OXALIC ACID	$C_2H_2O_4$	220 g/L (25°C)
MALONIC ACID	$C_3H_4O_4$	763 g/L (25°C)
SUCCINIC ACID	$C_4H_6O_4$	83 g/L (25°C)
GLUTARIC ACID	$C_5H_8O_4$	639 g/L (20°C)
ADIPIC ACID	$C_6H_{10}O_4$	14 g/L (20°C)
PIMELIC ACID	$C_7H_{12}O_4$	50 g/L (20°C)
SUBERIC ACID	$C_8H_{14}O_4$	12 g/L (20°C)
AZELAIC ACID	$C_9H_{16}O_4$	2.1 g/L (20°C)
SEBACIC ACID	$C_{10}H_{18}O_4$	0.1 g/L (20°C)

TABLE 11: Solubility of Azelaic acid

The monosodium and disodium salt of Azelaic acid are reasonably soluble in water, and well soluble at elevated temperature. The sodium salts can be obtained in-situ by neutralisation of Azelaic acid with sodium hydroxide. This enables processing of Azelaic acid in the water phase of emulsion systems or in gel preparations. Considering skincare products are in general formulated with acidic pH, Azelaic acid could be regenerated during the acidification and also during the storage with a mechanism of re-crystallization. The crystallized product will not contribute to the bio-availability of Azepur99®.

Neutralisation with organic amines is also possible, preferably with products that do not form stable N-nitrosamines. For pharmaceutical preparations tromethamine (TRIS, 2-amino-2-(hydroxymethyl)propane-1,3-diol) or AMP (2-amino-2-methylpropan-1- ol) are preferred. Upon neutralisation of Azelaic acid with TRIS or AMP simultaneously a powerful pH buffer is formed.

There is only a limited number of cosmetically/pharmaceutically suitable solvents available for Azelaic acid, to enable preparing clear solutions at ambient temperature: polyethylene glycol and (poly)propylene glycol ethers. Ethoxydiglycol (Transcutol® P; Gattefosse) is probably the best solvent for Azelaic acid available. Also butoxydiglycol is a good solvent for Azelaic acid. These solvents enable the production of clear gels of Azelaic acid, at high concentration (see Formulation of clear products).

Please consider that some of some glycols have cosmetic use restrictions in Europe (ethoxy diglycol and butoxy diglycol). Some esterbased products are suitable to incorporate Azelaic acid in emulsions: esters of dicarboxylic acids and/or esters derived from isostearic acid. In the tables below the solubility data of Azelaic acid in different medium are reported.

5.1 Solubility data

Option 1. Solubility of azelaic acid-propylene glycol system (1 atm, 20°C)

Azelaic acid (wt%)	0	2.0	4.0	8.0	12.0	20.0	25.0
Propylene glycol (wt%)	100	98.0	96.0	92.0	88.0	80.0	75.0
Solubility	○	○	○	○	○	×	×

Solubility (○: soluble, ×: nonsoluble)

Option 2. Solubility of azelaic acid-glycerin system (1 atm, 20°C)

Azelaic acid (wt%)	0	2.0	4.0	8.0	12.0	20.0	25.0
Glycerin (wt%)	100	98.0	96.0	92.0	88.0	80.0	75.0
Solubility	○	×	×	×	×	×	×

Solubility (○: soluble, ×: nonsoluble)

Option 3. Solubility of azelaic acid-sorbitol system (1 atm,

20°C) Azelaic acid (wt%)	0	2.0	4.0	8.0	12.0	20.0	25.0
Sorbitol (wt%)	100	98.0	96.0	92.0	88.0	80.0	75.0
Solubility	○	×	×	×	×	×	×

Solubility (○: soluble, ×: nonsoluble)

Option 4. Solubility of azelaic acid-polyethylene glycol system (1 atm, 20°C)

Azelaic acid (wt%)	0	2.0	4.0	8.0	12.0	20.0	25.0
Polyethylene glycol (wt%)	100	98.0	96.0	92.0	88.0	80.0	75.0
Solubility	○	○	○	○	○	×	×

Solubility (○: soluble, ×: nonsoluble)

Option 5. Solubility of Polysorbate 80-azelaic acid-propylene glycol system

Azelaic acid	2.0	4.0	8.0	12.0	20.0	25.0	30.0
Polysorbate 80 (25% with PG)	98.0	96.0	92.0	88.0	80.0	75.0	70.0
Solubility	○	○	○	○	○	×	×

(PG: propylene glycol)

Option 6. Solubility of Polysorbate 60-azelaic acid-propylene glycol system

Azelaic acid	2.0	4.0	8.0	12.0	20.0	25.0	30.0
Polysorbate 60 (25% with PG)	98.0	96.0	92.0	88.0	80.0	75.0	70.0
Solubility	○	○	○	○	○	×	×

(PG: propylene glycol)

Option 7. Solubility of Lysolecithin-azelaic acid-propylene glycol system

Azelaic acid	4.0	8.0	12.0	20.0	25.0	30.0
Lysolecithin (25% with PG)	96.0	92.0	88.0	80.0	75.0	70.0
Solubility	○	○	○	○	○	×

(PG: propylene glycol)

Option 8. Solubility of Polysorbate 80-azelaic acid-glycerine system

Azelaic acid	2.0	4.0	8.0	12.0	20.0	25.0	30.0
Polysorbate 80 (25% with GL)	98.0	96.0	92.0	88.0	80.0	75.0	70.0
Solubility	○	○	○	○	○	×	×

(GL: glycerine)

Option 9. Solubility of Polysorbate 60-azelaic acid-glycerine system

Azelaic acid	2.0	4.0	8.0	12.0	20.0	25.0	30.0
Polysorbate 60 (25% with GL)	98.0	96.0	92.0	88.0	80.0	75.0	70.0
Solubility	○	○	×	×	×	×	×

(GL: glycerine)

Option 10. Solubility of Lysolecithin - azelaic acid - glycerine system

Azelaic acid	2.0	4.0	8.0	12.0	20.0	25.0	30.0
Lysolecithin (25% with GL)	98.0	96.0	92.0	88.0	80.0	75.0	70.0
Solubility	○	○	×	×	×	×	×

(GL: glycerine)

Option 11. Solubilization of azelaic acid-surfactant-water system

	Water	5.0	37.0	50.0	60.0	95.0
Polysorbate 80	Polysorbate 80	71.3	48.0	48.0	30.0	3.8
(25% with PG)	Azalaic acid	23.8	15.0	12.0	10.0	1.3
	Solubility	soluble	soluble	recrystalize	recrystalize	recrystalize
	Water	5.0	20.0	35.0	60.0	95.0
Polysorbate 60	Polysorbate 60	71.3	60.0	48.8	30.0	3.8
(25% with PG)	Azalaic acid	23.8	20.0	16.3	10.0	1.3
	Solubility	separation	separation	recrystalize	recrystalize	recrystalize
	Water	5.0	20.0	35.0	60.0	95.0
Lysolecithin	Lysolecithin	71.3	60.0	48.7	30.0	3.7
(25% with PG)	Azalaic acid	23.7	20.0	16.3	10.0	1.3
	Solubility	soluble	soluble	soluble	recrystalize	recrystalize

Option 12. Solubilization of azelaic acid-surfactant-glycerine-water system

	Water	5.0	35.0	40.0	95.0
Polysorbate 80	Polysorbate 80	87.4	59.8	55.0	4.6
(25% with GL)	Azalaic acid	7.6	5.2	5.0	0.4
	Solubility	soluble	soluble	suluble	recrystalize
	Water	5.0	35.0	40.0	95.0
Polysorbate 60	Polysorbate 60	87.4	59.8	55.0	4.6
(25% with GL)	Azalaic acid	7.6	5.2	5.0	0.4
	Solubility	separation	separation	separation	recrystalize
	Water	5.0	35.0	40.0	60.0
Lysolecithin	Lysolecithin	87.4	59.8	55.0	36.8
(25% with GL)	Azalaic acid	7.6	5.2	5.0	3.2
	Solubility	soluble	soluble	soluble	soluble

5.2 How to avoid crystallization

Crystallization of Azelaic acid is best determined using optical microscopy using polarised light. Crystals of Azelaic acid in emulsions or gels are birefringent and are easily detected. To avoid crystallization suitable solvent(s) shall be used that is/are able to keep Azelaic acid mono-molecularly in solution. That is applicable for emulsions in both the water or oil phase, but also for aqueous/ hydrophilic gel preparations. Eventually also a solvent can be applied (see the solubility tables reported above), but the amount of Azelaic acid that can be solubilized is rather limited. An exception are gels based on phospholipids, more particularly phosphatidylcholine. These are the so-called organogels that exhibit an extreme potential for transdermal transport for pharmaceutical and cosmetic actives (see: 7.3 How to prepare organogels).

6. How to formulate with Azelaic acid

6.1 How to prepare clear / translucent products

Solubility and bio-availability are prime parameters for working with Azelaic acid. The use of Azelaic acid in the water phase of emulsions was already described (see 6. Solubility of Azelaic acid), and this also enables the use of Azelaic acid in waterborne gels based on carbomers, cellulose ethers or polysaccharides such as xanthan gum or sclerotium gum. However, these gels to be stable and clear enough, are characterized by a pH from neutral (close to 7) to slight alkaline 7.2-7.5) and could have a limited degree of bio-availability. For serum and gel based on high content of organic solvents such as ethanol, glycols, the pH value is not an important parameter as the water content is low.

The solubility of Azelaic acid in ethoxydiglycol is 360 g/l. A clear solution will be obtained that will not show crystallisation. Ethoxydiglycol is miscible with water in any proportion, and also soluble in many polar lipids. An example of such an application is given in table 12.

INGREDIENT	CONCENTRATION
ETHOXYDIGLYCOL	61.0%
AZELAIC ACID	20.0%
AQUA	11.5%
PEG-40 HYDROGENATED CASTOR OIL	4.5%
DIMETHYL ADIPATE	3.0%

TABLE 12: Clear Azelaic acid solutions

The formulation according to table 12 enables transdermal transport, as ethoxydiglycol is swiftly absorbed through the skin. This results in transport of Azelaic acid to the target location, such as in the hair follicles for the treatment of acne vulgaris. The preparation according to table 12 is very low viscous, but can effectively be converted into a transparent transdermal gel using hydroxypropylcellulose (HPC). For serum preparations 1-2% HPC is required, depending on the desired viscosity. For gel preparations 2-4% is needed. As an alternative for ethoxydiglycol butoxydiglycol may also be used although the solubility of Azelaic acid is less, estimated at 15%.

For personal care & cosmetic products both ethoxydiglycol and butoxydiglycol are limited in use because of their extreme penetration power. According to EU Regulation 1223/2009 the maximum allowed concentration ethoxydiglycol in leave-on products is 2,6% while for butoxydiglycol 9,0% is allowed. These concentration limitations are not applicable for medical devices and pharmaceutical products. Taking the risk of stating the obvious, anti-acne preparations, anti-rosacea preparations and products for the treatment of alopecia areata or hair growth products are not covered by EU Regulation 1223/2009.

Several other non-restricted glycol ethers may be used as solvents for Azelaic acid, although the solubility of Azelaic acid is markedly lower compared to ethoxydiglycol and butoxydiglycol. These products are commercially made available by DOW Chemical under the trademark Dowanol®. Some examples are:

- Triglycol Ethyl Ether Common name: ethoxytriglycol. CAS: 112-50-5. No INCI name assigned. Excellent solvent for Azelaic acid. Cosmetic limitations: none.
- Dipropylene Glycol Monomethyl Ether Acetate INCI name: PPG-2 Methyl Ether Acetate. CAS: 88917-22-0. Cosmetic limitations: none.
- 1-Butoxy-2-propanol INCI name: Propylene Glycol Butyl Ether. CAS: 5131-66-8. Cosmetic limitations: none.
- 1-Propoxypropan-2-ol Common name: Propylene Glycol Propyl Ether. CAS: 1569-01-3. Cosmetic limitations: none.

There is a massive set of other glycol ethers available, many of those are used in large quantities in chemical/technical applications, and some of those are suitable for use in personal care & cosmetic products. Attention shall be given to the residual monomer concentration (ethylene oxide/propylene oxide) and [substituted] p-dioxanes.

If the formulator is working to obtain a gel based on Azelaic acid, the addition of a rheology modifier should also be considered. In addition, to thicken a high concentrated Azelaic acid solution, it must have high resistance to electrolytes. For example, polyacrylate crosspolymer-6 is characterized by a high resistance to electrolytes. Such a polymer is, for example, commercialized by Seppic with the trade name Sepimax ZEN.

One possible formula to be used as a starting point for an R&D process to adjust a 10% Azelaic acid gel is reported below. According to the final use and to the claims to be reported on the label, other ingredients (soluble in this environment, to maintain the translucent aspect of the gel) can be added to this raw formulation. In this case, only propylene glycol (available worldwide, with a lower smell and also a better toxicological profile than the more efficient Azelaic acid solubilizers such as ethoxydiglycol and butoxydiglycol) is to be used to solubilize Azelaic acid. This is only a starting point, some small changes in terms of percentages could be required in case of different ingredients added, or in case other actives, fragrances or other ingredients in general have

PHASE	INREDIENT	% (BY WEIGHT)
A	1,3-PROPYLENE GLYCOL	35
	Azelaic acid	10
B	Water	27
	Sepimax ZEN	2
	1,3-propylene glycol	20
C	Salycilic acid	1
	1,3-propylene glycol	5

TABLE 13: Formulation Azelaic acid gel

Manufacturing procedure:

1. Add Azelaic acid in 1,3-propylene glycol, heat up to 65-80°C. Mix until homogeneous;
2. Disperse Sepimax ZEN in 1,3-propylene glycol. Add water and mix until homogeneous;
3. Add salicylic acid to 1,3-propylene glycol. Mix until homogeneous;
4. Mix the three phases, heating up to 55-65°C until homogeneous.

If during the storage test some precipitation is observed, the addition of 2-10% of Polysorbate-80 can improve the stability. Also, heptylglucoside can help in stabilizing the Azelaic acid solutions.

6.2 How to prepare emulsions

Solubility and bio-availability are very important parameters for working with Azelaic acid. The use of Azelaic acid in the water phase of emulsions was already described (see: Solubility of Azelaic acid), and this enables the use of Azelaic acid in waterborne gels based on carbomers, cellulose ethers or polysaccharides such as xanthan gum or sclerotium gum. However, these gels are alkaline and show only a limited degree of bio-availability.

For emulsion systems clarity of the Azelaic acid solutions is not significant. Especially polar esters are advantageously applied, preferably in water-in-oil (W/O) emulsions. Good solvents for Azelaic acid in the oil phase of emulsions are dimethyl, diisopropyl esters & diethylhexyl esters of succinic acid or adipic acid. Also some isostearic acid based esters, more particularly isopropyl isostearate and ethylhexyl isostearate, are good solvents for Azelaic acid in the oil phase of the emulsion. For all emollients mentioned is applicable that hot processing must be used to properly formulate Azelaic acid. The ratio of the before mentioned emollient(s) and Azelaic acid used is best set at 2:1, assuring that crystallisation will not occur. Control on the presence of Azelaic acid crystals is essential during the storage tests.

The choice of the emulsifier(s) for W/O emulsions is rather limited indeed. This limitation arises from the fact, that the emulsifier is also required to suppress crystallisation of Azelaic acid. Superior results are achieved with PEG-30 dipolyhydroxystearate (Cithrol® DPHS/Croda Oleochemicals, formerly Arlacel® P135). This emulsifier also tolerates high electrolyte concentrations. Polyglyceryl-3 diisostearate (Cithrol® PG32IS/Croda Oleochemicals; previously Prisorine® 3700) is an excellent co-emulsifier for PEG-30 dipolyhydroxystearate that enables to tune the sensorial and organoleptic properties of the final emulsion. The Azelaic acid loading of W/O-emulsions may be rather high, up to 15% without crystallisation.

For an industrial batch production, the solubilization of Azelaic acid is the crucial point of the formulation. Azelaic acid has to be added to oil phase gradually while stirring at temperature and keep stirring for at least 3 - 3.5 hours to be sure of the complete dissolution of the powder and no phases separation neither macroscopic nor after Centrifuge Test has noted. Sometimes a reduction of viscosity of the W/O emulsions based on PEG-30 dipolyhydroxystearate (detectable since the 1st month's check point) when stored at 40°C occurs. This is not to be considered critical because of the nature of the emulsion. Moreover, the emulsifier inside this formulation increases the viscosity of the product when subjected at high share rate so the packaging of the final cosmetic product in a container with pump will be the most indicated for these formulations. So, in detail, prepare the oil phase, being sure all the butters and waxes are completely dissolved. Add Azelaic acid to this phase gradually while stirring at temperature and keep stirring for at least 3-3.5 hours to be sure of the complete dissolution of the powder. A white/beige, creamy and without powder residues mixture will be obtained.

6.3 How to prepare organogels

Solubility and bio-availability are prime parameters for working with Azepur99®. The use of Azepur99® in the water phase of emulsions was already described in (see: Solubility), and this enables the use of Azepur99® in waterborne gels based on carbomers, cellulose ethers or polysaccharides such as xanthan gum or sclerotium gum. However, these gels are alkaline and show only a limited degree of bio-availability.

Organogels, for the first time introduced by Scartazzini, are formed from phospholipids, more particularly unsaturated phosphatidylcholine (PC. Phosphatidylcholine (Phospholipon® 85G; Lipoid, 5-10%), is dissolved in a suitable solvent that is also able to dissolve Azelaic acid (5-10%: dimethyl, diisopropyl esters & diethylhexyl esters) of succinic acid or adipic acid, and isostearic acid based esters, more particularly isopropyl isostearate and ethylhexyl isostearate. After complete dissolution of phosphatidylcholine, this may take considerable time, Azelaic acid is added while gently heating. A clear, transparent and low viscous solution will be obtained. To this solution an aqueous solution of poloxamer 407 (Synperonic® PE/F127) is added. The viscosity of the product will increase whereby a viscous emulsion-gel will be formed (sometimes abbreviated to “emulgel”).

These organogels are frequently used as a vehicle for transdermal application of pharmaceutical actives: pain relieve agents such as morphine or diclofenac, nicotine (smoking cessation), transdermal patches for contraceptives, etc. They distinguish themselves from regular emulsions & gels by the extreme degree of bio-availability, and thus high degree of functionality whereby the side effects are virtually completely suppressed compared to oral or intravenous application.

7. Azelaic acid: The Active Ingredient

7.1 General Information

Azelaic acid (1,7-hepanedicarboxylic acid) is a naturally occurring dicarboxylic acid. It occurs amongst others in cereals like wheat, barley and rye. Extracts of these cereals have been used since 3000 years in Ayurveda products to treat hyperpigmentation (skin lightening). Azelaic acid also exhibits bactericidal properties, and it is demonstrated to be effective for the treatment of acne vulgaris. Azelaic acid has also been shown to be effective for the treatment of baldness.

Azelaic acid extracted from natural resources is not economically feasible and then not commercially available; the extraction process is difficult and expensive. On the other hand, Azelaic acid can also be produced by ozonisation of oleic acid. Ozonisation is a hazardous reaction that can easily run out of control. The alternative is oxidation of the oleic acid chain largely present in the triglicerides of the most common vegetable oils with hydrogen peroxide. This route goes via the 9,10-epoxide, followed by subsequent oxidation of the epoxide. The oxidation of oleic chain results in the formation of Azelaic acid and nonanoic acid. Oleic acid can be for example obtained from sunflower oil. This choice of starting material enables to produce a grade of Azelaic acid of more than 99% purity where regular azelaic grades are specified at 85-90%.

Azelaic acid is an odourless, white, and highly crystalline solid with a melting point of 110°C. It is soluble in glycerol and glycols, but poorly soluble in water (2,1 g/l). The solubility of Azelaic acid is pH dependent, whereas the mono- and disodium salts are significantly more soluble. Also micro-emulsions based on sorbitan esters using glycerol and lauryl alcohol, as co-surfactants enable to dissolve Azelaic acid.

7.2 Azelaic acid grades

Azelaic acid is available in a variety of grades, ranging from pharmaceutical grade, cosmetic grade to industrial grade. The grade of Azelaic acid used in a product is important because it affects the product's efficacy. Besides purity, powder fineness is also an important indicator of product quality. The smaller the particle size, the higher the quality and the easier it is to formulate with.

Azelaic acid	INDUSTRIAL	COSMETIC	PHARMA	AZEPUR99®
PURITY	80–95%	min 98%	min 99,2%	MIN 99%
ORIGIN	ANIMAL / VEGETABLE / SYNTHETIC	ANIMAL / VEGETABLE / SYNTHETIC	ANIMAL / VEGETABLE / SYNTHETIC	VEGETABLE BASED
FINENESS	FLAKES	FLAKES / POWDER	MAX. 30 MICRON	MAX. 20 MICRON
CERTIFICATIONS	VERY LIMITED	LIMITED	REQUIRED	COSMOS APPROVED, NATRUE APPROVED, VEGAN COMPLAINT, REGULATORY FILE AVAIBLE UPON REQUEST
TECHNICAL SUPPORT	VERY LIMITED	LIMITED	REQUIRED	DEDICATED FORMULATION AND REGULATORY SUPPORT AVAILABLE

TABLE 1: Different grades of Azelaic acid.

Before adding the Oil Phase into the turboemulsifier you'll use for the union of the phases, slightly heat the machine (35-45°C) to avoid thermal shocks. The union of the phases (Water Phase into Oil Phase) has to occur very gradually, from the beginning to the end of the process, mixing only with blades at middle-low speed, without the use of the turbine. The turbine has to be used only after the union at low speed for 5 minutes at most. Then slowly cool the cream. After 3 month of accelerated stability (40°C In the oven), the production of Whitening Cream is stable and without any precipitate.

Azelaic acid loading for oil-in-water (O/W) emulsions is significantly lower compared to W/O-emulsions, while simultaneously avoiding crystallisation of Azelaic acid must be avoided. In O/W-emulsions non-ionic emulsifiers/emulsifier pairs must be used that form a liquid crystalline phase in the continuous phase of the emulsion (the water phase). There are numerous examples of emulsifiers that may be used. A small anthology, according to INCI, is given in table 14.

CETEARYL ALCOHOL / CETEARETH-6 / CETEARETH-25
STEARETH-2 / STEARETH-21
METHYL GLUCOSE SESQUISTEARATE / PEG-20 METHYL GLUCOSE SESQUISTEARATE
SORBITAN STEARATE / POLYSORBATE 60
SUCROSE STEARATE / SUCROSE DISTEARATE / CETEARYL ALCOHOL
CETEARETH-12 / CETEARETH-20 / GLYCERYL STEARATE

TABLE 14: Examples of emulsifiers

In these systems Azelaic acid is "dissolved" in the liquid crystalline double layer as described by Israelachvili, Ninham & Bingham (1976, Friberg & Shinoda). Numerous commercial examples of inclusion of physiologically active ingredients in the liquid crystalline double layer of emulsions have been reported. Processing is best done by combining the emulsifier pair and Azelaic acid at elevated temperature, followed by the addition of the water phase and the remaining ingredients of the oil phase.

In many situations the use of a hydrocolloid is required as the mechanical strength of the liquid crystalline double layer is frequently insufficient, and that may lead to emulsion instability. The addition of a hydrocolloid does not necessarily leads to an increased viscosity. For the hydrocolloid choice polymers (rheology modifiers) resistant to electrolytes could be the most indicated.

7.3 Azelaic acid ingredient combinations

Azelaic acid with niacinamide

Niacinamide is a highly stable, water-soluble form of vitamin B3 that addresses concerns such as uneven tone, enlarged pores, fine lines and dullness. Azelaic acid is valued for its anti-inflammatory properties and effectiveness against acne, rosacea and hyperpigmentation. When used together, they create a powerful combination that helps reduce redness, unclog pores, fade dark spots and strengthen the skin barrier. Niacinamide calms the skin and improves radiance, while Azelaic acid targets bacteria, inflammation and pigmentation. This partnership provides a balanced and comprehensive approach to clearer and healthier skin.

Azelaic acid with vitamin C

Vitamin C is one of the most trusted skincare ingredients, known for brightening, protecting and supporting collagen production. As a powerful antioxidant, it defends against pollution, UV rays and stress. L-ascorbic acid is the most effective form, although derivatives such as magnesium ascorbyl phosphate are often preferred for sensitive skin. Azelaic acid brings gentle exfoliation, reduces inflammation and clears pores. Used together, these actives improve clarity, tone and texture while also helping to fade post-acne marks and reduce redness. Clinical studies confirm that the combination of Azelaic acid, vitamin C and phytic acid increases hydration, elasticity and firmness while reducing wrinkles, hyperpigmentation and erythema.

Azelaic acid with retinol

Retinol, a derivative of vitamin A, is widely recognized for its anti-aging benefits. It stimulates collagen production and accelerates cell turnover, reducing wrinkles, fine lines and breakouts. Azelaic acid is gentler but supports similar processes by targeting acne, pigmentation and uneven skin tone. Combined, they complement each other and can be highly effective for acne-prone or aging skin. For individuals with sensitive or dry skin, Azelaic acid may be preferred on its own as it is less irritating, yet still delivers significant results.

Azelaic acid with hyaluronic acid

Hyaluronic acid is a naturally occurring substance that acts as a powerful humectant, attracting water into the skin to keep it plump and hydrated. Azelaic acid improves skin texture, reduces acne and fades pigmentation. Together, they combine hydration with clarity. While hyaluronic acid delivers lasting moisture and a youthful glow, Azelaic acid works to refine and balance the complexion, resulting in smoother and healthier-looking skin.

Azelaic acid with AHAs and BHAs

Alpha hydroxy acids and beta hydroxy acids are effective exfoliants, while Azelaic acid is milder and better tolerated. AHAs such as glycolic acid remove dead cells from the surface, improving texture and tone, while Azelaic acid reduces melanin production, inflammation and acne. The combination has proven effective for hyperpigmentation, acne and overall radiance, with fewer side effects than tretinoin. Salicylic acid, a BHA, penetrates deeply to unclog pores, while Azelaic acid works on the surface to reduce bacteria and redness. Used alternately or in combination under professional guidance, they deliver a thorough and well-tolerated approach to clear, smooth and balanced skin.

Azelaic acid with alpha arbutin

Alpha arbutin is a derivative of hydroquinone and works as a gentle brightening agent that fades dark spots and reduces pigmentation. Azelaic acid complements this action by promoting cell turnover and reducing melanin production. Together, they effectively improve radiance, even out tone and reduce blemishes. Clinical trials with moisturizers containing Azelaic acid and alpha arbutin have demonstrated significant improvements in brightness, smoothness, sebum control and post-inflammatory hyperpigmentation, confirming their synergistic effect.

Azelaic acid with peptides

Peptides are chains of amino acids that support repair processes, stimulate collagen and improve elasticity. They are widely used in anti-aging formulations to strengthen the skin structure, reduce wrinkles and improve resilience. Azelaic acid reduces inflammation and pigmentation, while peptides enhance firmness and repair. Used together, they provide complementary benefits that promote youthful, strong and healthy skin. Some peptides also benefit haircare by improving scalp condition and follicle vitality, further extending the potential of this combination.

Azelaic acid with minoxidil

Minoxidil is a well-known topical treatment for male pattern baldness and shows visible results after months of consistent use. Azelaic acid contributes to hair growth by inhibiting 5-alpha reductase, an enzyme involved in androgenetic alopecia, while also reducing oxidative stress and protecting follicles. When combined, Azelaic acid and minoxidil improve effectiveness without increasing the risk of side effects. Clinical studies suggest that this combination promotes stronger regrowth, improves scalp health and provides better protection against thinning and shedding.

8. Bio-availability of Azelaic acid

From a medical/physical point of view, bio-availability of Azelaic acid is the most important parameter enabling the product to demonstrate its ultimate abilities. In currently commercial gel & emulsion preparations containing Azelaic acid, crystallization is frequently encountered: these preparations may contain up to 15-20% Azelaic acid, but only a small % is bio-available.

9. Sustainability

Sustainability is about meeting the needs of society, living within the planet's ecological limits and without jeopardizing the ability of future generations to meet their needs.

Azepur99® is:

- 100% bio-based, 100% renewable, vegetable, palm oil-free origin
- Non animal-derived
- Sustainable innovative proprietary technology, Ozone-free, based on vegetable feedstock of European origin
- Formulating to sustainable, simplified personal care products
- Azeco Cosmeceuticals has developed some skin and hair formulations containing all the necessary ingredients to achieve the goal of more healthy skin, scalp and hair

9.1 Azepur99® as a sustainable cosmetic active ingredient

When applied in the context of chemicals, the concept of sustainability could be formulated as the ability of a chemical material/product/service to deliver its function without exceeding environmental and ecological boundaries along its entire life cycle, while providing welfare and socio-economic benefits. The safety concept is transversal to all sustainability dimensions: environmental, social, and economic. It is related to the absence of unacceptable risk for humans and the environment, preferably ensured by the absence of intrinsic hazard properties of chemicals.

Within the European Green Deal, the Chemicals Strategy for Sustainability (CSS) identified a number of interventions to reduce impacts on human health and the environment associated with chemicals, materials, products, and services commercialized or introduced in the EU market. The EU CSS action plan foresees the development of a framework to define Safe and Sustainable by Design (SSbD) criteria for chemicals and materials that should contribute to achieving the aforementioned ambitions, beyond current regulatory compliance.

In particular, this plan is presenting the dimensions, aspects, and indicators that can be used to assess chemicals and materials and how criteria can be defined in order to identify those that are SSbD:

1. Safe and environmentally sustainable chemicals/materials.
2. Safe and environmentally sustainable chemical production processes.
3. Safe and environmentally sustainable raw materials and inputs.
4. Safe and environmentally sustainable when recycled or reused, as well as when treated as waste.
5. Chemicals designed to contribute to sustainability that are generating benefits at the system level where applied.

Azepur99®, commercialized by Azeco Cosmeceuticals, a company founded in 2014 and specialized in Azelaic acid supply, was properly designed to satisfy the fixed criteria by the EU SSbD:

1. The obtained product is pure, safe for consumers and for the environment.
2. It is obtained with a safe, low energy consuming, sustainable process, safe for workers and for the environment.
3. It is obtained from a vegetable renewable source coming from European lands.
4. After use, safe waste is obtained, considering Azelaic acid is a safe molecule, readily biodegradable in the environment.

Sustainability is about meeting the needs of society, living within the planet's ecological limits and without jeopardizing the ability of future generations to meet their needs.

According to the Sustainable Cosmetics Summit (2019), which works to change the face of the beauty industry through sustainable development, the prioritization of sustainability is paramount:

1. Consumers are conscious of sustainability.
2. There are now more sustainable sourcing methods than ever: the personal care industry can today take advantage of ingredients originating from natural ingredients, sustainably sourced.
3. Sustainability-marketed products are driving growth.
4. In some cases, consumers have stopped buying cosmetic products with environmental concerns.
5. Sustainability investment within the personal care industry has increased significantly.
6. Consumers in developing markets are aware of the importance of buying green, healthy, and clean personal care products.

10. Clinical research

10.1 Clinical study: Anti Acne European Formula (SC002)

To evaluate the performance of the Anti Acne European composition (SC002) containing 10% azelaic acid, a clinical study was conducted in 8 patients presenting closed comedones. The formulation was applied twice daily for a period of 30 days on the affected areas. Efficacy was assessed at defined intervals using a standardized visual observation scale ranging from no improvement to complete recovery.

SC002 **Anti-acne European Formula** Triple action: anti-imperfections, anti-residual marks, anti-aging				
	INCI Name	Trade Name	% by weight	Function
A	Aqua	Water	45.45	Solvent
	Betaine	Betafin BP20 [1]	5	Emulsifier
	Glycerine	Pricerine 9083 [2]	5	Humectant
	Aqua, Sodium Hydroxyde	Sodium Hydroxyde, 18% Aqueous Solution	1.5	Neutralizer
B	Azelaic acid	Azepur99®	10	Active ingredient
	Tripelargonin	Matrilox CP601M [5]	15	Emollient
	Cetearyl Alcohol	Lanette O [4]	2	Body agent
	PEG-20 Glyceryl Stearate	Cutina E24 [4]	3	Emulsifier
	Glyceryl Stearate, Ceteareth-12, Ceteareth-20, Cetearyl Alcohol, Cetyl Palmitate	Emulgade SE [2]	10	Emulsifier
	Diethylhexyl Adipate	Crodalmol DOA [2]	2	Emollient
C	Phenoxyethanol, Sorbitan Caprylate	Nipaguard SCP [3]	1	Preservative
D	Parfum	–	0.15	Fragrance

TABLE 15: Anti-acne Formula

Suppliers:
[1] Dupont / Danisco Finnfeeds Oy
[2] Croda Oleochemicals
[3] Clariant / Nipa Preservatives
[4] BASF / Cognis
[5] Matrìca

Specifications:

Appearance	Soft cream
Colour	White
Odour	Characteristic
pH	4,9-5,6
Typical:	5,2
Brookfield Viscosity (S4, 20 rpm, 25°C)	7,200 11,400 mPas
Typical:	8,450 mPas

Manufacturing instructions:

1. The water phase (Phase A) is prepared by combining the ingredients. The water phase shall be alkaline as to (partially) neutralise Azelaic acid present in the oil phase. Ignoring to do so will inhibit emulsion formation. The water phase is heated to 70-75°C.

2. The oil phase (Phase B) is made by combining the ingredients and heating to 70-75°C. The oil phase shall be completely clear, and has a slight yellowish colour.

3. The oil phase is added to the water phase at 70-75°C while stirring with a planetary mixer. The mixture, that is still unstable, is stirred during 5 minutes (on a laboratory scale). Subsequently the mixture is homogenised using a high velocity rotor-stator mixer at maximum capacity. The pre-emulsion is cooled to 40-45°C and re-homogenised adding the preservative (Phase C). The obtained emulsion is white and is still low viscous. Upon further cooling the viscosity will continue to increase. At 25°C the fragrance is added (Phase D); stirring is continued during 15 minutes.

4. The pH is adjusted to the specifications with an 18% aqueous sodium hydroxide solution. The lotion is kept in quarantine for 5 days and committed for microbiological analysis. After 5 days the analytical data of the lotion may be adjusted to the specifications, if required. After the quarantine period the lotion may be committed for confectioning or transferred to bulk storage, provided it satisfies the specifications.

Results

The results are at least promising. In conclusion, Azepur99® can be regarded as a functional cosmetic ingredient which can successfully be used in formulations for the management of skin disorders. The following visual scale was used:

Visual observation rating:
0-1 No improvement
2-3 Clearly noticeable improvement
4-6 Good improvement
7-9 Excellent improvement
10 Complete recovery

Volunteer #	Gender	Age	Day #0	Day #5	Day #10	Day #15	Day #20	Day #25	Day #30
#1	Female	15	0	0	2	2	5	6	8
#2	Female	23	0	0	0	2	5	6	8
#3	Female	21	0	0	0	1	2	2	1
#4	Female	18	0	1	3	6	6	8	10
#5	Male	24	0	0	1	2	2	4	3
#6	Male	15	0	1	3	4	4	6	9
#7	Male	16	0	2	5	5	6	8	9
#8	Male	19	0	0	1	3	4	7	9

TABLE 16: Results

10.2 In vitro antioxidant efficacy: H-ORAC and CAA tests

Antioxidant activity is defined as the ability of a substance to protect cells against oxidative stress caused by free radicals. Free radicals are unstable molecules formed both by internal metabolic processes and by external environmental factors such as ultraviolet radiation and pollution. When not neutralized, these species may contribute to oxidative damage of proteins, lipids and DNA.

To evaluate the antioxidant potential of Azepur99®, two in vitro assays were performed: the H-ORAC test and the Cellular Antioxidant Activity (CAA) assay.

H-ORAC test
The ORAC (Oxygen Radical Absorbance Capacity) test is a well-established method to assess antioxidant capacity by comparison with Trolox, a vitamin E analogue used as a reference standard. In this assay, Azepur99® yielded a value of 49 µmol Trolox equivalents per 100 g. This result indicates that Azelaic acid possesses measurable antioxidant potential.

CAA test (Cellular Antioxidant Activity assay)
The Cellular Antioxidant Activity (CAA) assay is designed to quantify intracellular antioxidant activity in living cells. The method is based on the oxidation of dichlorofluorescin, a probe trapped inside the cell, which is converted into fluorescent dichlorofluorescein (DCF) upon exposure to peroxyl radicals generated by 2,2′-azo-bis(2-amidinopropane) dihydrochloride (ABAP).

The assay was performed using HaCaT cells (human keratinocytes). Cells were cultured to confluence and pre-incubated with a cell-permeable dye and six dilutions of the test item (non-cytotoxic dilutions), as well as a negative control and a positive control (quercetin reference standard), for 60 minutes at 37°C (n=3). After washing, a radical initiator was added to start the reaction. The kinetics were monitored using a fluorescence reader every 5 minutes for 1 hour at 37°C.
Under the experimental conditions (pH ≈ 4), the solid sample of Azelaic acid exhibited considerable intracellular antioxidant activity, with a CAA value of approximately 21.8. It should be noted that the acidic pH of the sample may have contributed to the apparent activity. Adjustment of the pH to approximately 6 did not significantly change the result. However, increasing the pH above 7 resulted in a CAA response below the limit of quantification.

Test	Model / Method	Result
H-ORAC	Trolox equivalents	49 µmol Trolox equivalents / 100 g
CAA assay	HaCaT human keratinocytes (pH ≈ 4)	CAA value ≈ 21.8

TABLE 17: Results

11. Evidence from other studies

The primary mechanism of action of Azelaic acid is its ability to inhibit the growth of Propionibacterium acnes, the bacteria responsible for causing acne. In a study by Searle et al. (2022), Azelaic acid was found to be more effective than other topical treatments, such as benzoyl peroxide and retinoid, in reducing the number of inflammatory lesions and non-inflammatory lesions in patients with mild-to-moderate acne. Furthermore, the study found that Azelaic acid was well-tolerated, with few reported side effects.

Azelaic acid has also been studied for its efficacy in treating rosacea. In a study by Szymańska et al. (2021), Azelaic acid was found to be more effective than metronidazole in reducing the incidence of papules, pustules, and erythema in patients with moderate-tosevere rosacea. Furthermore, Azelaic acid was found to be better tolerated than metronidazole, with fewer reported side effects.

In addition to its use in treating acne and rosacea, Azelaic acid has also been studied for its efficacy in treating melasma. In a study by Liyanage et al. (2022), Azelaic acid was found to be more effective than hydroquinone in reducing the severity of melasma in patients. Furthermore, the study found that Azelaic acid was well-tolerated, with few reported side effects.

Azelaic acid has also been studied for its efficacy in treating hyperpigmentation. In a study by Reznichenko et al. (2021), Azelaic acid was found to be more effective than hydroquinone in reducing the severity of hyperpigmentation in patients. Furthermore, the study found that Azelaic acid was well-tolerated, with few reported side effects. Acne vulgaris is a common skin disorder that affects millions of people around the world. The efficacy of Azelaic acid in treating acne vulgaris has been studied in multiple clinical trials. In a double-blind study, 20 patients with mild-to-moderate acne vulgaris were randomized to receive either topical Azelaic acid or a placebo twice daily for 12 weeks. At the end of the study, the Azelaic acid group showed a significant reduction in acne lesions compared to the placebo group (Singh et al. 2021).

Similarly, a randomized, double-blind study of 60 patients with mild-to-moderate acne vulgaris found that topical Azelaic acid was significantly more effective than a placebo in reducing acne lesions (Markiewicz-Tomczyk et al. 2022). Rosacea is a chronic skin disorder that affects the face, often resulting in redness, bumps, and visible blood vessels. The efficacy of Azelaic acid in treating rosacea has been studied in multiple clinical trials. In a randomized, double-blind study of 60 patients with rosacea, topical Azelaic acid was found to be significantly more effective than a placebo in reducing facial redness, bumps, and visible blood vessels (Chilicka et al. 2022).

Melasma is a common skin disorder characterized by dark patches of skin on the face. The efficacy of Azelaic acid in treating melasma has been studied in multiple clinical trials. In a randomized, double-blind study of 30 patients with melasma, topical Azelaic acid was found to be significantly more effective than a placebo in reducing the dark patches of skin (Bisht et al. 2021). Concurrently, a randomized, double-blind study of 20 patients with melasma found that topical Azelaic acid was significantly more effective than a placebo in reducing the dark patches of skin (Akl, 2022).

Hyperpigmentation is a skin disorder characterized by the darkening of the skin due to an overproduction of melanin. The efficacy of Azelaic acid in treating hyperpigmentation has been studied in multiple clinical trials (Kumar et al. 2020). In a randomized, doubleblind study of 30 patients with hyperpigmentation, topical Azelaic acid was found to be significantly more effective than a placebo in reducing the dark patches of skin. Szymańska et al. (2022) examined 20 patients with hyperpigmentation found that topical Azelaic acid was significantly more effective than a placebo in reducing the dark patches of skin.

12. Market trends

Scalp care as the new skincare

The cosmetics industry is undergoing a transformation in how the scalp is perceived. Instead of being treated separately from the skin, it is now increasingly understood as an extension of it. This change is particularly visible in Asia, where hot and humid climates aggravate scalp disorders such as dandruff and seborrheic dermatitis. Consumers are beginning to demand scalp serums, scrubs, and microbiome-friendly shampoos that restore balance and promote healthier hair growth. Azelaic acid plays a central role in this development because of its ability to calm inflammation, reduce irritation, and stimulate the hair follicle environment.

A holistic approach to hair health

The demand for holistic solutions is reshaping the haircare market. Consumers no longer settle for products that focus only on shine or volume but expect deeper benefits such as barrier protection, sebum regulation, and antioxidant defense. Clinical studies with Azelaic acid serums demonstrate measurable improvements in hair density, scalp barrier strength, and sensitivity reduction. This confirms that modern haircare is evolving into a dermatological category, creating opportunities for brands to deliver products that combine visible results with long-term scalp health.

Sustainability and safe design

Sustainability has become a decisive factor in ingredient selection. Both regulators and consumers expect cosmetics to be safe, transparent, and environmentally responsible. In the European Union, the Safe and Sustainable by Design framework sets clear standards for renewable and traceable cosmetic actives. Azepur99®, with its purity above 99% and bio-based origin, meets these expectations and provides formulators with a solution that combines high performance with sustainability.

Combination formulas and synergistic design

Another strong trend is the rise of multifunctional blends. Formulators are increasingly pairing active ingredients to achieve enhanced efficacy while ensuring product tolerance across diverse skin and scalp types. Azelaic acid shows exceptional versatility in this context. It works well with niacinamide to reduce redness and strengthen the skin barrier, with vitamin C to brighten and protect against oxidative stress, and with retinol to combat acne and photoaging. In haircare, its potential synergy with minoxidil has drawn significant attention as a promising strategy against hair loss. These examples highlight the role of Azelaic acid as a cornerstone active in advanced formulations.

Consumer acceptance and market opportunity

Clinical research becomes even more valuable when consumer perception confirms the results. Trials with Azelaic acid–based formulations not only demonstrated reduced hair loss and scalp irritation but also reported high satisfaction levels among participants. More than 70% of panelists indicated they would purchase the product, showing a strong link between scientific efficacy and commercial potential.

A future-proof ingredient

Taken together, these developments confirm that Azelaic acid is more than a proven dermatological active. It is also a future-proof ingredient that meets current demands for efficacy, safety, and sustainability. For formulators and brand managers, it represents a reliable and versatile tool to drive innovation in skincare, scalp care, and haircare, supported by both robust clinical science and strong consumer acceptance.

Skincare grade actives in body care

Body care is rapidly evolving from basic hydration to high performance skincare, driven by consumers who want targeted solutions for concerns such as body acne, rough texture, redness, and pigmentation. This shift is strengthened by social media influence, dermatological education, and the growing popularity of active body serums and leave on treatments. As a result, brands are increasingly developing body products with facial skincare level ingredients and measurable results. Azelaic acid fits perfectly into this trend thanks to its multifunctional benefits for skin clarity, tone improvement, and inflammation reduction. Its high skin tolerance makes it suitable for frequent use on larger body areas. This positions Azelaic acid as a strong active ingredient for advanced body lotions, body serums, and targeted body treatments.

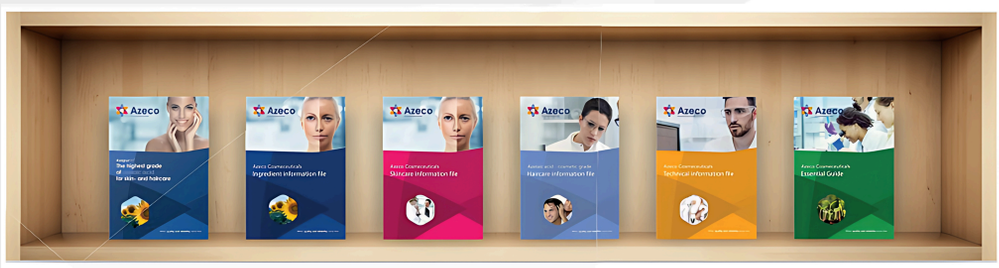
Pregnancy friendly skincare solutions

During pregnancy, consumers often simplify their skincare routine and actively look for mild, effective alternatives to stronger actives such as retinoids. This creates growing demand for ingredients that are widely seen as pregnancy friendly while still addressing common concerns like breakouts, redness, and uneven skin tone. Azelaic acid fits perfectly into this trend thanks to its gentle yet multifunctional performance and its strong positioning in dermatologist recommended routines. As a result, it is increasingly used in pregnancy focused skincare communication and sensitive skin formulations.

13. Discover the world of Azelaic acid

This essential guide on Azelaic acid has been compiled with the highest care. The most important information on Azelaic acid has been combined. Are you interested in specific example formulations for developing skincare or haircare products? The Skincare and Haircare brochures are available for that purpose. These can be requested free of charge via: service@azeco-cosmeceuticals.com or by subscribing to the VIP libary at www.azeco-cosmeceuticals.com.

Technical support
For specific questions, our technical support team is here to help and support you everything related to Azelaic acid. Feel free to contact us at: service@azeco-cosmeceuticals.com.



Feedback
Do you have feedback or want to know any information? Quality is our top priority, so feel free to always contact Azeco Cosmeceuticals. We will be happy to talk to you. You can reach us at: **service@azeco-cosmeceuticals.com** or fill in the contact form on the website **www.azeco-cosmeceuticals.com**

Newsletters
Stay up to date with everything around Azelaic acid. Get a subscription free of charge to the ''Discover the world of Azelaic acid'' newsletter. You can subscribe via our website.

Updates
By following us on social media, you will always be the first to know the latest information. We are active on the following platforms:

LinkedIn | Youtube | Instagram | Facebook

13. References

[1] Akl, E.M., 2022. Liposomal Azelaic acid 20% cream vs hydroquinone 4% cream as adjuvant to oral tranexamic acid in melasma: a comparative study. Journal of Dermatological Treatment, 33(4), pp.2008-2013.

[2] Bisht, A., Hemrajani, C., Upadhyay, N., Nidhi, P., Rolta, R., Rathore, C., Gupta, G., Dua, K., Chellappan, D.K., Dev, K. and Sourirajan, A., 2021. Azelaic acid and Melaleuca alternifolia essential oil co-loaded vesicular carrier for combinational therapy of acne. Therapeutic delivery, 13(1), pp.13-29.

[3] Chilicka, K., Rusztowicz, M., Rogowska, A.M., Szyguła, R., Asanova, B. and Nowicka, D., 2022. Efficacy of hydrogen purification and cosmetic acids in the treatment of acne vulgaris: a preliminary report. Journal of Clinical Medicine, 11(21), p.6269.

[4] Kumar, A., Rao, R. and Yadav, P., 2020. Azelaic acid: a promising agent for dermatological applications. Current Drug Therapy, 15(3), pp.181-193.

[5] Liyanage, A., Liyanage, G., Sirimanna, G. and Schürer, N., 2022. Comparative Study on Depigmenting Agents in Skin of Color. The Journal of Clinical and Aesthetic Dermatology, 15(2), p.12.

[6] Markiewic-Tomczyk, A., Budzisz, E. and Erkiert-Polguj, A., 2022. Clinical evaluation of anti-aging effects of combined therapy — Azelaic acid, phytic acid, and vitamin C applied layer by layer in females with Fitzpatrick skin types II and III. Journal of Cosmetic Dermatology, 21(12), pp.6830-6839.

[7] Reznichenko, N.Y., Reznichenko, Y.G., Reznichenko, G.I. and Veretelnyk, K.O., 2021. Efficacy and safety of 20% Azelaic acid cream for papulo-pustular acne vulgaris.

[8] Searle, T., Ali, F.R. and Al-Niaimi, F., 2022. The versatility of Azelaic acid in dermatology. Journal of Dermatological Treatment, 33(2), pp.722-732.

[9] Singh, S.K., Chaubey, S., Bansal, A., Kaur, G. and Malik, D.S., 2021. Cosmeceutical aptitudes of Azelaic acid. Current Drug Research Reviews Formerly: Current Drug Abuse Reviews, 13(3), pp.222-229.

[10] Szymańska, A., Budzisz, E. and Erkiert-Polguj, A., 2021. Efficacy of 30% Azelaic acid peel in the nonpharmacological treatment of facial acne. Journal of Dermatological Treatment, 32(3), pp.291-296.

[11] Szymańska, A., Budzisz, E. and Erkiert-Polguj, A., 2022. Long-term effect of Azelaic acid peel on sebum production in acne. Dermatologic therapy, 35(1), p.e15186.

For technical and / or sales service contact

Azeco Cosmeceuticals BV | The Netherlands
Customer service service@azeco-cosmeceuticals.com

www.azeco-cosmeceuticals.com