## KESANS:International Journal of Health and Science

e-ISSN: 2808-7178, p-ISSN: 2808-7380

Web: http://kesans.rifainstitute.com/index.php/kesans/index



### **Gluconolactone In Cosmetic (Review Article)**

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**Article Information** 

Submitted: 06 June 2023

Accepted: 08 June

2023

Online Publish: 20

**June 2023** 

Abstract

Introduction: Hidroxy acid is one of the active substances that is widely used in the cosmetic field. Its use is very wide, but there are several classes of hydroxy acid that are irritative. The use of hydroxy acids can cause skin redness, itching, and tension in the skin. Other hydroxy acids are needed that can meet consumer needs without unwanted side effects. Method: This article uses research methods through literature search methods by collecting journals related to research objectives. Articles were found on Google Scholar's seaching engine as many as 27 articles. Objective: To determine the effectiveness of gluconolactone as a skin barrier, antiaging, and as an antiacne. Result and Discussion: The antioxidant effect of gluconolactone can also be used as a sunscreen by capturing free radicals formed when the skin is exposed to the sun. Conclusion: From the search it was found that gluconolacntone can act as a skin barrier protector, anti-acne as well as antianging

Keywords: Gluconolactone; Skin Barier; Anti acne; Anti Anging;

#### Introduction

Nowadays, there are many cosmetic products available in the market that claim to have anti-aging, brightening, anti-acne, moisturizing, and other properties (Bhat et al., 2022). One of the active ingredients used is the group of hydroxy acids. Hydroxy acids are acid-based chemical substances with many derivatives. Some derivatives of hydroxy acids are AHA, BHA, and PHA. The function of hydroxy acids is as an effective exfoliating agent for the skin. These ingredients are also used to remove dead skin cells, regenerate the skin, and brighten the complexion. However, there are some side effects associated with the use of these preparations. The two main side effects of hydroxy acids are irritation and sensitivity to sunlight. Symptoms of irritation include redness, burning, itching, pain, or the development of scars.

The new generation of hydroxy acids includes polyhydroxy acids (PHA) and polyhydroxy bionic acids (PHBA). PHA and PHBA provide similar effects to HA but with fewer irritation responses. Some examples of PHA and PHBA are gluconolactone and lactobionic acid.

Gluconolactone is a type of hydroxy acid that has a larger molecular size compared to other hydroxy acids. This larger size minimizes its penetration into the deeper layers of the skin, resulting in fewer side effects. Despite its larger size, gluconolactone is equally effective as other hydroxy acid groups. Gluconolactone can be used as an active ingredient for anti-aging, anti-acne, and skin barrier protection, making it suitable for use as a moisturizer as well. This broad range of applications provides an opportunity for cosmetic manufacturers to produce comfortable and effective cosmetics for consumers.

Reviews on the active ingredient gluconolactone are still limited. Its role is not as popular as other hydroxy acid groups. Therefore, further literature research is needed for this active ingredient. This review article will discuss gluconolactone as a skin barrier protector, anti-acne agent, and anti-aging ingredient. It is hoped that this review article will provide a deeper understanding of gluconolactone as one of the active ingredients in the field of cosmetics.

Based on the above, the author is interested in analyzing the literature regarding the role of gluconolactone in cosmetics.

# Method

This type of research is review research through literature search methods by collecting journals related to research objectives. The preparation of the literature review began on April 20, 2022. Literature search using Google Scholar with the keywords "Gluconolactone" and "cosmetic". resulted in the discovery of 1060 articles and articles that fit into the inclusion criteria as many as 27 articles. The inclusion criteria used in this literature review are gluconolactone as a skin barrier, antiaging, and as an antiacne. Another inclusion criterion is journals published within the last 5 years and fully accessible. While the criteria for the exclusion of this research are research journals in the form of dissertations, literature reviews, and articles that are not in Indonesian or English.

The number of articles collected amounted to 27 journals. The flow of searching for articles in *the seaching engine* is shown in Figure 1

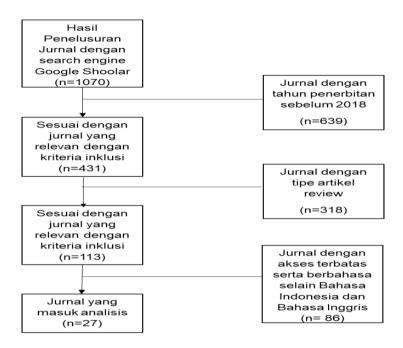


Figure 1, Article Search Flow on Seaching Engine

## **Result and Discussion**

### Result

In this article, the results and discussions are arranged by making a flow of presentation of research results as shown in Figure 2

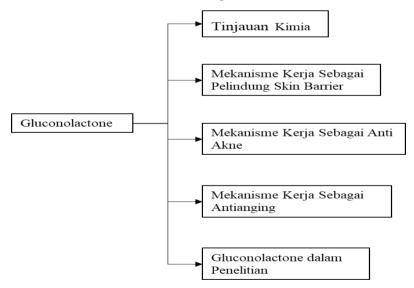


Figure 2. Flow of Presentation of Research Results

#### **Discussion**

## Gluconolactone and Hidroxy acid

Hydroxy acids are a group of organic chemicals consisting of a carboxylic acid group with one or more hydroxyl groups. This acid is naturally present in cane sugar, curds, honey, cucumbers, lemons, grapes, apples, etc. (Yu &; Van Scott, 2004). Hidroxy acid is also known as fruit acid because it is mostly found in fruit. α-hydroxy acids, β-hydroxy acids, polyhydroxy acids, polyhydroxy bionic acids and aromatic hydroxy acids are some examples of HA that can be found in skin care formulations.

## Type of Hydroxy acid (HA)

The first generation of HA was  $\alpha$ -hydroxy acids (AHAs), which are carboxylic acids with hydroxy groups attached to alpha carbons (e.g. glycolic acid and lactic acid) (Yu & Van Scott, 2004). Glycolic acid with its chemical name is hydroxy acetic acid, which was the first compound of this HA to be introduced into skin care products. This glycolic acid is the smallest compound of  $\alpha$ HA (Yu &; Van Scott, 2004). Lactic acid, with optimal biological activity in the l-form, is also used in various topical formulations for exfoliators and also to impart antiaging properties (Tasi Kostov et al., 2019)

 $\beta$ -Hydroxy acids ( $\beta$ HA) are carboxylic acids that have 1 hydroxy group attached to the carbon  $\beta$ . The most common form of  $\beta$ HA is  $\beta$ -hydroxybutanoic acid. The oil-soluble  $\beta$ HA is tropic acid (2-phenyl-3-hydroxypropanoic acid). Malic acid and citric acid can also be called  $\beta$ HA or  $\alpha$ HA because they have 1 hydroxy group attached to the carbon  $\alpha$  and also  $\beta$  carbon. Citric acid is widely known as an anti-oxidant and antiaging in topical formulations (Campos et al., 2021)

The new generation of HA, called PHA and bionic polyhydroxy acids (PHBA), provides effects similar to HA but with less irritant response. Polyhydroxy acids (PHA) are hydroxy acids that contain more than one hydroxy group (e.g., gluconolactone). Polyhydroxy acids with the addition of sugar molecules are called polyhydroxy bionic acids (PHBA) (for example; maltobionic acid and lactobionic acid) (Jarz bek Perz et al., 2021). PHBA can also be called Aldobionic acid (ABA) (Yu & Van Scott, 2004)

Aromatic hydroxy acids are carboxylic acids with phenolic rings, for example, salicylic acid (SA). In cosmetic and dermatological literature, SA is often described as βHA, but the calcification is false. Within SA, both hydroxyl groups and the carboxyl group are directly attached to the aromatic benzene ring and both exhibit acidic properties (Kornhauser et al., 2010). SA is used in cosmetic formulations for a wide range of applications, especially fat-soluble SA, which is useful in subjects with oily skin. SA can be used for the treatment of acne and post acne hyperpigmentation but side effects can occur salicylsus (How et al., 2020)

# Gluconolactone

Gluconolactone has several other names, including gluconic acid lactone, D-gluconic acid lactone, D-gluconic acid delta lactone, glucono delta lactone, delta-D-gluconolactone and D-glucono-1,5-lactone (Lee et al., 2021)

Gluconolactone, 3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-one with chemical formula C6H10O6 according to Figure 3

**Figure 3** Chemical Structure of Gluconolactone (Jarz bek Perz et al., 2021)

Gluconolactone is an oxidized lactone glucose derivative, in the form of a white, crystalline, almost odorless solid with a sweet taste and can be dissolved with water (Jarz bek Perz et al., 2021). Gluconolactone can only partially dissolve in ethanol solvent, which is 1 gram in 100 grams of alcohol, but Gluconolactone is insoluble in ether and acetone (Information & (2023), 2004) (Accessed at 17 June 2023)

The molecule is a directly substituted tetrahydropyrate ring with three hydroxyl groups, one ketone group and one hydroxymethyl group. Gluconolactone in a 6% aqueous solution has a pH value of 3.6. Over time, it will decrease to 2.5 in 2 hours due to rapid hydrolysis into gluconic acid (Information & (2023), 2004) (Accessed at 17 June 2023). The molecular weight of gluconolacton is 178 heavier than that of glicolic acid which weighs 76 (Information &; (2023), 2004) (Accessed at 17 June 2023). This smaller size does not allow gluconolactone to penetrate into the deeper layers of the skin than glycolic acid so it is minimal in irritant reactions. The melting point of Gluconolactone is at 155 <sup>0</sup> Celsius and its solubility at 250 C is 590000 mg/L (Information & (2023), 2004) (Accessed at 17 June 2023)

Gluconolactone is produced physiologically by skin cells, by converting glucose into ribose and then deoxyribose and can also be found in honey, wine and fruit juices (R. Li et al., 2018). Its pure form is obtained by fermentation of corn kernels or by the enzyme D-glucose oxidation, using bromine water as oxidant. In addition, it can be synthesized using aerobic acetic acid bacteria Acetobacter suboxidant (Jarz bek Perz et al., 2021)

Gluconolactone is a natural polyhydroxy acid (PHA) with metal-chelating, moisturizing and antioxidant activity. Gluconolactone can be produced by enzymatic oxidation of D-glucose oxidation. Its ability to extract free radicals contributes to its antioxidant properties. This property is used in cosmetic production and as a coagulant in tofu processing (Information &; (2023), 2004) (Accessed at 17 June 2023)

Although gluconolactone is softer than traditional AHAs, it has the same effect on improving facial texture. These improvements include smoothing, improving the cleanliness and brightness of facial skin, reducing the appearance of fine lines and wrinkles, and evening out skin tone. This gentle yet effective ingredient is suitable for all skin types. Gluconolactone can increase the skin barrier for protection against irritation and retain moisture (Information &; (2023), 2004) (Accessed at 17 June 2023)

#### **Manufacture of Gluconolactone**

Gluconolactone can be produced by oxidation of glucose with bromine water and by oxidation of glucose using *Acetobacter suboxydans* (Information &; (2023), 2004). Crystals of gluconolactone come from highly saturated gluconic acid solutions at temperatures of 36 to 57 °C. The Crystallization process occurs through two steps that continuously result in increased productivity per unit volume under favorable conditions in terms of energy consumption.

In the first step, a crystal suspension (3 to 10% crystalline material) is produced in a saturated gluconic acid solution maintained at 65 to 75 °C. The second step involves controlled cooling to 40 to 45 °C, followed by a period of crystal maturation at constant temperature. A portion of the resulting crystal suspension is then recycled to the first step.

Gluconolactone can also be obtained from gluconic acid solution in aqueous solution and then water removal involves azeotropic distillation with alcohol, followed by crystallization of alcohol-containing residues (Information & (2023), 2004) (Accessed at 17 June 2023)

# Gluconolactone mechanism as a skin barrier protector

The skin consists of one outermost protective layer called the epidermis. This layer allows the skin to be protected from liquids, solids, gases and attacks from viruses, bacteria, fungi and other microbes. The way of protection is physically, biochemically, redox, and immune. The epidermis protects physically as the first protection through the lipid layer, the acid mantle which is one of the contributors to the acidic pH of the epidermis, the calcium gradient that affects desquamation and cell turnover as well as epidermal differentiation, and many aspects of the skin's immune system (Lynde et al., 2006)

In this epidermis there are many corneocytes and between these corneocytes there is a lipid layer that serves to close the distance between corneocytes. The lipid layer is what we call the skin barrier. The lipid layer consists of ceramide (45–50%), cholesterol (25%), free fatty acids (10–15%) and cholesterol sulfate (less than 5%) ( Schwartz et al., 2019)

On skin whose skin barrier is disturbed, there will be several skin complaints, namely irritation, allergic contact dermatitis, atopic dermatitis, dry skin, skin aging, xerosis, rosacea, and ackne. This happens because when the skin barrier is disturbed, inflammatory mediators are activated, namely IL-1 and TNF $\alpha$ . Gluconolactone can be used well for the treatment of dry and sensitive skin (Jarz bek Perz et al., 2021). Gluconolactone is thought to inhibit IL-1a and PGE2 which are known as inflammatory mediators in the skin that can reduce and eliminate corneocyte cohesion (W. H. Li et al., 2018), An illustration of a picture of skin with a disturbed skin barrier is presented in Figure 4.

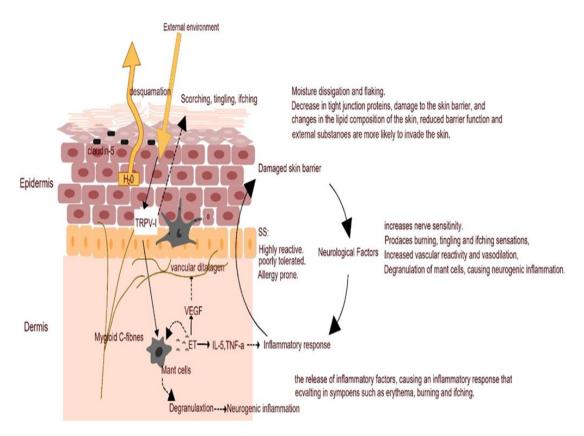


Figure 4. Processes That Occur in Sensitive Skin.

Disturbed skin barrier also results in increased TEWL (Trans Epidermal Water Loss) so that the skin will quickly lose water causing the skin to become dry and sensitive (Jarz bek Perz et al., 2021). Gluconolactone can improve skin barrier function by strengthening, sealing and reducing TEWL (Puigdemont et al., 2018).

Increased skin PH also occurs when the skin barrier is disrupted. Similar to lactobionic acid, gluconolactone can lower PH and can cause skin mood to become *hyperacidic*. This hyperacidification improves permeability and results in "supernormal" SC cohesion (Tasi Kostov et al., 2019). To obtain a hyperacid state in the stratum corneum can use 10% lactobionic acid or gluconolactone as a therapeutic strategy for inflammatory dermatosis. Gluconolactone preparation of 10-15% can also be used as a therapy for eczema and psoriasis. But for the most effective therapy for moderate to severe dry skin conditions requires a combination of gluconolactone, AHA, and antioxidants such as *Nacetyl-cystein* (Puigdemont et al., 2018)

α-hydroxy acids, β-hydroxy acids, polyhydroxy acids, and polyhydroxy bionic acids are used as exfoliatives used for several conditions such as dry skin, wrinkles, and aged spots, by thinning the stratum corneum, the outermost layer of skin (Puigdemont et al., 2018) . Stratus corneum contains dead keratinocytes also called corneocytes. Ionic interactions are responsible for keeping corneocytes stuck together. This ionic interaction arises as a result of electrostatic interaction between Ca2+ ions and negative ions such as SO4 2- and PO4 3-. Hydroxy acids can weaken these interactions by disrupting Ca2+ ions

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(Kim et al., 2019). The ability of  $\alpha$ -hydroxy *acids*,  $\beta$ -hydroxy *acids*, polyhydroxy *acids*, and polyhydroxy bionic acids to moisturize the skin is by absorbing water and exfoliating dead skin cells in the outermost layer of the skin. When the water content inside the corneum layer is high, the difference in charged ions will increase so that ion interactions will weaken. As a result, exfoliation of corneocytes will arise (Kim et al., 2019)

Gluconolactone can increase the acidity of the stratum corneum, increase fat metabolism in the skin so that Gluconolactone can reduce TEWL, reduce erythema, and protect the skin barrier (Lee et al., 2021)

### Mechanism of Gluconolactone as Antiackne

Acne arises one of them due to the blockage of hair follicles by dead skin cells, dirt, oil, and bacteria. Acne consists of inflammatory and non-inflammatory lesions. The prevalence of ackne arises during early adolescence to late adolescence. Acne can also arise due to increased sebum production, suboptimal keratinasisi processes in the stratum corneum and the production of inflammatory mediators (Hazarika, 2021). The most frequent acne-causing pathogenic bacteria is Propionibacterium acnes (Hazarika, 2021). In the pathogenesis of ackne, hyperkeratination plays an important role (W. H. Li et al., 2018). In hyperkeratinized stratum corneum, there is a group of sulphate cholesterol. This cholesterol sulfate is ionic, thus strengthening the bonds and adhesions between corneocytes resulting in decreased desquamation (W. H. Li et al., 2018)

In research conducted by Islami 2021, it shows that there is a relationship between lipid profiles and acne events. Research also reveals that skin sebum levels are also influenced by the severity of acne (Islami et al., 2021). The process of acne occurrence can also be triggered by a lack of moisture in the skin. Skin with a moisture content of less than 10% can result in disruption of the stratum corneum and inflammatory cytokine production. Therefore, adequate water content in the skin (10-20%) is very important in acne prevention (Yolanda et al., 2021). The mechanism of acne occurrence can be seen in Figure 5.

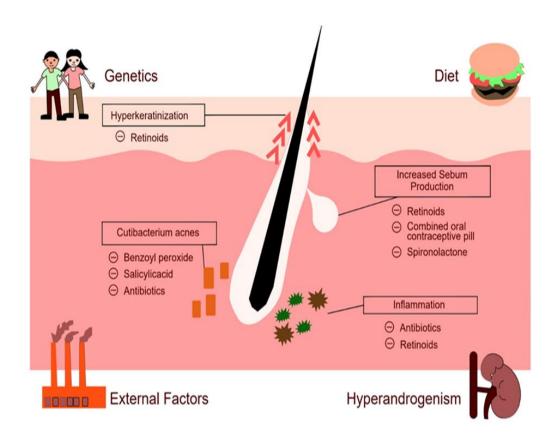


Figure 5. The Process of Acne Occurrence

Gluconolacton 14% has been studied as more effective in antiacne use than benzoyl peroxide 5%. This happens because when using 14% gluconolactone in mild to moderate lesions results in a decrease in the number of lesions and the number of inflamed acne. Side effects of benzoyl peroxide also do not occur when using gluconolactone such as dry, itchy skin and peeling (Jarz bek Perz et al., 2021)

The mechanism of action of gluconolactone as an antiacckne is the same as other hydroxy acid groups, namely by acting as an exfoliator. The role of the exfoliator is obtained by thinning the stratum corneum, the outermost layer of the skin. (epidermiolysis) Gulconolactone as well as other PHAs can help remove blackhead blockages from sebacean follicles (Jarz bek Perz et al., 2021)

Another condition that is similar to ackne but not ackne is rosacea. Rosacea is characterized by inflammation of the blood vessels where the blood vessels are vasodilated so that they appear reddened (Jarz bek Perz et al., 2021). Chronic vasodilation leads to telangiectation. Accne-like papules and pustules also often arise in rosacea patients. With the use of gluconolactone 5%-10% beneficial and effective for rosacea (Kantikosum et al., 2019)

#### Mechanism of Gluconolactone as an antianging

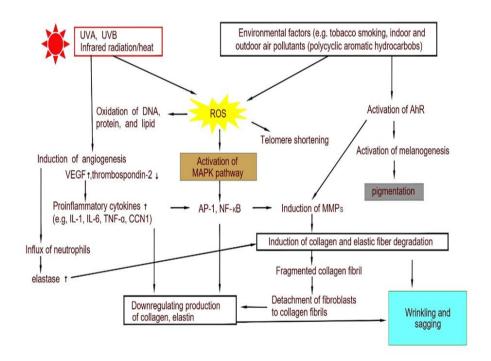
There are two causes of skin aging, namely intrinsic factor (chronological aging) and extrinsic factor (*photoaging*) (Weinm llner et al., 2020). In humans, the aging process

of the skin cannot be separated from the cause. Simultaneously, both intrinsic and extrinsic causes will jointly affect the aging process.

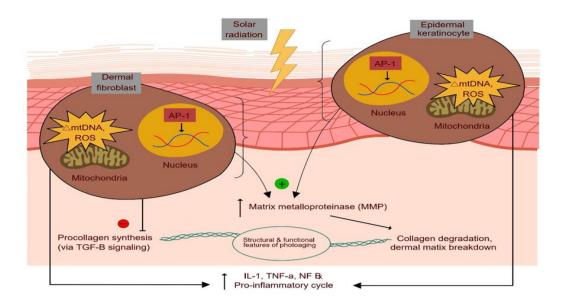
The process that occurs in intrinsic skin aging is a combination of three processes, including decreased proliferative ability of skin cells, decreased synthesis of the extracellular matrix of the skin, and increased activity of enzymes that degrade collagen in the dermis layer (Weinm llner et al., 2020)

Photoaging can aggravate intrinsic skin aging. This occurs due to chronic/repeated exposure to UV rays. Clinically, the skin becomes rough; The epidermis becomes thicker (hyperplasia) at first and then becomes thinner (atrophy). The skin will also look lethargic, pale with wrinkles, hyperpigmentation in some places, and the occurrence of lentigo and telangiectasis (Campione et al., 2021)

External factors that influence include repetitive facial expressions, the influence of heat, sleeping position, gravitational force, lifestyle such as smoking, pollution, and exposure to sunlight, especially UV rays. The extrinsic factor that plays the most role in skin aging is UV light, therefore often extrinsic aging is called photoaging (Campione et al., 2021). The process of aging can be seen in Figure 6 and Figure 7.



**Figure 6.** The Mechanism of Aging of the Skin.



**Figure 7**. The Mechanism of Aging of the Skin.

Skin aging has several clinical signs, namely: the emergence of wrinkles in the skin, changes in skin pigment color, and a decrease in skin volume (Milani &; Puviani, 2018)

The antianging effect of gluconolactone is obtained from its activity as a starum corneum esfoliator, repairing the skin barrier, moisturizing and as a skin humectant. An increase in the acidic state of the gluconolactone-induced stratum corneum can lead to improved lipid processing and an improvement of the skin's barrier function. Gluconolactone can reduce TEWL (Trans epidermal water loss) and erythema and improve skin brightness (Lee et al., 2021). In its function as an exfoliator, gluconolacton works by improving hyperkeratination of the stratum corneum so that it turns over corneocytes.

Gluconolactone also functions as an antioxidant by reducing the function of the MMP enzyme (Matrix MetalloProteinase) so that it can maintain the structure and function of collagen. Gluconolactone also aids in the synthesis of type V collagen in the skin and helps form heterotypic fibers produced by binding to type I collagen (Lee et al., 2021)

The antioxidant effect of gluconolactone can also be used as a sunscreen by capturing free radicals formed when the skin is exposed to the sun. In a study of mouse skin fibroblast cultures that have been exposed to UVB light, it was found that gluconolactone can protect elastin fibers from degradation of the effects of the sun (Jarz bek Perz et al., 2021)

#### Gluconolactone in Research

Some uses of gluconolactone from several articles obtained

**Table 1**Uses of gluconolactone from some articles

No.	Author and Country of Origin	Article tittle and Year	Research Result
1.	Brenda L. Edison, BA Heather A. Smith, BS Barbara A. Green, RPh, MS Neena K. Tierney, PhD USA	Skin exfoliation with low concentrations of alpha hydroxy acids and poly hydroxy acids when incorporated into wash-off or leave-on products using a novel abbreviated model to measure cell turnover rate	Body lotions containing 2% gluconolactone have skin cell turnover benefits which include: mild exfoliating skin (94%); skin feels new (100%); dry and dull skin revitalized (97%); and smoother skin texture (100%) (Edison et al., 2021)
2.	Sylwia Jarząbek-Perz Paulina Mucha Helena Rotsztejn	Corneometric evaluation of skin moisture after application of 10% and 30% gluconolactone, 2021	Corneometric measurements showed a significant improvement in facial skin hydration after gluconolactone application. No significant differences were observed between the application of 10% and 30% solutions (Jarz bek Perz et al., 2021)
3.	Kornphaka Kantikosum, Yuda Chongpison, Natcha Chottawornsak, and Pravit Asawanonda, Thailand	The efficacy of glycolic acid, salicylic acid, gluconolactone, and licochalcone A combined with 0.1% adapalene vs adapalene monotherapy in mild-to-moderate acne vulgaris: a double-blinded within-person comparative study, 2019	The combination of research products with active ingredients (glycolic acid, salicylic acid, gluconolactone and licochalcone A) compared with adapalene is not inferior to adapalene monotherapy in acne therapy with inflammatory lesions. Similar side effects exist in both formulations but slightly more burning is reported in the combination formula (Kantikosum et al., 2019)
4.	Vishal Saxena, Krishana Yadav, India	Glycolic Acid, Lactic Acid, Mandelic Acid, Salicylic Acid, Citric Acid, Gluconolactone: Skin Exfoliators inCombination Therapy of Acne Vulgaris	Treatment for an average of 6 weeks a combination of the composition of Glycolic acid 16%, lactic acid 8%, Mandelic acid 5%, citric acid& 1%, Gluconolactone7% and salicylic acid 2%. Has anti-acne effect and improves acne scars, without any side effects (Saxena & Yadav, 2020)
5.	Marisa Dufort, MS Hong Li, PhD Fa Zhang, PhD Fang Liu-Walsh, PhD Brenda L. Edison, BA Neena K. Tierney, PhD	Chelation properties demonstrated by a novel analytical method help elucidate polyhydroxy acids benefits for environmental oxidative stress and pigmentation	Consumers (n = 33) who used 10% Gluconolactone noted benefits for pigmentation namely: dark spots faded (82%), skin tone more evenly distributed (88%) and brighter and glowing skin (100%) with use twice daily for 4 weeks (Dufort et al., 2021)
6.	Rabab Hussain, PharmD Diana Friscia Wen-Hwa Li, MS, MBA Ramine Parsa, PhD Dara Miller Thomas Shyr	Appropriateness of a novel low ph 2% poly hydroxy acid-containing facial cleanser for patients with dry and sensitive Skin	During the use of Gluconolactone cleanser 2% used 2 times a day for 4 weeks obtained skin that is soft, supple, and looks healthiert (Hussain et al., 2021)
7.	Jin-Hyun KimID, Byungjun Ahn, Seon-Guk Choi, Sohyun In, A. Reum Goh, Sun Gyoo Park, Cheon-Koo Lee, Nae-Gyu Kang	Amino acids disrupt calcium- dependent adhesion of stratum corneum	In this study, it was shown that amino acids, such as serine, interfere with the adhesion of the Ca2+-dependent stratum corneum. As with Gluconolactone (Kim et al., 2019)

## Connclusion

Gluconolactone is a derivative of Hidroxy acid which has a relatively larger size than other hidroxy acid groups. Gluconolactone is a white solid, crystalline, almost

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odorless with a sweet taste and can be dissolved with water. Gluconolactone in a 6% aqueous solution has a pH value of 3.6. As time goes by, it will decrease to 2.5 in 2 hours due to rapid hydrolysis into gluconic acid.

Although gluconolactone is softer than traditional AHAs, it has the same effect on improving facial texture. These improvements include smoothing, improving the cleanliness and brightness of facial skin, reducing the appearance of fine lines and wrinkles, and evening out skin tone. From several articles, it was found that gluconolactone can function as a skin barrier protector, anti-acne and antianging.

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KESANS: International Journal Health and Science

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