

**Jungbunzlauer**

*From nature to ingredients®*

# facts

Glucono-delta-Lactone as a  
mild exfoliating agent with excellent efficacy  
in a minimalist formulation



## Introduction

As the skin care market continues to grow, so does the range of products available to consumers. Choosing between these products, with their many ingredients and claims, can sometimes feel overwhelming. Consequently, formulas featuring a short list of ingredients and simplified claims are increasingly appealing to consumers looking to establish a consistent, easy-to-follow routine. Furthermore, sustainability has become a major factor in consumer decision-making, leading to a growing interest in products developed using versatile natural and biodegradable ingredients. When it comes to exfoliation products, the trend is taking us away from harsh chemicals towards anti-inflammatory actives that are gentle on the skin.

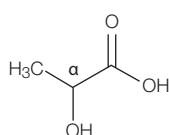
Among the most popular ingredients used for chemical peels are the alpha- and beta-hydroxy acids. With an organic acid structure containing multiple hydroxyl groups, the polyhydroxy acid glucono-delta-lactone (GdL) demonstrates similar exfoliating properties to those of alpha- and beta-hydroxy acids but also functions as a moisturiser.

## Hydroxy acids and their use in skin care

Although the biological mechanism behind the function of hydroxy acids has yet to be fully clarified, several studies have already investigated it. One study reported that alpha-hydroxy acids work by reducing the calcium ion concentration in the epidermis and removing calcium ions from the cell adhesion through chelation. This leads to disruption of cellular adhesion and hence exfoliates dead skin.<sup>[1]</sup> The same study also suggested that decreasing calcium ions in the epidermis could tend to promote cell growth. Another report showed that applying glycolic acid to sun-damaged skin increases epidermal thickness, epidermal and dermal levels of hyaluronic acid, and collagen gene expression.<sup>[2]</sup> This results in significant changes in epidermal and dermal hydration and therefore affects skin appearance, texture and function. Because they share the alpha-hydroxy acid structure, polyhydroxy acids have the ability to provide similar skin effects while additionally functioning as humectants and moisturisers, and providing an antioxidant chelation effect.<sup>[3]</sup>

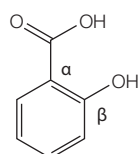
As shown in figure 1, the main structural difference between alpha-, beta- and polyhydroxy acids is the number of hydroxyl groups they possess.

Alpha-hydroxy acids



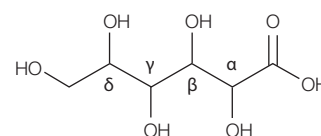
Lactic Acid

Beta-hydroxy acids



Salicylic Acid

Polyhydroxy acids



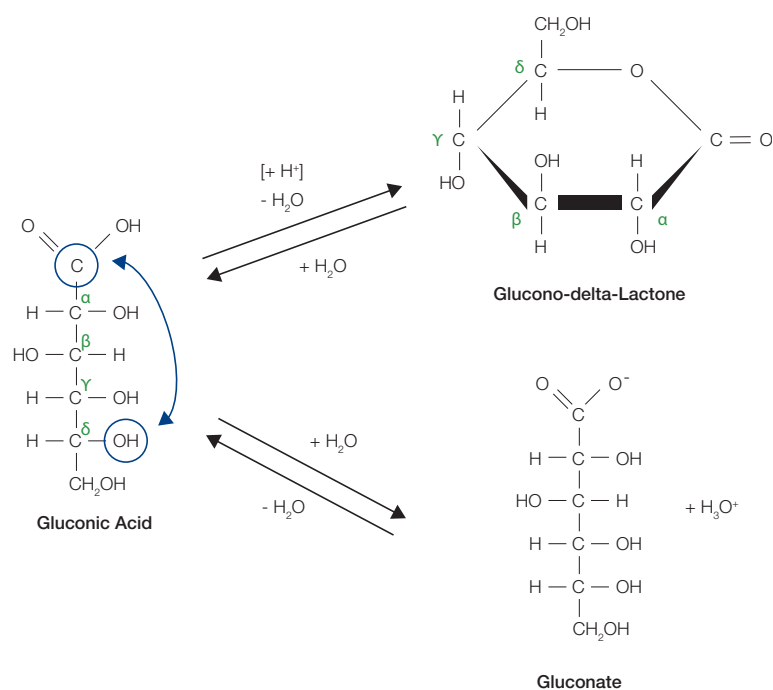
Gluconic Acid

Figure 1: Chemical structures of alpha-hydroxy acids, beta-hydroxy acids and polyhydroxy acids

The numerous hydroxyl groups of polyhydroxy acids such as GdL make these molecules bigger and bulkier than other hydroxy acids. This slows down their ability to penetrate into the skin, and prevents therefore the irritation and sensitivities often associated with alpha-hydroxy acids, while still allowing efficient exfoliation. In consequence, polyhydroxy acids would appear to be compatible with clinically sensitive skin conditions, including rosacea and atopic dermatitis. Furthermore, it has been proven that GdL can provide free-radical scavenging effects – specifically, protection against damage from UV radiation. This has been attributed to its ability to chelate oxidation-promoting metals.<sup>[4]</sup>

GdL is a neutral cyclic ester of gluconic acid. When added to an aqueous solution it rapidly dissolves and forms different chemical species: gluconic acid, gluconate, glucono-delta-lactone and glucono-gamma-lactone.<sup>[5]</sup> These species are shown in figure 2, with the exception of glucono-gamma-lactone, which is a minor species.

Two predominant, pH-dependent equilibrium processes occur between these chemical species. The first, the lactone hydrolysis, is a slow process forming gluconic acid, of which the proton dissociates and hence acidifies the medium. The deprotonation of gluconic acid, on the other hand, is a rapid process leading to the formation of gluconate ions.



**Figure 2: Equilibrium between Gluconic Acid and related chemical species**

The pH value of cosmetic formulations determines the predominant chemical species and must therefore be carefully adjusted to achieve the desired function of GdL. Detailed information relating to this aspect of GdL can be found in our flyer “How to use Glucono-delta-lactone in Personal Care”.<sup>[6]</sup>

For exfoliation to be efficient, the GdL or gluconic acid must be able to pass through the stratum corneum, which is the outermost layer of the epidermis and hence of the skin. The stratum corneum is composed of several layers of corneocytes, which are primary cells, being separated by a complex mixture of multilamellar lipid sheets.<sup>[7]</sup> In addition to these, there are lipids on the surface of the skin that are secreted by sebaceous glands and form part of the "acid mantle" of the stratum corneum. Therefore, to pass through the superficial layer of the epidermis, the GdL, or more generally the hydroxy acid, has to be in its uncharged, free acid form to create as many interactions as possible with the lipophilic, nonpolar stratum corneum. In other words, exfoliation products should have a pH value lower than the  $pK_a$  (acid dissociation constant) of the hydroxy acid used to ensure that the free acid form is predominant in the aqueous media.

## Objectives of the study

A study using a simple leave-on face serum as a vehicle and based on clinical-dermatological test criteria was conducted to assess the exfoliating and skin tolerance properties of GdL.

## Literature research

A literature research was carried out to identify representative values for the test formulation in terms of GdL concentration and pH, and to define the most promising performance parameters for study. It was not possible to draw definite conclusions as to a “standard” dosage or pH from studies investigating the effect of GdL (and other exfoliating acids) on the skin. Reported GdL concentrations ranged from 2.5% up to 14%, and pH values lay between 3.6 and 4.3.<sup>[4,8,9,10]</sup> Performance parameters also varied widely between studies, including parameters such as photodamage, skin irritation potential and anti-acne effect.<sup>[4,8,10,11]</sup> An overview of the literature is given in table 1.

**Table 1: Overview of studies on GdL efficacy with regard to skin-related parameters<sup>[4,8,9,10,11]</sup>**

Reference	Treatments	Concentration [%]	pH	Vehicle	Parameters
Berardesca <i>et al.</i> 1997	GdL	8	4.3	Cream	Skin barrier (evaporimetry), skin irritation (chromametry)
	Glycolic Acid		4.4		
	Lactic Acid		4.4		
	Tartaric Acid		3.4		
Bernstein <i>et al.</i> 2004	GdL	2.5	No info	Phosphate buffered saline solution	Photodamage
		5			
		7.5			
		10			
Edison <i>et al.</i> 2004	GdL	4	3.8	Day lotion	Anti-ageing, skin irritation
		10	3.6	Night cream	
	Glycolic Acid	8	3.8	Day cream	
		8	3.7	Night cream	
		8	3.7	Night cream	
Green <i>et al.</i> 2002	Glycolic Acid	8	4.1	Cream	Photodamage
	GdL		4.2		
Hunt and Barnetson 1992	GdL	14	No info	Lotion	Acne lesions, skin tolerance
	Benzoyl Peroxide	5			

## Formulation development

To study the efficacy of GdL as an active ingredient in leave-on products, a face serum with a short ingredient list comprising seven components overall was developed (table 2). In order to rule out any bias due to individual preferences, no perfume or colorant was included in the formulation. All selected ingredients were COSMOS compliant. Based on the GdL range described as effective in literature, a concentration of 8% was chosen for the formulation. To ensure that a high proportion of GdL would be present in the acid form, the pH of the face serum was adjusted to 3.5, which is a value below the  $pK_a$  of GdL of 3.6. The combination of a high dosage of 8% GdL at a very low pH promises a potentially highly effective treatment but does raise the question of skin tolerability. Therefore, it was an explicit aim of the study to confirm the product’s mildness and suitability for daily application.

The preservative system was chosen based on its COSMOS compliance and efficacy at the pH of 3.5, at which many commonly used preservatives such as sodium benzoate may crystallise due to low solubility of the free acid. Pentylene glycol was therefore used as a pseudo broad-spectrum preservative in the face serum formulation, in combination with a minimal amount of potassium sorbate as a preservative booster. The preparation of the formulation was a straightforward cold process. All ingredients were first dissolved in the water by thorough stirring, and the pH was adjusted after 24 hours once hydrolysis of GdL was completed.

The face serum formulation as shown in table 2 was stable for at least three months at 1°C, 40°C and room temperature and passed the antimicrobial preservation test according to Ph. Eur. 5.1.3. with Criterion A.

**Table 2: Minimalist formulation of face serum with GdL for home-use study**

Phase	INCI	Brand name	Supplier	%	Function
<b>A</b>	Aqua demin.	-	-	Qs	Bulk, solubiliser
	<b>Gluconolactone</b>	<b>Glucono-delta-Lactone Personal Care Grade</b>	<b>Jungbunzlauer</b>	<b>8</b>	<b>Exfoliating agent, moisturiser</b>
	Glycerine	-	-	5	Moisturiser
	Xanthan Gum	Xanthan Gum FNCSP-PC	<b>Jungbunzlauer</b>	0.5	Thickener
	Pentylene Glycol	dermosoft® Pentiol Eco	Evonik Dr. Straetmans	5	Broad-spectrum pseudo preservative
	Potassium Sorbate	-	-	0.1	Preservative booster
<b>B</b>	Sodium Hydroxide	-	-	Qs	Neutralising agent



## Study design

The skin tolerability and efficacy of the face serum formulation with GdL was evaluated in a clinical home-use test under dermatological control, led by the independent research institute Dermatest® (Münster, Germany). The user panel comprised eleven male and nine female persons older than 13 years, showing mild to moderate facial acne. The panellists were provided with a sample of the face serum filled in pipette flasks for easy dosing. They were instructed to apply the product onto the skin twice a day (morning and evening) after cleansing and drying the face, and to ensure homogeneous application and good absorption by applying gentle pressure to the skin. Panellists were allowed to continue using their standard products for routine skin care, but had to omit other peeling or exfoliating products. The overall study period was four weeks.

Upon completion of the study the panellists were asked for a subjective rating of the product based on a questionnaire. This comprised 22 questions about the occurrence of undesirable skin reactions, improvement of skin appearance, product haptics and overall liking of the product.

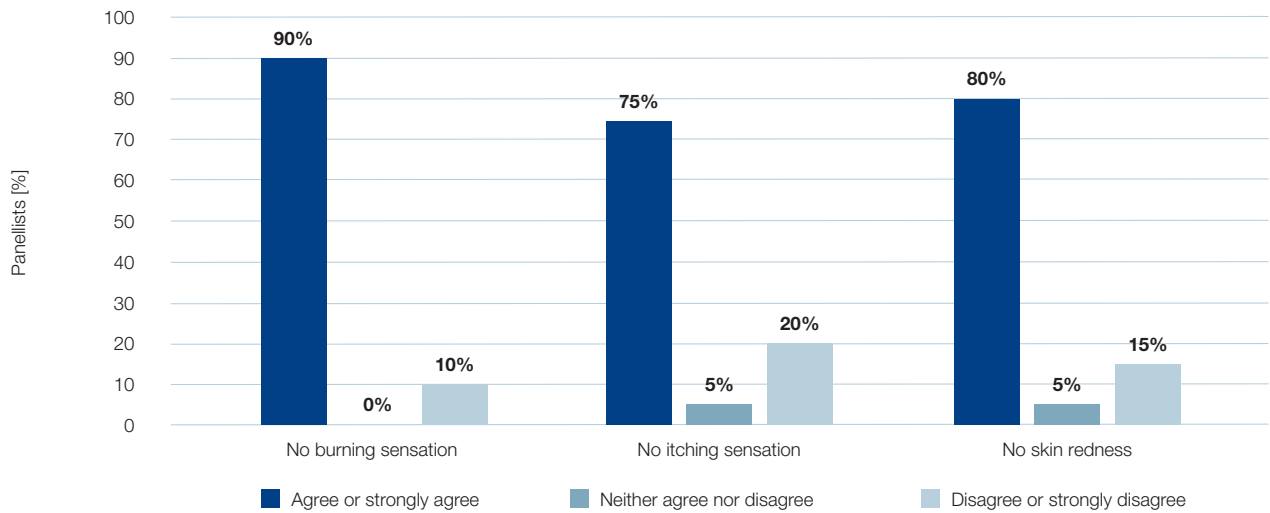
In addition, product performance was evaluated objectively. The skin sebum content was measured using a Sebumeter® SM 815 (Courage + Khazaka electronic GmbH, Cologne, Germany). Sebum is an oily substance secreted by sebaceous glands and is known to be one of the factors causing acne.<sup>[12,13]</sup> To analyse this, a cassette carrying a special mattified tape is pressed onto the skin, and the skin sebum makes the tape turn transparent without responding to skin moisture. The sebum content can then be quantified photometrically. These measurements were taken under constant conditions (20°C, 40–60% relative humidity) before and after the study period, probing three different spots within the test skin area each time.

For objective assessment of the change in skin appearance, efflorescences (blackheads, papules and pimples) were counted by a trained evaluator before and after the study period. Mean values were calculated from individual measurements and their percentage change over the study period was determined.

## Study results and discussion

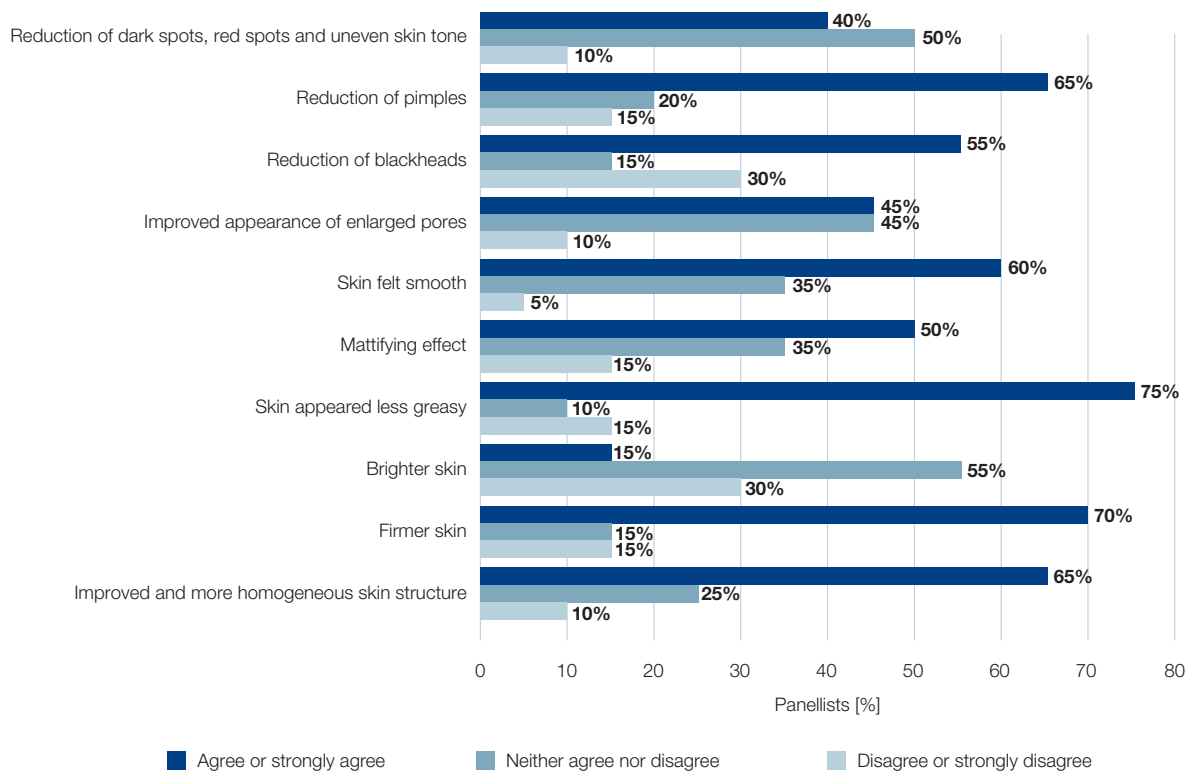
In the questionnaire, 75% of the panellists rated the product overall as good or very good, 20% were undecided and only 5% rated the product as poor. The main factor leading to a negative rating was the lack of a pleasant smell, which could be easily remedied by adding a suitable perfume. Panellists especially valued the product's simplicity of application, including easy spreadability and rapid absorption. They also highlighted aspects related to efficacy, such as improved skin appearance, refreshing and moisturising properties, and skin feeling soft and non-greasy.

In terms of skin tolerance, 85% of the panellists rated the product overall as good or very good. The majority of panellists did not perceive any burning sensations, itching or skin redness (figure 3). In fact, no intolerances such as skin irritation or allergic reaction were recorded in the clinical-dermatological examination. Therefore, the research institute confirmed the product's very good skin tolerability and awarded it the original Dermatest® 5-Star-Guarantee. This certifies formulations that have undergone long-term clinical testing with a representative and internationally recognised number of panellists applying the product to the area intended for its use.



**Figure 3: Rating of skin tolerance of the test face serum after the four-week study period**

A majority of panellists reported a significant improvement in the appearance of their skin at the end of the study period. As shown in figure 4, a reduction of skin impurities was often reported, particularly pimples (65%) and blackheads (55%). Furthermore, skin appearance was frequently perceived as less greasy (75%) and the skin seemed firmer (70%). Overall, 65% of the panellists attested that their skin structure seemed better and more homogeneous.



**Figure 4: Rating of the product performance of the test face serum after the four-week study period**

These overall positive results as obtained from the questionnaire were also confirmed by objective methods of study.

Skin sebum content was reduced by 21% during the study period, as determined by the Sebumeter® SM 815. High sebum concentrations promote the proliferation of undesirable bacteria, subsequent inflammatory responses and pore blockage.<sup>[14,15]</sup> Chemical peels based on acid exfoliants have been shown to reduce sebum production, thus effectively combating a causative agent of acne.<sup>[12,16]</sup>

Furthermore, the counting of efflorescences by trained study personnel showed that treatment with the face serum containing GdL led to the following improvements:

- Reduction of blackheads by 31%
- Reduction of pimples by 16%
- Reduction of papules by 4%

Thus, in many cases the skin appearance was visibly improved (figure 5).



**Figure 5: Example of improvement in skin appearance before (t = 0 d) and after (t = 28 d) the four-week study period**



## Conclusion

The excellent skin tolerability and efficacy of a face serum containing 8% GdL, formulated at pH 3.5, was demonstrated in a representative home-use study. A range of skin parameters were improved, such as occurrence of blackheads and papules, as well as sebum production. The positive product rating by the majority of panellists confirmed the great potential of GdL as an exfoliating agent in simple product formats. Jungbunzlauer GdL is obtained by fermentation of GMO-free renewable resources. It is safe, readily biodegradable and approved by COSMOS and NATRUE as a raw material for use in personal care. GdL is therefore a highly valuable ingredient for mild, natural yet efficacious personal care formulations.



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## About Jungbunzlauer

Jungbunzlauer is one of the world's leading producers of biodegradable ingredients of natural origin. We enable our customers to manufacture healthier, safer, tastier and more sustainable products. Due to continuous investments, state-of-the-art manufacturing processes and comprehensive quality management, we are able to assure outstanding product quality.

Our mission "From nature to ingredients®" commits us to the protection of people and their environment.

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