Jungbunzlauer

From nature to ingredients®

How to use Glucono-delta-Lactone in Personal Care

General properties of Glucono-delta-Lactone

INCI name	Gluconolactone	**Production process**	Fermentation of glucose syrup (from maize)
Characteristics	Free-flowing, white crystalline powder, practically odourless	**CAS number**	90-80-2
Solubility	Freely soluble in water (approx. 50% w/w), sparingly soluble in ethanol	**EC number**	202-016-5

NATRUE Approved

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Glucono-delta-Lactone and related chemical species

Glucono-delta-lactone (GdL) is a cyclic ester of gluconic acid. When added into an aqueous solution, it rapidly dissolves and forms different chemical species (figure 1): gluconic acid, gluconate, glucono-delta-lactone and glucono-gamma-lactone (Zhang et al., 2007).

The predominant, pH-dependent equilibrium processes are:

- Lactone hydrolysis (slow process) to form gluconic acid, leading to acidification of the medium
- Deprotonation of gluconic acid to form gluconate ions/ Protonation of gluconate to form gluconic acid (fast process)

pH adjustment in cosmetic formulations determines the predominant chemical species and is therefore crucial to achieve the desired function of glucono-delta-lactone.

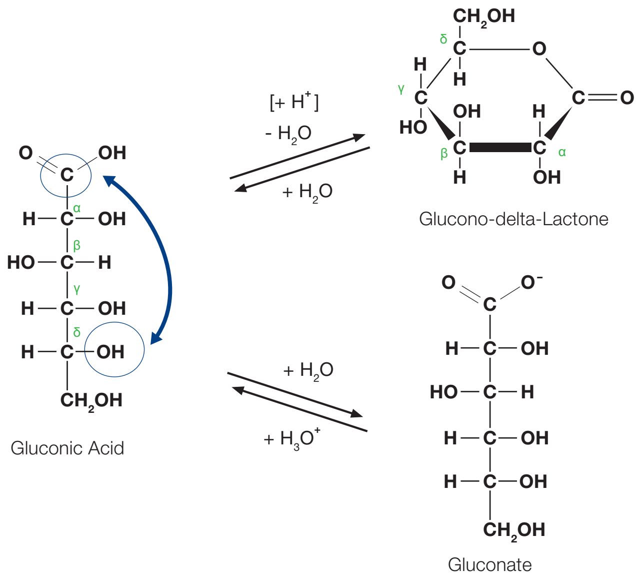


Figure 1: Equilibrium between Gluconic Acid and related chemical species

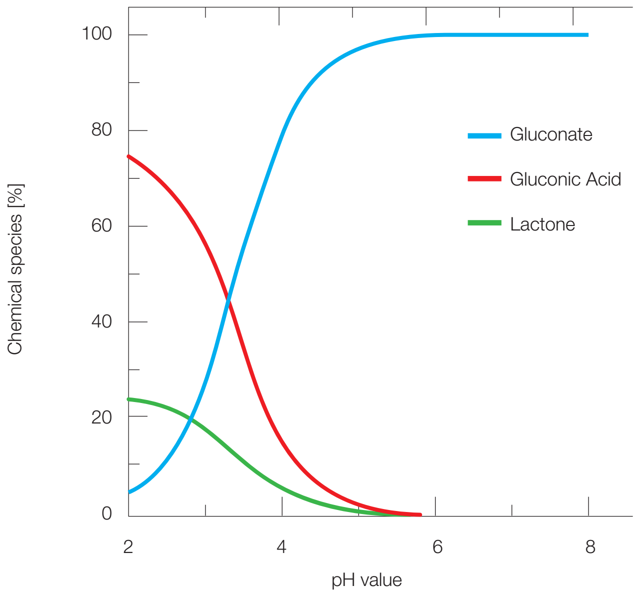


Figure 2: Distribution of chemical species depending on pH, graphic adapted from Zhang et al., 2007

The distribution of these different chemical species is represented in figure 2:

- At a pH of 3.6, there is a 1:1 ratio between gluconic acid and gluconate ions
- With increasing pH, the share of gluconic acid drops strongly: at a pH of 4.5, it is mostly in its deprotonated form (gluconate)
- Lactones are only formed at acidic pH (< 5)
- Lactones make up a minor share of chemical species

Functions of different chemical species

Purpose	Mode of action	Relevant chemical species	Favorable formulation conditions
Acidification	Proton donor	Glucono-delta-Lactone, Gluconic Acid	Aqueous phase ensuring full dissolution and hydrolysis
pH stabilisation	Proton donor/proton acceptor	Gluconic Acid, Gluconate	Aqueous phase ensuring full dissolution
Complexation	Free binding sites for positively charged divalent metal ions	Gluconate	pH > approx. 4 (increasing complexing capacity with rising pH)
Exfoliation	Penetration of skin barrier as unpolar (lipophilic) chemical species, acidification	Glucono-delta-Lactone, Gluconic Acid	Acidic medium (pH < 4.5)

Hydrolysis of Glucono-delta-Lactone into Gluconic Acid

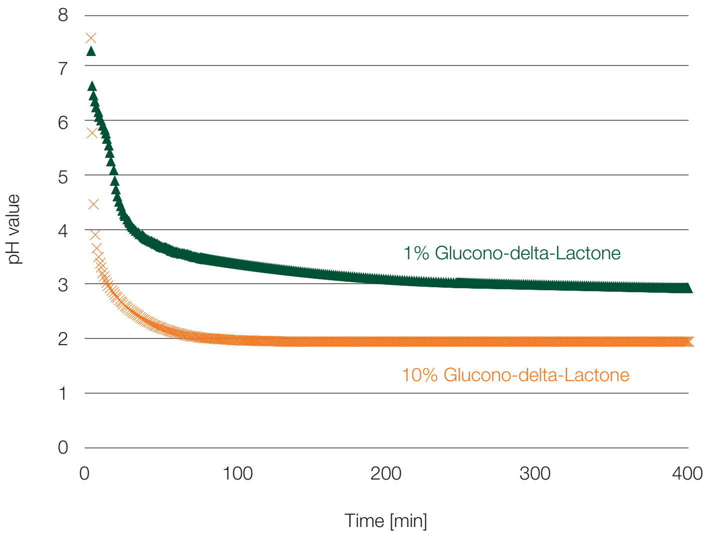


Figure 3: pH kinetics for different Glucono-delta-Lactone concentrations (T = 25 °C)

Different factors can influence the hydrolysis kinetics of glucono-delta-lactone.

- **Concentration**
  As illustrated in figure 3, the higher the glucono-delta-lactone concentration, the faster stabilises the pH
- **Temperature**
  Increasing the temperature speeds up the hydrolysis and hence the pH drop
- **Viscosity**
  Adding a thickener in the media to reach a higher viscosity does not show any impact on the pH drop as long as good mixing is ensured
- **Preservatives**
  A buffering effect is observed when adding salts of organic acids as preservative (e.g. sodium benzoate), leading to a less pronounced pH drop
- **Surfactants**
  As with preservatives, the presence of certain surfactants in the media can show a buffering effect and mitigate the pH drop

Key aspects to keep in mind when formulating with Glucono-delta-Lactone*

Viscosity and stability of emulsions
- pH and electrolytes impact emulsification, emulsion viscosity and emulsion stability
- The higher the electrolyte content, the more challenging the emulsification
- Increasing the pH of an emulsion with high glucono-delta lactone content requires a high electrolyte input, e.g. in the form of sodium hydroxide

Preservation
- Preservatives efficacy and solubility are pH dependent
- Low pH in exfoliating products requires thoughtful selection of preservatives

Viscosity of surfactant based-products
- pH and electrolytes (e.g. sodium ions) influence the viscosity of surfactant-based products
- Addition of glucono-delta-lactone acidifies the formulation and requires addition of neutralising agents (e.g. sodium hydroxide) bringing in sodium ions, potentially impacting viscosity

* *Note: these aspects are not specific to use of glucono-delta-lactone, but related to general use of acids.*

Focus on:
Emulsion stability with high content of Glucono-delta-Lactone

Matrix properties
- Leave-on product
- Emulsion
- pH = 3.2 – 4.0
- GdL content = 3 – 15% (active substance)
- GdL function: moisturising, mild but pronounced exfoliation

Product examples
- Face cream
- Body lotion

Testing of different approaches to adjust pH

Challenge
Acidification occurs slowly throughout the product manufacturing, so the momentary pH measured at the beginning of the processing is not equivalent to the one measured at the end. Especially in formulations with high glucono-delta-lactone load, large fluctuations in pH and salt concentrations occur throughout the process. Emulsification is pH- and salt-sensitive, which is why the timing of pH adjustment is important.

Goal
Identify suitable approach to add neutralising agent during emulsion preparation

Feasible approach 1
- Adjust momentary pH to target pH
- Further pH drop during processing to value below target pH
- Re-adjust final pH

Feasible approach 2
- No adjustment of momentary pH
- pH adjustment exclusively at the end of the production process

Approach 3 (not recommended)
- Adjust momentary pH to above the target pH (overcompensation) by adding a previously defined amount of base
- pH after processing = target pH
- No further adjustment of pH

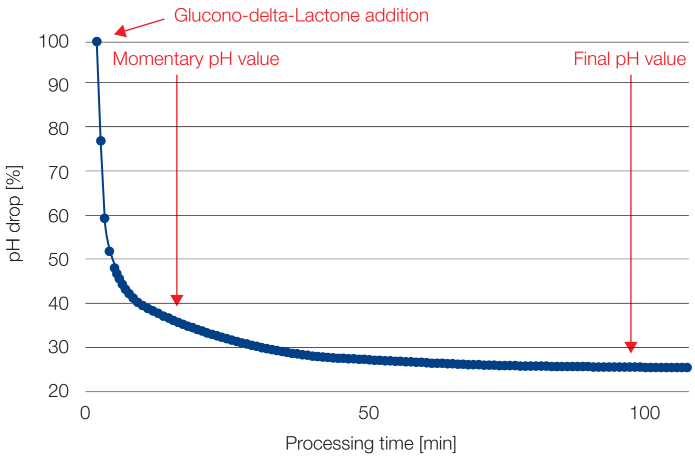
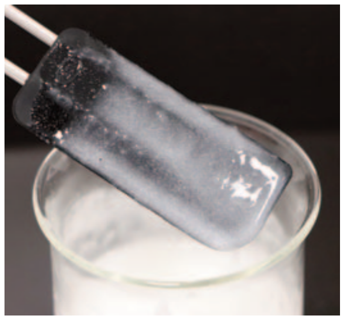


Figure 4: Exemplary pH drop during product manufacturing

Approaches 1 & 2:
Stable emulsion



Approach 3:
Instable emulsion, phase separation

Key learnings

Addition of neutralising agent
- Should be done after emulsification process to ensure a good and stable emulsion
- Sodium hydroxide is the most effective neutralising agent to adjust the pH (easy handling)
- Sodium citrate may be included as part of a buffering system

No further pH drop observed after final adjustment in the formulation
- High processing temperature of 80 °C (176 °F) for emulsions accelerates hydrolysis of glucono-delta-lactone
- Note: Emulsion stability also depends on type of emulsifier and their suitability for acidic pH

Focus on:
Preservation and exfoliating effect

Matrix properties
- Leave-on product
- Aqueous thickened, no surfactant
- pH = 3.5 – 4.5
- GdL content = 3 – 10% (active substance)
- GdL function: moisturising, mild but pronounced exfoliation

Product example
- Face serum

Choosing effective concentrations

With the multiple hydroxyl groups present within the organic acid structure, glucono-delta-lactone belongs to the category of polyhydroxy acids. Compared to alpha-hydroxy acids (AHAs) and beta-hydroxy acids (BHAs), polyhydroxy acids (PHAs) demonstrate milder exfoliating properties and hence reduce potential side effects, such as irritation or sun sensitivity.

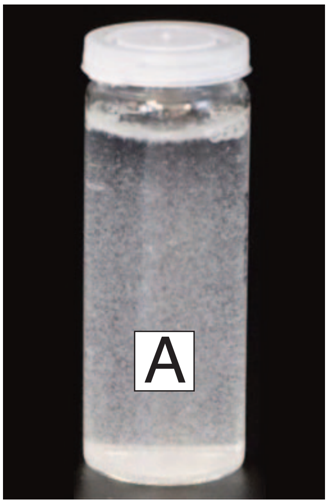
Several literature articles report about the exfoliating properties of glucono-delta-lactone:

Literature reference	Matrix	Glucono-delta-Lactone concentration	pH
Berardesca et al., 1997	Cream	8%	4.3
Edison et al., 2004	Day lotion	4%	3.8
	Night cream	10%	3.6
Green et al., 2002	Cream	8%	4.2
Hunt and Ross, 1992	Lotion	14%	–

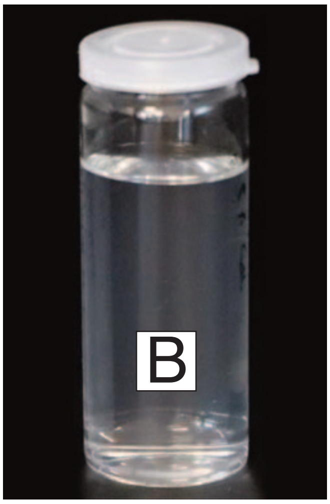
Aspects to consider regarding preservation

Explanation
- Salts of organic acids (e.g. sodium benzoate) represent an important class of preservatives
- The preservative dissociates when added in solution
- The addition of glucono-delta-lactone can lead to a drop of pH under the pK_a of the preservative
- The undissociated form of the preservative becomes predominant (e.g. benzoic acid)
- Having a low water solubility, the acid form of the preservative starts to crystallise

Recommendations
- Combine different preservative classes, e.g. organic acids and surfactants
- Consider solubility limit and pK_a of the preservative



A: Instable (crystallisation)
8.0% Glucono-delta-Lactone
0.5% Sodium Benzoate
0.1% Potassium Sorbate



B: Stable
8.0% Glucono-delta-Lactone
1.0% Benzyl Alcohol, Caprylyl Glycol

Key learnings

Exfoliating effect
- For mild exfoliating products, glucono-delta-lactone concentrations between 5 – 10% are a good starting point
- Formulating at a pH around 3.6 ensures the presence of significant amounts of effective acid and lactone forms

Preservation
- Identifying a suitable preservative system compatible with a high acid content and a low pH can be a challenge
- When using salts of organic acids, solubility limit and pK_a of the acid form should be taken into account
- Different preservative classes can be combined

Focus on:
Viscosity in surfactant-based products

Matrix properties
- Rinse-off product
- Aqueous, surfactant-based
- pH = 4.2 – 4.5
- GdL content = 0.1 – 1%
- GdL function: pH adjustment

Product example
- Shampoo
- Shower gel

Generic formulation example

Ingredients	%
Water demin.	Q.s.
Main and co-surfactant (active substance)	12%
Glucono-delta-Lactone	1%
Preservative	1%
Buffering agent (e.g. NaOH)	Q.s.

Challenge

- pH and electrolytes (e.g. sodium ions) influence the viscosity of products based on certain surfactant classes, e.g. alcohol ether sulfates
- With increasing sodium ions concentration, viscosity reaches a peak and then collapses
- Glucono-delta-lactone addition acidifies the formulation and requires addition of neutralising agents (e.g. sodium hydroxide, sodium citrate, sodium gluconate), which bring in sodium ions and can thus impact viscosity

Key learnings

Addition of neutralising agent
- Sodium hydroxide is one of the most effective bases to increase pH to the target range in a personal care formulation

Viscosity
- No effect on viscosity in this formulation example (further addition of salt to thicken)
- This may be different in surfactant-based products with high glucono-delta-lactone content
- Consider: Surfactant choice influences pH and possibility of salt-thickening

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