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Succinic acid:
a promising multi-functional ingredient for cosmetic and personal-care applications

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ABSTRACT

Formulators of cosmetic and personal-care products are on an endless quest for new and innovative ingredients that are effective, safe and sustainable.
Traditionally, Succinic Acid was produced synthetically (from fossil oil) or by distillation of amber (expensive), and therefore it is not yet extensively used as an ingredient in the industry. However, with the introduction of affordable, 100% natural succinic acid the interest for this raw material in cosmetics and personal care has strongly increased.

Furthermore, research shows that succinic acid can deliver multiple benefits when used in topical products. This paper highlights a number some of reported topical uses of succinic acid, as well as results of preliminary studies demonstrating the anti-microbial activity of Biosuccinium® S, a 100% natural succinic acid.

INTRODUCTION

It is estimated that the global personal-care market will be worth approximately USD 550 billion in 2020 with an annual growth of 3.5-4.5% (1).
The industry has been seeing a steady increase in demand for greener and more sustainable ingredients.
Green Chemistry has been playing a major role to provide cosmetic ingredients that are no longer based on non-renewable resources, e.g. petroleum, but on sustainable and renewable biomasses.
The publication of the principles of Green Chemistry in 1998 (2) was soon followed by a plethora of studies setting the foundations for the future manufacture of greener chemicals.
Traditionally distilled from amber, Succinic Acid was then commercially derived from petroleum (3).
However, studies on its production from microbial conversion of glucose have been published since the late 1990's (4).
BIOSUCCINIUM® S (INCI: Succinic Acid) is a 100% natural, ECOCERT-certified ingredient derived from non-GM, renewable vegetable feedstock.
It is readily biodegradable (OECD 301 E) and has shown a favourable toxicological profile.
The present article will outline novel uses of Succinic Acid in cosmetic and personal-care applications.

SUCCINIC ACID AND ITS POTENTIAL COSMETIC BENEFITS

Succinic Acid is an aliphatic dicarboxylic acid described by the empirical formula $C_4H_6O_4$; its chemical structure can be seen in Figure 1. It is a naturally occurring substance, and plays a crucial role in various biological processes in almost any living organism, The succinate anion is involved in the Tricarboxylic Acid (TCA) Cycle, a primary metabolic pathway used to produce chemical energy in the presence of O_2 (5). Furthermore, succinate links cellular metabolism, especially ATP formation, to the regulation of cellular function.

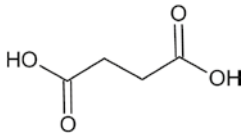

Figure 1. Chemical structure of Succinic Acid.

Succinic Acid is widely used in the food industry as a chelating agent and as a pH adjuster.
The FDA has granted Succinic Acid with the GRAS status (Generally Recognised as Safe Substance) (6).
Studies conducted within the food industry show Succinic Acid has anti-oxidant properties (7): even though this does not imply the same will be exerted when the substance is applied topically, it gives an indication that suitable tests could be carried out to understand whether Succinic Acid maintain such effect once formulated in a cosmetic product.
Succinic Acid is also used as an intermediate to manufacture several chemicals, amongst which raw materials for the cosmetic and personal-care industry, e.g. emollients, surfactants and emulsifiers.
Nevertheless, the use of Succinic Acid as an ingredient in cosmetic applications is very limited.
In the last 12 months (i.e. from December 2016 to December 2017), less than 0.1% of cosmetic and personal-care products launched globally contained Succinic Acid (8), mostly combined with other organic acids.
In the Authors' opinion Succinic Acid shows properties that can be of interest in cosmetic science.
Table 1 shows a summary of basic physico-chemical data.

Empirical Formula	$C_4H_6O_4$
Molecular Weight	118.09 $gmol^{-1}$
Appearance	White crystalline powder
Solubility (H_2O, 25°C)	83 gl^{-1}
Acidity	pKa_1 = 4.19
	pKa_2 = 5.48

Table 1. Physico-chemical characteristics of Succinic Acid.

Succinic Acid shows a favourable solubility in water when compared to other organic acids used in cosmetic products, e.g. Sorbic Acid (approx. 1.6 gl^{-1}, H_20/25°C), Benzoic Acid (approx. 3.4 gl^{-1}, H_20/25°C) and Salicylic Acid (approx. 2.4 gl^{-1}, H_20/25°C).

A literature study has revealed several publications suggesting that Succinic Acid offers a wide array of potential topical uses, such as:

- Anti-microbial activity: studies have shown a significant activity against *P. Acnes* (9).
  This property can find applications in anti-acne treatments as a potential replacement for more difficult to use ingredients such as Salicylic Acid or as a booster for other anti-acne ingredients.
  Further studies are needed in order to prove activity against more strains, which could extend the use of Succinic Acid in product preservation.
- Succinic Acid and its derivatives show antioxidant activity. It was found that Sodium Succinate can reduce intensity of the lipid peroxidation (7).
  This can suggest a potential use in applications such as aiding product preservation, anti-pollution, etc.
- Studies in the field of oncology (11) seem to suggest a possible role in inhibiting enzymes involved in collagen degradation, thus leading to further investigations to support the use of Succinic Acid and its derivatives in anti-ageing treatments.
- Succinate has been shown to inhibit cell proliferation stimulating mitochondrial respiration (12, 13).
  This ability may be useful in the prevention of hyperproliferation at skin level, e.g. in treating psoriasis or hyperkeratosis.
  Also the increase in oxygen consumption due to succinate may accelerate cell metabolism.
- Further evidence on the role of Succinic Acid in enhancing mitochondrial activity in skin cells (14, 15), may show a potential use in products claiming skin energising and revitalising effect.
  Also, the increased oxygen consumption may accelerate fat cell metabolism, proving useful in improving lipolysis, e.g. in anti-cellulite and slimming products.

INITIAL INVESTIGATIONS ON THE ANTI-MICROBIAL ACTIVITY OF SUCCINIC ACID

Substances with anti-microbial activity are of vital importance in the cosmetic and personal-care industry.
Not only is adequately preserving products a legal requirement set by the European Cosmetic Regulation EC/1223/2009, but it is also an ethical obligation.
Microbial spoilage of topical products can induce significant health issues especially for those products that are applied onto delicate body parts, e.g. eye, mouth and genitals.
Many substances featured on Annex V (*List Of Preservatives Allowed In Cosmetic Products*) of the EC/1223/2009 are under the spot light of Regulators and this seems to open opportunities for those Formulators willing to explore the chemistry and the anti-microbial properties of alternative substances (16).
Organic Acids, e.g. Sorbic and Benzoic, have been used for decades in both food and topical applications.
One of the main problems with these substances is their poor solubility in water.
It has previously been shown that Succinic Acid shows a much higher solubility in water which could make formulation easier.
Also, Succinic Acid appears to have potential skin benefits that could meet the demand for effective multi-functional ingredients.

An initial investigation into the Minimum Inhibitory Concentration of Succinic Acid (MIC) was carried out.
Salicylic Acid was used as a benchmark.
Bacterial strains were grown on tryptic soy agar (3-4days, 37°C), whereas Candida Albicans was grown on sabouraud dextrose agar (2-3 days, 37°C). The microbial growth was measured as absorbance at 650nnm and converted in CFU/ml using a predetermined standard curve for each of the tested strains. The MIC is considered effective the lowest concentration able to inhibit the microbial growth by at least 90%.

The following strains were chosen:

- *Streptococcus Mutans*: gram-positive bacterium normally found in the human oral cavity and a significant contributor to tooth decay.
- *Propionibacterium Acnes*: gram-positive bacterium linked to acne.
- *Candida Albicans*: commensal yeast that can become pathogenic under certain conditions.
- *Gardnerella Vaginalis*: gram-variable bacterium involved in bacterial vaginosis.

Table 2 shows results of the decrease of microbial growth generated by Succinic and Salicylic Acid:

DECREASE OF MICROBIAL GROWTH (%)					
SUCCINIC ACID (% w/w)					
STRAIN TESTED	**INOCULUM (CFU/ml)**	**2.0**	**1.0**	**0.5**	**0.1**
Streptococcus Mutans	2.3E+03	>99.9	>99.9	>99.9	>99.9
Propionibacterium Acnes	1.2E+04	>99.9	>99.9	>99.9	>99.9
Candida Albicans	4.5E+04	97.02	32.12	7.71	0.0
Gardnerella Vaginalis	3.4E+03	>99.9	>99.9	>99.9	>99.9
SALICYLIC ACID (% w/w)					
STRAIN TESTED	**INOCULUM (CFU/ml)**	**2.0**	**1.0**	**0.5**	**0.1**
Streptococcus Mutans	2.3E+03	N.P.	N.P.	>99.9	>99.9
Propionibacterium Acnes	1.2E+04	N.P.	N.P.	99.36	99.27
Candida Albicans	4.5E+04	N.P.	N.P.	95.68	57.98
Gardnerella Vaginalis	3.4E+03	N.P.	N.P.	>99.9	61.43

Table 2. Results of initial decrease of microbial growth (N.P. = Not Performed due to poor solubility).

It can be observed that Succinic Acid shows a decrease of microbial growth of above 99.9% at concentration as low as 0.1% against *S. Mutans*, *P. Acnes* and *G. Vaginalis*, thus outperforming Salicylic Acid.
The superior activity of Succinic Acid is particularly evident with *G. Vaginalis*.
C. Albicans is shown to be a rather resistant strain as none of the substances achieve a decrease of microbial growth of at least 90% under the test conditions. However, Salicylic Acid shows activity against *C. Albicans* that is significantly superior to that of Succinic Acid.
Table 2 enables some initial conclusions:

- S. Mutans and P. Acnes: Salicylic Acid and Succinic Acid perform quite similar.
- *C. Albicans*: MIC for Salicylic Acid is 0.5%, whilst it is 2.0% for Succinic Acid
- *G. Vaginalis*: MIC for Salicylic Acid is 0.5%, whilst it is 0.1% for Succinic Acid
- *S. Mutans* and *P. Acnes*: both Succinic Acid and Salicylic Acid will be tested at lower concentration to determine their MIC.

Table 3 shows results of the further tests conducted.

DECREASE OF MICROBIAL GROWTH (%)				
SUCCINIC ACID (% w/w)				
STRAIN TESTED	**INOCULUM (CFU/ml)**	**0.1**	**0.05**	**0.01**
Streptococcus Mutans	7.4E+04	>99.9	84.09	0.0
Propionibacterium Acnes	2.8E+04	97.98	78.67	0.0
Gardnerella Vaginalis	7.5E+04	94.67	51.04	23.93
SALICYLIC ACID (% w/w)				
STRAIN TESTED	**INOCULUM (CFU/ml)**	**0.1**	**0.05**	**0.01**
Streptococcus Mutans	7.4E+04	>99.9	88.59	0.0
Propionibacterium Acnes	2.8E+04	>99.9	84.63	0.0

Table 3. Further results of decrease of microbial growth.

The Minimum Inhibitory Concentration of the two acids was determined and is shown in Table 4.

	MIC (%)	
STRAIN TESTED	**SUCCINIC ACID**	**SALICYLIC ACID**
Streptococcus Mutans	0.1	0.1
Propionibacterium Acnes	0.1	0.1
Candida Albicans	2.0	0.5
Gardnerella Vaginalis	0.1	0.5

Table 4. MIC of Succinic Acid and Salicylic Acid.

Results obtained, even though initial and not conclusive, are supporting possible applications of Succinic Acid in products where decrease of microbial growth plays a role.
In the Authors' opinion, data particularly supports the use of Succinic Acid as a possible replacement for Salicylic Acid in anti-acne products.
Beside its anti-microbial activity against *P. Acnes*, water solubility of Succinic Acid (approx. 83 gl^{-1}, H_20/25°C) is significantly higher than that of Salicylic Acid (approx. 2.4 gl^{-1}, H_20/25°C), an ingredient notoriously difficult to formulate in aqueous media.
Succinic Acid skin friendliness combined with its activity against *G. Vaginalis* and *S. Mutans* could open possibilities respectively in feminine hygiene and oral care.
Further studies are being carried out to understand if Succinic Acid could be effectively used as an anti-microbial agent to aid product preservation.

FORMULATION EXAMPLE

A formulation example is given in Table 5.

INCI NAME	**% w/w**
Aqua	to make 100
Sorbitol	3.0
Sodium Gluconate	0.3
Pumpkin Seed Oil Polyglyceryl-4 Esters Succinate	10.0
Succinic Acid	1.0-5.0
Sodium Hydroxide	to pH 4.0-4.2
Zea Mays (Corn) Starch	3.0

Table 5. Demonstrative guidelines for the development of anti-acne and exfoliating topical treatments.

Succinic Acid is used between 1 and 5% and combined with Pumpkin Seed Oil Polyglyceryl-4 Esters Succinate, an innovative succinate-based ingredient (17) with self-emulsifying properties, to create topical treatments aimed at acne (lower use level) or gentle exfoliation (higher use level). Corn Starch (cold addition) imparts a pleasant and velvety touch and is able to absorb excess sebum.

CONCLUSIONS

Succinic Acid is not yet extensively used in cosmetic and personal-care products even though literature shows several non-topical properties that makes Succinic Acid worth testing in cosmetic applications, e.g. anti-microbial, anti-acne and anti-ageing.
Initial and not conclusive test results shown in the present article confirm some of the properties of Succinic Acid, particularly anti-microbial activity to replace less skin-friendly and less green ingredients currently used.
Further studies are needed to gain a deeper understanding of the skin and formulation benefits that Succinic Acid can deliver.
It is the Authors' opinion that Biosuccinium® S (INCI: Succinic Acid), a 100% natural, ECOCERT-certified ingredient derived from non-GM and renewable vegetable feedstock, can offer multiple opportunities to formulators of topical products seeking to use innovative and efficacious ingredients.

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