Preparation, separation and implementation of alpha-ketoglutaric acid in industrial applications

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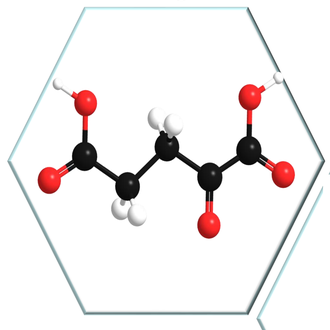
ABSTRACT and APPLICATIONS:
Keto acids such as alpha-ketoglutaric acid (AKG) are significant in biology as they are involved in anabolic metabolism, i.e. the construction of new compounds and tissues in an organism. AKG is widely used in many industries, f.e. precursor chemicals to produce food additives, diet supplements, pharmaceuticals, cosmetics, biodegradable polymers and preparations used in agriculture. Beneficial functional properties of AKG include cell protection against oxidative stress, supporting protein metabolism, immunomodulation, bone tissue regeneration, and cancer treatment.

Keto acids are currently produced by chemical synthesis. The production of keto acids involves multiple stages and the use of some toxic and explosive reagents, such as toluene, chloroform, absolute ethanol, diethyl ether or metallic sodium. Another disadvantage of chemical synthesis is the low process efficiency (below 75%) caused by the formation of undesirable by-products. Removing these by-products from the reaction mixture significantly increases the overall production cost.

Microbiological synthesis is a potential alternative to chemical keto acid production. Many species of bacteria and yeast such as *Arthrobacter paraffineus*, *Bacillus megatherium*, *Candida paludigena* and *Yarrowia lipolytica* are capable of keto acid biosynthesis. However, the cost of fermentation broth purification and preconcentration to extract the main metabolites is still high and accounts for over 50% of the cost of keto acid production by fermentation.

ADVANTAGES and FEATURES:
1. The application of a multi-stage separation process involving pressure and electrically-driven membrane processes allows for environmentally friendly and selective separation of AKG from the actual post-fermentation broth and to obtain the main product with a satisfactory purity.
2. The vacuum evaporation is high-energy consuming process and can significantly affect the total cost of AKG recovery.
3. Results from this study demonstrate the forward osmosis process as a promising method for AKG concentration.
4. The initial pH of the feed solution is an important parameter affecting mainly AKG rejection (99.7% at initial pH value equal to 5).
5. The use of the forward osmosis process allowed for a high-water recovery of 80%, even when real fermentation broth was used as the feed solution.
6. As a result of the pre-implementation work, an innovative cosmetic raw material was developed, which is a bioferment containing *Yarrowia lipolytica* yeast lysates and alpha-ketoglutaric acid obtained by biotechnology.
7. The innovative production technology of the cosmetic raw material is based on the assumptions of *Upcycling*, *Green technology and Zero waste* (low-temperature processes, eliminating the need to use toxic solvents, etc.).
8. The key competitive advantage of the proposed solution consists in: high concentration of functional substances, mainly with antioxidant potential, strong, multifunctional nourishing and regenerating, smoothing, immunomodulating and immunostimulating effect, a wide range of in vitro and in vivo test results confirming the effectiveness of the properties of the newly developed cosmetic raw material.



MEDICINES PRECURSOR

ANTI-OSTEOPOROSIS DRUG

DIETARY SUPPLEMENT

FOOD ADDIVANT

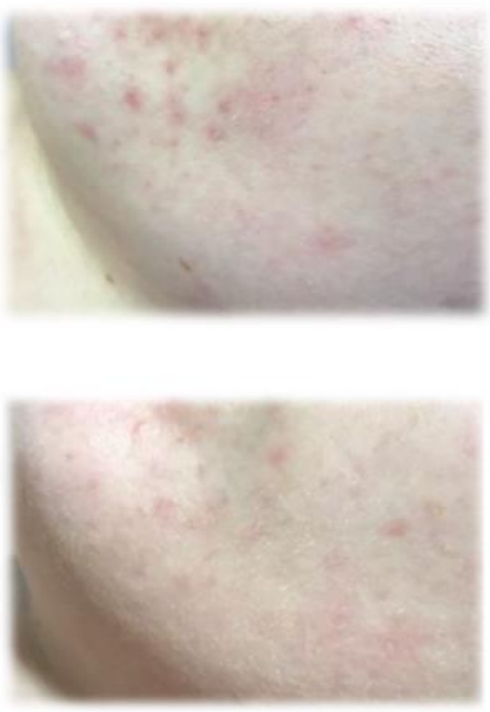
COSMETIC RAW MATERIAL

FEED ADDITIVE

CHEMICAL REAGENT

Face cream containing alpha-ketoglutaric acid obtained by biotechnological synthesis.

Improvement of skin condition and elimination of inflammation after 2 months.



Smoothing facial wrinkles after 2 months of using the cream.

INTELLECTUAL PROPERTY:
1. Method for production of alpha-ketoglutaric acid (AKG) from one-component water solutions (patent granted no PL 231635 B1)
2. Method of separating alpha-ketoglutaric acid (AKG) out of actual post-fermentation liquids by bipolar membrane electrodialysis (patent granted no PL 235896 B1)
3. Method for separation of alpha-ketoglutaric acid (AKG) from multi-component water solutions (patent granted no PL 232558 B1)
4. Method of concentration of alpha-ketoglutaric acid (AKG) from model and real digestate liquids by forward osmosis (FO) (patent granted no PL 242680 B1)
5. Method of separating alpha-ketoglutaric acid (AKG) from real digestate fluids using an integrated membrane system (patent granted no PL 242678 B1)
6. Separation of alpha-ketoglutaric acid by pressure-driven and current-driven membrane techniques from model and real fermentation broths (PhD dissertation)
7. Development of a production technology along with an assessment of the biofunctionality of an innovative cosmetic raw material containing alpha-ketoglutaric acid (know-how)

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