Modified nucleic acids as an anti-aging agents

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Abstract
The subject of the invention is the use of 4-furfurylcytosine and/or its derivatives in anti-aging compositions. As 4-furfurylcytosine and/or its derivatives possesses a series of biological properties it might be use as a composition having excellent anti-aging effect to prevent the sagging of skin and loss of luster and to improve sufficiently its aesthetic appearance without significantly change the growth rate and the total growth ability of the skin.

State of the art

Skin aging is a complex biological process influenced by a combination of endogenous or intrinsic and exogenous or extrinsic factors. Because of the fact that skin health and beauty is considered one of the principal factors representing overall “well-being” and the perception of “health” in humans, several anti-aging strategies have been developed during the last years (Ganceviciene et al., 2010)

Skin aging is a part of a natural human “aging mosaic” which becomes evident and follows different trajectories in different organs, tissues and cells with time. While the aging signs of internal organs are masked from the ambient “eyes,” the skin provides first obvious marks of the passing time. It is a complex biological process influenced by combination of endogenous or intrinsic (genetics, cellular metabolism, hormone and metabolic processes) and exogenous or extrinsic (chronic light exposure, pollution, ionizing radiation, chemicals, toxins) factors (Cevenini et al. 2008). These factors lead together to cumulative structural and physiological alterations and progressive changes in each skin layer as well as changes in skin appearance, especially, on the sun-exposed skin areas (Uitto, 1997; El-Domyati et al., 2002; Brincat et al., 2005; Scaffidi et al., 2006; Schmuth et al., 2007).

While natural aging is genetically determined, extrinsic aging can be prevented. Aesthetic dermatology should contribute to “healthy aging” not only in cosmetic means by trying to erase time vestiges in skin but by also playing a significant part in prevention, regeneration, and delaying of skin aging combining knowledge of possible local and systemic therapy, instrumental devices and invasive pro-
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The small molecules are one of the new most promising agents that could be subjected to use in cosmetology and dermatology. There was already shown a method for improving aesthetic appearance of mammalian skin by applying a composition including an effective amount of a substituted aminopurine cytokinin to mammalian skin (Bolund et al., 1992; Rattan, 1997). A composition including an effective amount of 6-(substituted amino)purine cytokinins (for example, kinetin (6-furfurylaminopurine) or the like) is applied to mammalian skin in such an amount that can improve sufficiently its aesthetic appearance, but does not significantly change the growth rate and the total growth ability of the skin. The method and composition for treating hyperproliferative skin diseases using 6-aminopurine cytokinins was also described. It has been discovered that 6-(substituted amino)purine cytokinins, such as kinetin, induce differentiation, and consequently reduce or eliminate the abnormally high rate of proliferation, of hyperproliferating associated with hyperproliferative skin diseases, such as psoriasis. Thus, this approach provides methods and compositions for treating hyperproliferative skin diseases in mammals, particularly such diseases associated with hyperproliferating epidermal cells in humans, by administering to the hyperproliferating cells associated with such a disease, in the skin of a mammal suffering from, a differentiation-inducing effective amount of a 6-(substituted amino)purine cytokinin.

The application of small molecules was also described in a method of and composition for treating inflammation and the immunological response (Clark, 1992). The plant cytokinins are effective to treat the inflammation, to accelerate healing of lesions, and to provide substantially immediate relief of pain, itching, and other immunological responses resulting from inflammation. The plant cytokinin is administered to the mammal in a suitable pharmaceutical preparation. A composition for topical use in accordance with the method comprises an effective amount of the plant cytokinin in a carrier suitable for topical application to the human skin, for example, hydrophilic ointment, isopropyl alcohol, or a powder formulation.

Despite the above described compounds, compositions and methods of manufacturing such compositions for external use showing improvement effect on skin wrinkle and inhibition effect on wrinkle-formation, compositions including cytokinins, substituted cytokinins and novel furfuryl derivatives which applied to mammalian skin in such an amount that can improve sufficiently its aesthetic appearance, there is still a need to obtain an optimal method of manufacturing compounds which show a cytostatic activity with less toxicity, used for skin preparations.

The goal of the invention is to provide a method which may be used to manufacture 4-furfurylcytosine and/or its derivatives facilitating its further use in the cosmetic and pharmaceutical industries and the use of this compound as an anti-aging preparation, to obtain an external composition for skin having excellent antiaging effect to prevent the sagging of skin and loss of luster. The embodiment of such a stated goal and the solution of problems dealing with the antiaging compositions, which may be utilized in the manufacture of anti-aging compositions and which applied to mammalian skin in such an amount that can improve sufficiently its aesthetic appearance, does not significantly change the growth rate and the total growth ability of the skin, have been achieved in the present invention.

The patent's claims:

- A cosmetic or pharmaceutical compositions comprise 4-N-furfurylcytosine and/or its derivatives, of the general formula wherein:
  - \( R_1, R_4, R_5 = \text{H, alkyl, alkenyl, alkinyl, hydroxyalkyl or aryl,} \)
  - \( R_4, R_5, R_6 = \text{H or alkyl,} \)
  - \( R_7, R_8 = \text{H, CH}_2\text{, alkyl, alkenyl, alkinyl, or hydroxyalkyl,} \)
  - \( R_9 = \text{H, D-2-deoxyriboside, D-riboside, or tetrahydro-pyranyl;} \)
The 4-N-furfurylcytosine and/or its derivatives can be apply to the cosmetic composition to the skin and that this composition includes up to 2% of the 4-N-furfurylcytosine and/or its derivatives.

The composition is a cosmetic composition that can be applied onto the skin (e.g. cream, serum, tonic, facial milk).

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