

NO-SYNTASE INHIBITORS

The present invention relates to a use of an effective quantity of at least one NO-synthase inhibitor in a cosmetic composition or for the manufacture of a pharmaceutical composition, this inhibitor or the pharmaceutical composition being intended to reduce the cutaneous irritant effect of products used topically in the cosmetic or pharmaceutical field.

It also relates to a cosmetic or pharmaceutical composition comprising an effective quantity of at least one NO-synthase inhibitor and a process of cosmetic treatment using the cosmetic composition according to the invention.

Within the framework of the present invention, the cutaneous irritant effect is a response of the skin which is most often manifested by blotches, pain or pricking, this response being generated by chemical products of natural or synthetic origin which are topically applied to the skin. This irritation is accompanied by impairment of the epithelial structure and/or function which is directly linked to the effect of the product having an irritant character.

Thus, the disruptions induced by a product having an irritant character are followed by a response of the skin which is intense to a greater or lesser degree aimed at restoring the homeostatic equilibrium which is broken or to repair the damages caused. This response may be infraclinical, that is to say without obvious inflammatory reaction to the naked eye. However, the reaction which is intense to a greater or lesser degree remains the most usual tissue response to aggression caused by an irritant product and the most disturbing for the user of this product having an irritant character.

When the product having an irritant character reaches the skin, it can react with certain pre-existing substances in the cells and the tissues and/or liberate intracellular substances. These liberated substances may, in turn, become active on other targets in the epithelium or the dermis. Thus, begins the cascade of reactions which, through the recruitment of blood cells and the substances which they liberate, give rise to the irritant process which is characterized mainly by irritation of the skin. This process is manifested in particular in various degrees, depending mainly on the quality and/or quantity of the product applied and/or the user of this product, by dysaesthetic sensations (inflammation, burning sensations, itching or pruritus, sensations of pricking, of twitching and the like), by blotches and/or by an oedema.

These products having an irritant character may be used in cosmetic or pharmaceutical, and more particularly dermatological, compositions quite obviously for other effects. Thus, they are generally used as active agents, surfactants, preservatives, perfumes, solvents or propellents for the said compositions.

However, because of their irritant character, these products are generally used in very low doses. The use of these products in small quantities may then prove to be of little advantage compared with the use of other products which are less active but less or not irritant and which are therefore used in a larger quantity.

Consequently, there is a need in the cosmetic and pharmaceutical field to find a means allowing these products to be used, without the latter exhibiting an irritant character which can be criticized by the user.

Now, the Applicant has discovered that the NO-synthase inhibitors make it possible to limit, or even suppress, the irritant character of these products.

Thus, the subject of the present invention is the use of an effective quantity of at least one NO-synthase inhibitor in a

cosmetic composition or for the manufacture of a pharmaceutical composition, this inhibitor or the pharmaceutical composition being intended to reduce the cutaneous irritant effect of products topically used in the cosmetic or pharmaceutical field.

The cosmetic or pharmaceutical composition comprising the NO-synthase inhibitor may comprise or otherwise the product capable of causing a cutaneous irritation.

In the case where these compounds exist in the same composition, the present invention also relates to a composition for topical, cosmetic or pharmaceutical use, characterized in that it comprises, in a cosmetically or pharmaceutically acceptable medium, an effective quantity of at least one NO-synthase inhibitor and at least one product capable of causing cutaneous irritation.

The pharmaceutical composition is preferably a dermatological composition.

The present invention also relates to a process of cosmetic treatment, characterized in that it uses the cosmetic composition according to the invention.

The effective quantity of at least one NO-synthase inhibitor according to the invention is a sufficient quantity of at least one NO-synthase inhibitor so that the cutaneous irritant effect decreases or even disappears. Thus, this quantity is variable depending on the quantity and the nature of the product having an irritant character which is applied. However, by way of illustration, a composition according to the invention may comprise at least one NO-synthase inhibitor at a concentration by weight of between $10^{-6}\%$ and 10% of the total weight of the composition and preferably between $10^{-4}\%$ and 1% of the total weight of the composition.

In the composition according to the invention, the quantity of the product capable of causing a cutaneous irritation may therefore correspond to a quantity which is sufficient to cause a cutaneous irritation if it was used alone (without the NO-synthase inhibitor).

Numerous topically applied products exhibit an irritant character, especially for people (users) with easily irritable skins.

Thus, even the products which are considered to be inert in a cosmetic or pharmaceutical, more particularly dermatological, composition may exhibit an irritant character when they are applied to the skin, the scalp, the nails or the mucous membranes, such as in particular preservatives, surfactants, perfumes, solvents or propellents.

Accordingly, products considered as active agents in cosmetic or pharmaceutical compositions may exhibit an irritant character when they are applied to the skin, the scalp, the nails or the mucous membranes, it is possible to speak of a secondary irritant effect, such as especially some sunscreens, α -hydroxy acids (glycol, lactic, malic, citric, tartaric, mandelic), β -hydroxy acids (salicylic acid and its derivatives), α -keto acids, β -keto acids, retinoids (retinol and its esters, retinal, retinoic acid and its derivatives, retinoids, especially those described in the documents FR-A-2,570,377, EP-A-199,636, EP-A-325,540, EP-A-402,072), anthralins (dioxanthranol), anthranoids (for example those described in the document EP-A-319,028), peroxides (especially benzoyl peroxide), minoxidil and its derivatives, lithium salts, antiproliferative agents, such as 5-fluorouracyl or methotrexate, some vitamins, such as vitamin D and its derivatives, vitamin B9 and its derivatives, hair dyes or colorants (para-phenylenediamine and its derivatives, aminophenols), perfuming alcoholic solutions (perfumes, toilet water, aftershave, deodorants), antiperspirants (some aluminium salts), depilatory or permanent waving active agents (thiols), depigmenting agents (hydroquinone), capsaicin,