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THE USE IN COSMETICS OF A NEW SYNTHETIC AMINO ACID: FURYLGLYCINE

By B. CIOCCA, P. ROVESTI and G. ROCCHEGGIANI*

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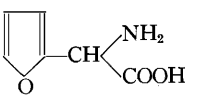
RECENTLY (1) WE REPORTED on the action of three new synthetic amino acids: *dl*-1-amino cyclohexane carboxylic acid, *dl*-1-amino 3-methyl carboxylic acid and *dl*-1-amino cyclopentane carboxylic acid.

The results obtained have induced us to continue further studies in this field. This time we have kept in mind the economic factor which plays an important part in our industry.

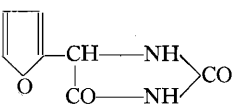
The studies have been directed toward the synthesis of an amino acid, furylglycine, whose basic material, furfural, is economically produced. Furfural is easily obtained from a variety of waste products, such as bran, straw, olive husks, wild plants, etc.

On the other hand, the chemical structure of furylglycine is of particular interest because there is a heterocyclic nucleus with a lipophilic characteristic linked to the amino and carboxylic functions (which are definitely hydrophilic).

We have also studied the action on the skin of the intermediate product in the synthesis of furylglycine (I), that is 5-furylhydantoin (II).



I



II

Quite a number of research workers having observed the close relationship between hydantoins and alpha amino acids, have suggested that hydantoic acids and hydantoins might be present in proteins.

* Piazza Amendola 1, Milan, Italy. Instituto di Ricerche su Derivati Vegetali, Milan, Italy.

The literature on this subject contains a number of interesting references. Both allantoin and derivatives of hydantoin have been used as healing agents.

Also remarkable is the stimulating action produced by these chemicals in the growth of healthy tissue and the solvent action on necrotic tissue.

You will find that the initial research on the amino acid and protein cosmetic field was carried out by the French School, followed by the Italian School which recently has been conducting research work in this field.

Essentially, amino cosmetics in their cutaneous action closely follow the principle on which is based what we call "isodermia" which considers the biochemical and physical-chemical properties of the skin in relation to the absorption of compositions of mixtures to be absorbed by the skin.

More specifically, amino cosmetics bring a special contribution to what we call "istofilia;" the necessary affinity which must exist between cosmetic raw materials and physiological and constituent properties of tissues.

The protein balance is of fundamental importance for the skin, not only in tissue growth, in production of specific proteins, hormones, enzymes, but also for the close relationship existing, for example, between lack of proteins and cutaneous dehydration, between lack of lipoproteins and dry skin and between a well-nourished skin and a healthy skin.

Like all proteins which constitute living matter, cutaneous proteins as well are not static but dynamic structures in continuous evolution and readjustment of the constituent amino acids.

And as in alimentation an indispensable minimum of proteins is necessary for sustenance, for the growth and for the energy expenditure, in order to compensate the daily consumption of amino acids, in the same way amino acid cosmetics represent an exogenous nourishment of the skin and an outside provision of nitrogenous substances needed to maintain and integrate its normal protein balance.

Treatments and beauty products which are intended to effectively "nourish" the skin cannot obviously disregard (as mainly happens today) the nitrogenous component; it is for this reason that they have to aim at a balanced composition.

Albert Fisher's studies (2) which are of fundamental importance, have demonstrated that the tissue cells are unable to demolish the blood plasma protein, while directly utilizing the amino acids for the synthesis of albuminoids necessary to create cytoplasm.

The use of the essential amino acids as predigested foods administered both parenterally and internally has long been successful in healing and substitution therapy. In dermatology a new use has been discovered. It is well known that amino acids, both in their biological complex and

isolated forms, applied locally or otherwise, do activate the cutaneous "nourishing" process, favoring granulation and healing.

Experimental

Chemical. Initially we have tried to synthesize furylglycine according to the classical Streker synthesis.

The reaction takes place in two fundamental phases: by the action of ammonia, ammonium chloride, potassium cyanide with a ketone or an aldehyde (in this case furfural), one can obtain the formation of the corresponding amino nitrile which by successive hydrolysis forms the corresponding amino acid. However, from the very beginning of the first phase, instead of the amino nitrile we have obtained some black resins.

Therefore, we had to adopt various modifications, such as working with a 50 per cent hydro-alcoholic solution; trying different emulsifiers in nitrogen atmosphere and finally at low temperature, but always with unsuccessful results.

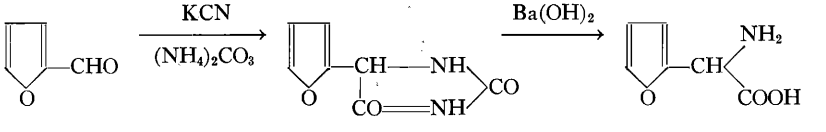
We have now adopted the method of synthesis suggested by Harvill and Herbst (4) and by Henze and Speer (5) which consists initially in the synthesis of Bückerer for the preparation of the hydantoins from aldehydes or ketones and successive opening and degradation of the nucleus with formation of the amino acid.

We have reacted 0.02 moles of furfural with 0.08 moles of ammonium carbonate and 0.04 moles of potassium cyanide in 50 cc. of 50 per cent alcoholic solution. The mixture is heated for about two hours at 58° to 60°C., and then the solution is concentrated to two-thirds of the initial volume.

After the acidification with hydrochloric acid, the 5-furylhydantoin is crystallized in an ice-bath. The product has a melting point of 147°C., and is obtained in a yield of 65 per cent.

The furylglycine is obtained by hydrolysis of 5-furylhydantoin and by means of concentrated solution of barium hydroxide. The melting point is 212° to 213°C., with decomposition. The yield is 52 per cent.

The reaction scheme is the following:



Cosmetic. The two referred chemicals have been tested in a facial mask on one-half of the face with the other half used as the control.

Then general cosmetic formulas were made as follows: the 5-furylhydantoin, which is partially liposoluble, has been previously dissolved in oleyl alcohol; the furylglycine, definitely hydrosoluble, is dissolved

in the watery phase. Both were gelatinized with bentonite 300 mesh with 10 per cent of sorbitol acting as the humectant.

After several tests made at the Dermatologic and Esthetic School of Milan and in other beauty laboratories, the following results were obtained:

(a) The best concentrations were found to be 1 per cent of 5-furylhydantoin and of 3 per cent furylglycine.
(b) The skin effects have been very evident for both chemicals. While the 5-furylhydantoin has a hydrating and tonifying action on the skin, the furylglycine has a clearing and smoothening effect on the skin. Both chemicals have also a remarkable "nourishing" effect on tissues. The tests through magnification revealed that the thin fissures of old and tired skins appear much less evident, while skin smoothness is increased.
(c) In cream, "nourishing" treatments and other cosmetics containing additional skin active constituents, the skin health improvement results are even more evident.
(d) Neither incompatibility nor allergy have been noticed up to now from the use of these two chemicals.
(e) The tests on the toxicity of the two chemicals have given results similar to those of the normal amino acids. Consequently, their use appears harmless.

Summary

In accordance with the tests carried out by us, 5-furylhydantoin and furylglycine have proved to be efficaciously active products for the skin.

Furylhydantoin (liposoluble) is different in its action from furylglycine because of its major hydrating power, while the amino acid has a marked action in minimizing skin lines.

Both products have a remarkable "nourishing" and "regenerating" action. In view of the low cost convenience of these products, we feel certain that they can find wide application in cosmetics.

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