BIOCHEMISTRY, PHARMACOLOGY AND THERAPEUTIC USE OF UREA

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Key words: Urea; Safety; Preservatives; Atopic Eczema

Synopsis

Modern dermatology looks more and more closely into "old" substances which proved to be effective and safe. In addition, most of them are much cheaper than the new compounds. Urea is one of the old substances which were used more and more often in topical therapy of dermatoses, either alone or in combination with a steroid, anthralin, retinoic acid or salicylic acid. In this paper, biochemistry and pharmacology of urea with special reference to its topical application were outlined. In many dermatoses, urea containing preparations may be successfully applied. Lastly, the possibilities of urea in cosmetology are briefly discussed.

Riassunto

L'urea è una delle sostanze più vecchie di uso dermatologico, utilizzata in terapia da sola o in associazione con steroidi, atralina, acido retinoico e acido salicilico. Viene descritto l'aspetto biochimico e farmacologico dell'urea in relazione soprattutto al suo uso topico. In molte dermatosi le preparazioni a base di urea vengono utilizzate con grande successo. Infine ne viene discusso il suo uso cosmetologico.
**Introduction**

Urea (carbamide, the diamide of carbonic acid) may be found in all organs, tissues, and body fluids.

Physiologically, urea is present on the skin surface, too, as a component of the hydrolipid emulsion. Urea here stems from sweat (content 0.4% urea) and from keratinization (end product of arginine degradation).

In former times, urea mainly was used as a diuretic and an antiedema drug. Doses amounted to 15 g per day orally or 1.0 g/kg/d intravenously. Urea was well tolerated even in these high doses.

From the beginning of the forties, urea was used for dermatological therapy in the form of creams and ointments (1, 2, 4). Numerous experimental investigations proved its valuable therapeutic actions. In the last years, urea is also increasingly found in cosmetic preparations.

In December 1988, a symposium was held in Salzburg on “Urea in dermatology”. The proceedings of this conference contain all the documentation on this topic (2).

**Pharmacological activities of urea upon topical use**

Applied externally, urea exerts a variety of dermatologically and cosmetologically important actions:

**Moisturizing action:** Urea binds water by including it into its crystal structure. In a concentration of 70%, urea is an important component of the natural moisturizing factor of normal human skin. In contrast to the effects of humectants (glycerol, propylene glycol), urea acts a moisturizer even in xerotic skin conditions. As water is the most important plastifying agent in stratum corneum, humidity significantly improves smoothness of the skin. Atopic skin with its lack of water binding capacity needs urea for its care.

**Keratolytic - keratinolytic action:** By splitting hydrogen bonds, urea in high concentrations (40%) exerts a proteinolytic (keratinolytic) activity. This effect may be used for a chemical onycholysis.

**Desquamating action:** Urea loosens the intercellular connections between the corneocytes thus facilitating desquamation of superficial cells and, on the other hand, increasing penetration. This effect may activate of drugs which are applied concomitantly with urea.

**Antimicrobial action:** By absorbing water, urea hinders the growth of microorganisms, without provoking an antimicrobial effect in the usual sense. Thus, preservation of urea-containing products needs less potential allergens in the form of the usual microbistic substances.

**Antiinflammatory action:** The antiinflammatory action of urea consists of several components: antiproliferative (in states of increased cellular turnover, only), antiedematous (topical

**Dermatotoxicology of urea**

The topical use of urea never provokes systemic resorptive effects as urea by itself is an atoxic substance.

On healthy skin, urea may be applied in concentrations up to 20%. (Due to chemical factors, such concentrations are not easy to reach!). On inflamed skin, concentrations of urea should be limited to 2 or 10%, depending upon the state of the lesions. Urea in a 40% concentration may be used for chemical onycholysis, e.g. in onychomycoses.

Urea lacks sensitizing and photodynamic activities. Urea is color- and odorless and does not stain either the skin or the linen.
“diuretic” effect, as could be demonstrated in cases of lymphostatic papillomatosis cutis verrucosa, and antipruritic (inhibitory action on enzymatic activities which promote itch).

**Dermatological indications for urea**

Topical preparations containing urea may successfully be used in a variety of dermatoses:
- Atopic eczema (therapeutic application, skin care in states of dryness and various forms of subacute and chronic, dry eczemas.
- Psoriasis vulgaris and other scaly diseases.
- Senile skin and other states of excessive dryness and itch.
- Ichthyosis
- Hyperkeratoses, keratoses.
- Chemical onycholysis, e.g. in onychomycoses.

**Urea combined with other drugs**

By its desquamating and hydrating actions, urea increases the bioavailability of other drugs. Furthermore, urea enhances the topical activity of some substances by influencing their solubility and crystal structure.

Urea can be successfully combined with the following substances:
- Glucocorticoids: The addition of urea increases the therapeutic activity of the glucocorticoids without changing the extent of undesirable actions. E.g., 1% hydrocortisone reaches the therapeutic effectiveness of 0.025% fluocinonide when 10% urea is incorporated. In combination with glucocorticoids, the antimicrobial action of urea is of special importance.
- Anthralin: The addition of 17% urea to anthralin 0.05 - 0.2% improves the antipsoriatic action, in short contact therapy as well as in day-time care. Irritation and staining by anthralin is diminished, so compliance is increased.
- Tretinoin: In severe ichthyoses, with the exception of the inflammatory and erythrodernolic forms, a combination of 0.03% tretinoin with 10% urea may be used. Such a product may also prove to be successful in stubborn cases of chronic psoriasis.
- Salicylic acid: In stubborn cases of hyperkeratoses, a combination containing 10% urea and 10% salicylic acid was recommended.

**Urea is cosmetology**

In cosmetic products, creams, ointments or best - lotions, urea is incorporated for skin care purposes in concentrations between 2 and 5%. For cosmetic purposes, the moisturizing action of urea is of greatest importance. Skin care products for senescent people should contain urea. One may assume that the use of urea is cosmetic products will steadily increase (3).

**References**