UREA REVISITED

Including clinical uses and evaluation by bioengineering techniques

EDITED BY

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INTRODUCTION

The development of modern cream emulsions has created a silent revolution in dermatology. Today, the use of emulsions as moisturizers and as a vehicle for active ingredients is a billion dollar business. However, dermatologists have shown only a relatively limited interest in the scientific evaluation of the effects of emulsions on the skin, interest being directed more towards other revolutions such as topical corticosteroids and retinoids. Consequently, scientific knowledge is concentrated mainly in the big international cosmetic companies, although this may not be very apparent, since marketing has to satisfy a world of dreams, and secrecy is a part of competition.

Urea has a long history in dermatology, originally being used for the treatment of ulcers. Today it is used as a keratolytic agent and as an active ingredient in moisturizing lotions for the treatment of ichthyosis, dry skin and various dermatitic conditions including atopy. Urea is antipruritic and antimicrobial; it potentiates also corticosteroids and dithranol. Chemically it is a small, polar molecule, having some features in common with other classical ingredients of lotions (see Fig. 1). Propylene glycol and glycerol exert some of the effects comparable to those exerted by urea, and they illustrate how the distinction between the effects of vehicles and those of active ingredients may be rather vague.

Interest in urea treatment declined in the 1970s, probably because many patients with atopic dermatitis complained of stinging sensations following the application of urea creams. This then was interpreted as being an irritant effect of urea on the skin. At that time the documentation of urea was mainly clinical. Furthermore, research methods and knowledge about the effects of irritants on the skin had not yet attained their recently achieved levels. Today, it is clear that stinging, resulting from 2%, 5% or 10% urea creams, is due to hyperosmolarity of the creams, and is not a true irritant effect of the cytotoxic type. Thus, by informing the patient, at the initiation of the treatment, that stinging is common yet harmless, misunderstandings and non-compliance may be prevented and the treatment course consequently carried to completion. Yet, in 40% occlusive application, urea is strongly keratolytic and nails may dissolve more or less selectively, with relatively minor influence on the nail bed; but this is not comparable to moisturizing treatments using creams with lower concentrations and open applications.

It was Professor Gunnar Swanbeck who, in Scandinavia, introduced modern treatment with urea. In Germany, Professor W. Wohlrab and other researchers have conducted a number of recent studies on urea. In December 1988, Professor W. Raab organized an international symposium in Salzburg, *Harnstoff in der Dermatologie*, resulting in a supplement to *Der Hautarzt* (no. IX, 1989). In Japan, Professor H. Tagami and his group have conducted a number of studies on urea and atopy, presented at different meetings. Thus, interest in urea internationally is increasing, and it may be undergoing a renaissance within dermatology.

Another revolution in dermatology was the increase in the quality of scientific documentation over recent decades and the introduction and validation of a number of new techniques. The introduction of new techniques has always been difficult. Paul Gerson Unna, the father of dermato-histo-pathology had his doctoral thesis rejected by the University of Strasbourg with a statement from Professor von Recklinghausen that: "it is not in keeping with the principles of science to draw conclusions from tissue sections that have been smeared with dyes". Staining really represents artefact, and biopsy processing changes the tissue, particularly the predominant element (i.e. water) which gets extracted. It took about 25 years for dermato-histo-pathology to be generally accepted and about 50 years to reach the high level of acceptance known today, where it is a golden standard and so well established that it is now a conservative force.

Since the introduction of urea, in the early 1970s, for the treatment of dermatitis and dry skin, a number of highly developed non-invasive or bioengineering methods have appeared. Due to noninvasiveness, in vivo situations can now be studied and followed in relation to treatments. A significant and increasing number of papers on the use of these methods are now being published in the dermatological literature. The discipline is still young, and education, standardization and interpretation may yet create significant problems. However, the methods have now reached a state where they are established and widespread in the academic community. A number of activities are initiated or organized by the International Society for Bioengineering and the Skin, and more recently by the International Society for Ultrasound and the Skin.

No man can see the water molecule, and "dry skin" (i.e. skin with literally no water content) is a fiction covering a clinical condition. The hydration state of the skin and the water barrier function clearly need to be measured. The lack of an accepted universal definition of "dry skin" allows much diversity and confusion in the field of research. Social and psychological factors contribute to the complexity. Thus there is a strongly felt need for clarification and objectivity.

One can therefore see there are good reasons to revisit urea and to update our knowledge on this useful agent, particularly in the light of developments in measuring techniques. The editor hopes that colleagues will read this supplement with interest and an open mind. The frontier of knowledge advances all the time.

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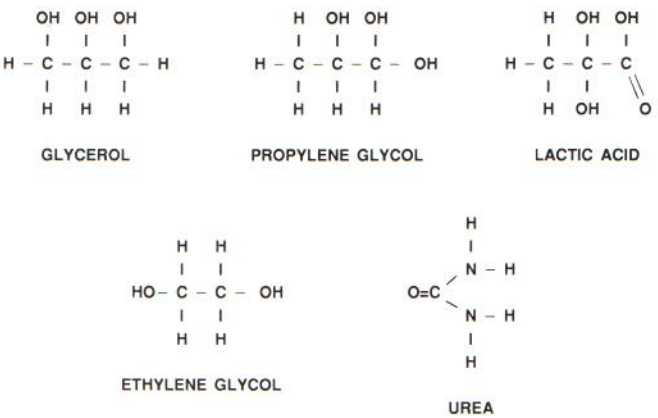

Fig. 1. Structure formula of glycerol, propylene glycol, lactic acid, ethylene glycol, and urea.

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