* THE MOLECULAR BASIS OF * SKIN IRRITATION *

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I. INTRODUCTION

A. Definitions

The molecular basis of skin imitation is defined as the adverse reactions of the cells and tissues of the skin, in terms of their constituent molecules, to the types of chemicals that may come in contact with the skin as a result of using cosmetics or skin products.

In a volume entitled "Cosmetic Science" in which skin irritation is discussed,' it should not be inferred that cosmetics and skin products in general cause skin irritation in man. Due to the stringency of national and international legislation and the social obligation of manufacturers not to market products that are hazardous to man, cosmetics may be considered to be non-irritant to the skin. Here, the phenomenon of skin irritation has been considered from the standpoint of the cosmetic chemist, whose aims include ensuring that products are non-irritant. This may be achieved by means of adequate pre- marketing safety tests to screen out potential irritants.

These tests usually involve laboratory animals and human panels, often with exaggerated conditions of application, and the total irritation potential is assessed by examination of the resultant skin reactions. Thus, an understanding of the chemical changes taking place in irritated skin may aid the interpretations of such tests.

1. Primary Imitation

Primary (non-allergic) irritation reactions are local skin responses that result in inflammation or injury at the site of application. They are elicited changes in the stratum corneum exposed to dimethyl sulphoxide that suggested it acted by dissolving the intracellular contents of the horny cells and altered the fibrillar components, but had no effect upon the cell membranes. Embery and Dugard (197 1) showed that extraction of human stratum corneum membranes with dimethyl sulphoxide removed substantial amounts of unidentified lipids and water soluble components. This was offered as a possible explanation of how the solvent reduced barrier function. But it is difficult to reconcile how extraction (i.e. removal or translocation) of such important structural components as lipids could induce changes in barrier function, when such changes were reversible after the solvent had been removed (Baker, 1968). Ember-y and Dugard also considered that reversible conformational changes in proteins of stratum corneum might result from the direct substitution by dimethyl sulphoxide molecules of water required for the integrity of the lipoprotein membranes: at high concentrations of dimethyl sulphoxide, substitution of water (solvation) is known (Rammler and Zaffaroni, 1967).

(d) *Extraction of non-lipid material from the stratum corneum* In 1952 Blank showed that the plasticity of stratum corneum was due to the presence of water, without which it would become dry and brittle. The work of Spier and Pascher (1957) identified a number of water-soluble and strongly hygroscopic substances in the stratum corneum (free amino acids, lactic, urocanic and pyrollidone carboxylic acids, urea, ammonia and sugars) that were shown to be responsible for the binding of water in the stratum corneum (Blank and Shappirio, 1955; Pier and Schwartz, 1962). Jacobi (1959) collectively described these components as the "natural moisturizer factor". Middleton (1968) proposed that the mechanism of water binding involved these hygroscopic substances that were held within the stratum corneum cells by semi-permeable lipoprotein membranes, and that treatment of the skin with lipid solvents dissolved the lipids of the semipermeable membranes, thus allowing the hygroscopic substances to be leached out and lost. Moreover, Middleton (1969) suggested that certain detergents (e.g. sodium lauryl sulphate) could dissolve these lipids and allow the intracellular hygroscopic substances to escape, as sodium lauroyl isethionate, which removed less lipids from the corneum, also had markedly less effect upon water binding capacity than sodium lauryl sulphate.

Smeenk and Polano (1965) and Smeenk (1969) showed that when human forearm skin was washed with various synthetic detergent solutions in a "washing simulator" (Vermeer *et al.,* 1963), free amino acids, soluble and insoluble proteins (i.e. horny cells) were all present in the wash liquors, in greater amounts than with just water washes.

* It is assumed that the reader is familiar with the structure and function of the skin, which have been described elsewhere to varying degrees of detail (for example, Zelickson, 1967; Breathnach, 1971; Harry, 1973; Jarrett, 1973; Menton and Eisen, 1971; Montagna and Parakkal, 1974; MacKenzie, 1975).