ABSTRACT

This thesis is concerned with contact allergy and skin irritation caused by autoxidized ethoxylated non-ionic surfactants, which are widely used components of household and industrial cleaners, topical pharmaceuticals, cosmetics and laundry products. Pure ethoxylated surfactants exert no allergenic activity, but these polyethers are susceptible to oxidation upon exposure to air, and certain of the products formed by autoxidation have been shown to act as skin sensitizers.

All compounds previously identified in such autoxidation mixtures are secondary oxidation products. Primary products formed by the autoxidation of ethoxylated surfactants are discussed on a theoretical basis in the literature, where they are described as peroxides and hydroperoxides. These types of compounds are often highly reactive and can thus be expected to cause biological damage. In the present study a primary product formed upon autoxidation of an ethoxylated surfactant has been identified for the first time. The structure of the predominant hydroperoxide thus formed from the homologously pure ethoxylated surfactant pentaethylene glycol mono-n-dodecyl ether (referred to as $C_{12}E_5$) was elucidated using HPLC-MS and NMR and this compound was subsequently synthesized, employing our experience from studies of the small model compound diethylene glycol monoethyl ether. On the basis of predictive testing in guinea pigs, this predominant hydroperoxide was identified as being a moderately potent contact allergen.

Hydroxyaldehydes, previously unknown secondary oxidation products, were also shown to be present in the mixture formed by autoxidation of $C_{12}E_5$. Analogues of these aldehydes lacking the carbon chain were synthesized and their sensitizing capacity was examined employing predictive animal testing, which revealed that the hydroxyaldehydes possess a weak sensitizing potential.

It is well known that most surfactants elicit irritant skin reactions, but possible alterations in their irritating potential as a consequence of changes in composition during handling and storage have not been studied previously. Using a patch test study with repeated exposures on human volunteers we found that autoxidized $C_{12}E_5$ is significantly more irritating to the skin than is the unoxidized surfactant.

It has been suggested that formaldehyde can be used as an indicator of the degree of autoxidation of ethoxylated surfactants and, thus, also of the sensitizing potentials of these products. Attempts to analyze formaldehyde in autoxidized ethoxylated surfactants using 2,4-dinitrophenylhydrazine derivatization and subsequent HPLC-analysis revealed that the corresponding hydrazone is formed not only from free formaldehyde, but also from primary autoxidation products during the derivatization reaction. We conclude that this derivatizing agent is inappropriate for the determination of formaldehyde in autoxidized ethoxylated surfactants.

Ethoxylated non-ionic surfactants are known to cause less skin irritation than other types of surfactants, which is why the former are often used as components of, e. g., skin-care products. The new insight presented here concerning the increase in irritation potential, as well as the formation of previously unknown allergenic oxidation products during autoxidation, may have important implications with respect to use of the ethoxylated surfactants and more detailed investigation of these phenomena is required.

Keywords: ethoxylated surfactants, autoxidation, contact allergy, skin irritation, CCET, patch testing, bioengineering methods, mass spectrometry, structural elucidation, hydroperoxides, formaldehyde

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