The 'Isothiazolinone Story'

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Over the past 10 years in Europe there has been an important increase in the use of the isothiazolinones as a biocide in industry (cutting oils, water cooling systems, paper mills, some adhesives and glues, latex emulsions, water colours and milk samplings) as well as in cosmetics (leave-on creams or shampoos) and in hygiene products such as toilet papers or moist papers [1-3]. Isothiazolinones were present in 42% of 156 cosmetic samples collected in Danish retail shops [4] and in 35% of 569 international cosmetics sold in Geneva drugstores up to the end of 1987 [pers. observation]. In fact the first cases of contact allergy were reported in 1984: 2 patients working in industry [2]. Since then, more and more observations related cases of sensitization with this preservative [see table 1 of the article by Luckner et al. in this issue (p. 91)] and an increase in contact allergy to Kathon CG [5, 6].

The isothiazolinone derivatives have more than 30 trade names, e.g. Kathon® CG, Kathon® 886 MW, Kathon® LX, Kathon® WT special, Acticide®, Algucid® CH 50, Amer-stat® 250, Euxyl® K100, Fennosan® IT21, GR 856 Izolin®, Grotan® TK 2, Mergal® K 7, Metatin® GT, Mitco® CC 31 L, Mitco® CC 32 L, Mx® 323, Parmetol® DF 35, Parmetol® DF 12, Parmetol® A 23, Parmetol® K 50, Parmetol® K 40, Parmetol® DF 18, P 3 Multan® D or Piror® P 109 [7]. Kathon CG contains 1.5% active ingredients in water stabilized by 23% of magnesium and calcium salts. The active ingredients are a mixture of 2 isothiazolinones: methylchloroisothiazolinone [5-chloro-2-methyl-4-isothiazoline-3(2H)-one] and methylisothiazolinone [2-methyl-4-isothiazoline-3(2H)-one] in a 3-to-1 weight ratio (fig. 1). Kathon CG is soluble in water, lower alcohols and glycols. It is a very effective preservative; even at low concentrations it is very active against gram+ and gram- bacteria as well as moulds and yeasts. The concentration limits recommended by the firm Rohm and Haas are 7-15 ppm (parts per million). Until recently in Europe the maximum concentration allowed was 30 ppm. The limit has been set at 15 ppm in the EEC countries since 1990.

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Methylchloroisothiazolinone

Methylisothiazolinone

Fig. 1. Composition of the active ingredients in Kathon CG.

The first Kathon CG study in Geneva was carried out between 1984 and 1986 using an epicutaneous patch test concentration of 15 ppm. This new patch test was then included in our standard battery. Eleven positive reactions (1.8%) [8] were observed out of 625 patients. This appeared to be relatively high in comparison with other results published in the meantime using a

100-ppm test concentration [9-12]. The Swiss Contact Dermatitis Research Group introduced the isothiazolinones at the concentration of 100 ppm recommended by the International Contact Dermatitis Research Group in their standard patch test series in 1987. An increasing rate of positive reactions was observed from 3.5% in 1987 [13] to 6.4% in 1988, and 5.6% from 1989 till January 1990 (see p. 94 in this issue).

Regional variations were very important between different Swiss centres as was also shown in Europe.

These could depend on: (a) the choice of the patch-tested patients; (b) the use of different cosmetics within a population. It would be very difficult, however, to trace a cosmetic containing a higher Kathon CG concentration than the recommended one!; (c) the pitfalls in patch testing [14].

In 1986, the isothiazolinone compound was accepted as a new allergen and reported in De Groot's book with 2,800 other allergens [15,16]. For this reason, it was introduced, on the recommendation of the International Contact Dermatitis Research Group, into the European standard patch testing battery among 22 other common allergens in 1989.

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However, it can be supposed that the presence of this new allergen in our environment could have been anticipated if the observations concerning the sensitizing capacity of the preservative Kathon CG [17] in the guinea pig had been taken into account. In effect, the use of the guinea pig maximization test in predictive patch testing is of great value. A compound that is a strong sensitizer in guinea pigs will be expected to show a high incidence of allergic contact dermatitis in humans when used in products of the leave-on type which are applied to both normal and damaged skin [18].

The labelling of cosmetics and toiletries must be generalized in order to prevent 'red face', perianal dermatitis or other forms of contact eczema in a Kathon-sensitized patient. Ingredient labelling should be introduced into EEC legislation as was the case in the USA 11 years ago. Both dermatologists and patients would be helped if cosmetic manufacturers declared all ingredients on their product labels and packaging. The dermatologist could then advise the patients to buy only products which are free from substances which they are allergic to [6]. This will finally benefit both the patient and the cosmetic industry! However, it must not be forgotten that the patient may also be inconvenienced by unsuspected isothiazolinone sources such as cleaning products, carpet cleaners or detergents [3]. In conclusion, every patch testing centre must be aware of cosmetic ingredients with an increasing sensitization rate, be able to trace possible sources of sensitization and discuss with the industry.

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