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Induction of contact sensitization to monotertiary butyl hydroquinone

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Key words: monotertiary butyl hydroquinone; TBHQ; contact sensitization; photosensitization; repeat insult patch test; antioxidant; CAS 1948-33-0; antioxidants; foods; cosmetics. © Munksgaard, 1997.

Monotertiary butyl hydroquinone (TBHQ) is an antioxidant. It has FDA clearance for use in foods at levels not to exceed 0.02% of oil or fat content (1). In addition, the Cosmetics Ingredients Review (CIR) Expert Panel has approved its use in cosmetics at concentrations not to exceed 0.1% (2, 3). Included in their review were 4 human repeat insult patch test (RIPT) studies in a total of 271 participants. No sensitization reactions were induced using concentrations ranging from 0.054–0.15%.

Methods and Results

There were 114 participants in an RIPT and 25 in a photosensitization study. Both studies used 0.20% TBHQ in pet., 0.2 ml of which was applied under an occluded Webril® patch (Kendall Health Care Products, Greenwood, SC, USA).

In the RIPT, induction patches were applied 3×/week for 3 weeks (4). After a 2-week rest period, a challenge

patch was applied for 1 day and reactions were scored 1 and 3 days after patch removal. In the photoallergy study, the test substance was applied to 2 different locations 2×/week for 3 weeks (5). 10 min after patch removal, 1 site was irradiated with UV light (16–20 J/cm²) while the other site acted as control. The induction period was followed by a 2-week rest period prior to application of the 1-day challenge patch. Patch sites were again irradiated and reactions were scored at 1 h and 1, 2 and 3 days post-irradiation. These studies identified 1 individual from each study with reactions suggestive of sensitization induction. The skin reaction observed in the individual from the photoallergy study occurred at both the irradiated and non-irradiated sites, indicating that irradiation was not needed for elicitation.

A 3rd study was conducted approximately 30 months later to reaffirm the sensitivity of these 2 individuals and to determine a no observable effect level (NOEL). Panelists were exposed to ascending concentrations of TBHQ (0.0003–0.02%) in 0.2 ml of pet. until a positive allergic response was elicited. Patches were left on for 2 days and sites were scored at 0.5 h and 2 days post removal. Both individuals exhibited reactions indicative of contact sensitization at concentrations of 0.010% and 0.020%. The NOEL for eliciting a reaction to TBHQ was determined to be 0.0050% (50 ppm).

Discussion

Monotertiary butyl hydroquinone has safely been used in the food and cosmetics industries for many years. There are isolated case reports of individuals exhibiting various dermatitis reactions who have tested positive to TBHQ in challenge patch tests (6–8). A lack of photosensitization in humans is in agreement with negative results seen in laboratory animal photoallergy studies

(3). Results of other guinea pig sensitization studies indicate that TBHQ is a weak sensitizer (2, 3). The studies above, along with those in laboratory animals and case reports, suggest that the potential for TBHQ to induce sensitization in humans is low when used as intended. However, these data substantiate that its use in cosmetics should be at the minimal level needed to achieve its intended effect and should not exceed the CIR recommended maximum of 0.1%. The small size of the data set, and our general information about human variation in sensitivity to contact allergens, mean that these numbers should be considered tentative approximations until more information becomes available.

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Photosensitivity due to doxycycline hydrochloride with an unusual flare

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A 42-year-old man was seen in July 1996 with scaly erythema and vesicles on the face, neck (Fig. 1), arms, and dorsa of the hands and feet that had started 3 days earlier. He had no past history of photosensitivity. He had been taking doxycycline hydrochloride (Vibramycin®, Pfizer Pharmaceut. Inc., Tokyo) 100 mg b. d., flavin adenine dinucleotide sodium 10 mg t. d. s., and pyridoxal phosphate 20 mg t. d. s. orally because of acne vulgaris for a week. There were no abnormal findings on hematological examination, blood chemistry, or uri-

nal analysis, including porphyrins of peripheral erythrocytes and urine. Histological findings of erythema on the nape of the neck demonstrated parakeratosis, hydropic degeneration of the basal layer, and perivascular edema and lymphohistiocytic infiltration. Sunburn cells were not seen.

We performed a screening phototest, as described before (1), with a Dermaray Model M-DMR-1 (Eisai Co. Ltd.) as a light source (2, 3). UVB-MED for this patient was normal (50 mJ/cm²), while 11.25 J/cm² of UVA-ir-

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