

CONTACT POINTS

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Positive rates to propyl gallate on patch testing: a change in trend

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Propyl gallate (E310) has, until recently, been used as a major antioxidant in fatty food and, in the cosmetic industry, in the manufacture of lipsticks. Propyl gallate has a high sensitizing potential; however, the frequency of allergic contact dermatitis from antioxidants of the gallate type was previously thought to be surprisingly low. Previous exposure and orally induced tolerance, as suggested by Khan and colleagues, may have explained the low rates of allergic contact dermatitis to propyl gallate in the past. The objectives were to assess the prevalence of allergic contact dermatitis to propyl gallate in our centre from 1988 to 2005. From 1988 to 2005, 9529 patients were patch tested to the face series, 6973 were females and 2556 were males. Patch tests were read at 2 D and 4 D. Positive reactions were scored as per International Contact Dermatitis Research Group recommendations as negative, +, ++, and +++ reactions. Propyl gallate was used at a 1% petrolatum (pet.). A total of 55 patients had positive reactions to propyl gallate 1% pet. (0.57%), 46 were female (0.65%) and 9 were male (0.33%). Using chi-square, there was a significant difference ($P < 0.05$) in the positivity rates between the 1988–96 period (0.45%) and the 1997–2005 period (0.77%). A review of our face series performed in the last 18 years has shown a statistically significant increase in propyl gallate-positive rates on patch testing over the last decade. An increase in its use in the cosmetic industry may well be the explanation for this. Nevertheless, a concomitant reduction of propyl gallate as an antioxidant in food, with oral tolerance being less likely to develop,

may also be a contributing factor in the increasing trend of allergic contact dermatitis caused by propyl gallate.

Key words: allergic contact dermatitis; antioxidants; lipsticks; oral tolerance; patch testing; propyl gallate.

Several chemicals are used in the cosmetic, pharmaceutical, and food industry as antioxidants to reduce oxidative deterioration and degradation of products which, otherwise, would cause rancidity. Some, like the parabens, are known to have a low sensitizing potential (1, 2). Propyl gallate (E310) has, until recently, been used as a major antioxidant in fatty food and, in the cosmetic industry, in the manufacture of lipsticks. Propyl gallate has a high sensitizing potential; however, the frequency of allergic contact dermatitis from antioxidants of the gallate type was previously thought to be surprisingly low (3). In 1992, Hausen and Beyer (4) reviewed the literature and frequency of allergic contact sensitization to gallates and found it to be increasing, propyl gallate being the most commonly implicated of the gallates. A recent report (in 2005) by the Cosmetic Review Expert panel published in USA states that in spite of an increased use of propyl gallate in the cosmetic industry (although at lower concentrations than in previous decades), sensitization rates have not increased (5). We assessed the prevalence of allergic contact dermatitis to propyl gallate in our centre from 1988 to 2005 and found it to be on the increase over the last decade. Previous exposure and orally induced tolerance, as suggested by Khan and colleagues, may have explained the low rates of allergic contact dermatitis to propyl gallate in the past. However, propyl gallate is no longer as frequently used in the food industry (D. A. Basketter, S.E.A.C. Unilever, Colworth House, Beds, UK, personal communication). The estimated average adult intake in the UK is 12–34% of the acceptable daily

intake (0.5 mg/kg) (6). It is possible that an increase in its use in the cosmetic industry and, perhaps, a reduction in oral intake, thus precluding the development of oral tolerance, may explain why the positivity rates in patch testing to propyl gallate have, indeed, experienced an increment over the last decade as predicted by Hausen and Beyer.

Methods

Patch testing at St John's Institute of Dermatology is performed according to recommendations of the International Contact Dermatitis Research Group (ICDRG). Finn Chambers are used and mounted on Scanpor tape. From 1988 to 2005, 9529 patients were patch tested to the face series, 6973 were females and 2556 were males. Patch tests were read at 2 D and 4 D. Positive reactions were scored as per ICDRG recommendations as negative, +, ++, and +++ reactions. Propyl gallate was used at a 1% petrolatum (pet.).

Results

A total of 55 patients had positive reactions to propyl gallate 1% pet. (0.57%), 46 were female (0.65%) and 9 were male (0.33%). Using chi-square, there was a significant difference ($P < 0.05$) in the positivity rates between the 1988–96 period (0.45%) and the 1997–2005 period (0.77%) (Table 1).

Discussion

Several of the antioxidants used in the cosmetic industry (creams, lotions, and lipsticks), food industry (bakery goods, frying oils, soups, sauces, chewing gum, and potato chips), and in pharmaceutical and industrial products (eardrops, suppositories, and transformer oils) include phenolic compounds such as propyl gallate, octylgallate, and laurylgallate (3).

It has long been suggested that the gallates are strong sensitizers. Khan

Table 1. Positives to propyl gallate on patch testing for face series 1988–2005

	Negatives to propyl gallate	Positives to propyl gallate	Total patch tested to face series
1988–96	5881	27 (0.45%)	5908
1997–2005	3593	28 (0.77%)	3621
Total	9474	55	9529

Degrees of freedom = 1, $\chi^2 = 3.91$, and $P < 0.05$.

and colleagues using an intradermal and epicutaneous method, this last one much less effectively, were able to sensitize guinea pigs to propyl gallate. Furthermore, they were also able to sensitize 5 of 10 human volunteers using 20% propyl gallate in 70% ethyl alcohol. By feeding some of the guinea pigs with propyl gallate prior to sensitization via an intradermal route, they were also able to suppress positivity to contact sensitization to propyl gallate. They postulated that animals that are given the contactant orally will not develop contact sensitivity to the substance when challenged later. Because propyl gallate 'contacts' virtually everyone, the minuscule magnitude of topical toxicity is best explained, according to the authors, by repeated exposures, especially via the oral route, such as occurs from chewing gums and foods (3).

Theoretically, antigen contact via the alimentary tract prior to sensitization may result in systemic immunological unresponsiveness, the so-called oral tolerance. Animal experiments with oral administration of nickel (7, 8) and, also, trinitrochlorobenzene (9) have shown induction of a high number of anergic T cells with persistent suppressor activity, leading to a down-regulation of contact sensitivity to these 2 allergens. Retrospective questionnaire studies have suggested that treatment with nickel-containing metallic orthodontic appliances before sensitization to nickel may reduce the frequency of subsequent nickel sensitization (10).

Another example of orally induced tolerance explaining low sesquiterpene lactone sensitivity in the Asian population may be due to repeated ingestion of chrysanthemum tea. The chrysanthemum flower is a member of the Asteraceae (Compositae) family. The major sensitizers, sesquiterpene lactones, are found in the leaves, stems, and flowers of this family of plants (11). In a retrospective study (13 729 patients patch tested to

standard series between 1998 and 2004) by Mak et al., the sensitization rates to sesquiterpene lactone mix 0.1% were 0.34% in Singapore and 1.37% in London. These differences were similarly seen in males and females and were statistically significant ($P \leq 0.01$) using the chi-square test. Perhaps, repeated exposure to sesquiterpene lactone through the ingestion of chrysanthemum tea induces down-regulation of any possible immune response to this allergen, thus, explaining the low sensitization rates to sesquiterpene lactone in East Asia (12, 13).

In 1992, Hausen and Beyer reviewed the literature and frequency of allergic contact sensitization to gallates and found it to be increasing, propyl gallate being the most commonly implicated of the gallates. They also predicted that this increasing trend will persist due to the fact that the excellent light protection properties of propyl gallate will make it the antioxidant of choice for the industry (4). A recent report (2005) by the Cosmetic Review Expert panel published in USA states that in spite of an increased use of propyl gallate (although at lower concentrations than in previous decades) in the cosmetic industry, sensitization rates have not increased (5). A review of our face series performed in the last 18 years do not support this and have shown a statistically significant increase in propyl gallate-positive rates on patch testing over the last decade. An increase in its use in the cosmetic industry may well be the explanation for this. Nevertheless, a concomitant reduction of propyl gallate as an antioxidant in food, with oral tolerance being less likely to develop, may also be a contributing factor in the increasing trend of allergic contact dermatitis caused by propyl gallate.

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