

CORRESPONDENCE

The effect of astaxanthin on allergic contact dermatitis in response to hair dye containing p-phenylenediamine

Hair colouring is currently widely used by women and men of all ages [1]. All hair-colouring agents can trigger allergic contact dermatitis, and *p*-phenylenediamine (PPD, 1,4-diaminobenzene) is the most common trigger. Oxidative stress may be an essential part of sensitization to contact allergy to *p*-phenylenediamine [2, 3]. Therefore, it appears that antioxidants could reduce the elicited reactions to *p*-phenylenediamine [4]. Astaxanthin has demonstrated antioxidant properties, approximately 6,000-fold stronger than that of ascorbic acid [5]. This study aimed to examine whether pre-treatment of the upper back skin with astaxanthin can reduce the elicited reaction to *p*-phenylenediamine in sensitized subjects. Thirteen volunteers with allergy associated with *p*-phenylenediamine were recruited into the trial. All participants had a history of skin symptoms after hair dying and a confirmed patch test reaction to 1% *p*-phenylenediamine. One percent *p*-phenylenediamine in petrolatum was supplied by Allertech (Smart Practice, Canada). A 0.07% Astaxanthin emulsion was purchased from Cosmaprof Company (Bangkok, Thailand). The

emulsion with or without astaxanthin (0.3 mL) was applied to the upper back on two different areas for 10 minutes and followed by the application of 1% *p*-phenylenediamine. Additionally, patch test chemicals comprising 1% *p*-phenylenediamine in petrolatum were applied to one area of the upper back and two other areas; the emulsion with or without astaxanthin was applied to the upper back as a control. Subsequently, on Day (D) 2, 3, and 7, the skin site reactions were interpreted by two experienced dermatologists according to the International Contact Dermatitis group criteria. The primary objective was to compare between the elicited reaction on the area pre-treated with an astaxanthin emulsion (Area B) and the elicited reaction on the area pre-treated with an astaxanthin-free emulsion (Area C). The results are summarised in *supplementary table 1*. A total of 13 subjects including 3 males and 10 females, aged between 20 and 70 years, participated in the study. Elicited reactions on the area pre-treated with the emulsion with astaxanthin are shown in columns 4 (D2), 7 (D3), and 10 (D7) of *supplementary table 1*. A comparison of columns 5 (D2), 8 (D3), and 11 (D7) (pre-treatment with an emulsion with non-astaxanthin) revealed that astaxanthin was associated with a lower grade of elicited reaction to the *p*-phenylenediamine in five of 12 subjects on D2 (*figure 1*), which was statistically significant ($p = 0.025$). However, a reduced reaction was demonstrated

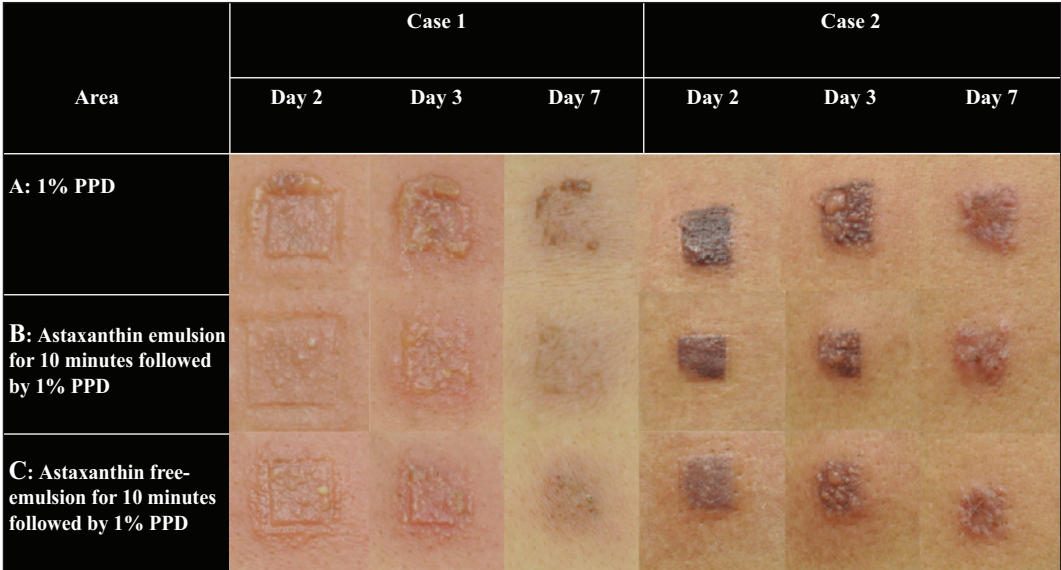


Figure 1. Characteristics of the elicited reactions on the back areas of two patients. Area A: exposure to 1% *p*-phenylenediamine in petrolatum; Area B: exposure to the emulsion with astaxanthin; Area C: exposure to the emulsion without astaxanthin.

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on D3 for one of 12 subjects ($p = 1.000$) and on D7 for two of 12 subjects which was statistically significant ($p = 0.046$).

The 0.07% astaxanthin with tocopherol, ethanol and glyceryl ester was used in our study. A previous study showed that a strong layer is formed by the co-antioxidants that helps to stabilize the emulsions. The penetration of emulsion may be more efficient with ethanol, making spreading on the skin easier [6]. No serious adverse effects were identified after the applied astaxanthin or vehicle emulsion.

In the present study, astaxanthin quenched singlet oxygen ($^1O_2$) far more rapidly and effectively than other antioxidants [7]. The role of antioxidants on the elicitation of contact allergic reactions to *p*-phenylenediamine has been elucidated in some studies; for instance, in 2016, Basketter *et al.* [8] demonstrated that adjacent skin to the hair-bearing area could be treated with ascorbic acid to reduce cosmetic allergic contact dermatitis due to hair dyeing in approximately 75% of cases, unlike the untreated skin. Furthermore, in the same year, Coenraads *et al.* [4] reported a comparison of pre-treatment with an ascorbic acid emulsion and an ascorbic acid-free emulsion and showed that ascorbic acid reduced the elicited reactions to *p*-phenylenediamine in three of 12 subjects on D3, which was statistically significant ($p = 0.046$), whereas one of the 12 subjects showed a decreased reaction ($p=0.41$) on D2. In our study, the significantly reduced elicited reactions of astaxanthin were observed on D2 after the occlusion patch test, which was earlier than that for ascorbic acid.

Application of astaxanthin emulsion pre-treatment reduced the allergenic response to *p*-phenylenediamine-containing hair dye. This study could be beneficial regarding attempts to reduce the burden of allergic contact dermatitis caused by hair dye cosmetics in sensitized subjects.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1684/ejd.2019.3654

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Radiotherapy-induced or focally enhanced autoimmune blistering diseases

Onset or exacerbation of cutaneous blistering diseases following radiotherapy is rarely reported. We report our experience by describing three clinical cases.

Patient 1: an 85-year-old woman treated by radiation therapy for Merkel cell carcinoma affecting the left elbow (*figure 1A*) developed blisters limited to the irradiated area of the left arm six months later (*figure 1B*). Histopathology revealed a subepidermal blister with an inflammatory infiltrate composed of eosinophils. Direct immunofluorescence (DIF) performed on a biopsy of irradiated skin revealed linear C3 and IgG deposition at the dermal-epidermal junction (DEJ). Indirect immunofluorescence (IIF) on salt-split skin showed linear deposition of antibodies on the epidermal side of the blister; IgG enzyme-linked immunosorbent assays (ELISAs) were negative for BP230 and BP180, but immunoblotting with epidermal extract identified anti-BP180 IgG. She was treated with clobetasol propionate 0.5% ointment for bullous pemphigoid (BP) with a four-month tapering period, without recurrence three years later. Patient 2: a 72-year-old woman with a history of two oropharyngeal squamous-cell carcinomas (2002: left tonsil treated by tonsillectomy, radiotherapy and chemotherapy; 2015: right velar treated by chemotherapy and radiotherapy) developed a pruriginous diffused blistering eruption with major involvement of the oral mucosa three years after the last course of treatment for the second squamous-cell carcinoma (*figure 1C-E*). Histopathology revealed a subepidermal blister with an inflammatory infiltrate of eosinophils. DIF identified linear C3 and IgG deposition at the DEJ with epidermal deposition on salt-split skin. ELISA revealed elevated BP180 antibodies (>199 U/mL). These findings led to the diagnosis of extensive BP with major oral involvement. Skin and oral lesions resolved under prednisone at 1 mg/kg and intravenous polyvalent immunoglobulins.

Supplementary table 1. Results of the close patch test on Day 2, Day 3, and Day 7

		Day 2			Day 3			Day 7		
Subject number	Previous patch test	PPD	AST+PPD	AST-free+PPD	PPD	AST+PPD	AST-free+PPD	PPD	AST+PPD	AST-free+PPD
1	++ (48h)	++	++	++	++	++	++	++	++	++
2	+(48h)	+	+	+	+	+	++	+	+	++
3	++ (48h)	+++	+++	+++	+++	+++	+++	+	+	++
4	+(48h)	++	++	++	++	++	++	++	+	++
5	++ (48h)	++	+	++	++	+	++	+	+	+
6	++ (72h)	++	++	++	++	++	++	++	+	+
7	++ (48 h)	+++	++	++	+++	+++	+++	++	++	++
8	++(48 h)	+++	++	+++	+++	++	++	++	+	++
9	+(72 h)	++	+	+	++	+	-	-	-	-
10	+(48 h)	++	+	++	++	++	+	++	+	+
11	+(72 h)	+++	++	+++	+++	++	++	++	+	+
12	+(48 h)	++	+	++	++	+	+	++	+	+
p-value										
AST ¹	vs PPD ²	0.008			0.025			0.014		
AST+PPD ¹	vs AST-free+PPD ²	0.025*			1.000			0.046*		
AST-free+PPD ¹	vs PPD ²	0.157			0.096			0.414		

Values are presented as frequency (%). P value corresponds to ¹Kruskal-Wallis test and ²Wilcoxon Signed Ranks test. AST: Astaxanthin; PPD: p-phenylenediamine; h: hour; +: weakly positive; ++: strongly positive; +++: extremely strongly positive.