

Potent skin sensitizers in oxidative hair dye products on the Swedish market

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Background: In recent years, the alarming increase in contact allergy to hair dyes has drawn much attention. It has been shown that many of the currently allowed hair dye substances are potent skin sensitizers.

Objectives: To study the prevalence of hair dye substances, categorized as potent skin sensitizer, in oxidative hair dye products on the Swedish market.

Materials and Methods: Ingredient labels of 122 oxidative hair dye products from 20 brands were examined. All ingredients were recorded, and the prevalence of hair dye substances categorized as potent skin sensitizers was assessed.

Results: According to ingredient labelling, 120 out of 122 examined oxidative hair dye products contained hair dye substances categorized as potent skin sensitizers. More than 80% of the products contained at least four such substances; 37 hair dye substances categorized as potent skin sensitizers were identified, and 10 of these were more prevalent than p-phenylenediamine.

Conclusions: Hair dye substances categorized as potent skin sensitizers are very common in oxidative hair dye products. A substantial number of potent skin sensitizers are more frequently used than p-phenylenediamine, while only a few are commercially available as patch test substances.

Key words: allergic contact dermatitis; consumer product safety; cosmetics; exposure analysis; hair dye; market survey; patch test; p-phenylenediamine; risk assessment. © John Wiley & Sons A/S, 2009.

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It is well known that hair dyes can cause contact allergy, sometimes resulting in reactions severe enough to require hospitalization (1, 2). Hair dye substances and other allergens are important factors in the development of occupational contact dermatitis among hairdressers, as they are more frequently and intensely exposed to these substances than the general population (3–5). Although hairdressers may be the occupational group with the highest prevalence of contact allergy to hair dyes, the majority of cases affected are probably related to consumer exposure (6). Market research indicates that the use of hair dye products has increased considerably over the last decade (7). In Denmark, 18% of men and 75% of women have dyed their hair, and the median age at first hair dyeing is 16 years (8).

Currently, oxidative hair dye products are by far the most frequently used and hold a market share of approximately 80% in the European Union and the USA (9–11).

The oxidative hair dyeing process is complex. Simplified, the products contain colourless precursors (bases and couplers), in general, aromatic amines and phenols. These are mixed with an oxidizing agent, typically hydrogen peroxide, prior to application to the hair. The low-molecular-weight precursors are taken up by the hair fibre and form larger molecules through oxidation and polymerization, resulting in coloured materials that become entrapped in the hair fibre (9, 10). p-Phenylenediamine, functioning as a base, is an extremely potent contact allergen and the most

well-known skin sensitizer in hair dye products (6, 12, 13).

More than 200 hair dye substances are currently used in hair dye products, and the risk that they may cause adverse health effects has been a focus of the European Commission hair dye strategy, where genotoxicity and carcinogenicity have been of high concern. Assessments of hair dye substances and further restrictions are in progress. In recent years, their skin-sensitizing properties have also drawn much attention in risk assessment by the European Commission's Scientific Committee on Consumer Products (SCCP) (14) and also by legislators. SCCP risk assessments are based on documentation submitted by industry, member states, and other stakeholders, including scientific publications and reports by industry on animal sensitization tests. The SCCP has categorized hair dye substances fulfilling the criteria for classification as skin sensitizers (R43) into one of three categories (moderate, strong, and extreme), according to their sensitizing potency (15, 16). Similar predictions of the skin-sensitizing properties of hair dye substances were performed based on their chemical structure (quantitative structure-activity relationship), assigning substances into the categories strong/moderate, weak, and extremely weak or non-sensitizer (17). The results of these studies indicate that many hair dye substances, currently allowed, are potent skin sensitizers in humans.

The present aim was to study the prevalence of hair dye substances, categorized as potent skin sensitizers, in oxidative hair dye products on the Swedish market.

Materials and Methods

The materials used in this study were collected during a market survey within the municipality of Botkyrka, in the County of Stockholm, Sweden. The municipality comprises approximately 80 000 people with an average age of 37, which is 3 years below the national average (18). The market survey was carried out between August and October 2008 in cooperation with the municipality's environment and health administration, which, together with the Swedish Medical Products Agency, is responsible for monitoring cosmetic products. The project also investigated whether children's cosmetic products conformed to existing regulations. The results of that study are not further discussed in this paper.

Selection of retailers, products, and target hair dyes

The study area held a varied selection of retailers of cosmetic products and the intention was that this would result in a rather representative picture

Table 1. Hair dye products included in a study of the prevalence of hair dye substances, categorized as potent skin sensitizers in oxidative hair dye products on the Swedish market. Market survey within the municipality of Botkyrka in the County of Stockholm, Sweden, August–October 2008

Company	Brand	Number of products
Creme of Nature	Super Conditioning Hair Color	2
Creme of Nature	Colors	2
Garnier	Naturligt resultat (Belle Color)	6
Garnier	Nutrisse Cream	9
Goldwell	Colorance–pH 6.8 Coloration Set	9
Jane Hellen	Mood	9
L'Oréal Paris	Casting Crème Gloss	6
L'Oréal Paris	Couleur Experte	6
L'Oréal Paris	Excellence	8
L'Oréal Paris	Récital Préférence	6
Revlon	ColorSilk	6
Schwarzkopf	Brilliance	9
Schwarzkopf	Country Colors	5
Schwarzkopf	Igora Vibrance Kit	4
Schwarzkopf	Men Perfect	3
Schwarzkopf	Poly Color	9
Schwarzkopf	Vital Colors	6
SoftSheen	Karizma	3
SoftSheen Carson	Dark and Lovely	5
Wella	Color Touch	9
Total number of hair dye products in the study		122

of the exposures of Swedish consumers. Twenty-nine retailers that were expected to sell a substantial quantity of cosmetic products to consumers were selected with the help of experienced officers at the municipality's environment and health administration. Out of the 29 retailers participating in the overall market survey, 13 were found to sell hair dye products to consumers, including grocery stores, hairdressers, hypermarkets, and beauty shops.

A total of 160 oxidative hair dye products from 20 brands (Table 1) were photographed (Canon eos 400D) on the shelves at the retailers. Then a systematic selection of products from each hair dye brand was applied, aiming at including two to three of the lightest shades, two to three of the darkest shades, and two to three shades in between, preferably with notable characteristics such as unusual colour (e.g. blue, purple, etc.) or intense colour. The purpose of this selection was to include as many brands as possible in the study and still attain a picture of which substances were present in the different brands. This strategy of selection was followed as far as possible, but could not always be applied, due to the limited number of products within some brands sold at the participating retailers. Selection was made based on the images on the packages, regardless of declared content.

Based on assessments performed by Søsted et al. (17) and the SCCP (16, 19) on the skin-sensitizing properties of hair dye substances, a list of target hair dyes was formed. The list comprised all hair dye substances categorized as strong/moderate

Table 2. Hair dye substances categorized as potent skin sensitizers (16, 17, 19), identified on the labels of 122 examined oxidative hair dye products on the Swedish market, August–October 2008. Maximum authorized concentration according to the Cosmetics Directive (76/768/EEC, consolidated version 2008-04-24) is given

INCI name	CAS No.	Maximum authorized concentration (in combination with hydrogen peroxide)	No. of products	Aromatic amine
m-Aminophenol	591-27-5	2% (1%)	83	X
o-Aminophenol	95-55-6	2% (1%)	1	X
p-Aminophenol	123-30-8	NR	31	X
5-Amino-6-chloro-o-cresol	84540-50-1	NR	4	X
2-Amino-6-chloro-4-nitrophenol	6358-09-4	2% (1%)	9	X
4-Amino-m-cresol	2835-99-6	3% (1.5%)	22	X
2-Amino-3-hydroxypyridine	16867-03-1	NR	19	X ^a
4-Amino-2-hydroxytoluene	2835-95-2	3% (1.5%)	43	X
4-Amino-2-nitrodiphenylamine-2'-carboxylic acid	117907-43-4	NR	1	X ^b
4-Amino-3-nitrophenol	610-81-1	3% (1.5%)	4	X
4-Chlororesorcinol	95-88-5	NR	22	
2,4-Diaminophenoxyethanol HCl	66422-95-5	4% (2%)	31	X
HC Red No. 3	2871-01-4	NR	5	X ^b
HC Yellow No. 2	4926-55-0	NR	7	X ^b
HC Yellow No. 5	56932-44-6	(c)	2	X ^b
Hydroxybenzomorpholine	26021-57-8	2% (1%)	9	
1-Hydroxyethyl-4,5-diaminopyrazole sulfate	155601-30-2	NR	6	X ^a
Hydroxyethyl-3,4-methylenedioxyaniline HCl	94158-14-2	3% (1.5%)	2	X ^b
Hydroxyethyl-2-nitro-p-toluidine	100418-33-5	2% (1%)	6	X ^b
Hydroxyethyl-p-phenylenediamine sulfate	93841-25-9	NR	6	X
6-Hydroxyindole	2380-86-1	NR	6	
4-hydroxypropylamino-3-nitrophenol	92952-81-3	5.2% (2.6%)	5	X ^b
Hydroxypropyl bis(N-hydroxyethyl-p-phenylenediamine) HCl	128729-28-2	3% (1.5%)	6	X ^b
2-Methyl-5-hydroxyethylaminophenol	55302-96-0	2% (1%)	18	X ^b
2-Methylresorcinol	608-25-3	2% (1%)	48	
1,5-Naphthalenediol	83-56-7	6% (3%)	4	
2,7-Naphthalenediol	582-17-2	1% (0.5%)	5	
1-Naphthol	90-15-3	2% (1%)	16	
N,N'-Bis(2-hydroxyethyl)-2-nitro-p-phenylenediamine	84041-77-0	NR	4	X ^b
N,N-Bis(2-hydroxyethyl)-p-phenylenediamine sulfate	54381-16-7	6% ^d	13	X ^b
p-Phenylenediamine	106-50-3	6% ^d	19	X
Phenyl methyl pyrazolone	89-25-8	0.5% (0.25%)	14	
Resorcinol	108-46-3	5% (2.5%)	100	
Sodium picramate	831-52-7	NR	6	X
Toluene-2,5-diamine	95-70-5	10% ^e	49	X
Toluene-2,5-diamine sulfate	615-50-9	10% ^e	49	X
2,5,6-Triamino-4-pyrimidinol sulfate	1603-02-7	NR	6	X ^a

INCI, inventory of cosmetic ingredients; CAS No., Chemical Abstract Service Registry Number; NR, no restriction under the Cosmetics Directive.

^aHeterocyclic aromatic amine.

^bN-Substituted aromatic amine.

^cThis substance is prohibited, and must not form part of the composition of cosmetic products.

^dThe accumulated content of free base of the substances is restricted to 6%.

^eThe accumulated content of free base of the substances is restricted to 10%.

skin sensitizers by Søstet et al. (17) and/or strong or extreme skin sensitizers by the SCCP (16, 19). In the present study, these substances are jointly referred to as target hair dyes or hair dye substances categorized as potent skin sensitizers.

Examination of the prevalence of target hair dyes

A total of 122 oxidative hair dye products were examined, and the study was based on information provided by their ingredient labelling and the European Commission database with information on cosmetic ingredients (CosIng) (20). No chemical analyses were performed. A relational database

and web application was created to be used as a tool in the survey of the substances of interest. All ingredients in the different parts of the products, such as colour crème, developer, and conditioner, declared on the label of each of the 122 hair dye products were manually entered into the database. An auto-text completion function linked to the downloaded inventory list (CosIng) (20) facilitated this process. Once the substances and products were in the database, it was possible to obtain information on the prevalence of target hair dyes in the examined products.

A rough categorization of products into black, dark brown, and light blonde shades was made

Table 3. The most frequently identified potent skin sensitizers on the labels of 122 examined oxidative hair dye products. Market survey in Sweden, August–October 2008

INCI name	Number of products (relative numbers in integers)	Patch test substance by C or AH
Resorcinol	100 (82%)	C, AH
m-Aminophenol	83 (68%)	C, AH
Toluene-2,5-diamine ^a	49 (40%)	AH
Toluene-2,5-diamine sulfate ^a	49 (40%)	C
2-Methylresorcinol	48 (39%)	
4-Amino-2-hydroxytoluene	43 (35%)	
2,4-Diaminophenoxyethanol HCl	31 (25%)	
p-Aminophenol	31 (25%)	C, AH
4-Amino-m-cresol	22 (18%)	
4-Chlororesorcinol	22 (18%)	
2-Amino-3-hydroxypyridine	19 (16%)	
p-Phenylenediamine	19 (16%)	C, AH
2-Methyl-5-hydroxyethylaminophenol	18 (15%)	
1-Naphthol	16 (13%)	
Phenyl methyl pyrazolone	14 (11%)	
N,N-Bis(2-hydroxyethyl)-p-phenylenediamine sulfate	13 (11%)	

C = Chemotechnique Diagnostics (2008), Malmö, Sweden.

AH = Almirall Hermal GmbH (2008), Reinbek, Germany.

^aToluene-2,5-diamine or toluene-2,5-diamine sulfate were identified on the labels of 98 (80%) of the examined products.

based on the images on the packages, regardless of declared content. The purpose was to get an indication of whether the distribution of target hair dyes differed markedly between the three groups.

Results

The results of the study are displayed in Tables 2 and 3 and Figs 1 and 2. A total of 122 oxidative hair dye products were examined. The list of target hair dyes comprised 179 substances categorized as potent skin sensitizers (16, 17, 19). Sixty-eight hair dyes assessed by Søstved et al. (17) had been prohibited for use by the Cosmetics Directive (21). They were, nonetheless, included in the list of target hair dyes in the present study, as it was considered that they could be part of hair dye products on the market.

A total of 37 different hair dye substances categorized as potent skin sensitizers were identified on the label of the 122 examined products (Table 1). Ten of the substances were more frequently identified than p-phenylenediamine. The most frequently identified are displayed in Table 3. Toluene-2,5-diamine or toluene-2,5-diamine sulfate was identified on the labels of 98 (80%) of the examined products and p-phenylenediamine on 19 (16%). Altogether, either of these substances were present in 117 (96%) of the examined products, as they were never present in the same product.

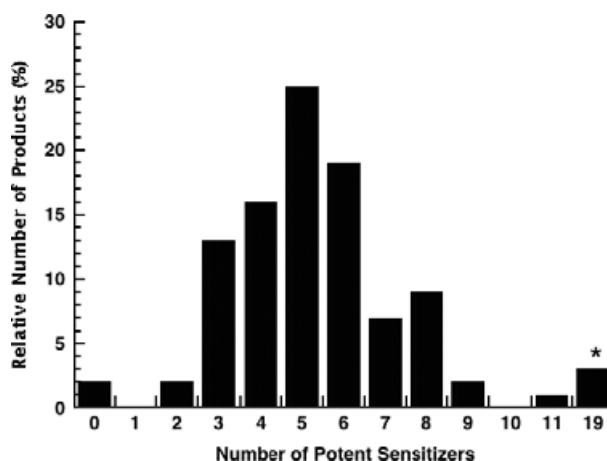


Fig. 1. Number of identified hair dye substances, categorized as potent skin sensitizers, on the labels of 122 examined oxidative hair dye products. Market survey in Sweden August–October 2008. *The symbol +/– preceded the declaration of hair dye substances in the ingredient labelling of these four products, which means that these substances *may* form part of the products' compositions. This symbol is legally restricted in the Cosmetics Directive to be used only when declaring colouring agents listed in annex IV (personal communication by Gunnar Guzikowski, Swedish Medical Products Agency). These products were, therefore, incorrectly labelled.

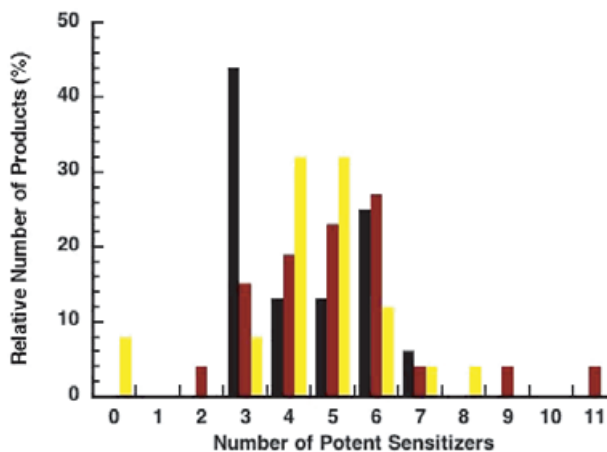


Fig. 2. Number of identified hair dye substances, categorized as potent skin sensitizers, on the labels of products with black shades (■) ($n = 16$), dark brown shades (■) ($n = 27$), and light blonde shades (■) ($n = 25$). Market survey in Sweden August–October 2008.

Out of 122 examined hair dye products, 120 were found to contain hair dye substances categorized as potent skin sensitizers. The number of hair dye substances categorized as potent skin sensitizers present in a single product ranged between 0 and 19, and more than 80% (101/122) of the examined products contained four or more, according to ingredient labelling (Fig. 1). Products with black, dark brown, and light blonde shades were declared to contain 3–7, 2–11, and 0–8 of these potent skin sensitizers, respectively (Fig. 2).

It was found that, from a legal aspect, six of the examined products were deficient. The prohibited hair dye substance HC Yellow No. 5 was found in two products, and four products were incorrectly labelled using the symbol $+/-$, indicating that the declared hair dye substances *may* be part of the products composition. This is not allowed for hair dye substances (Fig. 1).

Discussion

We found that, according to their ingredient labelling, 120 out of 122 examined oxidative hair dye products contained hair dye substances categorized as potent skin sensitizers. The results imply that these substances are very common in oxidative hair dye products on the Swedish market. A total of 37 target hair dyes were identified on the labels of the examined products, and 10 were more frequently identified than p-phenylenediamine.

p-Phenylenediamine has been the allergen of major concern in scientific reporting and diagnostic patch testing for hair dye contact allergy. Knowing that several other potent skin sensitizers now are used frequently, interest has to be broadened to include these hair dye substances. Patch test preparations are at present commercially available from Chemotechnique® or Almirall Hermal® GmbH for only 6 of 37 substances (Table 3), indicating that contact allergy to hair dye substances may be severely under-diagnosed in dermatitis patients. In a German study, 24 out of 29 patients with positive patch test reactions to their own hair dye or bleaching products had no positive reaction to any of the hair dye allergens commercially available for patch testing (22).

Several diagnostic patch test studies in dermatitis patients show high rates of contact allergy to toluene-2,5-diamine and toluene-2,5-diamine sulfate, closely following p-phenylenediamine with the highest rates (19). It has further been shown that contact allergy to toluene-2,5-diamine is an increasing problem among consumers (4, 23). Due to high and increasing rates of contact allergy, and its frequent use in hair dye products (table 3), we suggest that inclusion of toluene-2,5-diamine or its sulfate in the baseline series for patch testing should be taken into serious consideration.

In over 80% of the examined products, four or more target hair dyes were identified. This could help to explain the occasionally reported severe nature of allergic reactions to hair dyes. The combinations of potent allergens in these products may have synergistic effects on the elicitation response, due to cross-reactivity to allergens and/or multiple allergies in the subjects (2, 24). The authors' experience is that there is a general perception that

blonde hair dyes are safe to use. However, the blonde products examined in the present study did not markedly differ from other products in terms of presence of potent skin sensitizers. Although lower concentrations may be used, it is clear that these products contribute to the aggregative allergen exposure, and thus may both induce and elicit allergic contact dermatitis.

In the present study, the ingredient labelling of 122 oxidative hair dye products was examined, which, to the best of our knowledge, is the first of its kind. Sørensen et al. (17) presented data on tonnage amount used in hair dye products in Europe in the year 2002, based on information provided by industry, where the five most commonly used substances were, in descending order, toluene-2,5-diamine, resorcinol, p-phenylenediamine, 4-amino-2-hydroxytoluene, and p-aminophenol.

No chemical analyses were performed. Thus, any undeclared substance would not be detected and no information on concentrations was obtained. It is well known that cosmetic products may be incorrectly labelled and contain substances that are not declared, as has been observed with preservatives in skin creams (25, 26). Despite its limitations, studies based on ingredient labelling of such an extensive number of products and target substances can provide key information on exposure to allergens, which is not possible to obtain by chemical analyses of a limited number of substances and products. The hair dye brands included in this study are marketed both in Europe and internationally, and thus the results are of high relevance globally.

Interestingly, none of the examined products from the international brands L'Oréal Paris, Schwarzkopf, Wella, Garnier, and Goldwell contained p-phenylenediamine, according to their ingredient labelling. Is this an indication of a decreased usage of this important skin sensitizer? In contrast with this, all 12 products intended, according to manufacturers, for people of African descent were declared to contain p-phenylenediamine, indicating considerable differences in allergen exposures between consumer groups. The present study will present the baseline to a follow-up study, which could further elucidate the prevalence of potent skin sensitizers in hair dye products. Important information will be gained on how restrictions by the Cosmetics Directive may result in changed exposure to potent skin sensitizers in consumers and hairdressers. Two surveys concerning nickel on the Swedish market showed that nickel release from items covered by the Nickel Directive decreased significantly after entry into force (27, 28).

We have only focused on hair dye substances in this study. However, a wide range of other known

skin sensitizers were frequently present in the products. Apart from fragrances and preservatives, other ingredients are also worth noting. Ethanolamine was identified on the label of more than 60% (75/122) of the products. An increase in the prevalence of contact allergy to ethanolamine among dermatitis patients was recently reported, and it was suggested that they were exposed through dyeing their hair (23).

In summary, from the examination of the ingredient labelling of 122 oxidative hair dye products, we conclude that:

- (1) hair dye substances categorized as potent skin sensitizers are very common in oxidative hair dye products on the market;
- (2) a number of potent skin sensitizers are now more prevalent than p-phenylenediamine;
- (3) the majority of oxidative hair dye products contain several hair dye substances that are potent skin sensitizers; and
- (4) due to the current dominance of hair dye substances other than p-phenylenediamine, it should urgently be considered to add some of the most frequently used hair dye substances to the baseline and supplementary series for patch testing and to address these further in the regulatory control.

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