

Hair dye allergy and hair dyes in Thai market: A literature review and recommendations

Thanisorn Sukakul MD,
Pichaya Limphoka MD,
Waranya Boonchai MD.

ABSTRACT:

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DEPARTMENT OF DERMATOLOGY, FACULTY OF MEDICINE SIRIRAJ HOSPITAL, MAHIDOL UNIVERSITY, BANGKOK, THAILAND.

The era of aging population is approaching. Not only hair color provides insight into well-being, it is nowadays perceived to reflect youthfulness and attractiveness therefore greying hair is concerned by majority of population. There is increasing number of hair-dyed people along with hair dye allergy. Several chemical substances used in hair dyeing process are potent allergens; however, those substances have changed over time. Food and Drug Administration (FDA) of individual countries, including Thailand, have issued the ministerial regulations to control ingredients in hair dyes for safety of their people. As a consequence, we review all concerns of hair dyeing including categories of hair dyes, hair dye allergy, other adverse effects, hair dyes in Thai-market, and Thai-FDA regulations.

Key words: Hair dye, Hair dye allergy, Para-phenylenediamine, Herbal hair dye

From: Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Corresponding author: Waranya Boonchai MD., email: waranya.boonchai@gmail.com

บทคัดย่อ:

ธนิศร สุขะกุล, พิชญา ลิ้มโกคา, วรณญา บุญชัย เรื่องภาวะแพ้ยาย้อมผม ยาย้อมผมที่จำหน่ายในประเทศไทย และคำแนะนำที่เกี่ยวข้อง วารสารโรคผิวหนัง 2561; 34: 245-265.

ภาควิชาตจวิทยา คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล

ประชากรผู้สูงอายุเพิ่มมากขึ้นในปัจจุบัน สีมผมเป็นลักษณะหนึ่งที่บ่งบอกถึงความอ่อนเยาว์และสุขภาพที่ดี ดังนั้นการย้อมสีผมในยุคปัจจุบันจึงได้รับความนิยมมากขึ้น ยาย้อมผมประกอบด้วยสารเคมีหลายชนิด ซึ่งสารเคมีเหล่านี้สามารถทำให้เกิดผื่นแพ้ผิวหนังได้ สารเคมีในยาย้อมผมมักมีการเปลี่ยนแปลงตามยุคสมัย และพบอุบัติการณ์การแพ้สารเคมีในยาย้อมผมเพิ่มมากขึ้น ด้วยเหตุนี้ องค์การอาหารและยาในแต่ละประเทศ รวมถึงประเทศไทย จึงได้ออกกฎหมายเพื่อกำหนดสารเคมีที่สามารถใช้ในยาย้อมผม ทั้งนี้เพื่อความปลอดภัยของผู้บริโภค ดังนั้นบทความพินิจนี้จึงได้รวบรวมข้อมูลและองค์ความรู้เกี่ยวกับยาย้อมผม ได้แก่ ชนิดของยาย้อมผม ภาวะแพ้ยาย้อมผม ผลข้างเคียงของการย้อมผม และกฎหมายควบคุมสารเคมีในยาย้อมผมในประเทศไทย

คำสำคัญ: ยาย้อมผม ภาวะแพ้ยาย้อมผม พาราฟีนีนไดอะมีน ยาย้อมผมสมุนไพร

Introduction

As the era of aging population is approaching, greying hair is rather unacceptable to many people in society. Hair color reflects youthfulness and attractiveness. This results in a rising number of hair-dyed people along with hair dye allergy. Hair dyeing is the process of applying colors to natural hair. Hair dyes are widely used all over the world for the purposes of either covering the grey hair or cosmetic fashion. The history of hair dye use is estimated to begin about 4,000 years ago when the Egyptian used henna for dyeing the mummies. In the era of the Roman Empire, they used leaden combs immersed in vinegar in order to darken the grey hair.¹ There has been traced that African

and Asia women used henna or leaves of non-toxic herb for dyeing their hair.² At the present time, there are lots of newly developed hair dye products; either synthetic or botanical.

Many chemical substances used in hair dyeing process are potent allergens. Hair dye allergy was reported all over the world. Hair dyes substances have changed over time, so the new allergen has been continuously found.³ Food and Drug Administration (FDA) of individual countries, including Thailand, have to issue the ministerial regulations to control ingredients in hair dyes for safety of their people. We review all concerns of hair dyeing: categories of hair dyes, hair dye allergy, other adverse effects, hair dyes in Thai-market and Thai-FDA regulations.

Prevalence of hair dye allergy

Several ingredients in hair dye are potent sensitizers, which can cause hair dye allergy. Paraphenylenediamine (PPD), highly sensitizing compounds, and its derivatives are the most frequently agents causing allergic contact dermatitis worldwide.⁴⁻⁶ Each country has own legislation to control ingredients in consumer products, including hair dyes, sold in the market for safety of the consumers. Therefore, hair dye ingredients may be different in countries, which will reflect hair dye allergy frequently found in each population group.

Recent study of nearly 3,000 patients from 12 dermatology centers in Denmark found that 4.5% of patients resulted in positive for PPD, 2.8% to toluene-2, 5-diamine (PTD), 1.8% to *p*-aminophenol, 1% to *m*-aminophenol, and 0.1% to resorcinol.⁴ PTD was found in a higher prevalence in hair dyeing products than PPD.⁴ A study in Germany also found that PTD is the most common skin sensitizer used in hair dye.⁷

Kim H *et al* studied the potent skin sensitizers in hair dye products sold in Korea. Hair dyes sold in Korea contained numbers of potent skin sensitizers similar to those in Spain, Sweden and the United states.⁸ The common skin sensitizers in Korea were resorcinol, *m*-aminophenol, PPD, and *p*-aminophenol. Half of people who dyed hair showed positive patch test to hair dye components, 40% from PPD.⁶

Concerning, hair dye products in Thai market, there are 252 investigated products from a total of 49 brands.⁹ Twenty-five brands of those products are made domestically. Most of all hair dyes (78.6%) were oxidative permanent hair dyes. Of all products, two most common skin sensitizers were resorcinol (63.9%) and PPD (56%). Of primary intermediate, PPD were more commonly used in number of products twice as many as PTD. The most frequent skin sensitizer that was reported in domestic brands was PPD whereas the culprit of multinational brands was resorcinol.⁹ The prevalence of PPD allergy in Thai population was 2.7%.⁹ The incidence of PPD sensitization by monthly used of commercial hair dye products over a 6-month period was 1.3%.⁹

p-Phenylenediamine is the key patch test screening agent for hair dye contact allergy. Prevalence of PPD contact allergy is high across all continents.¹⁰ PPD positive patch test rates varied from 12.7-25.4% in European population.¹⁰ In Asia, the clinical relevance to hair dyes use and hair dye allergy were about 23-73% which were higher than those in Europe.¹⁰

Skin manifestations of hair dye allergy

The clinical manifestations of hair dye allergy vary according to types of allergic reactions. In general, there are 2 types of hypersensitivity

reactions: immediate type and delayed type hypersensitivity reactions.

Immediate type hypersensitivity reaction

Type I hypersensitivity reaction or immediate type hypersensitivity from hair dyes is rarely noted. Immediate reaction normally occurs within 0.5 to 1 hour after allergens contact to skin. This type of allergy can cause symptoms ranging from contact urticaria (CU), angioedema, rhinitis, bronchospasm, asthma, renal toxicity to even life-threatening condition, called anaphylaxis. Type I hypersensitivity from hair dyes can present as non-immunological CU, immunological CU, CU syndrome and CU of unknown origin. Non-immunological CU usually occurs on the site of contact without systemic reaction due to the absent of histamine released from mast cell. Thus, this type of CU cannot be inhibited by antihistamine. Immunological CU is caused by the coupling of specific IgE molecules on mast cells with specific antigens that absorb through the skin which causes the release of histamine. The diagnosis of CU syndrome includes 4 stages of symptoms ranging from local reactions to anaphylactic reactions. CU syndrome may be caused by either non-immunologic or immunologic CU mechanisms. For CU of unknown origin, overlapped clinical manifestations of both non-immunological CU and immunological CU can be observed. However, the pathological mechanism of this type of CU is not clearly understood.¹¹

Direct hair dyes, not require oxidation (peroxide) for the color to stain the hair, such as Basic Blue 99, Basic Brown 17, and patent blue dye were reported as causative agents of contact urticaria, which were confirmed by positive results in patch tests and skin prick tests in patients.¹¹ The worst clinical manifestation of this type of allergy, contact anaphylaxis caused by Basic Blue 99 in hair dyes had been reported.¹² Other composition in hair dyes such as henna, persulfate salts, PPD derivative, p-aminophenol, sodium methyl-oleoyl-taurate and 2,4-diaminophenoxyethanol-HCl were also reported to be the culprit chemical substances lead to this type of hypersensitization.^{11,13-14} Henna causing immediate reactions was infrequently reported, but it was found to be an occupational hazard causing contact urticaria in hair dressers.¹⁵

Delayed type hypersensitivity reaction

Type IV or delayed type hypersensitivity reaction is more common in hair dye allergy. The severity of reaction is vary, ranging from mild localized contact dermatitis to generalized dermatitis.^{13, 16} The typical clinical manifestations commonly present with itching, burning sensation, redness of the skin, papules, and vesicles over the scalp, forehead, hairline margin, periorbital area, ears, and neck.¹⁶⁻¹⁷ The onset may vary from a few hours to a few days after application.¹⁶⁻¹⁷ Dermatitis can find not only at head and neck, but also elsewhere, especially the hands. In

hairdressers, who have allergic reaction to hair dyes can present with chronic hand eczema as an occupational skin disease.¹⁸

PPD in permanent and semi-permanent hair dyes is the most mentioned cause of allergic contact dermatitis.¹⁹ Black or blue henna should be aware since it contains PPD that can cause skin reactions.¹⁵ However, red henna is considering safe and the exact allergen is still not identified although the compounds were tested in a few studies.¹⁵ Contact dermatitis from other substances such as direct dyes (Disperse Blue 106 and Acid Violet 43) and a coupler (resorcinol) had also been reported.²⁰⁻²¹

Other adverse effects of hair coloring

Hair dyeing can cause several adverse effects other than allergic contact dermatitis such as irritant contact dermatitis, photo-contact dermatitis and contact leukoderma.¹⁶ Other adverse reactions from hair dyes included hair loss, conjunctivitis, pigmentation, ulceration and redness.¹⁷ Brittle hair is another common adverse effect caused by the process of breaking the disulfide bonds, the hair shaft will become more hydrophilia. As a result, the hair become more swollen which made the hair more brittle. Unsurprisingly, skin staining of hair and scalp may easily cause by temporary synthetic hair dyes.⁵

Recently, there were some concerns about systemic adverse reactions from using hair dyes. Henna powder can spread into the air due to the lightness of particles and cause type I

hypersensitivity reaction of the respiratory tract which patients can be presented with rhinitis, conjunctivitis, sneezing, and asthma.¹¹ Although there were reports about genotoxicity from hair dyes in short term *in-vitro* tests, and PPD in hair dyes could induce oxidative stress with subsequent DNA damage to keratinocytes, but there is no recent consistent evidence of association between hair dyes and the toxicity in human.²²

Categories of hair dyes

Hair dyes are classified according to their origin as followings.

1. Vegetable hair dyes

Vegetable hair dyes originate from natural plants such as henna, chamomile and cinchona. The active ingredient in henna is 2-hydroxy-1,4-naphthoquinone that gives an orange shade of hair whereas chamomile results in yellowish shade.²³ In Asian countries, the walnut or logwood were used to yield for darker shade.²³ The differences shades may result from interaction of natural substance added such as lemon oil, vinegar and eucalyptus oil. Most of vegetable hair dyes are nontoxic and temporary.¹⁶ Those vegetable hair dyes contained none potent skin sensitizers.⁹ Most of Thai herbal hair dyes are vegetables hair dyes.

2. Mineral or metallic hair dyes

Mineral or metallic hair dyes such as lead acetate, lead sulfide (kohl), silver nitrate, salts of bismuth, copper, and cobalt are possible toxic

and tend to make hair brittle.¹⁶ They contained no potent skin sensitizers.⁹ The metallic hair dyes yielded darken shade of hair.²³ Red ochre (ดินเทส) is an earth pigment used for hair coloring found worldwide. It contains an anhydrous iron dioxide, a mineral hematite which gives reddish color.²⁴

3. Synthetic hair dyes

In order to understanding chemical process of synthetic hair dyes, main structures of hair are described in Figure 1. Hair shaft or hair fiber consists of 3 layers. The cuticle, the outermost part of hair shaft is made up of overlapping cells, which acts as a physical barrier against foreign matter in the environment. The cortex contains melanin pigments that determine hair colors. The medulla, an inner part of hair shaft, is a hollow core.^{5, 17}

Nowadays synthetic hair dyes are commonly used worldwide. The synthetic hair dyes are classified into four groups.^{5, 9, 17}

3.1. Temporary hair dyes

This type of hair dyes bond weakly and do not penetrate hair cortex (Figure 1a) because of their large particle size, so they easily rinse off by shampooing and reduce chance of hair damage. The dyes are made with cationic polymer to increase the ability to the bond with the hair cortex.⁵

3.2. Semi-permanent hair dyes

3.2.1 Non-oxidative semi-permanent hair dyes have no bleaching agents and are commonly

used to enhance color. Non-ionic nitro dyes are generally used. Owing to their low molecular weight, they can easily diffuse into middle layers of cuticle without binding to hair protein (Figure 1b). In addition, the dyes are also water-soluble, so they can be rinsed off after 6-8 shampooing.⁵

3.2.2 Oxidative semi-permanent synthetic dyes contain 2% hydrogen peroxide with monoethanolamine as low levels of alkalinizing agents. Therefore, their penetration property is more efficient than those of non-oxidative semi-permanent dyes.⁵

3.3 Demi-permanent hair dyes

Demi-permanent hair dyes are developed to have more long-lasting benefit than semi-permanent hair dyes. The properties of both semi- and demi-permanent hair dyes are nearly similar, except for that demi-permanent hair dyes do not contain ammonia. As they lack of ammonia, their property of lightening hair is limited.²⁵

3.4 Permanent hair dyes

Permanent hair dyes normally contain up to 6% hydrogen peroxide which is an oxidizing agent called color developer, and the alkalizing agent, ammonia. Both ammonia and hydrogen peroxide damage the cuticle to allow chemical or dye penetration. The precursors of permanent hair dyes have smaller molecules than other types of dyes, so they can easily penetrate the hair cortex (Figure 1c). Their penetration to the

hair cortex is more efficient than those of other groups of hair dyes. Their pH values usually range from 9-10.5.⁵ Dyeing hair with permanent hair dyes gives more damage to the hair fiber since they permanently bond with the hair cortex. Consequently, they are long lasting and irreversible until new hair growth. Hair coloring by permanent hair dyes occurs through the chemical processes.

The chemical processes of permanent hair dyeing

In general, the preparations of hair dyeing products in market usually have 2 kits. The first component contains primary intermediates together with couplers which called 'dye precursor' admixed with ammonia, and the other contains stabilized hydrogen peroxide solution. Permanent hair discoloration is occurred due to an oxidative process by mixing the chemicals.²⁶ The chemical process of dyeing includes oxidation process of primary intermediates, oxidation of dye precursors and coupling reaction of oxidized primary intermediates and dye precursors.

Oxidation process of primary intermediates

The first step is to lighten the natural hair color by oxidation process using alkaline hydrogen peroxide.²⁶ Primary intermediates such as arylamines (Para-Phenylenediamine; PPD, Para-toluenediamine; PTD) and para-aminophenols diffuse into the hair cortex and

dissolved melanin granules which later turn into partially fragmented melanin.^{5,17} Different shades depend on concentration of those primary intermediates, types of origin melanin and the time of reaction. Darker shades of hair require both longer time of this step and the higher concentration of primary intermediate.^{5,7}

Oxidation of dye precursors

The process of this step is to form several color couplers by oxidizing process and designate the final hair color. The couplers that commonly used are p-diamines, p-aminophenols, meta-substituted arylamines and their derivatives such as m-phenylene-diamines, m-aminophenols and resorcinol.^{5, 17, 27}

The coupling reaction of oxidized primary intermediate and color couplers

The shades of hair dye depend on the oxidization between each couplers and oxidized form of primary intermediates.⁵ This reaction forms water-resistant dye and results in large molecules of dye which are too large to diffuse back through the cuticle as shown in Figure 1.⁵

Thai herbal hair dyes

There are many herbal plants used for hair coloring. Some herbs are available worldwide, but some are traditionally planted and found only in Thailand or neighboring countries. Hair dyes from Thai herbs become popular nowadays because of rising concerns of chemical hazards in synthetic hair dyes. In the year of 2014,

Medical Plant Research Institute of Department of Medical science had promoted the application of Thai herbs in all aspects, including Thai herbal hair dyes.

Henna (เทียนกิ่ง)

Common names: Alcana, Cypress shrub, Egyptian Rivet, Henna Tree, Inai, Kok khau, Krapin, Madayanti, Mehadi, Mignonotte tree, Mong Tay, Lali, Reseda, Sinamomo²⁸

Scientific name: *Lawsonia inermis* L., *Lawsonia alba* Lam.

Henna leaves were used for hair dyeing. Henna itself can create only a golden-orange hair color. Therefore it was usually mixed with coffee or butterfly pea flowers to yield darker color.²⁹

Butterfly pea (อัญชัน)

Common names: Butterfly pea, Blue pea

Scientific name: *Clitoria ternatea* L.

Butterfly pea flower contains Anthocyanin which is used as a traditional medicine to enhance blood circulation as well as darken hair color.²⁸

Soap nut tree or Soapberry Tree (มะคำดีควาย หรือ ประคำดีควาย)

Common names: Soap nut tree or Soapberry Tree

Scientific name: *Sapindus rarak* DC. and *Sapindus trifoliatius*

Both herbs belong to SAPINDACEAE family and present the same properties. Its active

ingredients are β -Sitosterol, Emarginatoside, Quercetin, Quercetin-3-a-A-arabofuranoside, O-Methyl-Saponin, Sapindus – Saponin. Its fruit is able to reduce hair loss and can slow down grey hair.²⁸ It is used as an ingredient in hair mask products of Mamaherb® Thai brand which used for darkening hair color.

False daisy (กะเม็งตัวเมีย)

Common names: False daisy, White head, Yerbadetajo herb

Scientific name: *Eclipta prostrata* L.

False daisy trunk can be minced and mixed with coconut oil or sesame oil for hair dyeing.²⁸

Indigo (คราม)

Common name: Indigo

Scientific name: *Indigofera tinctoria*, l. sumat-rana

Indigo dye is an organic compound with dark blue crystallized powder extracted from plants. It is usually used for cotton yarn for a production of blue jeans and is occasionally used for hair coloring. Although most of herbal hair dyes rarely sensitize allergic reaction, indigo powder was reported as a culprit of allergic contact dermatitis together with henna and black tea in a 50-year-old male patient.³⁰

Cassia obovata (เทียนกิ่งขาว)

Common names: neutral henna, cassia

Scientific name: *Cassia obovata*

Neutral henna powder is extracted from *Cassia obovata* leaf which is used as a

conditioner for scalp hair. The preparation of this herb looks like red henna powder, but the color of the powder is green. It usually does not stain hair or hands except when use it with the water that dissolved with minerals. When those minerals react with the cassia, the hair can turn into green, dark brown, or greenish black.³¹

Turmeric (ขมิ้น)

Common names: Turmeric, Curcumin

Scientific name: *Curcuma longa*

Turmeric is a rhizomatous plant of the ginger family. The rhizomes can be extracted into

deep-orange color powder which is used for hair coloring.³²

Amla (มะขามป้อม)

Common names: emblic, emblic myrobalan, myrobalan, Indian gooseberry, Malacca tree

Scientific name: *Phyllanthus emblica*

The extraction of Amla fruit are used in Ayurvedic traditional medicine. It can be used in shampoos and hair oils for hair coloring and is believed to prevent premature grey hair.³³

Table 1. Showing the chemical substance that allowed to use as ingredients in hair dye products and their maximal concentration regulated by Thai FDA^{34, 36-9}

Types	Substances	Maximum concentration allowance
According to Government Gazette, book 129, part 162, 9 October 2008³⁴		
Oxidative hair dye products	1-Naphthol	2% before mixing * if mix with hydrogen peroxide, the concentration is maximal up to 1%
	Diaminophenols	10% of free base
	Hydroquinone	0.3%
	Inorganic sulfites and bisulfites	0.67% in SO ₂
	Methylphenylenediamines	10% of free base
	N-substituted derivatives of p-Phenylenediamine	6% of free base
	p-Phenylenediamine	2% of free base
	Resorcinol	5%
	Toluene-2,5-diamine	4% of free base
According to Government Gazette, book 129, part 162, 9 October 2008 (amendment 23 February 2012)³⁶		
non - oxidative hair dye	1,3-bis-(2,4-diaminophenoxy) propane	1.2% of free base, 1.5% of tetrahydrochloride salt
	Acid blue No. 9	0.50%
	Acid red No. 18	0.40%

Table 1. Showing the chemical substance that allowed to use as ingredients in hair dye products and their maximal concentration regulated by Thai FDA^{34, 36-9}(Cont.)

Types	Substances	Maximum concentration allowance
oxidative hair dye	Acid red No. 53	0.60%
	Acid yellow No. 23	0.40%
	Curry red	0.40%
	Dihydroxyindoline	2%
	1,3-bis-(2,4-diaminophenoxy) propane	1.2% of free base after mixture
	Acid red No. 52	1.5% after mixing
solvent of hair dye products	Butoxydiglycol	9%
solvent of non-oxidative hair dye	Butoxyethanol	2%
solvent of oxidative hair dye products	Butoxyethanol	4%
According to Government Gazette, book 129, part 1621, 9 October 2008 (amendment 6 July 2012)³⁷		
non - oxidative hair dye	2-Hydroxyethylamino-5-nitroanisole	0.20%
	3-Methylamino-4-nitrophenoxyethanol	0.15%
	Acid blue No. 62	0.40%
	HC blue No. 11	2%
	HC blue No. 2	2.80%
	HC yellow No. 10	0.10%
According to Government Gazette, book 125, part 1621, 9 October 2008 (amendment 27 November 2014)³⁸		
Non - oxidative hair dye	1,5-Naphthalenediol	1%
	2-Methylresorcinol	1.80%
	2-Amino-6-chloro-4-nitrophenol	2%
	3-Nitro-p-hydroxyethyl aminophenol	1.85%
	3-Amino-2,4-dichlorophenol	1.5%, calculated in hydrochloride form
	4-Nitrophenyl aminoethyl urea	0.50%
	4-Amino-3-nitrophenol	1%
	Dihydroxyindole	0.50%
	HC blue No. 12	1.5% after mixing, calculated in hydrochloride form
	HC violet No. 1	0.25%

Table 1. Showing the chemical substance that allowed to use as ingredients in hair dye products and their maximal concentration regulated by Thai FDA^{34, 36-9}(Cont.)

Types	Substances	Maximum concentration allowance
Oxidative hair dye	HC violet No. 1	0.25%
	Tetraaminopyrimidine Sulfate	3.4%, calculated in sulphate form
	Acid yellow No. 1	0.20%
	Basic yellow No. 57	2%
	Disperse black No. 9	0.30%
	HC blue No. 14	0.30%
	HC orange No. 1	1%
	HC red No. 1	1%
	HC red No. 10 + HC red No.11	1%
	HC red No. 7	1%
	HC yellow No. 13	2.50%
	HC yellow No. 2	1%
	HC yellow No. 4	1.50%
	HC yellow No. 9	0.5%, calculated in hydrochloride form
	HC yellow No.7	0.25%
	Hydroxyethyl-2-nitro-p-toluidine	1%
	Isatin	1.60%
	2,7-Naphthalenediol	1%
	2-Hydroxyethyl picramic acid	1.5% after mixing
	2-Methyl-5-hydroxyethyl aminophenol	1.5% after mixing
	2-Methyl-5-hydroxyethyl aminophenol	1.5% after mixing
	2,6-Dihydroxy-3,4-dimethylpyridine	1% after mixing
	3-Amino-2,4-dichlorophenol	1.5% after mixing, calculated in hydrochloride form
	4-Amino-3-nitrophenol	1.50%
	HC blue No. 12	0.75% after mixing, calculated in hydrochloride form
	HC red No. 13	1.25% after mixing, calculated in hydrochloride form
	Hydroxybenzo morpholine	1% after mixing
	Hydroxyethyl-p-Phenylenediamine Sulfate	2% after mixing, calculated in sulphate form
	m-Aminophenol	1.2% after mixing

Table 1. Showing the chemical substance that allowed to use as ingredients in hair dye products and their maximal concentration regulated by Thai FDA^{34, 36-9}(Cont.)

Types	Substances	Maximum concentration allowance
	p-Methylaminophenol	0.68% after mixing, calculated in sulphate form
	Phenyl methyl pyrazolone	0.25% after mixing
	1-Acetoxy-2-Methylnaphthalene	2% after mixing
	1,5-Naphthalenediol	1% after mixing
	2-Amino-3-Hydroxy pyridine	1% after mixing
	2-Methyl-1-Naphthol	2% after mixing
	2-Methylresorcinol	2% after mixing, calculated in hydrochloride form
	2-Amino-4-hydroxy ethylamino anisole sulphate	1.5% after mixing, calculated in sulfate form
	2-Amino-6-chloro-4-nitrophenol	2% after mixing
	2,4-Diaminophenoxy ethanol HCl and 2,4-Diaminophenoxy ethanol sulfate	2% after mixing, calculated in hydrochloride form
	2,6-Dimethoxy-3,5-pyridinediamine HCl	0.25% after mixing, calculated in hydrochloride form
	3-Nitro-p-hydroxyethyl aminophenol	3% after mixing
	4-Chlororesorcinol	2.5% after mixing
	4-Nitrophenyl aminoethyl urea	0.25% after mixing
	4-Nitrophenyl aminoethyl urea	0.25% after mixing
	4-Amino-2-hydroxytoluene	1.5% after mixing
	4-Amino-m-cresol	1.5% after mixing
	4-Nitro-o-Phenylenediamine	0.4% after mixing
	5-Amino-4-Chloro-o-Cresol HCl	1.5% after mixing, calculated in hydrochloride form
	6-Hydroxyindole	0.5% after mixing
	Acid Yellow 1	1% after mixing
	Dihydroxyindole	0.5% after mixing
	HC red No. 10 + HC Red No.11	1% after mixing
	HC violet No. 1	0.25% after mixing
	HC yellow No. 13	2.5% after mixing
	HC yellow No. 2	0.75% after mixing
	Hydroxyethyl-2-nitro-p-toluidine	1% after mixing
	Hydroxyethyl-3,4-methylenedioxyaniline HCl	1.5% after mixing

Table 1. Showing the chemical substance that allowed to use as ingredients in hair dye products and their maximal concentration regulated by Thai FDA^{34, 36-39}(Cont.)

Types	Substances	Maximum concentration allowance
	Hydroxypropyl bis (N-hydroxyethyl-p - phenylenediamine) HCl	0.4% after mixing, calculated in tetrahydrochloride form
	N, N-bis (2-Hydroxyethyl)-p-Phenylenediamine Sulfate	2.5% after mixing, calculated in sulphate form
	Tetraaminopyrimidine Sulfate	3.4% after mixing, calculated in sulphate form
According to Government Gazette, book 125, part 1624, 9 October 2008 (amendment 13 October 2015)³⁹		
Non oxidative dye hair	2-Chloro-6-ethylamino-4- nitrophenol	3%
Oxidative hair dye	2-Chloro-6-ethylamino-4- nitrophenol	1.5% after mixing

Thai-FDA regulations related to hair dyes

In the year of 2008, Thai FDA executed the law to regulate the cosmetic regulations in order to be consistent with the ASEAN Harmonized Cosmetic Regulatory Scheme.³⁴ The regulations altered the classification of hair dye from the specially controlled cosmetic to the controlled cosmetic. All the entrepreneur must inform and register the products which have to be permitted by Thai FDA before selling. Unfortunately, the government notification process and certification of the products took only 3 days without having enough information about manufacturing, storage places or labelling. In addition, some consumers were misunderstanding when reading the labels of cosmetic products.³⁵ In the year of 2012, 2014

and 2015, Thai FDA not only added more substances allowed to use in hair dyes products but also gave the clearer regulations (Table 1).³⁶⁻⁹ Later, in the year of 2016, Thai FDA listed the ingredients prohibited to use in cosmetic products (Table 2).⁴⁰

Recommendation of hair coloring substitutes in hair dye contact allergy

In case of the patients with hair dye contact allergy need to dye their hair, we recommend other materials as substitutes (Table 3). According to the products that replace PPD with para-toluenediamine (PTDS) as an intermediate, cross reactivity between PPD and PTDS may occur with about 60% chance.⁴¹

Table 2. Showing the substances prohibited to use in hair dye products regulated by Thai FDA ⁴⁰

Substances	Substances	Substances
1-Methyl-2,4,5-trihydroxybenzene and its HCl salt	Acid Red No. 95	HC Yellow No.3
1,2,4-Benzenetriacetate and its HCl salt	Acid Violet No. 9	HC Yellow No.5
1,3,5-Trihydroxybenzene (Phloroglucinol)	Acid Yellow No. 73 sodium salt	HC Yellow No.6
1,7-Naphthalenediol	Basic Blue No. 26	HC Yellow No.8
2-Amino-3-nitrophenol	Basic Blue No. 3	Hydroxyethyl-2,6-dinitro-p-anisidine
2-Aminomethyl-p-aminophenol and its HCl salt	Basic Blue No. 41	Hydroxyethylaminomethyl-p-aminophenol and its salt
2-Chloro-5-nitro-N-hydroxyethyl-p-phenylenediamine	Basic Blue No. 47	Hydroxypyridinone and its HCl salt
2-Methoxy-4-nitrophenol and its HCl salt	Basic Blue No. 6	N-(2-Methoxyethyl)-p-phenylenediamine and its HCl salt
2-Methoxymethyl-p-Aminophenol and its HCl salt	Basic Blue No. 7	N-Cyclopentyl-m-Aminophenol
2-Nitro-N-hydroxyethyl-p-anisidin	Basic Blue No. 9	N-Methyl-3-nitro-p-phenylenediamine and its salt
2-Nitro-p-phenylenediamine	Basic Brown No.4	N,N-Diethyl-m-Aminophenol
2,3-Naphthalenediol	Basic Green No. 1	N,N-Diethyl-p-phenylenediamine and its salt
2,4-Diamino-5-methylphenetol and its HCl salt	Basic Orange No. 1	N,N-Dimethyl-2,6-Pyridinediamine and its HCl salt
2,4-Diamino-5-methylphenoxyethanol and its salt	Basic Orange No. 2	N,N-Dimethyl-p-phenylenediamine and its salt
2,4-Diaminodiphenylamine	Basic Red No. 118	N,N'-Dimethyl-N-hydroxyethyl-3-nitro-p- phenylenediamine
2,6-Bis(2-hydroxyethoxy)-3,5-pyridinediamine and its HCl salt	Basic Red No. 2	Pigment Blue 15
2,6-Dihydroxy-4-methylpyridine and its HCl salt	Basic Red No. 22	Pigment Green 7
3-Nitro-4-aminophenoxyethanol and its HCl salt	Basic Red No. 46	Pigment Red 112
3,4-Diaminobenzoicacid	Basic Violet No. 14	Pigment Red 4
3,4-Methylenedioxyaniline and its HCl salt	Basic Violet No. 4	Pigment Red 48
3,4-Methylenedioxyphenol and its HCl salt	Basic Yellow No. 11	Pigment Red 5
4-Chloro-2-Aminophenol	Basic Yellow 28	Pigment Red 63
4-Diethylamino-o-toluidine and its salt	CI 50420	Pigment Red 64

Table 2. Showing the substances prohibited to use in hair dye products regulated by Thai FDA ⁴⁰ (Cont.)

Substances	Substances	Substances
4-Ethylamino-3-nitrobenzoic acid and its salt	CI Acid Black 131	Pigment Red 83
4-Hydroxyindole	CI Natural Red 25	Pigment Red 90, Acid Red 87 and Pigment Red 90
4-Methoxytoluene-2,5-Diamine and its HCl salt	Direct Black 51	Pigment Violet 19
4-Nitro-m-phenylenediamine and its salt	Direct Blue 86	Pigment Violet 23
4,4'-Diaminodiphenylamine and its salt	Direct Red 23	Pigment Yellow 12
4,5-Diamino-1-((4-Chlorophenyl)Methyl)-1H-Pyrazole Sulfate	Direct Red 80	Pigment Yellow 13
4,5-Diamino-1-methylpyrazole and its HCl salt	Direct Red 81	Pigment Yellow 73
4,6-Bis(2-hydroxyethoxy)-m-phenylenediamine and its salt	Direct Violet 48	Ponceau SX
5-Amino-2,6-dimethoxy-3-hydroxypyridine and its salt	Direct Yellow 12	propanediol
5-Amino-4-Fluoro-2-Methylphenol Sulfate	Disperse Blue3	Solvent Black 3
5-Hydroxy-1,4-benzodioxane and its HCl salt	Disperse Blue7	Solvent Black5
6-Amino-o-cresol and its salts	Disperse Brown 1	Solvent Green 3
6-Methoxy-2,3-pyridinediamine and its HCl salt	Disperse Orange 3	Solvent Green 7
6-Nitro-2,5-pyridinediamine	Disperse Red11	Solvent Orange 1
Acid Black 52	Disperse Violet 4	Solvent Red 1
Acid Blue 1	Fast Green FCF	Solvent Red 23
Acid Blue 3	Food Black 2	Solvent Red 3
Acid Brown 13	HC Blue No. 4	Solvent Red 43
Acid Green 1	HC Blue No. 5	Solvent Red 72
Acid Orange 24	HC Blue No. 6	Solvent Violet 13
Acid Orange 3	HC Blue No. 8	Solvent Yellow 29
Acid Orange 6	HC Blue No. 9	Solvent Yellow 33
Acid Red 27	HC Blue No. 10	Solvent Yellow 44
Acid Red 35	HC Brown No. 1	Toluene-3,4-diamine and its salts
Acid Red 51 and Pigment Red 172 Aluminium lake	HC Brown No. 2	VAT Red 1
Acid Red 73	HC Red No. 9	
Acid Red 87	HC Yellow No. 12	
1-Methyl-2,4,5-trihydroxybenzene and its HCl salt	Acid Red No. 95	HC Yellow No.3
1,2,4-Benzenetriacetate and its HCl salt	Acid Violet No. 9	HC Yellow No.5

Table 2. Showing the substances prohibited to use in hair dye products regulated by Thai FDA ⁴⁰ (Cont.)

Substances	Substances	Substances
1,3,5-Trihydroxybenzene (Phloroglucinol)	Acid Yellow No.73 sodium salt	HC Yellow No.6
1,7-Naphthalenediol	Basic Blue No. 26	HC Yellow No.8
2-Amino-3-nitrophenol	Basic Blue No. 3	Hydroxyethyl-2,6-dinitro-p-anisidine
2-Aminomethyl-p-aminophenol and its HCl salt	Basic Blue No. 41	Hydroxyethylaminomethyl-p-aminophenol and its salt
2-Chloro-5-nitro-N-hydroxyethyl-p-phenylenediamine	Basic Blue No. 47	Hydroxypyridinone and its HCl salt
2-Methoxy-4-nitrophenol and its HCl salt	Basic Blue No. 6	N-(2-Methoxyethyl)-p-phenylenediamine and its HCl salt
2-Methoxymethyl-p-Aminophenol and its HCl salt	Basic Blue No. 7	N-Cyclopentyl-m-Aminophenol
2-Nitro-N-hydroxyethyl-p-anisidin	Basic Blue No. 9	N-Methyl-3-nitro-p-phenylenediamine and its salt
2-Nitro-p-phenylenediamine	Basic Brown No.4	N,N-Diethyl-m-Aminophenol
2,3-Naphthalenediol	Basic Green No. 1	N,N-Diethyl-p-phenylenediamine and its salt
2,4-Diamino-5-methylphenetol and its HCl salt	Basic Orange No. 1	N,N-Dimethyl-2,6-Pyridinediamine and its HCl salt
2,4-Diamino-5-methylphenoxyethanol and its salt	Basic Orange No. 2	N,N-Dimethyl-p-phenylenediamine and its salt
2,4-Diaminodiphenylamine	Basic Red No. 118	N,N'-Dimethyl-N-hydroxyethyl-3-nitro-p-phenylenediamine
2,6-Bis(2-hydroxyethoxy)-3,5-pyridinediamine and its HCl salt	Basic Red No. 2	Pigment Blue 15
2,6-Dihydroxy-4-methylpyridine and its HCl salt	Basic Red No. 22	Pigment Green 7
3-Nitro-4-aminophenoxyethanol and its HCl salt	Basic Red No. 46	Pigment Red 112
3,4-Diaminobenzoic acid	Basic Violet No. 14	Pigment Red 4
3,4-Methylenedioxyaniline and its HCl salt	Basic Violet No. 4	Pigment Red 48
3,4-Methylenedioxyphenol and its HCl salt	Basic Yellow No. 11	Pigment Red 5
4-Chloro-2-Aminophenol	Basic Yellow 28	Pigment Red 63
4-Diethylamino-o-toluidine and its salt	CI 50420	Pigment Red 64
4-Ethylamino-3-nitrobenzoic acid and its salt	CI Acid Black 131	Pigment Red 83
4-Hydroxyindole	CI Natural Red 25	Pigment Red 90, Acid Red 87 and Pigment Red 90

Table 2. Showing the substances prohibited to use in hair dye products regulated by Thai FDA ⁴⁰ (Cont.)

Substances	Substances	Substances
4-Methoxytoluene-2,5-Diamine and its HCl salt	Direct Black 51	Pigment Violet 19
4-Nitro-m-phenylenediamine and its salt	Direct Blue 86	Pigment Violet 23
4,4'-Diaminodiphenylamine and its salt	Direct Red 23	Pigment Yellow 12
4,5-Diamino-1-((4-Chlorophenyl)Methyl)-1H-Pyrazole Sulfate	Direct Red 80	Pigment Yellow 13
4,5-Diamino-1-methylpyrazole and its HCl salt	Direct Red 81	Pigment Yellow 73
4,6-Bis(2-hydroxyethoxy)-m-phenylenediamine and its salt	Direct Violet 48	Ponceau SX
5-Amino-2,6-dimethoxy-3-hydroxypyridine and its salt	Direct Yellow 12	propanediol
5-Amino-4-Fluoro-2-Methylphenol Sulfate	Disperse Blue3	Solvent Black 3
5-Hydroxy-1,4-benzodioxane and its HCl salt	Disperse Blue7	Solvent Black5
6-Amino-o-cresol and its salts	Disperse Brown 1	Solvent Green 3
6-Methoxy-2,3-pyridinediamine and its HCl salt	Disperse Orange 3	Solvent Green 7
6-Nitro-2,5-pyridinediamine	Disperse Red11	Solvent Orange 1
Acid Black 52	Disperse Violet 4	Solvent Red 1
Acid Blue 1	Fast Green FCF	Solvent Red 23
Acid Blue 3	Food Black 2	Solvent Red 3
Acid Brown 13	HC Blue No. 4	Solvent Red 43
Acid Green 1	HC Blue No. 5	Solvent Red 72
Acid Orange 24	HC Blue No. 6	Solvent Violet 13
Acid Orange 3	HC Blue No. 8	Solvent Yellow 29
Acid Orange 6	HC Blue No. 9	Solvent Yellow 33
Acid Red 27	HC Blue No. 10	Solvent Yellow 44
Acid Red 35	HC Brown No. 1	Toluene-3,4-diamine and its salts
Acid Red 51 and Pigment Red 172 Aluminium lake	HC Brown No. 2	VAT Red 1
Acid Red 73	HC Red No. 9	
Acid Red 87	HC Yellow No. 12	

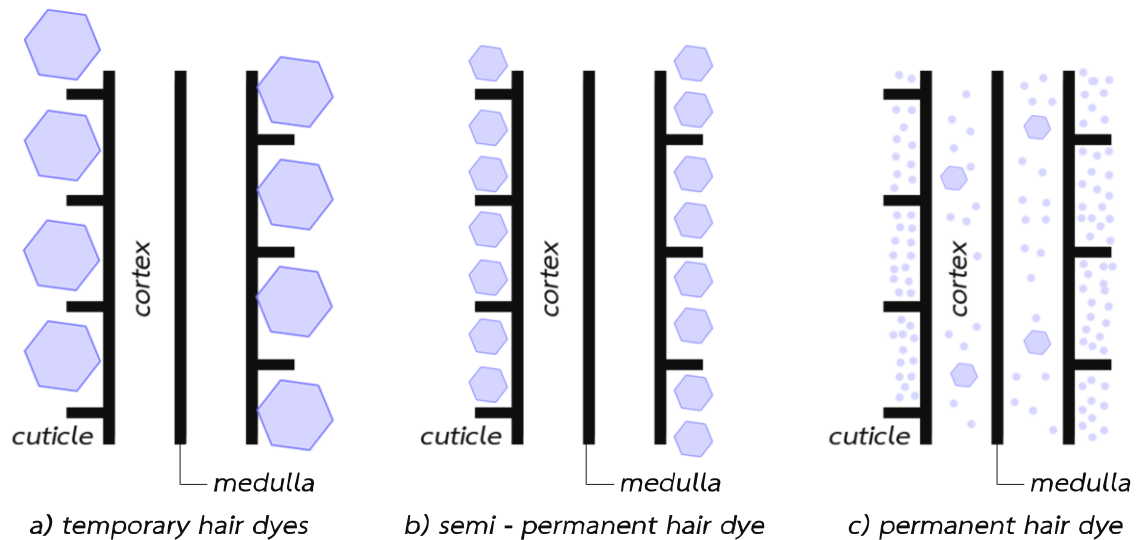


Figure 1. Showing the penetrating capacity of different types of hair dyes. The hexagons represent the different sizes of dye molecules in each type of hair dyes. A) Large molecules of temporary hair dyes are unable to penetrate the hair cortex. B) The molecules of semi-permanent hair dyes easily diffuse into middle layers of cuticle without binding to hair protein. C) Small molecules of permanent hair dyes are able to penetrate and diffuse in the hair cortex by breaking the cuticle

Table 3. Recommendation of hair coloring substitutes in hair dye contact allergy

Allergen	Substitution and examples of products sold in Thai market
PPD	PPD-free hair dyes containing PTDS • Beautylabo Whip Hair Color - Sweet brown • Biowoman Magic Pink Hair Color - B-01 Midnight black • Dipso TrioMatch Permanent Color Cream - D03 Natural warm brown • Garnier Olia Permanent Hair Color - 3.0 Soft black • Just Modern Hair Color - A2 Natural black • Schwarzkopf Essential Color - 299 Black berry • Schwarzkopf IGORA Colors - 1-0 Black / Dark brown • Schwarzkopf Palette Duluxe - 3-0 Dark brown • Schwarzkopf Palette Natural Colors - 4-0 Medium brown • Syoss Oleo Intense Permanent Intensive Oil Color - 4-00 Medium brown • Syoss Permanent Coloration - 1-0 Black

Table 3 Recommendation of hair coloring substitutes in hair dye contact allergy (Cont.)

Allergen	Substitution and examples of products sold in Thai market
PPD and PTDS	PPD-free and PTDS-free hair dyes • Catherine Bio Herbal White Hair Cover Cream - Natural black / Dark brown • Catherine Hair Mascara - Natural black / Dark brown • Cruset Herbal Spa Hair Colour Set - T1 Natural black / T2 Dark brown • Cruset Hair Mascara - Natural black / Light brown • Cruset Colour Restoring Cream • Restoria Discreet Colour Restoring Cream • L'oreal Professionnel Nuancelle - Natural brown DD

Conclusions

Hair dye allergy has been increasingly reported worldwide including Thailand. The hair dye allergy can be induced through both immediate type and delayed type hypersensitivity reactions. The most commonly reported allergens are PPD and its derivatives which are often used as primary intermediates in permanent hair dyes. However, many culprits in different types of hair dyes were also reported, especially in synthetic hair dyes. In contrast, vegetable dyes including Thai herbal dyes extracted from plants are usually safe for hair coloring.

Understanding the specifications of hair dye allergy and details of hair dyes in the market can help physicians taking good care of patients with hair dye allergy as well as pointing out the important issues to the consumers or hairdressers to beware of the potential hazards.

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