International Journal of Research in Dermatology
Gurusamy S et al. Int J Res Dermatol. 2024 Jul;10(4):220-224
http://www.ijord.com

DOI: https://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20241729

Review Article

Hair dye allergies: available alternatives

Sukanya Gurusamy, Celestin Geo Danny, Gayathri S.*, Divyabharathi Sundarara

Department of Dermatology, Venereology and Leprosy, Sri Balaji Medical College and Hospital, Chennai, Tamil Nadu, India

Received: 11 May 2024
Accepted: 11 June 2024

***Correspondence:**
Dr. Gayathri S.,
E-mail: devucharippurathu@gmail.com

ABSTRACT

P-phenylenediamine (PPD) is a well-known sensitizer of skin which forms a major component in permanent hair dyes. Allergic contact dermatitis induced by PPD is a major concern for hairdye industry and the population using hair dyes. To reduce the burden of contact dermatitis due to PPD in hair dyes, various alternative hair dye molecules have been developed over the years which include two-methoxymethyl-p-phenylenediamine (ME-PPD) molecule and hydroxyethyl-p-phenylenediamine (HE PPD) molecule. These both molecules have shown reduced sensitization to skin and much lower skin permeability which makes them as safer alternatives to PPD hair dyes in the market.

Keywords: Paraphenylenediamine, Allergic contact dermatitis, Two-methoxymethyl-p-phenylenediamine, Hydroxyethyl-p-phenylenediamine, Sensitizing potential, Hair dye molecules, Cross elicitation response

INTRODUCTION

Phenylenediamine (PPD) is a 108 Dalton low molecular weight compound. It belongs to the aromatic amines since the molecular structure consists of amino groups two in number (NH_2) which is connected in a meta position by an aromatic benzene ring.[1] PPD is usually found in white colour ranging to a shade of light purple that on darkening turns into crimson, brown, and finally black with (air) oxidation. As a result, it is employed as a dyeing intermediate.[1]

PPD, in addition to its dye precursor p-toluenediamine have been used as hair dye from 19th century and today it is among the frequently used precursor molecular dye in permanent hair colouring (PTD).

It's use in temporary 'black henna' tattoos has recently gained popularity as a way to speed up the process of darkening to achieve a long lasting look.

METABOLISM–OXIDATION VERSUS N-ACETYLATION

The reactions are given in the equations below.

PPD
$\rightarrow H_2O_2$ (oxidation)
-semiquinone diimine (SQD radical)
$\rightarrow H_2O_2$ (oxidation)–quinonediimine (QDI)

Quinonediimine (QDI)+PPD=Bandrowski's base

MECHANISM OF HAPTENATION OF P–PHENYLENEDIAMINE

PPD is an aromatic amine that can induce severe allergic contact dermatitis due to its high sensitizing potential. It is mostly employed in the form of preservative in hair dyes that are oxidizing in nature, and also in case of hair dyes that are temporary in nature.[2,3] Severe erythema and edema have been reported due to allergic contact dermatitis by PPD.[2,3]

ADVERSE EFFECTS

Adverse effects include: allergic contact dermatitis due to severe sensitizing capacity; the significant edema of the scalp and face caused by PPD induced allergic contact dermatitis is far more commonly misdiagnosed as angioedema; oral PPD intake has been linked to severe systemic toxicity, including angioneurotic oedema, respiratory distress, and rhabdomyolysis, which can lead to acute renal failure, according to a few case reports from India and East Africa; most of the cases were caused by ingestion of solid PPD, whether by mistake or on purpose; and PPD has been the subject of carcinogenicity investigations, particularly urothelial carcinogenicity studies, since various forms of aromatic amines previously used in hair dyes were found to have carcinogenic property.[2-4]

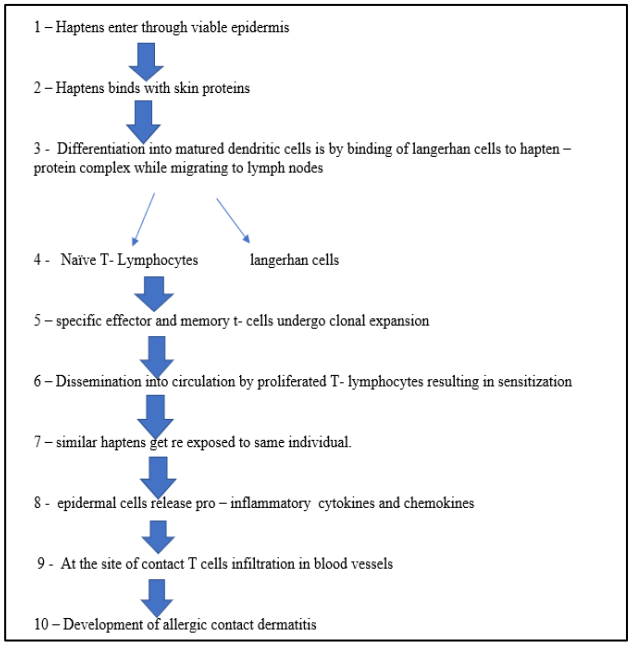

Figure 1: Pathogenesis of development of allergic contact dermatitis to hairdye.

HAIR DYE MOLECULES

Temporary, semi-permanent, and permanent hair dyes are divided into three groups based on their fastness. The latter, which account for 80% of the European Union's hair dye market, are comprised of 39 oxidizing colouring dyes.[5] A standard oxidizing colouring agent consists of a former molecule (such as PPD or PTD) and couplers (such as resorcinol or m-aminophenol) that are combined with H_2O_2 in an alkaline environment. Alkaline ingredient, which is commonly ammonia or ammonia replacements, opens up an inner layer so that former dye molecules can penetrate, thus the internal PH will be reduced, and this acclerates melanin bleaching.

H_2O_2, on the contrary, eliminates natural melanin content as well as any other artificial pigments. The oxidation of precursors is promoted by hydrogen peroxide penetrating hair shaft molecules, which are then connected to the coupler molecules. As a result, hair dye components that are huge in size for diffusion outside the hair will develop, resulting in a chemical compound that will give long lasting coverage usually permanent until hair shedding.

A broad range of dye reaction products ultimately resulting in variety of hair colours is produced by various combinations of precursors and couplers. PPD and PTD are the most often utilized former molecules in oxidizing dyes, usually regarded to contribute to contact dermatitis that is allergic among all other chemicals in hair dyes. Because of the strong cross-reactivity between these two compounds, being sensitized to one of them increases chances of becoming sensitized to the other.

Table 1: Susceptibility to sensitization: genes and exposure.

Antigen specific susceptibility	General (non-antigenic specific) susceptibility
Antigen recognition responses	Determinants of immunological 'hi/lo'
MHC class 1	Polymorphisms in TNF – alpha, IL-1, IL-6, IL-16
MHC class 2	
T cell receptor chains	Responses to chemical perturbation 2
	TLR's, PAMP's
Other relevant receptors	
TLR'S	Acute antioxidant defences
Catalase, vitamin C	Enzymes – superoxide dismutase
	Glutamyl cysteinyl glycine (GSH reductase, peroxidase)
	Non enzymatic scavengers: glutathione; response to chemical perturbation 2, epidermal barrier – permeability; xenobiotic detoxication, phase 1 enzymes – cyp450's, phase 2 enzymes – glutathione S –transferase

Methoxymethyl-p-phenylenediamine (ME-PPD) is a new hair colouring ingredient that was found recently.[6] This PPD products had excellent potential for hair dye coverage, but also had less percentage of sensitization. Unlike PPD, which has an EC3 value of 0.1 percent, and PTD, which has an EC3 value of 0.17 percent, ME-PPD has a potential of average sensitization with an EC3 value of 4.3 percent. A quantitative risk evaluation of capacity to induce sensitization according to usage under consumer settings demonstrated that ME-PPD has a significantly lower possibility of producing sensitizing capacity when compared to precursors. These are the recent advances

being made in hair dye molecules replacing PPD which is a potential sensitizer.[7]

CROSS ELICITATION RESPONSES TO ME-PPD IN PPD ALLERGIC INDIVIDUALS

ME-PPD, or 2-methoxymethyl-p-phenylenediamine, is a new PPD derivative. When combined with couplers (e.g. m-aminophenol) and an oxidising agent (e.g. hydrogen peroxide) in hair dyes, the addition of a methoxymethyl side chain to PPD resulted in a hair dye molecule giving outstanding colour coverage.[9] Furthermore, on comparison to PPD and its similar molecule p-toluylenediamine, ME-PPD has much lower skin sensitizing characteristics (PTD).[12]

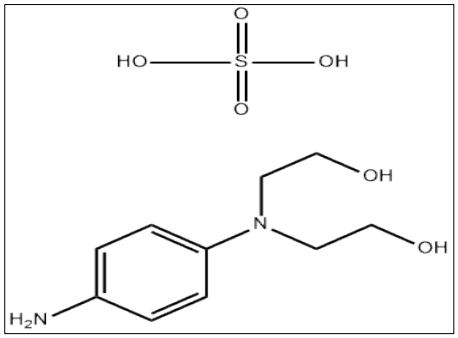

Figure 2: Chemical structure of 2-methoxy methyl-p-phenylenediamine.[8]

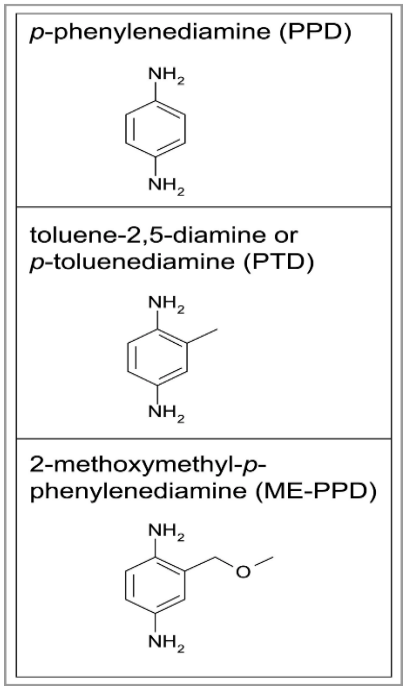

Figure 3: Chemical structure of paraphenylenediamine, p-toluenediamine, 2-methoxy methyl-p-phenylenediamine.[9]

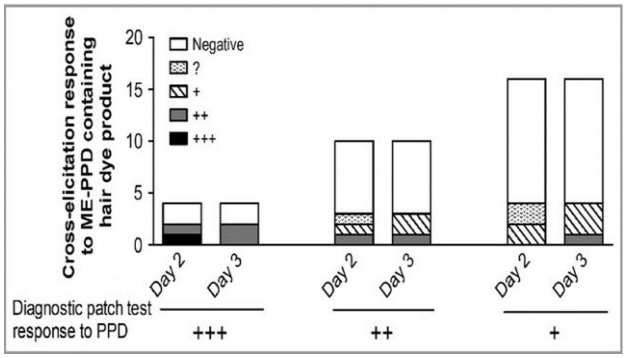

Figure 4: Diagnostic patch test response to paraphenylenediamine.[13]

Products that may contain PPD	Products that may cross-react
• Hair dye, permanent or semipermanent	• PABA (used in sunscreens)
• Fur dyes	• Azo dyes (used in some textiles)
• Printer's ink	• Certain local anesthetics based on ester groups; e.g., benzocaine, tetracaine, procaine
• Photographic or lithographic work	• Thiazide diuretics
• Rubber products† such as latex gloves and support stockings	

*In order of decreasing frequency of cases seen.
†PPD is sometimes used in rubber processing.

PABA = para-aminobenzoic acid.

Figure 5: Products that contain PPD with risk of cross reaction.[11]

Another benzene derivative is HPPS which has been shown to have less cross reactivity. It has been tolerated by small group of people who were previously sensitized to PPD with a history of contact dermatitis with hair dyes.

T cell receptor cross reactivity has a number of mechanisms. T cell receptor cross-reactivity generated on response by T cells which are allergen specific recognizing various molecules is typically explained by similar structural molecules, in which cross reactive ligands exhibit fundamental molecular as well as chemical properties.

As a result, ring replacements have been used to modify the basic para-structure of the PPD molecule, which has been shown to influence skin induction and elicitation.[12] When paratoluenediamine and p-aminophenol were evaluated in guinea pigs under controlled conditions, the cross-reactivity rate with PPD was 100% indicating that the introduction of a methyl side chain into PPD or the swap of an amino-group by a hydroxyl-group in p-aminophenol do not show a significant change in terms of cross-reactivity.[9]

Studies utilizing PPD-reactive T cell clones (created by sensitizing mice to a PPD-haptenated self-protein) have shown that, in addition to PPD, some of the T cell clones also identify p-aminophenol and PPD-self oxidation products, including Bandrowski's base.

As a result, the resultant cross reactivity in participants might be the effect of T cells that are unable to discriminate between distinct antigens. T cells that react to a hapten created by a common self-oxidation product of PPD and ME-PPD; and/or T cells that react to a hapten formed by a common self-oxidation product of PPD and ME-PPD.[10]

In contrast, the limited cross-elicitation to 2ME-PPD suggests significant change in the para-structure, resulting in lower state of T cell identification. Also it is consistent on the finding that lymphocytes from PPD-allergic patients identified protein changes due to PPD and was not recognized as 2,5-dimethyl-PPD, a modified PPD molecule with two additional methyl groups in the benzene ring.

NUVOTONE HAIR COLOUR (HENNA, INDIGO, AMLA, SHIKAKAI, COFFEE, TEA)

Cuticolor hair dye includes cetearyl alcohol, ethanolamine, steartrimonium chloride, stearamide DEA, ceteareth-20, toluene-2,5-diamine sulfate, steareth-21, stearamidopropyl dimethylamine, dimethicone, amodimethicone, *Boswellia serrata* extract, mineral oil, resorcinol, oleth-2, lanolin, *Portulaca oleracea* extract, behentrimonium chloride, m-aminophenol, cysteine HCl, allantoin, o-aminophenol, polyquaternium-10, panthenol, and ascorbic acid.

There is potential risk of cross reaction due to the presence of toluene-2,5-diamine sulfate which is a potential sensitizer in hair dye.

Vegetal safe hair color includes: indigo, henna, Manjistha, *Coffee arabica*, bhringraj, shikakai, brahmi, amla, and Kattha.

Indus valley organic hair colour includes henna, amla, basil, wheat germ, aloe vera, sunflower, jojoba, and orange.

Sesa natural hair colour includes: indigo and henna, mix infused with amla, shikakai, aritha, walnut and coffee.

HERBAL HENNA DYE (POWDER FORMULATION)

Natural plant extracts

Amla, henna, mandara, jatamansi, reetha, sariva, curry leaves, and methi seeds are popularayurvedic herbal medications that have routinely been in use to colour hair and promote hair growth.[13] Before the introduction of modern dyes, several different plant extracts were utilised for hair colouring in Europe and Asia.[6,13,14]

Henna

Henna has long been used in India to colour palms and hair. Many plants, such as kikar, bhringraj, patnag, akhrot, narra, jaborandi, jatamansi, amla, kuth, giloe, and behera, are utilised as important elements in hair care formulations, mostly for hair colouring. Henna, the basic powder, serves as a worldwide colouring agent. Helps to remove increased amount of oil from scalp while also conditioning.[13]

Reetha

Reetha rejuvnates the hair that has been dull, dry, or damaged. By giving additional nutrients to assist hair growth, Bhringraj helps to improve blood flow at the base of the hair. The jatamansi extract is a Hair growth is aided by this. It's also good for hair that's smooth, silky, and healthy.[13]

Indigo

Indigo, called as original fabric dye, is usually combined together with henna to create a variety of light brown to black hair colour shades.[6] Skin irritation, allergy, hair breakage, skin discoloration, and unexpected hair colour are all possible negative effects of using these drugs. Continuous use of such substances on natural hair has a number of negative consequences, including skin irritation, allergy, hair loss, dry scalp, erythema, and even skin cancer.[13]

Shikakai and amla

Shikakai is high in vitamins A, C, D, and K, which combine to make a potent antioxidant. This antioxidant is likely the sole thing hair requires to remove sebum accumulation from the scalp, unclog pores, kill infection-causing bacteria, and promote hair growth. Hair fall, dandruff, and greying can all be readily controlled by utilising hibiscus flower juice on a regular basis, even over 50 years old. It also has important fatty acids, which help to rebuild hair follicles and give them a fresh lease on life. Amla's high vitamin C content helps to prevent premature greying. It's an excellent hair conditioner and dandruff remover.[11]

Herbal hair pack is a gentle way to colour hair. Herbal-based cosmetics have the advantage of being nontoxic. It nourishes the scalp's and hair's skin. The skin receives essential nutrients from this hair product. It aids in the treatment of dandruff by reducing oil secretion in scalp. The usage of this pack on a regular basis results in manageable, frizz-free coloured hair. Pollution, ageing, stress, and severe temperatures can have a negative impact on hair quality. Natural cures are now widely welcomed with open arms because they are safer and have fewer negative effects than pharmaceuticals.[6]

CONCLUSION

Many hairdyes in recent times have been developed which are free from PPD, free from ammonia and hydrogen peroxide which have increased the usage and safety in PPD

allergic patients. There are various Indian brands that are PPD and ammonia and hydrogen peroxide free which is available in the market. Due to the increased need for hairdyes in the consumer market, these available PPD free hairdye alternatives shows promising results and safety.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Blömeke B, Pot LM, Coenraads PJ, Hennen J, Kock M, Goebel C. Cross-elicitation responses to 2-methoxymethyl-p-phenylenediamine under hair dye use conditions in p-phenylenediamine-allergic individuals. Br J Dermatol. 2015;172(4):976-80.
2. Martin SF. Immunological mechanisms in allergic contact dermatitis. Curr Opin Allergy Clin Immunol. 2015;15:124-30.
3. Schuttelaar ML, Vogel TA. Contact allergy to hair dyes. Cosmetics. 2016;3:21.
4. Dittmar D. Multiple Aspects of Contact Allergy. Thesis submitted to University of Groningen. 2019.
5. Kirchlechner S, Hübner A, Uter W. Survey of sensitizing components of oxidative hair dyes (retail and professional products) in Germany. J Dtsch Dermatol Ges. 2016;14(7):707-15.
6. Pal RS, Pal Y, Saraswat N, Wal P, Wal A. Current review on herbs for derma care. Open Dermatol J. 2019;13.
7. Goebel C, Coenraads PJ, Rothe H, Kunze G, Kock M, Schlatter H, et al. Elicitation of the immune response to p-phenylenediamine in allergic patients: the role of dose and exposure time. Br J Dermatol. 2010;163(6):1205-11.
8. Venkatesan G, Dancik Y, Sinha A, Kyaw HM, Srinivas R, Dawson TL Jr, et al. Development of novel alternative hair dyes to hazardous para-phenylenediamine. J Hazard Mater. 2021;402:123712.
9. Schuttelaar ML, Vogel TA. Contact allergy to hair dyes. Cosmetics. 2016;3:21.
10. Schuttelaar ML, Dittmar D, Burgerhof JGM, Blömeke B, Goebel C. Cross-elicitation responses to 2-methoxymethyl-p-phenylenediamine in p-phenylenediamine-allergic individuals: Results from open use testing and diagnostic patch testing. Contact Dermatitis. 2018;79(5):288-94.
11. Pal RS, Pal Y, Saraswat N, Wal P, Wal A. Preparation & assessment of poly-herbal anti-dandruff formulation. Open Dermatol J. 2020;14.
12. Kock M, Coenraads PJ, Blömeke B, Goebel C. Continuous usage of a hair dye product containing 2-methoxymethyl-para-phenylenediamine by hair-dye-allergic individuals. Br J Dermatol. 2016;174(5):1042-50.
13. Venkatesan G, Dancik Y, Sinha A. Development of novel alternative hair dyes to hazardous para-phenylenediamine. J Hazard Mate. 2021;402:123712.
14. Pal RS, Pal Y, Saraswat N, Wal P, Wal A. Synthesis and evaluation of herbal based hair dye. Open Dermatol J. 2018;12.

Cite this article as: Gurusamy S, Danny CG, Gayathri S, Sundarara D. Hair dye allergies: available alternatives. Int J Res Dermatol 2024;10:220-4.