Toxicological Effects of Hair Dye Paraphenylene diamine: a Threat to the Cosmetic World

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ABSTRACT

p-Phenylenediamine is primarily used as a dye intermediate and as a dye. It is toxic by skin absorption, inhalation or ingestion in mammalian specieces.This article deals with the toxic effects of Paraphenylenediamine (PPD) on different mammal including human being. Acute (short-term) exposure to high levels of *p*-phenylenediamine may cause severe dermatitis, eye irritation and tearing, asthma, gastritis, renal failure, vertigo, tremors, convulsions, and coma in humans. Eczematoid contact dermatitis may result from chronic (long-term) exposure in humans. In rats and mice chronically exposed to *p*-phenylenediamine in their diet, depressed body weights, but no other clinical signs of toxicity, were observed in several studies. No information is available on the reproductive, developmental, or carcinogenic effects of *p*-phenylenediamine in humans. EPA (Environmental Protection Agency) has not classified *p*-phenylenediamine with respect to carcinogenicity. Guineapigs dermally exposed to PPD has shown signs of hepatoxicity menifested by local degenerative changes in the hepatocytes along with fatty changes. Cytochemical studies in Guineapig also revealed some qualititative changes in DNA content of the nuclei of the hepatocytes and stored glycogen molecules in the cytoplasm leading to alternation in the functional efficiency of the organ. Sub chronic dermal exposure to PPD in adult albino rat can induce hyperglycemia, disturbed hepatic, renal and cardiac functions. Allergy to PPD may make a person sensitive to other related compounds. As a precaution one should avoid using any products containing PPD .

***Key words*:** Paraphenylenediamine, Hair dye, Hepatoxicity, Allergic reactions , Dermal exposure.

Sub Title: Health Hazards of Chemical Hair Dye Paraphenylenediamine

Para-Phenylenediamine (PPD) is widely present on the market since 1909, and it is still used in over 2/3 of permanent hair dyes. It is an organic compound with the formula $C_6H_4(NH_2)_2$ used also as a component of engineering polymers and composites, aramid fibers, rubber chemicals, textile dyes and pigments. Since the end of the 19th century the chemical *p*-phenylenediamine (PPD) has been described as a hair dye. Up till now it is used as an ingredient in more than 1000 hair dye formulations marketed all over the world (Dressler *et al*, 2006 and Stanley *et al.*, 2005). It is a used in dark coloured cosmetics, oils, greases, gasoline as well as a photographic developing agent and a chemical intermediate (Corbett et al.,1973). Paraphenylenediamine is also used as a vulcanization accelerator and as an antioxidant in rubber compounds. (Hawley,1971). It penetrates into the hair shaft to further undergo oxidative chemical reactions, resulting in a dark coloration of the hair. PPD is commonly mixed with henna in Africa, Middle East, and Indian subcontinent, which is traditionally applied to color palms of hands, soles and feet and to dye hair a dark red shade. Dermal exposure study of environmentally available chemicals is a new initiative in the field of toxicology research. This is particularly more relevant in case of chemicals that find its way into human system through the skin (Mathur, 1990). In USA, about one third of the adult women use PPD containing hair dyes. PPD is selected because of its high temperature stability, high strength, and chemical and electrical resistance.This product is added to real henna or used alone to create black tattoo-like body art. This compound is used in almost every hair dye on the market, regardless of brand. The darker the colour, usually, the higher the concentration. Even the so-

called "natural" and "herbal" hair colours, while ammonia-free, contain PPD. Some products sold as henna have PPD added, particularly "black henna". Using body art quality (BAQ) pure henna, or indigo is the only way to avoid PPD in hair dye. Sensitization by para-phenylenediamine (PPD) has been considered by some countries to be so great a hazard that its use in hair dyes was banned in Germany in the early 1900's. It was subsequently prohibited in France, and in 1964 in Sweden; however in Japan and India PPD is still used as a common component in hair dyes. The CDC (centers for disease control **and Prevention**) lists PPD as being a contact allergen. Exposure routes are through inhalation, skin absorption, ingestion, and skin and/or eye contact; symptoms of exposure include throat irritation (pharynx and larynx), bronchial asthma, and sensitization dermatitis (Tokumoto,2004 and Brow,1997). Sensitization is a lifelong issue, which may lead to active sensitization to products including, but not limited to black clothing, various inks, hair dye, dyed fur, dyed leather, and certain photographic products. It was voted Allergen of the Year in 2006 by the American Contact Dermatitis Society *(Ashraf, W.)* As a precaution we should avoid using products containing PPD.

Paraphenylenediamine exposure to Animal.

The experimental study on rat by Manal, *et al.* ,(2012) revealed the dermal exposure of rats to PPD that results in damages in the liver, kidney, heart and pancreas. This is proved by the biochemical changes that are consistent with the tissue damage. *p*-phenylenediamine exposure to Guineapig has been reported to penetrate the epidermis and hair shafts into the serum and excreated in the urine (Kiese *et al*., 1968). Guineapigs dermally exposed to PPD has shown signs of hepatoxicity menifested by local degenerative changes in the hepatocytes along with fatty changes. Retardation of blood flow through the organ as a result of fibrinous thrombi in the blood vessels causes local deficiency of oxygen in the tissues. This affects the organ as detoxification increases and cause toxic liver injury. Guinea pigs were dermally exposed to the hair dye PPD for 15 and 30 days showed the effects on selected enzyme activities, lipid peroxidation, and histamine content in the skin The activities of acid phosphatase, glutathione-s-transferase, and tyrosinase were enhanced after application of PPD. The lipid peroxidation, histamine, and PPD content of skin also showed marked elevation following dermal exposure to the chemical (Devi, 2004). The histopathological examination showed severe hyperkeratosis, thickening of collagen fibres and vacuolisation of epidermal cells in PPD (Mathur *et al,*2005). Cytochemical studies also revealed some qualititative changes in DNA content of the nuclei of the hepatocytes and stored glycogen molecules in the cytoplasm leading to alternation in the functional efficiency of the (Mathur *et al.,*1987). Manal *et al* in 2012 made an investigation on adult albino rat the results of which proved that sub chronic dermal exposure to PPD in albino rat can induce hyperglycemia, disturbed hepatic, renal and cardiac functions. The histopathological findings showed that PPD cause mild, moderate, and severe chronic inflammation in the heart and liver. In the kidney and pancreas it causes moderate and severe chronic inflammation. This study established the multivisceral toxic effects of sub chronic dermal exposure to paraphenylene-diamine (Saad H.A.,2000, and Abd-Elzahar *et al*, 2012).

Paraphenylenediamine exposure to human being.

Epidemiological studies demonstrated that workers in the textile dye rubber industries, and hair dye users incurred a high risk of bladder cancer, non-Hodgkin's lymphoma, multiple myeloma, and hemapoietic cancers ((Ed Rietschel *et a.l,*2001 and Stanely, 2005). In considering any potential replacement of a material or a chemical by another one due to safety concerns, the primary role must be above all "do not harm" which means that the use of any replacement candidate must ultimately result in decreased risk. Such a situation is considerably more complex when we address materials used for cosmetic applications. Cosmetic application is however, not a trivial use, as most human consider it, a quality of life improvement, that enhances appearance and improves self esteem. In fact, recent survey results indicate that in the

U.S., 42% of women and 25% of men use hair dyes. The use of dyes to alter the coloration of a human's hair represents a considerable added degree of complexity in the risk assessment process(Rosenkranz *et al*,2007).

Henna (*Lawsonia inermis*) is a flowering plant used since antiquity to dye skin, hair, fingernails, leather and wool. The name is also used for preparations used from the plant, and for the art of temporary tattooing based on these dyes. Additionally, the name is misused for other skin and hair dyes, such as black henna or neutral henna, which do not derive from the plant. Black henna powder may be derived from indigo, or it may also contain unlisted dyes and chemicals. Black henna may contain paraphenylene-diamine (PPD), which can stain the skin black quickly, but can cause severe allergic reactions. Allergic reactions to PPD include rashes, contact dermatitis, itching, blisters, scarring and potentially harmful systemic effects (Van den,*et al*., 2005).

The most frequent serious health consequence of having "black henna temporary tattoo" is sensitization to hair dye and related chemicals. If a person had a "black henna tattoo" and later dyes their hair with chemical hair dye, the allergic reaction may be life threatening and require hospitalization. Because of the epidemic of paraphenylene-diamine allergic reactions, chemical hair dye products now post warnings on the labels (Sosted *et al*., 2006)

In addition to the local effects, there is the risk of systemic toxicity. Transcutaneous absorption of PPD is rapid and may lead to systemic effects including angioedema, gastrointestinal disturbance, tremors, drowsiness, convulsions, dyspnea, liver atrophy, acute renal failure with oliguria, anuria and dark urine (a characteristic chocolate brown color), cardiac arrest or even death. Also dermal exposure to PPD may result into muscle pain, tenderness, rigidity, and rhabdomyolysis (Dressler, 2006). There is no evidence that PPD affects reproduction. Long term exposure to PPD can damage the red blood cells causing anemia.

For safety assessment of personal care products (PCP) the ingredients that pose complex safety issues must be used cautiously. PCP are generally applied to human skin and mainly produce local harmful effects, although skin penetration or via oral cavity, lips, eyes, face or mucosa also produce harmful systemic effects. Oxidative hair dyes contain arylamines, the most chemically reactive ingredients of PCP (Nohynek *et al*.,2010). A recent study investigated the dermal exposure of hairdressers to oxidative hair dyes. The study focused on hair dye residues on the hands of hairdressers after hair dyeing with or without gloves, as well as hand exposure during the cutting of dyed hair. Meanwhile, the given study did not investigate the systemic exposure, the significance in terms of a human health risk of small residues detected on the hair-dresser's hand is uncertain. Overall, the occupational systemic exposure of hairdressers to hair dye ingredients remains virtually unknown..

How to diagnose Allergic sensitivity of PPD

Most hair colour preparations, particularly those containing PPD, carry a warning on the packaging to the effect that a patch test should be done prior to use of the dye. There are basically 2 patch testing methods available to test for allergic sensitivity to PPD (Ed Rietschel *et al.,*2001).

Patch test method 1: uncovered

- Routine technique used by consumers for testing hair dye sensitivity.
- Instructions for testing should be included with every package of hair dye preparation.
- Essentially the test involves applying a 20 cent sized spot of solution (i.e. dye and developer mixed together) to either the neck (behind the ear) or the inner bend of the elbow. Allow to dry and leave uncovered for 48-72 hours. If no irritation or rash occurs during this time then the test is negative and one can assume that the risk of developing a rash will be much less when the dye is applied to the whole head.

- Any immediate signs of irritation or rash are more likely to be an irritant contact dermatitis (i.e. non-allergic, Fig-2) .
- A 1+ to 2+ reaction (scale measuring PPD sensitivity as shown in figure-1) to PPD hair dye usually indicates that dermatitis will develop if the mixture is used.

Patch test method 2: covered

- Diagnostic test used to determine PPD sensitivity.
- Patch testing using 2% PPD in petrolatum
- A +/- reaction (scale measuring PPD sensitivity) to this patch test method usually means that these individuals can use PPD hair dyes without difficulty.
- A 1+ to 3+ reaction indicates allergic dermatitis will most likely occur with use of hair dyes thus preventing their use.

  Positive reaction from both methods provides confirmation that PPD is the cause of dermatitis and PPD containing products should be avoided.

Treatment of PPD dermatitis

In acute severe cases of PPD hair dye dermatitis, wash the hair and scalp thoroughly with a mild soap or soapless shampoo to remove the excess dye. Apply a 2% hydrogen peroxide solution or compresses of potassium permanganate in a 1:5000 dilution to completely oxidise the PPD. To soothe, soften the crust and alleviate the tight feeling of the scalp, a wet dressing of cold olive oil and lime may be used. Further treatment with a topical application of an emulsion of water and water-miscible corticosteroid cream, or oral corticosteroids may be indicated. Management of PPD dermatitis on other parts of the body may be treated as for any acute dermatitis/eczema ; this may include treatment with topical corticosteroids and emollients (Ed Rietschel *et al.*,2001).

Conclusion : From above consideration, the replacement of Paraphenylene diamine with less hazardous ones represents an urgent challenge both from a chemical formulation and risk assessment perspectives. There is a strong care for the regulation and restriction of sale of paraphenylene-diamine. Semi-permanent hair dyes may be a suitable alternative but approximately 10% of individuals who are allergic to PPD also react to these.Metallic hair dyes and vegetable rinse hair dyes may be used but these do not provide permanent colouring. Some newer permanent and semipermanent hair dyes use para-toluenediamine sulfate (PTDS) instead of PPD. This is likely to be tolerated by about 50% of people who are allergic to PPD. Patch testing is recommended prior to use. In cases of occupational exposure, avoid contact with PPD by wearing suitable protective garments such as gloves and protective sleeves. Allergy to PPD may make a person sensitive to other related compounds. As a precaution we should avoid using products containing PPD.

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The real opportunity for success lies within the person and not in the job.

~ Zig Ziglar