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Review Article

Influence of Hair Dyes for Cancer

Components in Hair Dye and Possible Health Concerns from Using Straighteners, Including Cancer Risks

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Abstract: Acute toxicity of hair colours and their components ranges from moderately to low. Accidental human toxicity is uncommon and has only been associated with oral consumption. Hair colour interface sensitization is an ongoing safety concern, primarily due to unsupervised skilled description. While the usage of hair pigments has skyrocketed in developed nations over the past several decades, the prevalence of dye sensitivity in people of all ages and among professionals has steadied or even decreased. However, there is uncertainty regarding the organic category of oxidative hair dye ingredients' in vivo carcinogenicity (aromatic amines); in vitro, genotoxicity investigations on hair dye compounds typically produced good findings. Hair pigments seldom provide positive in vivo genotoxicity outcomes. No proof of genotoxic consequences of hair pigments or their components has been identified through research in men. Based on pharmacological investigations, a few favourable vivo positive hair dye chemicals (p-aminophenol, Lawsone) have been demonstrated to offer no danger or very little threat to people's health. Even though the newest case-control epidemiology research revealed a link between hair colour usage and bladder cancer, several additional studies, especially retrospective analyses on sizable populations, revealed no negative associations for bladder or other malignancies. Oral carcinogenicity studies on hair dye substances at doses taken orally up to the greatest tolerated dose (MTD) indicate that certain compounds are carcinogenic in rodents, despite research on the chemicals or commercial formulations of hair pigments' in vivo topical carcinogenicity producing insufficient proof for systemic toxicology or carcinogenicity.

Keywords: Hair dye, hair straighteners, p-aminophenol, hair colouring, p-phenylenediamine and local lymph node assay(LLNA)

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1. INTRODUCTION

Analyzing the toxicity and carcinogenicity of hair pigments and their constituents is essential. Many potential colouring compounds have passed safety evaluations before being used in hair pigments due to the scientific panel's Cosmetic Ingredient Review (CIR)[1]. Based on the nature of their composition, modern hair pigments can be categorised as oxidative or nonoxidative, and their colour permanence is temporary (8–12 washings), semi-permanent (24 items of washing), or permanent (until hair grows out). Chemically, nonoxidativehair pigments are categorised as temporary or semi-permanent, whereas oxidative hair pigments are sometimes referred to as permanent or semi-permanent. Interim and semi-permanent hair colours applied straight to natural hair include nonoxidative substances. In Asia, America, and Europe, enduringhair pigments have the largest revenue share of all contemporary hair pigments. Hair dyeing is currently identified as a risk to the public's health that needs immediate investigation of the toxicity and carcinogenicity connected to hair pigmentssince the expanding economic importance and user base. Since many hair colouring brands with particular chemicals were utilised in the past, findings regarding hair pigment-induced toxicity and carcinogenicity presented in research remain unclear. Leaden combs dipped in vinegar were frequently used in the Roman Empire to deepen greying hair[2]. Many people use hair pigments currently. These items have a significant and beneficial function in improving our quality of life since humans naturally desire to look better. Given the volume and frequency of human contact with hair colouring solutions, their components must be secure. The examination of transdermal absorption/penetration of hair pigments and their constituents began with the realisation that the human skin is not a formidable barrier for some topically applied compounds. When in vitro findings point to the likelihood of cumulative description in humans, the possible consequences for acute, subchronic, reproductive, and genetic toxicity and carcinogenicity must be examined. Alternative approaches, such as in silico and chemical models, are perhaps utilized to estimate the hazards related to the cumulative description. Regulatory decisions ought to be made in consideration of all available evidence. The safety of the public must be the primary concern. All stakeholders should be implemented in evaluating the risks and benefits of a given chemical or product[3]. The decision-making process must be transparent and accountable to ensure public safety and trust. These alternative methods can provide additional evidence to inform the regulatory decision, as the traditional risk assessment methods, such as animal tests and epidemiological studies, can be costly and time-consuming. Furthermore, transparency and accountability are essential to ensure that stakeholders know the assessment process and the decisions taken and that the public can trust the results. Therefore, alternative methods are utilised to supplement the traditional risk assessment methods and provide a more comprehensive understanding of the risks posed by a particular product or activity. This can result in better decision-making and protect the public's health and safety.

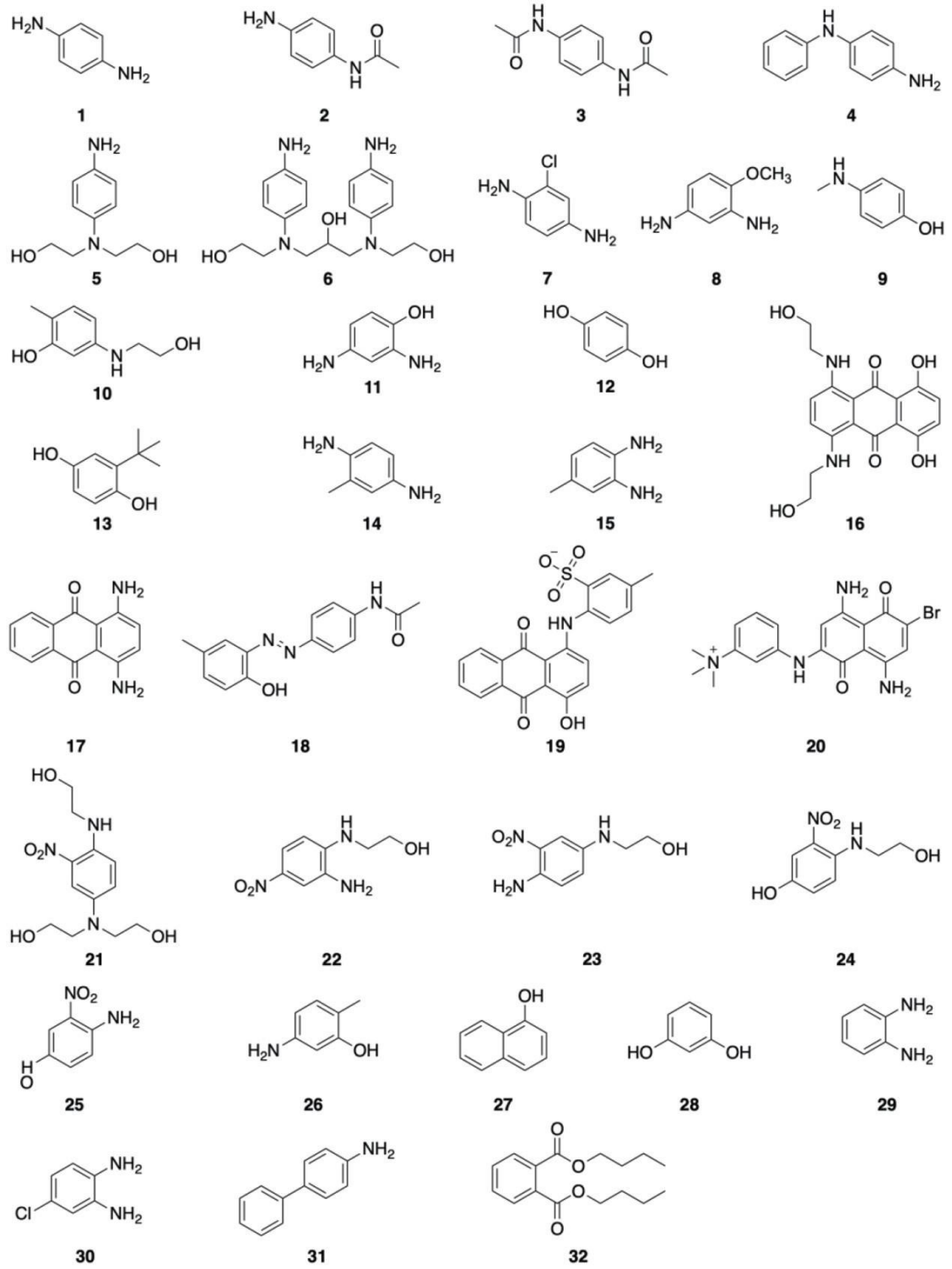

Fig 1: Chemical structures of hair dye ingredients. Chemical structures of the following hair dye ingredients are shown: p-phenylenediamine1

(PPD), N-monoacetyl-p-phenylenediamine2 (MAPPD), N,N-diacetyl-p-phenylenediamine3 (D-A-P-P-D), N-phenyl-p-phenylenediamine4, N,Nbis(hydroxyethyl)-p-phenylenediamine5, hydroxypropylbis(N-hydroxyethyl-p-phenylenediamine) 6, 2-chloro-p-phenylenediamine 7, 4-methoxym- phenylenediamine8, p-methylaminophenol9, 2-methyl-5-hydroxyethylaminophenol 10, 2,4-diaminophenol 11, hydroquinone 12, t-butyl hydroquinone 13, toluene-2,5-diamine (CAS no: 95-70-5) 14, toluene-3,4-diamine 15, Disperse Blue 7 16, Disperse Violet 1 17, Disperse Yellow 3 18, Acid Violet 43 19, Basic Blue 99 20, HC Blue no. 2 21, HC Yellow no. 5 22, HC Red no. 7 23, 3-nitro-p-hydroxyethylaminophenol 24, 4- amino-3-nitrophenol 25, 4-amino-2-hydroxytoluene 26, 1-naphthol 27, resorcinol 28, o-phenylenediamine29, 4-chloro-o-phenylenediamine 30, 4-aminobiphenyl31, and di-n-butyl phthalate 32. Only the core chemical structures are shown. The sulfate or hydrochloride salts are omitted for simplicity[4].

2. ELEMENTS FOR HAIR DYE: DISTINCT KINDS OF HAIR DYE

Semipermanent hair colours often maintain their colour after multiple shampooings. Permanent hair pigments enter the hair to change the colour, but they are better commonly linked to negative side effects and put human health at

greater risk. This is because permanent hair pigments use harsher chemicals to penetrate the hair shaft and change the colour. On the other hand, semi-permanent hair colors are less damaging as they only coat the outside of the hair shaft and do not penetrate it, making them less likely to cause any negative side effects. Three ingredients are necessary for permanent hair pigments: (1) precursor agents, which are elementary intermediates made of ortho- (o-) and para- (p-) aromatic amines replaced with groups of amino acids and hydroxides; (2) coupling agents, which are aromatic compounds meta- (m-) substituted with electron-donating groups, such as m-phenylenediamines, resorcinol, naphthol, and other derivatives; and (3) oxidising agents in alkaline. The precursor agents are responsible for the colouring of the hair, while the coupling agents, such as m-phenylenediamines, resorcinol, and naphthol, create the reaction between the precursor agents and the oxidising agents[5]. The oxidising agents, such as hydrogen peroxide, are necessary to make the colour permanent[6].

3. ELEMENTS IN HAIR DYE: CHEMICAL MAKEUP AND POTENTIAL TOXICITIES:

The primary class of substances used as antecedents in enduringhair pigments is aromatic amines, which include p-phenylenediamine (P-P-D, 1) (Figures 1 and 2). Previous research has shown that PPD has a variety of toxicological characteristics. For illustration, PPD promotes apoptosis by raising reactive oxygen species[7].PPD can enter the body through the skin during hair colouring; after that, it is subsequently taken up by the airways and biotransformed into N-monoacetyl-p-phenylenediamine (M-A-P-P-D, 2) and N, N′-diacetyl-p-phenylenediamine (D-A-P-P-D, 3; Figure 2)[8]. Using the restored human epidermis, researchers investigated how PPD transformed into MAPPD and D-A-P-P-D and discovered that the quantities of these metabolites depend on the PPD dosage[9]. After in vitro description of oxygen in the air, PPD causes dendritic cell (DC) activation and a positive local lymph node assay (L-L-N-A) response in vivo, demonstrating its intracorporeal sensitizing potential. PPD has been shown to be one of the potential inhibitors of oral cancer, as it stimulates the immune system to produce cytokines that can suppress the growth of cancerous cells. The anti-tumor activity of PPD has been demonstrated in various animal studies. It has also been demonstrated to have anti-inflammatory and antioxidant activities. In addition, PPD has been shown to have potential anti-viral activity. Studies have shown that PPD activates the immune response by inducing the production of cytokines, which are proteins involved in the regulation of the immune system. These cytokines can help to suppress the growth of cancer cells and also act as anti-inflammatory and antioxidant agents. Furthermore, research has revealed that PPD may also have anti-viral activity, which could be beneficial in the treatment of oral cancer.[29] Piperine has been found to have several anticancer properties, including the inhibition of cancer cell growth, induction of apoptosis, and suppression of inflammation. In the oral cavity, piperine has been found to have a protective effect against oral cancer, by preventing the formation of carcinogenic compounds and inhibiting oxidative damage. Piperine has also been shown to increase the bioavailability of some drugs, making them more effective. Additionally, piperine can reduce the side effects of certain drugs, making them more tolerable. It is believed that piperine works by blocking the enzymes that break down drugs in the liver and small intestine, increasing the amount of time the drugs stay in the body, and therefore increasing their effectiveness. It also binds to certain toxins, making them less harmful, and it can reduce inflammation in the oral cavity, which can help protect against cancer.[33]

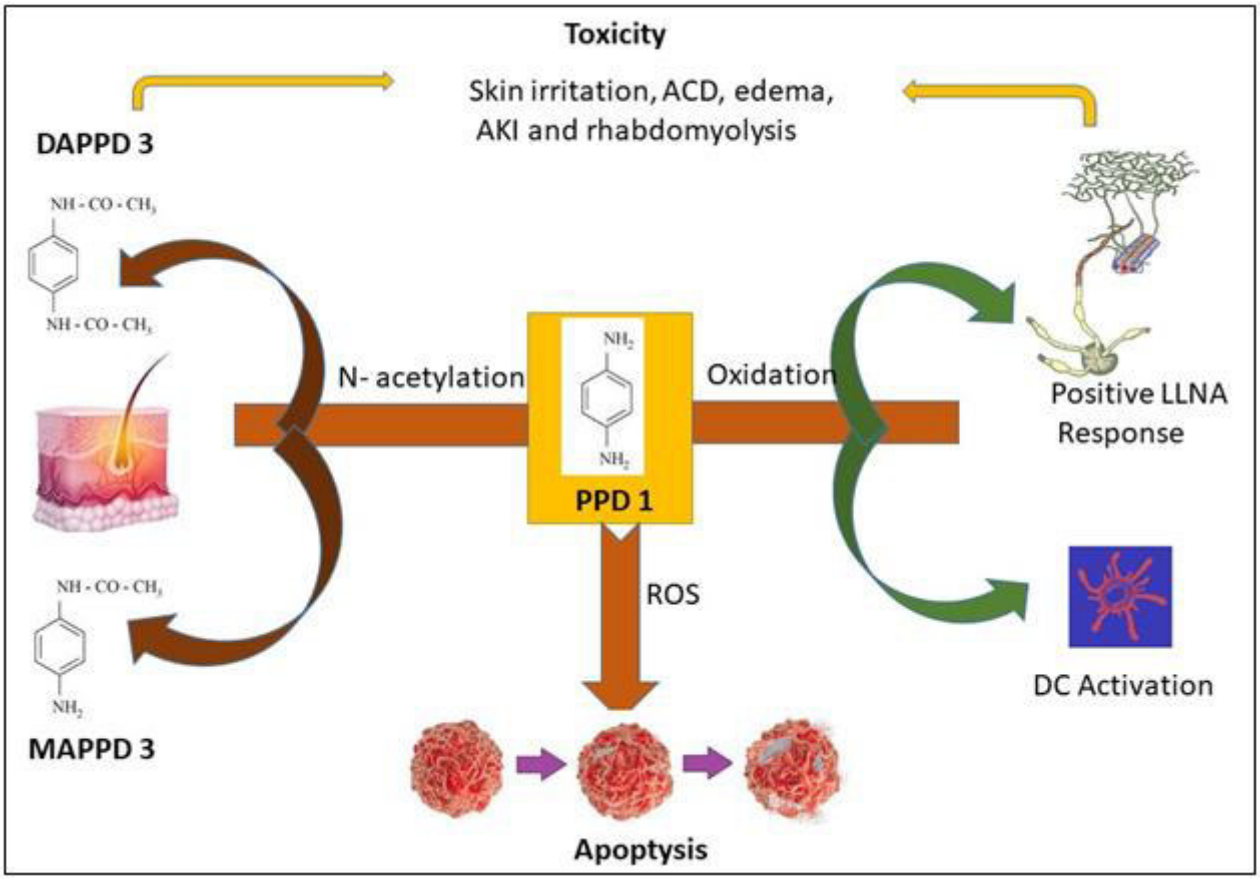

Fig 2:The technique of toxicity induced by p-phenylenediamine.

4. CONNECTION ACROSS USING HAIR DIES AND HEMATOPOIETIC CANCER

Personal hair colour is a risk factor for primary myelodysplastic syndrome. However, several studies have not found any conclusive evidence linking this behavior to an aggregate elevated risk of leukaemia. More research needs to be done to determine if there is a direct link between hair colouring and various forms of cancer. The potential risks should also be weighed against the benefits of using hair colour products. Diffuse large B cell lymphoma, a form of NHL, may be more likely in those who use hair colours for work. According to case-control research conducted at a hospital in Shanghai, individual hair dye usage is not linked to an increased risk of NHL or any of its subtypes[10]. However, further research needs to be conducted to determine if there are any long-term effects of using hair colour products. It is important to consider the potential risks associated with using hair colour products, especially for those in occupations requiring frequent use. It is also important to note that the Shanghai research did not take into account the cumulative effects of using hair colour products over some time. On the other hand, the routine application of enduring hair pigments was positively correlated with an elevated risk of NHL, according to population-based case-control research from the United States[11].This link was higher for a longer duration of use and younger age of initial use. Numerous long-term case-control investigations are also included. Strikingly, this correlation persisted despite other potentially influential factors, including smoking, alcohol use, race, education level, and others.

5. DISTINCT KINDS AND CHEMISTRY OF HAIR COLOURS: OXIDATIVE (PERMANENT) DYES

The most significant class of hair pigments accounts for approximately eighty percent of the EU or the US market. They vary from the other types of dye in that they include two elements that must be combined before usage for chemical processes to produce the colour on or in the hair. Multiple elements with various functionalities are present in contemporary oxidative dyes (see examples in Fig. 3. Primary intermediates: these include ortho- or para-aminophenols, substituted para-diamines, para-toluenediamine (PTD), para-phenylenediamine (PPD), and para-toluenediamine (PTD). These compounds are oxidised, and when they combine with adjustments, the resulting products are coloured. Primary intermediates are in hair pigments in concentrations ranging from 0.05% (light hues) to 1.5% (dark shades). Semipermanent and temporary direct dyes comprise the second group of economically significant hair colourants[12].Azo, triphenylmethane, anthraquinone, or indamine dyes are temporary colouring agents, while nitro-phenylenediamines, nitro-aminophenols, and certain azo dyes are semi-permanent colouring agents. Metal salts frequently depend on lead acetate, which is limited in the EU to a maximum lead level of 0.6% and is used mostly to conceal greying hair[13].Plant-based natural dyes have a modest but growing commercial significance. Henna, made from the leaves of the North African plant Lawsoniainermis, or its pure dye component, is used in many natural dyes.

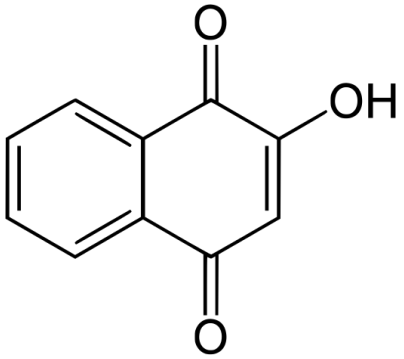

Fig. 3. Structure of Lawsone (2-hydroxy-1,4-naphthoquinone)

6. FACTORS OF HAIR DYE SAFETY - ACUTE TOXICITY/POISONING ACCIDENTS

According to the findings of acute toxicity testing, all significant components of hair dye, such as PPD, PTD, or resorcinol, have moderate to low acute toxicity characteristics. Only after oral administration have instances of unintentional human poisoning caused by chemicals in hair colour been documented. Despite the low toxicity of the components, it is important to follow the instructions for using hair dye and keep it out of reach of children. It should also be noted that prolonged and frequent hair dye use can still lead to health concerns. While there were a few reports of serious human poisoning from PPD, these incidents typically followed suicide attempts or murder. Angioneurotico edema, which causes acute respiratory distress, is the primary adverse effect of high acute doses of PPD in humans and higher mammals[14].Prolonged and frequent use of hair dye can also cause allergic reactions, such as contact dermatitis and contact urticaria, in some people. This is thought to be a reaction to the chemicals in the dye, such as para-phenylenediamine (PPD). Rhabdomyolysis, or the necrosis of skeletal muscle that causes acute renal failure, together with the atrophy of the optic nerve, causes vision loss in a patient who consumed an acute dose and has also been reported estimated amount of 7 g para-phenylenediamine[15]. Additionally, the rare case of rhabdomyolysis has been linked to ingesting an estimated amount of 7g of PPD, leading to the necrosis of skeletal muscle and optic nerve atrophy.

7. HAIR DYE SAFETY CONSIDERATIONS - CONTACT ALLERGIES

Contact allergies can be induced and elicited by PPD, among the least common precursors of oxidative carotenoids for hair, and its derivatives, such as PTD. Numerous research on humans and animals have supported this. Before using the

product, consumers are encouraged to do an allergy test, while hairdressers are urged to use gloves to protect their skin when dying their clients' hair. Primarily in cosmeticians and hairdressers, the allergenic potential of PPD and its derivatives continues to be a significant factor in occupational allergies. In Germany, routine patch tests revealed a high frequency of contact allergy to PPD, see Figure 04[16].Despite the rising usage of hair pigments in the industrialised world—from 40% of women reporting use in 1969 to 60% in 1996 (industry statistics), the relative prevalence of contact allergy to PPD appears to have declined in recent years. The consistent frequency has been related to the effective implementation of risk management strategies, such as precautionary labelling, improved adherence to occupational safety procedures, like donning protective gloves, reducing contact of the hair dye with the scalp during application, and raising consumer risk awareness. Nanotechnology strategies can include the use of nanomaterials to develop nanoscale drug delivery systems, nanomaterial-based sensors for detecting harmful substances, and nanosized particles for the detection and analysis of hazardous substances. Nanomaterials can also be used to create nanostructures for tissue regeneration and repair, as well as for the development of nanoscale diagnostic and imaging systems. Finally, nanotechnology can be used to create medical devices and treatments on a nanoscale. These nanomaterials are designed to interact with cells and biological molecules, allowing them to be used for targeted drug delivery, tissue engineering, and tissue regeneration. They are also used to create tiny sensors and probes that can be used to detect and monitor diseases. Furthermore, nanomaterials can be used to create nanostructures that can be used to repair damaged tissues or organs, as well as to create nanoscale imaging systems that can detect nanoscale changes in the body. Not only can nanomaterials be used for medical and diagnostic purposes, but they can also be utilized to create materials for a myriad of other applications, such as energy storage, water filtration, and even self-assembly of nanoscale parts.[31] Although PPD, PTD, or their analogs are the main cause of hair dye allergies, several direct dyes (such as those in the nitro- and anthraquinone classes) are recognized for their potential to cause sensitization;However, it appears that human allergies to direct dyes are not very common.

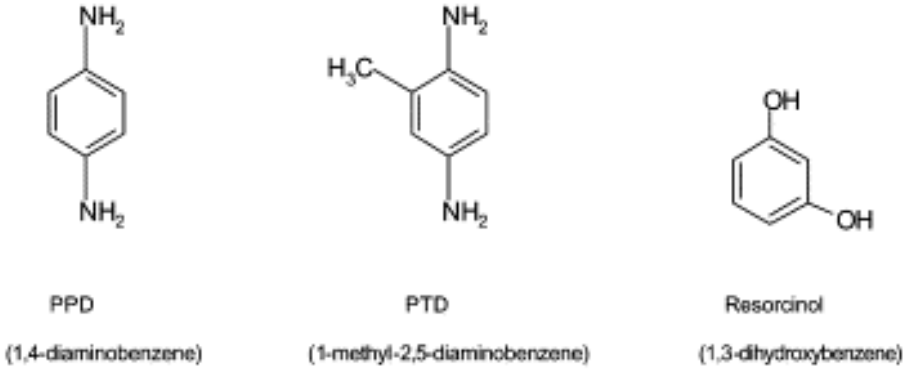

Fig. 4. Structures of primary oxidative hair dye intermediates paraphenylenediamine (PPD), para-toluenediamine (PTD), and resorcinol.

8. ASPECTS OF HAIR DYE SAFETY

While genetic testing for toxicity is now deemed informative for both mutagenic and carcinogenic dangers, they are still primarily seen as short-term screening studies to estimate a substance's carcinogenic capability. They are also used to determine the biological effects of a certain substance and its ability to cause genetic damage and mutations. Genetic testing is also used to examine the mechanism of action of a particular chemical or compound. Numerous authors and institutions have developed tiered test methodologies that combine in vitro and in vivo testing to assess the genotoxic risk of a chemical and its mechanism[17]. This is done by measuring the alterations in gene expression or the occurrence of DNA damage. It can also be used to establish if a particular chemical can cause mutation or if it has the potential to cause cancer. Furthermore, it is utilised to identify the potential mechanisms of action that allow a chemical to cause genetic damage. Genotoxicity testing may be utilised to assess the potential safety of a new drug or product before it is administered to human patients.

9. CARCINOGENICITY

For many years, toxicologists and epidemiologists have been interested in the possible carcinogenicity of hair dye components, primarily because several compounds are members of the broad chemical family of aromatic amines. Studies have shown that using hair colour might make some cancers more likely, such as breast and bladder cancer[18].However, more research is necessary to ascertain the precise risk of using hair colour. Some ofthe recognized human carcinogens found in aromatic amines, such as benzidine, 4-aminobiphenyl, and 2-naphthylamine, were identified as having an elevated incidence of bladder cancer among economically exposed dye industry employees as early as the latter part of the nineteenth century.This suggests that the same compounds in hair pigments may be linked to cancer. Research into the specific effects of these compounds on humans has been limited, so there is a need to investigate this link further and determine what risks, if any, are connected to hair dye use. The International Agency for Research on Cancer of the World Health Organization has examined the possible carcinogenicity of aromatic amines and hair colours[19]. Although certain aromatic amines have been linked to cancer in humans and other mammals, most compounds in this chemical family don't. Some aromatic amines have been used in the detection of oral cancer because they have been found to be selectively taken up by cells in the mouth that are indicative of pre-cancerous and cancerous lesions. Further research is needed to determine the effectiveness of using these compounds for cancer detection. As with any chemical, safety precautions should be taken when handling aromatic amines. Prolonged exposure

should be avoided to reduce the risk of developing cancer. In addition, further research is needed to determine the possible long-term effects of using these compounds for cancer detection. For example, it is unclear whether exposure to aromatic amines could potentially increase the risk of developing cancer over time, even if exposure is limited and safety precautions are taken. However, more research is needed to understand further the potential health risks associated with using hair colour products containing aromatic amines.

10. EPIDEMIOLOGY

Several epidemiological studies have been published on cancer occurrence in people who use hair colour and in groups exposed to it professionally. There is no correlation between the risk of cancer and consumer or workplace description of hair pigments, according to several evaluations of epidemiological research. However, further research is needed to rule out any possible threats associated with hair dye use. Moreover, it is important to note that other health risks may be associated with hair dye, such as allergies, skin irritation, and eye irritation. Female users of hair colour were shown to have a higher risk of urinary bladder cancer, according to a recent case-control research[20].A further study by the same authors on the same participants revealed that the N-acetyltransferase 2 (NAT2) slow acetylator phenotype of cancer was primarily responsible for the higher prevalence of bladder cancer among hair colour users[21].The study showed that slow NAT2 acetylators had a higher risk of bladder cancer when interacting with hair dye, while those with the fast NAT2 acetylator phenotype had a much lower risk. This suggests that the slow acetylation of hair dye metabolites, common among slow acetylators, is linked to the higher threat of bladder cancer among hair colour users[22]. However, because hair colouring mostly results in dermal contact with the components and substances like PPD may be acetylated in the skin by NAT1 and not NAT2, hair dye compounds such as these should be avoided. Therefore, it is important for hair colour users to be aware of the potential risks associated with slow acetylation of hair dye metabolites and to take necessary precautions when choosing hair pigments that do not contain compounds such as P-P-D.

11. DESCRIPTION OF HUMANS TO HAIR PIGMENTS

The possible detrimental effect of external human description to a chemical depends on its systemic toxicity, the human systemic contact, and the dose-response of the relevant toxic impact, with an instance of local effects such as skin sensitization or irritation. The toxicological evaluation of a chemical should consider the available information on the possible toxic effects, the description level, and the human population exposed. This will allow for the assessment of potential threats and the identification of any necessary risk management measures. As a result, a substance's hazardous potential is only important when considerable systemic description occurs[23]. The major safety concern with hair colour components is the potential consumer description, as occupational description has been demonstrated to be minimal when simple precautions are adopted. By assessing potential threats, it's possible to understand the likelihood of a hazardous effect occurring when a consumer is exposed to a particular substance. This also allows for implementing any necessary risk management measures to ensure that the description is kept to a minimum and the consumer is kept safe. Hair colours and their chemicals must first permeate the epidermal barrier to cause systemic description. Hair dye percutaneous absorption has lately been examined. Understanding the threat of a hazardous effect is essential for properly implementing risk management measures to reduce consumer description and keep them safe. Through research, the ability of hair colours and chemicals to permeate the epidermal barrier has been studied in depth, and further investigation is needed to understand the full extent of hair dye percutaneous absorption.

12. ENDOCRINE /REPRODUCTIVE EFFECTS

Additionally, the modest discrepancy between hairdressers and the reference group might have resulted from the strenuous nature of the profession. For instance, hair dye components are being examined for possible reproductive toxicity, including embryofoetal toxicity and, if appropriate, male/female fertility or peri-/post-natal toxicity[24]. Newer congeners of doxycycline, such as minocycline, are being studied for their potential to cause photosensitivity, allergic reactions, and antibiotic resistance. The potential for hormonal imbalances from long-term use of hair dye is also being studied. Similarly, there is concern about the possible carcinogenic effects of some components of hair dye. Finally, the potential for eye irritation is being investigated. Studies have shown that some of the chemicals in hair dye, such as parabens, can be absorbed through the skin and enter the bloodstream. This could lead to hormonal imbalances, and there is evidence that some of these chemicals could be carcinogenic. Additionally, the long-term use of doxycycline and minocycline can lead to antibiotic resistance, and there is a risk of allergic reactions and photosensitivity. Finally, the potential for eye irritation from hair dye is being investigated.[34] Hairstylists are exposed to other potentially hazardous chemicals, such as glues, dyes, and aerosols. Furthermore, they are at elevated dangerof musculoskeletal disorders since prolonged and awkward postures. Standing for over eight hours daily combined with physical activity has been identified as a threat elementfor LBWB CIR(Low Birth Weight Baby). Using a dye found in hair would be prohibited if a biological danger was found. Hair pigments contain plenty of chemicals that can be toxic if inhaled or have skin-based absorption. Prolonged descriptions of these substances may cause various health issues, such as respiratory problems, skin irritation, and cancer. Musculoskeletal disorders are also a risk, as the postures associated with hairstyling can be awkward and uncomfortable for long periods. Therefore, these chemicals are strictly monitored to ensure that hairstylists remain safe and healthy.However, it is uncommon for chemicals in hair colour to have biological impacts in animal experiments. Therefore, it is essential for hairstylists to be aware of the potential risks associated with the use of these chemicals and to take the necessary steps to reduce any potential harm.

13. METABOLISM, TOXICOLOGICAL AND TOXICOKINETIC ASPECTS

Early analyses of potential systemic descriptions of hair color ingredients were made on hypothetical worst-case presumptions. More thorough cutaneous absorption and metabolism investigations have been conducted in recent years. The key "primary intermediates" of oxidative hair pigments, p-phenylenediamine, and p-aminophenol, are the

subject of these investigations. The human percutaneous absorption of 14C-labeled chemicals included in oxidative hair pigments was assessed in certain investigations, while primary intermediates were the only focus of other studies[25]. Early diagnostics on oral cancer with a focus on the percutaneous absorption of hair pigments. This research showed that the percutaneous absorption of chemicals can be used as a biomarker for early cancer diagnosis. Additionally, this indicates that the absorption of hair pigments may have a role in cancer development. Further research is needed to understand the role of hair pigments in the development of cancer. With this research, it was determined that assessing the percutaneous absorption of certain chemicals could provide a reliable biomarker that would allow for an earlier diagnosis of oral cancer. This could potentially lead to better outcomes for those diagnosed with the condition, as earlier diagnosis has been linked to better treatment outcomes. Additionally, the findings suggest that hair pigments may play a role in the development of cancer, though further research is needed in order to understand the exact role they play. Further research may help elucidate how hair pigments influence cancer development, which could lead to even better treatment outcomes for those affected by the disease. A comprehensive review on bio-based materials that could potentially be used to create better hair pigments may provide a better understanding of their role in cancer development.[32,35]In humans, systemic penetration of oxidative and direct hair pigments has been predicted to be no more than 0.2% of the applied quantity, according to a review of prior research on the superficial absorption of hair pigments. Confidential industry papers filed to the EU Commission in 2005 describe another investigation on the uptake of hair dye reaction compounds (three dimers and one trimer) carried out in vitro using human and pig skin[26].Only 0.01 to 0.08% of the substances utilised on the skin were completely skin-based permeation. Therefore, there needs to be a more human description of the oxidative hair coloring procedure's dimeric or trimeric product reactions.

14. SUMMARY

Traditional commercial toxicology's classic subject is how specific aromatic amines cause urothelial carcinoma. Aniline, for example, has practically minimal ability to cause this sort of human neoplasia, but benzidine has a very high ability to do so[27].The key factors of the genotoxicity of aromatic amines are metabolism and the reactivity of metabolic intermediaries. As a result, several species variances exist in each compound's potency and organotropism. Similarly, it is claimedthat the almonella test has minimal predictive value for the ability of aromatic amines to cause cancer in rodents[28]. The aromatic compounds used as hair colourants also fall within these guidelines. In the 1970s, it was discovered that specific aromatic amines used in eternallyhair pigments had genotoxic qualities and were carcinogenic when given orally to rats. As a result, regulation was taken in Europe and other countries. Given that human urothelial malignancy chemically caused by industrial aromatic amines often have latency durations longer than twenty years, this brief period could still be relevant today.

15. AUTHORS CONTRIBUTION STATEMENT

M.S. Nandini conceived the study and was responsible for the overall direction, analysis, and planning. M.S. Nandini, Kishore Kumar S carried out the implementation. M.S. Nandini took the lead in writing the manuscript. Kishore Kumar S, Rajesh.E and Sankar Narayanan.R provided critical feedback, reviewed, and helped in the final corrections of the manuscript.

16. CONFLICT OF INTEREST

Conflict of interest declared none.

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