# Addressing Epidemic of Para-Phenylenediamine Sensitization by Going Forward into the Past

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The epidemic of sensitization to para-phenylenediamine will cause loss of client base for oxidative hair dye. Generalizing from the results of a broad UK sensitization assay of adolescents in 2014, 16% of adults in western industrialized nations are now sensitized to PPD; by the time they begin to gray in 2030, all of these people will be unable to use oxidative hair dye and other products containing coal tar derivatives and 7% may have reactions severe enough to require hospitalization.[i] Many with extreme PPD reactions were sensitized by 'black henna' temporary tattoos.[ii] In East Africa the practice of decorating skin with PPD to create 'black henna' temporary tattoos has been popular since the 1970's;[iii] levels of sensitization are very high; Khartoum, Sudan, now has over 300 hospital admissions each year from high systemic exposure to PPD.[iv] North Africa, the Arabian Peninsula, and South Asia, where people have used 'black henna' since the 1980's also have a high rate of hospital admissions related to the health consequences of PPD exposure.

The popularity of 'black henna' temporary tattooing is not the sole driver of this epidemic. Childhood use of hair dye, particularly inept applications of home hair dye kits by teenagers during the Punk, Emo, and Goth eras have elevated the number of sensitizations. The black henna temporary tattoos appear to be responsible for the severe reactions and cross-sensitization to related chemicals.[v] Black hair dye products imported from India, Pakistan, Japan, and China containing 20% to 40% PPD have contributed to the severity of sensitizations.[vi]

The current severe +++ sensitization reactions and deaths being reported now have not been seen since the early 1900's when PPD dyes for hair were not regulated at 6% PPD or lower.[vii] Because of the high dye percentage and large body area applications of PPD in 'black henna', many people are sensitized to other diamine-related chemicals and must avoid the entire portfolio of cosmetic chemicals which have proceeded from the initial synthesis of aniline dyes in the mid1800s. Development and promotion of 'safer oxidative' hair formulas may result in more injuries as many people sensitized through 'black henna' temporary tattoos are cross sensitized to chemically similar compounds.[viii]

According to a 2016 survey by the British Skin foundation, two-thirds of British dermatologists have seen an increase in patients with reactions to hair dyes, many of whom have previously had a 'black henna' temporary tattoo.[ix] If a significant number of the client base becomes unable to use chemical hair dye, and the chemical cosmetic industry does not want to lose that revenue, an alternative to coal tar derivative dyes must be developed.

**Why henna disappeared from cosmetology practice**

Before the invention of oxidative dyes, there was a permanent, gray-covering, non-fading hair dye technology based on henna, partially fermented indigo, cassia, and fruit acids. The older plant-based plant hair dye techniques were learned and shared in the village baths of North Africa, the Levant, Arabia, India, and the Middle East; these hair dye practices were refined generation after generation and regarded as the safest, most reliable, most attractive thing a person could use on hair. Colonial expansion into these countries brought these dyes to Europe, where they became the height of fashion in the late 1800's and into the early 1900's. Women's long, flowing red hair celebrated in Art Nouveau and the brilliant red hair shown in Toulouse Lautrec's paintings of women show European women's delight in henna, the newly available exotic wonder. Sarah Bernhardt hennaed her graying hair, as did many other divas, and their admirers followed suit.

The popularity and reliability of henna was disrupted when World Wars I and II interrupted the henna supply chain from the Ottoman Empire, Egypt, and North Africa. B. Paul and other American hair dye companies added mineral salts to inferior low grade henna base to stretch a scant and inferior supply when henna became difficult to import. These additives also were meant to compensate for the lack of traditional knowledge when henna products were sold outside of the native region. These products were marketed as 'henna compounds'. Compound henna hair dye products currently in the marketplace have a justifiably terrible reputation in the cosmetic industry based on the destructive cross reactions between mineral salts and the activators for oxidative hair dye. These are, most notoriously, sodium picramate, lead acetate, silver nitrate, copper, nickel, cobalt, bismuth and iron.[x] If these additives are undeclared, or the declaration is obscured, hairdressers conclude that henna itself is to blame.

Most compound henna products contain low dye content plant materials, misunderstood chemistry, and additives masking the poor botanical quality. These compromise the color outcome while pushing profits higher and undermine what once was, and what should be, a very beneficial product. The compound henna hair dye products presently in the marketplace are a case study in what can go wrong when market forces tinker with a reliable and serviceable product with the intent of improving convenience, uniformity, predictability, and profitability until the original good of the product is compromised to the point of near uselessness.

Pure henna, indigo, and cassia in varying proportions can dye hair the full range of human hair color and allow people who have been sensitized to PPD to transition away from oxidative hair dye without having to grow out their hair. If 16% of hair-dying population will need to switch to henna because of sensitization, how much supply must be obtained, and how will it be possible to re-educate the consumer and cosmetologists to transition these people to henna? One kilo of plant powder per year is sufficient for one person to permanently color hair, doing monthly root growth. Sufficient supplies will have to be planned for, grown, milled and harvested to the standards western consumers expect. The coarsely sifted henna presently in the marketplace will not be acceptable to western consumers accustomed to easy-to-apply, easy-to rinse dye. Henna, cassia, and indigo milling and sifting must be improved to 150 micron particle size; there must be no sand, adulterants, additives, or plant debris in the leaf powder. Double wall packaging is necessary for the powders to remain quality over several years. Indigo must be kept from freezing, or the dye will be spoiled. Henna must be kept under 90F to maintain dye quality.

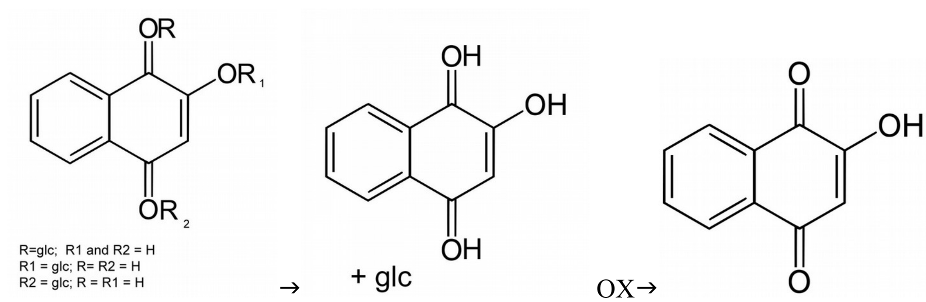
**Expanding and improving the resource base**

Most of the henna currently in the marketplace at present is grown in the Sojat region of India; about half of the annual crop is exported. India has improved henna milling facilities in Jodhpur and Farinabad. Henna sifted to western expectations of quality is available, but the quality of the crop varies from year to year; the highest lawsone content crops seem to coincide with El Nino events. To obtain consistent lawsone content for the market, more than one source will have to be developed to compensate for variation in annual crops. Sudan produces excellent henna, but more coarsely sifted than is acceptable. Yemen produces some of the highest dye content henna in the world, and the milling is good, but at present the infrastructure in the country by has been broken by civil war, and supplies are unreliable. Henna is available from Iran but trade restrictions have limited the supply to the USA for many years. All of the countries in the Sahel could be excellent henna producers, but the infrastructure of henna production to western market standard is not yet in place. Morocco and other North African countries have produced henna in the past, but have turned to more lucrative and modern agricultural products to serve the European market. The development of multiple henna growing areas will provide a more stable resource base.

An expanded and improved market for henna, indigo, and cassia with investment in plant breeding and milling infrastructure could improve economic and political ties to these areas. If the global henna supply must be increased to meet rising demand or if other strains of henna are desired for varied characteristics, other growing areas should be developed. A henna tree must grow for one year before leaf harvesting can begin; a henna tree can remain productive in the ground for up to fifty years. An initial investment in planting a henna crop can produce income for two generations. Indigo is grown and harvested annually. Cassia obovata is a perennial in frost-free zones.

Henna leaves contain 0.3% to 3% lawsone, 2-hydroxy-1,4-naphthoquinone. Since the lawsone content varies, HPLC batch testing is crucial to predict the color outcome. The longer henna paste is kept moist in the hair, the more intermediate lawsone molecules will have the opportunity to migrate into the keratin; six hours generally is enough for maximum absorption of henna. Warmth facilitates a faster uptake. As more lawsone molecules migrate into the cuticle and bind with the keratin, the more saturated the color result will be.

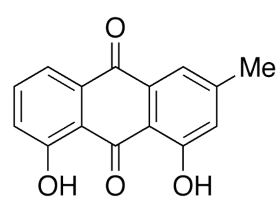
An HPLC test of powdered henna leaves generally shows 0.5% to 3% lawsone, a red-orange napthaquinone molecule[xi] which readily, harmlessly, binds with and stains keratin. The staining action is facilitated when henna leaf powder is mixed with a mildly acidic medium; a pH 5.5 paste mix is ideal [xii] to transform the precursor to the intermediate. The intermediate will bind to keratin via a Michael Addition creating a non-fading stable bond of the lawsone molecule with keratin. This red-orange stain can gradually oxidize to a brownish color by oxidation or contact with minerals commonly dissolved in tap water.




Lawsone is produced by precursors in the henna leaf: the sequence of henna dye release and binding.[xiii]

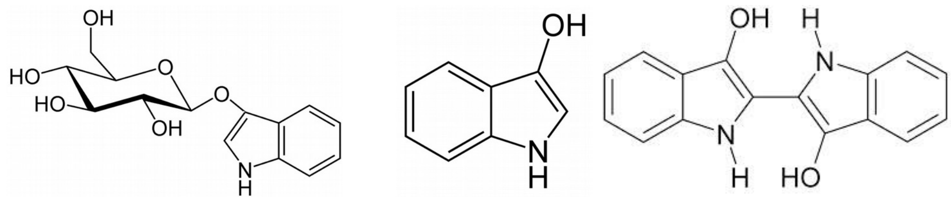
The lawsone precursor in the henna leaf is converted into the intermediate aglycone by mildly acidic hydrolysis. The aglycone intermediates will bind to keratin. Neither the precursor nor the final lawsone will bind as effectively to keratin as the aglycone intermediate. In mildly acidic henna paste at room temperature, the aglycone will become available after about an 8 hour soak, and remain at maximum content in the paste for 12 – 24 hour hours after which the percentage of the bindable aglycone form of the lawsone molecule will gradually diminish. Henna paste left out too long produces weak stains which shampoo out of hair. This transformation is gradual at room temperature, proceeding more quickly in warm conditions and slowing under cold conditions. When all of the unstable aglycone precursors have transformed to the stable form of lawsone in about one week at room temperature, the demised henna paste will keratin a weak orange color which will not darken.[xiv] The Michael Addition stain is permanent, and the color oxidizes to natural shades of red and auburn. After several days, the hair color matures and becomes very a stable color which does not fade even after daily shampoo for ten years.

Cassia obovata leaves contain chrysophanic acid (chysophanol), a golden yellow anthraquinone molecule, chrysophanol 1,8-Dihydroxy-3-methylanthraquinone. The crysophanic acid in cassia can dye pale or gray hair a golden-wheat color, but the stain is not as permanent as henna. The dye is translucent and does not make dark hair a lighter color. Proportional formulations of cassia, henna, and indigo can yield a wide range of blonde, strawberry blonde, ash blonde, and pale brunette tones for pale or graying hair. Cassia powder, like henna, gives best results when mixed with a mildly acidic liquid and allowed the mix to rest overnight to release the dye. As with lawsone, only the intermediate molecule will bind permanently to keratin and not wash out.




Chrysophanic acid (1,8-dihydroxy-3-methylanthraquinone)

Vashma indigo is fermented and powdered indigo leaves, used with henna to create brunette and black hair dyes. Indigo tinctofera leaves contain indican, a colorless molecule which is converted to indoxyl during alkaline fermentation. When indigo leaves are soaked in water and partially fermented, the indican molecule breaks into β-D-glucose and indoxyl. Indoxyl is the precursor to indigo; the intermediate indoxyl will dye keratin. The blue indigo molecule does not bind with keratin; it will wash out of hair.



When indigofera tinctoria leaves are fermented in an alkaline vat, the indoxyl molecule breaks from the indican molecule. The indoxyl molecule changes to the blue indigo molecule in contact with oxygen.

The vashma indigo powder is mixed with water to make a paste and applied to hair before contact with air changes the indoxyl to indigo. The indoxyl molecules will migrate from the indoxyl-rich paste into the keratin and bind with it. If the indoxyl molecule is converted to indigo before it has a chance to bind to and stain keratin, it will not bind, it will wash out of the hair. This chemical change happens rapidly so once water is stirred into the powder it has to be applied to hair before it can change to the indigo molecule.[xv] Indigo dye is not as permanent as henna, but the full length of the hair color remains stable for years with daily shampoo as long as the intermediate indoxyl is bound to the hair.

Only the intermediates in these plant powders bind permanently and efficiently with keratin. Henna stains hair when wetted with an acidic liquid. Cassia stains hair when wetted with an acidic liquid. Vashma indigo stains hair when wetted with a neutral or slightly alkaline liquid. Henna and cassia require time (usually 8 hours at 70F) to release the dye molecules to stain hair. The fermentation of vashma indigo pre-releases the dye molecule; vashma indigo must be used immediately after mixing. For these fundamental reasons, pre-mixed henna powders and pastes are unsatisfactory for dyeing hair, and adulterants are added to compensate for their poor outcomes. The plant powders must be mixed separately and added together at the time of application. The compound henna additives cross-react adversely with oxidative hair dyes. The pure henna, indigo, and cassia powders can be applied over oxidative hair dye without an adverse chemical reaction. This is why the future growth of non-coal tar derivative hair dye hinges on understanding and optimizing a centuries-old hair dye technology and methodology.

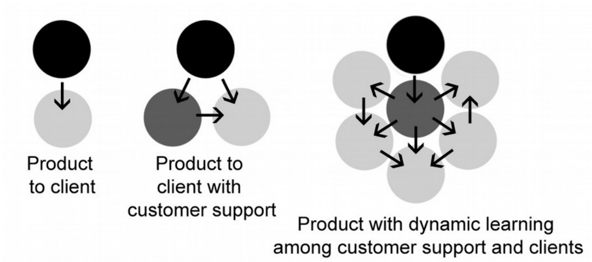
**Dynamic learning: an essential process for henna**

Modern industry has an underlying assumption that it is possible through science to tinker with a product until it suits consumer notions of convenience and expediency to compete for market placement. With henna, indigo, and cassia, people engaged with the physical requirements of natural plant dyes over centuries and gradually constructed a socially and personally positive practice of hair dye. If the hair dye industry is going to transition sensitized clients to henna, cassia, and indigo, it will be informative to look at the historical and anthropological records of how people successfully used these dyes, and create processes which duplicate these activities.

Before the 20th century, the understanding of henna hair dye process was transmitted person to person at the village bath; a person who wanted to cover gray had the cumulative expertise and assistance of all who went to the community bath.[xvi] Now that people bathe privately, they are cut off from the group knowledge of the henna process. The chemistry of henna, indigo, and cassia hair dye is simple, but requires experience to mix and apply, and adjustments by each person for optimal results. It is not possible to market henna successfully with brief, static instructions; the consumer cannot be a passive recipient of goods. Marketing henna will require education and interaction with consumers.

The subtleties of hair type, water supply, mixing times, and application time are each significant variables unique to each consumer. These cannot be learned from brief, static instructions. Web 2.0, the change from static web pages to dynamic or user-generated content and the growth of social media, can serve as a bridge among people who need to reconstruct community knowledge through shared experience.

Combining the information transmission of hair dye methods from before the 20th century and using parallel methods through the 'electronic village bath' creates a convivial educational and social support group for henna. Expert customer service engagement with clients through electronic interactive media is crucial to the success of henna in the 21st century, just as visits to the village bath and learning from other bathers was crucial to successful henna outcomes in the previous four hundred centuries. Using dynamic electronic support, we have successfully transitioned over fifty thousand severely sensitized people from oxidative hair dye to henna, indigo, and cassia in the last three years alone.[xvii]




Henna techniques are best learned interactively and dynamically

For the cosmetic industry to recapture hair dye clients lost to PPD sensitization and transition them to henna, a box of powder with one paragraph of written instructions will not be sufficient. A commitment to long term education of and engagement with clients will be as necessary as developing the product infrastructure. Re-educating stylists about how to incorporate henna into salons will be crucial. Engaging with stylists who have had to abandon their careers because of chemical sensitization, and establishing salons for 'plant-only' technologies serving highly sensitized patrons would be ideal. If, in 2030, 16% of graying clientele cannot use oxidative hair dye, the establishment of an alternative should be not only economically viable but essential to growth of the hair dye industry.

[i1] Smith V, Clark S, and Wilkinson M.. "Allergic contact dermatitis in children: trends in allergens, 10 years on. A retrospective study of 500 children tested between 2005 and 2014 in one U.K. centre." *British Association of Dermatologists' Annual Conference. Leeds Teaching Hospitals* NHS Trust, Leeds, U.K. (2015)
[ii] Cosmetic, Toiletry & Perfumery Association director-general, Dr. Christopher Flower, and Dr. Anjali Mahto, spokesperson for the British Skin Foundation (2016)
[iii] Hashim, S., Hamza, Y., Yahia, B., Khogali, F., and Sulieman, G., "Poisoning from Henna Dye and Para-phenylenediamine Mixtures in Children in Khartoum" *Annals of Tropical Pediatrics* **12**, 3 – 6 (1992)
[iv] Hooff GP, van Huizen NA, Meesters RJW, Zijlstra EE, Abdelraheem M, Abdelraheem W, et al. Analytical Investigations of Toxic *p*-Phenylenediamine (PPD) Levels in Clinical Urine Samples with Special Focus on MALDI-MS/MS. PLoS ONE **6**(8): e22191. doi:10.1371/journal.pone.0022191(2011)
[v] Schultz, E.; Mahler, V. "Prolonged lichenoid reaction and cross-sensitivity to para-substituted amino-compounds due to temporary henna tattoo." *International Journal of Dermatology*, v. **41** issue 5, p. 301-3. (2002
[vi] Chen, Thobile, Nkosi, Combrick, Viljoen, and Cartwright-Jones, C. "Rapid analysis of the skin irritant p-phenylenediamine (PPD) in henna products using atmospheric solids analysis probe mass spectrometry" *Journal of Pharmaceutical and Biomedical Analysis* (May, 2016)
[vii] Roher, J. *Rohrer's Illustrated book on Scientific Modern Beauty Culture*. New York City, N.Y.: Prof. Rohrer's Institute of Beauty Culture. (1924)
[viii] Ingram, John R., T. Meirion Hughes, and Natalie M. Stone. "Potential danger of hair dyes marketed as free from para-Phenylenediamine." *International Journal of Dermatology* **53**, no. 4: e257-e258. (2014)
[ix] Wellford, G. May 16, 2016. "Why you should avoid 'black henna' temporary tattoos this summer" *Sunderland Echo.* http://www.sunderlandecho.com/news/why-you-should-avoid-black-henna-temporary-tattoos-this-summer-1-7913496#ixzz48ugP05H7 (accessed June 11, 2016) (2016)
[x] Amro, B. I. "Dyeing with Henna and Related Materials" thesis for PhD at the University of Wales. (1989)
[xi] HPLC laboratory results, Alkemist Laboratories for TapDancing Lizard LLC, 2008 - 2016
[xii] Amro, I. H., James, K. C, and Turner, T. D.; 1993. "A Quantitative Study of Dyeing with Lawsone," *Journal of the Society of Cosmetic Chemistry*, **45**, 159 - 165
[xiii] Gallo, F., Multari, G., Palazzino, G., Pagliuca, G., Zadeh, S. M. M., Biapa, P. C. N., Nicoletti, M.; 2014. "Henna through the Centuries: A quick HPTLC analysis proposal to check identity." *Revista Brasiliera de Farma Cognisia*. **24**, 2
[xiv] Ruchi Badoni Semwala, Deepak Kumar Semwala, Sandra Combrinck, Catherine Cartwright-Jones, Alvaro Viljoen "Lawsonia inermis L. (henna): Ethnobotanical, phytochemical and pharmacological aspects." *Journal of Ethnopharmacology*, June 2014
[xv] Kerry G. Gilbert (nee Stoker) & David T. Cooke. "Dyes from plants: Past usage, present understanding and potential" *Plant Growth Regulation* **34**: 57–69 © 2001 Kluwer Academic Publishers. (2001)
[xvi] Cartwright-Jones, C. PhD. "The Hammam" *The Oxford Encyclopedia of Islam and Women*, Natana J. DeLong-Bas, Ed. Oxford University Press (2013)
[xvii] Cartwright-Jones, C. PhD. *Ancient Sunrise Henna for Hair* . TapDancing Lizard. http://www.tapdancinglizard.com/AS_henna_for_hair/index.html (2016)