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Review Article

Henna beyond skin arts: Literatures review

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Abstract Henna is the dried and powdered leaf of*Lawsonia inermis*and is a natural dye for hair, nails and skin for body arts in Islamic and Hindu cultures. Recently, it has been widely used in western countries as temporary black henna tattoo. Different experimental in vitro studies showed many pharmacological effects of *L. inermis*. Topical pure henna is generally safe and well-tolerated in humans but oral and topical henna with additives like para-phenylenediamine have many side effects some of them life threatening. This review highlights pharmacological effectiveness and adverse effects of henna.

Key words
Henna, *Lawsonia inermis*, para-phenylenediamine.

Introduction

The World Health Organization (WHO) has defined herbal medicines as finished labeled medicinal product that contain an active ingredient, aerial, or underground parts of the plant or other plant material or combinations.[1]Henna is the dried and powdered leaf of*Lawsonia inermis*.The plant henna (*Lawsonia inermis*, family *Lythraceae*) is a shrub that is naturally grown or cultivated from North-East Africa to India.[2,3] The chemical constituents of its extract include naphthalene derivatives, quinoids, beta sitosterol, flavonoids and gallic acid.[4] Henna is very popular in many countries especially in Middle East and South Asia; it is part of the culture and traditions in these countries and widely used in body art to dye skin, hair and fingernails. In addition, temporary henna tattoos or pseudo-tattoos have become increasingly widespread worldwide.[5]

The mechanism of dyeing is mainly related to the staining properties of constituent lawsone, and modified henna products such as black henna are available by adding para-phenylenediamine (PPD) to henna powder. In addition, several medicinal properties of *L. inermis*have been documented through *in vitro* studies. It has been used as an antimicrobial, antidiarrheal, anti-inflammatory, and analgesic; it has antipyretic effects.In this review, the author summarizes the effects attributed to henna regarding its non-dyingproperties including pharmacological properties and side effects.

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Pharmacology

1. Antimicrobial Activity

Natural antimicrobial therapy is an important research area because of antibiotic overuse and antibiotic resistance. Many *invitro*studies have evaluated the pharmacological activities of *L. inermis*. Its leaves, stem bark, roots, flowers and seeds have been used in traditional medicine.Henna leaves have a great potential to be used as a source of a potent eco-friendly antimicrobial agent.[6]Habbal*et al*.[7] reported that Omani henna has antibacterial activity against *Staphylococcus aureus,Escherichia coli* and *Pseudomonas aeruginosa*.[7]Abdullmomein[8] found that anthraquinones are a major constitute of henna leaves, and this compound has antimicrobial activities. Another study

done by Christy*et al*.[9] showed that the ethyl acetate and ethanol extracts of fruit and flower of *L. inermis*are potentially better source of antibacterial agents.Awadh*et al*.[10] investigated the Yemeni medicinal plants for antibacterial, and they found that ethyl acetate extract of *L. inermis* had activity against all bacteria in their study. *In vitro* studiesassessed the effect of henna powder on the growth of *E. coli*. There was obvious antibacterial activity against*E. coli*.[11]The tuberculostatic activity of henna was tested *in vitro* and *in vivo* and this study showed significant activity against *Mycobacterium tuberculosis* and*M. chelonae*.[12,13]Hexane extractsof *L. inermis* showed strong antifungal activity against*Trichophyton tonsurans*, *T. rubrum*, and *T. mentagrophytes*.[14]Antifungal effects of chloroformic, methanolic and aqueous extracts of henna (*L. inermis*) leaves on *Malassezia furfur*. The study reported that a chloroform extract of henna completely inhibited the growth of *M.furfur*.[15]These studies confirmed the antimicrobial activity of henna leaves and supported the traditional use of the plant in therapy of localized cutaneous infections.

2. Antioxidant activity

Research has shown that *L. inermis* extracts have antioxidant activities.*L. inermis*leaves inhibit carbon tetrachloride toxicity in rat liver.[16,17]In these studies, an ethyl acetate extract of *L. inermis*leaves caused a significant reduction in hepatic thiobarbituric acid reactive substances and increased antioxidant enzymes that inhibit the effectsof carbon tetrachloride. On the other hand, ethanolic and methanolic extracts of *L. inermis*have high antioxidant potential that simultaneously inhibits hexavalent chromium-induced oxidative toxicity and scavenges diphenyl-1-picrylhydrazyl and inhibit lipid peroxidation.[18,19] One study compared the antioxidant and immunomodulatory constituents of henna leaves with ascorbic acid, and this study showed comparable activity.[20] Additional studies are needed to isolate and characterize specific compounds to further assess antioxidant activity.

3. Wound healing activity

The ethanol extract of *L. inermis* has been used to evaluate wound healing in rats. One group treated with an ethanol extract of *L. inermis* showed increased collagen and enhanced wound contraction.[21,22] The methanolic extract, isoplumbagin and lawsaritol isolated from stem bark and root of *L. inermis*L. showed anti-inflammatory activity against carrageenan-induced paw edema in mice.[23,24]

4. Antiinflammatory, analgesic and antipyretic activity

The butanol and chloroform fractions of *L. inermis* showed potent anti-inflammatory, analgesic, and antipyretic effects that were comparable to phenylbutazone.[25] Studies found that crude ethanolic extracts of *L. inermis* in concentrations of 0.25-2.0 g/kg cause significant and dose dependent anti-inflammatory and analgesic effects in rats.[26]An interesting clinical study showed significant effect of topical henna in hand-foot syndrome induced by capecitabine, and the clinical improvement in these patients may be related to the anti-inflammatory, antipyretic and analgesic effects of henna.[27]

5. Immunomodulatory activity

The immuomodulatory activity was studied *in vitro*.A methanolic extract and naphthoquinone fraction of *L. inermis* leaves showed significant immunomodulatory effects through the promotion of T lymphocyte proliferative responses. Some of their effect was due to antioxidant and free radical scavenging activity of the henna extract.[20]

6. Anti-carcinogenic and cytotoxic activity

*L. inermis*also has cytotoxic effects.[28]The in vitro cytotoxic studies of 2-hydroxy-1,4-

naphthaquinone (lawsone) against two human cancer cell lines MCF-7 (human breast cancer) and HCT-15 (human colon carcinoma cells) using MTT assay revealed the cytotoxic effects in killing cancer cells even at low concentrations.[29,30]Also, the bicoumarin, biflavonoid and biquinone isolated from the flower of *L. inermis* showed cytotoxic activity against cancer cells.[31]An *in vivo* two-stage mouse skin carcinogenesis study using UV-B radiation for initiation and TPA for tumor promotion showed that oral feeding of henna (0.0025%) in drinking water ad libitum decreased tumor incidence by 66% and multiplicity by 40% versus a positive control at 10 weeks.[32]

7. Hypoglycemic and hypolipidemicactivity

A study to evaluate the effect of ethanolic extract of leaves of *L. inermis* in diabetic rats showed that a *L. inermis* extract at 400mg/kg BW had significant hypoglycemic activity in diabetic rats after oral administration.[33]The effect of the ethanolic extract 500 mg/kg of body weight was found to be better thanglibenclamide (10 mg/kg of body weight). These results suggest that the ethanolic extract possess significant antidiabetic effects.[34]The hypoglycemic effect may elicited through inhibiting alpha-amylase enzyme.[35]*L. inermis* hydroalcoholic extract may also show significantly improved lipid and lipoprotein patterns in diabetic rats. This could be due to improvement in insulin secretion.[36]

Complications of henna

Although most of complications of henna come from topical applications for traditional events or temporary tattoo, some serious complications have occurred after oral ingestion of henna.

1.Allergic contact dermatitis

Natural henna is usually hypoallergenic,[37,38] and allergic reactions occurred in mixed types including black henna. This was caused by diaminotoluene and diaminobenzene or cross-reactions of PPD with para-amino compounds (benzocaine, sulfa drugs, aminoazobenzene, IPPD, PABA) and hairdressing allergens (2,5-diaminotoluene sulfate, 2-nitro-4-phenylenediamine, 4-aminophenol, 3-aminophenol).[37,39]The clinical manifestations of allergic contact dermatitis varies in severity from an intensely itchy erythematous with patches of painful, itchy exudative bullous eruptions.[37-42]The patch test is the gold standard method for diagnosis of allergic contact dermatitis from henna, while the prevalence of the positive patch test in pure henna is 3%, and the prevalence of the patch test positivity to henna with PPD is 35% or more.[43,44] The high positive patch test results from high concentrations of PPD (15.7%) despite the directive of the European Community Cosmetics Directive, which allows the maximum concentration to be 6%.The USA Food and Drug Administration (FDA) advises that PPD should not be applied to the skin of patients with a history of atopy.[45]

2. Immediate-type hypersensitivity with urticaria

A few cases have been reported that describe immediate-type hypersensitivity reactions from direct contact to henna.[46,47]The clinical features are urticaria, rhinitis, acute bronchospasm and reported cases of severe, fatal angioneurotic edema.[48,49,50]This reaction was confirmed by both a skin prick test and radio allergen sorbent test (RAST), but the pathogenesis of this reaction is not clear. Immunologic contact urticaria reactions and non-immunologic contact urticaria may have a role.[51,52]

3. Erythema multiforme

Erythema multiforme is an acute, self-limited, skin eruption mediated by type IV hypersensitivity reaction and associated with certain infections, medications, and other triggers. Few cases have been reported from

topical henna. Most reactions are due to additive, especially PPD, which is an aniline derivative that is added to speed up the process of skin dying.[53,54,55]The clinical features range from classical erythema multiforme to generalized vesicular erythema multiforme-like reactions.[56,57]

4. Post-inflammatory hypo- or hyperpigmentation

The henna usually starts to fade within two weeks and is completely removed within 5 weeks. Cases of persistent hyperpigmentation have been reported.[58]The causes are either due to subclinical interface dermatitis caused by henna or its additives or the use of readymade henna paste of unknown origin. Hypopigmentation after non-permanent henna tattoo has been reported with a positive patch test to PPD. This may explain the residual hypopigmentiom.[59,60,61]

5. Hypertrichosis

Transient hypertrichosis has been reported in a few cases.[62-65] Hypertrichosis usually occurs within the first 20 days after initial application of black henna. This often resolves spontaneously after 3 to 5 months.Skin biopsy studies showed an increase in vellus hair follicles with slight peripheral fibrosis.[62]The pathophysiology is unknown but one of the additive substances may play a part in the pathophysiology.[62]

6. Keloids

Extensive keloid scarring in the pattern of the henna tattoo has been reported.[66,67,68]Keloid formation waspresided by severe allergic contact dermatitis, and a positive patch test to PPDwas documented in all cases.

7. Hemolysis

Hemolytic crises following external application of henna in glucose-6-phosphate dehydrogenase (G6PD)was documented in many cases.[69,70,71]Current scientific evidence suggests that lawsone acts directly as a hemolytic agent to induce oxidative stress. This is consistent with clinical observations of enhanced susceptibility to henna in G6PD-deficient individuals.[72,73]Oral ingestion of hennaeither accidentally, deliberate (suicidal), or homicidalcan cause acute renal failure,rhabdomyolysis and intravascular hemolysis.[74,75]

8. Vasculitis and renal impairment

Cutaneous vasculitis with rapidly progressive glomerulonephritis has been described with chronic use of henna mixed with PPD for dyeing of the hair. Indeed, hair dressers who use henna have been shown to have a high prevalence of renal impairment due to regular exposure to PPD.[77] Twelve patients ingested PPD (henna hair dye) in suicidal attempts with severe acute renal failure.[78]

Teratogenicity

Although pure henna is safe, but should be used with caution during pregnancy.Female mature BALB/c mice were intraperitoneally injected with 100 mg/kg of *L. inermis* for 7 days. On the 19th day, their embryos were examined for abnormalities. There were parietal bones absent in 90% of the embryos, and extra ribs were observed in 30%. This may be related to the 2-hydroxy-1,4-naphthoquinone in *L. inermis* extract.[79]Another study showed that hydroalcoholic extracts of henna can cause significant damage in newborn mice livers.[80]

Conclusion

There is some evidence showing the efficacy of topically applied natural henna, but it is necessary to identify and select a representative lead ingredient. More studies should be established for further observation of

the value of henna and to minimize side effects.

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