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REVIEW ARTICLE

Lawsonia inermis Linnaeus: Pharmacological Peculiarity and Modern Progression

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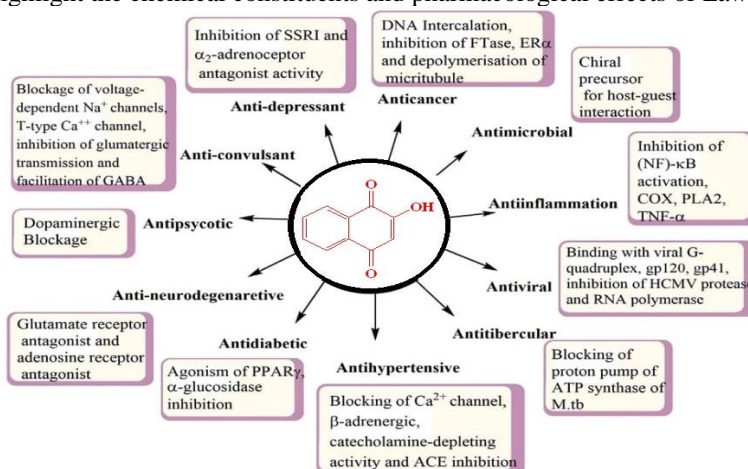
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ABSTRACT:

Lawsonia inermis (Family: Lythraceae) contained carbohydrates, phenolic, flavonoids, saponins, proteins, alkaloids, terpenoids, quinones, coumarins, xanthenes, fat, resin and tannins. It also contained 2-hydroxy-1,4-naphthoquinone (lawsone). Many alkaloids, naphthoquinone derivatives, phenolics and flavonoids were isolated from different parts of *Lawsonia inermis*. The pharmacological studies showed that *Lawsonia inermis* showed antibacterial, antifungal, antiparasitic, molluscicidal, antioxidant, hepatoprotective, central nervous, analgesic, anti-inflammatory, antipyretic, wound and burn healing, immunomodulatory, antiurolithiatic, antidiabetic, hypolipidemic, antiulcer, antidiarrhoeal, diuretic, anticancer and many other pharmacological effects. The current review will highlight the chemical constituents and pharmacological effects of *Lawsonia inermis*.



KEYWORDS: *Lawsonia inermis*, 2-hydroxy -1, 4- Naphthalenedione, antioxidant hobby, analgesic activity, lawsone, Constituents, Pharmacology, Naphthoquinone.

INTRODUCTION:

Henna dye is one of the world's oldest natural colours, dating back more than 5000 years to ancient Egypt. It takes the form of a little shrubby plant that grows to be a

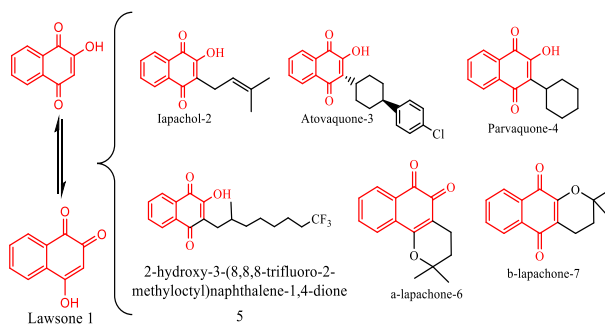
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2-6 metre monster with prickly branch tips. Soft, disputed, sub-sessile, elliptical, generally lanceolate, with well-down in the dumps ribs, the foliage is described. On the dorsal surface¹, visible. Rosemary flowers include four sepals and a two-millimeter calyx tube, as well as spherical, upright petals². The tree bears small tan fruits with 32 to 49 angular seeds per fruit. *Lawsonia inermis* leaves contain natural pigments such as (1, 4- Naphthalenedione,2-hydroxy), often known as Lawsone, which has been used to colour hair and hides since the 1400s³.

Lawsone is a vital part of the henna plant that is utilized to make anticancer drugs, for example, dichloroallyl Lawsone and lapachol¹¹. Whose antitumor impact has been supported¹². Plumbagin displays cell cycle movement and instigates apoptosis in melanoma, lung, and bosom disease cell lines¹³. Plant subordinates give a few advantages in the therapy of disease, including the capacity to be consumed and less adverse consequences¹⁴. Quinine is comprehensively dispensed in landscape and a lot of its counterfeit and natural product are exceptionally fundamental in bunches of different locales of science as well as organic chemistry¹⁵. They play a crucial capacity in various dwelling cells as electron merchants with inside the breathing arrangement, notwithstanding in blood coagulation with glutamate carboxylation. Due to the illuminate dating among quinones and biochemical methodologies in cells, these concentrates have been comprehensively utilized in the union of numerous natural dynamic substance fixings with anticancer activity.¹⁶ Molluscicidal¹⁷. Antiparasitic¹⁸, leishmanicidal¹⁹, mitigating²⁰, antimycotic²¹, against infective²² and trypanocidal action²³. As of now, henna extricates are quietly showcased for shading of foam,²⁴ fiber²⁵, and yarn²⁶ in various nations of Asia and Africa, in the Pali locale of Rajasthan in India individual the most really delivering rosemary remove, mainly as of *L. inermis* Linn²⁷. The henna separates are broadly utilized in people cure, especially in early stage countries²⁸ for the treatment of consume wounds tainted by various kinds of microbes²⁹ for example Mycobacterium³⁰ Staphylococcus, Pseudomonas, oxysporum, Aspergillus and albicans, in light of its antimycobacterial action³¹ notwithstanding migraines, myalgia, chest cool, extreme conjunctivitis, syphilis, lesion³².

Henna is a sacred plant normally utilized in profound functions and represents opulence. Naphthoquinones are go about as responsive oxygen species (ROS) generators as the primary terminating system In cells, the oxidation-decrease cycle includes the exchange of an e-from CYP450 oxido-reductase to the C=O gathering of the quinone cycle to create a semi-quinone particle revolutionary, that is in the long run moves that electron to O₂ and produces the superoxide extremist³³ Hydroxyl

bunch at C2 locales of Lawsone will in general lessen its electrophilic potential as well as in this manner influences its capacity to have an impact in redox cycles in production of receptive oxygen species³⁴. As a result of the inside and out information on its organic chemistry and hereditary qualities, as well as the effortlessness of cell control, the yeast *Saccharomyces cerevisiae* was picked as a natural model. Moreover, this animal offers half of its qualities with people as far as homology, including that multitude of whose changes are connected to human diseases³⁵ So as of late, only one review has utilized *S. Cerevisiae* to research the poisonousness of the law and its subordinate mixtures³⁶. The data presented here was important in concentrating on your business, however it can likewise be utilized as an aide for the drug business in the blend of a couple of subordinates with considerably more particular exercises and controlled methods of activity. These mixtures' helpful viability is gotten from their ortho or para quinonoid gatherings, which acknowledge a couple of electrons to produce the suitable revolutionary anions or di-anions in situ. Semiquinone revolutionaries, through making superoxide anions, accelerate the development of intracellular hypoxic conditions³⁷. Quinines might cause cytotoxicity in mammalian cells by this strategy, maybe by upsetting proteins such topoisomerases, a key chemical expected for DNA replicating in cells.³⁸ The quinone classification incorporates a few significant artificial materials as well as natural synthetics that have a hydroxy gathering in the quinone class. The Lawsone moiety, as well as its enantiomers 4-hydroxy 1, 2-naphthoquinone, are successive parts of synthetic substances with an assortment of naturally fascinating properties³⁹ Examples of which (1) lapachol (2), atovaquone (3), parvaquone (4), NQ1 (5),⁴⁰ β -lapachone (6) and α -lapachone (7)⁴¹.



Henna and lawsone separates, as per this review, were incredibly unsafe, making iron deficiency due anihilation of RBC and nephron apoptosis in rodents when given orally⁴², and furthermore shows awareness signs like hives, stodgy nose, and coronary obstructive pneumonic sickness (COPD).⁴³ Several fatalities of youths who take eat henna on cheerful, merry events have been reported.⁴⁸

Marzin and Kirkland revealed that lawsone, a characteristic henna tone, is to be sure a non-genotoxic threat in the mice undifferentiated organisms, micronuclei examine won't cause cell Damage in Chinese gerbil ovarian cells, making them the end that lawsone has no or little cancer-causing nature risk. Klotz and his accomplice analyze the oxidative problem flagging rear entryway all through refined human keratinocytes including a scope of 1,4-naphthoquinones and detailed that no other lawsone or lapachol (up to 100 M) were dynamic in any of these measures, however that these mixtures instigate phosphorylation of the (EGFR) and the connected ErbB2 receptor⁵⁰. Skin insurance against UV radiation, texture color⁵¹, hostile to maturing added substance to vulcanized normal elastic⁵², erosion hindrance for steel⁵³, and oxidation of chlorinated compounds are a couple of the applications found in the writing⁵⁴.

It likewise responds with amino corrosive deposits in unique mark layers on sheet surfaces, delivering an itemized light-earthly colored violet print that is additionally photoluminescent⁵⁵. As of late, lawsone was viewed as a touchy electrochemical and colorimetric sensor for negative particles, like Cn^- , CH_3COO^- , Fl^- and $H_2O_4P^{2-}$ (DHP) in CH_3CN . Different anions, like Cl^- , Br^- , I^- , or ClO_4^- , make a yellow orange-red change in arrangement lawsone that is imperceptible when these anionic species are present⁵⁶. Lawsone complexation strategies have been read up for an assortment of purposes, and various metal mixtures with different designs have been portrayed.⁵⁷ In three different oxidation states, lawsone and comparative mixtures can interface with metal particles: quinone, semiquinone, and quinone (the diminished one-electron type of quinone)⁵⁸. This limiting capacity, along with catechol, is believed to be answerable for quinones' significant job in organic cycles (the decreased type of two electrons)⁵⁹. Thus, lawsone iron buildings have been examined to impersonate the iron quinone pair found in the bacterial response place,⁶⁰ while lawsone copper edifices have been concentrated principally to grasp metal quinones communications and to emulate primary and practical models of copper-containing catalysts. Metals can likewise change the pharmacological impacts of regularly utilized prescriptions. Copper (II)- 9 buildings were recognized to enact apoptosis in HepG2 human malignant growth cells by caspase actuation and apoptosis-related protein guideline, utilizing this strategy to test Lawsone metal edifices for cytotoxicity against disease cells.⁶¹ Finally, the ruthenium (III) Lawsonate 10 a complex has been displayed to oxidize essential and auxiliary alcohols to aldehydes and ketones, individually, within the sight of N-methyl morpholine oxide as a co-oxidant⁶².

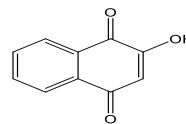


Figure 2. Lawsone (2-hydroxy-1,4 naphthoquinone)

Taxonomy

Table 1: Taxonomy of (Henna plant) *L.inermis*. Linn

Kingdom	Plantae
Sub-kingdom	Tracheobionta
Infra-kingdom	Streptophyta
Super-division	Spermatophyta
Division	Magnoliophyta
Sub-division	Spermatophytina
Class	Magnoliopsida
Subclass	Rosidae
Clade	Tracheophytes
Super-Order	Rosanae ⁷
Order	Myrtales
Family	Lythraceae
Subfamily	Lythroideae
Genus	<i>Lawsonia</i>
Species	<i>L. inermis</i> ⁸

Common Vernacular Name:-

Table 2: Common Vernacular Name

English	Henna plant, Cypress shrub, Samphire, Henna
Sanskrit	Ragangi, Timir, Mendika, Mendhi,
Hindi	Hena, Mehendi
Telugu	Goranta, Kormmi
Tamil	Alvanam, Aivani, Marithondi
Gujarat	Medi
Marathi	Mendhi, Mendi ⁹
Malayalam	Mailanchi
Bengali	Mendi
Arabic	Henna
French	Henne
German	Agyptische
Italian	Enne, cipro
Kannada	Mayilanchi
Oriya	Benjati
Punjabi	Mehndi
Turkish	Kena-ag ¹⁰

Sources of information retrieval:

From 10/2021 to 04/2022, a comprehensive literature search on *L. inermis* was conducted using textbooks, articles, abstracts, and peer reviews from bibliographic databases around the globe, including NISCAIR, SciELO (digital library), PUBMED, SCOPUS, INFLIBNET center, Sci-Finder, Sci-Hub, Science Direct, and Google Scholar. Keywords were used to find out information in the existing literature.

Cultivation and production:

However henna is a therapeutic plant that might develop to 6 Mt and live fA far reaching writing search on *L. inermis* was led from October 20, 2021 to February 2, 2022, utilizing reading material, articles, modified works, and companion audits from bibliographic data sets everywhere, including NISCAIR, SciELO (computerized library), PUBMED, SCOPUS, INFLIBNET focus, Sci-Finder, Sci-Hub, Science Direct, and Google Scholar. Watchwords were utilized to scan the accessible writing for data.

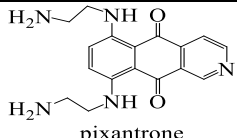
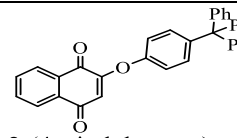
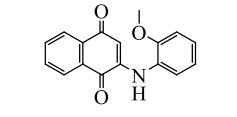
On the other hand 50 years, it is many times pruned back to short of what one meter high⁶³ and the important leaves gathered. Rosemary is planted in obstructions to protect the home nursery from desert winds and soil disintegration through its life span and diligent roots.⁶⁴ since henna requires no exceptional hardware or labor supply for the development and is developed close to smallholder family compounds, it is for the most part developed by the family ladies. In dry spell conditions, henna is a genuine type of revenue when different harvests evaporate. A smallholder's rosemary plant is likewise an important wellspring of home solutions for minor infirmities. Henna will fix ringworm and other parasitic diseases in youngsters, grown-ups, and animals⁶⁵ and speed up injury mending⁶⁶ The fungicidal, calming, and pain relieving impacts of henna give help to nursing moms whose areolas are tainted with thrush (*Candida albicans*). Both the antimicrobial and pain relieving impacts are valuable in family consume balms⁶⁷ Henna twigs are scoured.

Phytochemicals:

Table 3: phytochemicals present in *lawsonia inermis* linn

Sr No	Category	Trivial	Chemical Formula	Molecular weight
1	Alkaloids	Harmine	C ₁₃ H ₁₂ N ₂ O	212
		Harmaline	C ₁₃ H ₁₄ N ₂ O	214
2	Glycosides	Apigenin	C ₁₅ H ₁₀ O ₅	270
3	Tannins	1, 2, 3, 6-tetraO-galloyl-β-Dglucose & 1, 2, 3, 4, 6-penta-O-galloylβ-D-glucose	C ₃₄ H ₂₈ O ₂₂ C ₄₁ H ₃₂ O ₂₆	788 940
		4	Flavonoids	Acacetin Narigenin

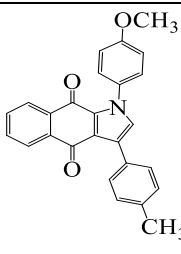
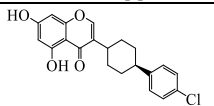
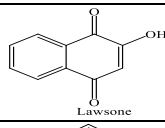
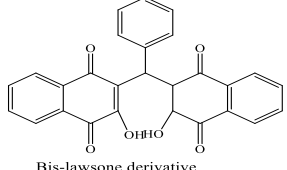
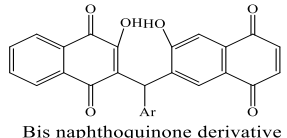
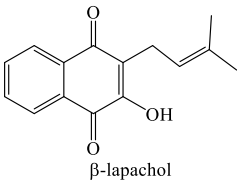
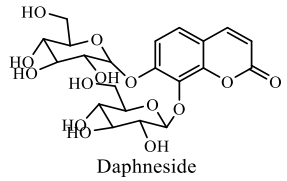
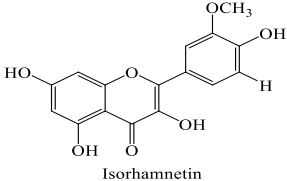
Table 4: Reported activity

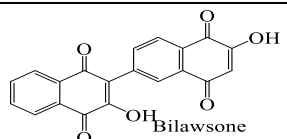
Bioactive studies	Nature of the extract	In vivo /vitro model system used in the studies	Dose range tested	Major finding	Reported drug Structure &IUPAC name	Ref
CNS activity(AD)	Petroleum ether, dichloromethane, ethanol and aqueous extract of the seed	Diazepam-induced sleeping time, open-field pentylenetetrazole and strychnine-induced convulsions models in swiss albino mice	100, 200 and 400 mg/kg bw	Aqueous and ethanolic fractions altered the vital body functions by causing sedation and preventing	 <p>pixantrone</p>	34
Antimicrobial activity	Leaf essential oil	Disc diffusion and micro-broth dilution assay against <i>B. cereus</i> , <i>E. coli</i> , <i>P. aeruginosa</i> , <i>S. aureus</i> , and <i>A. Niger</i>	1000 g/mL	All extract showed significant antibacterial activity on tested microorganism with maximum efficacy against <i>P</i>	 <p>2-(4-tritylphenoxy)naphthalene-1,4-dione</p>	37
Antioxidant activity	Ethyl acetate, ethanolic extract and aqueous decoction of leaf	ABTS and DPPH free radical assay	Not mentioned	The ethanolic extract was found best antioxidant (IC ₅₀ = 6.9 ± 0.1 mg/L) among other tested extracts	 <p>2-((2-methoxyphenyl)amino)naphthalene-1,4-dione</p>	113

5	Steroids	Apiin	C ₂₆ H ₂₈ O ₁₄	564
		Cosmosiin	C ₂₁ H ₂₀ O ₁₀	432
		Sterol	C ₁₇ H ₂₈ O	284
6	Xanthones	Lawsaritol	C ₂₉ H ₅₀ O	414
		Laxanthone-I	C ₁₅ H ₁₂ O ₆	288
		Laxanthone-II	C ₁₈ H ₁₄ O ₈	358
7	Coumarins	Laxanthone-III	C ₁₈ H ₁₆ O ₆	328
		Fraxetin	C ₁₀ H ₈ O ₅	208
		Scopoletin	C ₁₀ H ₈ O ₄	192
		Esculetin	C ₉ H ₆ O ₄	178
8	Naphthlenes	Daphnorin	C ₂₅ H ₂₂ O ₁₂	514
		Lawsoniaside	C ₁₉ H ₂₈ O ₉	400
9	Naphtho-quinones	Lawsone	C ₁₀ H ₆ O ₃	174
		2-methoxy-3-methyl-1,4 naphthoquinone	C ₁₂ H ₁₀ O ₃	202
10	Terpenes	Lupeol	C ₃₀ H ₅₀ O	426
		Betulin	C ₃₀ H ₅₀ O ₂	442
		Betulinic acid	C ₃₀ H ₄₈ O ₃	444

Pharmacological survey in henna:

The present pharmacological instruments of Henna have been widely employed over the past two centuries to analyse and validate a range of medicinal behaviours in henna plant extracts. The active activity of these active components is summarised in the following sections: Enzyme modulatory effect, Protein glycation inhibitory activity, CNS activity, Diuretics activity, wound healing activity, hypoglycaemic and antihyperlipidemic activity, antioxidant activity, antitumor and cytotoxic activity, Anti-inflammatory, antipyretic, analgesic and anti-diarrheal activity, Hepatoprotective activity, Anti parasitic activity, Antimicrobial activity, Activity on bone resorption, breast cancer, antifungal disease,etc. khael *et al* 2000.

Antitumor activity and cytotoxicity	Petroleum ether and ethyl acetate extract of leaves	In vitro cytotoxicity assay on MCF-7 cell lines by (3H)-hypoxanthine incorporation assay 22 and 27 mg/mL. Active against MCF-7 cell line by (3H)- hypoxanthine incorporation assay	22 and 27 mg/mL	Active against MCF-7 cell line	 1-(4-methoxyphenyl)-3-(p-tolyl)-1H-benzo[f]indole 4,9-dione	119
Antiinflammatory, antipyretic, analgesic and anti-diarrheal activity	1, 5-Diphenylpent-3-en-1-ynes and methyl naphthalene carboxylates (isolated from leaves and stem) Ethanolic (90%) and ethyl acetate fraction of seeds	In vitro biological assay by measurement of superoxide generation and elastase release in human neutrophils	Not specified	IC50 range 1.58–1.80 g/mL	 3-(4-(4-chlorophenyl)cyclohexyl)-5,7-dihydroxy-4H-chromen-4-one	108
Hepatoprotective activity	Aqueous and ethanolic extracts	CCl4-induced hepatotoxicity in rats	200–400 mg/kg bw	Validation of folklore use of L. inermis seeds in hepatotoxicity	 Lawsone	114
Diuretics activity	Petroleum ether and ethyl acetate extract of leaves	Lipschitz method of diuretic in male wistar rats	250 mg/kg and 500 mg/kg	Induction of diuresis was noted in animal model First in vitro	 Bis-lawsone derivative	8786
Antiparasitic activity	Methanolic leaf extract and isolated compounds	Cytotoxicity assays on P. falciparum (FcB1-Columbia and FcM29-Cameroon strains) by Incorporated (3H)-hypoxanthine method	27–33 mg/m L	report of antiplasmodial activity of leaf extracts	 Bis naphthoquinone derivative	
Enzyme Modulatory effect	Methanolic leaf extracts and lawsone derivatives A and B along with eight other phenolics compound	In vitro lymphocyte blast transformation, mitogenesis assay and lymphocyte transformation assay	0.50–2.50 mg/m L for extract and 3.5–6.09 mM for active constituents	Immunostimulant activity of the total methanolic extract (i.e., 90% lymphocyte transformation) was greater than individual solvent fractions	 β -lapachol	96
Activity on bone resorption	Leaf alcoholic extracts, lawsone, gallic acid	MTS Assay	Not specified	Daphneside and daphnorin showed a significant inhibition on receptor activator for nuclear factor-B ligand-induced osteoclast formation	 Daphneside	73
Protein glycation inhibitory activity	Hydroalcoholic leaf extract	In vitro spectro-photometric assay using bovine serum albumin and glucose	1500 g/mL (1000) g/mL and 1000 M, respectively	Alcoholic extract, lawsone and gallic acid showed 77.95%, 79.10% and 66.98% inhibition, of advanced glycated end products formation, respectively	 Isorhamnetin	25

Hypoglycaemic and antihyperlipidemic activity	Ethanollic extracts of leaves	Alloxan-induced diabetic model in swiss albino mice	100, 200, 400 and 800 mg/kg bw	Feeding 800mg/kg bw decreased the glucose concentration to normal condition after 14th day		49
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CNS activity:

In a mouse model, ligroin secluded from *L. inermis* leaves was examined for its adequacy in an assortment of CNS issues, including nervousness, amnesia, and conduct modifications transferred by the class of medication MAO synapses. An overly complex high shock detached aversion model was utilized to explore the results. By tweaking social changes managed by 5HT and nor-epinephrine, A Nootropic impact is accomplished.⁶⁸ Philip et al. (2011) utilized mice conduct models including, for example, rest time brought about by diazepam, open region, pentylenetetrazole, and ergot alkaloids actuated seizures to examine the viability of water, ethanol, pet-ether, and Ch2Cl2 concentrates of henna seeds on CNS exercises.⁶⁹ The concentrates were given orally in portions going from 100 to 400mg/kg body weight, upgraded rest span, and diminished locomotors activity, proposing that *L. inermis* seeds had A CNS depressant impact. Strychnine-instigated epilepsy was likewise eased back with the utilization of these concentrates. Moreover, ethanol removes at a measurement of 400mg/kg bodyweight safeguarded the mouse by creating tiredness and staying away from spasms through glycine receptors. In all models, pet-ether and Ch2Cl2 separates had a hurtful reaction and rushed to delay or safeguard mouse with Pentylenetetrazole Produced Epilepsy (PTZ) set off seizures.⁷⁰

Antimicrobial activity:

Interestingly, [Hanke and Talaat (1961) and Galal and colleagues] showed that *L. inermis* is a treatment for gastrointestinal loose bowels⁷¹. *L. inermis* removes were displayed to have antimycotic adequacy against *Pestalotiopsis mangiferae* by [Rai (1996)]⁷². Malekzadeh (1968) examined the antibacterial fluid leaves extricates against *Bacillus cereus*, *Bacillus anthracis*, *E. coli*, *Staphylococcus aureus*, *Proteus Vulgaris*, *Erwinia carotovora*, *Agrobacterium tumefaciens*, and *Xanthomonas campestris*.

Anti-microbials were demonstrated to be insufficient against *S. aureus*, in any case, development hindrance was viewed as the best against *B. anthracis*. No bacterial provinces were seen inside the zone of restraint in plate of *B. anthracis* and *X. Campestris*⁷³. (Tripathi and associates, 1978) the activity spectra of segregated lawsonone included fungicidal, parasites poisonous, and non-phytotoxic impacts⁷⁴. At 1:30 (W/V) weakening, the bark concentrate of henna had a fungistatic impact towards *Microsporum gypseum* and *Trichophyton*

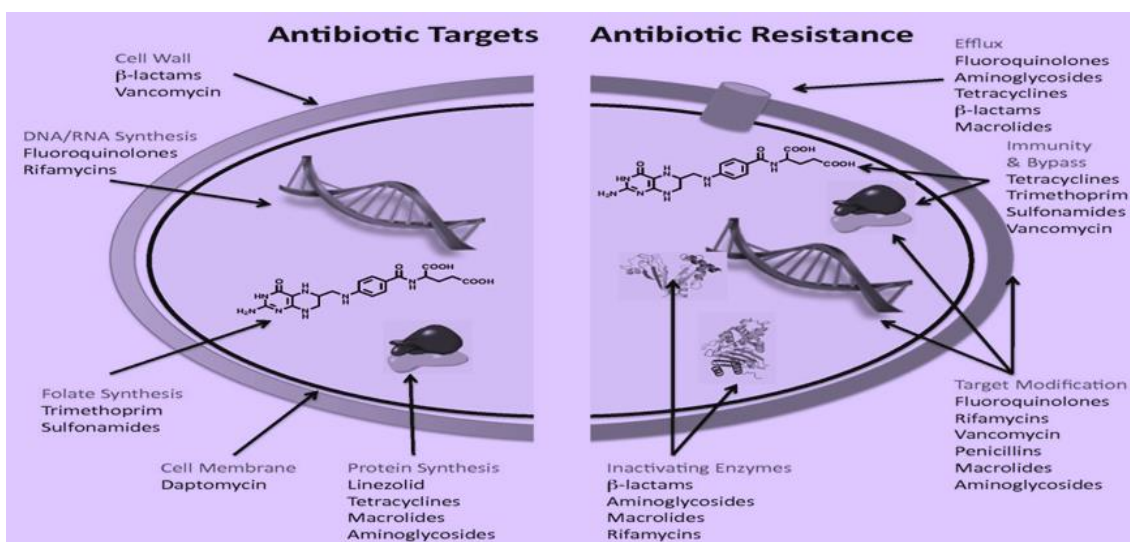
mentagrophytes, while at 1:10 (w/v) scattering, it became equipped for repressing the contamination. (Singh and Pandey, 1989)The concentrate additionally demonstrated that parasites have wide toxic viability that is unaffected by high temperatures⁷⁵. The tuberculostatic action of *L. inermis* against Tubercle bacilli and *M. Tuberculosis* (H37Rv) was examined in vitro and creature tests utilizing Lowenstein Jensen Conditions. It was found that a convergence of 6g/ml was sufficient to restrain microbiological development. Involving TB trial strategies in cavy and mice, scientists found that a measurements of five mg/kg BW diminished *Mycobacterium tuberculosis* H37Rv transmission fundamentally⁷⁶.

During the shrouding of 20 Yemeni balancing spices for antimicrobial and poisonous cells, the CH3COOC2H5 concentrate of *Lawsonia inermis* is dynamic.⁷⁷ Antibacterial action of the ethanollic extricate has additionally been shown against drug-safe microorganisms and pathogenic yeast variations⁷⁸ An ethanollic concentrate of *L. inermis* leaves showed antibacterial viability against MRSA lactamase makers in vitro, as well as synergistic impacts with antibiotic medication.⁷⁹ Fresh and handled leaves, as well as Hennas bits, were displayed to have powerful antibacterial action *S. aureus*, *E. coli*, and *Pseudomonas aeruginosa* clinical confines were tried. In vitro, dry leaves gave the best antibacterial action towards the *Shigella sonnei*, however they were incapable against *Candida albicans*.⁸⁰ The Ethanollic extricate consolidated well with antibiotic medication, chloramphenicol, and ciprofloxacin against *S. aureus* and *E. coli*. The AMES (TA 97 A, TA 100, TA 102, and TA 104) and mammalian (V79 hepatoprotective report) measures, as well as the mice lymphoma mutagenesis try, all showed that it was not unsafe to erythrocyte sheep, and no minutes of Typhimurium test kinds of *Salmonella*, and it gave no genotoxic risk in the chromosomal bending examine⁸¹ The watery, Ethanollic, chloroform and ethereal segregates of *L. inermis* had the most grounded suppressive impacts against Gram-positive (*Bacillus cereus*, *Bacillus subtilis*, and *Staphylococcus aureus*) and Gram-negative (*Escherichia coli*, *Proteus Vulgaris*, and *Pseudomonas aeruginosa*) microorganisms in an agar stock weakening examine⁸² The antibacterial action of fluid, ethanollic, and greasy concentrates of *L. inermis* leaf towards secluded bacterial settlements of cutaneous irresistible infections was tried utilizing ampicillin, ciprofloxacin, gentamycin, and antibiotic medication. The base inhibitory convergence of alcoholic

concentrates against the microscopic organisms concentrated in vitro demonstrated critical benefits over as of now accessible anti-toxins.⁸³ Henna, as per [Ahmadian and his associates (2009)], can likewise forestall mycotic ailment⁸⁴. The antibacterial action of henna leaf separates in n-hexane, chloroform, and alcoholic structure against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Proteus mirabilis* was significant⁸⁵.

Leaves have high antibacterial affectivity, forestalling (UTI) in individuals by inciting critical interruptions in *E. coli* protein, amylase, and glycoprotein divisions.⁸⁶ The alcoholic concentrate of *L. inermis* leaves has likewise been shown to be defenseless to *Staphylococcus aureus*, *K. pneumonia*, *Proteus* species, *Escherichia coli*,

Pseudomonas aeruginosa, and *Candida albicans*.⁸⁷ C_2H_5OH and $C_2H_5COCH_3$ confines of blossoming, berry, and leaves showed uncovered hesitance against the tried microorganisms at centralizations of more than 1 mg/100ml⁸⁸. When lawsone and 6 other detaches of *L. inermis* in H_2O , Dimethyl sulfoxide, C_2H_5OH , $CHCl_3$, $CH_3COC_2H_5$, and $C_2H_5COC_2H_5$, that are utilized by Algerian individuals customary medication for the treatment of an assortment of infectious disease, were evaluated for antimicrobial exercises against 5 endophytes, lawsone recognized possibly huge MICs of 12g/mL and 50g/mL against *Fusarium oxysporum* and *Aspergillus flavus*, separately, Against *F. oxysporum* the ethanolic segregates had a MIC of 230g/ml towards different concentrates¹⁰⁶.



Antioxidant activity:

There are numerous phenolic glycosides like (Lalioside, Lawsoniaside, 2,4,6-Trihydroxyacetophenone-2-O-d-glucopyranoside, 1,2,4-Trihydroxynaphthalene-1-O-d-glucopyranoside, and luteolin-7-O-d-glucopyranoside) were found in the leaves, butanol segment. In DPPH model and carotene measures, *inermis* has shown better cell reinforcement limit.⁹⁰ There was a ton of rummaging free extremists and linoleic corrosive oxidation aversion. In FTC and TBA measures, the fragrant oil of *L. inermis* showed strong cancer prevention agent capacity, suggesting that it very well may be utilized as a nutraceutical to address the cell reinforcement need.⁹¹ DPPH (2,2-diphenyl-1-picryl-hydrazyl-hydrate) and ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic corrosive) extremists, ferric particles, Lipid peroxidation, and destruct to DNA were all altogether decreased in fluid as well as alcoholic concentrates of the ethereal plant.⁹² Alcoholic *L. inermis* disconnects and 12 unique Malaysian botanicals were demonstrated to be more compelling revolutionary foragers than watery confines,

demonstrating that absolute phenolic content and cell reinforcement limit are associated. At a convergence of 100g/mL, extricates were not cytotoxic to 3T3 and 4T1 cells, showing that they restrain lipid peroxidation.⁹³

The alcoholic concentrate of *L. inermis* displayed improved (2,2-diphenyl-1-picryl-hydrazyl-hydrate) revolutionary searching, decreased MO6+ to MO5+ chelation, Fe^{3+} to Fe^{2+} decrease, and stayed away from oxidative harm when contrasted and 2-(1,2-dihydroxy ethyl)-4,5-dihydroxy-furan-3-one.⁹⁴ The alcoholic separates of *L. inermis* and furthermore 7 separates (p-coumaric corrosive, 2-methoxy-3-methyl-1,4-naphthoquinone, apiin, lawsone, apigenin, luteolin, and cosmoiin), shows cancer prevention agent and invulnerable modulatory action in lymphocyte change, ABTS, and free revolutionary rummaging immunoassay.⁹⁵

Henna berries have been tried for cell reinforcement capacity and decreasing power extraordinarily low IC50 values, lower phenols (72.1 and 75.8mg/g), yet great

enemy of revolutionary (16.2 and 14.4) and diminishing powers (0.7 and 0.6 ASE/mL) when inspected (Prakash et al., 2007).¹¹⁵

Wound healing activity (WHA):

The WHA of the alcoholic separates of *L. inermis* leaf (200mg/kg bw/day) had been depicted in female Male Sprague - Dawley rodents taking advantage of extirpation, scratch, and killed region slash situations.⁹⁶ In contrast with control creatures, treated creatures had A 71 percent decrease in scraped spot region. Skin treatment of the alcoholic disconnects (220mg/kg/body weight) and oral conveyance of lawsone (50mg/kg/body weight) both prompted impressive injury recuperating movement in mouse entry point and extraction models, with the skin application being altogether more apparent than the oral methodology.⁹⁷ In male Wistar rodents, wound mending was speedier with a 5 and 10% w/w cream of Ethanolic leaves disengages than with a 0.2 percent nitrofurazone salve.⁹⁸ Henna tattoos glue has additionally demonstrated to be entirely ideal for twisted recuperating in an assortment of film diseases⁹⁹.

Antitumor activity and cytotoxicity:

The WHA of the alcoholic withdraws of *L. inermis* leaf (200mg/kg bw/day) had been portrayed in female Male Sprague - Dawley rodents exploiting extirpation, scratch, and killed locale slash circumstances.⁹⁶ interestingly, with control animals, treated animals had A 71 percent decline in scratched spot area. Skin treatment of the alcoholic separates (220mg/kg/body weight) and oral transport of lawsone (50mg/kg/body weight) both affected broad injury retouching development in mouse cut and extraction models, with the skin application being essentially more clear than the oral approach.⁹⁷ In male Wistar rodents, wound repairing was speedier with a 5 and 10% w/w cream of Ethanolic leaves detaches than with a 0.2 percent nitrofurazone ointment.⁹⁸ Henna tattoos stick has also shown to be genuinely really great for wound patching in a combination of layer infections⁹⁹.

Anti-inflammatory, antipyretic, analgesic, and anti-diarrheal activity:

In light of its pharmacological impact, *L. inermis* is regularly recommended to victims of palmer-grower erythrodysesthesia¹⁰⁹. In juxtaposition to watery leaves confines (0.25-2.0g/kg body weight), alcoholic leaves separates (0.25-2.0g/kg body weight) and its CHCl₃ and n-CH₃-CH₂-CH₂-CH₃ portions had astounding portion subordinate mitigating, analgesics, and antipyretic impacts in rodents¹¹⁰.

Lawsone, as per these specialists, protracted pentobarbitone-set off resting in calming rodents. Two mixtures, lawsochylin An and lawsonaphthoate-A, repressed superoxide anion creation (IC50 1.80 and 1.90

g/mL) and conveyance of the elastase compound made by unambiguous tissue in the pancreas (IC50 1.58 and 3.17g/mL) in human neutrophils because of cytochalasin-B fMLP. Apigenin, luteolin, 2-butoxysuccinic corrosive, and 4S-4-hydroxyl tetralone all forestalled the age of superoxide anion (IC50 0.75-1.78 g/mL) and the arrival of elastase (IC50 1.62-3.61 g/mL) in these examines (Liou et al., 2013). Gupta et al. (1986) found the mitigating impacts of luteolin, - sitosterol, and lawsone in rodents¹¹¹. In rodents, fluid alcoholic leaf secludes of *L. inermis* have been demonstrated to have huge enemy of joint movement when contrasted with Freud's strong actuated and HCHO-initiated joint inflammation models¹¹². In mice models, alcoholic leaves disengages had huge analgesics and an enormous antidiarrheal side interest, offering clinical help for its conventional use contrary to free development and edge torment¹¹³.

Hepatoprotective activity:

Due to its pharmacological impact, *L. inermis* is every now and again endorsed to victims of palmer-grower erythrodysesthesia¹⁰⁹. In juxtaposition to watery leaves separates (0.25-2.0g/kg body weight), alcoholic leaves secludes (0.25-2.0g/kg body weight) and its CHCl₃ and n-ch₃-ch₂-ch₂-ch₃ parts had astounding portion subordinate calming, analgesics, and antipyretic impacts in rodents¹¹⁰. Lawsone, as indicated by these analysts, extended pentobarbitone-set off resting in mitigating rodents. Two mixtures, lawsochylin An and lawsonaphthoate-A, restrained superoxide anion creation (IC50 1.80 and 1.90g/mL) and conveyance of the elastase protein made by unambiguous tissue in the pancreas (IC50 1.58 and 3.17g/mL) in human neutrophils in light of cytochalasin-B fMLP. Apigenin, luteolin, 2-butoxysuccinic corrosive, and 4S-4-hydroxyl tetralone all forestalled the age of superoxide anion (IC50 0.75-1.78g/mL) and the arrival of elastase (IC50 1.62-3.61g/mL) in these examines (Liou et al., 2013). Gupta et al. (1986) found the mitigating impacts of luteolin, - sitosterol, and lawsone in rodents¹¹¹.

In rodents, fluid alcoholic leaf disengages of *L. inermis* have been demonstrated to have critical enemy of joint action when contrasted with Freud's steady initiated and HCHO-instigated joint pain models¹¹². In mice models, alcoholic leaves separates had huge analgesics and an enormous antidiarrheal side interest, offering clinical help for its customary use contrary to free development and edge torment¹¹³.

Diuretic activity:

According to Reddy et al., each watery and alcoholic extract of *Lawsonia inermis* verified an amount of the drug increase in urine (2011). Alcoholic isolates had a higher level of natriuresis than aqueous isolates, reflecting a higher rate of H₂O, Na⁺, K⁺, and Cl⁻ excretion¹¹⁹.

Enzyme modulatory effect:

L. inermis has a 'double impact' in mice's hepatic cells, increasing the performance of Phase-2 enzymes involved on carcinogenic cleansing while lowering the substrates of Phase-1 enzymes. Over ambient limits, treatment with *L. inermis* isolates enhanced the distinctive sports of hepatic GSTs and DT-Diaphorases. *L. inermis* and lawsonie ethanolic isolates with IC50 values of 64.87 and 48.6g/mL, respectively, have been shown to inhibit trypsin¹²⁰.

Activity on bone resorption:

Lawsoniasides A and B, as well as eight other phenolics (particularly daphneside and daphnorin) isolated from alcoholic isolates of *L. inermis* leaf, were shown to inhibit nuclear factor transmitter chemicals. The -B ligand increased bone cell synthesis in mouse bone marrow macrophages, which helped to prevent pathology-related rapid bone reuptake¹²¹.

Protein glycation inhibitory activity:

The ethenolic isolates of henna leave efficaciously guard the proteins against damage, and it was determined that 2-hydroxy 1, 4-naphthoquinones is responsible for the protein's non-enzymatic glycosylation inhibitory motion.¹²² Gallic acid, which is one of the key Phenolic isolates, was also involved in the degradation and non-enzymatic glycosylation of protective proteins. The ethanolic isolates, 1, 4- Naphthalenedione, 2-hydroxy, and Gallic acid considerably prevented the development of glycosylated waste material, with blockage rates of 77.95%, 79.10%, and 66.98%, respectively, at concentration of 1500g/mL, 1000g/mL¹²³.

Hypoglycaemic and antihyperlipidemic activity:

A 70 percent ethanolic extract of henna leaf isolates supplied at a dosage of 800mg/kg mass for two weeks in a Swiss odd person mice model demonstrated a decrease in glucose intensity in alloxan-induced polygenic disease. There was also a little amount of real steroid alcohol-associated lipids present. The hypoglycaemic substance produced by duct glands from pancreatic islets improved glucose transport to peripheral tissue, resulting in an antihyperglycemic effect¹²⁴. The symptomatic severity of sickle fruit fenugreek isolates was substantially greater in neutral and alkaline medium than in acid media when methanolic extracts of leaves were combined with Magnoliopsida genus jambolana, dicot genus charantia, genus Morus alba, flower Sativa genus.

Antiparasitic effects:

The antihelmintic action of ChCl₃, maturation liquor, and fluid segregates of the henna leaf (10, 20, 50, and 100mg/ml) on mature *Eisenia fetida* has been analyzed. *Lawsonia inermis* removes caused neurological impacts bountiful right away and thus the chance to mortality was more limited¹²⁶. In vitro, the counter Strongyloides viability of henna (stems 70% alcoholic detaches) have

been examined. Different scopes of *Lawsonia* (1, 10, 100 mg/ml) were utilized to develop hatchlings and non-parasitic females for changing timeframes (24, 48, 72, and 96 h). *Lawsonia inermis* at a portion of 10mg for 24 hours impacted the parasite fingernail skin interface inside the type of even and vertical breaks as well as level wretchedness, contrasted with no epidermal modification using flubendazole (100mg/ml)¹²⁷. In vitro examination was done on the antimalarial pharmacological movement of the henna separate. Oil ether extricate had A 27mg/l antimicrobial potential and alkyl revolutionary concentrate had 33mg/l antimalarial impacts against each and every variation of *Plasmodium* species¹²⁸.

The antiplasmodial action of synthetically characterized detaches and its essential fixing on the chloroquine-delicate NF-54 variation was analyzed in vitro. In vitro testing, the ester concentrates of leaves (IC50 9.00 0.68 g/ml) with fraxetin (IC50 19.21 1.04 M) have been the most productive, and they have been likewise decided for in situ in *Plasmodium berghei* contaminated mice. The polluted mice got an ester arrangement of leaves combined with fraxetin, which came about in essential (p 0.05) and fundamentally diminished erythrocyte osmotic delicacy and malondialdehyde. The review presumes that leaf concentrate of henna decreased trypanosomosis histology in rodents, with respect to giving an antitrypanosomal movement to words the *T. congolense*, in all probability by shielding the RBC film from trypanosome-initiated erythrocyte oxidative harm¹²⁹. The activity of produced valuable metallic nanoparticles to words the head hatchlings of Head mite bugs Diamond State Geer (arthropod parasite) and the sheep body mite *Bovicola Ovis Schrank* was contemplated (Mammal biting lice). The rate demise for manufactured respectable metallic nanoparticles against *B. Ovis* has been 33, 84, 91, and 100 at 10, 15, 20, and 35 minutes, correspondingly. The parallel compound leaves disengages of henna 1 mol AgNO₃ arrangement and created Ag NPs showed the best viability towards *P. humanus capitis*. Ag NPs had the best enemy of lousicidal action, as indicated by the exploration.

Molluscicidal effects:

Lymnaea acuminata and *Indoplanorbis exustus* were used to test *L. inermis* aerial portions for molluscicidal activity. Seed powders were far more toxic than fresh leaves and bark against *I. exustus*. Precompiled mixtures of henna grain by Himalayan cedar and neem oil, crushed garlic, or stem ginger rootstock natural resins were substantially more damaging to the snails *L. acuminata* and *I. exustus* than individual diagnostics. The neem isolates mixture also became riskier than the individual substances and combinations.

Abortifacient effect:

Lawsonia inermis extract's abortifacient effect was investigated in heavy with child mice. From the 1st to 17th day of pregnancy, pregnant mice have been given 1 and 10mg/kg body mass of *Lawsonia inermis* hydroalcoholic extracts intraperitoneal injection. Abortions were shown to be more common (p0.01) in *Lawsonia inermis*-treated groups, which had considerably higher blood estrogen levels (p0.01) and considerably lower progesterone levels (p0.01). In mice, rats, and guinea pigs, although, the methanolic extract induced abortion in a dose-dependent manner.

Immunomodulatory effect:

The immunomodulatory effect was produced by activating T-lymphocyte proliferative responses in methanolic isolates of the henna leaf at a 1 mg/ml concentration of 1mg/ml. Similarly, naphthoquinone produced from the leaves had a significant immunomodulatory effect¹³⁰.

Gingivitis healing activity

The effectiveness of *Lawsonia inermis* leaves methanol extracts (62.500, 31.250, and 15.625 µg/ml) in healing gingivitis was studied in Sprague Dawley rats with induced artificial inflammation in the mandibular labial gingiva by 10% H₂O₂. There was no difference in healing between the three concentrations of *Lawsonia inermis* leaves methanol extract and povidone-iodine, while there were differences among the 3 concentrations. Higher concentration (62.500 µg/ml) can accelerate the inflammatory cells reduction and epithelial connective tissue repair¹²⁹. The effect of *Lawsonia inermis* leaves infusion in gingivitis healing was studied clinically. Sixty-three gingivitis patients were instructed to rinse with 3 concentrations (50000, 10000 and 5000 µg/ml) of *Lawsonia inermis* leaves infusion, 0.1% hexetidine solution, and placebo as control. Bleeding index was decreased in *Lawsonia inermis* leaves infusion at 10000 µg/ml concentration (80%), more than hexetidine 0.1% (76%)¹³⁰.

Antiurolithiatic activity

The curative and protective effects of the alcoholic extract of *Lawsonia inermis* bark against ethylene glycol induced urolithiasis and its possible underlying mechanisms were studied in rats

Other effects

The ethanolic extract of *Lawsonia inermis* leaves and lawsone possessed an IC₅₀ value of 64.87 and 48.6 µg/ml trypsin inhibitory activity, respectively¹³⁴. Compounds, lawsone, (E)-methyl 3-(4-hydroxyphenyl) acrylate, (E)-ethyl 3-(4-hydroxyphenyl)acrylate, caffeoyl alcohol, 2-hydroxy-1,4-naphthoquinone and 1,4-naphthoquinone isolated from *Lawsonia inermis* were evaluated for inhibition of

nitric oxide production in LPS-stimulated product of nitrite in RAW 264.7 cell, they showed IC₅₀ values of 6.12, 16.43, 18.98, 9.30, 9.30 and 14.90 µg/ml, respectively³⁴. Side effects and toxicity The aqueous extract of *Lawsonia inermis* was found to be safe up to 2g/kg bw orally in mice. After 24 h there was no mortality and signs of toxicity^{24, 105}. The minimum lethal dose of ethanol-water (1:1) extract of henna was greater than 2 g/kg bw orally in mice¹⁰⁷.

The toxicity of the aqueous root extract of *Lawsonia inermis* (200, 400, 800, 1200 and 1600 mg/kg bw, ip) was investigated in rats. Dizziness, loss of appetite, partial paralysis, temporary amnesia and spontaneous abortion in the pregnant females, were recorded in rats treated with 800-1600 mg/kg bw. Rats received 200-400 mg/kg bw remained active and healthy. No mortality was recorded in all doses. The results indicated delayed toxicity after intraperitoneal administration of the extract at various concentrations^{79, 135}.

In acute toxicity study, a volume of 0.1 ml of the test substance (approximately 58 mg) was instilled into the conjunctival sac of the right eye of each of 3 New Zealand white rabbits. Transient inflammation of the iris and moderate conjunctival irritation were observed up to a maximum of 48 and 72 h. *Lawsonia inermis* was slightly and transiently irritating to the eyes of New Zealand white rabbits. *Lawsonia inermis* exhibited no potential to induce dermal sensitization in Guinea pigs. On the other hand, no skin findings were observed on the tested skin area of any of the volunteers at any time during the 3 w of the induction phase and at challenge after a one week rest period. However, it was shown that lawsone penetrated through the pigskin in vitro. After exposure of 30 min and a follow-up period of 72 h, about 0.28% of the applied dose of lawsone was penetrated and 0.06% remained in the skin. The respective absolute skin penetration rate was 703 ng/cm². In using of radioactive of test substance, the mean percutaneous absorption of the test substance amounted to 0.20% of the administered radioactivity after 72 h, corresponding to an absolute absorption of 1.70 µg/cm². A 13-week oral toxicity study was conducted in rats with a 0.5 % aqueous methylcellulose solution of henna administered once daily by gavage. The treated animals received the test substance corresponding to daily dosage of 40, 200 and 1000 mg/kg bw. No mortality was observed during the study. In the high dose group, animals occasionally presented signs of poor clinical condition: loud breathing, piloerection and ptialism. Brown urine was noted in all males and females, accompanied by a brown tail in some animals. All clinical signs were reversible after 4-weeks recovery period, except for brown-coloured tail. Henna was tested for mutagenicity, it did not induce bacterial (*Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538) and

mammalian cell gene mutation. Henna was administered by daily gavage to 100 pregnant female rats on day 6 through 15 of gestation at the dose levels of 40, 200 and 1000 mg/kg/day bw. No clinical signs, no abortions and no mortalities were recorded in any female of any group during the study. A very slight (<10%) but statistically significant decrease of body weight gain and food consumption was observed in the dams receiving 1000 mg/kg/day. Pre and postimplantation loss, fetal body weight and sex-ratio were similar between control and all treated groups. At the external examination, no treatment-related anomalies or malformations were observed¹³⁶.

The toxic effect of aqueous extract of *Lawsonia inermis* seeds was studied in rats. 78.57 mg/kg orally, of the extract for 4 w, caused body weight gain, significant decrease on hematological parameters and potassium concentration, significant increase in the AST, ALP, total protein, albumin and urea concentrations with no histopathological changes. 78.57, 392 and 785.7 mg/kg/day orally for 1 w, increased AST, ALP and total protein concentrations. 785.7 mg/kg/day of the extract increased the ALT activity and decreased potassium concentration. 78.57 and 785.7 mg/kg/day of the extract increased urea and cholesterol concentrations, while 392 and 785.7 mg/kg/day of the extract induced hepatocytic necrosis, dilatation of the renal tubules and desquamation of the intestinal epithelium¹³⁷.

The safety of 500 and 1000g/kg dose of *Lawsonia inermis* ethanolic seeds extracts was studied in mice. The acute dose of 500 mg and 1000 mg/kg caused no death in animals after 24 h, and no signs of change in feeding, behavior, diarrhea or loss of fur were observed. WBC, RBC haemoglobin and platelets count were minimally affected. Serum Na, K, creatinine and urea were not deviated from control. Liver enzymes, protein, blood glucose and lipids profile were not affected by chronic administration of henna extract. However a slight but significant elevation in AST was recorded in the high dose group. Post mortem examination showed no signs of toxicity¹³⁸.

The teratogenic effects of 10 and 100 mg/kg bw, ip, of 80% ethanol extract of the aerial organs of *Lawsonia inermis* (for 7 d) were studied in mice. Both doses of the extract caused significant decrease in embryos' height and weight in comparison with the control ($p < 0.001$). However, no significant difference was observed between 10 and 100 mg/kg of the extract in embryos' height and weight. Skeletal abnormalities including rib and parietal bone abnormalities, anencephaly and exencephaly of embryos were recorded in both *Lawsonia inermis* treated groups with different frequencies⁴³.

A case of acute kidney injury was recorded in 34 y old man with G6PD deficiency from Yangon, Myanmar, after ingesting a herbal remedy of boiled henna leaves. He developed hemoglobinuria, and he underwent 5 sessions of hemodialysis. His condition improved within 7 w with full recovery¹³⁹.

CONCLUSION:

Lawsonone and its derivative have promising potential for treating several disease due to their antibacterial, antifungal, antiviral, antitumor and antiparasitic effect and have the potential to control pest via their molluscicidal and insecticidal properties. For the synthetic derivative of this compound for their pharmacological activity; in the future, synthetic derivative of lawsonone could potentially be used to treat disease and be used as pesticides. It was found that lawsonone is biologically active and further studies can be performed. Methanolic extract of *Lawsonia inermis* (MELI) bark (300 and 500 mg/kg, po) were administered once daily from 15th day to 28th day as curative regimen and from 1st day to 28th day as a preventive regimen. Treatment with the extract significantly restored all elevated parameters including calcium, phosphate and oxalate in urine and kidney homogenate; and creatinine, uric acid and urea nitrogen in serum compared to the control group. The histopathological study of the kidney also supported the biochemical results¹³¹. The antiurolithiatic activity of hydroethanolic extract of the leaves of *Lawsonia inermis* was studied in ethylene glycol with ammonium chloride model in rats. Hydroethanolic extract showed significant antiurolithiatic activity against calcium oxalate type stone. It modulated the levels of serum urea, urea nitrogen, uric acid, creatinine, kidney weight, urine volume, urine PH, urinary total protein, calcium, phosphorus, and magnesium¹³².

CONFLICT OF INTEREST:

The authors have no conflicts of interest regarding this review literature.

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