



E-ISSN: 2278-4136
P-ISSN: 2349-8234
JPP 2019; 8(1): 256-262
Received: 02-11-2018
Accepted: 05-12-2018

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Phytochemical and pharmacological benefits of *Hemidesmus indicus*: An updated review

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Abstract

Hemidesmus indicus (L.) is a potential source of several active principles of therapeutic value. It is an important medicinal herb used in the traditional system of medicine in India. Phytochemical studies have shown the presence of many valuable compounds such as alkaloids, steroids, terpenoids, flavonoids, saponins, phenolic compounds, tannins, lignin, inulin and cardiac glycosides. Over the past decades, several reports highlighted the potential pharmacological properties with numerous lines of evidence from *in vitro* and *in vivo* studies. Main pharmacological activities include anti-oxidant, inflammatory, anti-arthritis activity, anti-cancerous activity, anti-diabetes activity, anti-cataractous activity, anti-diarrhoeal activity, anti-HIV-1 activity, monophenolase activity, antivenom activity, anti-hepatocarcinogenic activity, anti-angiogenic activity, acetylcholinesterase and butyrylcholinesterase inhibitory activity. Due to the effective usage of this herb in biomedical science, it is essential to optimize the standard protocols for its propagation and enhancement of bioactive molecules. The present work reviews recent studies and updates on the phytochemical and pharmacological properties of this herb.

Keywords: Medicinal plant, anticataractous, antivenom, anticancer and anti-HIV

1. Introduction

Medicinal plants have been exploited for centuries to treat several disease conditions. The quest for safer and improved drug efficacy is an endeavour that triggers an upsurge in exploring natural sources for therapeutics. Recently, there was an escalating utilisation of Indian valuable medicinal plant resources in drug discovery and pharmaceutical industry. *Hemidesmus indicus* (HI) or Indian sarsaparilla is one such medicinal plant used in Indian traditional medicine [1] and also as a drug in Indian Pharmacopoeia [2] and British Pharmacopoeia. Its Chromosome $2n = 22$ [3]. The Plant List includes 5 scientific plant name species rank for the genus *Hemidesmus*. Of these 2 are accepted species name. viz, *Hemidesmus indicus* (L.) R. Br. ex Schult. *Hemidesmus cordatus* (Poir.) Schult (www.theplantlist.org). It belongs to the family Asclepiadaceae [4-7]. The main focus of the review deals with the recent updates on the pharmacological properties.

Table 1: Taxonomical Classification of *Hemidesmus indicus*

Kingdom	Plantae
Phylum	Tracheophyta
Class	Magnoliopsida
Order	Gentianales
Family	Asclepiadaceae
Genus	<i>Hemidesmus</i>
Species	<i>Indicus</i>

Table 2: Vernacular names of *Hemidesmus indicus*

English	Indian Sarsaparilla
Hindi	Magrabu
Kannada	Namada-beru
Sanskrit	Anantmul
Tamil	Arakkam

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Fig 1: *Hemidesmus indicus*

2. Tissue Culture

Tissue culture of this plant species has been carried out by various groups of scientists. *In vitro* multiplication was reported through axillary bud culture [8]. A tissue culture protocol was developed for rapid multiplication through multiple shoot cultures obtained in MS medium supplemented with 1 mg/L BAP and 0.5 mg/L NAA. The rooting was induced using 2 mg/L IBA and 1 mg/L NAA [9]. Similar results were obtained using low concentrations of BAP alone or in combination with auxin for the production of multiple axillary shoots [3, 10, 11]. Plant growth regulators such as 2, 4-D, Kinetin and NAA were reported to produce high percentage of callus formation in 1 mg/L NAA and 2 mg/L Kinetin. NAA 1 mg/L with BAP 2 mg/L produced a maximum number of shoots (7-8) per explants having a minimum response time of 4 days. Maximum elongation of shoot buds was achieved within 30- 35 days after inoculation [12]. A protocol for somatic embryogenesis (92%) with indole-3-butyric acid (IBA) was standardised [13]. The synthetic seeds prepared using somatic embryos, sodium alginate and calcium chloride germinated even after 120 days of storage at 4 °C.

2.1 Hairy root culture

Hairy root cultures were genetically and biosynthetically stable, easily maintained and faster in growth. A wide range of chemical compounds was produced from hairy roots of HI [14, 15]. Many plant species of hairy root cultures were widely studied, to produce secondary metabolites with potential applications in pharmaceuticals, food supplement, and cosmetics [16, 17]. Hairy root cultures were initiated, from the leaf and stem explants of HI incubated with *Agrobacterium rhizogenes* (MTCC532) along with acetosyringone in the medium [18]. The leaf explants were transferred, onto a hormones medium cefotaxime containing 500 mg/L medium. Then hairy roots were cultured on MS medium fortified with IAA 0.3mg/L exhibited improved biomass dry matter content. HI produces the aromatic compound 2-hydroxy 4-methoxy benzaldehyde as secondary metabolite [19].

3. Phytochemical studies

Phytochemical constituents indicate the presence of alkaloids, steroids, terpenoids, flavonoids, saponins, phenolic compounds, tannins, lignin, inulin and cardiac glycosides in HI. These phytochemicals could contribute to the anti-inflammatory, antipyretic, antidiarrheal, antinociceptive, antioxidant, antithrombotic, antitumor and hepatoprotective

activity of the plant [20]. Several phytochemicals were isolated from various parts of HI.

Root: Roots were reported to be the predominant source of several phytochemicals with therapeutic values. It possesses hemidesmol, resin and glucoside, tannin and resin [21]; lupeol, β -sitosterol, α - and β - amyrins [22]; lupeol, α -amyrin, lupeol acetate, β -amyrin acetate, hexa-Triconic acid, lupeol 1-octacosanol, steroid, terpenoid, flavonoid, and saponin [23]. HI contains 80% of crystalline material glucose hemidesmol, 2-hydroxy-4-methoxy benzaldehyde, glucoside, resin acid, sterol, and tannins [24].

Stem: Glycosides like hemidine and indicine were isolated from the stem [25]. Chloroform and alcohol extracts of the stem yield two pregnane glycosides, hemidesmine and emidine [26].

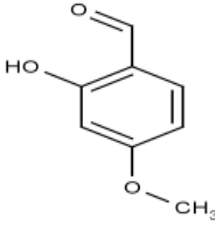
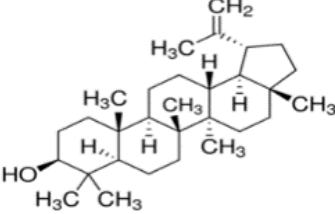
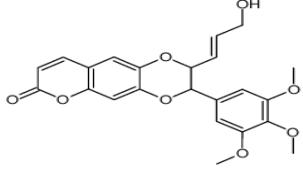
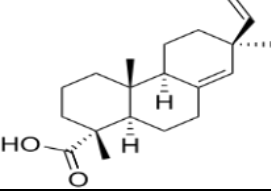
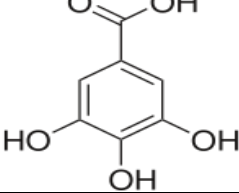
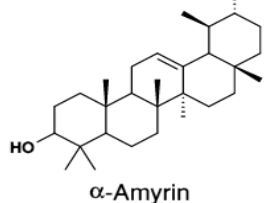
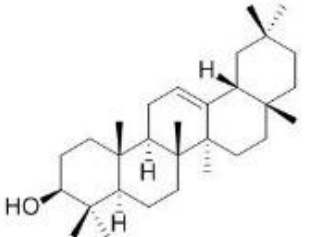
Leaves: Leaf represents 2.5% of tannins [27]. Coumarin oligonoids hemidesminine, hemidesmin 1, and hemidesmin 2 were also isolated from leaves [28]. Coumarin oligonoids were new and rare group naturally occurring compound, with cytotoxic and antihepatotoxic properties [29].

Flowers: Flowers of HI contain glycosides, hyperoxide, Isoquercetin, and rutin [29].

3.1 Chemical constituents

Different parts of the HI plant mainly root contain various compounds, such as 2-hydroxy 4-methoxy benzaldehyde, 4-hydroxy 3-methoxy benzaldehyde, lupeol, ledol, nerolidol, linalyl acetate, dihydrocarvyl acetate, cis-caryophyllene, isocaryophyllene, β -selinene, dodecanoic acid, hexadecanoic acid, camphor, borneol, dehydrolupanyl-3 acetate, dehydrolupeol acetate, 3-hydroxy 4-methoxy benzaldehyde, hexadecanoic acid, hexatriacontane, lupeol octacosanoate, β -amyrin acetate, lupeol acetate, α -amyrin, β -amyrin, sitosterol, drevogenin β -3-O- β -D-oleandropyranosyl, hemidesmin-1, hemidesmin-2, hemidesminine, phytosterols, triterpenes, saponin, resin acid, tannins, tetracyclic triterpene alcohols, fatty acids, glycosides, 16-dehydropregnenolone, pregnane ester diglycoside (desimine), indicine, hemidine and rutin [6, 22-35]. HPLC analysis of HI methanolic root extracts from seven ecotypes exhibited variation in peak number when compared to 2-hydroxy 4-methoxy-benzaldehyde and its concentration was more in ecotype 6 and less in ecotype 3 [36]. New condensed phenylpropanoid glucoside and three new pregnenolone glycosides were isolated from the roots [37].

Table 3: Chemical structures of major compounds present in *Hemidesmus indicus* (L.) R. Br.

Name of the compound	structure	Biological activity	Ref
2-hydroxy, 4-methoxybenzaldehyde (2H4MB)		Anti-oxidant Antifungal	[38]
Lupeol		Anti-oxidant	[39]
Hemidesminine		Anti-cancerous	[28]
Resin acid		Antibacterial Antioxidant	[40]
Tannins		Antioxidant	[40]
α -amyrin	 α -Amyrin	Anti-inflammatory	[21-23]
β -amyrin		Anti-inflammatory	[21-23]

4. Pharmacological Aspects

Medicinal properties of *Hemidesmus indicus* have been mentioned in several articles from ancient to the modern day scripts. The plant roots are used as an antipyretic, anti-diarrheal, blood purifier. They are used for the treatment of blood diseases, biliousness, dysentery and diarrhoea, respiratory disorders, skin diseases, leprosy, leucorrhoea, leukoderma, itching, syphilis, bronchitis, asthma, eye diseases, epileptic fits in children, lack of appetite, burning sensation, rheumatism, kidney and urinary disorders [1, 41-44].

4.1 Anti-inflammatory activity

Ethyl acetate root extract of HI exhibited anti-inflammatory activity in acute and subacute inflammation evident from the significant inhibition of inflammation caused by carrageenan, bradykinin, S-hydroxy tryptamine in rats. The extract was less active than phenylbutazone. HI root aqueous extract showed sufficient anti-inflammatory activity compared to diclofenac sodium gel [45]. Anti-inflammatory effect of HI root ethanol extract (100, 200 mg/kg, p.o) exhibited prominent dose-dependent inhibition in the experimental rat and mice models [46].

4.2 Antioxidant activity

Methanol extracts of HI root bark exhibited inhibition of lipid peroxidation, hydroxyl, and superoxide radicals [47]. HI extracts protected against free radical-mediated oxidative stress in the plasma, erythrocytes, and liver [48, 49].

4.3 Anti-arthritic activity

HI root display protective activity against arthritis, probably assigned by the presence of terpenes, sterols, and phenolic compounds in hydroalcoholic root extract and ethyl acetate fraction. These fractions showed higher anti-arthritic activity than chloroform and residual fraction [50]. The effect of HI root ethanolic extract on osteoporosis was evaluated in ovariectomised rats and reported that it prevents bone loss in dorsal ovariectomy-induced osteoporosis without estrogen-like side effects [51].

4.4 Anti-cancerous activity

Roots of HI exhibit protective activity against hepatocarcinogenesis and other cancers [52]. Studies on chemopreventive effects of soxhlet HI extract on the acute lymphoblastic leukemia cell line (CCRF-CEM) showed cytotoxic effect via intrinsic as well as extrinsic apoptotic pathways; hindered cell cycle in S phase and alleviated DNA damage [53]. Aqueous extracts and fractions of *Rubia cordifolia*, *Mimosa pudica* and HI were assessed for their wound healing potential and were found to enhance angiogenesis in chorioallantoic membrane (CAM) model [54]. Cytotoxic, cytostatic and cytodifferentiative activity of HI roots decoction was reported in the human promyelocytic leukemia cell line (HL-60) [55].

4.5 Anti-hepatocarcinogenic effect

The decoction prepared using HI root, *Smilax glabra* rhizome and *Nigella sativa* seed was evaluated for cancer therapy through p53 and p21 gene expression in Human hepatoma cells (HepG2) and Mouse liver with chemically-induced hepatocarcinogenesis. They found that the decoction increased the expression both genes in HepG2 cells and mice, probably by modulating the activities of genes in tumour suppression and cell cycle arrest [56]. The mechanism of anti-hepatocarcinogenic action of the decoction revealed that it induces apoptosis in human hepatocellular carcinoma HepG2 cell by caspase-3 and caspase-9 activation, pro-apoptotic Bax up-regulation and anti-apoptotic Bcl-2 genes down-regulation [57].

4.6 Anti-angiogenic activity

In vitro anti-angiogenic activity of HI root decoction was assessed on human umbilical vein endothelial cells. The compounds showed several interactions with crucial steps in angiogenic cascade targeting VEGF expression triggered by HIF-1 α , and also endothelial cell migration and differentiation [53].

4.7 Acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) inhibitory activity:

Progressive neurodegenerative disorders cause impaired memory and behavior manifestations. Cholinesterase inhibitors are the approved drugs for the treatment. Six plant extracts along with HI were screened for AChE and BChE inhibition. Among the six plant extracts HI root extract exhibited considerable IC₅₀ for both cholinesterases inhibition followed by *Vernonia anthelmintica* and *Saussure alappa* Clarke [58]. 2-hydroxy-4-methoxybenzaldehyde

(MBALD) and 4-hydroxy-3-methoxybenzaldehyde (vanillin) produced from root and pod extracts of HI and *Vanilla planifolia* respectively showed significant acetylcholinesterase (AChE) inhibitory activity [59].

4.8 Anti-diabetes activity

2-hydroxy-4-methoxy benzoic acid was isolated from HI roots and its effect on erythrocyte membrane-bound enzymes and antioxidant status was evaluated in streptozotocin-induced diabetic rats. 2-hydroxy-4-methoxy benzoic acid treatment significantly elevated the activity of total ATPases, Na/K ATPase, Mg²⁺-ATPase and Ca²⁺-ATPase; decreased catalase, superoxide dismutase, glutathione peroxidase, glutathione-S-transferase in erythrocytes; enhanced vitamin E; low level of vitamin C and glutathione level in plasma and erythrocytes of rats [60]. Active principle β -amyrinpalmitate was reported from root extract with anti-diabetes mellitus potential at low concentrations in alloxan and streptozotocin-induced diabetic rats [61].

4.9 Anti-cataractous activity

The anti-cataractous activity of HI was assessed in streptozotocin-induced diabetic cataract in a rodent model. Methanol root extracts inhibited aldose reductase activity, lowered blood glucose, delayed progression of cataract, decreased osmotic stress and prevented loss of antioxidants [62].

4.10 Corrosion inhibitor

Ethanol leaf extract of HI was assessed for their inhibition of metallic corrosion of steel in the accelerating system of H₂SO₄. They found that the extract inhibited the corrosion of the metal as confirmed by Gravimetric, gasometric, potentiodynamic polarisations, EIS methods and thermodynamic parameters analysis [63].

4.11 Antivenom activity

Inflammation induced by Viper venom was reported to be treated by HI root extract possibly by reducing reactive oxygen species and inflammatory cytokines. It nullifies *Naja kaouthia* venom-induced cardiotoxicity, neurotoxicity, and respiratory changes. Viper venom-induced coagulant and anticoagulant activity were neutralised by the root extract [64].

4.12 Anti-HIV-1 activity

Many antiretrovirals have been reported, but there is a demand for novel therapeutics from natural sources. Phytocompounds have been reported to possess their efficacy towards HIV-1 [66-70]. The anti-HIV-1 activity of HI was evaluated and found to inhibit RT-associated RNase H function, HIV-1 RT-associated RNA-dependent DNA polymerase activity and cellular α -glucosidase [71].

4.13 Nanoparticles

Spherical silver nanoparticles were synthesized and assessed for its antibacterial efficacy on poultry gut isolated *Shigella sonnei* and showed that silver nanoparticles of HI plant leaves exhibited higher inhibitory activity against the isolated bacteria [72].

4.14 Diuretic activity

The acute diuretic activity of HI roots in rats was evaluated using aqueous and ethanol crude extracts which significantly increased the urine output in higher doses using acute rat models, without alterations in pH and specific gravity [73].

Aqueous extract significantly increased urinary Na⁺ and K⁺ levels. Aqueous root extract conferred a better protective effect against bromobenzene induced mitochondrial dysfunction in rat kidneys than vitamin E [74].

4.15 Monophenolase activity

2-hydroxy-4-methoxybenzaldehyde (MBALD) exhibited inhibitory activity against diphenolase activity of the tyrosinase. The crude root extract of HI displayed greater inhibition against monophenolase activity compared to pure MBALD, evidenced by the extension in lag time [59].

4.16 Combinatorial treatment

HI root is also used in combinatorial treatment along with other traditional medicines. Aqueous extracts and fractions of *Rubia cordifolia*, *Mimosa pudica* and HI were reported to enhance angiogenesis in chorioallantoic membrane (CAM) model. Chloroform fraction of methanol extract of *Buchanania axillaris*, *Hemidesmus indicus* and *Rhus mysorensis* exhibited dose-dependent inhibitory activities against AChE, BuChE, α - and β -glucosidase enzymes and also neuroprotective activity [75]. Antibacterial action of ethanol extracts of *Hemidesmus indicus* (L.), *Leucas aspera*, *Plumbago zeylanica* and *Tridax procumbens* was dose and time dependent [76]. The mechanism involves bacterial membrane disruption, permeabilization and leakage. HI root extracts might cause vasodilation, positive inotropic effect, and cardioprotection [77].

5. Conclusion

The demand for novel, safe and efficient therapies is on the rise. The naturally-derived phytochemicals of medicinal value are the potential sources of the new drugs and one such source is *Hemidesmus indicus*. The isolated active principle compounds from this herb need to be further evaluated for their applications as chemotherapeutic and chemopreventive agents. The active compounds have molecular versatility which has to be clinically exploited. *In vitro* and *in vivo* studies need to be focussed to decipher the mechanisms of action of the active compounds. Pure compounds isolated from HI can be used for preclinical studies and consequent translation to clinical application by drug design and development. The current pharmaceutical knowledge of HI has to be potentially tapped in a commercial way for the production of therapeutic products.

6. Acknowledgement

Authors are thankful to DST-SERB, DST-PURSE for providing infrastructure and UGC, CSIR-New Delhi for providing fellowship.

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