Advances in Bioresearch
Adv. Biores., Vol 5 (3) September 2014:208-213

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
ICV 7.20 [Poland]

Advances in Bioresearch

REVIEW ARTICLE

Medicinal Importance of *Hemidesmus indicus*: a Review on Its Utilities from Ancient Ayurveda to 20th Century

Aparna Banerjee[1] and Subha Ganguly[2]*
1Department Of Biotechnology, Vidyasagar University, Midnapore, West Bengal - 721 102, India
2AICRP On Post Harvest Technology (ICAR), Department Of Fish Processing Technology, Faculty Of Fishery Sciences, West Bengal University Of Animal and Fishery Sciences, P.O.- Panchasayar, Chakgaria, Kolkata - 700 094, WB, India
*Corresponding Author Email: ganguly38@gmail.com

ABSTRACT
Hemidesmus indicus commonly known as Anantmool belongs to the family of Periplocaceae and it is used as a folk medicine and found to be an important medicinal ingredient from ancient ayurveda period to this 20th century. This climbing vine plant is a common inhabitant of Gangetic India and West Benagl. It has several medicinal properties varying from anti-cancerous activity, chemopreventive activity, wound healing power to immuno-modulatory activity, anti-diarrheal activity, antioxidant properties; also anti-venom properties, anti-leprotic properties to diuretic activities.
KEYWORDS: Hemidesmus indicus, Phytochemical contents, Medicinal properties

Received 12/06/2014 Accepted 16/08/2014

How to cite this article:
Aparna B and Subha G. Medicinal Importance of Hemidesmus indicus: a Review on Its Utilities from Ancient Ayurveda to 20th Century. Adv. Biores., Vol 5 [3] September 2014: 208-213. DOI: 10.15515/abr.0976-4585.5.3.208213

INTRODUCTION

Hemidesmus indicus commonly known as Anantmool belongs to the family of Periplocaceae and is synonymously known as *Periploca indica* [1]. *H. indicus* has long been used as a folk medicine and found to be an important ingredient in ayurvedic and unani preparations. This is a climbing vine plant found in Upper Gangetic plain, eastwards to Bengal and Sundarbans and from Central provinces to Travancore and South India. *H. indicus* root is sweet, cooling and demulcent. It is used as tonic, diuretic and aphrodisiac. Whole root and root-bark are useful in syphilis, leucoderma, hemicrania, rheumatism and in several liver and kidney disorders. Powdered root mixed with cow's milk treats scanty and highly coloured urine and is used as a popular folk medicine.
Chromosome number 2n= 22 [1].

DESCRIPTION OF THE PLANT

IT IS A PERENNIAL, SLENDER, LATICIFEROUS, TWINING, WIRY SHRUB.
Stems - Numerous slender stems having thickened nodes.
Leaves – Simple, opposite, very variable from elliptic-oblong to linear lanceolate and 5-10 cm long. It is dark green in colour with reticulate veins
Flowers – Greenish purple crowded in subsessile cymes with opposite axils.
Fruits – Slender and cylindrical, approximately 10 cm long
Seeds – Seeds are black, 6 to 8 cm long
Roots – Roots are cylindrical in shape, irregularly bent, slightly twisted and aromatic.
1.5 -2 cm in diameter. It is externally dark brown and internally yellowish brown in colour.

PHYTOCHEMICALS PRESENT IN THE PLANT

Roots- Roots of *H. indicus* are reported to contain chemical constituents like - essential oil containing 80% of 2-hydroxy 4-methoxy benzaldehyde, a ketone, fatty acids, saponin, tannins, resinal fractions, resin acids, sterols, β-sitosterol, stigmasterol and sarsapic acid. Hemidesmin 1, hemidesmin 2, alpha-amyrin, beta-amyrin, lupeol and 2-hydroxy-4-methoxy benzoic acid have been isolated and identified from roots of *H. indicus*.

Stem- Gupta et al. [2] isolated and characterized a terpene lactone, 3-keto-lup-12-ene-21 to 28-olide from hexane soluble fraction of ethanol extract of stem of *H. indicus.* Lupanone, delta12-dehydrolupanyl-3beta-acetate, delta12-dehydrolupeol acetate, hexadecanoic acid, 4-hydroxy-3-methoxybenzaldehyde and 3-hydroxy-4-methoxybenzaldehyde were also isolated. Chloroform and alcohol extract of stem yields pregnane glycoside, emdine and hemidescine. [10] Glycosides like- indicine and hemidine were also reported to be isolated from stem.

Leaves- Leaves of *H. indicus* contain cardiac glycosides, Tanins, Saponins. Coumarinolignoids like- Hemidesmine, Hemidesminine and Flavonoids like- rutin, hyperoside are also isolated from leaves of *H. indicus*

Flowers- Flavonoid glycosides identified in flowers of *H. indicus*, are hyperoside, rutin and isoquercitin.

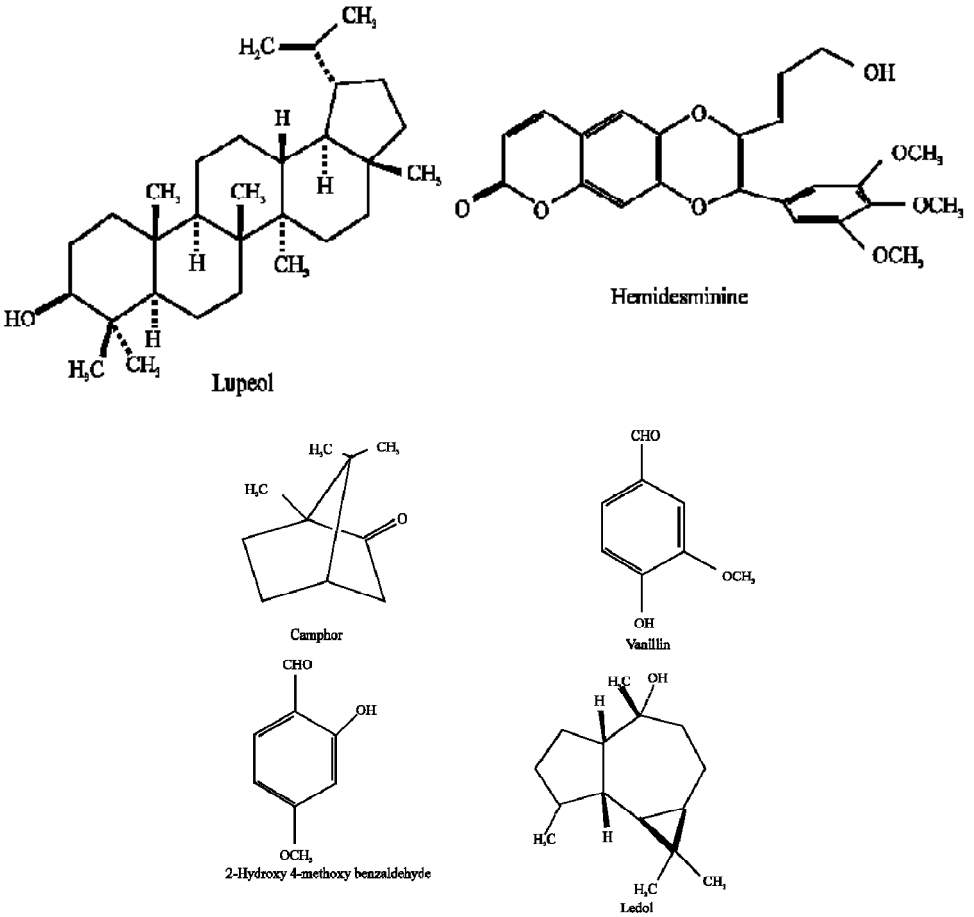

Fig: Different Phytochemicals isolated from *Hemidesmus indicus* and its chemical structures

MEDICINAL PROPERTIES OF THE PLANT

Anti-cancerous activity- *H. indicus* have remarkable anticancer potentials against MCF7 Brest cancer cell lines. Methanolic extract of rhizomes of *H. indicus* could be an excellent drug for treating breast cancer. Cytotoxic effect against HT29colon cancer cell line is also demonstrated by rhizomes of Hemidesmus indicus. So it can be used as a potential anticancer herb against colon cancer too. *H. indicus* methanolic root extract showed a significant cytotoxic activity against Ehrlich Ascites Tumor too. [9] *H. indicus* modulated many components of intracellular signaling pathways involved in cell viability and proliferation and altered protein expression, finally leading to tumor cell death, mediated by a loss of mitochondrial transmembrane potential and increased Bax/Bcl-2 ratio. Hemidesmus induced mitochondrial depolarization. Hemidesmus induced a significant Ca^{2+} raise through mobilization of intracellular Ca^{2+} stores. Moreover, Hemidesmus significantly enhanced antitumor activity of 3 commonly

used chemotherapeutic drugs- methotrexate, 6-thioguanine, cytarabine. It indicates molecular basis of antileukemic effects of Anantmool.[10]

Chemopreventive- *H.indicus* is an effective chemopreventive agent in skin and capable of betterment of cumene hydroperoxide induced cutaneous oxidative stress and further tumor promotion [8]. Shetty et al [6] reported that radioprotective effect on lipid peroxidation in rat liver microsomes protected microsomal membrane by minimizing lipid peroxidation, which ultimately protect DNA from radiation effect.

Immunomodulatory activity- Methanol: Iso- propyl alcohol: acetone extract of *H. indicus* shows an immunomodulatory activity related to IgG secretion and Adenosine deaminase (ADA) activity. Herbal extract promotes the release of IgG by lymphocytes in vitro and also the ADA activity after 72 h of culture [12].

Wound healing activity- Leaves of *H. indicus* possess marked wound healing activity and play a promising role in the treatment of wounds especially chronic wounds and in diabetic and cancer patients. The alcoholic extract of *H. indicus* formulated as 5% and 10% ointment increase the rate of wound contraction and period of epithelisation [4].

Antiulcer activity- Austin [3] established the antiulcer activity of *H. indicus*. It acts by mucoprotective action and selectively inhibiting prostaglandins. Even standard drugs, like- omeperazole, rantidine have less mucoprotective activity than *H. indicus* have.

Nootropic effect- The *n*-butanol fraction of ethanolic *H. indicus* root extract significantly improved learning power and memory at mice. Hence, *H. indicus* proved to be a useful memory restorative agent in the treatment of dementia seen in the Alzheimer's disease and other neurodegenerative disorders [5].

Antioxidant and free radical scavenging activity- Doxorubicin (Dox) is an anthracycline antibiotic widely used in the treatment of cancers including hematological malignancies, many carcinomas and soft tissue sarcomas. However, the clinical use is restricted due to its toxicities to cardiac tissues. The Dox-induced cardiotoxicity is shown to be mediated by lipid peroxidation, free radical formation, mitochondrial damage and decreased activity of Na+–K+ ATPase. Antioxidant enzymes-SOD, CAT and GPx, as well as GSH levels in heart tissue decreased drastically after doxorubicin injection. *H. indicus* root extract, due to its antioxidant properties significantly reduced the oxidative stress and thereby toxicity induced by doxorubicin [9].

Phytochemicals, like flavonoids and polyphenols, terpenoids, coumarins and glycosides have antioxidant properties. Evaluation of antioxidant activity of methanolic extract of *H. indicus* root bark in *in vitro* and *ex vivo* models is done (like radical scavenging activity by DPPH reduction, superoxide radical scavenging activity in riboflavin/light/NBT system, nitric oxide radical scavenging activity in sodium nitroprusside/greiss reagent system and inhibition of lipid peroxidation induced by iron-ADP-ascorbate in liver homogenate and phenyl hydrazine induced haemolysis in erythrocyte membrane stabilization study) [13]. 70% methanolic extract of *H. indicus* root, which contains large amounts of flavonoids and phenolic compounds, exhibits high antioxidant and free radical scavenging activities. It also chelates iron and has reducing power. These in vitro assays indicate that the extract contains constituents that can be a significant source of natural antioxidant.

Hepatoprotective activity- Oral administration of 50% ethanolic extract of *H. indicus* significantly prevented rifampicin and isoniazid induced hepatotoxicity.[14] CCl4 and paracetamol induced hepatic damage can be cured upto an extent by *H. indicus* root extract. Biochemical parameters, like- Alkaline phosphatase (ALP), Serum glutamate oxaloacetate transaminase (SGOT), Serum glutamate pyruvate transaminase (SGPT) were found to be in normal range only after oral administration [15]. Many phytoconstituents present in *H. indicus* are reported to possess hepatoprotective property, like phenolic compounds, glycosides, coumarins and saponins.

Anti-inflammatory effect- It is found that ethyl acetate extract of H. indicus root shows much anti-inflammatory effect in acute and subacute inflammation. Oral administration of *H. indicus* root extracts exhibited a dose dependent antinociceptive activity in all models and it blocked both neurogenic and inflammatory pains. Comparative studies on anti-inflammatory activity of *H.* indicus are also done in carrageenan-induced rat paw oedema. The ethanolic extracts of roots exhibited significant anti-inflammatory activity at a dose of 350 mg/kg p.o. as compared to control [16].

Diuretic- Aqueous extract of *H. indicus* root caused an increase in urinary flow in rats. *H. indicus* along with aminoglycosides therapy, like- Gentamicin; is able to reduce nephrotoxicity at a significant level [17].

Anti-hypergycemic effect- Upon treatment with *H. indicus* root extract to diabetic rats, reduced level of glycogen content in muscle tissues was significantly improved. During diabetes, excess glucose present in the blood reacts with hemoglobin to form glycosylated hemoglobin. So level of glycosylated hemoglobin is directly proportional to blood glucose level. Diabetic rats showed higher levels of glycosylated

hemoglobin indicating their poor glycemic control. Treatment with *H. indicus* root extract showed a significant decrease in the glycosylated hemoglobin level, which could be due to improvement in glycemic control [7].

Antidiarrhoeal activity- Methanolic extract of *H. indicus* elicited significant antidiarrhoeal activity than standard drugs. It was found that aqueous extract of *H. indicus* root increase water absorption and Na+-K+ from jejunam. He also suggested that extract can be incorporated as a oral dehydrating salt solution (ORS) for its increasing efficacy [18].

Antivenom- *H. indicus* root extracts effectively neutralized Viper venom induced lethal, haemorrhagic, coagulant, anticoagulant and inflammatory activity. Lupeol acetate isolated from the root extract of Indian sarsaparilla *H. indicus* could significantly neutralize lethality, haemorrhage, defibrinogenation, edema, PLA2 activity induced by *Daboia russellii* venom. It also neutralized *Naja kaouthia* venom induced lethality, cardiotoxicity, neurotoxicity and respiratory changes in experimental animals [19]. Methoxy benzoic acid isolated from *H. indicus* root particularly has antivenom potential.

Antileprotic activity- Aqueous extract of *H. indicus* was orally administered at 2% concentration in mice. The mice were infected with *Mycobacterium leprae* from leprosy patients and it was observed that cutaneous hypersensitivity stimulation was delayed. It also possessed immunomodulatory and immunosuppressant activities. Phogocytosis was also decreased.[20]

Antimicrobial activity- *H. indicus* is traditionally used in Indian folklore medicine for the treatment of various bacterial and fungal infections.

H.indicus showed Maximum zone of inhibition against *Staphylococcus aureus, Pseudomonas aeruginosa* and *Escherichia coli.* Chloroform extract of *H.indicus* showed promising activity against the clinical isolates of *Helicobacter pylori. H. indicus* have a stronger and broader spectrum of antimicrobial activity against pathogenic microorganisms and extracts may be used to discover bioactive natural products that would serve as basic source for development of new antimicrobial compounds to overcome the increasing antibiotic resistance. 95% ethanolic extract and aqueous extract both were shown to be effective against *Corynebacterium diptheriae*, *Diplococcus pneumoniae*, *Streptococcus viridans*, *and Streptococcus pyogenes.* It was found that *H. indicus* demonstrated high activity against ESβL (Extended spectrum β-lactamase) producing multidrug resistant enteric bacteria, when fractionated into acetone, ethyl acetate and methanol. The chloroform and ethanol (95%) extracts of *H. indicus* showed antifungal activity against *Aspergillus niger.*

Clinical trials of "RENALKA" syrup [containing extracts of *Tribulus terrestris, Crataeva magna, H. indicus, Cyperus rotundus, Vetiveria zizanoides, Asparagus racemosus* and *Elletaria cardamomum* and Trikatu] is done for effectiveness in curing and relieving the symptoms of UTI. The drug was found to be safe and effective against *E. coli, B. proteus, Klebsiealla* and *Pseudomonas* [22].

Antiarthritis activity- *Hemidesmus indicus* root has protective activity against arthritis and the activity is might be attributed by presence of terpens, sterols and phenolic compounds in hydroalcoholic root extract, as well as in ethyl acetate fraction [21].

IN VITRO *STUDIES WITH THE PLANT*

Studies on steroids in cultured tissues and also mature plant of *H. indicus* was reported.[3] Regeneration of *H. indicus* by organogenesis and somatic embryogenesis, induced from callus initiation from leaf and stem explants cultured on MS and B5 medium supplemented with 2.4-D, NAA, BA and Kinetin. Somatic embryogenesis depended on explant type, growth regulator and callus age. Callus induced on MS medium containing 2,4-D and Kinetin (1mg/L) developed somatic embryos on half strength MS basal medium. Organogenesis was induced in callus cultured on MS medium containing NAA (2mg/L) and Kinetin (0.5mg/L), and subcultured on Kintein (1.5-2 mg/L) and 10% coconut milk. Isolated shoots were then rooted in half strength MS basal medium [3].

Rooting was achieved in MS basal medium NAA and Kinetin (1 mg/L both). Micropropagation and production of 2-hydroxy-4-methoxy benzaldehyde from this root cuture of *H. indicus*. Nodal explants of in vitro raised shoots subcultured in same medium. These shoot cultures were rooted in quarter salt strength of MS medium containing 9.8μM IBA [3].

Multiple shoot induction from nodal segments and shoot tip of *H. indicus* in MS medium was supplemented with NAA, BA and Gibberelic acid [3].

Micrpropagation of *H. indicus* is achieved through axillary bud culture. Highest shoot multiplication rate with 95% frequency was achieved in five weeks on MS medium supplemented with 1.15μM Kintetin and 0.54μM NAA. Micropropagation was also achieved in MS basal medium supplemented with Benzyl adenine/BA (3mg/L). Addition of low concentration of ammonium nitrate increased shoot thickness and length of internode significantly. Regeneration of *H. indicus* plants from root segments was derived from seedlings. Formation of shoot bud from root segment failed to initiate from auxin and cytokinin

individually, but shoot formation from proximal end of root segments was observed on medium with Cytokinin and α-NAA in 2-3 weeks. Highest number of shoot was produced on medium with 6- BAP at 3mg/L and α-NAA at 0.5mg/L. Rapid elongation of shoot bud was observed on half strength MS medium. Improvement in micropropagation of *H. indicus* is done by adding adenine sulphate. Excised shoot tips and nodal segments from field grown mature plant of *H. indicus* were used to establish *in vitro* clonal propagation. Selected nodal segments were cultured on MS with BA at a concentration of 0.1-4.0 mg/l. Maximum number of usable shoots was found in 1.0 mg/l BA with slight concentration 0.01 mg/l NAA. Higher concentrations of BA or NAA stimulate for considerable callusing at the cutting base which decreased shoot proliferation [3].

Somatic embryogenesis and plant regeneration from leaf cultures is possible on *H. Indicus* [3].

Phytochemical Studies

In vitro biosynthesis of antioxidants, like- lupeol, vanillin and rutin; is reported from *H. indicus* root culture [23]. Production of phytochemicals, lupeol and rutin on shoot culture of *H. indicus* MS basal medium is supplemented with BAP and NAA.

CONCLUSION

The present review highlights on the varying phytochemical contents in the herb, *Hemidesmus indicus* which makes it as a popular choice for folk medicine and also must be considered as the source for alternative medicine.

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