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AN UPDATE ON THE THERAPEUTIC POTENTIAL OF HEMIDESMUS INDICUS (*INDIAN SARSAPARILLA*)

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ABSTRACT: *Hemidesmus indicus* (*H. indicus*), also known as Indian Sarsaparilla or Anantmul, is a plant with diuretic, demulcent, and diphoretic properties. It treats various illnesses, detoxifies the blood, and reduces Vata, Pitta, and Kaphadoshas. It has been shown in pre-clinical trials to reduce illnesses in everyday clinical practice. In order to effectively promote this herbal medicine, clinical trials and patient studies conducted in hospitals are necessary. The intent of this review is to update the numerous medicinal qualities of *H. indicus* and demonstrate its therapeutic potential, enabling it to be used as an alternative to contemporary or modern medicine to treat a variety of disorders. The taxonomy, pharmacological components, and unique medicinal qualities of *H. indicus* are all outlined in this paper. It showed a proven effective and beneficial on the long-standing illness, therefore the need of the multicentre clinical trials is needed on the herbal medicine to be used as a complementary approach in future.

INTRODUCTION: *Hemidesmus indicus* (*H. indicus*) or Indian Sarsaparilla is a member of the Apocynaceae family and is known by a variety of names depending on the language it is spoken in, including anantmul in Hindi, nannari in Tamil, sugandhipala in Telugu, ananta in Sanskrit, and namdaberu and sogadaberu in Kannada [1–4]. The climber plant is cultivated and growing in the Gangetic plains, as well as some regions of Madhya Pradesh and West Bengal. For plants to flourish, the right climate must be present, and the soil must have enough humus and an alkaline pH of 7.5 to 8.5 and stem and rootstock cuttings are all necessary for plants to thrive.

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The requirements include creating planting trenches that are 30 cm x 30 cm x 30 cm in size with a 60 cm x 60 cm field and adding 1-2 kg of farmyard manure along with a mixture of soil and sand in equal parts [4]. The leftover propagules are then moved to the pit while the plants with roots are moved to the field in August and September month. Sweta Sariva is intercropped with orchards since these plants needed support [5]. After being harvested for two and a half years, roots typically reach maturity before being washed and dried.

Hemidesterol, hemidesmol, tannis, and resins are the major components of the roots, and it is a slender, perennial, twining undershrub with woody and aromatic qualities. It has properties such as powerful (Virya), heavy (guru), cooling (sheeta), bitter (atikta), greasy (snigdha), and sweet (madhura) flavour (ras), and also has variety of effects, including the elimination of ama (amahara), purifying of the blood (raktaprasadana), elimination

of odour (durgandhanashana), diuretic activity (mutra-janana and mutravirajaniya), alleviation of searing pain (daahanaasana), and anti-inflammatory effects (sothahara). It reduces the effects of the temperature regulator (Pitta Jwaraprasamana) for vata, pitta, and kapha (Doshakarma). It is recommended for use in the treatment of poisoning as well as for fever, loss of appetite, urticaria, menorrhagia, vomiting, and diarrhoea [4, 6]. Hence, with the presence of such beneficial medicinal properties and its usage in treatment of various ailments, this review was carried out with the aim of highlighting its applications of *H. indicus* in future clinical practices along with the modern medicine.

Morphology and Phytochemical Constituents of Hemidesmus Indicus Taxonomy [1]:

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Gentianales

Family: Apocynaceae

Subfamily: Periplocoideae

Genus: Hemidesmus

Species: indicus

Leaves: The herbs' 5–10 cm long, dark green, smooth, shiny, hard leaves have a variety of sizes and forms and are opposed to one another. They also include 2.5% of tannis, cardiac glycosides, and saponins. It also includes the coumarno lignoid shemidesmin 1 and hemidesmin 2, respectively. Additionally, it includes flavonoids such hyperoside and rutin [6, 7].

Flowers: Flowers are small and arranged in dense clusters; they are outwardly green and interior deep purple. It contains the flavonoid glycosides hyperoside, isoquercitin, and rutin [3].

Fruits: The fruit of *H. indicus* consists of two oblong, flat, and straight follicles that are both straight and narrowly cylindrical, with approximately 6 to 8 cm long black seeds [6].

Stem: Hemidine and indicine are two glycosides found in the stem of *H. indicus*. The hexane-soluble fraction of the ethanolic stem extract yielded lactone, luparone, delta 12 dehydrolupanyl-acetate, 4-hydroxy-3-methoxybenzaldehyde, and delta dehydro-lupeol acetate. Pregnane, glycosides, hemidescine, and emdine are extracted from the stem of *H. indicus* using chloroform and alcohol [6]. *H. indicus* stem is used to treat syphilis, kidney, liver, and brain disorders as well as a diuretic, diaphoretic, laxative, and other conditions. Additionally, it is employed for bronchial asthma, coughing, toothaches, and uterine ailments [7].

Roots: *H. indicus* has cylindrical, twisted, and irregularly bent roots that have a pleasant scent. It has hemidesmin 1, hemidesmin 2-hydroxy 4-methoxy benzoic acid, lupeol, -sitosterol, and -amyrin. *H. indicus* root oil contains tannis, saponin, sterols, 2-hydroxy-4-methoxybenzaldehyde, resin

acid, and other compounds. Astringent, antipyretic, blood purifier, anti-diarrheal, diuretic, and tonic are other uses for roots. In blood disorders, skin disorders, itching, asthma, burning, and rheumatism, roots are helpful. Root powder is used to treat a variety of skin diseases, including eczema, urticaria, and erysipelas, as well as white discharge, or leucorrhoea in females. The indicusin steroid is present throughout the entire *H. indicus* plant. Using spectroscopic methods, triterpenes from the entire plant were found, including two oleanenes, three ursenes, and a lupine [6–8].

Nagrajan *et al.* investigated the chemical structure of the volatiles of *H. indicus*. They claimed that ledol and 2-hydroxy-4-methoxybenzaldehyde are present in HI volatiles. According to GC/MS analysis, residual oil contains active principles with aromatic properties such as nerodilol, linalyl acetate, borneol, dihydrocarvyl acetate, isocaryophyllene, and 1–8 cineole [9].

Medicinal Properties of Hemidesmus Indicus:

Antioxidant and free Radical Scavenging Activity of *Hemidesmus indicus*: *H. indicus* has antioxidant properties that have been studied *in-vitro* using many techniques, particularly with help of FRAP assay. It was noted in previous research that *H. indicus* exhibited hydroxyl radical and nitric oxide radical scavenging activities. The iron in *H. indicus* plays a significant role in oxygen transport, respiration, and various enzyme activities, but it is also highly reactive and can cause oxidative damage to lipids, proteins, and other cellular structures. It is also noteworthy that *H. indicus* has the ability to chelate iron due to the presence of polyphenols, which protects the cell from damage brought on by free radicals. The aqueous extract of root of *H. indicus* has high total phenol content (3.45±0.12) as well as high total flavonoid content (2.19±0.03). The root bark of the *H. indicus* plant's methanolic extract has antioxidant properties that are particularly effective in scavenging superoxide radicals and only moderately effective in scavenging NO radicals. Additionally, it inhibits liver homogenate lipid peroxidation and phenyl hydrazine-induced hemolysis, indicating that it has membrane stabilising properties. Due to its ability to scavenge free radicals, it can be used to cure a variety of ailments [10, 11]. Since, the presence of doxorubicin may produce cardiotoxicity due to lipid peroxidation, damage to mitochondria, production of free radicals, and decreased Na+-K+ ATPase activity, the antioxidant capabilities significantly lowered the oxidative stress and toxicity induced by doxorubicin. It causes levels of antioxidant enzymes like SOD, CAT, GP, and GSH decline. It also inhibits the cleavage of DNA strand [12]. Several investigations have been conducted to examine the free and bound phenolic radicals' antioxidant activity. These radicals are considered "free radical scavengers" due to their ability to donate hydrogen from the phenolic hydroxyl group to form a stable compound and hinder further lipid peroxidation. Additionally, it revealed an apparent correlation between *H. indicus's* antioxidant activity and total phenolic concentration. As a result of *H. indicus's* antioxidant properties, another study found that it reduced oxidative stress in individuals with pulmonary tuberculosis and hypertension [13, 14].

Antinociception: Verma *et al*. reported that the alcoholic extract of *H. indicus* exhibits antinociceptive effect when administered orally in a dose-dependent manner using the tail flick method, acetic acid-induced writhing, and hot plate of analgesic drug evaluation. Inflammatory and neurogenic pain is inhibited by the flavonoids, steroids, and triterpenes that are present in it [7].

Anti-inflammatory Action: In both acute and subacute types of inflammation, *H. indicus* ethyl acetate root extract exhibits anti-inflammatory activity. Rats' paw oedema caused by carrageenan was inhibited by the roots of *H. indicus*, demonstrating the plant's anti-inflammatory properties [6]. *H. indicus's* ability to reduce inflammation may be due to the presence of 2hydeoxy-4-methoxybenzaldehyde in the plant's roots [15].

Hepatotonic and Hepatotoxic Effects: According to researches, *H. indicus* methanolic extract exhibits hepatoprotective effects at doses of 250 mg/kg in cases of Carbon tetra chloride (CCL4)-induced liver damage and 500 mg/kg in cases of paracetamol-induced liver damage, and liver enzyme levels return to normal. Its' effects were contrasted with those of the widely used hepatoprotective drug Silymarin, 100mg/kg body weight [6]. Additionally, *H. indicus* ethanolic extract

(70%) at a dose of 100 mg/kg for 15 days showed hepatoprotective effects against Rifampicin and Isoniazid-induced hepatotoxicity in rats. Another study reported that ethanolic extracts of *H. indicus*, var. indicus and var. pubescens (50%) generate hepatomegaly as revealed by biochemical and histological analyses, which may be related to the extraction process [7]. *H. indicus* contains phenols, coumarins, saponins, and glycosides that shield the liver from harm [6].

Diuretic Action: Considering that the aqueous root extract of *H. indicus* has a diuretic effect and increases urine production in rats, it is suggested to employ it as an adjuvant therapy to minimise the nephrotoxicity brought on by gentamicin [7].

Genitourinary Action: *H. indicus* is helpful in resolving urinary tract infections because it lessens the burning sensation and acts as a cooling agent. To treat urinary tract infections, it can be used with sandalwood or coriander [3].

Anticancer action of *Hemidesmus indicus*: *H. indicus's* methanolic extract has anticancer activity against the MCF7 breast cancer cell line and cytotoxic activity against the HT29 colon cancer cell line. By modifying intracellular signalling, the expression of proteins regulating cancer cell growth, and viability, it helps in inhibition of tumour cells. Cytarabine, 6-thioguanine, and methotrexate's anticancer effects are increased by *H. indicus* [6].

Antimicrobial Activity: *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Helicobacter pylori,* Corynebacterium diphtheriae, *Diplococcus pneumoniae,* Streptococcus viridans, and *Streptococcus pyogenes* are all susceptible to *H. indicus'* antibacterial properties. It was shown to have excellent action against enteric bacteria that produce an extended spectrum -lactamase and are multidrug resistant. Additionally, it works against *Aspergillus niger's* fungus [12].

Antivenom Action: *Hemidesmus indicus* methanolic extracts were reported to be effective at reducing the effects of viper venom on haemorrhage, defibronogenation, PLA2 activity, and edoema in rats and mice. It was discovered that lupeol acetate from *H. indicus* root extract considerably reduced bleeding, edoema, and defibrinogenation brought on by the venom of Daboliarussellii. Because methoxy benzoic acid is present in the roots of *H. indicus,* it has antivenom properties [6].

Antidiarrhoeal Action: Due to its antimicrobial effects and reduction in intestinal motility, the methanolic extract of *H. indicus* exhibits antidiarrheal efficacy at doses of 500 to 1500mg/kg body weight. Additionally, *H. indicus* aqueous root extract improves water and salt absorption from the gut. Consequently, it can be added to ORS [7].

Antileprotic Action: Gupta *et al.* administered a 2% concentration aqueous extract of *Hemidesmus indicus* to mice that had been infected with *Mycobacterium leprae bacilli*. They discovered that *Hemidesmus indicus* caused delayed cutaneous hypersensitivity at a dose of 100 mg/kg. It also has immunosuppressive and immunomodulatory effects at this dose [7].

Skin Conditions: *H. indicus* may be beneficial for treating psoriasis, urticarial, eczema, and acne rosacea due to its ability to reduce inflammation and affinity for raktadhatu. For skin irritation, H. indicus, neem, manjishtha, gotu, sandalwood, and licorice in paste or creamform are used [3].

Anti-arthritic Activity: In a rat model of arthritis, hydroalcoholic extract of *H. indicus* at 450 mg/kg po and its ethyl acetate fraction exhibits strong antiarthritic activity that is comparable to methotrexate [16].

Nootropic Effect: *H. indicus* ethanolic root extract contains n-butanol, which improves learning and memory in rats and may be used to treat Alzheimer's disease [12].

Chemoprotective Effect: *Hemidesmus indicus* has demonstrated an antioxidant defence against oxidative stress caused by cumenehydroperoxide and in the inhibition of cancer growth. By suppressing lipid peroxidation and protecting DNA from radiation-induced damage, *Hemidesmus indicus* root extract has also demonstrated radioprotective effects on lipid peroxidation in rat liver microsomes [17].

Renoprotective Effect: When combined with calamus, anantmul demonstrated nephroprotective

effects by reducing serum creatinine levels in rats with cisplatin-induced nephrotoxicity. Additionally, it lessens the nephrotoxicity brought on by aminoglycosides. By shielding rat kidneys from bromobenzene-induced mitochondrial dysfunction, it has demonstrated to have renoprotective effects. This may be due to its free radical scavenging action [3].

Hypoglycemic Effect: According to a study, *H. indicus* root extract significantly reduced the amount of glycosylated haemoglobin in diabetic rats [5]. To study the hypoglycaemic activity of H. indicus in streptozocin-induced diabetic rats, these rats were divided into six groups, with group I serving as the control group, group II as the streptozocin-treated diabetic rat, group III as the positive control group, receiving tolbutamide (100mg/kg bw/day), group IV including the fasted rat model both diabetic and non-diabetic rats were examination of blood electrolytes, enzymes that break down glucose, hepatic microsomal enzymes, and lipid peroxidation following administration, group V contains rat meal and 500mg/kg/BW/day of an oral aqueous root extract from *H. indicus* group VI includes glucose-loaded animals.

After administering a root extract of *H. indicus* to diabetic rats, blood electrolytes, glucose metabolising enzymes, hepatic microsomal enzymes, and lipid peroxidation were assessed. Aqueous extract of *H. indicus* lowered blood glucose levels in diabetic rats that were fed, fasted, and given glucose after 5 hours, according to the study. After 12 weeks of treatment, it restored glycolytic enzymes, serum electrolytes, and hepatic cytochrome p-450 dependent enzymes by avoiding lipid peroxidation in the liver and kidney, which may be due to its hyperglycaemic and antioxidant activity [18].

Wound Healing and ulcer Healing Property of *Hemidesmus indicus*: It has also been researched on 30 patients with persistent wounds and shows wound healing properties. On the wound, distilled water and *H. indicus* root powder were administered. Follow-ups were done, and detail such the location of the wound, its size, shape, granulation, scar, and symptoms were recorded. Only 10% of patients had noticeable reductions in signs and symptoms, and 86.6% were completely cured, 3% of patients showed slight improvements in wound healing in more than 39 days after treatment with *H. indicus*. Following therapy with *H. indicus*, the scar colour in 86 individuals restored to normal, confirming the herb's capacity to cure wounds. Another study revealed that *H. indicus* is useful for lowering the oxidative stress associated with traumatic mouth ulcers and for promoting ulcer healing [19].

Immunomodulatory Effect: The root extract from *H. indicus* also has immunomodulatory effects on lymphocytes in peripheral blood. The whole extract of *H. indicus* was used in the investigation, along with varied concentrations, together with isolated peripheral blood cells.

For the proliferation of lymphocytes in the presence or absence of various concentrations of *H. indicus*, phytohaemagglutinin or lipopolysaccharide was utilised. Adenosine deaminase and IgG secretion activities of cultured lymphocytes were also assessed in the study. After 72 hours, they discovered that *H. indicus* extract had stimulatory action at a dosage of 1 mg/ml. It also increases the synthesis of IgG from peripheral blood cells [20].

Antiulcer Activity: It becomes apparent that *H. indicus* has an antiulcer effect. On the gastrointestinal mucosa, it exerts gastroprotective effects. It has stronger antiulcer properties than proton pump inhibitors like omeprazole [6].

Antigenotoxic Effect: *Hemidesmus indicus* root extract shown antigenotoxic action in cytogenetic damage brought on by Cisplatin. Additionally, it safeguards bone marrow cells from harm [21].

Antipsychotic Effect: *Hemidesmus indicus* aqueous root extract reduces Apomorphine-induced stereotypical behaviour in rats. It enhances the catalepsy brought on by haloperidol [21].

Larvicidal Activity: The aqueous root extract of H. indicus possesses larvicidal activity against the lymphatic filariasis vector, *Culex quinquefasciatus*. [21]

Anticonvulsant Action: *H. indicus* ethanolic root extract has demonstrated anticonvulsant activity by maximum electroshock technique at various doses, including 100, 300, and 500 mg/kg body weight [21].

Antithrombotic Action: Platelet aggregation is hindered by methanolic root extract. It has been discovered that when administered intravenously, it slows the period until plasma re-calcifies and stimulates the activity of the enzyme lipoprotein lipase, leading to fat breakdown [21, 22].

Antipyretic Activity: Compared to paracetamol 100 mg/kg body weight, hydroalcoholic extract at doses of 100, 300, and 400 mg/kg body weight reduces yeast-induced rectal temperature [21].

Anti-acne Activity: Due to the existence of Terpenoidal, *H. indicus* root extract possesses anti-acne effect against Staphylococcus epidermis and Propionibacterium acne [21, 23].

Anti-angiogenic Activity: *H. indicus* has demonstrated anti-angiogenic activity on human umbilical vein endothelial cells in hypoxemia and normoxiain *in-vitro* study, and thus it suppresses VEGF in normoxia. In hypoxia, HIF 1 is inhibited, and VEGF and VEGFR-2 are down regulated, which have an anti-angiogenic effect [21].

Anti-hyperlipidaemic Effect: *H. indicus* has an anti-hyperlipidemic action due to presence of 2-hydroxy-4-methoxy benzoic acid and thus lowers cholesterol levels (VLDL, LDL, & HDL) and raising levels (HDL) when given at a dose of 16 mg/kg from a cell culture extract [21].

Antianxiety Action: A clinical study by Jogdand *et al.* on *H. indicus* root extract revealed antianxiety activity, and concluded that it significantly reduces anxiety compared to clonazepam because of its antioxidant properties [22].

Miscellaneous use: Additionally, it made notable contributions as a blood purifier in snakebite and scorpion sting patients and showed a cooling effect on stomach ulcers. In addition, it is used to treat high fever, skin conditions, and venereal disorders. *H. indicus* roots are utilised in the creation of a sweet beverage [7].

CONCLUSION: The current review focuses on *H. indicus'* phytochemical components, which are responsible for its numerous therapeutic qualities. It has a variety of qualities, including immunomodulatory, anti-cancer, wound-healing, hepatic and reno protecting, and antioxidant effects. Preclinical research comprises up nearly all of studies. Therefore, multiple clinical trials must be conducted to demonstrate its therapeutic potential in various illness conditions so that it can be utilised in various diseases as an alternative to contemporary medication if there are contraindications to its usage.

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