

HEMIDESMUS INDICUS: A REVIEW

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Summary

Natural products have served as a major source of drugs for centuries and about half of the pharmaceuticals in use today are derived from natural products. *Hemidesmus indicus*, also popularly known as 'Anantmul' is a semi erect shrub belonging to family Asclepiadaceae is widely distributed throughout India. It is traditionally used in dysentery, diarrhoea, skin diseases, syphilis, dyspepsia, leucoderma, diuretic, blood purifier, burning of body, chronic fever and asthma. Pharmacological studies carried out with its extract and purified compounds indicate that this plant possess antioxidant, hepatoprotective, anti-ulcer, antimicrobial, anticancer, hypoglycemic, antithrombotic, antihyperlipidemic, otoprotective, analgesic, anti-inflammatory and immunomodulatory activities. It has been reported to possess various phytoconstituents such as hydrocarbons, glycosides, oligoglycosides, terpenoids and steroids. In the present review attempts have been made to bring in light the potential benefits and uses of this plant.

Key words: *Hemidesmus indicus*, Asclepiadaceae, Anantmul, Saarivaa, Phytochemical Constituents, Pharmacological Actions.

Running Title: Effects of *Hemidesmus indicus*

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Introduction

Hemidesmus indicus is a semi-erect shrub found throughout India from upper Gangetic plain eastwards to Assam and throughout central, western and southern India [1]. The name “*Hemidesmus*” is derived from Latin word “*Hemidesmos*” which means ‘half bond’. It is so named in allusion to sub connate filaments at their base – joint pods and connected stamens. Word “*indicus*” stands for ‘of India’. *Hemidesmus indicus* belongs to family Asclepiadaceae which is derived from word “*Asklepos*” – means ‘God of Medicine’ [2]. Vernacular name “*Anantmul*” is a Sanskrit word which means ‘endless root’ [3]. Plant has two varieties namely black variety, also called as ‘*Krishna Saarivaa*’ and white variety which is called as ‘*Saarivaa*’ [2]. *Hemidesmus indicus* is accepted by Ayurvedic formulary as white variety whereas, *Cryptolepis buchananii* Roem. and Schytt as black variety. *Ichnocarpus frutescens* is also used as black variety by the people of West Bengal and Kerala [4].

It is a slender, laticiferous twining shrub distributed to greater part of India. Leaves are opposite, shortly petioled, elliptically oblong to linear lanceolate. Flowers are greenish outside but purplish inside. Seeds are black, flattened with a silvery white coma [5]. Pictures of entire plant as well as roots are as shown in Figure 1 and Figure 2 [6, 7].



Figure 1. *Hemidesmus indicus* plant



Figure 2. Roots of *Hemidesmus indicus*

Pharmacognostical Studies

Macroscopy - Dark brown roots are 30cm long and 3-8mm in diameter, cylindrical, thick, hard, sparsely branched and are provided with few thick rootlets along with secondary roots. Bark is brownish and shows transverse cracks and longitudinal fissures.

Microscopy – Transverse section of roots shows periderm consisting of three layers of tissues, cork, cork cambium and secondary cortex. Cork cells are radially flattened, rectangular and filled with dark brown contents. Cork cambium is 2 or 3 layered, compressed and is filled with deep brown contents. Secondary cortex consists of 3-4 layers of cells and contains little or no dark brown contents. Secondary phloem consist of sieve elements, parenchyma, phloem ray cells along with several scattered laticiferous ducts.

Parenchyma cells are filled with starch grain and occasionally show presence of prismatic crystal of calcium oxalate. Cambium is very narrow. Xylem is transverse by narrow medullary rays. Vessels and trachieds show pitted marking. Pith is absent and central region is occupied by woody tissues [1].

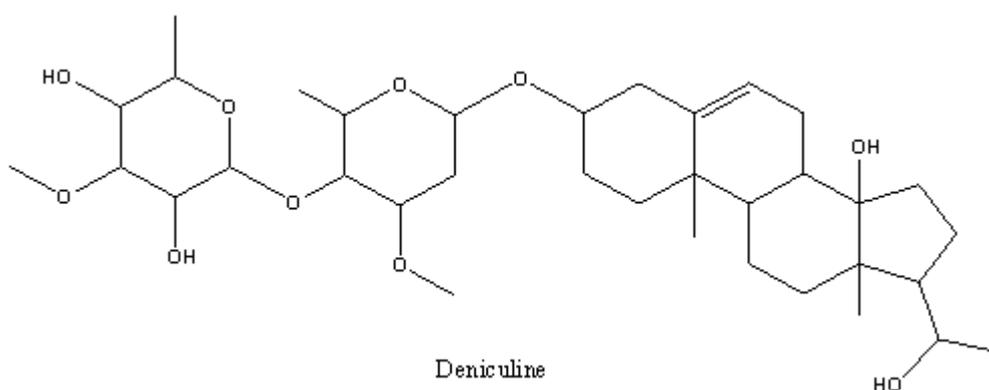
Phytochemistry

Phytoconstituents of *Hemidesmus indicus* ranges from hydrocarbons, glycosides, oligoglycosides, and terpenoids to steroids [8, 9]. The phytoconstituents isolated so far from different parts of *Hemidesmus indicus* is presented in Table 1.

Table1. Phytoconstituents reported from different parts of *Hemidesmus indicus*. [8, 9]

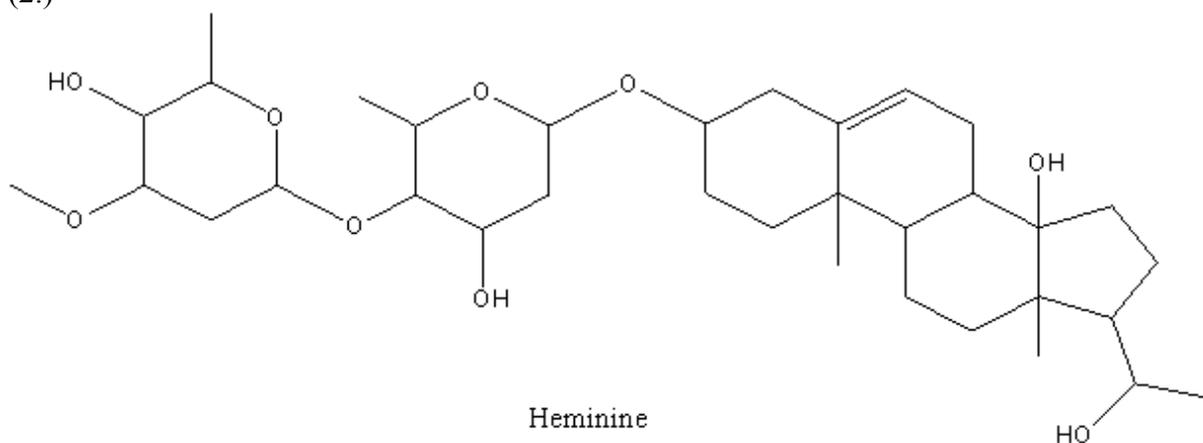
Sr. No.	Parts	Constituents
1.	Roots	Pregnane glycoside viz. Hemindicin. Coumarinolignoids viz. Hemidesmin-1 and Hemidesmin-2. Others - β -amyrin acetate, α -amyrin, β -amyrin, lupeol acetate, β -sitosterol, hexadecanoic acid, hexatriacontane, lupeol octasonate. Oil contains 80% crystalline matter, glucose, hemidesmol, hemidesterol, 2-hydroxy-4-methoxy benzaldehyde, resin acid, glucoside, α -amyrin triterpene, β -amyrin triterpene, and benzaldehyde.
2.	Stem	Glycosides such as Indicine and Hemidine. Pregnane glycoside such as Hemidescine and Emidine. Pregnane oligoglycosides viz. demicunine and heminine. Desinine, Indicisin, Medidesmine, Hemisine and Demicine. Steroidal compounds viz. Calogenin-3-o- β -D-digitoxopyranosteroid, desminine steroid, hemisine steroid. Triterpenoids viz. 3-keto-lup-12-ene-21->28 olide triterpene, lup-12-ene-3- β -ol acetate triterpene.
3.	Leaves	Coumarinolignoids viz. hemidesminine, hemidesmin-1, hemidesmin-2. Flavonoids viz. hyperoside and rutin. 2.50% tannins.
4.	Flowers	Flavanoid glycosides viz. Hyperoside, Isoquercetin and Rutin

Also the structures of pharmacologically active constituents are mentioned below [10].

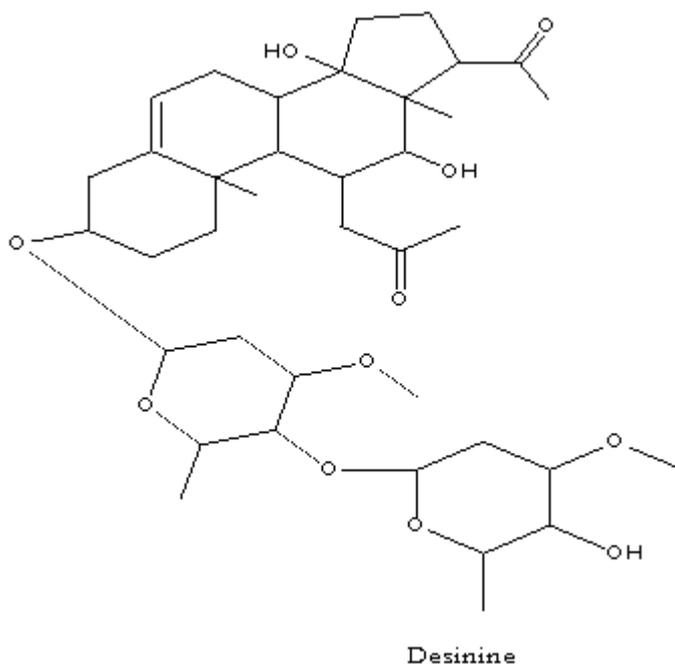


(1.)

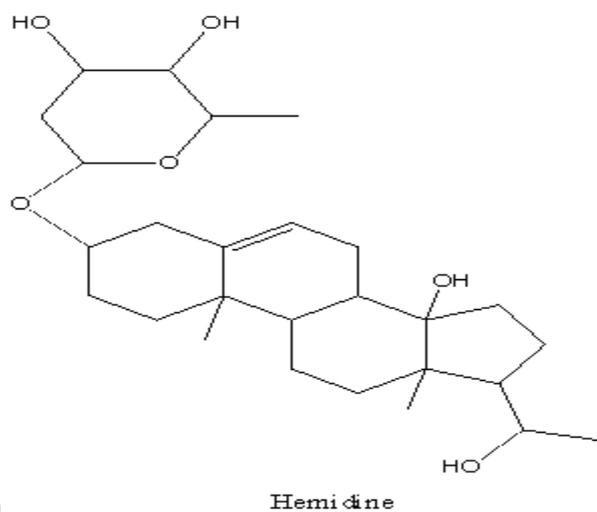
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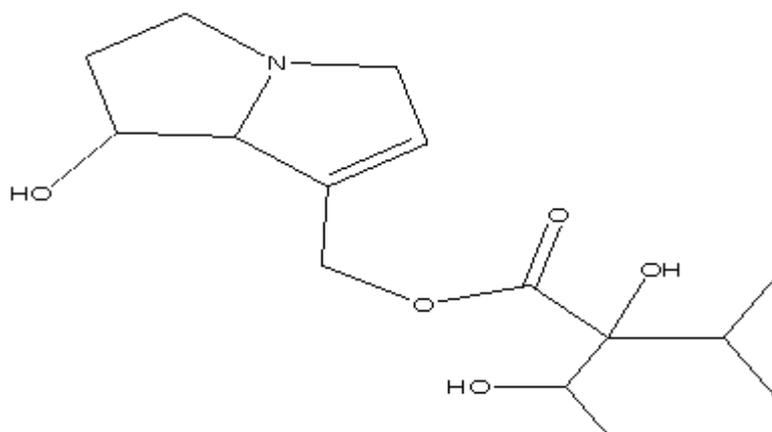
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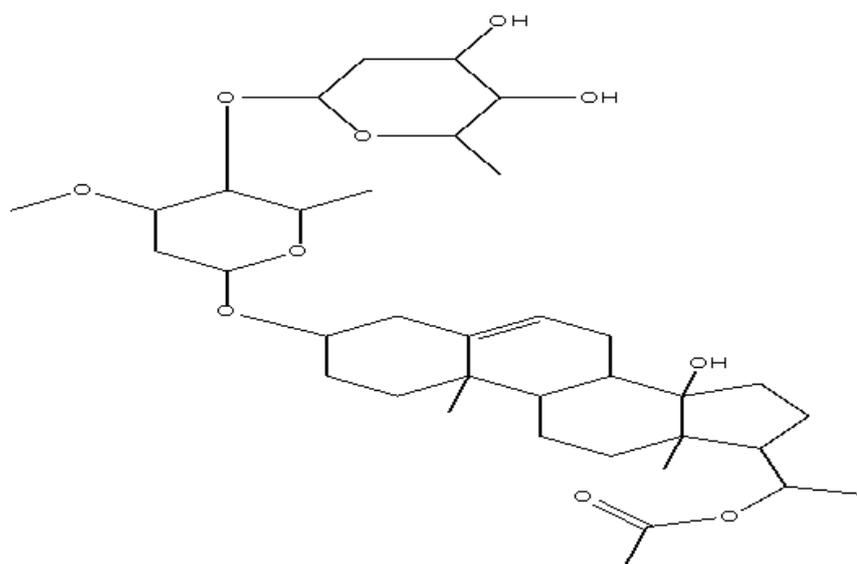


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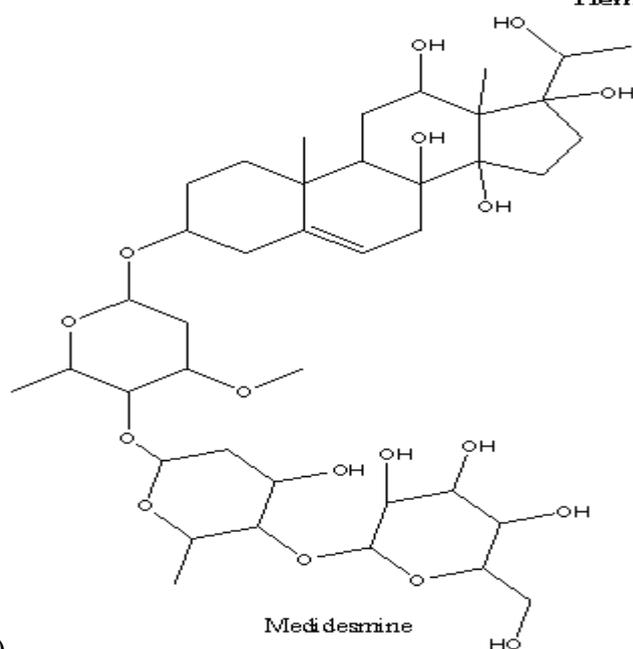


Indicine

(6.)



Hemidesmine



Medidesmine

(7.)

Traditional uses

Decoction of leaves of Saarivaa i.e. white variety of *H. indicus* was prescribed by Charaka in sallow complexion, loss of voice, cough, menstrual disorders and dysentery whereas entire plant is prescribed for treating asthma, cough, abdominal swelling and aching limbs. Krishna Saarivaa i.e. black variety has been indicated by Sushruta in respiratory infection and wasting diseases [4]. Traditionally medicated ghee containing *Hemidesmus indicus* along with few other plants is used in chronic fever, asthma, cough, hiccup, headache, burning of body and vitiation of digestive fire [3]. Syrup prepared from root of *Hemidesmus indicus* was made official in British Pharmacopoeia (BP) of 1864 and is also included in Indian Pharmacopoeia. In Ayurvedic system this syrup is prescribed in dyspepsia, loss of appetite, fever, skin diseases and ulceration due to syphilis, chronic rheumatism, and leucorrhoea. It also has demulcent and diuretic properties. Infusion of root powder is used as blood purifier and possesses sudorific properties. This infusion along with milk and sugar is used in children as tonic in cases of chronic cough and diarrhoea. Parts of Anantmul, roots of Bala (*Pavonia odorata*), tubers of mustaka (*Cyperus rotundus*), ginger and kutki root (*Picrorhiza kurroa*) are prescribed by Ayurvedic experts to clear bowels and relieve fever [11]. According to Unani system of medicine, roots and stems of *H. indicus* act as laxative, diaphoretic, diuretic and are useful in treatment of syphilis and leucoderma. In central India, a special "Herbal Mala" is made from the root pieces of Anantmul and Semal (*Bombax ceiba*) which is used in the treatment of Marasmus. The roots are used by the tribal India to cure gonorrhoea, leucoderma, bleeding piles, jaundice and dysentery. Powdered root is used in pre and post-natal care. The tribals of Rajasthan use the paste of roots in scorpion sting. Syrup prepared from roots is used for flavoring medicinal mixtures and it is often called 'Sugandha' because of the wonderful fragrance [12].

Pharmacological Activity

Antioxidant activity

In the study conducted by Ravishankara and coworkers methanolic extract of *Hemidesmus indicus* roots showed a concentration/dose dependent inhibition of 1, 1-diphenyl-2-picrylhydrazyl (DPPH) radical, superoxide radicals and moderate nitric oxide scavenging activity due to the presence of polar components. Lipid peroxidation induced by Ferric-ADP and ascorbate in rat liver homogenate was also inhibited. Haemolysis of erythrocytes by phenylhydrazine was also effectively inhibited [13]. Similar effects were reported by Mohana and coworkers by using 50% aqueous ethanolic extract of *Hemidesmus indicus* along with hepatoprotective effect [14]. Topical application of cumene hydroperoxide in rats caused depletion of cutaneous glutathione and activities of antioxidant enzyme viz. glutathione reductase (GR), glutathione peroxidase (GPx), glucose 6-phosphate dehydrogenase, and catalase leading to enhanced cutaneous microsomal lipid peroxidation. Topical application of ethanolic extract of *Hemidesmus indicus* in acetone prior to application of cumene hydroperoxide showed significant inhibition of cutaneous oxidative stress and increased level of above antioxidant enzymes by an unknown mechanism [15]. Nadana and coworkers postulated that in rats with ethanol induced nephrotoxicity, ethanolic extract of *Hemidesmus indicus* showed potent antioxidant effect and provided protection against free radical-mediated oxidative stress in kidney. Administration of 500mg extract/kg of body weight/day for last 30 days of experiment significantly reduced the level of serum-urea, uric acid, creatinine and kidney-thiobarbituric acid reacting substances (TBARS), lipid peroxides and conjugated dienes. *H. indicus* extract also increased level of kidney superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and reduced glutathione (GSH) [16].

Kumar and coworker reported that the terpenoidal fraction obtained from successive extraction of *Hemidesmus indicus* roots possess potent free radical scavenging activity [17]. In another study Mahalingam and coworkers showed that in streptozotocin induced diabetic rats, administration of aqueous extract of *Hemidesmus indicus* roots (500mg/kg/day) for a period of 12 weeks decreased lipid peroxidation index which is attributed to its antioxidant action [18].

Hepatoprotective activity

Mookan and coworkers reported that the ethanolic extract of *Hemidesmus indicus* roots has protective effect against Rifampicin and Isoniazid (INH) induced liver toxicity. Extract (100mg/kg body weight/day, for 15 days) prevented alteration in activities of isocitrate dehydrogenase, α -ketoglutarate dehydrogenase, succinate dehydrogenase, malate dehydrogenase, cytochrome C oxidase and NADH dehydrogenase. The authors postulated that these effects were probably due to presence of coumarino lignoids viz. hemidesmin-I and hemidesmin-II which has free radical scavenging activity [19]. Mohana and coworkers have demonstrated that 50% aqueous ethanolic extract of *Hemidesmus indicus* (400mg/kg, per orally) showed similar effects against carbon tetrachloride (CCl₄) induced liver damage. These effects were attributed to its free radical scavenging and antilipid peroxidative activities [14]. Similar effects were reported by Baheti and coworkers with methanolic extract of roots of *H. indicus* against carbon tetrachloride (CCl₄) and paracetamol induced liver damage. *H. indicus* extract decreased elevated level of serum glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT), alkaline phosphatase (ALP), total and direct bilirubin in rats with hepatic damage [20]. Nadana and coworkers reported that the ethanolic extract of *Hemidesmus indicus* also showed protective effect against ethanol induced liver injury. *H. indicus* extract significantly decreased level of liver collagen and hydroxyproline content, lipid peroxidation and increases solubility of liver collagen and ascorbic acid level. The extract also decreased activities of matrix metalloproteinase-2 and matrix metalloproteinase-9 which are implicated in extracellular matrix degradation during ethanol intoxication [21].

Antimicrobial activity

Hiremath and coworkers showed that chloroform and 95% ethanolic extracts of roots of *H. indicus* possess antifungal activity against *Aspergillus niger* [22]. Das and coworkers reported potent *invitro* antimicrobial activity of methanolic extract of *H.indicus* roots against *Salmonella typhimurium*, *Escherichia-coli* and *Shigella Flexneri*. The extract decreased colony forming unit (CFU)/ml in extract treated broth culture. Further the extract also inhibited castor oil induced diarrhoea in rats which was evidenced by decrease in amount of wet faeces when rats were pretreated with extract at a dose of 500-1500mg/kg. The effect might be due to inhibition of intestinal motility and by its bactericidal activity [23]. Das and coworkers further studied the antienterobacterial activity of both methanolic and chloroform extracts of *H.indicus*. Both the extracts inhibited growth in dose dependent manner and were found to be most effective against *S. flexneri*, moderately effective against other strains and least effective against *S. dysenteries*. This antienterobacterial activity was attributed to the presence of antimicrobial trace elements such as copper and zinc [24]. Das and coworkers demonstrated that glycosides obtained from *Hemidesmus indicus* inhibited adherence of *S.typhimurium* to host cell and hence reduced its pathological effect. Glycoside showed this action by mimicking host cell receptor saccharide and blocks bacterial ligands from binding to the host cell. Further, glycosides also reduced bacterial surface hydrophobicity [25]. Khanna and coworkers demonstrated that the aqueous extract of *H. indicus* showed larvicidal effect against *Culex quinquefasciatus* mosquito larvae which was responsible for

transmission of lymphatic filariasis caused by *Wuchereria bancrofti*. Aqueous extracts showed 100% mortality at concentration of 5% on 2nd day [26].

Antiacne activity

Most common skin disorder of pilosebaceous unit is Acne vulgaris, which is caused by bacteria *Propionibacterium acnes*, *Staphylococcus epidermis* and *Malassezia furfur*. Most of antiacne drugs target *Propionibacterium acnes*, *Staphylococcus epidermis* as they are the main culprit. In a study conducted by Kumar and coworkers, the roots of *Hemidesmus indicus* showed strong inhibitory effect on *P.acne* and *S.epidermis*. Minimum inhibitory concentration for *P.acne* and *S.epidermis* was found to be 0.051mg/ml and 1.25mg/ml. But high concentrations were required to act as bactericidal agent [27]. In another study conducted by Kumar and coworkers, terpenoidal fraction obtained during successive extraction of *Hemidesmus indicus* was evaluated for antiacne activity. This terpenoidal fraction showed potent antiacne activity and minimum inhibitory concentrations determined by broth dilution assay was found to be 38ug/ml for both *P. acne* and *S. epidermis* and minimum bactericidal concentrations were 38ug/ml and 46ug/ml respectively [17].

Anticarcinogenic activity

Studies conducted by Sultana and coworkers showed that treatment of mouse skin with extract prior to application of cumene hydroxide prevented induction of ornithine decarboxylase activity and DNA synthesis which is considered to be a biochemical marker to evaluate tumor promoting potential of an agent. Thus extract inhibited tumor growth in mouse skin and hence can be considered as a potent chemopreventive agent [15]. Iddamaldeniya and coworkers evaluated the decoction of *Hemidesmus indicus*, *Nigella sativa* and *Smilax glabra* for its effect on diethylnitrosamine (DEN)-induced hepatocarcinogenesis. Carcinogenic potential was scored by comparing number, area and staining intensity of glutathione S-transferase placental form (GST-P) positive foci and number of cell/cm² of the positive foci in livers of rats. The decoction significantly inhibited DEN-mediated GST-P expression in rat liver and hence inhibited early DEN initiated phase of hepatocarcinogenesis. Mechanism of action of decoction was not clear but the authors hypothesized it to be either by detoxification of carcinogen, antioxidant activity, immunomodulatory action or cytotoxicity [28]. In another study using same decoction Iddamaldeniya and coworkers found that long term treatment of rats with decoction not only inhibited DEN induced GST-P expression but also the carcinogen mediated development of overt tumor and histopathological changes leading to tumor development. Also a marked reduction of angiogenesis was observed in rats treated with DEN and decoction, but mechanism by which decoction inhibit angiogenesis was not clear [29]. Chloroform fraction containing phytosterol and fatty acid obtain from crude methanolic extract of roots of *H. indicus* was investigated by Das and coworkers for protective effect against cytotoxicity induced by *Salmonella typhimurium* in human intestinal cell lines (Int 407). Int 407 cells infected with *S. typhimurium* treated with 100ug/ml of chloroform fraction had 10 times less cytotoxicity compared to those cells which were infected by wild type bacteria. Adherence and invasive ability of *S. typhimurium* when treated with chloroform fraction to Int 407 cells was decreased by 40 times and 10-15 times respectively. Further, Int 407 cells infected with chloroform fraction treated *S.typhimurium* showed almost normal morphology with normal mitochondrial cristae. But few cells had one or two invaded bacteria and cells with altered morphology were rarely observed [30]. Shetty and coworkers have shown that *Hemidesmus indicus* (HI) root extract protect microsomal membranes by reducing lipid peroxidation and also protect DNA from radiation induced strand breaks [31].

Antithrombotic activity

Mary and coworkers have demonstrated that the methanolic extract of roots of *H. indicus* inhibit platelet aggregation. Intravenous administration of root extract of *H. indicus* delayed the plasma recalcification time. Further, authors also reported that the extract of *H. indicus* increased release and activation of enzymes which results in metabolic degradation of lipids [32]. In another study Mary and coworkers investigated the antiatherogenic effect of a polyherbal formulation called Caps HT2 having *Hemidesmus indicus* as one of the ingredient. The putative mechanism of action for the said effect is proposed to be by inhibiting platelet aggregation, delaying plasma recalcification time in rabbits and enhancing lipoprotein lipase activity [33].

Antihyperlipidaemic activity

Bopanna and coworkers reported that in normal rats, cell culture extract of *Hemidesmus indicus* (CCH) administered at a dose of 16mg/kg decreased low density lipoproteins (LDL) and very low density lipoproteins (VLDL), Cholesterol and significantly increased high density lipoproteins (HDL): cholesterol ratio. In hypercholesterolemic rats, CCH administered at a dose of 2, 4 and 16 mg/kg showed significant reduction in total cholesterol, triglycerides, LDL cholesterol and phospholipids. The possible mechanism of action for the above effect can be an increase in liver LDL receptor activity with a concomitant decrease in hepatic triglyceride (TG) synthesis. Also faecal excretion of cholesterol and phospholipids were increased in hypercholesterolemic rats after administration of CCH (4 and 16 mg/kg) [34]. As mentioned above the polyherbal formulation Caps HT2 was also found to possess hypolipidemic activity as it raised HDL cholesterol level in hyperlipidemic rats [33]. In another invivo study Anoop and coworkers proposed that 2-hydroxy-4-methoxy benzoic acid (HMBA) present in *Hemidesmus indicus* may be responsible for its antihyperlipidemic action. Administration of HMBA 200ug/kg/day for 30days after oral administration of ethanol for 30days to rats decreased plasma total cholesterol, TG, lipoproteins, phospholipids, free fatty acids and increased plasma lipoprotein lipase concentration [35]. Few other reported biological investigations are presented in Table 2.

Table 2. Other Biological Investigations of *Hemidesmus indicus*

Activity	Observation	Mechanism	Reference
Anti ulcer	Aqueous ethanolic extracts decreased formation of gastric and duodenal ulcers by various ulcerogenic procedure and cytodestructing agent.	Probably by increasing hexosamine and carbohydrate/protein ratio and decrease in pepsin content which result in increase in mucous secretion. It also selectively increases prostaglandin and shows mucoprotective activity.	36
Otoprotective	Eighty percent ethanolic extract (25 and 50µg/ml) significantly counteract toxic effect of Gentamicin on hair cells i.e. decreased apoptosis of hair cells.	Due to specific inhibition of Gentamicin induced apoptosis as well as antioxidant action of extract.	37
Hypoglycemic	Aqueous extract (500mg/kg) decreased	May be due to stimulation of β-cells to produce more	18

	blood glucose level within 5hr. in Streptozotocin induced diabetic rats. Also restored decreased level of metabolic enzymes of glucose as well as hepatic metabolizing enzymes to normal level.	insulin as well as increase in peripheral glucose utilization.	
Antinociceptive	Ethanollic extract dose dependently counteract both neurogenic and inflammatory pain.	Not clear	38
Anti-inflammatory and anti pyretic	Methanolic extract showed dose dependent reduction in volume of paw odema and in body temperature up to 4hr.	Not clear	39
Renoprotective	Protects against aminoglycosides induced nephrotoxicity.	Not clear	40
Immuno-modulatory	Enhances both cellular and humoral immunity	Increases production of immunoglobulin-G and increases activity of adenine deaminase which in turn increases lymphocyte proliferation.	41
Venom neutralization	Lupeol acetate isolated from methanolic extract reversed lethal effect induced by venom of <i>Daboia russelli</i> and <i>Naja kaouthia</i> .	Not clear but might be related to antioxidant action of lupeol acetate.	42
Miscellaneous action	Aqueous suspension enhanced absorption of water, sodium ion and potassium ion. But ethanolic extract decreased the same.	Not clear	43

Toxicity Studies

The toxicity profile of *H. indicus* has been studied by Arseculeratne and coworkers. The plant was toxic to liver but no toxicity was observed in kidney and lungs. Dried stem administered at a dose of 25% showed hepatotoxic activity with diffuse hydropic degeneration and focal hepatocellular necrosis. Anoop and coworkers also reported occurrence of hepatomegaly and sclerosed glomeruli when aqueous alcoholic extract of *H. indicus* was administered. [9].

Marketed Formulations

Various polyherbal formulations containing *Hemidesmus indicus* as one of their major constituents are used in treatment of various ailments. Table 3 represents various formulations along with their reported use.

Table 3. Marketed Formulations

Sr. No.	Formulation	Marketed by	Indications	Reference
1.	Praas	Komal Herbals, Inc., United States	Used as tonic, as restorative agents, prevent health stresses; helps enhance memory power, prolongation of antioxidant capabilities.	44
2.	Skinelle Tablets	Charak Pharma, India.	Used for treatment of <i>Acne vulgaris</i> and premenstrual acne.	45
3.	ELGER	Healing Power, Inc., New York.	To provide resistance against all airborne allergies.	46
4.	Renalka Syrup	Himalaya Herbal Healthcare, India.	Used in variety of urinary disorders viz. burning micturition, recurrent urinary tract infection and dysuria.	47
5.	Psorcure Oil and ointment	Clinic Psoriasis, Canada.	Treatment of Psoriasis.	48, 49
6.	Uriflow	Merazon Health Products, Inc., USA.	Used in kidney stone	50
7.	Pressure Control	Vadik Herbs, California.	In regulating the blood pressure.	51
8.	Stresnil	Naturalypure health products, California.	Relieves stress, anxiety, tension, fatigue, poor memory and disturbed sleep.	52

Conclusions

H.indicus is commonly found throughout India and is widely recognized in traditional system of medicine. Various pharmacological studies carried out have shown the potential of plant as an anti-inflammatory, antimicrobial, antiulcerogenic, otoprotective, anti-oxidant, anti-atherogenic and anti-carcinogenic agent. Roots of the plant are used in various herbal formulations that are available in market for treating various ailments.

However, not much information regarding the effect of this plant as an anti-fertility or anti-leprotic agent is available. Therefore, further studies may be carried out to explore the hidden potential of this plant. Further, the plant has become an endangered species now and hence one needs to focus on the agricultural and climatic needs of this plant, which favours its growth and survival.

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