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A systematic analysis of the ethnopharmacological relevance of an Indian traditional plant, *Hemidesmus indicus* (L.) R.Br. for the past 10 years

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ABSTRACT

Hemidesmus indicus (L.) R.Br., an Indian traditional plant belonging to the family Apocynaceae is a climber growing in the Indian subcontinent. The plant popularly known as "Anantmool," is a vital ingredient in medicinal formulations (Ayurveda, Siddha, and Unani). In the present study, we performed a systematic review analysis on the research progress of *H. indicus* (L.) R.Br. conducted during the past 10 years. The data was retrieved from several online databases and search engines- PubMed, Google Scholar, Scopus, and Science Direct. Since the 20th century, it has been used as a traditional folk remedy for various ailments such as snake bites, leprosy, arthritis, bacterial infections, syphilis, fever, headache, dysentery, and diarrhea. The major pharmacological properties of *H. indicus* include antioxidant, anti-diabetic, anti-cancer, anti-ulcerogenic, anti-inflammatory, anti-microbial, hepatoprotection, neuroprotection, cardioprotection, and nephroprotection. The phytochemical screening of *H. indicus* identified the presence of flavonoids, terpenoids, tannins, steroids, and lignans. Several formulations of *H. indicus* are commercially available to the public as herbal powder and topical creams/oils. Evidence support that *H. indicus* can be potentially explored for further drug discovery process in terms of bioactive against various disease conditions thus helping in the clinical setting to discover promising drugs.

INTRODUCTION

Hemidesmus indicus (L.) R. Br. (*H. indicus*), is an ayurvedic medicinal plant popularly known as Indian Sarsaparilla, a major component of many traditional formulations and health drinks [1]. *Hemidesmus indicus* is a slender, laticiferous, twining shrub that belongs to the Apocynaceae family. The plant is widely distributed in the Indian subcontinent and is locally known as "Anantmoola" or "Anantamuli" [2]. It is an official drug in both Indian and British Pharmacopoeia [3]. The plant is traditionally used for various ailments such as diabetes, leprosy, skin diseases, urinary diseases, sexually transmitted diseases, syphilis, snakebites, scorpion stings, dyspnea, inflammation, rheumatism, menorrhagia, pyrosis, abdominal colic, dysentery, diarrhea, anorexia, respiratory disorders, fever, cough, bronchitis, cancer [4,5].

Hemidesmus indicus has different vernacular names like Sariva, Sarsapilla, Nannari, Naruneendi, Narunari, Anantoola, Karala, Krishodari, Hindisalsa, Upalsan, Suguddimalo, Sugandhipala, Ushba, Anantvel, and Onotomulo in various parts of India. It is a key ingredient in folk medicine and several Ayurveda and Unani formulations [6]. Historically, it is reported that the numerous biological activities of *H. indicus* are associated with the roots. The roots of *H. indicus* are rich in phytochemical components, including tannins, alkaloids, flavonoids, lignin, steroids, terpenoids, inulin, phenolic compounds, and cardiac glycosides [7]. Besides the roots, recent studies report that the stem, leaves, and flowers

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also serve as potential sources of valuable phytoconstituents [8]. According to recent phytochemistry studies, *H. indicus* includes volatile oils, hemidesmol, hemidesmine, hemidesterol, stearoptin, flavonoids, pregnane glycosides, coumarin, saponins, and triterpenes [3]. A few review articles provide a comprehensive review of *H. indicus*. However, we emphasize the traditional medicinal plant research updates conducted over the past 10 years to know the plausibility of clinical translation.

METHODOLOGY

The data was collected from online databases like *Google Scholar, PubMed, Science Direct,* and *Scopus*. The literature review analysis was performed with the literature of the recent 10 years. The keywords used for data collection include "*Hemidesmus indicus*," and "*H. Indicus*," "*H. Indicus* phytochemistry," "geographical areas," "biological activities," "pharmacological activities," "Nannari extracts," "Sariva root," "Naruneendi," "traditional uses," "home remedies," "Anantmula effects," "*in vitro* studies," "*in vivo* studies," etc. A total of 561 articles were initially identified from which 250 articles were screened after duplicate removal. Among these, 90 full-text articles were assessed to be eligible for the study. 60 full-text articles are included in the review after checking the exclusion criteria. The methodology adopted for the literature review is represented in Figure 1.

Botany

The plant possesses several narrow, slender, and terete stems. The top, larger leaves are dark green without any lines, while the lower leaves are thinner and frequently have white lines on the upper surface [2]. Leaves are opposite to each other with smooth, shiny, and firm petiolate. According to their age, the leaves vary in their size and shape. The flowers are small greenish on the outer area and deep purple in the inner parts crowded as tiny dense clusters at the axillary cymes [7]. Fruits or follicles are cylindrical, paired, slender, and pointed. The seeds are white, coated with tiny silver hairs. The roots of *H. indicus* are thick and hard with very few branches of rootlets. The roots are aromatic, bitter, astringent, and anthelmintic. The roots are dark brown externally whereas yellowish at the center enclosed by a white cortical layer. The plant has a brownish bark with longitudinal fissures and transverse cracks at the cork [7,9].

Distribution

Hemidesmus indicus is native to India, primarily in South Asian countries such as India, Pakistan, Sri Lanka, Bangladesh, Maldives, Iran, and Moluccas [10]. The plant has been found mostly throughout India from the Indo-Gangetic plains, eastern parts up to Assam, and across Southern India in mesophytic and semidry environments. It grows in moistened deciduous woods, shrubs, and deteriorated areas with untamed soils. Usually, they are cultivated at an altitude of 600 m [11].

Phytochemistry

Different secondary metabolites such as flavonoids, saponins, triterpenoids, and glycosides, were reported from the different parts of *H. indicus*. The phytochemical investigations report the presence of 2-hydroxy-4-methoxybenzaldehyde, 4-hydroxy-3-methoxybenzaldehyde, hexa-tricostate acid, lupeol acetate, β-amyrin acetate, lupeol-1-octacosanol, flavonoids, steroids, saponins, terpenoids, lignins, phenolic compounds, tannins, cardiac glycosides, insulins, carbohydrates, and proteins, from the roots [12]. Hemidesmol, lupeol, linalyl acetate, dihydrocarvyl acetate, camphor, borneol, sitosterol, hexadecanoic

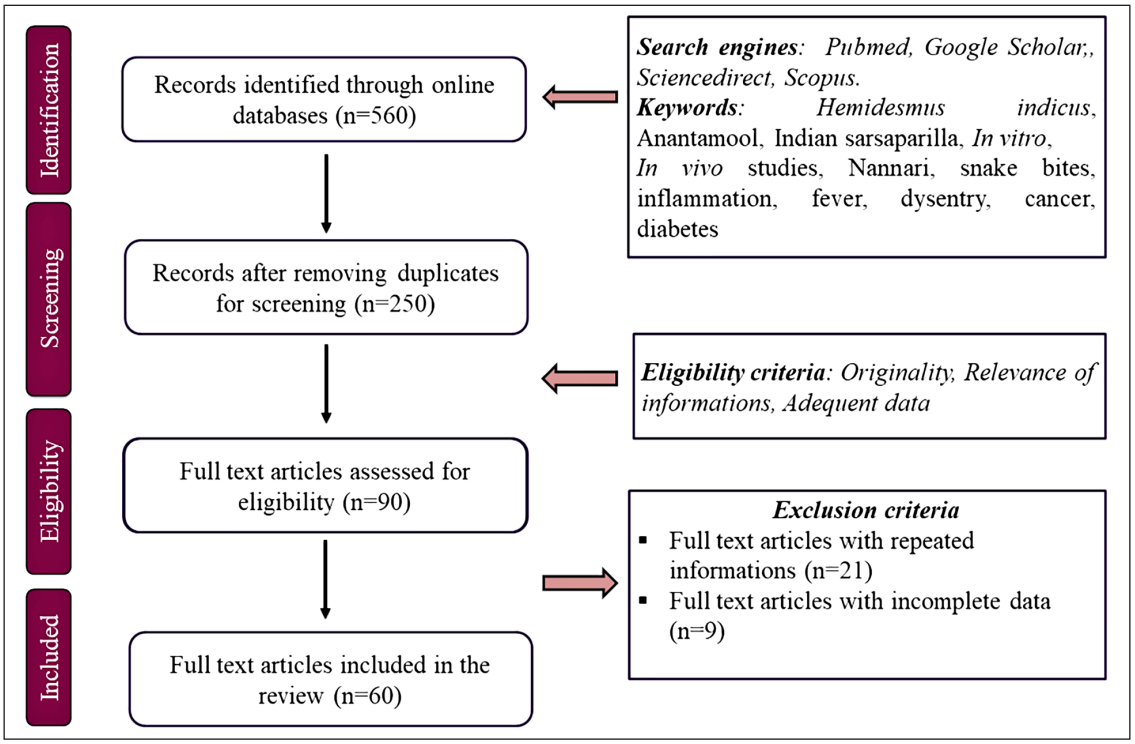

Figure 1. Methodology adopted for the systematic analysis.

acid, ledol, nerolidol, and drevogenin were also isolated from the roots. *Hemidesmus indicus* stem contains hemidescine, hemidine, emidine, indicasin, hemisine, hindicusine, medidesmine, demicine, di-O-acetylhindicusine (pregnane glycoside), indicine, denicunine, desinine, heminine (pregnane glycoside), 3-keto-lup-12-ene-21 28-olide (triterpene lactone), 12-dehydrolupeol acetate, hexadecanoic acid, vanillin, and isovanillin [13]. Its leaves and flowers contain tannins, phenolics, flavonoids, and flavonoid glycosides (isoquercetin, rutin, and hyperoside), respectively. Flavonoids play a variety of biological activities and also impart color and aroma to the flowers [14]. The phytoconstituents isolated from *H. indicus* are listed in Table 1.

Table 1. The table illustrates the phytoconstituents of *H. indicus* reported till date.

Plant part	Phytoconstituents	Reference
Roots	2-hydroxy-4-methoxy benzaldehyde, 4-hydroxy-3-methoxy benzaldehyde, hexa-triconate acid, lupeol acetate, β-amyrin acetate, lupeol-1-octacosanol, steroids, flavonoids, terpenoids, lignins, saponins, phenolic compounds, tannins, proteins, insulins, cardiac glycosides, and carbohydrates	[2]
Stem	Hemidine, hindicusine, desinine, di-O-acetylhindicusine (pregnane glycoside), indicineindi-cusin, denicunine, hemisine++, heminepregnane glycoside hemidescine, emidine, medidesmine, hexadecanoic acid, demicine, Δ12-dehydrolupeol acetate, 3-keto-lup-12-ene-21 → 28-olide (triterpene lactone), Δ12-dehydrolupanyl-3β-acetate, 3-hydroxy-4-methoxybenzaldehyde (isovanillin) and 4-hydroxy-3-methoxybenzaldehyde (vanillin)	[13]
Leaves	Tannins, phenolics, flavonoids	[2]
Flowers	Flavonoid glycosides (isoquercetin, rutin, hyperoside)	[2]

Commercial formulations of *H. indicus*

Various extracts of *H. indicus* roots are used against leukemia, breast, hepatic, colon, and skin cancers in traditional medicine. They also benefit from epileptic fits, diarrhea, arthralgia, leprosy, and burning sensations. The leaves help to cure vomiting, wounds, and leukoderma [15]. Due to the extensive traditional use of *H. indicus*, the plant is a major ingredient in many traditional formulations including Ayurveda. About 46 Ayurvedic formulations contain *H. indicus* alone or in combination with other herbal ingredients. *Dhanwamthara Taila*, *Pinda Taila*, *Amrithadi Enna*, *Gandha Taila*, *Triphaladi Taila*, *Neelidaladi Taila*, *Chandanadi Taila*, *Anuthaila,* and *Aswagandhadi Yamaka* are some of the Ayurvedic topical preparations containing *H. indicus*. Banyan botanicals commercialize *H. indicus* products like the *Anantmul root powder*, *herbal skin care tablets*, *Mahanarayan oil*, and *Kidney formula tablets.* Apart from this, the root powder of *H. indicus* is marketed as a hair care product [9,16].

PRECLINICAL STUDIES

Anti-inflammatory activity

Inflammation is a natural defensive response of the body against injury or pathogen invasion. However, chronic inflammation leads to various disorders like cancer, diabetes, rheumatoid arthritis, cardiovascular diseases, etc. [17]. *Hemidesmus indicus* roots exhibit anti-inflammatory action in human leukemia monocytic cell lines (THP-cell lines). The anti-inflammatory property of the alcoholic and water extracts of *H. indicus* roots was evaluated on lipopolysaccharide/ phorbol 12-myristate 13-acetate (LPS/PMA)induced human monocytic cells. The remarkable suppression of pro-inflammatory markers interleukin-6, macrophage inflammatory protein-1, tumor necrosis factor-α (IL-6, MIP-1, TNF-α) was noticed [18].

Anti-diabetic activity

Diabetes mellitus is a common, chronic metabolic disorder that leads to the dysfunction of various organ systems such as kidneys, heart, eyes, and blood vessels. In many countries, traditional medicinal systems are used to manage diabetes mellitus as it is cost-effective and non-toxic [19]. Senadheera *et al.* [20] investigated the potential of rice-based herbal porridges containing *H. indicus* leaf extracts in streptozotocin (STZ)-induced diabetic Wistar rat models. The study showed a marked decrease in the glucose level in the test group animals within 3 months [20]. Another research study investigated the influence of methanolic *H. indicus* root extracts on cataracts (a secondary complication of diabetes) in rats, where diabetes was induced by STZ. The results indicated that the methanolic *H. indicus* root extracts extract remarkably inhibits the aldose reductase enzyme activity. Aldose reductase converts glucose to sorbitol using nicotinamide adenine dinucleotide phosphate hydrogen (NADPH) causing osmotic stress and cataractogenesis in a dose-dependent manner [21]. β-amyrin palmitate extracted from *H. indicus* roots showed anti-diabetic activity at 50 µg/kg body weight compared to 500 µg/kg glibenclamide (anti-diabetic drug in clinical use) in alloxan-induced and STZ-induced diabetic Wistar rat models [22,23]. Siraj *et al.* [24] studied the impact of ethanolic *H. indicus* root extract on intestinal glucose absorption. The results showed that the 500 mg/kg root extract of the plant steadily decreased the gastrointestinal tract (GIT) absorption of glucose compared to the control. These findings strongly suggested that the ethanolic root extract has remarkable anti-diabetic activity [24].

Anti-oxidant activity

Oxidative stress has been identified as the primary cause of various chronic disorders. However, increasing the endogenous antioxidant potential of the body limit the consequences of reactive oxygen species-induced oxidative damage. Since ancient times, herbal plants have been valued as good antioxidants. *Hemidesmus indicus* is used traditionally for several chronic diseases based on its antioxidant potential. Different extracts (hexane, ethyl acetate, and ethanol) of *H. indicus* root were used to determine the antioxidant activity using the 2,2-diphenylpicryl hydrazyl (DPPH) method. The hexane (IC_{50} 14.53 g/ml), ethyl acetate (IC_{50} 6.793 g/ml), and ethanolic (IC_{50} 6.510 g/ml) extracts of the plant exhibited strong scavenging activity as compared to that of standard butylated hydroxytoluene (IC_{50} 7.621 g/ml) [1,25]. The antioxidant properties of *H. indicus* crude extracts were evaluated

using the phosphomolybdenum method. The antioxidant capacity was calculated as ascorbic acid equivalents. The IC_{50} value of *H. indicus* was obtained as 190.09 g/ml compared to ascorbic acid (IC_{50} values 18.80 g/ml) [26]. Kaffoor *et al.* [27] compared the antioxidant capability of various extracts of *H. indicus* (methanol, chloroform, petroleum ether, and water) root in which the methanol and aqueous extracts showed better antioxidant activity with IC_{50} values of 51.92 ± 11.19 and 70.10 ± 8.28 µg/ml, respectively [27].

Anticancer activity

Cancer is a chronic disease marked by the spread of abnormally growing cells to different body parts. According to GLOBOCAN reports, mortality due to cancer will increase from 9.96 to 1.63 million by 2040 [28]. Natural products possess an excellent capacity to prevent the spread or risk of acquiring various forms of cancer. *Hemidesmus indicus* also possess efficient anticancer potential which is validated through various preclinical studies. The anticancer potentials of ethanolic *H. indicus* root extracts on hepatoblastoma cell lines (HepG2 cell lines) were compared with Vero cell lines. The cytotoxicity study results indicated that the maximal cell death of HepG2 cells with the extracts was 72.110% ± 004% at 160 g/ml concentration. The IC_{50} of the root extract of the plant was 65.58 g/ml. The maximal cell death of Vero cells with root extracts was found to be 20.690% ± 003% at 160 g/ml concentrations, and the IC_{50} was found to be 386.66 g/ml. The microscopic observations revealed the *H. indicus* extract exhibited significant anti-tumor activity against HepG2 cells [29].

Another *in vitro* study showed that rhizomes of *H. indicus* exhibit cytotoxic effects on the HT-29 colon cancer cell lines. Similarly, the methanolic extract of *H. indicus* significantly exhibit cytotoxicity to Ehrlich ascites tumor (EAT) at the IC_{50} of 274.83 µg [1]. Another study indicated that the decoction of the roots of *H. indicus* exhibits chemopreventive effects against HL-60 (Human promyelocytic leukemia) cell lines. *Hemidesmus indicus* decoction inhibited the G0/G1 phase of the cell cycle, thus altering the cell cycle progression. Moreover, it increased the differentiation of the cancer cells [30]. Another research study examined the chemopreventive efficacy of the hydro-alcoholic root extract of *H. indicus* on the acute lymphoblastic leukemia cell line. The phytochemical analysis of the extract revealed the presence of 2-hydroxy-4-methoxybenzaldehyde (2H4MB), 2-hydroxy-4-methoxybenzoic acid (2H4MBA), and 3-hydroxy-4-methoxybenzaldehyde (3H4MB) as bioactive compounds. The extract induced apoptosis in a dose-dependent manner. It was also analyzed for its anti-tumor action on DLD1 cells (colorectal adenocarcinoma cells). The extract showed a cytostatic effect on the cells by inhibiting the G2/M phase (growth 2/mitosis) of the cell cycle [31].

Anti-venom activity

Snake bites are considered a major health concern in India that causes mortality. The only effective treatment available for snake bites is antivenom. However, the use of antivenom has been hampered by several drawbacks, such as allergic reactions, high cost, and scarcity, which makes it challenging. Since ancient times, *H. indicus* was shown to be highly effective at neutralizing snake bite venom. An ethnobotanical study of traditional herbs used to treat snakebites in southern Tamil Nadu, India exhibited the effective potential of Sariva as an antivenom. It is revealed that 2-hydroxy-4-methoxybenzoic acid isolated from *H. indicus* suppressed the free radical production brought on by viper venom-induced inflammation and antagonized fatal, hemorrhagic and coagulant action in experimental rodents [16].

Another study investigating the anti-venom property of "lupeol acetate," a component isolated from the roots of Sariva neutralizes the venom of *Daboiarussellii* and *Najakaouthia*. The results indicate that lupeol acetate significantly inhibits the lethality, bleeding, defibrinogenation, and edema brought on by *Daboiarussellii* venom [32]. Additionally, it reversed the cardiotoxicity, neurotoxicity, and respiratory problems that Najakaouthia venom caused in Swiss albino mice [7,33,34]. The mortality caused by viper venom (Viperarussellii) and hemorrhage in albino rats and mice were significantly neutralized by the methanolic extract of *H. indicus* [8]. Another research study established the anti-scorpion venom property of an aromatic compound isolated from methanolic *H. indicus* root extracts in Swiss albino mice and Wistar albino rats. The antivenom activity was assessed by various tests like qualitative analysis of urine, levels of alanine transaminase and aspartate transaminase (hepatotoxicity markers), urea and creatinine (renal toxicity markers), creatine phosphokinase and lactic dehydrogenase (myotoxic markers) and oxidative stress markers lipid peroxidation (LPO), glutathione peroxidase, glutathione. The results indicated that the compound isolated from *H. indicus* exhibits significant antioxidant potential [35].

Anti-hyperlipidemic activity

Hyperlipidemia is a chronic condition caused by aberrant lipid metabolism which leads to various diseases such as diabetes, obesity, atherosclerosis, hypertension, and coronary heart disease. Low-density lipoprotein (LDL), total cholesterol, and triglycerides are higher in the blood indicating hyperlipidemia. A research study investigating the protective effect of *H. indicus* root extracts in Wistar rats indicated that methanolic root extract produced significant dose-dependent protection against oxidative stress-induced through a high-fat diet. Significant differences in the levels of triglycerides, phospholipids, free cholesterol, total cholesterol, ester cholesterol, atherogenic index, and the body weight of the treatment group and the control group animals were observed. Moreover, intake of *H. indicus* extracts protected the rats from fat-induced hepatic damage [36,37]. Choudhury *et al.* [18] investigated the anti-hyperlipidemic property of alcoholic and aqueous extracts of *H. indicus* roots in Wistar rats. The extracts administered at 200 mg/kg bw/day showed that serum lipid markers induced by high-fat diet consumption (total triglycerides, LDL, and total cholesterol) are reduced significantly. Moreover, the treatment with extracts of *H. indicus* roots maintained a healthy level of High density lipoprotein (HDL) in the test group [18].

Anti-ulcer activity

An ulcer is caused by the imbalanced production of digestive juices and the protective elements of the stomach lining. Anti-ulcer medications work by inhibiting the generation of stomach acid, neutralizing the acid, or protecting the gastrointestinal mucosa from damage. One of the research studies investigated the potential of ethanolic extract of *H. indicus* (whole plant) against ulcers (induced by indomethacin) in Wistar rats. The results indicated that oral consumption of the extracts (at 200 and 400 mg/kg) exhibited remarkable antiulcer activity by strengthening the gastric mucosa [38]. Another research study compared the potential of the aqueous root extracts (500 mg/kg) and alcohol root extracts (100 mg/kg) of *H. indicus* in protecting the gastrointestinal mucosa of indomethacin-induced peptic ulcers in Wister Albino rats. The results showed an efficient ulcer healing action for alcohol root extracts than aqueous extracts [39].

Another study revealed that the ulcer index significantly decreased with the alcoholic extract of *H. indicus* roots at doses, 200 and 400 mg/kg in Wistar rats with indomethacin-induced gastric ulcers. Omeprazole 20 mg/kg provided ulcer protection of 78.91%, whereas *H. indicus* root extract offered 73.59% and 76.82% protection, at 200 and 400 mg/kg, respectively [8,40]. Anti-ulcerogenic property of ethanolic *H. indicus* root extract was investigated in pyloric ligated Wistar rats. The aqueous ethanolic extract of the *H. indicus* roots decreased the destructive factors such as pepsin and proteins whereas subsequently increased the defensive factors of pH, hexosamine, fucose, hexose, and sialic acid. The results showed an increased carbohydrate-to-protein ratio, indicating high mucin action [41].

Hepatoprotective activity

The liver, the most essential organ in the body, is responsible for many physiological processes like metabolism and detoxification. Hepatic disorders are a major concern to public health worldwide. Despite the advancements in modern medicine, there are still no specific therapeutic agents to enhance

Table 2. The table summarizes the *in-vitro* studies of *H. indicus* reported over the past 10 years.

Plant extracts	Model *in-vitro* cell lines	Assay used	Concentration IC_{50}	Result	Reference
Alcoholic and aqueous extract of the root	LPS/PMA-induced human monocytic (THP-1) cells	MTT assay	-	• ↓IL-6, TNF-α, MIP-1α • ↓Secretion of TNF-α protein	[18]
Hexane, ethylacetate, and ethanol root extract		DPPH radical scavenging activity assay	IC_{50}—6.510 µg/ml	• ↑Scavenging activity with ethanolic extracts	[25]
Methanolic rhizomes extract	MCF7 breast cancer cell lines HT29 colon cancer cell line Ehrlich Ascites tumor	-	IC_{50}—274.83 µg	• Efficient anti-cancer activity against MCF7 Breast cancer cell lines, HT29 colon cancer cell line, and Ehrlich ascites tumor	[1]
Crude extract	-	DPPH scavenging method	IC_{50}—190.09 g/ml	• ↑Anti-oxidant capacity	[26]
Ethanolic and aqueous root extract	-	Free radical scavenging activity on nitric oxide radical scavenging activity and hydrogen peroxide scavenging activity	-	• Efficient antioxidant capacities	[49]
Aqueous and methanol leaf extracts	-	DPPH and ABTS+ free radical scavenging activities	IC_{50}—51.92 ± 11.19 and 70.10 ± 8.28 µg/ml, respectively	• ↑Extract concentration • ↑DPPH radical scavenging activity	[27]
Root extract	HepG2 cell line	-	IC_{50}—386.66 g/ml	• ↑Cytotoxicity	[29]
Root decoction	Human promyelocyticleukemia cell line (HL-60)	-	IC_{50}—0.31 mg/ml	• Inhibit G0/G1 phase	[30]
Hydroalcoholic, ethylacetate, chloroform root extract	Acute lymphoblastic leukemia cell line	-	-	• Chemopreventive action	[6,50]
Ethanolic root extract	-	-	-	• ↑Antibacterial action	[25]
Ethanolic extract	Various bacterial strains	Colony-forming assay	-	↑Antibacterial activity in dose dependant manner	[47]

hepatic function, protect the whole organ, or support liver cell regeneration [42]. Das *et al.* [5] reported that ethanolic extract of *H. indicus* roots (100 mg/kg, for 15 days) administered orally prevented isoniazid (INH) and rifampicin (RMP) induced hepatotoxicity in Wistar rats. The results showed that in comparison to control rats, INH and RMP-intoxicated rats possessed significantly lesser levels of the mitochondrial protein in the liver, iso-citrate dehydrogenase, succinate dehydrogenase, malate dehydrogenase, α-ketoglutarate dehydrogenase, NADH dehydrogenase, and cytochrome c oxidase. The antiperoxidative enzymes chloramphenicol acetyltransferase and superoxide dismutases exhibited a considerable decline in activity after intraperitoneal treatment of INH and RMP, which also caused an inclination in LPO in the mitochondria [5].

Hydroalcoholic extract of *H. indicus* roots (400 mg/kg, orally) was effective against carbon tetrachloride (CCl_4)-induced liver damage. In a similar study, methanolic extract of the roots of *H. indicus* showed hepatoprotective activity against CCl_4-induced liver damage. The oral administration of the extract rats significantly reduced the elevated levels of serum glutamate pyruvate transaminase, alkaline phosphatase, glutamate oxaloacetate transaminase, and bilirubin [5,34]. In another research study, the influence of ethanolic *H. indicus* extract and 2-hydroxy 4-methoxy benzoic acid (HMBA) against liver fibrosis was evaluated in ethanol-fed rats. The extract and the compound remarkably reduced LPO and the levels of hepatic collagen and hydroxyproline content. It was also noticed that the ascorbic acid level and the solubility of hepatic collagen were increased in the treatment group. The levels of matrix metalloproteinases (MMP-2 and MMP-9) relevant during the extracellular matrix degradation on ethanol intoxication were found to be less in the extract and HMBA-treated group [34,43].

Anti-microbial activity

"Microbial infections" is a collective term for the infections caused by bacteria, parasites, viruses fungi, etc. The infectious agents invade an organism, grow, and are confronted by the host tissue leading to microbial infection [44]. Phytochemicals are reported to be effective antimicrobials with negligible toxicity. Aqueous extracts of the *H. indicus* roots (0.04–0.1 mg) exhibited anti-microbial activity against *Staphylococcus aureus, Klebsila pneumonia,* and *Pseudomonas aeruginosa* [5]. *Hemidesmus indicus* roots extracted using methanol were formulated as an ointment to check its wound-healing activity in Wistar rats. The herbal formulation exhibited remarkable wound healing action by promoting the proliferation of the cells, stimulating granulation tissue formation, and enhancing the healing index [45]. Another study investigated the effects of various solvent fractions of the roots of *H. indicus* (methanol, chloroform, petroleum benzene, acetone) against some of the uropathogenic bacteria, including *S. aureus, Escherichia*

Table 3. The table illustrates the summary of *in-vivo* studies of *H. indicus* reported in the last 10 years.

Plant part/extracts	*In-vivo* animal models	Doses	Result	References
Aqueous and ethanolic extract of leaves and stem	Carrageen induced paw oedema	400 mg/kg	• ↓Inflammation	[51]
Aqueous leaf extract	STZ-induced diabetic Wistar rat model	60 mg/kg	• ↓Activity in diabetic rats compared with in normal control group	[20]
Methanolic root extract	STZ-induced diabetic cataract in a rodent model	22.76 µg/ml	• ↓Osmotic stress and progression of diabetic cataract in STZ-induced diabetic rats	[21]
β-amyrin palmitate	STZ-induced diabetic rats	500 µg/kg	• ↑Anti diabetic action	[23]
Plant extract	Albino rats	600 mg/kg	• ↑Antivenom activity in 600 mg/kg	[33]
Ethanolic root extract	Wistar rats	100 mg/kg	• Anti-peroxidative enzyme level restoration↑ • Mitochondrial LPO↓	[5]
Aqueous ethanolic extract	Wistar rats	400 mg/kg	• LPO↓ • Sodiumnitroprusside formation↓	
Ethanolic extract	The pylorus ligation model in Wistar rats	100, 200, 400, and 800 mg/kg	• ↑Anti-ulcer activity	[40]
Aqueous and alcoholic extracts	Wistar rats	200 and 400 mg/kg	• Effective ulcer healing property for alcoholic extract than aqueous root extracts • ↓Oxidative stress	[38]
Methanolic extract	Wistar rats	200 mg/kg	• ↓Hyperlipidaemia • ↓Liver damage	[37]
Ethanolic root extract	Wistar rats	250 and 500 mg/kg	• ↓GIT's absorption of glucose than control at 500 mg/kg • ↑Anti-diabetic activity	[24]

coli, and *Enterococcus faecalis*. Among these strains, *S. aureus* is a multi-drug resistant strain. The results indicate the effectiveness of the methanolic extract of *H. indicus* roots for the treatment of urinary tract infections [46].

Another research study investigated the anti-microbial efficacy of hexane, ethanol, and ethyl acetate extracts of *H. indicus* roots by disk diffusion method against *Bacillus megaterium, P. aeruginosa, S. aureus,* and *K. pneumonia*. It was observed that in the extract-treated group, there was a marked decrease in the bacterial load [25]. Saritha *et al.* [47] studied the efficacy of ethanolic extract of *H. indicus* against *E. coli.* The extract showed its activity through cellular content leakage, inner membrane permeabilization, blebbing, and membrane potential disruption [47]. Purohit and Bais [48] studied the anti-bacterial activity of ethanol and aqueous extracts of *H. indicus* roots against *E. coli, Bacillus subtilis, S. aureus, and P. aeruginosa* compared to those of the standard drug, ciprofloxacin. The results showed that the ethanol extract was highly efficient against Gram-positive bacteria (*E. coli* and *B. subtilis*) whereas moderately active against Gram-negative (*P. aeruginosa* and *S. aureus*). The aqueous extract was comparatively efficient against *B. subtilis* and *S. aureus* whereas moderately efficient against *P. aeruginosa* and *E. coli* [48].

CONCLUSION

The present review discusses the research progress of *H. indicus* during the last 10 years. Since ancient times, the plant has been used for leprosy, piles, itching, leucoderma, skin disease, asthma, bronchitis, syphilis, paralysis, leucorrhoea, urinary disorders, dysentery, diabetes, and snake bites. The extensive uses of this folk remedy for various ailments have considered it to the commercial market as a health supplement. Various pharmacological actions of the plant have been validated through preclinical studies (Tables 2 and 3). *Hemidesmus indicus* is effective as an anti-inflammatory, anti-arthritic, anti-oxidant, hepatoprotective, antiulcer, anti-venom, anti-hyperlipidemic, and anti-microbial agents. Even though there are many preclinical studies with *H. indicus* extracts, there are very few research works for identifying the phytoconstituents responsible for the bioactivity. Preclinical studies show that *H. indicus* roots are effective against a wide spectrum of ailments however, the clinical data on the drug's effectiveness is very limited. More clinical studies are necessary to validate the traditional usage of this medicinal plant scientifically.

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This study does not involve experiments on animals or human subjects.

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The authors report no financial or any other conflicts of interest in this work.

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AVAILABILITY OF DATA AND MATERIALS

The authors confirm that the data supporting the findings of this study are available within the article.

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