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PHARMACOLOGICAL AND PHYTOCHEMICAL IMPORTANCE OF *SIDA CORDIFOLIA*: A REVIEW

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ABSTRACT: *Sida cordifolia* is locally known as Bala is one of those precious medicinal herbs of Malvaceae that are still included in un-utilized herbs in spite of the variety of useful pharmacological properties it possesses. *Sida cordifolia* have anti-inflammatory, anti-ulcer, anti-diabetic, nephroprotective, cytotoxicity, anti-hypercholesterolemia, hepatoprotective, analgesic, anti-stress and adaptogenic activity, cardiovascular, anticancer, antibacterial, antimelanogenesis, anticandidal activity, anti-parkinson's disease, CNS depressant, fat loss, hypotensive, ultrastructure and antioxidant properties. Here, we have reviewed all the reported pharmacological properties and phytoconstituents of this valuable herb to highlight the effectiveness and potentials of this herb.

Keywords: *Sida cordifolia*, Malvaceae, Pharmacological properties, Chemical constituents

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INTRODUCTION: The plant under investigation, *Sida cordifolia,* is locally known as Bala. *Sida cordifolia* is a perennial subshrub of the mallow family Malvaceae. The specific name, *cordifolia*, refers to the heart-shaped leaf. Native from tropical America, it has spread along many tropical regions in the world and propagates so fast to be considered an invasive herb. This plant mostly occurs in very spoilt soils due to the heavy rains, excessively hot or uncontrolled grazing.

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This plant usually used in Brazilian folk medicine for the treatment of inflammation of the oral mucosa, blennorrhea, asthmatic bronchitis, and nasal congestions, stomatitis of asthma and nasal congestion and in many parts of Africa for various ailments, particularly for respiratory problems. It has been investigated as an anti-inflammatory, for preventing cell proliferation and for encouraging liver re-growth. As a consequence of the presence of ephedrine, it possesses psychostimulant properties and affecting the central nervous system as well as the heart. However, a good quality fiber is obtained from the plant; it can be used like jute (*Corchorus spp*.) The drug is well reputed in Ayurvedic and Siddha system of medicine for an ailment of different diseases. Though seed contains the maximum amount of active constituents, the root is used extensively.

Root is used as astringent, diuretic, and tonic. The infusion of the root is given for the treatment of neurological and urinary problems as well as blood and bile disorder. It is also used for the treatment of bleeding piles, cystitis, leucorrhoea, gonorrhea, chronic dysentery, and asthma. The root powder is given along with cow milk to treat leucorrhoea and frequent micturition. It is also useful in throat diseases and insanity. The root bark is used mixed with sesame oil *(Sesamum indicum*, Pedaliaceae) and cow milk in curing facial paralysis and sciatica pain. Root decoction mixed with ginger is effective in curing intermittent fever and healing of wounds. Seeds are aphrodisiac, given in gonorrhea, cystitis, colic pain, piles, tenesmus, *etc*. Leaves are demulcent and febrifuge, used in dysentery. The cooked leaves are eaten in case of bleeding piles. The extract of the whole plant, mixed with water, is prescribed to cure spermatorrhoea, rheumatism, and gonorrhea [1].

General Botanic Description: *Sida cordifolia* is an erect perennial that reaches 50 to 200 cm (20 to 79 in) tall, with the entire plant covered with soft white felt-like hair that is responsible for one of its common names, "flannel weed." Structural features of this plant are given below:

Stem: Stem up to 1 m high, erect, grayish-green, densely pubescent with minute stellate hairs mixed with simple hairs.

Leaves: Leaves 2.5-6.5 × 1.5-3.5 cm, orbicular, ovate to oblong, cordate at base, obtuse or acute, occasionally rounded or truncate at apex, crenate-serrate along the margin, 5-7 nerved atbase, densely velutinous with stellate hairs on both surfaces; petioles 2-3 cm long; stipules free-lateral, filiform, densely stellate-hairy mixed with few simple hairs.

Flowers: Flowers 10-15 mm diam., axillary, solitary, or 2-5 in cymes, clustered particularly towards the apical portion of twigs; pedicels 4-6 mm long. Calyx campanulate, accrescent; lobes triangular, 4-6 mm long, acute to acuminate, densely stellate pubescent mixed with some simple hairs outside.

Corolla light yellow or creamy white, 10-15 mm across; petals obovate, truncate at apex, 6-8mm long. Staminal column 6-8 mm long, either with simple hairs or glabrous. Ovary conical, stellate hairy; style 5-7 mm long; stigma penta-fid.

FIG. 1: DIFFERENT PARTS OF *SIDA CORDIFOLIA*

Fruits: Fruits depressed-globose, schizocarp, with a pair of the horny structure at the lateral sides of the apex.

Seeds: Seed 1.5 mm across, flattened, reniform, glabrous, dark brown or black.

Habit: An erect, small, annual, under a shrub, hairy with soft and with stellate hairs all over.

Flowering and Fruiting Time: The flowering and fruiting period is between October-December of the year.

Inflorescence: Solitary or few together [2].

Vernacular Names: [3, 4, 5, 6] Hindi- Barial, Bariar, Khareti, Kharenti, Kungyi, Variyara; English- Country mallow; Sanskrit- Badiyalaka, Bala, Baladhya, Balini, Bhadra, Bhadrabala, Bhadrodani, Brela, Jayanti, Kalyanini, Kanaka, Kathorayashtika, Kharakakashtika, Kharayashtika, Krura, Motapati, Nilaya, Odanavha, Odani, Odanika, Phanijivaka, Prahasa, Raktatandula, Samanga, Samansha, Shitapaki, Suvarna, Svetherela, Variga, vataghni, Vatyalaka, Vatyali, Vatyapushpi, Vilala; Tamil- Mayir-manikham, Arivalmanaippundu, Nilatutti, Paniyaratutti; Bengali- Bala, Barila, Brela, Svetberela, Badela; Gujarati- Junglimethi, Baladana, Khareti, Bal, Bala; Malayalam- Kutturam, Velluruma; Punjab- Simak, Kharent, Kharayati; Maharashtra- Chikana; Kannada- Hettuti; Marathi- Chikana, Khiranti; Telegu- Antisa, Chirubenda, Muttavapulagamu, Suvarnamu, Tellagorra, tellantisa.

Synonyms: [7, 8, 9, 10] Baladhya, Bhadrabala, Bhadraudani, Bhadra, Kharakasthika, Kalyanini, Motavati, Mahasamanga ,Odanika, Odanahvaya, Sitapaki, Samamsa, Udanika, Vati, Vatya, Vatyalika, Vatyodarahvaya, Vatyalaka.

Taxonomic Hierarchy: [2]

Kingdom: Plantae
Class: Magnoliopsida
Order: Malvales
Family: Malvaceae
Genus: Sida L.
Species: *Sida cordifolia* L.

Distribution: [11, 71] Country Mallow of Malvaceae family is widely distributed along with other species are common throughout the tropical and sub-tropical plains all over the world.

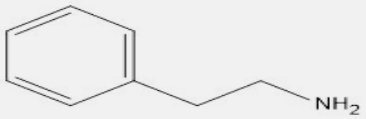
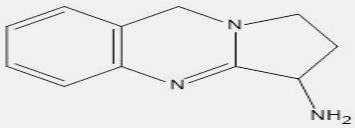
In Asia- Bangladesh, Bhutan, Cambodia, China (Fujian, Guangdong, Guangxi, Hainan, Sichuan, Yunan), India (Madhya Pradesh, Odisha, Tamil Nadu, West Bengal), Indonesia, Israel, Japan, Jordan, Laos, Malaysia, Myanmar, Nepal, Pakistan, Philippines, SriLanka, Taiwan, Turkey.

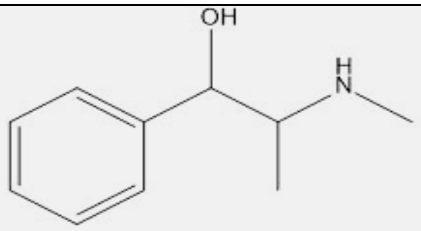
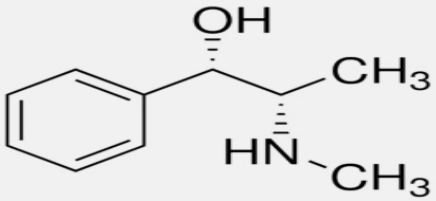
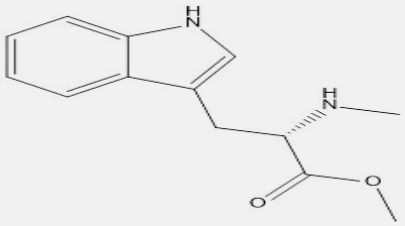
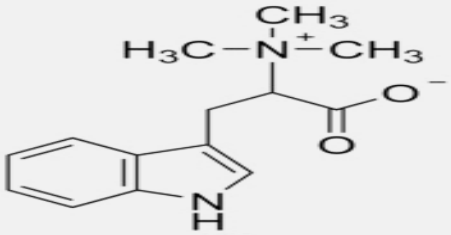
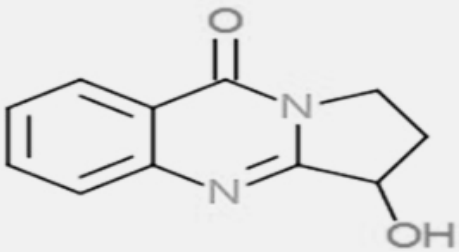
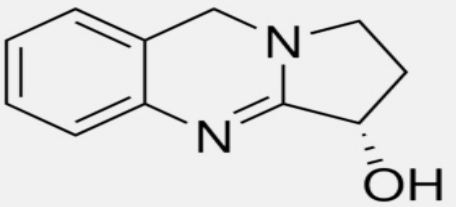
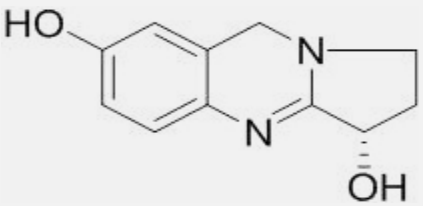
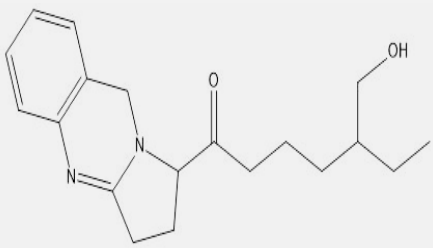
In Africa- Angola, Benin, Botswana, Burkina Faso, Burundi, Cameroon, Central African Republic, DR Congo, Egypt, Equatorial Guinea, Ethiopia, Gabon, Ghana, Guinea, Kenya, Madagascar, Mali, Mauritius, Mozambique, Namibia, Nigeria, Rwanda, Senegal, Seychelles, Somalia, South Africa, Sudan, Tanzania, Togo, Uganda, Zaire, Zambia, Zimbabwe. In North America /Europe- Mexico, USA (Florida, Hawaii, Texas), Europe: Croatia, Italy.

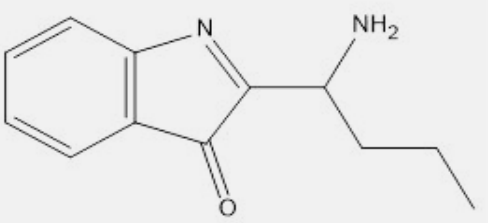
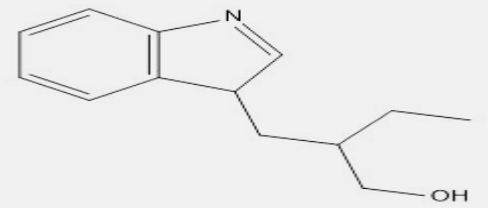
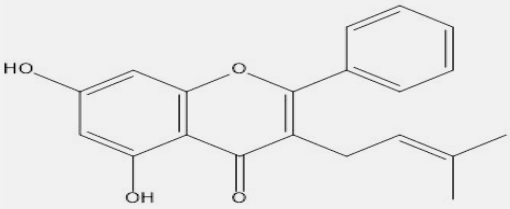
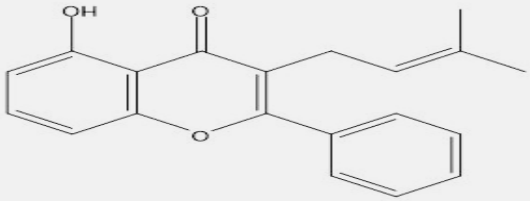
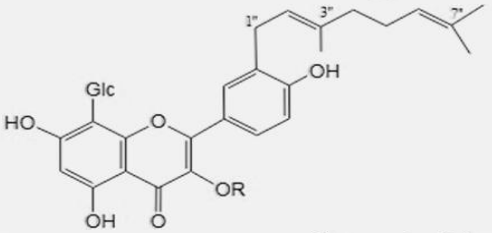
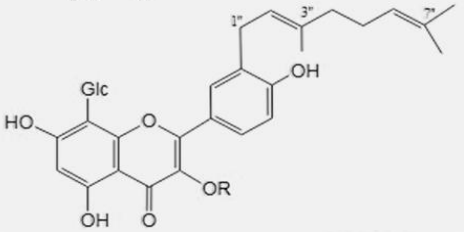
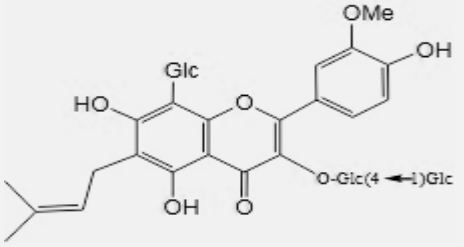
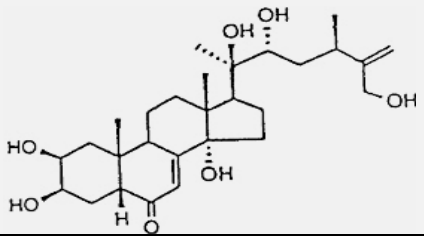
In Central America and Caribbean- British Virgin Islands, Costa Rica, Cuba, Dominica, ElSalvador, Guatemala, Haiti, Honduras, Jamaica, Martinique, Netherlands Antilles, Nicaragua, Panama. In South America- Argentina, Bolivia, Brazil (Paraiba, Sao Paulo) Chile, Colombia, Ecuador, French Guinea, Guyana, Paraguay, Peru, Uruguay. In Oceania- Australia (Northern Territory), Cook Islands, Fiji, French Polynesia, Guam, Nauru, New Caledonia, Papua New Guinea, Tonga, Vanuatu up to an altitude of 1050 m., growing wild along the roadside.

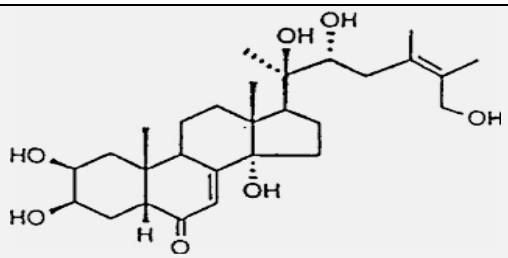
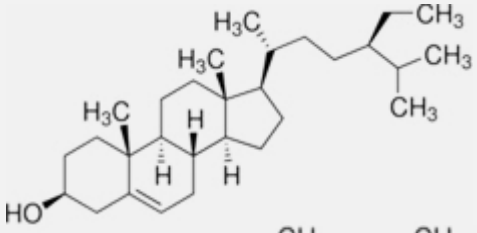
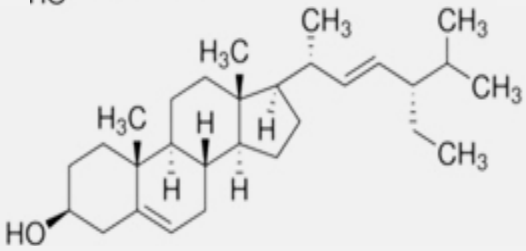
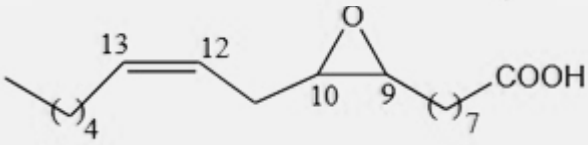
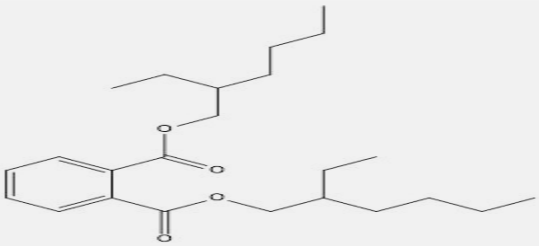
Chemical Constituents: A considerable work has already been done to identify and isolate the chemical constituents from different extracts of *Sida cordifolia*.

TABLE 1: IMPORTANT CHEMICAL CONSTITUENTS ISOLATED FROM *SIDA CORDIFOLIA* EXTRACTS [60-70]

S. no.	Chemical constituents	Structure	References
1	*β* – Phenethylamine		60
2	1,2,3,9-Tetrahydropyrrolo[2,1-*b*]-quinazolin-3-yl-amine		72

3	Ephedrine		60, 61
4	*Ψ*-(Pseudo) -Ephedrine		61
5	*S*-(+)-*Nb*Methyltryptophanmethyl ester		60
6	Hypaphorine		60
7	Vasicinone		60
8	Vasicine		60
9	Vasicinol		60
10	5′-Hydroxymethyl-1′ (1,2,3,9-tetrahydropyrrolo[2,1 *b*]-quinazolin-1-yl)-haptan-1-one		72, 66

11	2-(1′-Aminobutyl)-indol-3-one		72
12	2′-(3H-Indol-3yl *methyl*)-butan-1′-ol		72
13	5,7-Dihydroxy-3-isoprenylflavone		69
14	5-Hydroxy-3-isoprenyl flavone		69
15	3′-(3″,7″-Dimethyl 2″,6″-octadiene)-8-C *β*-Dglucosyl-keampferol 3-*O*-*β*- Dglucoside		72, 65
16	3′-(3″,7″-Dimethyl-2″,6″-octadiene)-8-C *β*-D-glucosyl-keampferol-3-*O*-*β*-D-glucosyl [1→4]-*α*-D glucoside		72
17	6-(Isoprenyl)-3′ methoxy-8-C-*β*-D glucosylkeampferol3-*O*-*β*-D-glucosyl [1→4] *α*-D-glucoside		72
18	Sidasterone A		62

19	Sidasterone B		62
20	*β*-Sitosterol		72
21	Stigmasterol		72
22	(10*E*, 12*Z*)-9 Hydroxyoctadeca10,12-dienoic acid		70
23	Sterculic acid		66
24	Malvalic acid		66
25	(+)-Coronaric acid		66
26	Choline		60
27	Betaine		60
28	Di- (2-ethylhexyl) phthalate		63

Alkaloids, ecdysteroids, and flavonoids are the most abundant constituents of this genus. Alkaloids and flavonoids are the major bioactive principles of the extracts. Various studies have exposed that different extracts of *Sida cordifolia* contain several bioactive compounds including ephedrine, β-Phenethylamine, vasicinone, *β*-Sitosterol, malvalic acid, and stigmasterol. So far, β-phenethylamines, 2-carboxylated tryptamines, quinazoline, and quinoline alkaloids have been reported from *Sida cardifolia* [60, 62 72, 73] indole alkaloids [67] β-phenethylamine and quinazoline alkaloids, (-) ephedrine, ψ- ephedrine and vasicinone [60] are therapeutic principles of the plant extracts. All the reported flavonoids are flavones, flavonols, and their glycosides. Some of the flavonoids namely, 5, 7-dihydroxy-3-isoprenylflavone , 5-hydroxy-3-isoprenylflavone 8 and 3'- (3",7"-dimethyl-2",6"-octadiene)-8-C-β-D-glucosyl-kaempferol 3-O-β-D-glucoside isolated from *Sida cordifolia* demonstrated analgesic and anti-inflammatory activities in animal models [65,69].

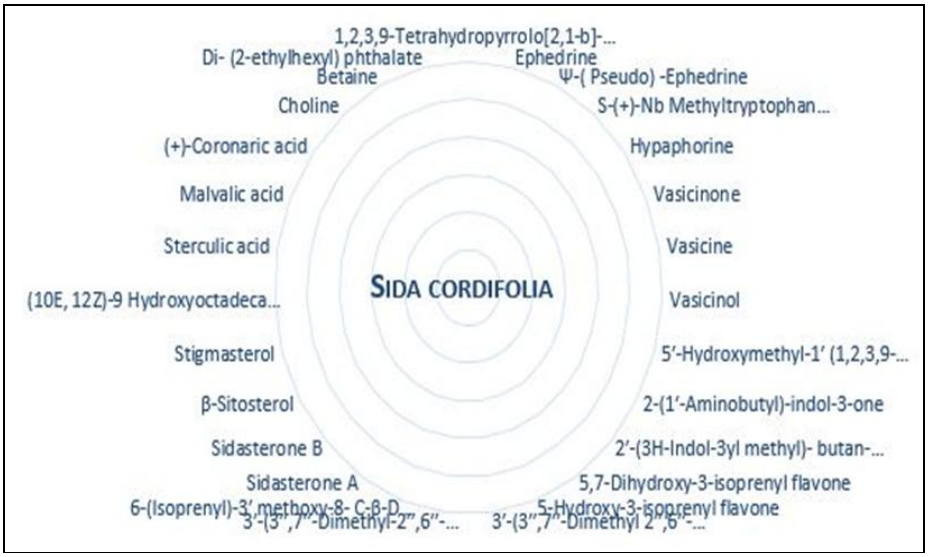


FIG. 2: IMPORTANT CHEMICAL CONSTITUENTS ISOLATED FROM *SIDA CORDIFOLIA* EXTRACTS

TABLE 2: PHYTOCONSTITUENTS OF DIFFERENT PARTS OF "*SIDA CORDIFOLIA*" PLANT WITH % ALKALOIDS

Plant parts	Phytoconstituents	Alkaloids percents
Whole parts (include leaves, stems, seeds and roots	Large amount of ephedrine	Extend of 0.085 %
Seeds	Sterculic, malvalic and coronary acid along with other fatty acids	0.32 %
Leaves	Ephedrine, pseudoephedrine	0.28 %
Stems	Ephedrine	0.22 %
Roots	Ephedrine, saponins, choline pseudoephedrine, beta-phenethylamine, vasicine, hypaphorine, ecdysterone and related indole alkaloids	0.06 %
Aerial parts	Ephedrine, pseudoephedrine, Palmitic, stearic and β – sitosterol, hexacosanoic acids, 6-phenyl ethyl amine, carboxylatedtryptomines, quinazoline, hypaphorine, vasicinol	0.31 %

HPLC Analysis: The presence of two bioactive compounds, vasicine and vasicinone, was confirmed in methanolic root extracts (10% w/v) of *Sida cordifolia*, by using high performance liquid chromatography (HPLC) method [12].

Pharmacological Properties:

Antimicrobial Activity: An antimicrobial evaluation has been done by using different extracts of *Sida cordifolia* against bacteria and fungi by disc diffusion method. Dimethyl sulphoxide (DMSO), the solvent control, showed no effect against the tested bacteria and fungi. On the other hand, the aqueous extract showed the highest inhibitory activity compared to other extracts [13 14]. Ethanolic leaf extract showed significant activity than methanolic extract with a zone of inhibition 9.5 mm for *Klebsiella*

pneumonia and 11 mm for *Pseudomonas aeruginosa* at 75 ml/disc concentration [15]. An antimicrobial evaluation has been done among five medicinal plants against *Bacillus subtilis* and *Staphylococcus aureus*. *Sida cordifolia* showed the highest antibacterial activity among them and the highest antifungal activity for *Fusarium verticillioides* [16]. The anti-microbial activity of the oil, obtained from *Sida cordifolia* seeds, has been evaluated against *E. coli*, *Staphylococcus aureus*, *Candida albicans*, and *Aspergillus niger* by using cup-plate method and the property was comparable with standard drug norfloxacin and griseofulvin disc [17, 18].

The antibacterial activities of methanol, ethanol and acetone extract of *Sida cordifolia* was evaluated by using agar well diffusion method against four bacterial pathogens, among which three were gram-negative (*Escherichia coli, Pseudomonas aeruginosa, E. faecalis)* and one was gram-positive (*Staphylococcus aureus*). The result obtained that *Sida cordifolia* showed potent antibacterial activity against designated bacterial pathogens, where methanol extract of this medicinal plant exhibit greater inhibitory effect over the microorganisms [44].

The ethanol leaves extract of *Sida cordifolia* exhibited good antibacterial activity, against *Staphylococcus aureus, Bacillus subtillus, Escherichia coli* and *Pseudomonas aeruginosa* by using cup plate method, with zone of inhibition ranging between 10 mm to 16 mm at concentration of 5 mg/mL, 10 mg/mL, 15 mg/mL and 20 mg/mL. The MIC and MBC results indicated that ethanol extract is both bacteriostatic and bactericidal on the test organisms at a concentration of 6.250 mg/mL. On the other hand, the petroleum ether fraction did not show activity on the test organisms[45]. Ethyl acetate roots extract of *Sida cordifolia* showed significant antibacterial activity against two Gram-positive (*Staphylococcus aureus* MTCC 96, *Klebsiella pneumonia* MTCC 109) and two Gram-negative (*Escherichia coli* MTCC 1303, *Pseudomonas aeruginosa* MTCC 2453) bacteria, where Chloramphenicol used as standard [46].

Anti-Inflammatory and Analgesic Activity: Aqueous extract of *Sida cordifolia* showed anti-inflammatory, analgesic, and acute toxicity effects in rats and also increased the latency period of mice in the hot plate method. Also, at the oral dose of 400 mg/kg, the aqueous extract inhibited several writhes produced by acetic acid [19]. Ethanolic extract of *Sida cordifolia* L. showed acute inflammatory activity at doses of 100mg/kg (48.83% inhibition) and for 200 mg/kg (53.48% inhibition) was observed. The capability of inhibiting the increasing number of fibroblast and synthesis of collagen and mucopolysaccharides in the course of granuloma tissue formation indicates the efficiency of anti-inflammatory agents in sub-acute inflammatory states. Ethanolic extract of *Sida cordifolia* L. showed significant ($p<0.05$) anti-inflammatory activity by decreasing granulomatous tissue in cotton pellet granuloma method and hence found to be effective in sub-acute inflammatory conditions [20, 21].

Petroleum ether extract of the seeds of *Sida cordifolia* was screened for acute toxicity test in albino mice to establish an effective dose. It is concluded that at an oral dose of 400 mg/kg body weight in the form of suspension by triturating with water and 0.5% gum acacia CMC, the seed extract significantly ($p<0.01$) reduced carrageenan-induced paw edema at 0, 30, 60, 180, 300 min in comparison with the control group and standard drug diclofenac sodium. Which means the test sample may act in both early and late phase of carrageenan-induced acute inflammation [18].

Cyclooxygenase and lipoxygenase are the indicators of inflammatory responses which were increased in the quinolinic acid-treated rats, and this was reduced upon administration of the ethanolic extract of the roots of *Sida cordifolia* and the standard drug Deprenyl [23]. Aqueous leaves extract of *Sida cordifolia* showed most significant anti-inflammatory activity even at the dose of 10 µg/ml than other medicinal plants such as- *Malva sylvestris* and *Pelargonium graveolens* [24]. A new alkaloid (5' - hydroxymethyl -1'- (1, 2, 3, 9 - tetrahydro - pyrrolo) [2, 1- b] quinazoline -1- yl) - heptan - 1 - one), was isolated from *Sida cordifolia* and was investigated its analgesic and anti-inflammatory properties in rats. Acetic acid induced writhing inhibition method helped to determine the analgesic activity, and the result exhibited a significant reduction. The anti-inflammatory activity was experimented using

carrageenan-induced rat paw edema, and the alkaloid showed significant ($p<0.01$) activity. These results specified that possessed analgesic and anti-inflammatory activities [36]. Aqueous extracts of *Sida cordifolia* was administered intraperitoneally at a dose of 6 mg/kg for 14 days. It was analyzed for analgesic properties using acetic acid-induced writhing in mice. The extracts produced significant inhibition due to the use of acetic acid. Similarly, for formalin-induced nociception the extracts of *Sida cordifolia* produced higher inhibition [37].

Anti-Ulcer Activity: Antiulcer activity of *Sida cordifolia* Linn extracts had been experimented by inducing ulcer using aspirin, aspirin plus pylorus ligation, and ethanol treatment in 36 h fasted albino rats. The result showed that the extract had significant antiulcer activity against different ulcer-causing agents in all the three experimental models [25]. The methanolic extracts of *Sida cordifolia* (MESC) possessed the anti-pyretic and anti-ulcerogenic properties in rats [26].

Anti-Diabetic Activity: Aerial and roots extracts of *Sida cordifolia* possessed hypoglycemic, analgesic, and anti-inflammatory activities [27]. Alcoholic extract of *Sida cordifolia* at a dose of 200 and 400 mg/kg possessed hypoglycemic, anti-hyperlipidemic, and antioxidant activities. In streptozotocin-induced diabetes rats (55 mg/kg) *Sida cordifolia* (400 mg/kg) extracts showed significant reduction of the blood glucose level as well as the reduction in total cholesterol, triglycerides, low-density lipid, plasma-creatine, and plasma-urea nitrogen. A significant increase in antioxidant enzymes such as catalase and superoxide-dismutase was reported [28].

Nephroprotective Activity: Both ethanolic and aqueous extracts of *Sida cordifolia* L. possessed nephroprotective activity in comparison with gentamicin. *Sida cordifolia* might have demonstrated nephroprotective activity due to potent antioxidant activity [29]. Aqueous extract of *Sida cordifolia* exhibited nephroprotective activity at a dose level of 200 mg/kg and 400 mg/kg in comparison with gentamycin 100 mg/kg and cisplastin 7mg/kg. The presence of flavonoids and phenols in *Sida cordifolia* might be contributed for antioxidant potentiality that exhibits nephroprotective activity [30].

Cytotoxicity: The extract of *Sida cordifolia* plant exhibited a cytotoxic effect on HeLa cell lines. The result showed that cells with uncontrolled growth had been arrested by the extract of *Sida cordifolia*, and there is a decline level of cancerous cells [31].

Anti - hypercholesterolemia Activity: The methanol and ethanol extracts of *Sida cordifolia* at a dose level of 500, 750, and 1000 mg/kg were administered orally to streptozocin-induced diabetic rats. The result showed that the level of cholesterol, triglyceride, LDL, and VDL were decreased significantly in the rats which were treated with the extract (1000 mg/kg), along with that the level of HDL was increased by the treatment with the extract of *Sida cordifolia*. The alkaloids and flavonoids present in the extract may be contributed in the inhibition of the pathway of cholesterol synthesis and activates LDL receptors of hepatocyte, which is responsible for the uptake of LDL into the liver [32]. Alcoholic extract of *Sida cordifolia* at a dose of 200 and 400 mg/kg showed a significant reduction in total cholesterol, triglycerides, low-density lipid, plasma-creatine, and plasma-urea nitrogen [28].

Hepatoprotective: Powdered roots, aerial parts and their extracts of *Sida cordifolia* showed hepatoprotective activity against carbon tetrachloride, paracetamol, and rifampicin-induced hepatotoxic rats. It was reported that significant hepatoprotective activity had been shown by the powdered aerial and root parts against carbon tetrachloride followed by methanolic and aqueous extracts [33]. The leaf extracts of *Sida cordifolia* possessed the capability of regenerating the liver cells [34]. 50% ethanolic extract of the roots of *Sida cordifolia* L possessed the hepatoprotective activity against alcohol intoxication. Alcohol-induced toxicity is facilitated through oxidative stress; then it can be supervised by detecting lipid peroxidation products. After administration of ethanolic extracts of *Sida cordifolia* in rats, Malondialdehyde, hydroperoxides and conjugated dienes were significantly reduced in liver and protein carbonyls in the serum which were observed in the rats. Although the mRNA level of cytochrome P450 2E1, NF-KB, TNF-α and transforming growth factor-β were found to be increased in the alcohol treated rats, their expressions were found to be decreased in the *S. cordifolia* extracts treated rats[35].

Anti-stress and Adaptogenic Activity: The extracts of *Sida cordifolia* Linn. were prepared and administered orally in rats. Ashwagandha, which was used as reference standard antistress drug, was used in water-soluble powder form. The result showed that *Sida cordifolia* extracts reduced plasma cortisol level along with blood glucose[38].

Cardiovascular Activity: The hydroalcoholic extract of *Sida cordifolia* possessed cardiovascular activity at a dose of 5, 10, 20, 30, and 40 mg/kg in normotensive non-anesthetized rats. It might be due to subsidiary cardiac muscarinic activation as well as direct activation of endothelial vascular muscarinic receptors by using atropine (2mg/kg) [39]. It was concluded that administration of hydroalcoholic extract of *Sida cordifolia* (HESC) at a dose of 500 mg/kg has cardioprotective potential[40]. Myocardial infarction (MI) was induced by isoprotenolol or by ischemia-reperfusion injury (IRI) in the Albino rats and rats were administered with *Sida cordifolia* extracts at the doses of 100 and 500 mg/kg and propranolol at a dose of 10 mg/kg to evaluate the biochemical and antioxidant properties of the extract. The endogenous markers and antioxidant were assessed in serum/ perfusate and heart tissue homogenate. The activities of endogenous markers were raised in heart tissue homogenate and depleted in serum/ perfusate of *Sida cordifolia* extracts and propranolol[41].

Anticancer Activity: The ethanolic extracts of *Sida cordifolia* was administered orally against Aflatoxin B1 (AFB1) induced hepatocellular carcinoma (HCC) in Wistar rats at a dose of 250 and 500 mg/kg. The results exhibited a significant restoration of abnormal serum and tissues, indicating the protective effect [42]. Cryptolepine from *Sida cordifolia* induces growth arrest in MG63 cells through the p53-independent activation mediated through specific Sp1site in the promoter region. It points out the probability that treatment with cryptolepine can be used as chemotherapy for osteosarcoma [43].

Antimelanogenesis: Tyrosinase or phenol oxidase is a prime enzyme for melanin synthesis, a copper-containing monooxygenase. So that tyrosine inhibitors are the substances which lead to skin whitening by reducing or blocking melanin synthesis. The study discovered that the alcoholic extracts of *Sida cordifolia* could be used to develop a new antityrosinase inhibitor. However, more research is required to be done in isolating active constituent from *Sida cordifolia,* so that it can be practically used and are compatible with the safety food additive [47].

Anticandidal Activity: The results of the experiment showed a low immune stimulatory effect, and this can be happened due to the lack of biologically active antioxidants such as polyphenol compounds lowly contained in the alkaloid compounds. The results of this experiment showed that alkaloid compounds in combination with antifungal references such as nystatin and clotrimazole demonstrated antimicrobial effects against candida strains tested, besides the results also supported the utilization of these plants in infectious diseases especially in the treatment of candida infections [48].

Anti-Parkinson's Disease: Parkinson's disease Ayurveda treatment objects at balancing disturbed data where massage therapy, enema, medication methods are applied. *Sida cordifolia* is used as the prime herb in Parkinson's disease Ayurvedic treatment [49].

CNS Depressant: The hydroalcoholic extract of *Sida cordifolia* at a dose of 1000 mg/kg (i.p. and p.o.) produced sedation, decrease of the ambulation, reduction of answer to the touch, analgesia and decrease of urination same dose caused significant reduction ($P<0.001$) of the spontaneous locomotors activity in comparison with the control group at 30 and 60 min, besides did not cause a significant difference in the motor coordination of the treated animals in comparison with the control group. Along with that, the hydro alcoholic extract of *S. cordifolia* at a dose of 1000 mg/kg (i.p. or p.o.) did not produce a significant modification of the latency and the time of sleep of the reacted animals in comparison with those from control group [1]. Further research appears to confirm that *Sida cordifolia* does not stimulate the CNS [50].

Fat Loss: The oral administration of extract of *Sida cordifolia* in rats caused a reduction in both heart rate and blood pressure. If it was due to the stimulatory effect, then both heart rate and blood pressure would increase. Since, *Sida cordifolia*

missed the mark to increase CNS activity, it cannot promote fat loss through CNS stimulation [50]. In the present day numbers of companies are promoting *Sida cordifolia* for anti-obesity effect. In experts opinion anti-obesity effect is not limited to ephedrine content; other components may play a synergistic role. Further, chemical analysis exposes that seasonal variation of alkaloids in *Sida cordifolia* less in comparison with *Ephedra sp*. *Sida cordifolia*, maybe a worthwhile substitute to *Ephedra sp*.

Hypotensive: The effect of aqueous fraction of hydro alcoholic extract of *Sida cordifolia* induced hypotension and bradycardia on mean arterial pressure and heart rate had been evaluated in the non-anesthetized rat. Administration of atropine eliminate the aqueous fraction of hydroalcoholic extract of *Sida cordifolia* induced hypotensive and bradycardic responses. Administration of hexa methonium potentiates significantly the hypotensive response and significantly attenuate the bradycardic response. The administration of hexamethonium significantly attenuates the same extraction induced a hypotensive response, on the other hand, did not affect the bradycardic response [50, 51].

Ultrastructure: It was observed that air pollution caused by air pollutants like SO_2, O_3 and CO_2 showed marked modifications in photosynthetic pigments (chlorophyll, carotenoid, & phaeophytin), and relative water content was decreased, in spite of the fact anti-oxidative enzymes like catalase and peroxidase were found to be enriched. Plants growing in the urban locations arrange for a great respite to us from the brunt of auto pollution by captivating the pollutants at their foliar surface. Foliar surface structure and biochemical alterations in plant species, namely, *Sida cordifolia* L. The experiments have revealed that modifications in epidermal traits, with reduced number of stomata, stomata indices, and epidermal cells per unit area can be solved while length and breadth of stomata and epidermal cells were found to be greater than before in leaves samples which can be used as biomarkers of auto pollution [52].

Antioxidant Activity: The antioxidant activities of ethanol and aqueous extract of the whole plant of *Sida cordifolia* Linn. are evaluated by various antioxidant assays like α, α-Diphenyl-β-picrylhydrazyl (DPPH) free radical scavenging, total reducing power, nitric oxide scavenging and hydrogen peroxide scavenging in comparison with the standard antioxidants such as ascorbic acid. In case of antioxidant activity, due to the presence of various phytoconstituents such as alkaloid (asparagine, ephedrine, vas-cicinone, vascinol, pseudoephedrine), flavonoids (5,7- dihydroxy-3-isoprenyl flavone and 5-hydroxy-3-iso- prenyl flavone) and phenolic compounds ethanolic extract was more significant than aqueous extract [53 54].

Antioxidant capability noticed that the reduction capability of DPPH radicals obtained the greatest result in comparison with the other methods of free radical scavenging [48]. The results of the ABTS assay showed that the ethanolic extract of *Sida cordifolia* was found to be most potent (IC50 16.07 mg/ml) than other experimental plants. The result of the relative antioxidant capacity for the water infusions was observed for *Sida cordifolia* (IC_{50} 342.82 mg/ml), and the results of water infusions of the plants on lipid peroxidation were *Sida cordifolia* IC50 126.78 mg/ml [55]. The *in-vivo* antioxidant activity of aqueous extract of *Sida cordifolia* using d-ROMs and ROS tests and by phosphomolybdate methods recommends that this plant is an effective and significant antioxidant, where either acute or chronic stress is produced by introducing potassium dichromate [56].

The methanolic root extract of *Sida cordifolia* can be a good source of polyphenols, which also demonstrated the highest antioxidant activity among the eight selected *Sida species* [57]. The ethanolic extract of *Sida cordifolia* (SAE) most likely stimulates its antioxidant potential by decreasing oxidative stress, enhancing the translocation of Nrf_2 to the nucleus and thus regulating glutathione metabolism, leading to enhanced GSH content [58]. In the presence of sunlight, *Sida cordifolia* leaf extract was successfully used to synthesize stable AgNPs. UV–vis spectroscopy, Fourier Transform Infrared spectroscopy (FTIR), Transmission Electron Microscope (TEM), Scanning Electron Microscope (SEM) was used to confirm the formation of biosynthesized AgNPs. Significantly, the biofunctionalized AgNPs showed remarkable antioxidant and anticancer activities [59].

CONCLUSION: The literature review of *Sida cordifolia* represents that it has extensive pharmacological properties which effectively perform to treat several disorders. The extracts from different solvents had successfully identified the exertion of different therapeutic purposes including anti-inflammatory, anti-ulcer, anti-diabetic, nephroprotective, cytotoxicity, anti-hyper-cholesterolemia, hepatoprotective, analgesic, antistress and adaptogenic activity, cardiovascular, anticancer, anti-bacterial, anti-melanogenesis, anti-candicidal activity, anti-Parkinson's disease, CNS depressant, fat loss, hypotensive, ultrastructure and antioxidant activity. The study demonstrated on its phytochemistry, and various biological properties of the extracts and constituents might provide incentive for proper evaluation of the use of the plant in medicine.

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