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A REVIEW OF SIDA CORDIFOLIA A TRADITIONAL HERB FROM A CONTEMPORARY PERSPECTIVE

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ABSTRACT

In India, China, Brazil, and other nations, *Sida cordifolia* is used in traditional medicine for a variety of conditions, such as bronchitis, asthma, nasal congestion, oral mucosal inflammation, rheumatism, neurological illnesses, chronic dysentery, and gonorrhea. It is also utilized as a hypoglycemic agent and has antiviral, analgesic, antipyretic, laxative, diuretic, and aphrodisiac qualities. To confirm the presence or absence of ephedrine and cryptolepine in the species of *Sida*, extensive studies involving various *Sida* species and a large number of samples obtained from various geographical regions and at different plant growth stages are warranted. Sida cordifolia has a strong bronchodilator called vasicinone, which may support its use in Ayurvedic medicine for ailments that are comparable to those that ephedrine treats. Although *S. cordifolia* has not been linked to any toxicity, the existence of alkaloids including vasicine-type alkaloids and cryptolepine, which have not yet undergone a thorough evaluation, raises questions regarding its potential toxicity and safety.

Keywords: *Sida Cordifolia,* Traditional Medicine, Ayurvedic Medicine, Alkaloids.

I. INTRODUCTION

Herbal remedies are used all around the world. It is a medication made entirely of plant components, including leaves, stems, roots, flowers, seeds, and more. Herbal medicine is sometimes referred to as phytomedicine or botanical medicine. According to WHO data, 80% of the population presently uses herbal medications for some form of primary healthcare. Herbal remedies are typically regarded as effective and safe treatments. Because they have fewer adverse effects, individuals choose herbal remedies over allopathic ones. Herbal remedies have been utilized in India since the Vedic era, as recorded in the Rig-Veda and referenced in the Charaka Samhita. In India, herbal remedies from Ayurveda, Siddha, the Homoeopathic system, and Unani are utilized. One excellent source of medicinal herbs is India. In India, 8,000 herbal treatments are arranged according to AYUSH systems. Herbal remedies are employed in India's Ayurvedic, Siddha, Unani, and homeopathic medical systems. The Department of AYUSH, ICMR, and CSIR collaborate to create novel medications and safe and efficient AYUSH products for ailments that may be identified. The AYUSH department established a certification program for AYUSH pharmaceuticals. India creates guidelines for conducting herbal medicine clinical trials, however, the registration procedure is not adequately controlled. (1)

PLANT PROFILE

Classification

Kingdom Plantae
Phylum Tracheophyta
Class Equisetopsida
Order Malvales
Family Malvaceae
Genus *Sida*.
Species *cordifolia* (2)

Common Names

Assamese Boriala, Son-borial
English Bala, Country Mallow
Kannada Benne garage, Cittuharalu, Hethuthi
Malayalam Anakurunthoti, Kattooram, Kurunthotti
Tamil Arivalmanaippundu, Arivalmukkan

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Telugu Chirubenda, Muttavapulagamu, Suvarnam (2)

Synonyms: *Sida herbacea; S. holosericea; S. hongkongensis; S. rotundifolia.* (3)

Description

Sida species can be shrubs, under shrubs, perennial herbs, or annuals. Stems procumbent or upright, pubescent with glandular and stellate hairs, or glabrous. Simple, seldom lobed, lanceolate-ovate to obovate-elliptic, with a base that is obtuse to cuneate, margins that are whole, serrate-dentate or lobed, and an apex that is acute to acuminate, petiolate, and stipulate, the leaves alternating. By reducing the top leaves, the inflorescence often consists of axillary single, paired, or terminal panicles or racemes. Bisexual flowers with a thin pedicel that is joined above the center, an epicalyx that is missing, a calyx that is five-lobed or serrated, campanulate or cupular, and a corolla that is showy, yellow, cream white, base connate, and adnate to the stamina column are typically plicate in bud. Shorter than petals, glabrous or hairy, with basifixed anthers, the staminal column points toward the apex. Stigma capitate, ovules 1 per locule, style 1 per carpel, and ovary 5–14 carpellate. Fruit is schizocarp, oblate or discoid, minutely pubescent or glabrous, reniform, smooth or reticulate, minutely stellate pubescent, and indehiscent or partially dehiscent by the central dorsal line, and infrequently by the lateral or basal walls when dry. One seed, ovoid to reniform, glabrous or minutely hairy, is present in each mericarp. (2)

Distribution

Sida is distributed in Africa, Australasia, North America, South America, Bhutan, China, India, Indonesia, Nepal, Pakistan, the Philippines, Sri Lanka, Taiwan, and Thailand. Arunachal Pradesh, Assam, Bihar, Delhi, Goa, Daman Diu, Gujarat, Himachal Pradesh, Jammu & Kashmir, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Manipur, Meghalaya, Rajasthan, Tamil Nadu, Tripura, Uttar Pradesh, Uttarakhand, and West Bengal are among the Indian states where it is locally distributed. (2)

Traditional uses

S. cordifolia, often known as "bala," has been used extensively since ancient times and is regarded as one of the most beneficial medications in Ayurvedic medicine in India. The roots, leaves, and stems are used as traditional remedies for asthma, gonorrhea, and chronic dysentery. Additionally, it is used to treat neurological illnesses including Parkinson's disease, induce or increase aphrodisia, and treat piles. S. cordifolia roots are used as a treatment for urinary problems and neurological conditions like facial paralysis and hemiplegia.The root bark is used as an antiviral, diuretic, astringent, bitter, tonic, stomachic, demulcent, and aromatic agent. S. cordifolia seeds have long been used as an aphrodisiac and are also recommended for the treatment of tenesumus, piles, colic, gonorrhea, and cystitis. (3)

Phytochemistry

In addition to the bases choline and betaine present in the water-soluble alkaloid fraction, the roots of S. cordifolia provided β-phenethylamines, carboxylated tryptamines, (S)-(+)-Nb-methyltryptophan methyl ester, hypaphorine, and quinazoline alkaloids, vasicine, vasicinone, and vasicinol. Ephedrine has been identified in S. cordifolia and related species. S. cordifolia roots that were six months old mostly generated quinazoline alkaloids.

The main constituents of two-year-old roots were carboxylated tryptamines. Nonetheless, it was noted that as this plant ages, its alkaloid content decreases. From the aerial portions of S. cordifolia, another quinazoline alkaloid was identified as 5`-hydroxymethyl-1`-(1,2,3,9-tetrahydro-pyrrolo [2, 1-b] quinazoline-1-yl)-hepta-1-one). Cryptolepine, a well-known indoloquinoline alkaloid, was recently identified from S. cordifolia and may be a component of this plant.

The aerial portions of S. cordifolia were used to isolate 5,7-dihydroxy-3-isoprenyl flavones and 5-hydroxy-3-isoprenyl flavones, as well as 3`-(3``,7``-dimethyl-2``,6``-octadiene) - -8-C-β-D-glucosyl-kaempferol 3-O-β-D-glucoside. Following more research, three flavonol C-glycosides were identified from the same source. These include 3′-(3′′,7′′-dimethyl-2′′,6′′-octadiene)-8-C-β-Dglucosyl-kaempferol 3-O-β-D-glucosyl [1→4]-αD-glucoside, 6-(3′′-methyl-2′′-butene)-3′-methoxy-8-C-β-D-glucosyl-kaempferol 3-O-β-D-glucosyl [1→4]-β-D-glucoside.

Oil, β-sitosterol, stigmasterol, epoxy, and cyclopropenoid fatty acid are found in S. cordifolia seeds. Malvalic and sterculic acids were the primary compounds found in S. cordifolia oil, together with coronaric acid and other

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fatty acids (C14:0, C15:0, C18:0, C18:1, C18:2, C18:3). There were no trans-unsaturated lipids. A hydroxyl unsaturated fatty acid was isolated from the MeOH extract of S. cordifolia by bioassay-directed fractionation; (10E, 12Z) (9-hydroxyoctadeca-10,12-dienoic acid). (3)

Reported activities

Aerial parts of Sida cordifolia were serially extracted using Soxhlet equipment. The DPPH, H2O2, and NO radical scavenging abilities were used to assess the in vitro antioxidant capacity. Human breast cancer (MCF7), ovarian cancer (PA1), colon cancer (HT29), melanoma (A375), liver cancer (HepG2), and normal mouse embryonic fibroblast (NIH3T3) cell lines were treated with increasing concentrations of the extract for 24 hours to evaluate the extract's antiproliferative activities using the MTT test. The ethanolic extract demonstrated good DPPH, H2O2, and NO radical scavenging activity (IC50 values of 20.93µg/mL, 85.14µg/mL, and 320.99µg/mL, respectively). Additionally, the extract demonstrated dose-dependent cytotoxicity against every cancer cell line employed in the investigation. The sensitivity of A375 and HT29 was higher than that of the other cancer cell lines (IC50 values of 16.51 and 49.86µg/mL, respectively). (4)

The plant's aerial parts were extracted hot and continuously using a Soxhlet device and ethanol as a solvent. The MTT test was used to evaluate the extract's cytotoxicity in a variety of cancer cell lines, including those from breast, ovarian, colon, skin, and liver cancer. Every cell line IC50 value was determined. Melanoma cells were exposed to 12.5 and 25 µg/ml extract to investigate the extract's mechanism of anticancer action. The outcomes were compared with the control. DNA laddering analysis was done using gel electrophoresis. Using SDS-PAGE, the expression of proteins from the TP53, Bcl, and Caspase gene families was identified. Using the JC-1 kit, the potential of the mitochondrial membrane was examined. A flow cytometer was used to analyze the cell cycle. ANNOVA was used for statistical analysis, while Tucky post hoc analysis was used to further examine significant data. Statistical significance was defined as a P value of less than 0.05. With an IC50 value of 16.51µg/ml, the MTT experiment demonstrated the extract's highest cytotoxicity against melanoma. When the extract was applied to melanoma cells, dose-dependent DNA laddering was seen. Additionally, the extract showed a dose-dependent rise in the levels of the proteins p53, caspase 3, caspase 9, and bax. There was a considerable decrease in Bcl2 protein expression. The extract significantly reduced the mitochondrial membrane potential of melanoma cells. The number of melanoma cells in subG_0 and G2/S was noticeably higher. Based on these findings, it may be deduced that S. cordifolia ethanol extract is cytotoxic to melanoma cells. It works by using an internal mechanism to trigger apoptosis. Additionally, melanoma cells in the G2/M phase are arrested by the extract. (5)

Using spectroscopic analysis and phytochemistry, the ethanolic extract of Sida cordifolia was examined for 5,7-dihydroxy-3-isoprenyl flavone and 3'-(3``,7``-dimethyl-2``,6``-octadiene)-8-C-β-D-glucosyl-kaempferol-3-O-β-D-glucoside. Using the Disc Diffusion Method, the antibacterial activity of the plant extract (zone of inhibition in mm) was investigated. The ethanolic extract contains bioactive compounds susceptible to V. cholera, according to preliminary experiments. These compounds are more than the ciprofloxacin, norfloxacin, and ofloxacin prescribed for cholera patients, and their susceptible zone size is comparable to that of the antibiotics Tetracycline, Doxycycline, and Azithromycin. (6)

The roots of Sida cordifolia were successively extracted using hexane, chloroform, methanol, and water. Through a series of tests measuring the reactions of macrophages, splenocytes, and an in vivo model of innate immunity (Galleria mellonella), immunomodulatory activity was found. By calculating the minimum inhibitory/bactericidal concentrations (MIC/MBCs) for different strains of both Gram-positive and Gram-negative bacteria, antibacterial activity was evaluated. The aqueous extract was shown to have immunomodulatory activity, and further fractionation and biochemical analysis produced a very effective polysaccharide-enriched fraction (SCAF5). Immune cell proliferation, antibody secretion, phagocytosis, nitric oxide generation, and elevated expression of pro-inflammatory cytokines are only a few of the immunomodulatory effects of SCAF5, a complex combination of several polysaccharides. In addition, Galleria mellonella pre-treated with SCAF5 had a 98% decrease in bacterial load in pre-treated larvae as compared to the negative control, and they generated more hemoglobin and were more resistant ($P<0.001$) to infection with methicillin-resistant Staphylococcus aureus (MRSA). The methanolic fraction of Sida cordifolia was shown to have antimicrobial properties. Two molecules, rosmarinic acid, and its 4-O-β-d-glucoside derivative, were identified by extensive fractionation to have strong anti-gram-positive antibiotic-resistant bacteria, including

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MRSA. Sida cordifolia fights bacterial infections in two ways. To fully realize its potential as an anti-infective drug, immunomodulatory polysaccharides from this plant need to be separated and characterized. For example, qualities might be created as a substitute for antibiotics in the medical setting and as a different growth stimulant for the agricultural-food sector. (7)

When the ethanolic extract of S. cordifolia was subjected to GC-MS analysis, methyl 5-methylimidazolidine-2,4-dione (5R), 2-hydroxybenzoate, 4-methylbenzaldehyde, and methyl (2S)2-carboxylate-5-oxopyrrolidine, It is also known as 1,3-dimethyl-1,2,3,4-tetrahydropyrimidine-2,4-dione, 1-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione, or 2-(3,4-dimethoxyphenyl)ethan-1-ol, 3-hydroxybenzohydrazide, 2-methyl-3H-pyrimidine-2,4-dione, and 2,4-di-tert-butylphenol (or) (2R,6S) 2-(3,4-dimethoxyphenyl)ethanol(2E)-N-[1-(dimethylcarbamoyl)propyl], -2,6-dimethylcyclohexan-1-oneThe compound N-propylbut-2-enamide Butan-2-one, 5-(2,6,6-trimethylcyclohex-1-en-1-yl), and 5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)3-(pyrrolidin-2-yl)propanoic acid, decan-3-one, 3-[(3E,7E)-3,7-dimethyl-9-(phenylsulfanyl)nona-3,7-dien-1-yl](3S) -2,2-dimethyloxirane3,5-diazatricyclo, 3-acetyl-6-methyl-3,4-dihydro-2H-pyran-2,4-dione[7.4.0.0^{2,6}]3,7,9,11-hexaene, 4-[(1E)-3-hydroxy prop-1-en-1-yl], trideca-1(13),2(6)-2-methoxyphenol, 1,7-dimethyl-6,7-dihydro-1H-purin-6-one (also known as 1,7-dimethylpurin-6-one), and 1-ethyl-N,2-dimethyl-N-phenyl-1H-1,3-benzodiazole-5-carmoxamide. The glide scoring function, which is frequently used to screen compounds from virtual screening, approximates the ligand binding free energy.

The ligand 15 [3-[(3E,7E)-3,7-dimethyl-9-(phenyl sulfanyl) nona-3,7-dien-1-yl]-2,2-dimethyloxirane] was shown to be effective in binding to BCL2, according to the glide scoring. Similarly, VEGFR2 was effectively bound by ligand 6 [1-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (or 1-methyl-3Hpyrimidine-2,4-dione). (8)

In mouse models, the aqueous leaf extract of S. cordifolia was tested for acute toxicity and antimalarial qualities. The plant's aqueous extract was tested for its ability to control and cure malaria in rodent Plasmodium berghei-infected mice with chloroquine-sensitive ANKA strains. Rats were used to evaluate acute toxicity by OECD 425 standards. In suppressive and curative trials, the extract's ED50 values were 117.49 ± 15.22 mg/kg and 144.84 ± 18.17 mg/kg, respectively, indicating anti-plasmodial action in vivo. In the suppressive and curative investigations, the maximum percentage of parasitemia suppression was 76.90 ± 0.64% and 61.50 ± 0.97%, respectively. The extract significantly extended the survival of sick mice. This was partially correlated with the percentage of parasitemia reduction; however, it was reliant on the extract's dosage. Related antimalarial metrics, such as the experimental mice's temperature, body weight changes, and % hematocrit, showed that the treated animals' malarial symptoms had subsided. Rats did not exhibit any toxicity from the extract. Sida cordifolia is harmless and contains antimalarial qualities. It extended the lives of diseased animals receiving therapy, was non-toxic to animals, and lowered parasitemia in both suppressive and curative experiments. (9)

The LC-MS/MS study of three Sida cordifolia tissues showed that procyanidin and acacetin are two significant metabolites that have been shown to contribute to the plant's therapeutic usefulness. The biosynthesis of phenylpropanoid and flavonoid compounds depends on several essential enzymes, including phenylalanine ammonia lyase, which may be a significant rate-limiting enzyme. Phenylalanine ammonia-lyase (PAL), cinnamonyl alcohol dehydrogenase 1 (CAD), cinnamonoyl-CoA reductase 1 (CF1), and transcinnamate 4-monooxygenase (TCM) were among the enzymes identified by Real-Time Quantitative Reverse Transcription Polymerase Chain Reaction (qRT-PCR) analysis as being primarily expressed in root tissue as opposed to leaf and stem tissue. In Sida cordifolia, the work offers a theoretical understanding of metabolic engineering and active metabolite screening. (10)

Sida cordifolia aqueous extract and 5-fluorouracil impact on colon carcinogenesis brought on by 1,2-dimethylhydrazine (1,2-DMH). The frequency of aberrant crypts was decreased by the extract in comparison to the positive control, but there was no discernible difference between the mice receiving the extract, the conventional anticancer medication, and the positive control. Therefore, in animal models, the aqueous extract of Sida cordifolia 800 mg/kg had no statistically significant effect on carcinogenesis, but it had a notable anti-inflammatory effect on the mucosa of the colon. (11)

The study's goal was to evaluate the spermatogenesis effect of an aqueous extract of S. cordifolia roots in clinical trials. Through placebo-controlled clinical trials on males with low sexual desire and an unsatisfactory sexual life, the study evaluates the therapeutic efficacy of research formulation using qualitative criteria like primary

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and secondary symptoms and quantitative investigations like hematological investigations, hormonal analysis, and semen analysis. Primary symptoms including low libido, trouble ejaculating, or little semen, as well as secondary symptoms like headache, nausea, body aches, indigestion, appetite loss, and overall weakness, were found to be extremely inhibited in the research group. The non-toxic character of the research formulation is shown by the absence of any negative changes in the biochemical parameters (bilirubin, protein, SGPT, SGOT, and ALP) and hematological parameters (blood sugar, hemoglobin, ESR, RBC, and WBC). During the clinical investigation, the research group's hormone levels significantly increased, particularly the testosterone level (8.53%). Sperm count, motility, and morphology measurements of semen quality revealed a notable improvement in the research group, indicating that the use of the research drug in stress-related sexual problems protected healthy cells by lowering ROS generation and assisted in maintaining spermatozoa quality parameters during spermatogenesis. By inhibiting primary and secondary symptoms and improving hormonal and seminal parameters, the research formulation derived from S. cordifolia roots demonstrates good and significant therapeutic efficacy, validating its spermatogenesis effect without any harmful or toxic side effects. (12)

Using transfer latency (TL) and step-down latency (SDL) tests, the nootropic effect of Sida cordifolia aqueous and hydroethanolic extracts (AESC and EESC, respectively) was examined in mice. Different groups received varying dosages of AESC and EESC (50, 100, and 250 mg/kg; p.o.) for 15 days in a row, along with the conventional medication (donepezil; 5 mg/kg). On the sixteenth day, TL and SDL tests were administered to them. When compared to the control group, EESC dose-dependently raised the SDL and lowered the TL in mice; this effect was similar to that of the conventional medication. After receiving AESC at different doses, no discernible change in TL or SDL was seen. These results indicate to the nootropic effect of EESC and forecast its potential use in the management of illnesses like Alzheimer's disease that are linked to memory loss. (13)

Patients frequently experience joint discomfort brought on by arthritis. The purpose of this study was to determine the effectiveness of a decoction of Sittamatti (Bala-Sida cordifolia Linn) as an anupanam (drug vehicle). Within three months, a control clinical investigation examined the treatment's impact by determining if there was a substantial reduction in arthritis symptoms. This study combines qualitative analysis with a clinical control study.

The first steps involve selecting 60 samples and preparing our new research medication at the same time. Data gathering and monitoring of the study drug's effect progressed after that. Lastly, it was examined using tables, charts, and statistical methods. Based on the results of the charts and tables, each table provided an explanation of the several perspectives used to gather the data and observations at the total of numbers and percentage level. In the research sample population, 40% of the samples are female and 60% are male. Out of the entire research outcomes, 73.3% indicate a very marked improvement and 26.6% indicate a moderate improvement. Thus, medicine with anupanam (Group-I) is superior to medicine without anupanam (Group-II). Clinical effectiveness is higher for Vatha Gajendra Singhe Rasa with Sida decoction and Mudakku Chooranam with Sida decoction therapy than for Vatha Gajendra Singhe Rasa without Sida decoction and Mudakku Chooranam without Sida decoction treatment. According to the statistical findings, the difference between sample groups I and II within three months of therapy was 0.0001. Ultimately, we found that our medication-assisted vehicle was considerably more successful in reducing joint condition symptoms than the medication-controlled Group II. Within three months, all symptoms of arthritis, including joint pain, soreness, mobility restriction, and edema, were reported to have decreased. (14)

The purpose of the study was to evaluate how Sida cordifolia leaf aqueous extract, affected liver regeneration. The Sida100 group's hepatocyte regeneration index was noticeably higher than that of the control group and every other group. Additionally, compared to the control group, it revealed a statistically significant increase in regeneration rate. Following several investigations, the impact of a few regulatory elements that initiate or govern the liver regeneration phenomena on hepatocyte proliferation was established. Using cultured rat hepatocytes and the gene expression pattern following partial hepatectomy, the processes behind this phenomenon have been clarified. Some of these compounds influence DNA synthesis either directly or indirectly. They are referred to, respectively, as mitogens and co-mitogens. Hepatocyte growth factor (HGF), acidic fibroblast growth factor (aFGF), transforming growth factor alpha, and epidermal growth factor (EGF) are the primary mitogens. Co-mitogens include immunosuppressive drugs, bradykinin, angiotensin-converting

enzyme inhibitors, vasopressin, angiotensin I and II, insulin, glucagon, estrogens, testosterone, norepinephrine and alpha-1 adrenoreceptors, tumor necrosis factor-alpha, prostaglandins, and hepatic stimulatory substance (HSS). Wistar rats were given the plant's alcoholic extract orally at doses of 150, 300, and 600 mg/kg. After that, a notable drop in glucose levels was seen. These results suggested that Sida cordifolia functions as a sulphonylurea, stimulating the release of insulin by pancreatic cells. (15)

In the petroleum ether extract of Sida cordifolia leaves, the fat and oil tested positive, but the ethanol extract included glycosides, tannins, alkaloids, flavonoids, carbohydrates, proteins, and polyphenols. Because the ethanol extract included flavonoids and polyphenols, it was chosen for more research. Ascorbic acid and ethanol extract both had IC50 values of 48.13 µg/ml and 92.84 µg/ml, respectively, for neutralizing the DPPH radical. It was discovered that ascorbic acid and ethanol extract have dose-dependent scavenging capabilities. Ethanol extract of Sida cordifolia has TPC and TFC of 74.61 mg/gm and 78.24 QE mg/gm, respectively. Column chromatography was used to test the Sida cordifolia ethanol extract, and the fractions were eluted using the gradient polarity of ethanol and ethyl acetate. In the TLC mobile phase solvent ratio of chloroform: methanol (1:1), column fractions 48–54 containing ethyl acetate: ethanol (80:20) had an Rf value of 0.46, which is equivalent to that of standard quercetin. The separated flavonoid may therefore be regarded as a quercetin compound. Animals in the control group saw a progressive improvement in local edema following the subplantar injection of carrageenan. Following the injection of the isolated flavonoid, a significant reduction in the rats' edema was noted. Also, indomethacin significantly decreased the rats' edema. Rats administered isolated flavonoids showed a significant reduction in the weight of both wet and dry cotton pellets. Rats given regular drugs had comparable outcomes. (16)

The purpose of the study is to examine the underlying mechanism and osteo-protective effect of S. cordifolia root and leaf ethanolic extracts (RE and LE). RE and LE antioxidant activity was measured. The total amount of flavonoids and phenols was measured. The polyphenol content of RE and LE was investigated using HPLC profiling. Primary calvarial osteoblast culture was used to assess the impact of RE and LE on osteoblast cell proliferation, differentiation, mineralization, and expression of the protein linked to osteogenesis. The effects of S. cordifolia RE and LE on the skeleton were examined in C57BL/6J ovariectomized mice. To assess the change in trabecular and cortical bone microarchitecture, micro-CT was utilized. The isolated vertebra was subjected to histology investigations. To verify the important bone markers, western blotting and qPCR analysis were performed. Because of their high polyphenol content, RE and LE demonstrated strong antioxidant activity. While neither RE nor LE changed the survival of the cells, they both markedly enhanced the mineralization, differentiation, and proliferation of osteoblast cells. Additionally, they increased osteogenic genes' mRNA expression. The activation of ERK, AKT, and CREB was stimulated by both RE and LE. While neither RE nor LE directly impacted osteoclastogenesis, they both raised the expression of the Opg/Rankl ratio in osteoblast cells. By raising bone mineral density, bone volume fraction, trabecular number, and trabecular thickness while lowering trabecular separation and structural model index in ovariectomized mice, RE and LE at 750 mg/kg/day markedly enhanced the trabecular and cortical microarchitecture of the femur and tibia. Additionally, by promoting osteoblast function and suppressing osteoclast function, RE and LE considerably increase the vertebral bone mass and have osteo-protective effects, according to the vertebral histology of the lumbar vertebrae. (17)

The purpose of the study was to assess the ability of hydrogel containing methanolic extract of Sida cordifolia (MeOHSC) to repair wounds in diabetic rats. The hydrogel-based methanolic extract was given topically to the wounds of fructose-fed streptozotocin-induced diabetic rats. The excision wound model was used to assess the percentage of wound contraction, the duration of epithelialization, the hydroxyproline content, and the histological examination; the incision wound model was used to determine the tensile strength. In terms of percentage wound contraction, period of epithelialization, hydroxyproline content in the excision model, and tensile strength in the incision model, the results demonstrated that the hydrogel of MeOHSC exhibited significant wound healing activity in both models when compared to diabetic wound control. Compared to the diabetic wound control group, collagen fibers, and more robust epithelial cell proliferation were seen in the MeOHSC hydrogel. According to the research, MeOHSC hydrogel may help improve the healing of wounds in diabetes patients.
The presence of gallic acid and phenolic chemicals in the extracts may be the reason for this. (18)

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In p53-mutated human osteosarcoma MG63 cells, the indoloquinoline alkaloid cryptolepine (CLP) extracted from Sida cordifolia causes growth arrest and p21WAF1/CIP1 expression. Four micromolar of CLP resulted in G2/M-phase arrest and total inhibition of MG63 cell growth. In a dose-dependent manner, CLP increased the expression of p21WAF1/CIP1 at the mRNA and protein levels. We discovered that the CLP-responsive element is a Sp1 site at -82 concerning the transcription start site of the p21WAF1/CIP1 promoter using several mutant p21WAF1/CIP1 promoter constructs. These results imply that CLP inhibits MG63 cell proliferation by p53-independently activating the p21WAF1/CIP1 promoter via the particular Sp1 site. Furthermore, the deletion of the p21WAF1/CIP1 gene in human colon cancer HCT116 cells decreased CLP-mediated cell cycle arrest, indicating that the elevation of p21WAF1/CIP1 expression was at least largely responsible for the cell cycle arrest induced by CLP. (19)

Sida species, including S. acuta, S. cordata, S. cordifolia, S. indica, S. mysorensis, S. retusa, S. rhombifolia, and S. spinosa, were examined using methanolic root extracts (10% w/v). Sida cordifolia had the highest levels of total phenolic content (TPC: 1.92 ± 0.10 mg Caffeic Acid Equivalent/g and 2.13 ± 0.11 mg Tannic Acid Equivalent/g), total flavonoid content (TF: 2.60 ± 0.13 mg Quercetin Equivalent/g), and antioxidant activities in assays for DPPH radical scavenging (51.31 ± 2.57%), Trolox Equivalent Antioxidant Capacity (566.25 ± 28.31µM; Ascorbic acid Equivalent Antioxidant Capacity: 477.80 ± 23.89 µM), and ferric reducing antioxidant power (TEAC: 590.67 ± 29.53 µM; AEAC: 600.67 ± 30.03 µM). In contrast to DPPH and FRAP activity, S. indica exhibited the greatest levels of ABTS+ antioxidant activity (TEAC: 878.44 ± 43.92 µM; AEAC 968.44 ± 48.42 µM). The fact that AEAC (µM) values were greater than TEAC values for every antioxidant activity examined was noteworthy. The antioxidant qualities of some Sida species are directly correlated with the high concentrations of phenolic compounds found in their root extracts. Finally, it can be said that S. cordifolia roots may be a good source of antioxidants and polyphenols. (20)

By measuring the urine volume, electrolyte content, and diuretic efficacy in male albino rats, the diuretic qualities of petroleum ether, chloroform, ethyl acetate, and methanol extract of Sida cordifolia roots were assessed. After five hours of treatment, the urine output of hydrated rats was assessed immediately after being given varying doses of petroleum ether, chloroform, ethyl acetate, and methanol extract (250, 500 mg/kg). The reference drug was furosemide (10 mg/kg), while the control was a standard saline solution (0.9%). Every extract, except petroleum ether extract, demonstrated dose-dependent diuretic effects. The diuretic effect started quite quickly (within an hour) and persisted for the full study time (up to five hours). Additionally, extracts significantly raised the levels of Na+, K+, and Cl-. (21)

The purpose of the study was to assess the chloroform extract of Sida cordifolia leaves' antibacterial and antifungal properties in vitro. The harmful bacterial strains Escherichia coli and Staphylococcus aureus were used to assess the antibacterial activity. Additionally, antifungal activity was evaluated against Candida albicans, a human pathogenic fungus strain. The disc diffusion technique was used to test the extract of S. cordifolia for antibacterial and antifungal properties. S. cordifolia chloroform extract exhibited no zone of inhibition against E. coli at 50µgm/mL and the highest zone of inhibition (10mm) against S. aureus. Additionally, it had stronger antibacterial action against S. aureus. It was discovered that the chloroform extract was more efficient against the human pathogenic fungus C. albicans. (22)

Using plant extract from Sida cordifolia, iron oxide (α-Fe2O3) nanoparticles were synthesized, and their antibacterial properties were assessed. Using LC-MS/TOF and HPTLC, the phytochemical content of the methanolic plant extract of Sida cordifolia was examined. Using FTIR, UV spectroscopy, TG-DTA, scanning and transmission electronic microscopy, and X-ray diffraction, the green-produced iron oxide nanoparticles (α-Fe2O3 NPs) were studied. The produced α-Fe2O3 nanoparticles' crystallite size, as determined by the Debye-Scherrer formula and the Williamson-Hall plot, was around 20 nm, consistent with the particle size shown in TEM images. The iron-oxide nanoparticles mediated by S. cordifolia exhibit strong antibacterial activity against B. subtilis, as evidenced by the highest zone of inhibition (ZOI) of 16.00 ± 1.00 mm. It also had a zone of inhibition of 13.67± 0.58, 11.33± 0.58, and 12.00± 1.00 mm against S. aureus, E. coli, and K. pneumonia, respectively. (23)

The goal of the current work is to create silver nanoparticles (Ag NPs) using an aqueous extract of the whole Sida cordifolia plant as a possible bio-reducing agent and evaluate the antibacterial activity of these particles. A surface Plasmon resonance peak at 420 nm was seen in a constructed silver colloidal solution using UV-Vis

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spectroscopy. XRD and TEM investigation identified the shape as ultra-small, monodispersed spherical nanoparticles with a mean particle size of 3–6 nm and a face-centered cubic structure. The long reaction time and phytochemicals in the S. cordifolia extract may be the cause of this minuscule nano size. Ag NPs have been shown to have antibacterial efficacy against humans (Escherichia coli, Klebsiella pneumonia, Bacillus subtilis, and Staphyloccocus aureus) and fish (Aeromonas hydrophila, Pseudomonas fluorescence, Flavobacterium branchiophilum, Edwardsiella tarda, and Yersinia rukeri) bacterial infections. (24)

The purpose of this study was to assess the hypoglycemic, anti-hyperlipidemic, and antioxidant properties of an alcoholic extract made from the areal portion of S. cordifolia in wistar rats with streptozotocin-induced diabetes. Streptozotocin was administered intraperitoneally at a dosage of 55 mg/kg to cause diabetes. Glibenclamide (5 mg/kg) and an alcoholic extract of S. cordifolia at 200 and 400 mg/kg were administered sub-acutely to diabetic rats for 28 days. In diabetic mice, an alcoholic extract of S. cordifolia at 400 mg/kg considerably reduced blood glucose levels while also improving body weight. The alcoholic extract of S. cordifolia, however, demonstrated a positive impact at 400 mg/kg, showing a notable reduction in triglycerides, low-density lipids, plasma-creatinine, plasma-urea nitrogen, and lipid peroxidation and a notable rise in diabetic rats' high-density lipid levels. It's interesting to note that the diabetic rats showed a considerable increase in antioxidant enzymes like catalase and superoxide-dismutase activity at 400 mg/kg. The alcoholic extract of S. cordifolia at a level of 200 mg/kg did not significantly alter the diabetic rats. The presence of bioactive substances including glycosides, resins, alkaloids, sterols, saponins, and flavonoids may be the reason for the alcoholic extract of plant parts' high medicinal potential. (25)

The microwave-assisted extraction (MAE) method was used to create the ethanolic extract of Sida cordifolia seeds. The extract was qualitatively examined for several phytochemicals, and the amount of flavonoids was measured as quercetin equivalent, while the extract's total phenolic content was quantified as gallic acid equivalent (GAE) per gram of dry extract. In the DPPH and FRAP assays, the IC50 values were 10.29 and 33.36, respectively. Additionally, the levels of the antioxidant enzymes SOD, CAT, and POD were 19.46, 38.94, and 4.75 units/mg, respectively. Additionally, at 1000 mg/ml, it exhibits 13.32% thrombolytic activity, which is typical for improving blood circulation to tissues. The diameter (mm) of the zones of inhibition in the chosen bacterial colonies was used to gauge the plant's antibacterial activity. Gentamicin is a common medication.In S. aureus, B. cereus, E. coli, and P. aeruginosa, Sida cordifolia possesses ZOI of 17 mm, 20 mm, 18 mm, and 17 mm, respectively. with 40 mg/ml, the ethanolic extract of Sida cordifolia generated a 15 mm zone of inhibition, but with 10 µg of ketoconazole, a 25 mm ZOI was achieved. (26)

Thin-layer chromatography and RP-HPLC were used to analyze the ephedrine, and UV-Vis Spectrophotometry was used to validate its identification. After 60 days of callus development, active production of ephedrine began. 2,4-D significantly suppressed the ephedrine bioproductin. greatest cell growth was seen in the presence of 1 mg/l NAA and 5 mg/l Benzyl Adenine (BA) (889 mg dry weight), but the greatest ephedrine accumulation was noted in callus cultured in (MS) medium containing 1 mg/l (NAA) and 5 mg/l Kinetin (Kin) (462 µg/g). According to a growth and ephedrine accumulation time course research, ephedrine only began to actively accumulate in the callus cultures after 90 days of growth, and it increased further until the end of 150 days, at which point it began to decline. (27)

The aqueous-methanolic extract (Sc.Cr) of Sida cordifolia was assessed using models of ferric chloride-induced carotid artery thrombosis, carrageenan-induced tail vein thrombosis, acute pulmonary embolism, and clot lysis test. In a dose-dependent fashion, hemostasis parameters were raised. The restoration was demonstrated by histological investigations, which revealed reduced red blood cell congestion and clean alveolar gaps. A notable drop in the platelet count (PC), an increase in coagulation parameters, and a significant reduction in the infarcted length of the thrombus were noted. With a dose-dependent decrease in thrombus weight and a notable rise in PT and APTT, arterial occlusion duration was prolonged. Additionally, the antioxidant capacity and phytochemical components of Sc. Cr was examined. Sc. Cr's antithrombotic and thrombolytic properties were established by the results employing both in vitro and in vivo experimental methods. (28)

The investigation conducted on Malva sylvestris leaves and flowers, as well as Sida cordifolia and Pelargonium graveolens leaves. Hexane, chloroform, ethyl acetate, and residual extracts and fractions were tested for their anti-inflammatory properties by measuring the quantity of prostaglandins (PG) and thromboxane B2 in the supernatant of RAW 264.7 cells that had been stimulated with lipopolysaccharide (LPS). For plants, the crude

extract, ethyl acetate fraction, and residual fraction showed the greatest inhibition of the release of anti-inflammatory mediators. Even at the lower dose examined (10 µg/mL), the superior activity of S. cordifolia greatly reduced the levels of all mediators following treatment with its residual fraction. When treated with leaf crude extracts (50 µg/mL), M. sylvestris and P. graveolens had comparable outcomes, such as the decrease of all mediators. (29)

The goal of the study was to describe the antioxidant characteristics of Sida cordifolia, paying particular attention to its thorough biochemical investigation. According to the study, S. cordifolia floral tissue had the greatest levels of chlorophyll A (0.9 ± 0.3 mg/g), total chlorophyll content (3.0 ± 0.7 mg/g), total carotenoid content (0.3 ± 0.1 mg/g), total soluble proteins (7.5 ± 0.1 mg/g), and total phenolic contents (5.6 ± 1.3 mg/g). Nevertheless, the leaf tissues had the highest levels of peroxidase (POD) (118 ± 31 units/g) and superoxide dismutase (SOD) activity (64 ± 1.5 units/g), whereas the flowers of S. cordifolia had higher levels of catalase (CAT) (133 ± 25 units/g) and ascorbate peroxidase (APX) (145 ± 44 units/g) than else. (30).

II. CONCLUSION

Sida cordifolia is considered a very powerful medicinal plant in Ayurveda, and the majority of its components have long been used to cure a variety of ailments. SC is also referred to as "Bala" in Hindi and is regarded as a "Rasayana," meaning that it has restorative qualities. It is abundant in alkaloids, flavonoids, steroids, fatty acids, and other kinds of secondary metabolites, according to phytochemical research. Numerous investigations have demonstrated the anti-inflammatory, antioxidant, antibacterial, antiviral, anticancer, antihyperglycemic, and wound-healing qualities of Sida cordifolia extracts and their phytochemicals or isolated metabolites in both in-vitro and in-vivo studies. These findings provide substantial evidence for the potential therapeutic use of SC extracts in contemporary medicine.

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