

Exploring the Pharmacological Potential of *Cocculus hirsutus* { Review }

Ramakrishna S¹, Ujaneshwar Mayachari, Narayana murthy G¹, Likhitha K

Ramakrishna.S , Assistant Professor , Department of Pharmacognosy,
National College of Pharmacy,Shivamogga,Karnataka, India.

Dr.Narayana Murthy.G Principal, National College of
Pharmacy,Shivamogga,Karnataka, India.

, **Ujaneshwar Mayachari** , UG Scholar,

National College of Pharmacy,Shivamogga,Karnataka, India.

Likhitha K . Lecturer, , Department of Pharmacognosy, National College of
Pharmacy,Shivamogga,Karnataka, India

Corresponding author : Ramakrishna.S Assistant Professor , Department
of Pharmacognosy, National College of Pharmacy,Shivamogga,Karnataka,
India.

ABSTRACT

Cocculus hirsutus (L.) Diels, a climbing plant belonging to the Menispermaceae family, has been highly valued in traditional medicine for its wide range of therapeutic benefits. Abundant in bioactive components like alkaloids, flavonoids, and terpenoids, the plant demonstrates diverse pharmacological effects, including anti-inflammatory, antimicrobial, antioxidant, antidiabetic, liver-protective, and neuroprotective actions. Recent studies highlight its potential in cancer research, showcasing specific phytoconstituents with cytotoxic properties against cancerous cells. Although widely used traditionally, it lacks thorough scientific validation through detailed pharmacokinetic and toxicity studies.

KEY WORDS: *Cocculus hirsutus*, Neuroprotective, Flavonoids, Antioxidant, Antidiabetic,

The well-known traditional medicinal herb *Cocculus hirsutus* (L.) W. Theob (family: Menispermaceae) is also referred to as "patalagarudi" in Ayurveda. It is a climber that is frequently found in Asian nations, particularly India, that have tropical and subtropical temperatures [1-3]. Almost everywhere in India, including in Karnataka, Uttar Pradesh, Gujarat, Orissa, Rajasthan, Tamil Nadu, Bihar, West Bengal, and Maharashtra, it may be found in arid

and open environments. Its detoxifying properties are very strong. Gonorrhoea, cough, ophthalmia, cephalalgia, neuralgia, and skin infections and itchy skin, including rheumatism, can all be treated with the leaves [4]. The Menispermaceae family comprises about 70 genera and 500 species. North America, Africa, Asia, and Australia are home to the roughly ten species that make up the genus *Cocculus* [5]. *Cocculus hirsutus* (L.) W. Theob (Figure 1) has the following synonyms: *Cocculus aristolochiae* DC., *Cocculus hastatus* DC., *Cebatha hirsuta* (L.) Kuntze, *Cebatha villosa*, *Cocculus hirsutus* (L.) Diels, and *Cocculus holopeira-torrída* C.Ch. *Menispermum hirsutum* L., Broun & R.L. Massey, *Cocculus villosus* DC, *Cocculus linnaeanus* Kurz, and *Cocculus sepium* Colebr. [6]. *Cocculus hirsutus* (L.) Diels (Family: Menispermaceae) is a plant that grows extensively in dry regions of the Indian plains. Indian tribes use it medicinally for a variety of ailments, including constipation and kidney problems [7, 8]. There have been reports of analgesic and anti-inflammatory properties in *C. hirsutus* roots.

Mucilage, applied topically as a cooling and soothing treatment for prurigo, dermatitis, and impetigo, as well as used as a diuretic for gout, is formed when the juice from *C. hirsutus* leaves coagulates in water [10].

Cocculus hirsutus, *Cocculus pendulus*, and *Cocculus laurifolius* represent the three species of *Cocculus* that inhabit the Western Ghats. Primarily dioecious, the Menispermaceae family consists of lianas, along with a few small trees or shrubs and perennial herbs. The leaves are petiolate, exstipulate, arranged alternately, and sometimes peltate. The lamina features palmate veins and can be either entire or lobed. This family encompasses several plants known for their notable pharmacological properties recognized by modern science [11,12]. It serves as an initial treatment for minor injuries. *C. hirsutus* may also provide significant benefits in the management of diabetes mellitus.

Pendulus cocculus (J.R. & G. Forst.) is a climbing shrub known as diels that thrives among rocks and in dry mountainous areas. A soothing remedy for gonorrhea can be prepared from the mucilage-rich leaf juice, which forms a jelly-like substance when mixed with water [14]. The stem and foliage contain alkaloids with anticancer and blood pressure-lowering effects [15].

Cocculus laurifolius DC., commonly called the snail tree due to its laurel-like leaves, has also been utilized as a worm expeller and a diuretic. Research has revealed that *Cocculus laurifolius* possesses blood pressure-lowering and muscle-relaxing effects. With its traditional applications in alleviating rheumatic pain, headaches, hypertension, gastrointestinal discomfort, and various other conditions, this plant holds considerable importance.

Figure 1 COCCULUS HIRSUTUS



Figure 2 COCCULUS PENDULUS



Figure 3 COCCULUS LAURIFOLIUS



Table Displaying The Local Names In Different Languages: [17–19].

Language	Name(s)
Bengali	Huyer
English	Broom creeper, Ink Berry
Hindi	Farid buti, Jamti ki bel
Kannada	Kaage Mari, Dagadi balli
Urdu	Farid buti
Malayalam	Paathaalagarudakkoti
Nepali	Kaanse laharo
Sanskrit	Garudi, Patalagarudi
Telugu	Chipuru-tiga
Tamil	Kattu-k-koti

Taxonomic classification

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Ranunculales

Family: Menispermaceae

Genus: *Cocculus*

Species: *hirsutus*

Morphology:

Jamti-ki-bel, known scientifically as *Cocculus hirsutus* Diels, belongs to the Menispermaceae family and is a climbing shrub. Its leaves may exhibit various shapes, including mucronate, retuse, obtuse, or sub lanceolate, and can also be three-lobed, with a base that is subcordate or truncate, featuring juvenile villosus on both surfaces; the petiole measures approximately half an inch in length. The roots emit a peculiar, caustic odor, possess a bitter and unpleasant flavor, and are characterized by a keeled structure, rarely branching, and exhibiting significant twisting. (21) In Ayurvedic medicine, *Cocculus* is incorporated into several formulations, such as 'Guduchi Satwam.' It is recognized in the Ayurvedic pharmacopoeia as the most potent bitter tonic, ranking first among beneficial bitter tonics. It is recommended for various ailments, including rheumatism, diabetes, splenic disorders, chronic gonorrhea, diarrhea, dyspepsia, and urinary

issues. Historically, the leaves and roots of *Cocculus hirsutus* have been particularly valued for their medicinal properties. The plant is utilized as a cooling remedy for ocular conditions and as a soothing treatment for dermatitis, impetigo, and dyspepsia. The juice from the leaves is known to coagulate in water, while a decoction of the roots is employed in the treatment of rheumatism.(22)

Chemical Constituents;

preliminary phytochemical screenings and isolation and identification of a few alkaloids such as trilobine, isotrilobine, cocclaurine and magnoflorine . and other compounds i.e., β -sitosterol, ginnol and monomethyl ether of inositol . Three flavonoids rutin, liquiritin and quercetin were also reported from the leaves . Similarly, β -sitosterol and 28-acetyl botulin were isolated from the aqueous extract of aerial parts . Many studies have reported the preliminary phytochemical screening of the extracts and presence of carbohydrates, steroids, alkaloids, glycosides, flavonoids, tannins , saponins . Jaminine, Jamine *N*-oxide, Haiderine, Hirsutine, Cohirsutine, Cohirsutinine, Cohirsine, Cohirsinine, Corsutine, Cocclaurine, Shaheenine, Magnoflorine, Trilobine, Isotrilobine & Cocsuline-*N*-2-oxide were isolated from whole plant, stem & roots. [23–41].

Microscopical STUDIES

Cocculus hirsutus

The cork's outer two layers are characterized by reddish, highly compressed cells with thick walls, while the inner three to four layers consist of colorless cells with thinner walls. The cortex comprises six to eight layers of collenchymatous cells. A continuous ring of sclerenchyma, linked by prism-shaped crystals and stone cells, encircles the stelar area, which is made up of sequential vascular bundle rings. Externally, six to eight layers of phloem surround 23 to 25 distinct wedge-shaped xylem strips. The thin medullary rays, which are lignified parenchyma, connect neighboring vascular bundles. The cambium is formed of three to four layers of loosely stacked thin-walled cells. The xylem, which has a greater number of large vessels, consists of vessels, tracheids, parenchyma, and fibers. Small, single, and sometimes paired vessels are circular to oval in shape. The pith consists of densely packed, large, thin-walled parenchymatous cells. The dimensions of fibers and the height and width of xylem rays increase from the center of the stem to its outer edges.(41)

Cocculus pendulus

Ten to twelve layers of dark brown, tangentially elongated cells make up the outer layer of the cork, while three to four layers of colourless, thin-walled cells make up the inner layer. Collenchymatous cells are arranged in four to six layers to form the cortex. Stone cells connect the continuous ring of sclerenchyma that encircles the stelar region. Comprising 20–22 different wedge-shaped strips of xylem and successive rings of vascular bundles, the stellar area is surrounded by 5–6 layers of phloem. The

adjacent vascular bundles are connected by parenchymatous high and thin medullary rays that are multi-crystal and unlignified. The cambium is composed of four to six layers of loosely packed, thin-walled cells. . Fibres, tracheid, parenchyma, and vessels—the latter being larger and more numerous—are the constituents of xylem. Small, round to oval vessels are frequently observed alone, though sometimes in pairs. Pith is composed of large, thick-walled, closely packed parenchymatous cells. *C. pendulus* wood's wide xylem channels enhance water transport to the upper canopy, and the xylem's abundance of ray parenchyma cells provides exceptional flexibility. The plant's capacity to endure in the harsh environment depends on these traits [42].

Cocculus laurifolius

The outer four to five layers of the cork are composed of reddish brown, thick-walled, strongly compressed cells, while the inner two to three layers are composed of colourless cells with thin walls. Three to five layers of parenchymatous and five to seven layers of collenchymatous cells comprise the outermost layer of the cortex. The continuous ring of sclerenchyma is connected by stone cells. The stelar region is composed of two successive rings of vascular bundles [43], and it is surrounded on the exterior by 10–12 phloem layers and 30–32 discrete wedge-shaped xylem strips. The parenchymatous high medullary rays connecting the nearby vascular bundles lack crystals. These are lignified and multiseriate rays.

Cambium is composed of loosely stacked layers of three to four thin-walled cells. Xylem is composed of vessels, tracheid, parenchyma, and fibres; it has a greater number of tiny xylem vessels [43]. Some of these jars are small, round to oval, and sometimes paired. There isn't any tylose. The pith is composed of large, irregularly shaped, thick-walled parenchymatous cells [44, 45].

Traditional Uses:

South Asian ethnic groups' traditional uses of *C. hirsutus* have been the subject of several investigations. The Koyas put leaf paste on their heads for cooling purposes. The leaves are also used for eczema, impetigo, prurigo, cuts, wounds, sores, and other skin disorders. Stomach disorders are treated with the stem

Sesame oil and the plant's juice are applied to the head and body to help them chill. The plant paste can be applied to the navel region to cure blood dysentery and reduce stomach heat. Leaf treatment also includes fever, acute gonorrhoea, leucorrhoea, and urinary issues. The leaves and stems are used to treat conjunctivitis and other eye diseases.

Taking the leaf powder orally helps cure diarrhoea and dysentery.

Every part of this plant is used in traditional medicine; in tropical and sub-tropical nations, people have made remedies from it to treat a variety of ailments, including anorexia, bronchitis, diarrhoea, jaundice, and leprosy. The plant's dried leaves and stems have been used to make a decoction that has been used to treat eczema, diarrhoea, eye disorders, and urinary tract infections. It is known that root extracts contain antidiabetic, anti-inflammatory, analgesic, spermatogenic, antibacterial, and antioxidant qualities.

Analgesic and anti-inflammatory properties of *C. hirsutus* roots have been reported. When the juice from *C. hirsutus* leaves coagulates in water, a mucilage is created that is administered topically to cure gout, eczema, impetigo, and prurigo. It also has diuretic properties.

The bitter, alterative, and laxative roots are used to treat syphilitic cachexia, cough, rheumatism, gout, fever, and stomachaches in youngsters. Root and stem preparations are used for their spasmolytic, cardiotonic, relaxing, and hypotensive effects. Some people grind the root into a paste, mix it with water, and take it orally to relieve gastrointestinal distress [46-73].

Table Summarizing The Uses Of Different Parts Of *Cocculus Hirsutus*:

Plant Part	Uses
Roots	Used to treat rheumatoid arthritis, sunstroke, migraines, intestinal worm infestations, and anorexia in Ayurvedic medicine. Additionally used externally to treat poisonous bites.
Leaves	Used traditionally to treat digestive problems, urinary disorders, and skin diseases. Its antimicrobial qualities are also well known.
Stem	Includes alkaloids that have pharmacological effects, such as immunomodulatory, hepatoprotective, antidiabetic, and antibacterial qualities.
Whole Plant	Used to treat fever, rheumatism, and congenital conditions as well as as a detoxifying agent.

Pharmacological Activities:

Anti-T.B. Activity

As Jethva et al. examined the water-based extract of *C. hirsutus*. With an inhibition percentage of 80.26%, they discovered that *hirsutus* possesses potent anti-mycobacterial activity against *Mycobacterium tuberculosis* H37Rv [74]. Gupta & Co. evaluated *C.*'s ability to combat mycobacteria.

Hirsutus leaf ethanoextract protects against several MDR strains of *M. tuberculosis* H37Rv. For MDR strains JAL-19187, JAL-19126, JAL 19049, JAL 19111, and JAL-191888, as

well as *M. tuberculosis* H37Rv, the extract demonstrated potent anti-mycobacterial activity, with MIC values of 500, 250, 500, 250, 500, and 500 µg/mL, respectively [75].

Anti-Bacterial activity

Devi & Co. Methanol, ethanol, and an aqueous extract of *C* were tested for antibacterial activity using clinical bacterial isolates, such as *Salmonella typhi*, *Escherichia coli*, *Micrococcus luteus*, *Staphylococcus aureus*, *Acetobacter laffi*, *Proteus mirabilis*, and *Bacillus cereus*. *hirsutus* leaves in volumes of 25, 50, 75, and 100 microliters. The extracts showed potent antibacterial properties [76]. The antibacterial activity of multiple *C. species* was assessed by Nayak and Singhai. Strong antibacterial activity was demonstrated by the ethanol extract of *hirsutus* root extracts against *Salmonella typhi*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* [77].

Anti-Fungal activity

water-based extract of *C. Devi* and colleagues evaluated the antifungal properties of *hirsutus* against strains of the fungi *Rhizopus arrhizus*, *Sclerotium rolfsii*, and *Fusarium solani*. Antifungal activity against *F. and S. rolfsii* was demonstrated by the extract. *solani* [78].

Anti-Cancer Activity

The moment De Wet et al. examined the unrefined alkaloidal extract from *C. A* modest anticancer effect was demonstrated by the extract of *hirsutus* rhizomes on three cancer cell lines: the kidney (TK10), melanoma (UACC62), and breast (MCF7) cell lines [79]. Following Thavamani et al. evaluated *C*'s methanolic extract. The results showed that *hirsutus* had an IC₅₀ value of 111 µg/mL against the HeLa cell line [80]. Another study evaluated the plant *C. properties* of *hirsutus* that inhibit the growth of Dalton's lymphoma ascites (DLA) cells in mice. In vitro tests using the MCF-7 cancer cell line revealed that the methanolic extract of *C. Significant* cytotoxic action was shown by *hirsutus*, with an IC₅₀ value of 84–56 mg/mL. Furthermore, the extract showed in-vivo anticancer efficacy, as dosages of 200 and 400 mg/kg body weight significantly reduced the packed cell volume and tumor cell count while bringing the serum biochemical and haematological parameters back to normal [81].

Anti-Malarial and Insecticidal Activity

Various *C* extracts. *hirsutus* roots were evaluated for their in vitro antimalarial effectiveness against two strains of *Plasmodium falciparum*: K1 (a chloroquine-resistant strain) and 3D7 (a chloroquine-susceptible strain). Both the chloroform and methanol extracts showed strong activity against both strains. 82. Elango & Co. evaluated the larvicidal efficacy of *C. protection* of *hirsutus* leaves from malaria-carrying *Anopheles subpictus* larvae. The following extracts showed high activity with emergence inhibition values and percentage mortality at 24 hours: methanol extract (81 ± 1.08), hexane extract (60 ± 2.04 and 75 ± 2.44), chloroform extract (78 ± 2.56 and 85 ± 1.50),

ethyl acetate extract (86 ± 1.29 and 69 ± 1.71), and acetone extract (100 ± 0.00 and 68 ± 2.13). Furthermore, extracts of C in acetone and ethyl acetate. Elango et al. demonstrated that hirsutus leaves had larvicidal effects on *Culex tritaeniorhynchus* and *Anopheles subpictus*. 84.

Anti-Oxidant Activity

Srikanta and Dharmesh evaluated the antioxidant capabilities of the aqueous extract of C using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical and reducing power assay. hirsutus foliage. With IC₅₀ values of 2.75 ± 0.3 μ g gallic acid equivalents (GAE)/ml and reducing power activity of 65.17 ± 4.8 U/mg GAE, the extract effectively scavenged DPPH free radicals. A total phenolic content of 31.83 ± 3.1 mg GAE/g was also found in the extract [85]. Researchers Rakkimuthu and associates looked into C. Antioxidant properties of hirsutus. Strong DPPH, ABTS, and nitric oxide free radical scavenging activity, as well as reducing power, lipid peroxidation prevention, and metal chelating activity test ascorbic acid, were all shown in the results [86].

Hepatoprotective Activity

In ethanol-induced hepatotoxicity in albino Wister rats, Thakare et al. examined the C methanolic extract. Hepatoprotective properties of hirsutus. Oral administration of the extract at doses of 100, 200, and 400 mg/kg resulted in a significant reduction of AST, ALT, ALP, LDH, direct and total bilirubin, and cholesterol [87].

Diuretic and Nephroprotective Activity

The diuretic properties of an aqueous extract derived from the aerial sections of C. hirsutus were examined by Ganapaty et al., utilizing normap mice. The extract, administered at doses of 100 and 200 mg/kg, orally, exhibited a marked increase in the urine concentrations of sodium (Na⁺) and potassium (K⁺), suggesting robust diuretic activity [88]. Badole et al. assessed the acute and long-term diuretic effects of the ethanolic extract of C. hirsutus leaves in healthy rats, and the extract demonstrated a notable increase in the levels of Na⁺ and K⁺ in the urine [89]. Gadapuram et al. uncovered the strong nephroprotective effects of the ethanolic extract of C. hirsutus leaves in a 5/6 nephrectomised rat model [90].

Immunomodulatory Activity

Mallik and Nayak evaluated the immunomodulatory effects of 1:1, 2:1 and 1:2 ratios of C. hirsutus leaves and *Sesbania grandiflora* (L.) Pers. (Fabaceae) flowers. The 1:1 combination mixture showed strong immunostimulatory action [91]. Rastogi et al. tested the immunostimulatory properties of water and ethanolic extracts of C. hirsutus aerial parts in normal and immunosuppressed rats. The authors concluded that the extract was effective in both stimulating the immune system and in protecting against immunosuppression, as it was shown to increase the carbon clearance, the humoral antibody (HA) titre, the delayed type hypersensitivity (DHT) and the white blood cell (WBC) count, depending on the dose [92].

Anti-Diabetic Activity

In mice given alloxan to induce diabetes, Badole et al. evaluated an aqueous extract of C's anti-hyperglycemic effect. *Hirsutus* foliage. Blood glucose levels significantly decreased on the 28th day following oral administration of the extract at doses of 250, 500, and 1000 mg/kg. The oral glucose tolerance test (OGTT) showed improved glucose tolerance in normal mice after receiving 1000 mg/kg of extract orally [93]. The anti-diabetic qualities of C were evaluated by Sangameswaran and Jayakar in rats with streptozotocin-induced diabetes. *hirsutus*, and methanolic extract administered orally at 400 and 800 mg/kg decreased blood glucose levels [94].

Analgesic and anti-inflammatory activity

C. hirsutus methanol extract shows both central and peripheral analgesic effects when administered orally to male Swiss albino mice at doses of 100 mg and 200 mg kg. Substitution chemical processes should therefore be developed using materials of natural origin which have low negative impacts. The analgesic effect of *C. hirsutus* leaf extract in methanol was tested by using the Eddie method on a hot plate and on mice by acetic acid-induced thrashing. Both in vitro and in vivo models were used to investigate antiinflammatory properties of *C. hirsutus*. Human red blood cell membrane stabilisation was used to test the antiinflammatory efficacy of cotton balls and carrageenan by inducing oedema and granuloma in rats. Miscellaneous substance secreted by *C. hirsutus* methanol extract. It shows how the concentration of the extract affects its anti-inflammatory properties both immediately and over time.[95]

Patents :

The formulation and its components have been the subject of patents for the use of *C. hirsutus* extract in the prevention and treatment of dengue and tuberculosis. [96, 97, 98, 100]

MARKETED PRODUCTS



Conclusion

With countless therapeutic potential, *Cocculus hirsutus* is a powerful medicinal plant. Despite the well-established ethnobotanical significance of this plant, systematic pharmacological research, standardization, and toxicity profiling are necessary to translate its benefits into clinically approved treatments. Future research should concentrate on identifying the active ingredients, clarifying how they work, and carrying out clinical trials to guarantee both safety and effectiveness. Prioritizing sustainable conservation methods is also necessary to preserve its availability in the face of ecological difficulties. *Cocculus hirsutus* has great potential for integrative medicine and could lead to the development of innovative natural medication formulations with further scientific research.

Reference:

- [1] World Flora Online (WFO) *Cocculushirsutus* (L.) W.Theob; Published on the Internet.[(accessedon3November2020)]; Availableonline: <<http://www.worldfloraonline.org/taxon/wfo-0000613546>> .
- [2] H. De Wet, M. Struwig, B.E. Van Wyk, Taxonomic notes on the genus *Cocculus* (Menispermaceae) in southern Africa, *S. Afr. J. Bot.* 96 (2015) 99–104.
- [3] R. Logesh, N. Das, A. Adhikari-Devkota, H.P. Devkota, *Cocculus hirsutus* (L.) W. Theob. (Menispermaceae): A review on traditional uses, phytochemistry and pharmacological activities, *Medicines* 7 (11) (2020) 69.
- [4] Chadha YR. The wealth of India. A dictionary of Indian raw materials and industrial products. New Delhi: CSIR; 1950, p. 258.
- [5] De Wet, H.; Struwig, M.; Van Wyk, B.E. Taxonomic notes on the genus *Cocculus* (Menispermaceae) in southern Africa. *S. Afr. J. Bot.* 2015, 96, 99–104. [CrossRef]
- [6] World Flora Online (WFO). *Cocculus hirsutus* (L.) W.Theob; Published on the Internet. Available online: <http://www.worldfloraonline.org/taxon/wfo-0000613546> (accessed on 3 November 2020).
- [7] Ganapaty S et al. Diuretic, laxative and toxicity studies of *Cocculus hirsutus* aerial parts. *Fitoterapia* 2002; 73: 28–31.
- [8] Caius JF. The Medicinal and Poisonous Plants of India. Jodhpur, India: Scientific Publisher, 1986: 166–171.
- [9] Nayak SK, Singhai AK. Anti-inflammatory and analgesic activity of roots of *Cocculus hirsutus*. *Indian J Nat Prod* 1993; 9: 12–14.
- [10] Nadkarni AK. *Indian Materia Medica*. Vol. 1, 3rd edn. Mumbai: Popular Prakashan, 1982: 362, 387–388.
- [11] Troupin, G, *Flora of tropical East Africa*, 1, Royal botanical gardens, Kew, 1956.
- [12] Botha DJ, 'N Taksonomiese studie van die Suid-Afrikaanse verteenwoordigers van die Menispermaceae (Doctoral dissertation, Universiteit van Pretoria.), 1975.
- [13] Sangameswaran B & Jayakar B, Antidiabetic and spermatogenic activity of *Cocculus hirsutus* (L) Diels, *African Journal of Biotechnology*, 6(10), 2007.
- [14] Jangir S, Mathur K, Goyal M & Yadav SK, A Review on *Cocculus Pendulus* (jr Forst. & g. Forst.) Diels: Traditional Uses, Phytochemistry and Pharmacological Properties, *Indian Journal of Drugs*, 4(2), 2016, 57-62.

- [15] Bhakuni DS, Alkaloids from Indian medicinal plants and their biosynthesis. In Proceedings of the Indian Academy of SciencesChemical Sciences, 1984, pp. 661-676).
- [16] Thakur S & Sidhu MC, Medicinal plant remedies for dermatological problems, Current Botany, 8, 2017, 23-33
- [17] Panda, B.R.; Mohanta, S.R.; Mishra, U.S.; Kar, S.; Panda, B.K.; Chakraborty, P. Antibacterial activity of the leaves of *Cocculus hirsutus*. Indian Drugs 2007, 44, 108–116.
- [18] Shrestha, K.K.; Bhattarai, S.; Bhandari, P. Gymnosperms and Angiosperms: Cycadaceae—Betulaceae. In Handbook of Flowering Plants of Nepal; Scientific Publishers: Jodhpur, India, 2018; Volume 1
- [19] India Biodiversity Portal. *Cocculus hirsutus* (L.) Diels. Available online: <https://indiabiodiversity.org/species/show/229234> (accessed on 3 February 2020).
- [20] The Wealth of India — A Dictionary of Indian, Raw Materials, Vol. 2, Publications and Information Directorate, CSIR, New Delhi; 1950:35-36.
- [21] Chatterjee Tk, "Herbal Options", 1996,1st edition,published by M/s Eastern Traders, Calcutta :157-178
- [22] Chadha YR, The Wealth of India- A dictionary of Indian Raw Materials and industrial products. CSIR, New Delhi; 1950: 258.
- [23] Tripathi, V.J.; Ray, A.B.; Dasgupta, B. Alkaloids of *Cocculus hirsutus* DC. Indian J. Chem. Sect. B Org. Chem.Incl. Med. Chem. 1976, 14, 62–63.
- [24] Jagannadha Rao, K.V.; Row, L.R.M. Chemical examination of *Cocculus hirsutus* DC. J. Sci. Ind. Res. 1961,20b, 125–126.
- [25] Naik, R.M.; Merchant, J.R. Chemical investigation of *Cocculus hirsutus*. Curr. Sci. 1956, 25, 324–325.
- [26] Merchant, J.R.; Naik, R.M.; Hirwe, S.N. Chemical investigation of *Cocculus hirsutus*. J. Indian Chem. Soc. 1962,39, 411–416
- [27] Patil, V.; Angadi, S.; Devdhe, S.; Wakte, P. Recent Progress in Simultaneous Estimation of Rutin, Quercetin and Liquiritin in *Cocculus Hirsutus* by HPTLC. Res. J. Pharmacogn. 2015, 2, 49–55.
- [28] Iyer, S.V.; Shankul, K.; Parikh, P.M. Isolation of phytoconstituents from the aerial parts of *Cocculus hirsutus* Linn. J.Pharm.Res. 2011, 4, 1946–1947.
- [29] Meena, M.K.; Singh, N.; Patni, V. Determination of bioactive components of the leaves of *Cocculus hirsutus* (L.) Diels using GC-MS analysis. Int. J.Pharm. Pharm. Sci. 2014, 6, 327–329.
- [30] Ahmad, V.U.; Iqbal, S. Jamtinine, an alkaloid from *Cocculus hirsutus*. Phytochemistry 1993, 33, 735–736.[CrossRef]

- [31] Ahmad, V.U.; Iqbal, S. Haiderine, a new isoquinoline alkaloid from *Cocculus hirsutus*. *Nat. Prod. Lett.* 1993,2, 105–109. [CrossRef]
- [32] Ahmad, V.U.; Atta-ur-Rahman; Rasheed, T.; Habib-ur-Rehman. Jamtine-N-oxide—A new isoquinoline alkaloid from *Cocculus hirsutus*. *Heterocycles* 1987, 26, 1251–1255.
- [33] Rasheed, T.; Khan, M.N.I.; Zhadi, S.S.A.; Durrani, S. Hirsutine: A new alkaloid from *Cocculus hirsutus*. *J. Nat. Prod.* 1991, 54, 582–585. [CrossRef]
- [34] Ahmad, V.U.; Iqbal, S. Cohirsitine, a new isoquinoline alkaloid from *Cocculus hirsutus*. *J. Nat. Prod.* 1992,55, 237–240. [CrossRef]
- [35] Ahmad, V.U.; Atta-ur-Rahman; Rasheed, T.; Habib-ur-Rehman; Khan, A.Q. Cohirsine—A novel isoquinolone alkaloid from *Cocculus hirsutus*. *Tetrahedron* 1987, 43, 5865–5872. [CrossRef]
- [36] Ahmad, V.U.; Rasheed, T.; Iqbal, S. Cohirsinine, an alkaloid from *Cocculus hirsutus*. *Phytochemistry* 1991,30, 1350–1351. [CrossRef]
- [37] Yadav, S.B.; Tripathi, V. A minor phenolic alkaloid from *Cocculus hirsutus* Diels. *Indian J. Chem.-Sect. B Org. Med. Chem.* 2005, 44, 212–214. [CrossRef]
- [38] Tripathi, V.J.; Ray, A.B.; Dasgupta, B. Alkaloids of *Cocculus hirsutus* DC. *Indian J. Chem. Sect. B Org. Chem. Incl. Med. Chem.* 1976, 14, 62–63.
- [39] Jagannadha Rao, K.V.; Row, L.R.M. Chemical examination of *Cocculus hirsutus* DC. *J. Sci. Ind. Res.* 1961, 20b, 125–126.
- [40] El-Shabrawy, A.O.; Schiff, P.L., Jr.; Slatkin, D.J.; Das Gupta, B.; Ray, A.B.; Tripathi, V.J. Cocsuline-N-2-Oxide, a New Alkaloid from *Cocculus hirsutus* DC. *Heterocycles* 1984, 22, 993.
- [41] Rao KS, Rajput Kishore S, Cambial variant and xylem structure in the stem of *cocculus hirsutus* (menispermaceae), *IAWA Journal*, 24(4), 2003,411–420.
- [42] Masrahi, Yahya S, Ecological significance of wood anatomy in two lianas from arid southwestern Saudi Arabia. *Saudi Journal of Biological Sciences*, 2014, 21(4), 334–341.
- [43] Carlquist Sherwin, "Wood and Stem Anatomy of Menispermaceae," *Aliso: A Journal of Systematic and Evolutionary Botany*, 14(3), 1995.
- [44] Fan JP, He CH, Simultaneous quantification of three major bioactive triterpene acids in the leaves of *Diospyros kaki* by highperformance liquid chromatography method, *Journal of Pharmaceutical and Biomedical Analysis*, 41(3), 2006,950–956.
- [45] Jethva Khushboo, Bhatt Dhara, Dhru Bhavita, Patel Sonal, Zaveri Maitreyi, *Phyto Pharmacognostical Evaluation of Leaf of Cocculus Hirsutus*, *Int. J. Pharm. Sci. Rev. Res*, 38(1), 2016,165-170.
- [46] Rama Rao, N.; Henry, A.N. *The Ethnobotany of Eastern Ghats in Andhra Pradesh, India; Botanical Survey of India: Kolkata, India*, 1996.

- [47] Jain, S.K. Glimpses of Indian Ethnobotany; Jain, S.K., Ed.; Oxford and IBH Publishing Co.: New Delhi, India, 1981; pp. 13–36.
- [48] Bedi, S.J. Ethnobotany of the Ratan Mahal Hills, Gujarat, India. *Econ. Bot.* 1978, 32, 278–284. [CrossRef]
- [49] Saxena, H.O.; Brahman, M.; Datta, P.K. Ethnobotanical Studies in Orissa. In *Glimpses of Indian Ethnobotany*; Jain, S.K., Ed.; Oxford and IBH Publishing Co.: New Delhi, India, 1981; pp. 232–244.
- [50] Chaudhuri, R.H.N.; Pal, D.C.; Tarafdar, C.R. Less known uses of some plants from the tribal areas of Orissa. *Bull. Bot. Surv. India* 1975, 17, 132–136
- [51] Shah, G.L.; Yadav, S.S.; Badri, N. Medicinal plants from Dahanu forest division in Maharashtra state. *J. Econ. Taxon. Bot.* 1983, 4, 141–151.
- [52] Joshi, P. An ethnobotanical study of Bhils-A preliminary survey. *J. Econ. Taxon. Bot.* 1982, 3, 257–266
- [53] Hemadri, K.; Rao, S.S. Leucorrhoea and menorrhagia: Tribal medicines. *Anc. Sci. Life* 1983, 3, 40–41.[PubMed]
- [54] Goel, A.K.; Sahoo, A.K.; Mudgal, V. A contribution to ethnobotany of Santal Pargana, Bihar. *Bot. Surv. India* 1984, 31, 22–26.
- [55] Ahmad, V.U.; Iqbal, S. Haiderine, a new isoquinoline alkaloid from *Cocculus hirsutus*. *Nat. Prod. Lett.* 1993, 2, 105–109. [CrossRef]
- [56] Audichya, K.C.; Billore, K.V.; Joseph, T.H.; Chaturvedi, D.D. Role of indigenous folk remedies for certain acute illnesses in primary health care. *Nagarjun* 1983, 26, 199–201.
- [57] Gairola, S.; Sharma, J.; Gaur, R.D.; Siddiqi, T.O.; Painuli, R.M. Plants used for treatment of dysentery and diarrhoea by the Bhoja community of district Dehradun, Uttarakhand, India. *J. Ethnopharmacol.* 2013, 150, 989–1006. [CrossRef]
- [58] Y. Chadha, *The Wealth of India*, CSIR, New Delhi, India, 1950.
- [59] S. Ganapaty, K. Vijay, Hypoglycemic activity of aerial parts of *Cocculus hirsutus* on alloxan-induced diabetes, *Indian J. Nat. Prod.* 22 (4) (2006) 17–20.
- [60] S.K. Nayak, A.K. Singhai, Anti-inflammatory and analgesic activity of roots of *Cocculus hirsutus*, *Indian J. Nat. Prod.* 9 (1993) 12–14.
- [61] Nayak SK, Singhai AK. Anti-inflammatory and analgesic activity of roots of *Cocculus hirsutus*. *Indian J Nat Prod* 1993; 9: 12–14.
- [62] Nadkarni AK. *Indian Materia Medica*. Vol. 1, 3rd edn. Mumbai: Popular Prakashan, 1982: 362, 387–388.

- [63] Shah, G.L.; Yadav, S.S.; Badri, N. Medicinal plants from Dahanu forest division in Maharashtra state. *J. Econ.Taxon. Bot.* 1983, 4, 141–151.
- [64] Goel, A.K.; Sahoo, A.K.; Mudgal, V. A contribution to ethnobotany of Santal Pargana, Bihar. *Bot. Surv. India* 1984, 31, 22–26.
- [65] Ahmad, V.U.; Iqbal, S. Haiderine, a new isoquinoline alkaloid from *Cocculus hirsutus*. *Nat. Prod. Lett.* 1993, 2, 105–109. [CrossRef]
- [66] Singh, U.; Wadhwani, A.M.; Johri, B.M. *Dictionary of Economic Plants of India*; Indian Council of Agricultural Research (ICAR): New delhi, India, 1965.
- [67] Agrawal, V.S. *Economic Plants of India*; Bishen Singh Mahendra Pal Singh and Kailash Prakashan: Calcutta, India, 1986.
- [68] Sudhakar, S.; Rolla, R.S. Medicinal plants of Upper East Godavari District (Andhra Pradesh) and need for establishment of medicinal farm. *J. Econ. Taxon. Bot.* 1985, 7, 399–406.
- [69] Shah, G.L.; Manon, A.R.; Gopal, V. An account of Ethnobotany of Saurashtra in Gujarat state (India). *J. Econ. Taxon. Bot.* 1981, 2, 173–182.
- [70] Shah, G.L. Some economically important plants of Salsette island near Bombay. *J. Econ. Taxon. Bot.* 1984, 5, 753–765.
- [71] Malhotra, S.K.; Moorthy, S. Some useful and medicinal plants of Chandanpur district (maharashtra State). *J. Econ. Taxon. Bot.* 1973, 15, 13–21.
- [72] Singh, V.; Pandey, R.P. Medicinal plantlore of the tribals of eastern Rajasthan. *J. Econ. Taxon. Bot.* 1980, 1, 137–147.
- [73] Rajan, S.; Sethuraman, M.; Mukherjee, P.K. Ethnobiology of the Nilgiri Hills, India. *Phyther. Res.* 2002, 16, 98–116. [CrossRef] [PubMed]
- [74] Jethva, K.; Bhatt, D.; Zaveri, M. Antimycobacterial screening of selected medicinal plants against *Mycobacterium tuberculosis* H37Rv using agar dilution method and the microplate resazurin assay. *Int. J. Mycobacteriology* 2020, 9, 150–155.
- [75] Gupta, V.K.; Kaushik, A.; Chauhan, D.S.; Ahirwar, R.K.; Sharma, S.; Bisht, D. Anti-mycobacterial activity of some medicinal plants used traditionally by tribes from Madhya Pradesh, India for treating tuberculosis related symptoms. *J. Ethnopharmacol.* 2018, 227, 113–120. [CrossRef]
- [76] Devi, M.D.; Kaviyarasu, S.; Arunsagararaj, I.; Ranjithkumar, J. Optimization of Conditions for Flavonoid Extraction from the Leaves of *Cocculus hirsutus* (L.) And its Antibacterial Activity. *Int. J. Microbiol. Res.* 2019, 10, 42–47.
- [77] Nayak, S.; Singhai, A.K. Antimicrobial activity of the roots of *Cocculus hirsutus*. *Anc. Sci. Life* 2003, 22, 101–105. [PubMed]

- [78] Devi, K.B.; Pavankumar, P.; Bhadraiah, B. Antifungal activity of plant extracts against post-harvest fungal pathogen. *Int. J. Curr. Microbiol. Appl. Sci.* 2017, 6, 669–679. [CrossRef]
- [79] De Wet, H.; Fouche, G.; Van Heerden, F.R. In vitro cytotoxicity of crude alkaloidal extracts of South African Menispermaceae against three cancer cell lines. *Afr. J. Biotechnol.* 2009, 8, 3332–3335.
- [80] Thavamani, B.S.; Mathew, M.; Dhanabal, S.P. In vitro cytotoxic activity of menispermaceae plants against HeLa cell line. *Anc. Sci. Life* 2013, 33, 81.
- [81] Thavamani, B.S.; Mathew, M.; Palaniswamy, D.S. Anticancer activity of *Cocculus hirsutus* against Dalton's lymphoma ascites (DLA) cells in mice. *Pharm. Biol.* 2014, 52, 867–872. [CrossRef]
- [82] Brahman, P.; Sunita, K. Phytochemical investigation and in vitro antimalarial activity of *Acalypha indica* (L.) and *Cocculus hirsutus* (L.) from Prakasam district, Andhra Pradesh, India. *Biomed. Pharmacol. J.* 2018, 11, 2123–2134. [CrossRef]
- [83] Elango, G.; Rahuman, A.A.; Kamaraj, C.; Bagavan, A.; Zahir, A.A. Efficacy of medicinal plant extracts against malarial vector, *Anopheles subpictus* Grassi. *Parasitol. Res.* 2011, 108, 1437–1445. [CrossRef] [PubMed]
- [84] Elango, G.; Rahuman, A.A.; Bagavan, A.; Kamaraj, C.; Zahir, A.A.; Venkatesan, C. Laboratory study on larvicidal activity of indigenous plant extracts against *Anopheles subpictus* and *Culex tritaeniorhynchus*. *Parasitol. Res.* 2009, 104, 1381–1388. [CrossRef] [PubMed]
- [85] Srikanta, B.M.; Dharmesh, S.M. Anti-*Helicobacter pylori*, proton pump inhibitory and antioxidant properties of selected dietary/medicinal plants. *Int. J. Phytomed.* 2012, 4, 573–581.
- [86] Rakkimuthu, R.; Kavithakrishna, R.; Suganyadevi, P.; Aravinthan, K.M. Quantitative phytochemical analysis and their antioxidant activity of *Cocculus hirsutus* (L.) Diels fruit. *Int. J. Phytomedicine* 2012, 4, 447–455.
- [87] Thakare, S.P.; Deore, H.V.; Patil, S.D.; Yende, S.R.; Upadhyay, U.M. Evaluation of hepatoprotective effect of *Cocculus hirsutus* (L.) diels on ethanol induced hepatic damage in albino wistar rats. *Pharmacologyonline* 2010, 3, 810–816.
- [88] Ganapaty, S.; Dash, G.K.; Subburaju, T.; Suresh, P. Diuretic, laxative and toxicity studies of *Cocculus hirsutus* aerial parts. *Fitoterapia* 2002, 73, 28–31. [CrossRef]
- [89] Badole, S.L.; Bodhankar, S.L.; Patel, N.M.; Bhardwaj, S. Acute and chronic diuretic effect of ethanolic extract of leaves of *Cocculus hirsutus* (L.) Diels in normal rats. *J. Pharm. Pharmacol.* 2009, 61, 387–393. [CrossRef]
- [90] Gadapuram, T.K.; Murthy, J.S.N.; Rajannagari, R.R.; Kandati, V.; Choda, P.K.; Shukla, R. Nephroprotective activity of *cocculus hirsutus* leaf extract in 5/6 nephrectomized rat model. *J. Basic Clin. Physiol. Pharmacol.* 2013, 24, 299–306. [CrossRef]

- [91] Mallik, A.; Nayak, S. Study the Immunomodulatory Effects of Combined Extracts of *Sesbania grandiflora* Flowers and *Cocculus hirsutus* Leaves on the Circulating Antibody Response. *Am. J. Phytomed. Clin. Ther.* 2015, 3, 199–208.
- [92] Rastogi, B.; Tiwari, U.; Dubey, A.; Bawara, B.; Chauhan, N.S.; Saraf, D.K. Immunostimulant activity of *Cocculus hirsutus* on immunosuppressed rat. *Pharmacologyonline* 2008, 3, 38–57.
- [93] Badole, S.; Patel, N.; Bodhankar, S.; Jain, B.; Bhardwaj, S. Antihyperglycemic activity of aqueous extract of leaves of *Cocculus hirsutus* (L.) Diels in alloxan-induced diabetic mice. *Indian J. Pharmacol.* 2006, 38, 49–53.
- [94] Sangameswaran, B.; Jayakar, B. Anti-diabetic and spermatogenic activity of *Cocculus hirsutus* (L) diels. *Afr. J. Biotechnol.* 2007, 6, 1212–1216.
- [95] Ranjan, P.B.; Mohanta, S.R.; Sii, S.; Das, G.K. Preliminary Phytochemical Analysis and Wound Healing Activity from the Leaves of *Cocculus hirsutus* Diels. *Int. J. Pharm. Sci. Nanotechnol.* 2009, 2, 675–678. [CrossRef]
- [96] Elango, G.; Rahuman, A.A. Evaluation of medicinal plant extracts against ticks and fluke. *Parasitol. Res.* 2011, 108, 513–519. [CrossRef]
- [97] Nayyar, K.; Arora, U.; Palla, S.; Saravan, A.; Prasad, M.; Madan, S.; Sood, R.; Khanna, N.; Potdar, A.; Shukla, R.; et al. Use of *Cocculus hirsutus* Extract for Treating Dengue. Indian Patent Application IN 201,821,046,412, 2020. (Filing date 9 December 2019).
- [98] Nayyar, K.; Arora, U.; Palla, S.; Prasad, M.; Saravan, A.; Madan, S.; Sood, R.; Khanna, N.; Potdar, A.; Shukla, R.; et al. Use of *Cocculus hirsutus* Extract for Treating Dengue. PCT International Application WO2,020,115,723, 2020.
- [99] Dhirajal, J.K.; Narendrakumar, Z.M.; Shrikant, D.S. Herbal Formula Containing *Cocculus Hirsutus* Extract for the Treatment and Management of Tuberculosis. Indian Patent Application IN 201,821,050,047, 2019.
- [100] Mina, M. Herbal Omposition for Therapeutic Managemnt of Respiratory Tract Diseases. Indian Patent Application IN 201,611,023,226, 2018.