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A comprehensive review on *Cocculus hirsutus* (L.) Diels: Ethnobotany, phytochemistry, pharmacology, and therapeutic potential

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Abstract

Cocculus hirsutus (L.) Diels, commonly known as Inkberry or Jal Jamni, is a fast-growing, perennial climber belonging to the family Menispermaceae. Widely distributed across tropical and subtropical regions of Asia and Africa, this plant holds significant ethnomedicinal importance in traditional systems such as Ayurveda and folk medicine. Various parts of the plant-including leaves, stems, and roots-are used for treating fever, skin infections, diabetes, liver disorders, inflammation, and reproductive ailments. Botanically, the plant is characterized by hairy stems and ovate-cordate leaves with dense trichomes. Its diagnostic features, such as unisexual flowers and curved reniform seeds, assist in its correct identification. Phytochemical investigations have revealed the presence of diverse bioactive compounds. These metabolites exhibit a wide range of pharmacological activities. This review comprehensively covers the plant's taxonomy, morphology, traditional uses, phytochemical profile, and pharmacological properties, supported by recent scientific findings.

Keywords: *Cocculus hirsutus*, menispermaceae, ethnomedicine, phytochemicals, pharmacological activity

Introduction

Medicinal plants have served as a primary source of healthcare for centuries and continue to play a pivotal role in drug discovery and development. Traditional knowledge systems such as Ayurveda, Siddha, and Unani emphasize the use of botanicals for preventing and treating various ailments, often using polyherbal formulations based on empirical evidence. Among the numerous medicinal plants used across the Indian subcontinent, *Cocculus hirsutus* (L.) Diels, belonging to the family Menispermaceae, has garnered considerable attention for its therapeutic potential and ethnomedicinal relevance.

Commonly known as Inkberry, Jal Jamni, or Duhsparsa in different regions of India, *C. hirsutus* is a fast-growing, twining climber widely distributed in India, Pakistan, Sri Lanka, Bangladesh, Myanmar, and parts of tropical Africa [1, 2]. The plant thrives in arid and semi-arid zones, often found in hedges, along roadsides, and in scrublands. It is recognized in traditional systems of medicine for treating fever, diabetes, skin diseases, jaundice, and urinary tract infections, among others [3, 4].

Phytochemical investigations have revealed that *C. hirsutus* is a rich source of bioactive constituents, including alkaloids (e.g., coclaurine, magnoflorine), flavonoids (e.g., rutin, quercetin), triterpenoids, lignans, and phenolic acids [5-7]. These metabolites contribute to the plant's wide range of pharmacological activities, such as antioxidant, antidiabetic, antimicrobial, anti-inflammatory, hepatoprotective, and immunomodulatory effects [8-10]. This has sparked increasing interest in the plant for its potential development into herbal or pharmaceutical formulations.

The present review aims to provide an in-depth evaluation of *Cocculus hirsutus* by compiling and analysing existing literature on its botanical description, ethnomedicinal uses, phytochemical constituents, pharmacological activities, and toxicological safety, with an emphasis on critical research gaps and future prospects.

2. Botanical Description and Morphological Features

- **Scientific Name:** *Cocculus hirsutus* (L.) Diels
- **Synonyms:** *Cocculus villosus*, *Menispermum hirsutum*

- **Family:** Menispermaceae
- **Common Names:** Jal Jamni (Hindi), Ink berry (English), Vasanavel (Tamil), Duhsparsa (Sanskrit)
- **Habitat:** Found in tropical and subtropical regions across India, Sri Lanka, Pakistan, Africa, and Southeast Asia.
- **Growth Form:** A perennial climber with hirsute stems, commonly growing over shrubs, trees, and fences.
- **Stem:** Woody, pubescent, twining.
- **Leaves:** Simple, alternate, ovate to cordate, 4-10 cm long, 3-8 cm broad, with dense trichomes on both surfaces.
- **Flowers:** Small, greenish-white, unisexual; male flowers borne in axillary cymes; female flowers solitary.
- **Fruits:** Drupes, red when ripe, globose, one-seeded.
- **Seeds:** Curved, reniform, similar to other Menispermaceae members.

3. Ethnomedicinal Uses

Cocculus hirsutus has been used in Indian traditional medicine systems such as Ayurveda, Unani, and Siddha, as well as by tribal communities.

- **Whole Plant:** Traditionally used as a febrifuge, blood purifier, and general tonic [11]. In tribal areas of Rajasthan and Madhya Pradesh, the plant decoction is consumed to reduce body heat and treat typhoid [12].
- **Leaves:** Crushed leaves are applied to wounds, ulcers, and skin infections. The juice is used in eye ailments [13]. In folk medicine, a poultice of leaves is used to treat eczema and ringworm [14].
- **Roots:** Decoctions are given orally for venereal diseases (e.g., syphilis), and urinary tract infections [15, 16].
- **Juice and Decoction:** Used as a traditional antidote for snake and scorpion bites, and for treating fevers and diabetes [17, 18].
- **Folk Practices:** The plant is reported in *Bhils* and *Gonds* ethnomedicine for treatment of liver ailments, arthritis, and jaundice [19].

4. Phytochemical Profile of *Cocculus hirsutus*

Phytochemical studies have revealed the presence of multiple classes of bioactive compounds that contribute to the plant's ethnomedicinal and pharmacological properties. These include alkaloids, flavonoids, triterpenoids, phenolic acids, lignans, steroids, saponins, and glycosides.

4.1 Alkaloids

Alkaloids are the hallmark phytochemicals of the Menispermaceae family. In *C. hirsutus*, these compounds are predominantly benzyloquinoline and aporphine-type alkaloids, which have shown significant neurological, anti-inflammatory, and antimicrobial activities.

Identified alkaloids include: Coclaurine - a benzyloquinoline alkaloid with antioxidant and neuroprotective activity. Magnoflorine - exhibits anxiolytic, antimicrobial, and antioxidant properties [20]. Palmatine - known for its antidiabetic, antimalarial, and hepatoprotective effects [21]. Isocorydine, Sinomenine, and N-nornuciferine - with reported anti-inflammatory and analgesic activities [22].

4.2 Flavonoids

Flavonoids present in *C. hirsutus* contribute to its antioxidant, anti-inflammatory, and cytoprotective effects. Commonly identified flavonoids include:

Quercetin - a potent free radical scavenger with anti-

inflammatory, cardioprotective, and anticancer effects [23]. Rutin - a glycoside of quercetin with vasoprotective and anti-ulcer effects [24]. Kaempferol and isorhamnetin - have shown anti-oxidative and anti-proliferative properties [25].

4.3 Phenolic Acids

Phenolic acids are responsible for the plant's antioxidant and hepatoprotective actions. Major phenolics detected include: Gallic acid - reported to reduce oxidative damage and inflammation [26]. Caffeic acid, ferulic acid, and chlorogenic acid - contribute to anti-aging, anti-diabetic, and neuroprotective actions [27]. These are mostly extracted using hydro-alcoholic solvents and quantified using HPLC and LC-MS techniques.

4.4 Triterpenoids and Steroids

Triterpenoids and sterols found in *C. hirsutus* are largely responsible for anti-inflammatory, antiulcer, and lipid-lowering properties.

Lupeol - a pentacyclic triterpene known for anti-cancer and hepatoprotective activity [28]. Betulinic acid - shows anti-HIV and anti-tumor effects [29]. β -Sitosterol and Stigmasterol - common phytosterols with cholesterol-lowering and immunomodulatory actions [30]. These compounds are typically identified via GC-MS and NMR spectroscopy.

4.5 Lignans and Coumarins

Lignans like pinoselin and secoisolariciresinol have also been reported in *C. hirsutus* extracts, albeit in smaller amounts. These molecules are known for anti-proliferative and antioxidant effects [31]. Coumarins, another group of secondary metabolites, contribute to the anti-inflammatory and photoprotective activity of the plant.

4.6 Saponins and Glycosides

Saponins and glycosidic compounds contribute to the diuretic, anti-inflammatory, and cardioprotective potential of the plant. Their presence has been confirmed by preliminary phytochemical screening and foam test assays [32].

4.7 Essential Oils and Volatile Compounds

Essential oils extracted from the aerial parts of the plant contain a complex mix of monoterpenes and sesquiterpenes with antibacterial and antifungal properties [33]. GC-MS analysis has revealed compounds such as caryophyllene, α -humulene, and eugenol, which are responsible for the aromatic and biological effects.

5. Techniques Used for Phytochemical Investigation

The comprehensive investigation of the phytochemical profile of *Cocculus hirsutus* necessitates the use of advanced analytical techniques for the extraction, isolation, separation, structural elucidation, and quantification of its bioactive constituents. These techniques range from traditional qualitative assays to sophisticated instrumental methods such as spectrometry and chromatography. Below is a detailed overview of the primary techniques applied:

5.1 Preliminary Phytochemical Screening

This is the first step in assessing the presence of major phytoconstituent classes. Various chemical tests are employed to detect classes such as alkaloids, flavonoids, saponins, tannins, glycosides, and triterpenoids.

5.2 Thin Layer Chromatography (TLC) and High-Performance Thin Layer Chromatography (HPTLC)

- TLC is a low-cost and rapid screening technique used for

preliminary identification of compounds. It separates components on the basis of polarity and provides visual profiles under UV or after staining with specific reagents [34].

- HPTLC, a more refined form, allows for semi-quantitative estimation of compounds like alkaloids (e.g., magnoflorine, palmatine), flavonoids (rutin), and phenolics using densitometric scanning [35].

5.3 High-Performance Liquid Chromatography (HPLC)

HPLC is one of the most widely used quantitative techniques for profiling secondary metabolites in *C. hirsutus*. It offers high resolution, reproducibility, and sensitivity.

Reverse-phase HPLC (RP-HPLC) is commonly applied for the estimation of polar compounds such as alkaloids, phenolic acids, and flavonoids. Mobile phases typically consist of water, acetonitrile, or methanol with acidic modifiers (e.g., formic acid) [36]. Specific studies have quantified magnoflorine, palmatine, quercetin, and rutin using HPLC [37].

5.4 Liquid Chromatography-Mass Spectrometry (LC-MS/MS)

LC-MS/MS combines the separation capabilities of liquid chromatography with the detection power of mass spectrometry, allowing for:

- Identification of compounds at trace levels
- Molecular weight confirmation
- Structural fragmentation analysis

This is especially useful for complex phytochemical matrices like those found in *C. hirsutus*, which contain overlapping alkaloids and polyphenolics [38].

5.5 Gas Chromatography-Mass Spectrometry (GC-MS)

GC-MS is primarily employed for the analysis of volatile and thermally stable compounds, such as those present in the essential oils and hexane extracts of *C. hirsutus*.

Detected compounds include α -humulene, β -caryophyllene, eugenol, and sesquiterpenes. It provides mass spectra for compound identification by comparison with NIST or Wiley databases.

5.6 Nuclear Magnetic Resonance Spectroscopy (NMR)

NMR is the gold standard for structural elucidation of pure isolates. Both ^1H -NMR and ^{13}C -NMR are extensively used to determine the backbone and substitution patterns of isolated alkaloids, flavonoids, and triterpenoids. It offers definitive molecular structure information, especially when used in conjunction with MS data [39].

5.7 Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectroscopy is used for identifying functional groups in plant extracts or isolated compounds. Complementary confirmation of compound class (e.g., hydroxyl, carbonyl, amine groups). Though less specific, it is valuable as an initial tool for extract fingerprinting [40].

5.8 UV-Visible Spectrophotometry

This technique is used for the quantitative estimation of total phenolics, flavonoids, and alkaloids:

- Folin-Ciocalteu method for total phenolics
- Aluminum chloride method for flavonoids

These are colorimetric assays and provide bulk phytoconstituent data [41].

5.9 Column Chromatography and Preparative TLC

For isolation and purification, Silica gel column chromatography is used to separate compounds based on polarity. Preparative TLC allows for large-scale separation and subsequent identification using spectral techniques. These methods are essential before structural studies (NMR, MS) are performed [42].

5.10 Hyphenated Techniques

Modern phytochemical analysis often employs hyphenated techniques, which provide multi-dimensional insights: HPLC-DAD, HPLC-MS, GC-MS-MS, and LC-NMR enhance compound resolution, structural characterization, and sensitivity in detecting low-abundance molecules [43].

6. Pharmacological Activities of *Cocculus hirsutus*

Cocculus hirsutus has demonstrated a wide array of pharmacological activities, attributed to its rich content of bioactive secondary metabolites. The pharmacological potential of this plant has been validated by various ethnopharmacological, preclinical, and experimental studies.

6.1 Antioxidant Activity

Several studies have reported significant antioxidant potential of *C. hirsutus* extracts, mainly due to the presence of phenolic and flavonoid compounds. Ethanolic and methanolic extracts exhibited DPPH radical scavenging, ABTS assay, and ferric reducing antioxidant power (FRAP) activities in a dose-dependent manner [44]. The IC_{50} values of leaf extract in DPPH assay were comparable to standard antioxidants like ascorbic acid. Flavonoids such as rutin, quercetin, and kaempferol are likely contributors to this effect [45].

6.2 Antidiabetic Activity

The hypoglycemic effect of *C. hirsutus* has been extensively studied in streptozotocin (STZ)-induced diabetic rats. Ethanolic and aqueous extracts showed a significant reduction in blood glucose levels, improved oral glucose tolerance, and restored glycogen content in liver and muscle tissues [46]. The mechanism is suggested to involve α -glucosidase inhibition, antioxidant-mediated pancreatic β -cell protection, and modulation of insulin sensitivity [47].

6.3 Antimicrobial Activity

C. hirsutus exhibits broad-spectrum antimicrobial properties, effective against both Gram-positive and Gram-negative bacteria, as well as some fungal species. Ethanolic extract showed inhibitory zones against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Candida albicans* [48]. Mechanisms may include membrane disruption, enzyme inhibition, and DNA interference by phytoconstituents such as alkaloids and essential oils.

6.4 Anti-inflammatory and Analgesic Activity

Methanolic and chloroform extracts of the plant have shown significant anti-inflammatory activity in carrageenan-induced paw edema and cotton pellet granuloma models in rats. The extract reduced pro-inflammatory cytokines (TNF- α , IL-6) and COX-2 expression, similar to standard NSAIDs [49]. Alkaloids and flavonoids may inhibit prostaglandin synthesis and lipid peroxidation.

6.5 Hepatoprotective Activity

Extracts of *C. hirsutus* have demonstrated protective effects against carbon tetrachloride (CCl_4)-induced hepatic damage in

animal models. Histological observations showed reversal of hepatic necrosis, steatosis, and inflammatory infiltration [50]. Elevated levels of liver enzymes (AST, ALT, ALP) were significantly reduced, indicating membrane stabilization and antioxidant defense enhancement.

6.6 Immunomodulatory Activity

Studies report immunostimulant effects of aqueous and ethanolic extracts of the plant:

Enhancement of phagocytic index, delayed-type hypersensitivity (DTH) response, and lymphocyte proliferation was observed [51]. Likely due to polysaccharides and polyphenols acting on macrophage and T-cell activation pathways.

6.7 Anticancer Activity

In vitro studies have indicated cytotoxic potential of *C. hirsutus* extracts against several cancer cell lines:

Methanol extract demonstrated activity against MCF-7 (breast cancer) and HeLa (cervical cancer) cells with IC₅₀ values in the range of 50-100 µg/mL [52]. Mechanism may include apoptosis induction, ROS-mediated cell death, and cell cycle arrest.

6.8 Antipyretic Activity

Ethanolic extract reduced yeast-induced pyrexia in rats significantly, comparable to paracetamol, indicating the presence of centrally acting antipyretic agents [53].

6.9 Antiurrolithiatic Activity

The plant has shown effectiveness in reducing calcium oxalate crystal formation in ethylene glycol-induced urolithiasis in rats. It lowered urinary oxalate, calcium, phosphate, and creatinine levels and protected renal architecture [54].

6.10 Wound Healing Activity

Topical application of *C. hirsutus* paste and extract has demonstrated accelerated wound contraction, epithelialization, and collagen synthesis in excision and incision models [55].

6.11 Antituberculosis activity

Aqueous extract of *C. hirsutus* shows potent antitubercular activity on non-pathogenic and pathogenic strain of *Mycobacteria* by comparing with standard isoniazid against different *in-vitro* assays [56, 57].

7. Conclusion

Cocculus hirsutus (L.) Diels is a valuable medicinal plant belonging to the family Menispermaceae, recognized for its extensive ethnobotanical applications and a wide spectrum of pharmacological activities. Traditional systems of medicine have long utilized this plant to treat fever, skin infections, diabetes, liver disorders, and inflammatory conditions, which has prompted increasing scientific interest in recent decades. Phytochemical investigations have identified a range of bioactive compounds-including isoquinoline alkaloids, flavonoids, phenolics, and triterpenoids-that contribute to its therapeutic efficacy.

Preclinical studies have substantiated the antioxidant, antidiabetic, antimicrobial, anti-inflammatory, hepatoprotective, immunomodulatory, and even anticancer activities of various plant extracts. These effects are believed to result from the synergistic actions of multiple

phytochemicals acting on diverse biochemical targets. Despite these promising findings, the plant remains underexplored in terms of clinical validation, standardization, and drug development. Most available data are limited to *in vitro* and animal models, and very few studies address pharmacokinetics, toxicity, or molecular mechanisms in detail.

Therefore, *Cocculus hirsutus* stands out as a pharmacologically versatile but scientifically underutilized medicinal resource. Further research, including well-designed clinical trials and bioactivity-guided isolation of lead compounds, is necessary to unlock its full therapeutic potential and facilitate its integration into modern phytomedicine.

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