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PHARMACOLOGICAL AND PHYTOCHEMICAL SPECTRUM OF TRADITIONAL MEDICINAL PLANT *ADINA CORDIFOLIA* FAMILY- RUBIACEAE: A REVIEW

Sweta Negi *, Arvind Negi and Manish Kumar Mishra

GRD (PG) IMT, Department of Pharmacognosy, 214- Rajpur Road Dehradun - 248001, Uttarakhand, India.

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Correspondence to Author:
Sweta Negi

GRD (PG) IMT,
Department of Pharmacognosy,
214- Rajpur Road Dehradun - 248001, Uttarakhand, India.

E-mail: swetanegi398@gmail.com

ABSTRACT: *Adina cordifolia* is the yellow Saffron Teak; belonging to the subfamily Cinchonoideae; family *Rubiaceae* is found in Southern Asia, from India and Srilanka east to southern China and Vietnam. It is a substantial, deciduous tree, hinge disintegrated in deciduous forests all through the significant part of India, levitates up to an altitude of 900 m in the sub-Himalayan stretch. *Adina cordifolia* was used by historical healers as the remedy of chronic cough and jaundice, stomach ache, fodder, and swelling in the stomach; the Roots are astringent and constipating and are useful in diarrhea and dysentery. The bark is bitter, acrid, refrigerant, astringent, vulnery, demulcent, diuretic, aphrodisiac, and tonic. It is efficacious in deprave pitta conditions, wounds and ulcers, skin disease, strangury, gastropathy, fever and burning sensation. The buds are an antidote to snake venom, flowers used in headaches; leaves are antiseptic utilized in dressing wounds. These are also used in cuts, boils and to cure hemicrania. *Adina cordifolia* has an extensive array of medicinal applications. It has been used as Antiamoebic, Anti-inflammatory, Anti-aging, Antinociceptive, and Antifertility. In the present review compassed on plant *Adina cordifolia*, more prominence was given to literature review, chemical composition, pharmacological and biological studies on *Adina cordifolia* plants. This dissertation will be benevolent to push scientists to co-ordinate their studies because it's a disputable kind of drug with sparse research.

INTRODUCTION: Nature has provided a complete storehouse of remedies to cure all ailments of mankind. The knowledge of drugs has accumulated over thousands of years due to man's inquisitive nature so today we possess many effective means of ensuring health care. The human being appears to be afflicted with more diseases than any other animal species.

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In the past, almost all the medicines used were from plants, the plants being man's only chemist for ages. Today, a vast store of knowledge concerning the therapeutic properties of different plants has accumulated. All phyla of plants *viz*. Thallophyta, Bryophyta, Pteridophyta, Spermatophyta, contain species that yield official and unofficial products of medicinal importance.

By far, the greatest number of these are derived from plants and include three hundred or more recognized families of spermatophyte [1]. Medicinal plants contain some organic compounds which provide definite physiological action on the human body and these bioactive substances include tannins, alkaloids, carbohydrates, terpenoids,

steroids, and flavonoids [2]. Awareness of medicinal plant usage results from the many years of struggles against illnesses due to which man learned to pursue drugs in barks, seeds, fruit bodies and other parts of the plants [3]. The knowledge of the development of ideas related to the usage of medicinal plants, as well as the evolution of awareness, has increased the ability of pharmacists and physicians to respond to the challenges that have emerged with the spreading of professional services in the facilitation of man's life [4]. Among the 7,000 species of medicinal plants recognized all over the world. The medicinal value of plants lies in some chemical substances that produce a definite physiologic action on the human body [5]. The most important of these bioactive compounds of plants are alkaloids, flavonoids, tannins, and phenolic compounds.

The phytochemical research based on ethnopharmacological information is generally considered an effective approach to discovering new anti-infective agents from higher plants.[6] Scientists estimate that there may be as many as 10,000 different phytochemicals potentially affecting diseases such as cancer, stroke metabolic syndrome [7]. Plants are rich in a wide variety of secondary metabolites such as tannins, terpenoids, alkaloids, and flavonoids, which have been proved *in-vitro* to have anti-microbial properties. The use of plant extracts and phytochemicals with known anti-microbial properties can be of great significance in Therapeutic treatments [8].

Herbal and Medicinal plants are a source of various alkaloids, flavonoids, terpenoids, and other chemical substances essential for mankind. The use of indigenous drugs of plant origin forms a major part of complementary, alternative, and traditional medicine and the total global herbal drug market is estimated to be US$ 62 billion. It is expected to grow up to US$ 5 trillion by the year 2050. India has a great wealth of traditional knowledge and wisdom, and the value of medicinal plant-related trade in India is estimated at ₹5000 crores per annum. As the demand for plant-derived pharmaceutical compounds increases, possibilities for mass production need to be explored. Plant tissue culture techniques offer the rare opportunity to tailor a phytochemical product's chemical profile by manipulating the chemical or physical microenvironment, to produce a compound of potentially more value for human use. Availability of the plant is subjected to seasonal variation, leading to uncertainty in stable supply throughout the year. Plant production under controlled conditions of *in-vitro* systems can eliminate these problems. Therefore, establishing a suitable micropropagation protocol for the high-yielding lines will potentially provide a better source for a continuous supply of plants in the field of drug research as well as manufacturing of drugs [9, 10].

History of Medicinal Plants: The history of herbal medicine and plants is as old as human civilization. The documents, many of which are of great antiquity, revealed that plants were used medicinally in China, Egypt, and Greece long before the beginning of the Christian era. The text of documented by more than 800 formulae and 700 different drugs. The drugs such as acacia, castor oil, and fennel are mentioned, along with references to compounds such as iron oxide, sodium chloride, sodium carbonate, and sulphur. Most of the medicinally active substances identified in the nineteenth and twentieth centuries were used as crude extract [1]. Plants have been used for medicinal purposes from 5000 BC with the emergence of the Indus Valley Civilization. The oldest known herbal is *Pen-t'sao*writte by Emperor Shen Nung around 3000 B.C. It contains 365 drugs, one for each day of the year [1]. The indigenous system of medicine, viz.-Ayurvedic, Siddha, and Unani, has existed for several centuries. The country has 45,000 different plant species and 15000 medicinal plants, including 2000 plants used in Ayurveda, 700 in Unani, 600 in Siddha, 450 in Homoeopathy, and 30 in modern medicine. The drugs are derived from the whole plant or from different parts like leaves, stem, bark, root, flower, seed, *etc*. Some drugs are prepared medicines. (from excretory plant products such as gum, resins, and latex) [11].

Significance of Medicinal Plants in Human Life [1, 3, 8, 10]:

- Medicinal plants & plant-derived medicines are widely used in traditional cultures.
- At least 7,000 medical compounds in modern pharmacopoeia are derived from plants.

- In Africa and Asia, 80% of the population still uses traditional remedies.
- Annual worldwide market for traditional herbal medicine approaches 60 billion US$.
- Medicinal plants are resources of new drugs. It is estimated there are more than 250, 000 flower plant species.
- Many modern medicines are produced indirectly from medicinal plants, such as aspirin.
- Plants are directly used as medicines by most cultures around the world, such as Chinese medicine and Indian medicine.
- Many food crops have medicinal effects, for example, garlic.

Several herbal traditions have come to dominate the practice of alternative medicine. These include the western herbal tradition based on Greek, Roman, and medieval sources, the essentially Ayurvedic tradition of India, and the Chinese herbal medicine. Traditional Chinese medicine continues as a distinct branch of modern medical practice.

The traditional herbal remedies as alternative medicine also play a significant role in South Africa, where it forms a part of the culture and beliefs of the indigenous population and also features significantly in primary health care. Botanicals or phytomedicines have always been a major component of traditional healing systems in developing countries, which have also been an integral part of their history and culture. In the ancient Indian system of medicine, Ayurveda and Siddha are such examples [9]. The widespread use of herbs in traditional medicine has also prompted demands that herbal remedies be regulated as drugs to ensure quality standards and to prove their scientific basis. Herbs hold promise not only for prevention but also for the treatment of various types of diseases. The drugs of natural origin constitute very important and valuable segments of modern medicine. Traditional medical practitioners and scientists are turning towards medicinal plants for curing ailments such as inflammation, rheumatoid arthritis, cancer, diabetes, and many more because they possess lesser side effects due to their natural origin. These extracts are formulated into different formulations for ease of administration. The novel formulations have remarkable advantages over conventional formulations of plant actives and extracts. These include enhancement of solubility, bioavailability, toxicity protection, pharmacological activity enhancement, stability enhancement, tissue macrophage distribution, sustained delivery, and protection from physical and chemical degradation [15].

Herbal Drug Research Today: The goal of the herbal drug research and development program is to discover single entity and multi component bioactive natural products that may lead to the development of new pharmaceuticals that address unmet therapeutic needs.

Traditional knowledge-driven drug discovery will serve as a powerful search engine and, most importantly, will greatly facilitate the focused and safe natural products research to rediscover the drug discovery process. There are over 750,000 plants on earth. Only a very few of healing herbs have been studied scientifically. Of these, only about 6% have been screened for biologic activity, and a reported 15% have been evaluated phytochemically [16].

Revival of Traditional Medicine: There is a rising recognition of the value of experience and historical knowledge gathered by indigenous cultures with medicinal plants. The revival of interest in herbal medicines is firstly due to increased awareness of the limited horizon of synthetic pharmaceutical products to control major diseases and secondly due to the current widespread belief that 'green medicine' is safe and more accessible and affordable than the costly synthetic drug many of which have adverse side effects. The past decade has witnessed a tremendous resurgence in the interest and use of medicinal plant products, especially from developed countries. According to a WHO estimate, about 80% of the world population relies on traditional systems of medicines for primary health care, where plants form the dominant component over other natural resources [17].

Plant Profile:

FIG. 1: LEAVE WITH SEEDS

FIG. 2: LEAVE WITH A FLOWER

FIG. 3: *ADINA CORDIFOLIA* TREE

FIG. 4: SEEDS OF *ADINA CORDIFOLIA*

- *Adina cordifolia* is a large deciduous tree, under good conditions grows, over 30 m., but is normally about 14-20 m tall.[12,18,19]

- Leaves up to 25 cm or more across, broadly oval or circular in shape, acute at the apex, heart-shaped at the base, slightly hairy, especially when young, green or tinged with red or pink; nerves a strong one running from the base to the tip of the leaf and 5-6 pairs of lateral ones, which unite in a wavy line near the margin of the leaf. Leaves come out in pairs, one on either side of a branch, their stalks connected by a pair of stipules. These are two leaf-like structures, up to 2.5 cm. long, enclosing and protecting the very young leaves and shoot apex; when the stipules fall away, they leave two clear lines, each encircling half of the branch. Leaf stalks are 5-10 cm, long [19, 20].

- Flowers are insignificant individually, being very small, but they come out in balls 2-3 cm. across; the tiny flowers are yellow or yellowish

in color, often tinged with pink. When the little flowers open out, the most prominent parts are the styles, which form a sort of halo round the floral ball [18-22].

- Fruits are minute, forming an almost solid ball, which, when ripe is black or nearly black. Fruits are capsules like, splitting into two dehiscent cocci [18, 20, 21].
- Seeds are many, narrow, small and tailed [19-21].
- Leaves are shed about February, and the tree remains leafless until about may-june; the stipules covering the buds are conspicuous. Flower balls are at their best from June to August. After the fruit proper has been shed at about the beginning of June of the following year, the fruit heads appear black and are about 12 mm. across: the monsoon rains may bring them down and prepare the tree for the new flower balls [21-25].

History of *Adina cordifolia*: The history of *Adina cordifolia* can be traced back to Vedas, Puranas, and Samhita. There is a reference to roots and branches of *Adina cordifolia* in different books of vedic period. It was used for dantadhavana. In paraskara Guhyasutra 1/21, Atharvaparishista 26/5/1-4, Yajnavalkyashiksha 34, Mandukishiksha 4/1 *etc*., Adina has been mentioned. It is mentioned as Nipa in Panineeya Asthadhyayi, Pathanjali Mahabhashya, Gubhilagruhya sutra, and Shulwa Prathishakhya [18-25].

Distribution: It is a South East Asian species. It is distributed throughout India, Burma, Srilanka, Bangladesh, Nepal, Thailand, South China, Bhutan, Vietnam, Myanmar, and Malaysia. It is found scattered in deciduous forests throughout the greater part of India (except in arid regions of Rajasthan), ascending to an altitude of 900 m in the sub-Himalayan tract. It is also common in the forests of South India. It grows well under 300-1000m altitude and prefers well-drained soil. Suitable soil pH range from 5.5 to 6.5. The annual temperature requirement is 250C-350C and prefers a mean annual rainfall between 1000-2000mm. It is not frosted tolerant. The tree grows in various geological formations such as granite, gneiss, schist, quartzite, trap, and late rite up to 1000 MSL [12, 18-25].

TABLE 1: TAXONOMIC CLASSIFICATION [18-25]

Kingdom	**Plantae**
Class	*Magnoliopsida*
Sub-class	*Asteridae*
Superorder	*Gentiananae*
Order	*Gentianales*
Family	*Rubiaceae*
Subfamily	*Cinchonoideae*
Genus	*Adina*
Specific epithet	*Cordifolia*
Botanical name	*Adina cordifolia (*Roxb.) Benth& Hook. F.
Synonym	*HaldinaCordifolia* (Roxb.)

Family: Rubiaceae family includes plants that have medicinal use and contain secondary metabolites. Rubiaceae is by far the substantial family in the flowering plants order-sgentianales.

It is also the oldest family that branched off on the gentianales family tree. Rubiaceae comprises about 450 genera and 6500 species and includes trees and thousands of infrequently herbs7-10. Among the many plants, *Adina Cordifolia* is one from the Rubiaceae family [12, 18-25].

Genus: *Adina cordifolia*, is the sole species in the genus Haldina [12, 18-25].

TABLE 2: CLASSICAL CATEGORIZATION OF *ADINA CORDIFOLIA*

S. no.	**Classical texts**	**Gana & Varga**
1	Bhavprakash Nighantu 26	Pushpa Varga
2	Madanpala Nighantu. 27	Vatadi Varga
3	Nighantu Adrash 28	Manjisthadi Varga
4	Raja Nighantu 29	Prabhadradi Varga
5	Dravyaguna Vijanam 30	Jwarghnadi Varga

TABLE 3: VERNACULAR NAMES OF HARIDRU [30, 31]

S. no.	**Language**	**Names**
1	Sanskrit	Haridru
2	Hindi	Haldina
3	Bengali	Kelikadamba
4	Marathi	Hed
5	Gujarati	Haldarvo
6	Tamil	Manjkadamba
7	Urdu	Halnd
8	English Name	Yellow Teak, Saffron Teak

USES [23-25, 30-33]:

- Fresh bark is ground with brown sugar and taken internally for stomachache.

- Bark and leaves are used for cholera, cold cough, fever, headache, Scars, and skin yellowish of body, urine complaints.
- Laves are used on coughs and cold.
- Fresh stem bark juice is taken in rheumatism.
- Latex is applied on aching tooth.
- Stem bark used on fever.
- Leaves are applied over swollen portion to remove pain and swelling.
- Bark is used as an antibacterial, eczema, Scabies, Bark paste is applied to eczema, Scabies, or bacterial infections on the skin.

Chemical Composition of *Adina cordifolia*: A yellow colouring matter adinin, belonging to naphthaquinone group of pigments, was isolated along with tannins from the heartwood [23, 34].

A detailed examination of the heartwood confirmed the occurrence of a compound agreeingin physical properties with adinin, which was shown to be an alkaloid of the Bcarbolineseries and renamed the compound adifoline. The other constituents identified were cordifoline; [35] benzoic acid, B-sitosterol, and umbelliferone. The flavanones isolated from the heartwood were identified as 7, 4-dimethoxy-5-hydroxyflavanone and 5, 7-dimethoxy-4-hydroxyflavanone. The heartwood also yielded saturated aliphatic hydrocarbons *viz.* nheneicosane, n-tricosane, n-pentacosane, and n-pentatriacontane b-sitosterol. Theoleoresin obtained by the incision of the trunk yield 5.2-6.8 percent of essential oil [24, 36]. In a preliminary chemical study, the stem bark was found to contain alkaloids. The ethanolic extract of the root bark was found to contain a new coumarin glycoside adicardin, characterized as 7-apiglucoside of umbelliferone [35, 36].

Phytocompound in A*dina cordifolia*: Identification of phytocompounds was based on the principles of molecular weight (MW), retention time (RT), molecular formula (MF), and concentration (peak area %).A total of 66 constituents were identified in the study contributing: [37, 38]

- 61.74% of the chloroform extract,
- 80.42% of the ethyl acetate extract,
- 60.88% of the acetonic extract,
- 45.59% of the methanolic extracts.

The dominating constituents in respective leaves extracts of "*Adina cordifolia"* were:

- Transsqualene (15.4-42.1%),
- Vitamin E (2.9-5.8%),
- Phytol (1.1-9.42%),
- Neophytadiene (2.0-2.4%).

TABLE 4: THE PHYTOCOMPOUNDS IDENTIFIED IN LEAF OF *A. CORDIFOLIA* IN DIFFERENT SOLVENTS [37, 38]

Chloroform extract	Ethyl acetate extract	Acetonic extract	Methanolic extracts
Tetradecanal (0.93%)	Tetradecanal (1.09%)	Phenol (7.33%)	Phenol (1.14%)
Neophytadiene (2.46%)	Neophytadiene (2.05 %)	Neophytadiene (2.09%)	Naphthalene (1.16%)
Trans-squalene (42.13%)	Trans-squalene (15.42 %)	Trans-squalene (27.44%)	Epiglobulol (3.23%)
Phytol isomer (2%)	Phytol isomer (9.42%)	Trimethylsilylpalmitate (3.36%)	Caryophyllenoxide (4.14%)
Ergost-5-en-3-ol (3.38%)	Gamma.-sitosterol (4.11%)	Phytol isomer (1.18%)	Loliolide (1.32%)
Vitamin E (4.22%)	Vitamin E (5.84%)	Vitamin E (2.99%)	Pentyloctanoate (3.44%)
Campesterol (1.71%)	Hexadecanoic acid methyl ester (1.10%)	Campesterol (1.05%)	Behenylbehenate (6.53%)
Naphthalene (3.48 %)		Tetradecanal (0.68%) Naphthalene (3.77%)	

Pharmacological and Biological Studies: Anti-ulcer*:* *A. cordifolia* had also been evaluated for its anti-ulcer potential active constituent and showed interesting H+/K+ ATPase inhibitory activity. Four compounds isolated from the stem of *Adina cordifolia* were identified as stigmasta-5, 22-diene-3P- O – a – rhamnopyranosyl - (1 - 4) – P – Dxylo-pyranoside, a-amyrin, octacosanol and naringenin-7-methyl ether-4'-O-a-rhamnopyranoside on the basis of spectral and chemical evidence [21, 37, 45].

Anti-microbial: The crude extract of the bark showed antibacterial activity against *Bacillus anthracis, Bacmycoides, Bacsubtilis, Pseudomonas sp., Salmonella paratyphi*, *Staphylococcus albus*, *Xanthomonas campestris* and *Xanth malvacearum* [20, 39, 44].

Flavone isolated from the heartwood exhibited broad spectrum antibacterial activity against *Vibrio cholerae*, *Neisseria gonorrhoea*, mild activity against *Escherichia coli* and moderate antifungal activity against *Aspergillus fumigatus* and Cryptococcus neoformans [20, 44].

Hepato-protective Action: The acetone (*AEAC*) and aqueous extracts (*AQEAC*) of *Adina cordifolia* were studied for hepatoprotective activity against Wister rats with liver damage induced by ethanol. It was found that *AEAC* and *AQEAC*, at a dose of 500 mg/kg bodyweight, revealed hepatoprotective effect by diminishing the Serum Glutamate Pyruvate Transaminase (SGPT), Serum Glutamate Oxaloacetate Transaminase (SGOT), alkaline phosphate and total bilirubin to a remarkable extent and also significantly increased the levels of total protein. Histopathological studies of liver tissue also mounted the hepatoprotective activity. The effects of *AEAC* and *AQEAC* were comparable with standard drug silymarin [40, 44].

Antimalarial: The alcoholic extract of the stem bark screened for *in-vivo* and *in-vitro* antimalarial activity against the NK 65 strain of plasmodium Bergheim was found inactive [41, 44].

Anti-oxidant Property: Percentage of DPPH radicals' inhibition and IC_{50} values (µg/ml) was expressed as antioxidant activity of extracts. IC_{50} values ranged from 20.39 to 38.96µg/ml. The total phenolic content ranged from 17.48 to 20.83 mg/g of the dry weight of extract, expressed as gallic acid equivalents. The total flavonoid concentrations varied from 17.49 to22.48 mg/g, expressed as quercetin equivalents. The significant linear correlation was confirmed between the values for the total phenolic content and antioxidant activity of plant extracts. *Adina cordifolia* (Roxb.) can be estimated as auspicious candidate for natural plant sources of antioxidants with high value [42, 44].

Antifertility: The ethanolic extract of the dried leaves administered to female rats for 5d after mating did not reveal antifertility activity (anti-implantation and abortifacient) as observed on the 10 d of pregnancy [22, 44].

Antidiabetic: The hydro-alcoholic extract of *Adina cordifolia* (Roxb.) leaves in alloxan-induced diabetic rats at 250, and 500 mg/kg doses showed antidiabetic activity. Glibenclamide (10 mg/kg, s.c.) was used as the standard, which produced a notable decrease in blood glucose levels. The blood glucose levels of experimental animals were examined at 0, 2,4, and 6 h after giving plant extract by using glu-oxidase peroxidize reactive strips and glucometer. Treatment with hydro-alcoholic extract of *Adina cordifolia* (Roxb.) leaves at 500 mg/kg dose reduced the blood glucose level significantly. However, the lower doses (250 mg/kg) of hydro-alcoholic extract of *Adina cordifolia* (Roxb.) leaves produced a little decrease in blood glucose level. It was demonstrated that there was a dose-dependent decrease in blood glucose level in the alloxan-induced diabetic rats compared to the control group. This study revealed that hydro-alcoholic extract of *Adina cordifolia* (Roxb.) leaves possessed significant antidiabetic activity [44].

Anti-proliferative: Anti-proliferative activity of methanolic extract of *Adina cordifolia*, was determined using cell lines. Cells (5 × 103) were seeded in 12-well plates containing respective medium at 370C with 5% CO_2 and 95% air and in 100% relative humidity. After 24 h, various concentrations of *Adina cordifolia*, extracts (0-100 µg/ml) were added. At the end of 72 h incubation, the medium in each cell was replaced by fresh medium containing 5 mg/ml of MTT. 3 hours later, the Formosan product of MTT reduction was dissolved in DMSO and absorbance was measured using a multi-plate reader. The IC_{50} values were calculated by plotting the percentage survival versus the concentration of extract [46].

CONCLUSION: The present work was carried out on the plant *Adina cordifolia* family: Rubiaceae here; more emphasis was given to literature reviews of Phytochemical & Pharmacological of *Adina cordifolia Plants*. After a thorough investigation and literature search, it was observed that less work had been done on this plant, especially its leaves. Traditionally the plant *Adina*

cordifolia has a large demand due to its treatment of many chronic and acute diseases with great benefits. This study attempts to lighten high the Therapeutic potential of *Adina cordifolia* and its constituents in the prevention or therapy of the disease. We can conclude from this study that the results reviewed are aimed at attracting the attention of researchers seeking new drugs from *Adina cordifolia* and its chemical compounds. The isolated compounds can hopefully be considered in the future for more clinical evaluations and possible applications and as an adjuvant to current medications. We should continue to consider and valorize our natural patrimony and conduct more research on *Adina cordifolia* and its Pharmacological aspects.

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