

Review Article

ARTABOTRYS HEXAPETALUS (L. F.) BHANDARI: A PLANT WITH ENORMOUS BIOMEDICAL POTENTIAL

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ABSTRACT

This review is intended to investigate the published report regarding phytochemical, ethnomedicinal, and pharmacological activities and put forth the therapeutic potential of *Artabotrys hexapetalus* (L. f.) Bhandari. (*A. hexapetalus*). It belongs to the family *Annonaceae*, one of the therapeutically important plants, broadly distributed throughout the world. An extensive review of the literature available in various recognized databases including logical writing and scientific literature, search engines such as Springerlink, ScienceDirect, SciFinder, PubMed, Scopus, Google Scholar, and BioMed Central as well as relevant books, websites, scientific publications, and dissertations were utilized as a source of information that provided an up-to-date review. Phytochemical profiling of these species revealed the presence of some imperative phytochemicals alkaloids, terpenoids, anthraquinones, butyrolactones, flavonoids, neolignans, phenolic compounds, and leucoanthocyanins as the basis of its valuable therapeutic properties. The other imperative phytoconstituents which contribute to the therapeutic properties are isoamericanin A, isoamericanol, americanin, artabotricinol and artabotriol, β -unsaturated- β -butyrolactones, arapetaloside taxifolin, apigenin-7-O-apiosylglucoside, glucoluteolin, and artabotrine. The pharmacological activities exhibited by *Artabotrys hexapetalus* as antimicrobial, antileishmanial, antioxidant, antifungal, antifertility, and anthelmintic properties are attributed to the presence of valuable bioactive phytoconstituents. Considering these facts an effort was made to present a comprehensive review enlightening the taxonomical, phytochemical, and pharmacological activities of plant *Artabotrys hexapetalus*. Future research can be directed to an extensive investigation about phytochemistry, clinical trials, pharmacokinetics, and acquiring safety data to add new dimensions to the therapeutic utilization of *Artabotrys hexapetalus* and other *Artabotrys* species.

Keywords: *Artabotrys hexapetalus*, *Annonaceae*, Pharmacological, Phytochemicals

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INTRODUCTION

Artabotrys is a genus of woody trees, shrubs, and vines comprising about 130 genera and 2,300 species, which is distributed mainly in tropical and subtropical regions of the world, especially tropical Africa and Eastern Asia and the Indomalayan region [1, 2]. Plants of *Artabotrys* genus are climbing herbs bearing recurved hooks borne on lateral branches and scandent shrubs are one of the largest genera of the custard-apple family [3]. *Artabotrys hexapetalus* (L. f.) (*A. hexapetalus*) Bhandari generally described as a folk drug that has a wide range of medicinal uses belonging to family *Annonaceae*. The family includes trees, shrubs, and lianas, found in almost all vegetation types. It is generally considered to be a natural family and one of the six members of *Magnoliales* [4]. It is an ornamental, medium-sized woody climber that produces aromatic flowers with fragrance. *A. hexapetalus* is native to India and widely distributed in the southern part of China, and is used in traditional Chinese medicine for the treatment of malaria [5]. It is a medium-sized climbing shrub, largely cultivated in India. Leaves are oblong, lanceolate, and glabrous. Flowers solitary or paired, often fragrant, usually on woody, hooked recurved branches (Peduncles) [6]. It is widely distributed throughout the southern part of China and also in the southern part of Asia. As a Chinese traditional folk medicine, its roots and fruits are used for treating malaria and scrofula, respectively [7]. The flower is acrid, bitter; useful in vomiting, diseases of the blood and the heart, leucoderma, headache. A decoction of leaves is given for cholera. Phytochemically it contains alkaloids, anthraquinones, butyrolactones, flavonoids, neolignans, phenolic compounds, leucoanthocyanins, terpenoids, and volatile oils [8-10]. Many phytochemicals in the form of flavonoids of *A. hexapetalus* possibly be modified or used as "lead" for developing more effective drug molecules. Hence, extensive pharmacological and phytochemical screening, together with the pharmacokinetic and toxicological assay can be aimed at future investigations. Hence an attempt is made to highlight selected phytochemical and biomedical potentials of *A. hexapetalus* species in this review.

Introduction to *Artabotrys hexapetalus* (L. f.) Bhandari

Taxonomical classification [11]

Domain: Eukaryota
Kingdom: Plantae
Subkingdom: Tracheophytes
Division: Magnoliophyta
Subphylum: Angiosperms
Class: Magnoliopsida-Dicotyledons
Subclass: Magnoliidae
Order: Magnoliales
Family: *Annonaceae*
SubFamily: *Annonoideae*
Genus: *Artabotrys*
Species: *Artabotrys hexapetalus*
Common Name: Ylang-Ylang, Hari Chafa

Vernacular names [12]

Sanskrit: Harachampaka.
Tamil: Manoranjidam.
Telugu: Manoranjidamu.
Marathi: Vilayati Champa.
Genus: *Artabotrys*
Species: *Hexapetalus*

Synonym: *Hornschuchiaceae*

Etymology

A. hexapetalus Indochina: Day cong chua.

Artabotrys = arta+botrys (artao= Support, botrys=bunch of grapes)
Hexapetalus = 6 petals

A plant with 6 petalled flower and fruits resembles a bunch of grapes [13].

Geographic distribution of *A. hexapetalus*

A. hexapetalus probably native to South India and largely cultivated in India, Sri-Lanka, Burma, Southern China, and Taiwan. In different parts of the world, it is largely known as an ornamental plant. Within India, it is indigenous to South India and very commonly cultivated in gardens throughout the country for its fragrant flowers. Plant is propagated through stem cutting and seed. Group of fruits (usually 6) grow together at the end of the long peduncle [14].

Characteristics of plant *A. hexapetalus*

The plant is a climber with lateral branches straight, lenticellate, glabrous, dark brown when dry, young twigs sparsely pubescent shown in fig. 1.

Leaves

The leaves are simple, alternate, petiolated (3-8 mm), exstipulate, and distichously arranged. They are thinly pubescent; oblong-lanceolate 6-10 mm long, shortly acuminate, elliptic, glabrous on both surfaces with a thinly coriaceous blade, and the base is acute

cuneate. The colour of the leaves is pale green when dry. The midrib of the leaf is flat on the upper epidermis and raised at the lower epidermis with lateral anastomosing veins flat on both surfaces [15, 16].

Inflorescence

It has a flat peduncle, solitary or in pairs that are sparsely pubescent with two branches; 1-2 flowers; bract elliptic to oblong and bud broadly ovoid.

Flowers

The flowers are bisexual and actinomorphic, possessing 3 whorls of perianth with 3 segments in each whorl. Entire parts of floral are distinct, yellow, solitary or in pairs, 3.2-3.8 cm long, pedicels 15-20 mm long, sepals are 6 cm long that erect to reflexed sparsely pubescent. Flowers are thinly fleshy, ovate, with acute apex and pubescent. The petals are fleshy, connate below, tips reflexed petals are lanceolate above the saccate base, clothed with appressed silky hairs. Inner petals are narrower, flat, 20-30 x 3-6 mm; torus convex; stamen are oblong. Apical possess a cylindrical carpels prolongation flat, obovoid, glabrous with 2-3 cm in diameter. The stamens are very short and tightly packed generally fertile with central anther portion, a distal pad of fleshy connective tissue, and a short fleshy basal portion [17, 18].

Fruit

Appeared berries, obovoid to ellipsoid, 3.5-4 x 1.5 cm, apex mucronate; stalk 20 x 1.5 mm, sparsely pubescent. It bears berry-like fruits but sometimes forms multiple fruits like the custard apple [19].

Seed

Two large, ellipsoid oblong little flattened, deeply grooved on one side, more than 13 mm long. Sectioned seeds reveal channels or partitions in the ruminant endosperm [20].

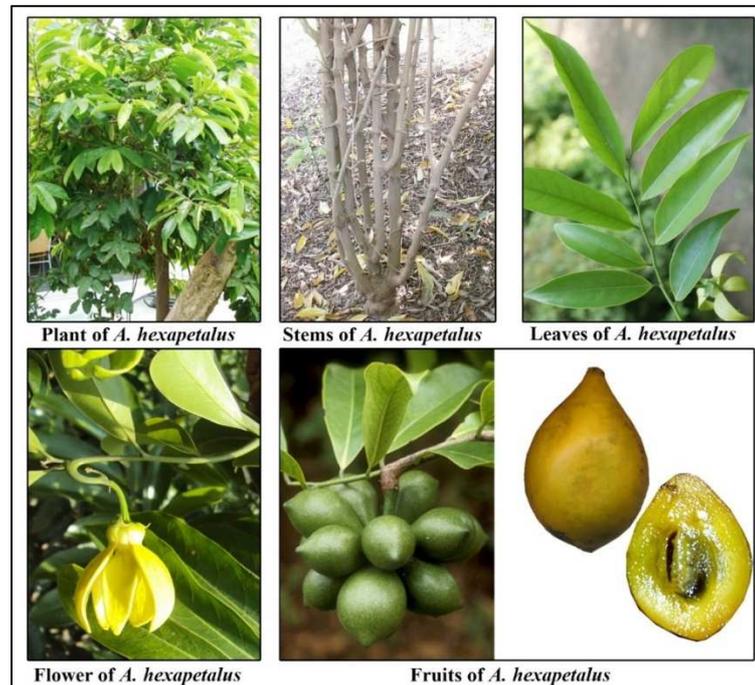


Fig. 1: Morphology of the *A. hexapetalus* plant

Traditional uses of *A. hexapetalus*

Medicinal plants and traditional systems of medication is been continuously allied as the backbone of these systems. India has an ironic natural heritage of traditional systems of medicine. These traditional systems of medications with the perceptions of safety, efficacy, and quality will urge to protect the customary heritage [21]. The flowers of *A. hexapetalus* are tonic and stimulant. The fruits and the bark are used to treat fever, diarrhea, skin diseases, wounds,

ulcers, inflammation, cough, asthma, and bronchitis. The leaves extract has antibacterial, antifertility, and antifungal activity [22]. The pulp of ripened fruits has been used traditionally in some parts of Assam for the fungal infections in the domestic animals the tribes of Malay Archipelago use a decoction of leaf for treatment of Cholera. Roots of this plant are used to treat Malaria according to Chinese traditional systems of medicine. The volatile oil from the flower in the Unani system of medicine is used in aromatherapy [23, 24]. In Ayurveda and Siddha systems of medicines flowers used as tonic

and stimulant. Fruit and bark are used to treat fever, diarrhea, flatulence, colic, constipation, skin disorders, wound healing, cough, and bronchial asthma. The decoction of leaves used as an antimicrobial, antifertility, muscle relaxant, and cardiac stimulant [25]. Flowers used as a flavoring in tea Southern India; Sri Lanka Used in perfumery as the source of essential oils. In Salem, Tamil Nadu, Southern India used in the preparation of stimulating tea-like beverages. In Java, Indonesia, Philippines, Southern China, India

whole plant is used as an ornamental plant and for screen planting in large gardens. In traditional Chinese systems of medicine prescribed for the treatment of malaria and scrofula [26-28].

Phytochemical composition of *A. hexapetalus*

The literature proposes that *A. hexapetalus* possess important bioactive compounds, as shown in fig. 2.

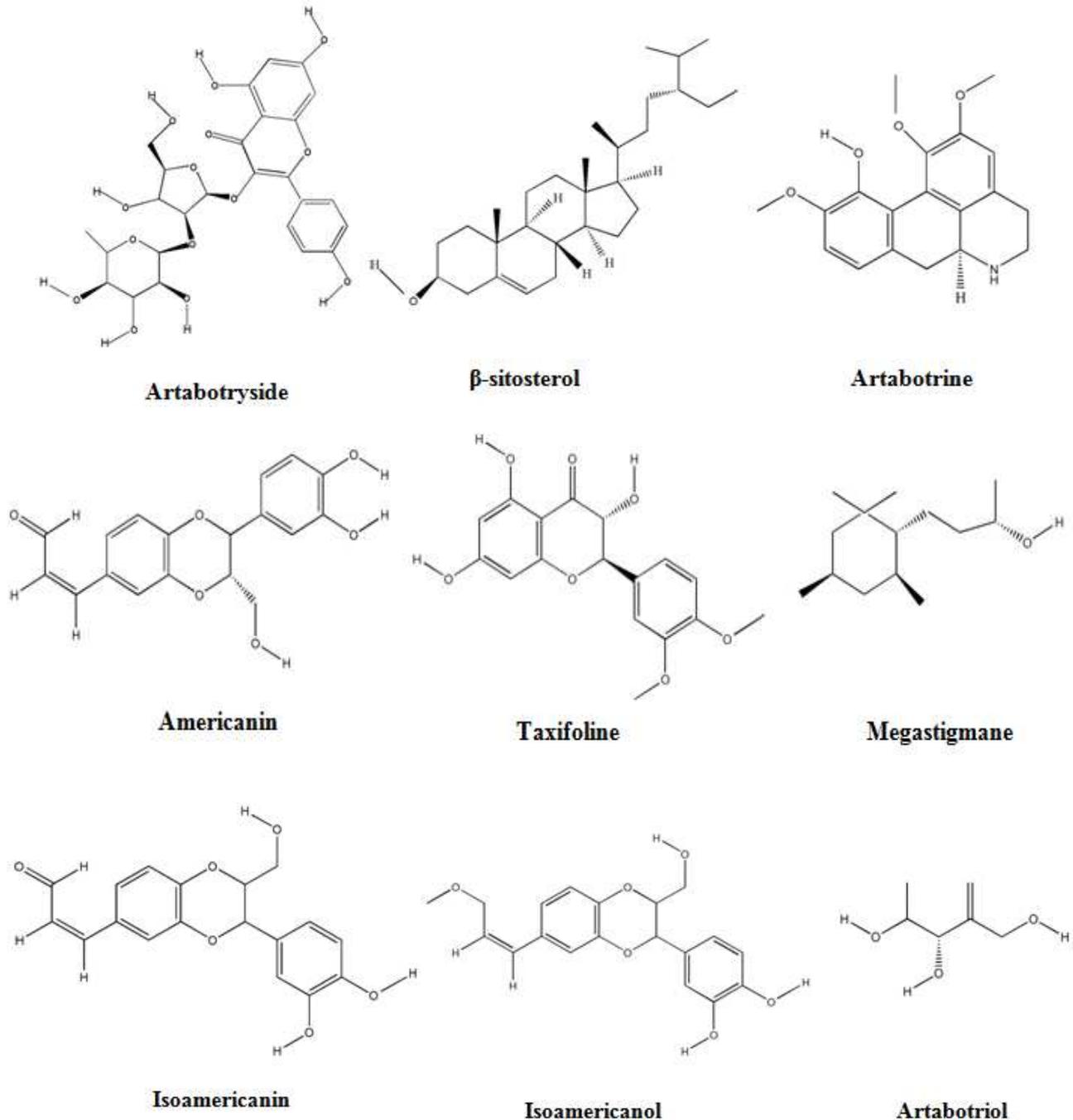


Fig. 2: Phytoconstituents of *A. hexapetalus*

Interestingly almost all parts of the *A. hexapetalus* species have been explored for phytochemical analysis and various phytoconstituents are isolated to date. Various important phytoconstituents have been reported are 4-neolignan, namely isoamericanin A, isoamericanol A,

americanin B and artabotricinol a semi terpenoid: (R) artabotriol. It contains β -unsaturated- β -butyrolactones. Flavonol glycosides namely arapetaloside A and B are reported, Flavonoids: taxifolin, apigenin-7-O-*apiosyl*glucoside, and glucoluteolin. Alkaloid: artabotrine [29] table 1.

Table 1: Chemical constituents of *A. hexapetalus*

S. No.	Phytochemical		Plant part	Reference
1.	4-neolignan	Isoamericanin A, Isoamericanol A, Americanin B and Artabotricinol	Seeds	Yu J <i>et al.</i> [30]
2.	Semi-terpenoids	Artabotriol	Seeds	G. Yu <i>et al.</i> [32]
3.	Lactones.	β -unsaturated- β -butyrolactones.	Aerial parts	Wong <i>et al.</i> [31]
4.	Flavonol glycosides	Arapetaloside A and B	Roots	Tong-mei <i>et al.</i> [34] Singh <i>et al.</i> [39]
5.	Flavonoids	Taxifolin, apegenin-7-O-Apiosylglucoside, and glucolutioline	Roots, Leaves	Li T [33] Somanawat <i>et al.</i> [35]
6.	Alkaloid	Artabotrine hexapetalines A and B	Roots Stem	QiZhou <i>et al.</i> [31]
7.	Organic acid	Succinic, Fumaric acid	Fruits	Yao Xue <i>et al.</i> [30]
8.	Sterols	β -sitosterol, Daucosterol	Seeds	G. Yu <i>et al.</i> [32]
9.	Sesquiterpenoids	β -caryophyllene, Caryophyllene oxide	Flowers, Roots	Feng-Min Xi <i>et al.</i> [36] Phan <i>et al.</i> [40]

A. hexapetalus.: *Artabotys hexapetalus* (L. f.) Bhandari

Yu J *et al.* 2002 have isolated four neo-lignans-isoamericanin A, isoamericanol A, americanin B, and artabotricinol and a hemiterpenoid: (R)-artabotriol and other compounds from the seeds of *A. hexapetalus* and reported the presence palmitic acid, β -sitosterol, and daucosterol [30]. Wong H *et al.* 2002 have reported that the dichloromethane extract of the aerial parts of *A. hexapetalus* contains β -methoxy- γ -methylene- α , β -unsaturated- γ -butyrolactones which are anticipated to be derived from a C-18 unsaturated fatty acid [31]. Yu J *et al.* 2001 have studied the chemical constituents of the seeds of *A. hexapetalus*. Eight compounds were isolated and identified as four Neolignans-isoamericanin A, isoamericanol A, americanin B, and artabotricinol, a semiterpenoid: (R)-artabotriol and others [32]. Li T *et al.* 1997 reported the isolation of various constituents from *A. hexapetalus* leaves. They isolated two new flavonol glycosides derivatives of artabotryside and three known flavonoids: taxifolin, 7-O-glucoluteolin, apigenin glycoside, and two organic acids as succinic and fumaric acid. Based on spectral analysis structures elucidated were quercetin and kaempferol [33]. Tong-Mei Li *et al.* 1997 reported the isolation of two novel flavonol glycosides from the leaves of *A. hexapetalus*. Isolated compounds were named as arapetaloside A and B. Additionally taxifolin, apigenin glucoside, and glucoluteolin flavonoids were also isolated [34]. Somanawat J *et al.* 2012 isolated and identified a megastigmane glucoside along with four flavonoid glycosides from the leaves of *A. hexapetalus*. They identified these compounds by applying various spectroscopic techniques. Also for the first time occurrence of megastigmane glucoside and quercetin triglycoside in this plant is being reported [35]. Feng-Min Xi *et al.* 2017 isolated seven pairs of sesquiterpene from the roots of *A. hexapetalus* identified as a new peroxy-bridge sesquiterpene and peroxy-bridge norsesquiterpene with five known compounds. Their structures of compounds were confirmed by elucidation based on spectroscopic characterization. Seven pairs of stereoisomers were confirmed by chiral HPLC [36]. Qi Zhou *et al.* 2015 reported the isolation of two new alkaloids as benzylisoquinoline derivatives named hexapetalines A and B from the stems of *A. hexapetalus*. The structures of hexapetalines were elucidated by using extensive spectroscopic methods and compounds were identified by comparisons with the literature [37].

Yao Xue *et al.* 1998 have isolated two new flavonol glycosides, artabotryside A and B, three known flavonoids: taxifolin, 7-O-glucoluteolin, apigenin-7-O-apiosyl glycoside, and succinic and fumaric acid from the leaves of *A. hexapetalus*. The structures of compound artabotryside and its derivative were elucidated based on spectral analysis. For the first time, compound quercetin-3-O-alpha-L-rhamnopyranosyl (1->2)-alpha-L-arabinofuranoside and kaempferol-3-O-alpha-L-rhamnopyranosyl (1->2)-alpha-L-arabinofuranoside were isolated [38]. Singh A *et al.* 1997 have reported the isolation of the flavonol glycosides-quercetin, quercetin 3-O-glucoside, 3-O-arabinoside, and 3-O-galactoside along with kaempferol, myricetin, and gallic acid from the leaves of *A. hexapetalus* [39]. Phan, G *et al.* 2007 reported extraction, identification, and analysis of essential oil from the flower of *A. hexapetalus*. Compounds were analyzed by using GC and GC/MS spectroscopic techniques. Twenty-six components of the oil that were identified as sesquiterpene hydrocarbons and oxygenated sesquiterpenoids, β -caryophyllene, and caryophyllene oxide [40]. Mahidol C *et al.* 2005. Investigated compositions of the essential oils from flowers of *A. hexapetalus*. The flowers were subjected to hydrodistillation, solvent extraction, solid-phase microextraction, and simple headspace solvent-trapping technique. By hydrodistillation, thirty-one components and five unidentified ones were identified together as β -caryophyllene, β -gurjunene, and globulol. Employing solvent extraction method thirty-one components were identified as 3-methyl butanol, 2-methylbutanol, ethyl butanoate, isopentyl acetate, 2-methyl butyl acetate, limonene, linalool, and two unidentified components. The other two unconventional extraction methods were employed as simple headspace solvent-trapping techniques. Using this method, seventeen components were identified as ethyl acetate, ethyl isobutanoate, isobutyl acetate, and ethyl butanoate. Employing the Solid-phase microextraction technique the headspace vapor of the fresh flowers was absorbed on the viscous liquid, polydimethylsiloxane (PDMS), and injected directly into the GC-MS. By using this method Thirtynine components were identified with three unidentified ones were Ethyl acetate, ethyl isobutanoate, isobutyl acetate, ethyl 2-methyl butanoate, ethyl isovalerate, ethyl 3-methyl-2-butenate, isobutyl isovalerate, and β -caryophyllene [41].

Table 2: Biological activities of *A. hexapetalus*

S. No.	Part of plant	Activity reported	Reference
1.	Leaf	Antioxidant Activity:	Satya <i>et al.</i> [58]
2.		Antifertility Activity	Karthik <i>et al.</i> [62]
3.		Hepatoprotective activity	Veena <i>et al.</i> [63]
4.	Bark	Antibacterial and Antifungal activity	Grainge <i>et al.</i> [54]
5.		Anthelmintic and Cytotoxic activities	Morshed <i>et al.</i> [64]
6.		Antimicrobial activity	Shankar <i>et al.</i> [52]
7.	Root	Antileishmanial activity	Bajaj <i>et al.</i> [56]
8.		Mosquito repellent activity	Rajabu <i>et al.</i> [62]
9.	Flower	Antimalarial	Wijesekera [66]
		Antipyretic	Rahini <i>et al.</i> [65]

A. hexapetalus.: *Artabotys hexapetalus* (L. f.) Bhandari.

Biological and pharmacological activities of *A. hexapetalus*

Herbal drugs have been playing a substantial role throughout the world in treating and preventing several diseases [42]. The essential oil of this plant has shown excellent antihelmintic property against tapeworms, earthworms, and roundworms [43]. Fruits of this plant are recoded as containing fixed and volatile oil, glycosides, and resins. Extracts are reported to show hypotensive and spasmogenic, as well as cardiac stimulating effects on some animals and a cardiac depressant on others [44]. Ethanolic and benzene extracts of leaves have shown irregular oestrus cycle in albino rats. Also used as a remedy to treat abdominal and kidney pains [45]. Decoction used in the treatment of cholera. It is used as a cardiotoxic, cardiac stimulant, muscle relaxant, and uterine stimulant [46-51] (table 2).

Antimicrobial activity

Shankar P, *et al.* 2011 investigated acetone and ethanolic extracts of leaves of *A. hexapetalus* for antibacterial efficacy. The phytochemical analysis confirmed the presence of flavonoids, alkaloids, tannin, sterols, and terpenoids. Ethanolic extract showed significant antibacterial activity against *E. coli*, *Bacillus subtilis*, and *Salmonella typhi*. Acetone extract showed the maximum zone of inhibition against *Staphylococcus aureus* [52]. Sowjanya K, *et al.* 2013 reported antibacterial and antifungal activity of methanolic extracts of *A. hexapetalus* leaves. This antimicrobial activity was carried out using the agar well diffusion method. Different concentration of extracts (25-100µg/ml) was tested against *Salmonella typhi*, *Streptococcus entericus*, *Lactobacillus casei*, *Streptococcus mutans*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Bacillus megaterium*, *Enterococcus faecalis*, *Xanthomonas campestris*, *Candida albicans*, *Aspergillus niger*, *Rhizopus oryzae* and *Candida rogasa*. The results proved noteworthy microbial inhibition calculated from zones of growth inhibition [53]. Grainge M, *et al.* 1987 in this investigation tested leaf extracts of *A. hexapetalus* against *Xanthomonas Campestris* and *Drechslera oryzae* (*Cochliobolus miyabeanus*) and 10 other bacterial strains. The leaf extracts showed inhibition in the growth of *X. campestris pv campestris* [54]. Haseena S, *et al.* 2019 reported the green synthesis of CuO nanoparticles using *A. hexapetalus* extract by co-precipitation method. The antibacterial ability of CuO nanoparticles was determined against gram-negative *E. coli* pathogen by the agar-agar diffusion method. Results revealed that CuO nanoparticles showed significant antibacterial activity against gram-positive *E. coli* strain [55].

Antileishmanial activity

Bajaj S, *et al.* 2018 evaluated the *in vitro* antileishmanial activity of extracts of *A. hexapetalus* against the *Leishmania donovani* (L. donovani) promastigotes. The plant extracts inhibited the growth of *L. donovani in vitro* after 24, 48, 72, and 96 h of incubation and had 50% inhibitory concentration (IC₅₀). The lowermost concentration of extract showed inhibition of growth of *L. donovani* parasites it was measured as the maximum inhibitory concentration. This indicated after incubation at 24 and 48 h. all extracts showed antileishmanial activity in a dose-dependent mode [56].

Antioxidant activity

Manjula M, *et al.* 2011 reported screening of antioxidant and antimicrobial activity of *A. hexapetalus* flower extracts. 2,2,1-diphenyl-1-picrylhydrazyl (DPPH) and reducing power method was utilized in the screening of antioxidant activity. Results indicated reducing the power of extracts increased with increase in the concentration of extracts. DPPH free radical-scavenging of chloroform, methanol, aqueous extracts, and Gallic acid as standard with half-maximal inhibitory concentration IC₅₀ values at the concentration range of 50-250µg/ml were determined as 378.73µg/ml, 72.0µg/ml, 118.49µg/ml and 68.75µg/ml respectively [57]. Satya K, *et al.* 2017 determined free radical scavenging activity of methanol extract of *A. hexapetalus* utilizing ascorbic acid as standard antioxidant. DPPH method was used for screening of antioxidant activity. *A. hexapetalus* extracts showed a 52.99% scavenging activity in the DPPH assay [58]. Rahini D, *et al.* 2014 carried out *in vitro* free radical scavenging assays of *A. hexapetalus*

flower extract. This assay was performed by determination of total antioxidant capacity, reducing ability Nitric oxide radical, and scavenging of hydrogen peroxide. *A. hexapetalus* flower extract effectively scavenged free radicals at all different concentrations and showed its potent antioxidant activity [59]. Bollapragada M, *et al.* 2018 determined *in vitro* antioxidant activity of methanolic extract of *A. hexapetalus* leaves. The antioxidant assay was determined using DPPH, ferric reducing antioxidant power, and total antioxidant capacity. The activity of methanolic extract at lower concentrations 10-50 µg/ml. IC₅₀ values were 33.95 µg/ml in comparison to that of standard ascorbic acid 33.2µg/ml. The results demonstrated that the extract of *A. hexapetalus* had a significantly higher (p<0.05) value. Hydroxyl radical scavenging activity of methanolic extract of *A. hexapetalus* showed 200.3±3.11 µg/ml IC₅₀ value [60].

Mosquito repellent activity

Rajabu A, *et al.* 2014 investigated mosquito repellent activity of their essential oils of leaves and stem bark of *A. hexapetalus*. The composition of oil from the stem bark and leaves showed both β-caryophyllene oxide and 11-hexadecyn-1-ol as the main components. Essential oil from the leaves of *A. hexapetalus* displayed strong activity with Repellent concentrations (RC₅₀) values 1.81×10⁻⁵ mg/cm² and 2.79×10⁻⁵ mg/cm². Against mosquitoes female *Anopheles gambiae* s. s. The repellency activity of essential oil in comparison to standard citronella oil used (RC₅₀ = 4.1×10⁻⁶ mg/cm²) was found to be moderate [61].

Anti-fertility activity

Karthik Y, *et al.* 2012 evaluated the antifertility activity of hydroalcoholic extract of *A. hexapetalus* leaves *in vivo* on male Wistar rats and female Sprague Dawley rats and rabbits. In this study, male Wistar rats were orally fed with hydroalcoholic extract at a concentration of 200, 400, 600 mg/kg. p. o. for 45 d. This effect of the extract on reproductive organs, sperm count, serum testosterone, testicular cholesterol, and alkaline phosphates levels was noted and changes in testicular histology were compared with the control rats. Progestogenic activity assay was determined by pregnancy maintenance test in female Sprague Dawley rats. The result showed a decrease in weight of testis, seminal vesicles and sperm count, serum testosterone testicular cholesterol and alkaline phosphates level and the histological examination of testis demonstrated that decrease in the diameter of seminiferous tubule server hypercellularity of Leydig cells. The Pregnancy maintenance assay displayed non-progestogenic, progestational, or anti-progestational activities [62].

Hepatoprotective activity

Veena R, *et al.* 2016 screened the alcoholic extract of *A. hexapetalus* for *in vivo* hepatoprotective activity in rats, which were intoxicated by paracetamol. The hepatoprotective activity and oxidative stress of *A. hexapetalus* were determined using parameters like serum enzyme levels like SGOT, SGPT, ALP, ACP, Total Bilirubin, Direct Bilirubin, SOD, GSH, Vitamin C and catalase levels of the animals treated with hepato-toxic paracetamol. The alcoholic extract of *A. hexapetalus* overturned the hepatotoxicity that was induced by paracetamol in the rats, indicating their hepatoprotective action. This histopathological studies revealed structural damage occurred due to paracetamol, which was further supported by the DNA fragmentation studies that showed the absence of fragmentation of DNA in alcoholic extract-treated groups, indicating the hepatoprotective activity of *A. hexapetalus* [63].

Anthelmintic activity

Niaz M, *et al.* 2012 investigated the methanolic extract of bark of *A. hexapetalus* for *in vitro* anthelmintic and cytotoxic activities. Brine shrimp lethality bioassay was used for the evaluation of the cytotoxic activity. The methanolic extract presented noteworthy cytotoxic potential (LC₅₀ value of 7.688 µg/ml) in comparison to standard vincristine (0.839 µg/ml). To evaluate anthelmintic activity where albendazole was used as the reference standard and methanolic extract of barks (50 mg/ml) showed paralysis of the worms at 68.33 min and death at 84.0 min. In comparison to the standard albendazole at the concentration of 10 mg/ml worms were

paralyzed and killed at the respective 17 min and 48 min. Thus it confirmed the significant anthelmintic activities of bark extract of *A. hexapetalus* [64].

Antipyretic activity

Rahini D, *et al.* 2014 reported antipyretic activity of ethanolic extract of flowers of *A. hexapetalus* tested on yeast induced pyrexia in albino rats. To carry out screening of the antipyretic flower extract at oral doses of 100, 250, and 500 mg/kg was used. A significant reduction in body temperature on yeast induced pyrexia was observed at a dose of 500 mg/kg body weight when compared with standard Paracetamol drug (200 mg/ml). [65]

CONCLUSION

The present review comprises of a perspective to show current advances in the phytochemical and pharmacological activities of *A. hexapetalus* as a prognostic therapeutic agent. According to the literature review, it is uncovered that *A. hexapetalus* possesses valuable therapeutic uses as antimicrobial, antileishmanial, antioxidant, antifungal, antifertility, anthelmintic, mosquito repellent, hepatoprotective, and cytotoxic activity. It has a potent free radical scavenging property which sufficiently demonstrated in different assays. Its potential as an antioxidant and antimicrobial agent needs to be undermined in future research work. It may perhaps be advised that alkaloids, terpenoids, anthraquinones, butyrolactones, flavonoids, neolignans, phenolic compounds, and leucoanthocyanins might be valued as a principal molecule in the development of new drugs to treat various diseases. Various unique constituents in the form of flavonoids of *A. hexapetalus* can also be chemically modified or used as "lead" for developing more effective drug molecules. Therefore, extensive pharmacological and phytochemical screening, together with the pharmacokinetic and toxicological assay, will be a focus for forthcoming investigation. Furthermore, a well-designed study to measure its toxicity from its long-term use is another urgency. This review article emphasizes the potential of *A. hexapetalus* that can be employed in new therapeutic drugs and will offer the base for future research on the application of herbal medicines.

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AUTHORS CONTRIBUTIONS

Abhijeet Puri: Being a single author, I carried out a compilation of literature, an inscription of a manuscript, read-through, revising, and improving the standard of the manuscript. No other co-author contributed to this work.

CONFLICTS OF INTERESTS

The authors declare that he has no conflicts of interest.

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