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A Review on Phytochemistry, Bio-Efficacy, Medicinal and Ethno-Pharmaceutical Importance of *Artocarpus altilis*

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ABSTRACT

In recent years, herbal medicine is being the sources of many imperative drugs of modern world. Use of potent medicinal plants like Breadfruit (*Artocarpus altilis*) against various ailments to reduce the adverse effects of various orthodox allopathic medicines and detrimental side effects of conventional antibiotics has emerged as an evolved technique in pharmaceutical science. The present review emphasizes the antimicrobial potentiality of various parts of *A. altilis* along with their known therapeutic properties in context of biologically active compounds (phytoconstituents). Research investigations on ethno-pharmacological study of the plant parts with their nutritional value, multifarious medicinal uses and antibacterial effect are being quoted in the present review. This review will provide detailed information to future researchers on phytoconstituent analysis, bioefficacy assessment and ethno-pharmaceutical importance of *A. altilis* in the field of medical science.

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INTRODUCTION

In recent years research on the emergence of multiple drug resistance to various human pathogenic bacteria has gained utmost importance all over the world which necessitated a search for new antimicrobial substances from other sources including plants. In the present scenario, there has been a startling enhancement in the occurrence of new and emerging infectious diseases. Early people confronted with illness and disease, discovered a wealth of useful therapeutic agents in the plant and animal kingdoms. The empirical knowledge of these medicinal substances and their toxic potential was passed on by oral tradition. According to World Health Organization (WHO), about 80% of the world population relies chiefly on the plant based traditional medicine especially for their primary healthcare needs [1].

Nowadays medicinal plants occupy an important position in allopathic medicine, herbal medicine, homoeopathy and aromatherapy, as being the sources of many imperative drugs of the modern world. Numerous plants have immeasurable ability to synthesize secondary metabolites of which at least 12,000 have been isolated and these substances serve as plant defense mechanism against predation by microorganisms, insects and herbivores (Wink, 1998). In comparison to various orthodox medicines, the plants being used as therapeutic agents have lower incidence of adverse effects after use. These are cheaper and easily available to most people in the developing countries. Researches on the medicinal values and antimicrobial properties of plants have gained utmost attention throughout the world. The detrimental side effects of conventional antibiotics can be easily overcome by use of ethnic medicinal plants as an alternative treatment of diseases by producing a variety of compounds of known therapeutic properties [1, 2]. In the recent past, attention has been paid to the use of plant extracts and their biologically active compounds [1].

Artocarpus altilis (Family-Moraceae) commonly known as breadfruit is originated from New Guinea and extensively grows in the Southern parts of India. Breadfruit (*Artocarpus altilis* (Parkinson) Fosberg.) is a multipurpose agroforestry tree crop which is primarily used for its nutritious, starchy fruit with rich source of carbohydrates, calcium and phosphorus [1]. The multifarious importance of breadfruit includes food, medicine, clothing material, construction

materials and animal feed. The other species of *Artocarpus* has been studied for its antimicrobial activity by several researchers [1, 2].

The medicinal values of different plant parts of *Artocarpus* for the treatment of tongue thrush, skin infections, sciatica, diarrhoea, low blood pressure and asthma have gained immense importance in countries like Trinidad and Bahamas. The leaf juice is employed as eardrops. A powder of roasted leaves is used as a remedy for enlarged spleen [3]. Breadfruit has long been an important staple food in the Pacific Islands. Extracts from roots and stem barks showed some antimicrobial activity against Gram-positive bacteria and have potential use in treating tumors [2]. The root and stem bark extracts were being used against some bacteria [4]. The chromatographic study of breadfruit revealed high content of amino acid, fatty acids, and carbohydrates [5]. Atrocarpin, isolated from Thai Breadfruit heartwood extract exhibits inhibitory effect on melanogenesis showing high antioxidant activity. These effects indicate the potential use of heartwood of Bread fruit in cosmetics [6].

The medicinal uses of breadfruit are being actively researched; however still there is a huge dearth of information regarding the antimicrobial activity of different plant parts of breadfruit. Therefore it is imperative to intensify investigations aimed at evaluating the potentiality of this plant against various microbial pathogens. The study on comparative effect of leaf extracts using different solvents to detect the inhibitory effect of leaf extracts of *A. altilis* on the growth of *Staphylococcus aureus, Pseudomonas aeruginosa, Streptococcus mutant* and *Enterococcus faecalis* was carried out by Pradhan et al., [7]. This review is a concise report with an overall view on phytoconstituent analysis, bioefficacy assessment and ethno-pharmaceutical importance of *A. altilis* in the field of medical science.

PLANT TAXONOMY AND DESCRIPTION

Breadfruit (*Artocarpus altilis*) is a species of flowering tree in the mulberry family, Moraceae. (Figure 1).

Figure 1. *Artocarpus altilis* with leaves and fruit. [Source: Pradhan et al., [2]

It is a member of the genus *Artocarpus* (Moraceae) which contains about 50 species. Its name is derived from the texture of the cooked moderately ripe fruit, which has a potato-like flavor, similar to freshly baked bread. The plant has been assigned to following taxonomic position (Table 1).

Table 1: Taxonomic position of *Artocarpus altilis*

Rank	Scientific Name and Common Name
Kingdom	Plantae – Plants
Subkingdom	Tracheobionta – Vascular plants
Superdivision	Spermatophyta – Seed plants
Division	Magnoliophyta – Flowering plants
Class	Magnoliopsida – Dicotyledons
Subclass	Hamamelididae
Order	Urticales
Family	Moraceae – Mulberry family
Genus	*Artocarpus* J.R. Forst. & G. Forst. – breadfruit
Species	*Artocarpus altilis* (Parkinson) Fosberg – breadfruit

Some species are locally valuable as timber trees, while breadfruit, jackfruit (*Artocarpus heterophyllus* Lamarck) and champedak (*Artocarpus integer* (Thunberg) Merrill) are grown for their fruits [8]. The generally accepted name for breadfruit is *Artocarpus altilis* (Parkinson) Fosberg which has taxonomic priority and replaced *Artocarpus incisus* (Thunb). L. f. Suppl. 411. 1781 (*A. incisa* variant spelling), and *Artocarpus communis* Forst. Char. Gen. 101. 1776. These names for breadfruit are based solely on specimens or descriptions of seedless Tahitian breadfruit collected during Captain Cook's voyages there in 1768-1771 [8]. Throughout the Pacific, breadfruit exhibits great morphological variability, ranging from true seedless fruits to fruits with numerous, minute, aborted seeds, to fruits with one to few viable seeds, to fruits with numerous seeds.

Ecology and Distribution of breadfruit

Breadfruit, an equatorial lowland species, grows best below elevations of 650 metres (2,130 ft), but is found at elevations of 1,550 metres (5,090 ft). Its preferred rainfall is 1,500–3,000 millimetres (59–118 in) per year. Preferred soils are near neutral (pH of 6.1-7.4) and either sand, sandy loam, loam or sandy clay loam. Breadfruit is able to grow in coral sands and saline soils. It is a widely grown and nutritious tree fruit which grows in the hot, moist regions of the throughout Southeast Asia, South India and most Pacific Ocean islands [8]. It is also grown in the Leeward Islands and Windward Islands of the Caribbean and in Africa. Though they are widely distributed throughout the Pacific, many breadfruit hybrids and cultivars are seedless or otherwise biologically incapable of naturally dispersing long distances. Therefore, their distribution in the Pacific was clearly enabled by humans, specifically prehistoric groups who colonized the Pacific Islands.

Documented Species Distribution

The map (Figure 2) shows countries where the species has been planted. It does neither suggest that the species can be planted in every ecological zone within that country, nor that the species can not be planted in other countries than those depicted. Since some tree species are invasive, you need to follow biosafety procedures that apply to your planting site.

Native: Malaysia, Papua New Guinea, Philippines

Exotic: Antigua and Barbuda, Australia, Bahamas, Barbados, Brazil, Byelarus, Colombia, Cook Islands, Costa Rica, Cuba, Dominica, Dominican Republic, Fiji, French Guiana, French Polynesia, Gambia, Grenada, Guadeloupe, Guatemala, Guinea, Guyana, Haiti, India, Indonesia, Jamaica, Kiribati, Madagascar, Maldives, Marshall Islands, Martinique, Mauritius, Mexico, Montserrat, Netherlands Antilles, New Caledonia, New Zealand, Norfolk Island, Puerto Rico, Samoa, Seychelles, Solomon Islands, Sri Lanka, St Kitts and Nevis, St Lucia, St Vincent and the Grenadines, Taiwan, Province of China, Tonga, Trinidad and Tobago, US, Vanuatu, Virgin Islands (US).

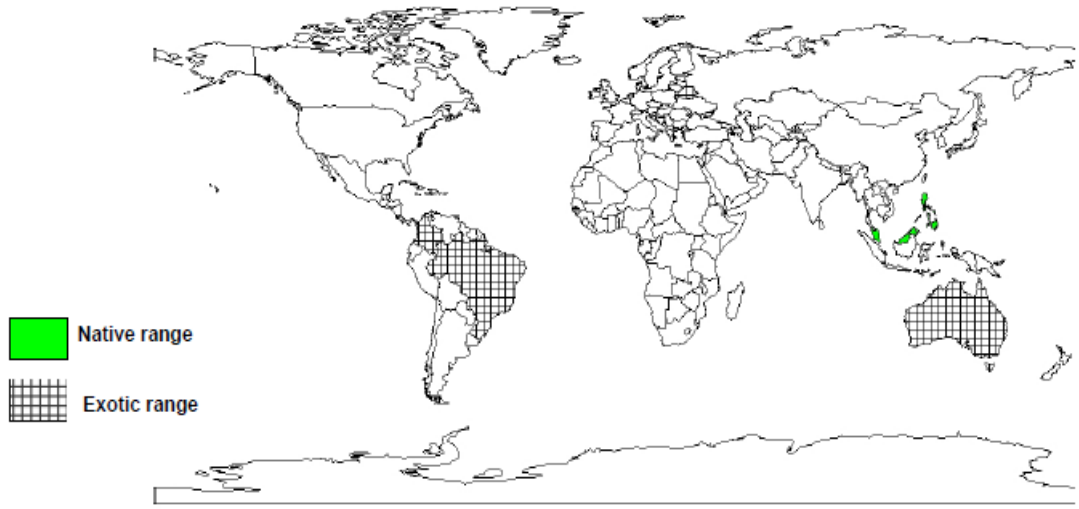


Figure 2 The map above shows countries where the species has been planted. It does neither suggest that the species can be planted in every ecological zone within that country, nor that the species cannot be planted in other countries than those depicted. Since some tree species are invasive, you need to follow bio-safety procedures that apply to your planting site.

(**Source-** ***Agroforestry Database 4.0 (Orwa et al.2009)***)

MORPHOLOGICAL DESCRIPTION

The breadfruit is closely related to the breadnut, from which it might have been selected, and to the jackfruit.

Tree

Breadfruit trees are very large, evergreen reaching up to heights of 15 to 20 meters. Or even to 25 m (82 ft) [9]. The tree comprises smooth, light-colored bark, and the trunk is large in 1.2 m in diameter. All parts of the tree yield milky latex, a milky juice, which is useful for boat caulking.

Leaves

The large, thick and leathery leaves are deeply cut into pinnate lobes and with a dark-green colour on the dorsal side, which often appears to be glossy. At the end of the branches, the leaves are seen as clusters with varying size and shape. The crown is conical in shape when the trees are young or grown under shaded condition and they become rounded and irregular when it turns older. Blade is generally smooth, glossy dark green with green or yellow-green veins and many white to reddish-white hairs on the midrib and vein.

Flowers

Breadfruit tree monoecious and bears a multitude of tiny flowers. The male flowers emerge first, followed shortly afterward by the female flowers, which grow into capitula, which are capable of pollination just three days later. Club shaped spikes are found in Male flowers whereas the female flowers are elliptical, green, pricky head measuring. Flowers undergo cross pollination with small powdery pollen grain spread by both the wind and insects. Once both the male and female flowers are fused together, it develops into a fleshy and edible fruit.

Fruits

The compound, false fruit develops from the swollen perianth, and originates from 1,500-2,000 flowers. These are visible on the skin of the fruit as hexagon-like discs. The ovoid fruit has a rough surface, and each fruit is divided into many achenes, each achene surrounded by a fleshy perianth and growing on a fleshy receptacle. The fruits are variable in size, shape and surface texture. Mostly they are round, oval and oblong in shape and usually weighing around 0.25-6 kg. The colour of the breadfruits are usually light green, yellowish green or yellow in colour when mature. The flesh of the fruit is usually creamy, soft with a pleasant fragrant. Breadfruit is one of the highest-yielding food plants, with a single tree producing up to 200 or more grapefruit-sized fruits per season.

Seeds

Breadfruits are available with seeds and also without seeds. The seeded types of breadfruit are available in south western Pacific, whereas seedless types of breadfruit are common in Micronesia and Eastern islands of Polynesia. All the breadfruit varieties elsewhere especially in topic region are of seedless type. Seeds are brown in colour, shiny, round or ovoid in shape and irregularly compressed. Moreover, the seeds have little or no endosperm, no period of dormancy and they can germinate immediately. Since they can germinate immediately, they are not able to be dried or stored. Trees that grow with the help of seeds can produce their fruits in a timeline of 6-10 years or sooner. On the contrary, asexually propagated trees can start to produce their fruits in 3-6 years of time [5, 8, 9].

BIOLOGICALLY ACTIVE COMPOUNDS WITH SPECIAL REFERENCE TO MAJOR PHYTOCONSTITUENTS

Phytoconstituents are the biologically active secondary metabolites of plant origin, which are commercially important as drugs, flavours, pesticides or other types of specialty chemicals. Plants produce a wide variety of phytochemicals in order to attract animals, protect from infection, parasitism and predation etc [9]. The search for natural antioxidants, especially of plant origin, has notably increased in recent years. In view of this, various plant fruits and vegetables are under investigation for the detection of these bioactive compounds. Not even the fruits but the seeds, barks and leaves also are considered to be containing large number of bioactive components which can have therapeutic uses.

Artocarpus species are noted as an abundant source of phenolic constituents. These constituents can be classified into isoprenylflavonoids, stilbenoid and 2-arylbenzofuran derivatives, phenolic compounds with oxepine ring and natural Diels-Alder type adducts. Biological studies on the phytochemicals isolated from these plants showed some interesting findings which some how justified the usage of *Artocarpus* plants in traditional practices.

A.heterophyllus, A.altilis, A.camans and A.integer contain various chemical constituents such as morin, dihydromorin, cynomacurin, artocarpin , isoartocarpin, cyloartocarpin, artocarpesin, oxydihydroartocarpesin, artocarpetin, norartocarpetin, cycloartinone, β-sitosterol, ursolic acid,

betullic acid acetate and artocarpanone. It has been reported that the heart wood contains cellulose 59.0 %, glucosides 38.0%, moisture 6.7%, lipids 0.7% and albumin 1.7%. The plant also contains some essential Amino acids like Arginine, Cystine, Histidine, Leucine, Lysine, Metheonine, Theonine, Tryptophan and free suger (sucrose), fatty acids, ellagic acid. Bark contains betullic acid and two new flavone pigments, cycloheterophyllin. Triterpenic compounds like cycloartenyl acetate, cycloartenone have also been reported. Heterophylol a phenolic compound was obtained from *Artocarpus heterophyllus*. There is only 3.3% tannin in the bark. The leaves and stem show the presence of sapogenins, cycloartenone, cycloartenol, β-sitosterol and tannins, they show estrogenic activity. A root contains β-sitosterol, ursolic acid, Betulinic acid and cycloartenone. Arcommunol C, D and E, squalene, stigmasterol, phytol, ployprenol, dihydrochalcones, hydroxyartoflavone, artogomezianone, furanocyclocommurin, prenylated stilbenes.

Antimicrobial potentiality of *A. altilis* to assess its bio-efficacy

The methanolic leaf extracts at a high concentration and ethyl acetate and petroleum ether leaf extracts of *A. altilis* at low concentration were found very much effective against all the four types of microbes studied and showed highest antimicrobial activity. This result showing the bioefficacy of different leaf extracts of *Artocarpus altilis* against various human pathogens might be due to the presence of different phytoconstituents which was further evidenced through their individual action on the growth of these pathogens, especially the presence of tannins [7]. An effective defense mechanism against these human pathogens was developed by the action of these secondary metabolites through inhibiting their growth [7].

The methanolic leaf extracts of *Artocarpus altilis* containing tannins have been found to form irreversible complexes with proline-rich proteins and these compounds are known to be biologically active resulting in the inhibition of the cell protein synthesis as a result of which microbial growth is inhibited [1]. Tannins also react with proteins and act as stable and potent antioxidants which fight against various toxins released from the microbes. The activity of proteolytic enzymes used by plant pathogens were highly inhibited by tannins. Many plants contain non-toxic glycosides that can get hydrolyzed to release phenolics that are toxic to microbial pathogens. Screening of different phytoconstituents of medicinally important

Artocarpus altilis for its multifarious antimicrobial activity has gained utmost importance in recent years.

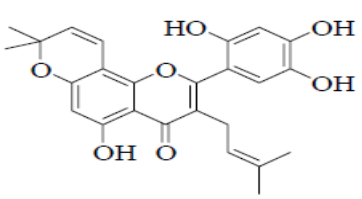
Research investigation by Pradhan et al. [2] showed that the zone of inhibition for *Streptococcus mutans, Staphylococcus aureus, Pseudomonas aeruginosa* increases with increasing dose of methanolic leaf extract of *Artocarpus altilis*. MIC values of different leaf extract of *Artocarpus altilis* against different pathogenic microorganisms also varied significantly. The MIC values of leaf extract of *Artocarpus altilis* was found to be 0.6 mg/ml against *Streptococcus mutans* (Inhibition Zone: 9 mm) and *Pseudomonas aeruginosa* (Inhibition Zone: 10 mm) whereas these MIC values of different leaf extract of *Artocarpus altilis* ranges from 0.3 mg/ml to 0.45 mg/ml for inhibition of *Enterococcus faecalis and Staphylococcus aureus* at different solvent media used. Increased antimicrobial activity against *Pseudomonas aeruginosa* was shown by the action of steroid at a lower concentration i.e. up to 30 µl (extracted from 0.9 mg of leaf) whereas the application of 50 µl of steroid was effective against *Staphylococcus aureus* [2]. Phytosterol has no effect on growth of *Pseudomonas aeruginosa* but most effective against *Streptococcus mutans* in comparison to other three phytochemicals. The growth of the organism *Enterococcus faecalis* was highly suppressed by phytosterols followed by steroids as revealed from their zone of inhibition [2]

Medicinal and Ethno-pharmaceutical importance of *A. altilis*

Medicinal importance of Artocarpus has been attributed to the presence of bioactive phytoconstituents (Figure 3.) which may be elaborately discussed as follows. Number in parentheses present the serial number of structure of compounds given just below their description.

Artonin E (1) and B (2) which were isolated from *A. communis* showed stronger activity against cancer cells, mouse L-1210 and colon 38 compared to the critical drug, theafulvin (3). Artonin E (1) also exhibited the most potent inhibition on arachidonate 5-lipoxygenase with IC50 value of 0.36 µM [3, 4]. Artonin E (1) was also expected to be an anti-tumor promoter based on the similarity of the structure with morusin (4) which was isolated from the root bark of *Morus alba* L. The latter compound had been reported as an anti-tumor promoter in a two-stage carcinogenesis experiment with teleocidin [5, 6]. Both compounds have an isoprenoid moiety at

the C-3 position. The difference is in the B ring where morusin (4) has a structure bearing a 2′,4′-dioxygenated pattern while artonin E (1) has a structure bearing a 2′,4′,5′-trioxygenated pattern. Thus, the inhibitory effect of the *Artocarpus* flavonoids on tumor-necrocis factor-α (TNF-α) release stimulated by okadaic acid using BALB/3T3 cells has been examined [7, 8]. All the tested compounds inhibited the TNF-α release stimulated by okadaic acid at suitable lower concentration. Artonin E (1) was found to be the most potent inhibitor. Heterophyllin (5) and artobiloxanthone (6) inhibited stronger than cycloheterophyllin (7), cycloartobiloxanthone (8), and morusin (4). The compounds which exhibited strong activity have three hydroxyl groups in the B ring. This characteristic feature might be one of the important factors for their biological activity.



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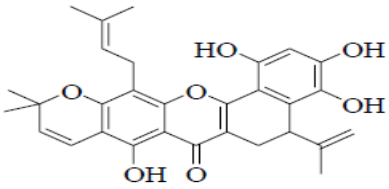

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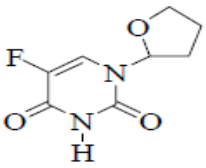

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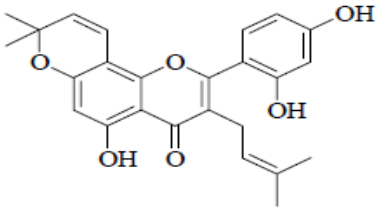

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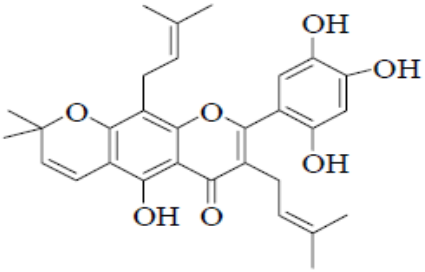

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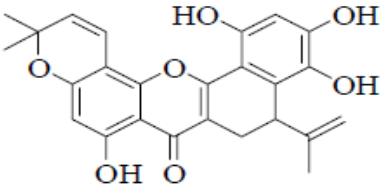

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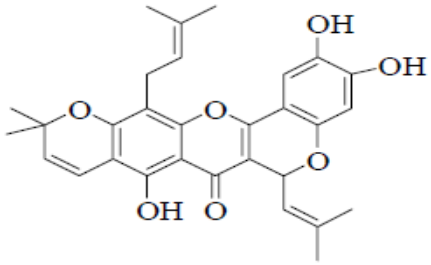

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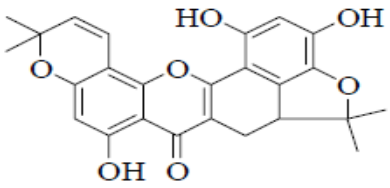

(8)

Figure 3. Bioactive phytoconstituents of *Artocarpus* species (Number in parentheses present the serial number of structure of compounds given just below their description).

Recently there has been a large upsurge in application of ethno-medicinal knowledge for curing various diseases. Application of traditional medicine as source of potentially useful compounds.

Artocarpus species are used traditionally in various disorders. The different parts of the plants have been reported to posses various activities. The leaves are used in fever, boils, wounds and skin diseases. The young fruits are used as astringent and carminative. The ripe fruits are supposed to posses laxative, aphrodisiac activities. The seeds are diuretic, and constipating. The wood is used as antidiabetic, anti-inflammatory, sedative and in convulsions. The latex is used in dysopia, ophthalmic disorders, pharyngitis and as antibacterial agent. The dried latex possesses marked androgenic action and also latex promotes healing of abscesses, snakebite and glandular swellings. The root is a remedy for skin diseases, asthma, fever and diarrhea [10]. *Artocarpus* sps. with its wide distribution [11, 12] enable the plant as a potent pharmaceutical tool for ethno medicinal purposes [13,14].

Literature reveals that lot of pharmacological investigations have been carried on *Artocarpus* species. Some reported are anti-inflammatory, antioxidant, antifungal, control of sexual behaviour, immuno-modulatory effect, antidiabetic effect, antibacterial effect, anti-cholinergic, chelating activity, nutritional assessment, cosmetic agent, toxicity to cancer cell, anthelmintic effect, protease inhibitors, regulation of oestrogens and inhibition of melanin biosynthesis [10].

CONCLUSION

An insight for discovery of therapeutic agents and information on disclosure of new sources of tannins, oils, gums, flavonoids, saponins, essential oils, precursors for the synthesis of complex

chemical substances in *A. altilis* have been provided by the knowledge of its various phytochemical constituents and the activity against tested pathogens. There are a number of plants with immense ability to synthesize secondary metabolites and serve as plant defense mechanism against predation by microorganisms, insects and herbivores through providing unlimited prospects for the development of new drugs. Further purification of the secondary metabolites, structural studies and isolation of bioactive compounds from this plant on tested animal models against various other pathogens could lead to new inventions in pharmaceutical sciences. Taking into account the various important aspects of *A. altilis* in context of pharmaceutical science it could be of potential value in commercializing the plant for its multifarious uses.

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