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REVIEW ARTICLE

ARECA CATECHU: A COMPREHENSIVE PHARMACOLOGICAL

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ABSTRACT

Nature has been a source of herbal medicinal agents for thousand of years and an impressive number of modern drugs have been isolated from natural sources. About 80% of the world's population rely mainly on traditional medicines for their primary health care. Areca catechu L. (Palmaceae), commonly known as Areca nut in English, is a perennial tree occurring throughout the Indian subcontinent and used traditionally for several medicinal purposes. *Areca catechu* is the most widely cultivated species in the genus *Areca* and has been distributed by humans throughout the tropics. Its various parts are used against wide range of ailments. The plant has traditional uses which consist of wound healing, antidiabetic, anti-fungal, antidepressant, antioxidant, and anti malarial. Areca is used for treatment of schizophrenia and glaucoma. It is also used as a mild stimulant; and as a digestive aid. Some people use areca as a recreational drug because it stimulates the central nervous system (CNS). Its medicinal properties is due to presence of numerous secondary metabolites like alkaloids, tannins and terpenoids. Hence this article aims to provide a comprehensive review on past work done on *Areca catechu* with special emphasis on its pharmacological properties.

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INTRODUCTION

Herbal medicines have been main source of primary healthcare in all over the world. From ancient times, plants have been catering as rich source of effective and safe medicines. About 80% of world populations are still dependent on traditional medicines. There has been an increasing demand for the pharmaceutical products of Ayurveda all over the world because of fact that the allopathic drugs possess great side effects. Safe, effective and inexpensive indigenous remedies are gaining popularity among the people of both urban and rural areas especially in India and China (Singh, 2007). *Areca catechu* is the most widely cultivated species in the genus *Areca* and has been distributed by humans throughout the tropics. As a result of its long history of domestication, the geographic origin of this palm is not known with certainty (similar uncertainty surrounds the origin of Coconut (Cocos nucifera), Peach Palm (Bactris gasipaes), and Sugar Palm (Arenga pinnata) (Grieve, 1995). The plant is known by various names in different languages as supari in Hindi, betel palm in English. The areca nut is not a true nut, but rather a drupe. It is commercially available in dried, cured and fresh forms.

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While fresh, the husk is green and the nut inside is soft enough to be cut with a typical knife. In the ripe fruit, the husk becomes yellow or orange and, as it dries, the fruit inside hardens to a wood-like consistency. The present review will emphasis on the contribution of *Areca catechu* in modern system of herbal medicine and its traditional uses which will heal the ailments and cure mankind for a better and healthy living (Jaiswal *et al*., 2011).

The Areca nut is used to make medicine. Areca nut is chewed alone or in the form of quids, a mixture of tobacco, powdered or sliced areca nut, and slaked lime wrapped in the leaf of "betel" vine (Piper betel). The plant has traditional uses which consist of wound healing, antidiabetic, anti-fungal, antidepressant, antioxidant, and antimalarial. Areca is used for treatment of a mental disorder called schizophrenia and an eye disorder called glaucoma; as a mild stimulant; and as a digestive aid. Some people use areca as a recreational drug because it speeds up the central nervous system (CNS). In veterinary medicine, an extract of areca is used for expelling tapeworms in cattle, dogs, and horses; to empty animals' bowels; and for treating intestinal colic in horse. It is thought that areca affects chemicals in the brain and other parts of the central nervous system (Farnswoth, 1988).

PLANT DETAILS

The plant is known by various names in different languages as under;

Hindi - Supari
India – Indian nut, Areca palm,
English – Betel palm
Filipino – Bunga
Indonesia – Pinang
Trade name – Areca nut
Botanical name – Areca catechu
Family – Arecaceae

GENERAL BOTANICAL DESCRIPTION

The areca nut is not a true nut, but rather a drupe. It is commercially available in dried, cured and fresh forms while fresh, the husk is green and the nut inside is soft enough to be cut with a typical knife. In the ripe fruit, the husk becomes yellow or orange and, as it dries, the fruit inside hardens to a wood-like consistency. At that stage, the areca nut can only be sliced using a special scissors-like cutter (known as *adakattera* in Telugu, *adake kattari* in Kannada,*bajjeai* in Tulu, *adakitta* in Marathi, *puwak* in Sinhala, *jaanti* in Bengali, *adakka* in Malayalam, *pakku* in Tamil, *sarautaa* in Hindi, *guaa* in Oriya, and *sudi* in Gujarati).

DISTRIBUTION AND CULTIVATION

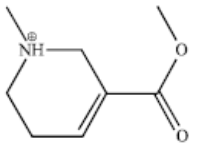
Areca catechu is the most widely cultivated species in the genus *Areca* and has been distributed by humans throughout the tropics. As a result of its long history of domestication, the geographic origin of this palm is not known with certainty (similar uncertainty surrounds the origin of Coconut (*Cocos nucifera*), Peach Palm (*Bactris gasipaes*), and Sugar Palm (*Arenga pinnata*). However, several origins have been suggested, including the Philippines, Malaysia, Celebes (Sulawesi), Java, New Guinea, and the Andaman Islands (Kapoor *et al*., 1990).

Areca palm seed is now among the most important stimulant products in the world, used by around 200 to 600 million people globally. It is often said to rank in extent of use below only caffeine, tobacco, and alcohol among addictive plant products. When seeds of this species are unavailable, seeds of certain wild palm species such as *Pinanga dicksonii* in South India or *Areca macrocalyx* in the Moluccas and New Guinea are sometimes substituted as inferior alternatives (Harvey, 2000).

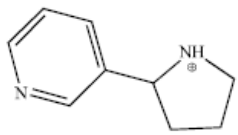
CHEMICAL COMPOSITION

The main constituents of the areca nut are carbohydrate, fats, fibre, polyphenol including flavonoids and tannins, alkaloids and minerals (IARC, 2004). The fatty acid constituents of the *A. catechu* nut oil are; lauric 19.5, myristic 46.2, palmitic 12.7, stearic 1.6, decanoic 0.3, oleic 6.2, linoleic 5.4, dodecenoic 0.3, tetradecenoic 0.6 and hexadecenoic 7.2%. The chief component glycerides are 56% of fully saturated (trimyristin, dimyristins and lauromyristopalmitin); 30% monounsaturated-disaturated (mainly hexadeceno-lauromyristins) and 14% of diunsaturated-monosaturated (oleolinoleo-glycerides, mostly oleolinoleopalmitin). The amino acids present are traces of tryptophan, methionine and larger amounts of proline, tyrosine, phenylalanine and arginine. *Areca catechu* nut contains; tannin 8-18, non-tannin 7-15 and insolubles 42.44%. The tannins, commonly known as chogaru, are predominantly catechol tannins which closely resemble *Mimosa* bark tannins and are used to convert the putrefiable hides and skins into leather, for treating fishing nets and for making inks. The tannins of *Areca catechu* may also be used as a substitute for synthetic food colours. The polyphenols of *Areca catechu* seed are mainly flavonoids and their concentration decreases with the maturity of the nut (Anonymous, 1985).

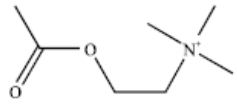
Areca catechu seed contains several alkaloids belonging to the pyridine group. Most important of them physiologically is arecoline (Chu, 2001). Other alkaloids present are arecaidine, arecolidine, guvacine, guvacoline, isoguvacine, norarecaidine and norarecoline (Anonymous, 1985; Giri *et al*., 2006). Arecoline has an effect similar to pilocarpine. It is reported to be cholinergic, exerting a sialagogue and diaphoretic action in normal dosage but in very large doses it depresses the central nervous system and paralyzes the muscles (Anonymous, 1985). It also has a stimulant effect on the occulomotor nerve causing mydriasis, followed by slight paralysis and dilation of pupil. In the liver homogenate, arecoline is decomposed to arecaidine which has no paralympathomimetic effects but only stimulating properties. Arecaidine does not affect the general activity of an animal but in higher doses exerts a sedative effect. Arecoline hydrochloride is found to be a mild antagonist of reserpine at a dose of 1 mg kg^{-1} intraperitoneally. Arecoline hydrobromide, a commercial salt, is a stronger stimulant to the salivary glands than pilocarpine and a more energetic laxative than eserine. It is used for colic in horses (Grieve, 1995). The active principle of *A. catechu* is an alkaloid, arecoline, which is considered to be the major constituent responsible for the toxicity (Anonymous, 1985). Arecoline, like nicotine, binds to certain receptors for acetylcholine.



Arecoline



Nicotine



Acetylcholine

MEDICINAL USES OF *ARECA CATECHU*

Areca nut is chewed alone or in the form of quids, a mixture of tobacco, powdered or sliced areca nut, and slaked lime wrapped in the leaf of "betel" vine (Piper betel). Areca is used for treatment of a mental disorder called schizophrenia and an eye disorder called glaucoma; as a mild stimulant; and as a digestive aid. Some people used areca as a recreational drug because it speeds up the central nervous system. In veterinary medicine, an extract of areca is used for expelling tapeworms in cattle, dogs, and horses; to empty animals' bowels; and for treating intestinal colic in horse (Farnworth, 1984). It is seems that areca affects chemicals in the brain and other parts of the central nervous system (Dar *et al*., 2000).

PHARMACOLOGICAL ACTIVITIES

The plant is also claimed to be used as antifungal, antimalarial, antibacterial, antidepressant, antioxidant, antidiabetic and used in wound healing in traditional system of Indian medicine (Kumosani, 2010).

Antimicrobial

Reena *et al*. (2012) evaluated antifungal activity of *Areca catechu* L . The purpose of this investigation was to study the antifungal activity of hot water extract of *Areca Catechu* nuts collected from coastal region of Kerala. Disc diffusion method was used to evaluate the zone of inhibition against fungi by taking nystatin as standard. The largest zone of inhibition was observed against *Candida albicans*. The most effective concentration needed for 85% inhibition of the production of aflatoxin by *Aspergillus flavus* was between 100-250 µg/ml (Reena *et al*., 2012). Chin *et al.* (2013) also investigated the antimicrobial potentiality of ethanolic extract of *Areca catechu* seeds against mixed oral-flora from tooth scum and gram negative laboratory isolates. They found that the highest antimicrobial action were seen against the *Proteus vulgaris* and *Vibrio cholera* (Chin *et al*., 2013). Raphael *et al.* (2014) reported the potential antimicrobial, anthelmintic and antioxident properties *of Areca catechu* L. root. It was observed that ethanolic extract produced significant anti-bacterial, anti-fungal and anthelmintic properties in a dose-dependent manner. DPPH free radical scavenging assay exhibited IC 50 value of 65.7 ± 1.53 and super oxide anion scavenging assay showed 201.7 ± 0.76, IC 50 value (Raphael *et al*., 2014). Cyriac *et al*.,(2012) observed the antimicrobial properties of *Areca catechu* husk extract against the oral pathogens. in this the aquos extract of *Areca catechu* were prepared and antimicrobial properties against the oral pathogens like *Streptococcus mutan, Streptococcus mitis, Streptococcus salivarius, candida albicans, prevotella intermedia* were performed by agar well diffusion method. alcoholic extract of *Areca catechu* husk fiber showed dose dependent positive inhibitory effect against the *candida albicans* (Cyriac *et al*., 2012).

Antidiabetic

Rajkumari *et al.* (2013) reported the effect *of Areca catechu* L. leaf extract on Type II diabetes in rats. Diabetes mellitus was induced in rats by High fat diet, high fat emulsion and intraperitoneal injection of Streptozotocin (STZ, 35mg/kg body weight).Oral glucose tolerance test was performed and diabetic animals were separated. Hyperglycemic rats were treated with Ethanolic extract of dose 100 mg/kg and 200 mg/kg p.o. The treatment was given for 15 days and at an interval of 5 days the blood glucose level was measured. The extract showed significant antidiabetic activity at 100 and 200mg/kg (Rajkumari *et al*., 2013). Mondal *et al*. (2012) evaluate antidiabetic activity of *Areca catechu* leaf extracts against streptozotocin induced diabetic rats. Diabetes mellitus was induced in rats by single intraperitoneal injection of streptozotocin (STZ, 50 mg/kg body weight). The present study concludes that *Areca catechu* leaf confirmed promising anti diabetic activity in streptozotocin-induced diabetic Wister rats (Mondal *et al*., 2012). Meutia Sari *et al*. (2014) carried out acute oral toxicity study with *Areca catechu* L. aquous extract using Sprague-dawley rats. The acute oral toxicity of A. catechu L. nuts extract was investigated in rats, as per OECD Guidelines 423 for acute protocols. The body weight, possibility of death, and activity parameters were measured for 14 days to ascertain the median lethal dose (LD50) of the extract. The LD50 was found to be >15.000 mg/kg body weight. There was significant weight increase ($p<0,05$). No mortality was observed during the course of whole 14 days study period. No detectable alterations were found in activity parameter in treated group when compared to control group (Meutia *et al*., 2014).

Antioxidant

Lee *et al*. (2003) have screened out methanolic extracts of nine medicinal plants traditionally used in Chinese medicine for antioxidant activity versus resveratrol which has been shown to protect cells from oxidative damage. The extracts of *A. catechu* strongly enhanced viability against H(2)O(2)-induced oxidative damage in Chinese hamster lung fibroblast (V79-4) cells. Relatively high levels of 1,1- diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity were detected in *A. catechu*. The activities of superoxide dismutase**,** catalase and glutathione peroxidase were dose dependently enhanced in V79-4 cells treated with most of the plant extracts. The extracts of *A. catechu* showed higher antioxidant activity than resveratrol in all experiments (Lee *et al*., 2003).

Wound healing

Verma *et al*. (2012) reported *e*ffect of topical ethanolic extract of Areca catechu on burn wound healing in albino rats. Ethanolic extract of *Areca catechu* kernel was prepared and an ointment was made with 2% of this extract. Burn wound was induced by standard procedure. Rats with burn wound model received either vehicle, standard drug or test drug. The result was found that the wound contraction rate was significantly increased in *Areca catechu* treated group in all the days compared to control (Verma *et al*., 2012). Masuram *et al*. (2014) evaluated the burn wound healing activity of orally administered ethanolic extract of *Areca catechu* kernel in normal as well as dexamethasone treated rats. The parameters observed were wound contraction rate and period of epithelialization. *Areca catechu* has shown significant enhancement of wound contraction rate in all the days compared to control (Masuram *et al.,* 2014).

Antiovulatory and abortifacient

Jyoti *et al*. (2010) investigated antiovulatory and abortifacient effects of *Areca catechu* (betel nut) in female rats For antiovulatory effect, ethanolic extract of *A. catechu* at 100 and 300 mg/kg doses was administered orally for 15 days. Vaginal smears were examined daily microscopically for estrus cycle. Rats were sacrificed on 16th day. Ovarian weight, cholesterol estimation, and histopathological studies were done. Abortifacient activity was studied in rats at 100 and 300 mg/kg doses administered orally from 6th to 15thday of pregnancy. Rats were laparotomised on 19thday. The number of implantation sites and live fetuses were observed in both horns of the uterus. The ethanolic extract of *A. catechu* at doses of 100 and 300 mg/kg has antiovulatory and abortifacient effects (Jyoti *et al.,* 2010).

Antidepressant

Dar *et al.* (1998) reported the antidepressant activities in *Areca catechu* fruit extract and observed that the hexane and aqueous fractions of Areca catechu (A. catechu) have demonstrated anti-depressant properties in screens used to detect such activity. Similar properties had previously been detected in the plant's aqueous ethanolic extract. The aqueous ethanolic extract (F1), and the hexane (F2) and aqueous (F5) fractions inhibit monoamine oxidase (MAO) in rat brain homogenates. The aqueous fraction seems to be the most potent inhibitor of MAO and its effect is similar to that of clorgyline (a specific MAO-A inhibitor). The extract and fractions from A. catechu, therefore, merit further research in the quest for new anti-depressants (Dar *et al*., 1998).

Sullivan *et al.* (2000) investigated the effects of chewing betel nut (Areca catechu) on the symptoms of people with schizophrenia and observed that Betel chewers with schizophrenia scored significantly lower on the positive (P=0.001) and negative (P=0.002) sub-scales of the PANSS than did non-chewers. There were no significant differences in extrapyramidal symptoms or tardive dyskinesia (Sullivan *et al*., 2000).

Learning memory And Behavior

Joshi *et al.* (2012) performed pharmacological investigation of *Areca catechu* extracts for evaluation of learning, memory and behavior in rats. The present study was done to evaluate the effect of *Areca catechu* Linn extract on learning and memory in rats using radial arm maze. The extract used for study was of two different types of *Areca catechu* namely, wet and dried *Areca catechu*. Three groups of rats each consisting of seven animals were used for the purpose. Test groups were given 500mg/kg p.o of wet *Areca catechu* extract and dried *Areca catechu* extract respectively. It was observed that wet *Areca catechu* extract showed greater increase in spatial memory and learning in comparison to the control group of rats. Hence increase in spatial memory could be because of higher amount of arecoline present in wet *Areca catechu* extract (Joshi *et al*., 2012).

Conclusion

There are number of plants which are used traditionally by the tribal people of India but they are not been validated. Thus an alternative approach by natural remedies are viable to allopathic medications as they cause undesirable side effects. From this study, it is clear that the medicinal plants play a vital role against various diseases. Our review revealed that *Areca catechu* could be used to prevent from microbial and fungal, ulcer, diabetes, depression, and other disease. A variety of botanical products have been isolated and reported to possess that activity. Hence the review study is concluded that the herbal drug *Areca catechu* is a promising plant possessing antiulcer, antifungal, anti-diabetic, anti-microbial, anti-depression activity and it has been proved by different animal models in the near future too.

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