



Received on 21 January 2015; received in revised form, 22 March 2015; accepted, 28 April 2015; published 01 May 2015

ARECA CATECHU: ENFOLDING OF HISTORICAL AND THERAPEUTIC TRADITIONAL KNOWLEDGE WITH MODERN UPDATE

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Keywords:

Supari, *Areca catechu*,
Unani medicine, Ethnomedicine
uses, Anti-HIV activity

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ABSTRACT: *Areca catechu* has been in use as a social drug from the time immemorial and usually chewed by at least 10% of the world's population. *Areca catechu* commonly known as supari consists of dried ripe nuts and belongs to the family Palmae which is cultivated in tropical India, Sri Lanka, Malaysia, South China, the East Indies, the Philippines Islands and part of East Africa (including Zanzibar and Tanzania). Large quantities are exported from Madras, Singapore, Penang, and Sri Lanka. *Areca* nut (seed) contains tannin, gallic acid, gum, and alkaloids, viz. arecoline, arecaine, arecaine, guvacoline, guvacine and choline and various minerals such as copper, calcium, phosphorus, and iron. It also contains vitamin B₆ and vitamin C. In Unani medicine, it is used for stomatitis, bleeding gums, gingivitis, conjunctivitis, glaucoma, leucorrhoea, antiperspirant, urinary disorders, anorexia, diarrhoea and improves foul breath. Experimental studies of *A. catechu* showed antioxidant activity, hypoglycemic activity, anti-depressant activity, and anti-HIV activity, etc. The present review is an attempt to compile and explore comprehensively the ethnomedicine uses, phytochemical properties and pharmacological uses of *Areca catechu*.

INTRODUCTION: *Areca* nut is chewed usually by at least 10% of the world's population and is fourth most ranked psychoactive substance after nicotine, caffeine and alcohol¹. Drug Fufal consists of dried ripe nuts of *Areca catechu* Linn. of Palmae family². Immense quantities have been consumed in the East from very early times in the form of a masticatory known as betel, which consists of a mixture of areca nuts, the leaves of piper betel, and lime. The value of areca as a taenicide was also known in the East³.

According to ancient Greek, Sanskrit, and Chinese literature, it is clear that betel nut has been in use from I century BC. Innumerable references are available to support the fact that areca nut was also used in ancient Sanskrit period. Apart from various references, the most important is of 'Anjana Charita' (Sisy Mayana 1300 BC).

The practice of chewing betel leaves after meals had become common in the period of 75 AD to 300 AD as mentioned in Charaka and Sushruta Samhitas. It was believed in the period of 300 to 750 AD that chewing of betel leaves with some fragrant spices, helpful in digestion, remove the phlegm, and make the mouth fragrant. Its medicinal properties were known to the famous Indian scholar Vagbhatta (500 AD). Its use has also been documented by ancient historians in Ceylon and Persia around 600 AD and parts of the Arab world

QUICK RESPONSE CODE 	DOI: 10.13040/IJPSR.0975-8232.IJP.2(5).221-28
	Article can be accessed online on: www.ijpjournal.com
DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.IJP.2(5).221-28	

in the 8th and 9th centuries. It is believed that the nut was carried to Europe by Marco Polo around 1300 AD and became an important commodity in the western Pacific. The word 'Areca' is derived from the Malay word *adakka* (areca nut) or *adakeya*, the Indian equivalent⁴.

Vernacular Names:

Arabic: Fufal, Fofal^{2,5,6}
 English: Betel Nut^{2,6,7,8}
 Hindi: Supari^{6,7,8,9,34}
 Persian: Popal^{2,6,10}
 Sanskrit: Ghonta;² Kramuka;^{2,11} Gubak;
¹² Poogaphalam^{8,11,12,13}
 Unani: Fufal, Chhalia, Supari¹⁴
 Urdu: Chalia, Supari^{2,15}

Habitat and Distribution: The palm requires a moist tropical climate for luxuriant growth; it is very sensitive to drought. It thrives in areas with

heavy rainfall (500 cm), provided drainage is good and also drier areas if irrigation all around the year is assured. The palm can flourish between 15 °C and 38 °C, but it does not tolerate extremes of temperature and wide diurnal variations. A cool, moist atmosphere is essential.

A tree can stand a wide range of altitude, from sea level to about 1,000 m; but at an altitude above 850 m, the percentage of germination of the nut and the proportion of dry weight of kernel to whole fruit are less than at the lower altitudes. It is a shade-loving plant, especially in earlier stages, and is generally grown as a mixed crop with banana and coconut. Sometimes it is also grown in mango, orange, jackfruit, and guava trees. A mixed plantation is said to cool down the atmosphere, but it has the disadvantage of subjecting the crop to competition.



FIG. 1: ARECA CATECHU



FIG. 2: LABORATORY SAMPLE OF ARECA CATECHU

Areca nut is cultivated in three types of land, viz. the plains, the hill slopes, and the very low lying valleys; and thrives on a variety of soils, such as

laterite soils along the west coast, the red loamy soils of Coimbatore (Tamil Nadu), the loam of Orissa, the alluvia of West Bengal and Assam, and coastal alluvia of North Konkan consisting of a high amount of lime. Ill-drained, saline or alkaline soils, lands with much admixture of kankar nodules, calcareous segregations, and light and sandy soils are not suitable for areca nut cultivation¹². A feather-palm 15-17 m high, which is cultivated in tropical India, Sri Lanka, Malaysia, South China, the East Indies, the Philippines Islands and part of East Africa (including Zanzibar and Tanzania). Large quantities are exported from Madras, Singapore, Penang, and Sri Lanka³. In India, this plant is commercially cultivated in W. Coast, West Bengal, and Assam¹⁶.

Botanical Description: Trunk solitary, quite straight, 12-30 m. high, usually about 50 cm. in circumference, uniformly thick, Leaves 1.2-1.8 m., leaflets numerous, 30-60 cm. upper confluent, glabrous. Spathe double compressed glabrous. Spadix much branched, bearing male and female flowers. Rhachis stout compressed; branches with filiform tips. Male flowers very numerous, sessile, without bracts; calyx 1-leaved, small, 3-corned, 3-parted; petals 3, oblong, rigid, striated; stamens 6, anthers sagittate. Female flowers solitary, or 2 or 3, at or near the base of each ramification of the spadix, sessile, without bracts; sepals 3, cordate, rigid, fleshy, permanent; petals 3, like the sepals, permanent; staminodes 6, connate; style scarcely any; stigma 3, short, triangular. Fruits 3.8-5 cm long, smooth, orange or scarlet¹⁵.

The betel-nut has the shape of a very short, rounded cone, scarcely an inch in height; it is depressed at the center of the base. The testa, which seems to be partially adherent to the endocarp, is obscurely defined, and inseparable from the nucleus. Its surface is marked with a network of veins, running chiefly from the hilum; these veins extend into the white albumin, giving the seed a strong resemblance to a nutmeg. The small conical embryo is situated at the base. The ripe nut is feebly astringent.¹⁸

Phyto-Chemical Studies: Watery extract yields betel nut catechu. "kernels" (seeds) contain catechu, tannin 15%; gallic acid, gum, and alkaloids, viz. arecoline 0.07%, arecaine 1%, arecaidine, and guvacoline, guvacine and choline occur in traces only. All these alkaloids are chemically related; arecoline C₈H₁₃NO₂ is colorless volatile resembling nicotine, with a boiling point of 230 °C, is methyl arecaidine and is prepared by the action of formaldehyde and formic acid on guvacaine by hydrolysis. Arecoline is the most important alkaloid and an anthelmintic principle forms white crystalline salts with acids, i.e., hydro-bromide which in several pharmacopoeias in Europe. It is soluble in water, alcohol, and ether¹¹.

Only arecoline, which is present to the extent of 0.1 - 0.5%, is medicinally important. Ether extraction yields about 14% of fat, consisting mainly of the glycerides of lauric, myristic and oleic acids; subsequent extraction with alcohol yields about

15% amorphous red tannin matter (areca red) of phlobaphene nature³. A study was carried out by Chetan Trivedi et al., they examined that *Areca catechu* contains copper of amount 1.5-11.6% and 7.1-11.3% was soluble when areca nut products were extracted *in-vitro* in distilled water and *in-vivo* in human saliva²⁷. The mineral matter includes calcium (0.05%), phosphorus (0.13%) and iron (1.5 mg/100g). It also contains vitamin B₆ (286.9 mg) and vitamin C (416.2 mg)²⁸.

Pharmacological Actions: Astringent^{6, 7, 10, 11, 14, 15, 17, 21, 22, 28}, strengthen of teeth^{6, 5, 7, 10, 17, 23, 24}, strengthen of gums^{5, 6, 7, 9, 11, 15, 18, 19, 22, 24, 33}, anti-inflammatory^{5, 6, 7, 10, 11, 17, 23}, nerve tonic^{5, 10, 15, 20, 21}, exhilarant^{5, 11, 15, 18}, appetizer^{5, 15}, diuretic^{5, 10, 15, 21}, stomachic^{5, 22, 23, 27}, emmenagogue^{10, 15, 21}, antihelmintic^{5, 15, 20, 21}, digestive^{15, 23, 35}, tonic^{7, 21}, stimulant^{5, 11, 14, 15, 18}, cardio tonic^{9, 10, 15, 23, 25}, aphrodisiac^{5, 15, 18, 20, 21}, antiemetic⁵.

Medicinal Uses: Stomatitis^{5, 15, 23}, improves foul breath^{5, 11, 15, 18, 22}, bleeding gums^{5, 6, 15, 17}, gingivitis²³, conjunctivitis^{5, 6, 7, 10, 15, 19, 17}, sialagogue^{5, 10, 11, 23}, glaucoma^{8, 14, 17, 23}, leucorrhoea^{5, 7, 14, 15}, antiperspirant^{5, 11, 25}, urinary disorders^{5, 8, 15, 21, 22}, anorexia^{7, 21, 23}, diarrhoea^{5, 6, 10, 26, 32}, antioxidant²³, taeniicide (Confined to Veterinary Medicine)^{8, 13, 14}, improve the tone of digestive organs^{21, 22}, anti-malarial^{8, 14, 23}.

Parts Used: Dried ripe seeds^{2, 21}

Therapeutic Dose: 3-5 (gm)^{6, 7}

Mizaj (Temperament): Cold 2° and Dry 2°^{5, 6}

Mazarrat (Adverse Effects): Muwallid-e-sange gurde wa masana (Produces stones in kidneys and bladder)^{6, 17}. Mukhashshin sadr (Causes khushoonat (dryness) in the thorax)^{5, 7, 10}.

Musleh (Correctives): Choona (Lime)⁶, Kateera (*Cochlospermum religiosum*), Ilaichi (*Elettaria cardamomum*)^{5, 6}.

Badal (Substitute): Sandal (*Santalum album*)^{6, 7}, Dhania (*Coriandrum sativum*)¹⁷.

Compounds: Majoon Supari Pak^{2, 6, 17}, Majoone Muqawwie Rahem², Habbe Hamal², Mufarre Rahem^{2, 17}, Sufufe Salab^{2, 17}.

Pharmacological Studies:

Linked to Oral Sub Mucous Fibrosis: A study was carried out by Chetan Trivedy *et al.* They suggested that substantial amounts of copper released from areca products induces lysyl oxidase activity up-regulating collagen synthesis by fibroblasts, facilitating its cross-linking and, thereby, inhibiting its degradation. The role of copper from areca products in the pathogenesis of oral submucous fibrosis merits further investigation, particularly since it is thought to be involved in other fibrotic diseases such as scleroderma and liver fibrosis²⁷.

Antioxidant Activity: Ethanolic extract from areca nut showed potent anti-oxidative, free radical scavenging, and anti-hyaluronidase activity. Anti-oxidative effect of the extract was lower than butylated hydroxytoluene but similar to tocopherol and higher than ascorbic acid²⁹. *Areca* nut extract showed 1, 1 diphenyl 2-picryl (DPPH) free radical scavenging activity³⁰. And strong scavenging activity against superoxide anion radical (*O₂) evaluated by electron spin resonance (ESR) technique³¹. *Areca* nut extract showed *in vitro* inhibitory effect of on H₂O₂ induced RBC hemolysis³².

Anti - inflammatory / Anti - Melanogenesis Activity: Kuk Kook *et al.*, reported that *Areca* nut extracts topical application inhibits hyaluronidase activity *in-vivo* on delayed hypersensitivity and croton-oil induced ear edema in mice. This study indicates that areca nut extracts effective anti-inflammatory/anti-melanogenesis agent and can be used as a new agent for cosmetics³³.

Skin Aging and Cosmetics: KK Lee and JD Choi reported that the anti-aging effects of *Areca catechu* L., on the skin were investigated both *in-vitro* and *in-vivo*. The treatment with areca nut extract showed an increase in collagen synthesis, improvement in skin hydration, the skin elasticity, and skin wrinkles and suggested that areca nut extract can be used as a new anti-aging component for cosmetics *Areca* nut extract reported to have inhibitory activity on elastase and hyaluronidase enzymes present in the skin tissues and areca nut extract purified by solvent fraction and identified to be phenolic substance which showed competitive inhibition with the substrate. Results suggested that

phenolic substance purified from *A. catechu* has an anti-aging effect by protecting connective tissue.³⁴

Hypoglycemic Activity: A study was carried out that arecoline to investigate the hypoglycemic activity in an animal model of diabetes upon subcutaneous administration. Subcutaneous administration of an alkaloid fraction of *Areca catechu* to alloxanized rabbits showed a significant hypoglycemic effect lasting for 4/6 h³⁵.

Vascular-Relaxation: Hirozo Goto *et al.*, reported that *Areca catechu* extract found to have relaxed aortic ring preparations of isolated rat aorta that contain endothelium and relaxation have not occurred in specimens without endothelium, while, inhibition had found during pretreatment with NG-nitro-1-arginine methyl-ester (L-NAME)²².

Arecoline found to have relaxed the human umbilical artery and vein rings in a concentration-dependent manner; the higher the concentration of arecoline, the greater the relaxation of the rings and that relaxation was decreased after the endothelium removed or pretreated with L-NAME, a nitric oxide synthase inhibitor. Arecoline increased in a dose-dependent way the cGMP levels of human umbilical arteries and veins. Therefore, the relaxant effects of arecoline on the umbilical artery and vein rings were endothelium-dependent through the NO-cGMP systems³⁶.

Antimicrobial Activity: Sumitra Hada *et al.* reported that areca nut fatty acids (myristic and oleic acids) and procyanidins from betel nuts (the seed of *A. catechu* L.) were respectively revealed to be the major antibacterial principles against a primary cariogenic bacterium, *Streptococcus mutans*, and the major inhibitory activity against glucosyltransferase from *S. mutans*³⁷.

CM De Miranda *et al.*, also reported that areca nut extracts inhibited the growth of the salivary organisms, which were cultured from the saliva after chewing boiled areca nut, such as *Streptococcus mutans*, *Streptococcus salivarius*, and *Fusobacterium nucleatum* and *Staphylococcus aureus*, in a concentration-dependent manner, baked and boiled nuts were reported to show more potent than raw nut³⁸. *Areca catechu* reported showing inhibitory effects on the growth of *Streptococcus mutans* and *Streptococcus salivarius*,

respectively and 5'-nucleotidase inhibitory activity, which may be useful dental anti-plaque preventing agents³⁹.

Wound Healing Profile of *Areca catechu* Extracts: A study carried out by Shameena Azeez et al., that the arecoline alkaloid, a polyphenol of areca nut and the combined formulation enhanced the breaking strength in the incision wound model. All the extracts increased the wound contraction on the 4th and 16th day and the period of epithelization. This study showed that the alkaloid of areca nut and polyphenols of areca could be used to enhance the healing of burn wounds, leg ulcers, and skin graft surgery⁴⁰.

Protective Effect of *Areca catechu* Extract on Ethanol-Induced Gastric Mucosal:

Lesions: The antiulcerogenic activity was reported by Shameena Azeez et al. They concluded that 250mg/ kg have protective effects on the ethanol-induced gastric mucosal injury⁴⁰.

Anti-Allergic Activity: Anti-allergic activity of *Areca catechu* reported by JH Lee et al., that it has the most potent inhibitor of antigen-induced degranulation in mast cells. *A. semen (Areca catechu)* inhibited DNP-BSA-and compound 48/80- induced degranulation in mast cells and found to have shown inhibitory activity on compound 48/80-induced systemic anaphylaxis by 46% in mice. *A. semen* also inhibited the expression of TNF- α and the activation of mitogen-activated protein kinase, ERK1/2, which is critical for the production of inflammatory cytokines in mast cells, as indicated by the suppression of the activating phosphorylation of ERK1/2. These results suggest that *A. semen (Areca catechu)* may be useful for the treatment of various immediate and delayed allergic diseases⁴¹.

Platelet Aggregation Inhibitory Activity: A study was carried out by MN Ghayur et al. that areca nut crude extract inhibited platelet aggregation induced by arachidonic acid, adenosine phosphate, platelet activating factor and epinephrine and Ca⁺ ionophore. *Areca* nut crude extract showed more potent inhibitory activities on ADP and Ca⁺ ionophore-induced aggregation. *Areca* nut crude extract showed significant acetylcholine esterase inhibitory activity⁴².

Prevention of Dental Cavities: JC Kurian reported that previously betel nut used in toothpaste to prevent cavities. Laboratory studies suggest that betel nut may have antibacterial effects, which may reduce the development of cavities. *Areca* nut made into a dentifrice on account of its astringent properties. It is considered to strengthen the gum, sweeten breath. The seed reduced to charcoal and powered forms excellent dentifrices⁴³.

Anti-HIV Activity: Various active constituents like procyanidins, *Areca* tannin B1 and extracts of the areca nut seed showed HIV protease inhibition activity⁴⁴.

The Effect of *Areca catechu* (Nut) Chewing in Pregnant Women: Amy L. Chue et al., have specifically examined the effects of areca (betel) nut use in pregnant women of Thai Myanmar border. After study, they revealed that areca (betel) nut-related adverse pregnancy outcomes were not observed in this population, whereas smoking was clearly harmful. *Areca* nut use alone was not associated with any adverse effects on maternal or neonatal outcomes in pregnant Karen and Burmese women, in contrast to all, except one. Smoking (cheroots) was a significant risk factor for adverse neonatal outcomes. Smoking and areca nut use in this population did not result in worse outcomes than smoking alone, lending support to the lack of adverse findings in users of areca only⁴⁵.

Anti-Migraine Activity: *Areca catechu* nut extract is a popular folk remedy for the treatment of migraine in Kerala and Tamil Nadu states of India. To prove the claimed utilization of plant, a study was carried out by Amol Bhandarea et al. Findings of the study collectively indicate that the extract exhibited significant inhibition of iNOS, which may be the probable mechanism for its anti-migraine activity, providing evidence, at least in part, for its folkloric use⁴⁶.

Anti - Depressant Activity: Anti - depressant activities of *Areca catechu* fruit extract had shown by A. DAR et al., in the rat brain that the hexane and aqueous fractions of *Areca catechu* 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 (Fs) 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)⁴⁷.

Antihypertensive Activity: *Areca* tannin has been suggested as having a blood pressure regulatory effect through its ability to inhibit the pressor response to both angiotensins I and II. FU-MEI Chung *et al.*, proposed that the cardiovascular effects of chronic BQ (betel quid)/ *Areca nut* usage can be affected by the polymorphism of the angiotensin-converting enzyme (ACE) gene. This study revealed that BQ chewing might be related to blood pressure regulation, which supports the hypothesis that concomitant genetic susceptibility and environmental factors determine the level of blood pressure. *Areca* tannin has been suggested to have properties as a hypotensive drug through its ability to inhibit the pressor response to both angiotensin I and II.⁴⁸

Hypolipidemic Activity: Chun-Pin Chiang *et al.* reported that they established a hamster model of chewing BQ (Betel quid) or *Areca* nut (AN). A total of 81 2-week-old hamsters were randomly divided into three groups: 25 for the control group, 28 for BQ-chewing group, and 28 for AN-chewing group. These animals were fed with a powdered diet with/without BQ or AN for 18 months. Although the consumption of BQ or AN showed some variations, hamsters fed with powdered diet could chew and grind AN or BQ into small pieces of coarse fibers during the entire experimental period. The survival rate of AN-chewing hamsters decreased significantly after 6 months of exposure. The mean survival time was 15.6 ± 0.9 months for control animals, 13.6 ± 0.98 months for AN-chewing animals, and 15.7 ± 0.55 months for BQ-chewing animals.

The body weight of BQ- or AN-chewing animals also decreased after 4-13 months. Hamsters fed with AN for 18 months showed hyperkeratosis in 80% and acanthosis in 50% of cheek pouches. Animals fed with BQ for 18 months also showed hyperkeratosis in 93% and acanthosis in 14% of cheek pouches. These results indicate that AN and BQ components may induce alterations in

proliferation and differentiation of oral epithelial cells. An animal model of chewing BQ or AN can be useful for future tumor initiation, promotion and chemoprevention experiments simulating the condition of BQ chewing in humans⁴⁹.

Antioxidant Activity: A study was carried out by M.N. Hamsar *et al.*, *Areca* nut (*Areca catechu* L.) or Pinang is one of the most widely used psychoactive substances with several hundred million users worldwide, predominantly in Southern Asia. This study evaluates the antioxidant activity and the total phenolic compound of methanolic and aqueous extract of seeds (ripe and unripe seeds), root and adventitious root. They concluded that *areca* nut extracts have the potential to prevent oxidative damage in normal cells due to their antioxidant characteristics⁵¹.

Aphrodisiac Activity: Reena R *et al.*, evaluated the aphrodisiac effect of *A. catechu* along with another plant, *Pedaliium murex* L., which is used in herbal aphrodisiac formulations. Oral administration of the extract at a dose of 150 mg/kg body weight produced significant augmentation of sexual activity in male rats. It significantly increased the mounting frequency, intromission frequency, intromission latency and caused a significant reduction in the mounting latency and post-ejaculatory interval.

The extract was also observed to be devoid of any adverse effects. There was a sustained increase in the sexual activity of normal male rats without any conspicuous adverse effects indicating that *A. catechu* possesses aphrodisiac activity. The study thus provides a scientific rationale for the traditional use of *Areca* nut in the management of male sexual disorders⁵¹.

CONCLUSION: This article provides an overview of many characteristics of *areca* nut and therapeutic effect of phytochemical effect of its biochemical on various disease conditions. *Areca* nut biochemical compounds have been recently recognized as functionally active molecules, possessing antioxidant, hypoglycemic activity, anti-allergic and other useful properties, as well as exert protective effects against cardiovascular and other diseases. As mentioned in the article that further studies are required to know the underlying mechanisms and

type of biochemical compounds involved in this beneficial effect and to ensure these studies, it would facilitate for utilization in modern medicine.

ACKNOWLEDGEMENT: The authors are grateful to the Department of Ilmul Saidla of National Institute of Unani Medicine, Bangalore.

CONFLICT OF INTEREST: Nil

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How to cite this article:

Rashid M, Shamsi S, Zaman R and Ilahi A: *Areca catechu*: Enfolding of historical and therapeutic traditional knowledge with modern update. Int J Pharmacognosy 2015; 2(5): 221-28. doi link: [http://dx.doi.org/10.13040/IJPSR.0975-8232.IJP.2\(5\).221-28](http://dx.doi.org/10.13040/IJPSR.0975-8232.IJP.2(5).221-28).

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