



Review Article

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ANTIMICROBIAL PROPERTIES OF ARECA NUT, *ARECA CATECHU*, L: A REVIEW

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ABSTRACT

Areca palm, *Areca catechu* L., is widely cultivated in several South Asian and Southeast Asian countries. The seeds of areca nut have been widely used in clinical practices. Areca nut has an important place in the ancient Indian system of medicine such as Ayurveda, Unani and Homeopathy. It is traditionally used in a number of ailments for its laxative, digestive, carminative, antiulcer, antidiarrhoeal, anthelmintic, antimalarial, antihypertension, diuretic, prohealing, antibacterial, hypoglycaemic, antiheartburn activities. The observations in this review proved that the areca nut palm is a reservoir of potentially useful chemical compounds which could be served as drugs and might provide newer leads and clues for modern medicine. The bioactive components present in areca nut were worthy enough for further detailed studies and exploit them for their inherent ability as antimicrobial agents.

Keywords: *Areca catechu* L., Tannins, Areca nut, Antibacterial, Antifungal

INTRODUCTION

Areca palm, *Areca catechu* L., is widely cultivated in several South Asian and Southeast Asian countries including India, China, Bangladesh, Indonesia, Myanmar, Thailand, Malaysia, Vietnam, Philippines, etc.¹ Its fruit or seed is also called areca nut / betel nut or 'supari'. It has a characteristic astringent and slightly bitter taste.² In most parts of India, areca nut is marketed after processing.

One type of areca nut is 'Red Supari'. It is obtained by boiling and drying unripe dehusked nuts at different stages of maturity. The other type is 'White Supari' which is obtained by mere drying of ripe nuts and dehusking later on.³ Since ancient times, areca nut has been used for chewing as it is believed to have medicinal properties, both in India and abroad.⁴⁻¹⁵ Areca nut is generally masticated as betel quid. It is a mixture of areca nut, leaf or inflorescence of betel (*Piper betle*) vine and slaked lime. Some people also add tobacco (*Nicotiana tabacum*), catechu (*Acacia catechu*) and certain sweeteners and condiments.¹⁶

Recently, the medicinal uses and properties of areca nut were investigated. It has antioxidant, anti-inflammatory and analgesic¹⁷, anti-diabetic¹⁸, hypolipidemic¹⁹, anti-malaria²⁰, anti-aging²¹, learning and memory improvement²², wound healing²³, anti-ulcer²⁴, anti-migraine²⁵, antihypertensive²⁶, anti-depressant²⁷, anti-allergic²⁸, anthelmintic²⁹, aphrodisiac³⁰, hepatoprotective³¹, cytoprotective³², anti-tumour³³ etc. In spite of all these medicinal values of areca nut, its chronic consumption or chewing may cause several adverse effects including carcinogenesis.^{16, 34}

The major constituents of areca nut on the basis of dry weight are polyphenols, including flavonoids and tannins (up to 29.8%), polysaccharides (up to 25.7%), proteins (up to 9.4%), fats (up to

15.1%), fibers (up to 15.4%), alkaloids (up to 0.24%) and minerals (up to 2.5%).^{35,36} Several scientific reports have been written on antimicrobial properties of areca tannins, especially on microbes causing human diseases.³⁷⁻⁴⁰

In this paper, an attempt has been made to review the available scientific literature on the antibacterial, antifungal, antimalarial and anti-HIV properties of areca nut.

Antibacterial Properties

Almost all parts of areca palm including its nuts, leaves and roots show good antibacterial properties. The hot water extract of areca nut was effective against both gram negative and gram positive bacteria. The concentration needed for 100% inhibition of growth was reported to be 3.3 to 7 µg/ml for gram negative and 16 µg/ml for gram positive bacteria.⁴¹

Natural polyphenols including tannins have been reported to be of medicinal importance.⁴²⁻⁴⁴ While preparing the 'Red Supari' of areca nut, the nuts are boiled first and during this process lots of concentrated liquid called *Chogaru* which contains good amount of tannin comes out of the nut.⁴⁵ This liquid is generally wasted by farmers. Such by-product of areca nut was also reported to be antibacterial against *Enterobacter aerogenes*, *Staphylococcus aureus*, *Escherichia coli* and *Bacillus subtilis*.⁴⁶ Hence, even a waste material like *Chogaru* could be used for medicinal purposes.

It was reported that the butanol fraction of areca nut was more potent than the methanol, ethylacetate, and water extract against four strains of bacteria such as *S. aureus* 96, *S. aureus* 2940, *Streptococcus mutans* and *Mycobacterium smegmatis*.⁴⁷ The minimum inhibitory concentrations for these bacteria were 62.5, 125, 250, and 250µg/ml, respectively.

Apart from polyphenols of areca nut, its protein molecules, especially the peptides were also reported to be antibacterial. The peptides such as 68kDa and 65kDa present in areca nut kernel (isolated by acetone extraction at 1:2 ratio) were reported to be antibacterial against *Staphylococcus epidermidis*, *E. coli* and *Proteus mirabilis*.⁴⁸ The minimum inhibitory concentrations varied from 250 to 500µg/ml and the minimum bactericidal concentrations were more than 1000µg/ml.⁴⁸

Among the gram positive and gram negative bacteria, the latter was observed to be more susceptible to these peptides. Hence, the protein molecules of areca nut could also be used as an alternative to the synthetic antibiotics. The hydroalcoholic extract of areca nut was also antibacterial against three skin infesting bacteria, *Staphylococcus aureus*, *E. coli* and *Bacillus subtilis*.⁴⁹ It was found that the extract, at a concentration of 100mg/ml was effective against *S. aureus*, whereas at 200mg/ml, it was very effective even against *E. coli* and moderately effective against *B. subtilis*. In Ayurveda system of medicine, areca nut is already known for the treatment of several skin diseases.⁸

Not only the nuts of areca palm, but also its leaves and roots have antibacterial properties. The antibacterial effect of areca leaf extract was reported against *Bacillus cereus* and *Pseudomonas fluorescens*.⁵⁰ The root extract of areca palm was found to be more potent than its leaf extract against several bacteria. The ethanol extract of areca root was found to be highly effective against *Pseudomonas aeruginosa* and even more effective than that of the conventional chemical bactericide, Chloramphenicol.⁵¹ The zone of growth inhibition at the recommended dose of Chloramphenicol was 9.3mm, whereas with a concentration of 100µg/ml the areca root extract inhibited even up to 12.6mm and it increased to 14.6 and 15.4mm at a concentration of 250 and 500µg/ml, respectively. It was also found that the root extract was effective even against several other bacterial species such as *Klebsiella pneumonia*, *Salmonella typhi*, *Bacillus cereus*, *Streptococcus pyogenes* and *Staphylococcus aureus* with the zone of inhibition ranging from 12.2 to 14.6mm at a concentration of 500 µg/ml.⁵¹

Effect of Areca nut on oral microorganism

In Ayurveda system of medicine, areca nut, along with turmeric (*Curcuma longa*), is known for its action as tooth cleaner.⁸ In recent years, attempts were made to identify the antibacterial properties of areca nut on oral microorganisms. Several scientific observations reveal that chewing areca nut protects teeth against dental caries.⁵²⁻⁵⁵ It is the stain of areca nut which acts as a protective varnish against microorganisms on tooth surface. Betel nut stained teeth were even reported to withstand acids (pH of 3.5 to 4.5) for several months.⁵⁵

The tannic acid component of areca nut is responsible for the cariostatic effect. While investigating the inhibitory effects of areca nut extract and its components (arecoline and tannic acid) on certain common periodontal bacterial pathogens in vitro, it was found that the tannic acid component at a dose of more than 9mg/ml inhibited the growth of *Eikenella corrodens*, *Porphyromonas gingivalis*, *Campylobacter rectus*, *Tannerella forsythensis* and *Fusobacterium nucleatum* but not the arecoline component.⁵⁶

The procyanidines from the seeds of areca nut were reported to be the actual antibacterial principles against the primary cariogenic bacteria, *Streptococcus mutans*.⁵⁷ It was identified that two polyphenolic substances (nucleotidase inhibitors), NF-861 and NF-8611 from areca nut were also responsible for the

growth inhibition of *S. mutans* MT8148(c) and MT6715(g) strains.⁵⁸ These compounds might be used as anti-plaque agents. Prolonged intraoral exposure to the nut was reported to suppress bacteria in the mouth and the extract of baked and boiled nuts was found significantly more potent than raw nuts.⁵⁹ Baked and boiled nuts are mainly obtained from tender areca nut.³ It was reported that polyphenols are more in tender areca nut as compared to mature nuts.⁶⁰ This might be the reason why the boiled areca nut are more effective than raw nuts in their cariostatic effects.

As far as the extract of areca nut is concerned, it is the ethanolic extract which was reported to be very effective against several oral microorganisms such as *E. coli*, *K. pneumonia*, *Proteus vulgaris*, *P. aeruginosa*, *S. non-typhi*, *S. typhi*, *Shigella flexneri* and *Vibrio cholera*.⁶¹ Highest antibacterial activity was observed against *P. vulgaris* and *V. cholera* with zone of growth inhibition of 16mm at 50% concentration for *P. vulgaris* and 18mm at 70% concentration for *V. cholera*. They further found the result comparable to that obtained with the conventional antibiotic Ciprofloxacin for *P. vulgaris* in which the zone of growth inhibition at the recommended concentration was only 15mm. The water extract of areca nut was found equally effective to that of ethanol extract against *E. coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Staphylococcus aureus* but hexane extract did not give any positive result.⁶²

Not only the aerobic bacteria, but also the anaerobic bacteria such as *Enterococcus faecalis*, which is responsible for human endodontic infection was susceptible for areca nut extract. The aqueous extract of areca nut was found even better than that of Chlorhexidine (the chemical disinfectant presently used during root canal treatment) in inhibiting the growth of *E. faecalis*.⁶³ With areca nut extract, the growth of inhibition was noticed at a concentration of as low as 0.062mg/disk whereas with chlorhexidine the inhibition was not noticed at that concentration, but it commenced only at a concentration of 0.25mg/disc.

Though areca nut extract has antimicrobial properties against several oral pathogens and its chewing may reduce dental caries, there is ample evidence to show that chronic chewing of betel quid increases periodontitis,⁶⁴ and might induce several other complications.^{16,34}

Antifungal Properties

The areca nut extract was also reported to be antifungal. The aqueous extract of areca nut at 50 µg/ml effectively inhibited the growth of the unicellular fungus such as *Candida albicans*.⁴¹ In another study, a zone of inhibition of 18mm was obtained on *C. albicans* with aqueous extract of areca nut at 16.67 µg/ml concentration.⁶⁵ However, the hydroalcoholic extract of areca nut was moderately active against *C. albicans* at a concentration of 100mg/ml and very active at 200mg/ml concentration.⁴⁹

The aqueous extract of areca nut was also effective against other fungi such as *Mucor sp*, *Cladosporium sp* and *Aspergillus niger* with the zone of inhibition of 12mm, 13mm and 14mm, respectively at 16.67 µg/ml concentration.⁶⁵ The aqueous extract of areca nut even inhibited the development of aflatoxin producing fungus, *Aspergillus flavus* by 85.71% at a concentration of 100 to 250 µg/ml and reduced the aflatoxin content from 35 ppb to 5 ppb. These results indicate that the chewing betelnut might have properties of a disinfectant. Further studies are needed to determine the chemical compound responsible for such antifungal activity.

In a study on the antifungal effects of different solvent extracts (aqueous, ethyl acetate and hexane) of areca nut against *C. albicans*, it was reported that ethyl acetate extract was the most active one followed by aqueous extract.⁶⁶ The hexane extract was least effective. In various studies, it was found that, the ethyl acetate extract of areca nut mostly contained tannins and polyphenols. This is in conformity with the earlier findings that Polyphenols of plants are also antifungal.⁴²⁻⁴⁴

Not only the areca nut seed but also its husk (pericarp) and root were reported to exhibit antifungal properties. It was reported that the alcoholic extract of areca nut husk fibres exhibit dose dependent positive inhibitory response against *C. albicans* with zone of inhibition of 5 to 9mm.⁶⁷ Hence, this plant material could be a potential source for developing natural antifungal agent for this common oral pathogen. The ethanol extract of the roots of *A. catechu* was even more effective against several fungi such as *C. albicans*, *A. niger*, *A. flavus* and *Penicillium notatum* with zone of growth inhibition ranging from 16 to 28.3mm at different concentrations between 100 to 500µg.⁵¹ They also got an interesting result that the *C. albicans* which was resistant to the conventional chemical fungicide, Fluconazole succumbed to the root extract of areca palm with zone of growth inhibition of 16.7 and 24.0mm at concentrations of 100 and 500µg/ml, respectively.⁵¹

The areca nut extract was observed to be antifungal against plant pathogens as well. It was reported that the hexane, ethyl acetate and methanol extracts of the pericarp (husk) of areca nut were antifungal against *Colletotrichum gloeosporioides*, an important anthracnose fungus causing fruit rot in plants.⁶⁶ Studies conducted revealed that three triterpenes, namely fernenol, arundoin and a mixture of stigmaterol and alpha-sitosterol and one fatty acid, lauric acid inhibited the mycelia growth of this fungus *in vitro* with EC50 values of 36.7, 47.5, 56.7 and 111.5mg/l, respectively. They also studied the fungal growth and found that the fernenol, arundoin and the mixture of stigmaterol and β-sitosterol inhibited spore germination and germ tube elongation and were significantly more effective than benomyl, a common systemic fungicide, for controlling post harvest anthracnose disease in mango fruits.⁶⁶

Antiviral Properties

The antiviral activities of areca nut extracts have also been studied. The works carried out by different researchers on the uses of several plants (herbal medicines) for treatment against the sexually transmitted diseases (STDs) and acquired immunodeficiency syndrome (AIDS) in man have been reviewed.⁶⁸ They reported that the areca nut extract had inhibitory effects against viral pathogens responsible for HIV and herpes simplex virus (HSV-1). Plant tannins and alkaloids were found responsible for antiviral properties.⁶⁹

Among 39 crude drugs tested for their inhibitory effects against human immunodeficiency virus (HIV), it was found that the extract of areca nut was the most potent antiviral agent against HIV-IPR with a growth inhibition activity of more than 70% at a concentration of 0.2mg/ml.⁷⁰ They also isolated the procyanidine, areca tannin B1 responsible for this activity. The areca nut extract was also observed to inhibit the viral growth of the New Castle Disease Virus (NDV) and Egg Drop Syndrome Virus (EDS) grown in embryo cultures.⁴¹

Antimalarial Properties

Malaria is caused mainly by four species of the protozoan parasite, *Plasmodium falciparum*, *P. vivax*, *P. ovale* and *P.*

malariae. In a study on the antimalarial activity of areca nut extract, it was found that the treatment of malaria- infested mice with butanol extract of areca nut at a dose of 150mg/kg/day for 4 days, resulted in an increase in the survival rate by 60% over control.^{71,72}

In another study, it was reported that the butanol fraction of areca nut extract was most potent against *P. falciparum* with an LC 50 of 18 µg/ml.⁴⁷ These observations have been really useful for pharmacology industry as there were reports of *Plasmodium* becoming resistant against Chloroquine, the common drug presently used for the treatment of malaria.

CONCLUSION

These observations proved that areca palm is a reservoir of several useful chemical compounds which could be served as potential therapy and might provide newer leads and clues for modern medicine. The bioactive components present in areca palm were worthy enough for further detailed studies and to exploit them for their inherent ability as antimicrobial agents.

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