

## American Journal of Oral Medicine and Radiology



Journal homepage: www.mcmed.us/journal/ajomr

## **ARECA NUT AND ITS EFFECTS ON THE HUMAN BODY**

### Anjana Mohan Kumar, Kota Sravani\*, Veena K.M, Prasanna Kumar Rao J, Laxmikanth Chatra, Prashanth Shenai, Rachana V Prabhu, Tashika Kush Raj, **Pratima Shetty, Shaul Hameed**

Department of Oral Medicine and Radiology, Yenepoya Dental College, Yenepoya University, Mangalore, Karnataka, India.

### **Article Info**

Received 23/12/2014 Revised 16/01/2015 Accepted 23/02/2015

Key words:- Areca catechu, Arecoline, Tannin, Oral mucosa. Leukoplakia.

#### **INTRODUCTION**

## ABSTRACT

Areca nut (also known as betel nut) is the seed of the fruit of the areca palm (Areca catechu). Betel nut chewing is an important cultural practice in some regions in south and south-east Asia and the Asia Pacific. It has traditionally played an important role in social customs, religious practices and cultural rituals. The chewing of areca nut has always been a topic of controversy worldwide. Though when used occasionally areca nut has many beneficial effects, its excessive use causes dangerous adverse effects hence the good effects are masked. This article gives an overall review on areca nut, its origin, cultivation, composition, and general uses and side effects.

The areca nut, also commonly known as betel nut, is the seed of the Areca catechu palm tree, and is the fourth most commonly used psychoactive substance, after caffeine, nicotine and alcohol. There are an estimated 600 million people who chew betel nuts worldwide making it more popular than chewing gum but less popular than tobacco. Areca catechu palm is an un branching, long plant extending up to 15m and crowned with 6 to 9 palm fronds.<sup>[1]</sup> The nut is the seed are found within the fruit, the outer surface of which is green when unripe and orangevellow when ripe. The seed is separated from the outer layer of the fruit and may be used fresh, dried, boiled, baked, roasted or cured [1].

#### History of origin

Unknown in the wild, betel nut is a cultigen that grows only where people grows it. The actual source of origin of areca nuts is uncertain. Its cultivation is said to date back to the pre-Christian era [2]. It is mentioned as being cultivated in Malacca before 1593.

Corresponding Author

Kota Sravani Email: - kota sravani@yahoo.co.in

De Candolle in his work 'The origin of cultivated plants' mentions that its origin is probably the Sunda Islands. It is now believed that areca nut is indigenous to southern Asia, Indonesia and possibly the Philippines. It is an aboriginal introduction into New Guinea, the Solomon Islands and western Micronesia and a recent introduction into Fiji, Samoa and other islands [3].

Betel nut's origins in India cannot be precisely dated but it has been mentioned in ancient literature and texts for almost 2,000 years. Betel nuts also feature in ancient traditional medicine. Ayurvedic medical texts dating back 2000 years discuss the ingredients of betel quid, and Sanskrit writings list different types of betel quid. More precise references to betel nut chewing dates from the Gupta period in the 5th century AD. By this time, it appears to have been a widespread practice [4].

#### Cultivation of areca nut

Areca nut almost always exists in cultivation; therefore, conditions of its natural habitat are difficult to assess. It however thrives in areas of high rainfall. Although tolerant to moderate elevations, it generally grows best in low altitudes. Being a shade-loving species, areca nut always does well when grown as a mixed crop with fruit trees.



The planting of areca nuts are done during premonsoon period of May-June [5]. The areca nut palm is prone to a number of diseases as the warm, damp interval of monsoon showers is an ideal environment for diseases to occur. To prevent fungal diseases, growers spray 1% Bordeaux mixture (a fungicide which is prepared by adding milk of lime to a solution of copper sulphate until alkaline reaction is obtained) as a prophylactic spray just before the onset of monsoon. This helps the areca palms to withstand the heavy rainfall. The spray gives a coating on the tender palms and prevents it from rotting and falling off [6].

#### Worldwide distribution

There are more than .5 million betel nut vendors and 5 million people who make their living in the betel nut industry. As per the Food and Agriculture Organization (FAO), the world production of areca nut was around 8.54 lakhs metric tons with a total area of around 7.03 lakh hectares in the year 2006. India's share in production comes to 55 per cent and that of Indonesia 17 per cent, Bangladesh 10 per cent, China 8 per cent, Myanmar 4 per cent and Thailand was around 2 per cent [7]. The share of Sri Lanka, in total production of areca nut in the world is hardly 1.6 per cent and that of Nepal, Malaysia, Maldives and Kenya as per this source, is very negligible [Fig 1].

#### Chemical and metal constituents of areca nut

The major constituents are carbohydrates, fats, proteins, crude fibre, polyphenols (flavonols and tannins), alkaloids and mineral matter [8]. The concentrations of various constituents vary between raw and ripe areca nuts [9]. Polyphenols form the major constituents of the nut and it also gives the astringent taste to the nut. Arecaidine, arecoline, guvacine and guvacoline are the four main alkaloids conclusively identified in areca nut. [10] The other alkaloids include arecaine, arecolidine, isoguacine and conine [11]. The metallic constituents include copper, iron, zinc, nickel, manganese, potassium and sodium etc [Table 1]. Certain varieties of areca nut have lead, magnesium, chromium, cobalt and arsenic. The metallic constituents can vary depending on the fertilizers and fungicides used while cultivation [12].

# Effect of the various constituents of areca nut on the body

According to Sushruta, who lived in the 1<sup>st</sup> century BC areca nut chewing tends to cleanse the mouth, impart a sweet aroma to it, enhance its beauty and cleanse and strengthen the voice, tongue and teeth, the jaws and the sense organs' [13]. Chewing betel also evokes a mild euphoria, and it is this general feeling of 'well-being' that contributes mainly to the popularity of the custom [14]. This feeling of well being is brought about by arecacoline which acts as an agonist at the muscarinic acetylcholine receptors causing stimulation of the central and autonomic nervous system thereby increasing the secretion of nor

adrenalin and acetylcholine [15]. Betel chewing produces an increase in heart rate, blood pressure, sweating and body temperature. In addition, EEG shows widespread cortical desynchronization indicating a state of arousal. In autonomic function tests, both the sympathetic skin response and RR interval variation are affected. Arecaidine shows anxiolytic properties through inhibition of gamma amino butyric acid reuptake. Areca tannin has a blood pressure regulatory effect due to its ability to inhibit the pressor response to both angiotensin I and II [16]. The pulp of the nut is used for relieving pain in the stomach of humans. As an astringent it hardens the mucous membranes of the stomach. A decoction of betel nut and khair (khadira) taken with honey can be used to cure urinary infections. And betel nut powder can be used to cure syphilitic ulcers. Areca-nut is widely used in veterinary medicine, mainly to expel parasitic worms. Some claim that the areca-nut is an aphrodisiac. The raw and unripe nuts are poisonous and harmful to the eye. But the cured hard center of the nut can cure the same complaint. It is said that betel nuts are poisonous when young, purgative in middle age but an elixir when fully ripe and dry.

Arecoline is also reported to have cytotoxic, genotoxic and mutagenic effects in various cells [17]. The cellular level of glutathione was diminished by areca nut extract leading to suppression of T – cells activation and Th1 cytokine production. Intra cellular antioxidative activity is increased in response to increased oxidative stress and genetic damage in human keratinocytes [18]. The addictive properties of areca chewing are reflected in the withdrawal symptoms shown by even mild habituated users [19].

In rare instances, heavy use of betel nut has resulted in an acute reversible toxic psychosis characterised by hallucinations and delusions. Cholinergic toxicity with the SLUDGE syndrome (salivation/sweating, lacrimation, urinary incontinence, diarrhea, gastrointestinal upset, emesis) can be seen with initial or heavy use of the betel nut. In large quantities, it can cause pulmonary edema, broncho-constriction, and even death. An overdose of betel nut can mimic insecticide poisoning [20]. Expectant mothers who chew areca nut causes adverse effects on baby like low birth weight, low birth length and early term.

#### Effects on the oral cavity

Areca-nut chewing has significant effects on the hard and soft tissues of the oral cavity [21]. The most common effect of areca chewing on the hard tissue is staining of teeth due to areca deposits [Fig 2]. The habitual chewing of areca may result in severe wear of incisal and occlusal tooth surfaces leading to exposure of dentine and tooth sensitivity. Some studies have described a protective effect of areca-nut chewing on dental caries, cariostatic properties of areca is thought to be due to the betel stain, which often coats the surface of the teeth, may act as a protective varnish. It is also seen that the nuts exhibits a direct anti-bacterial effect on the oral bacteria [22]. It is seen that areca extracts containing Arecoline may be cytotoxic to periodontal fibroblasts and may exacerbate pre-existing periodontal disease as well as impair periodontal reattachment. Areca-induced lichenoid lesions [Fig 3] mainly on buccal mucosa or tongue, have been reported at sites of quid application, which is a type IV contact hypersensitivity-type lesion but resembles oral lichen planus clinically. It is usually seen at the site of quid placement in areca chewers and may be unilateral in nature with fine keratotic lines radiating from a central red or atrophic area.

Betel chewer's mucosa is characterised by brownish-red discolouration of the oral mucosa accompanied by encrustation of the affected mucosa with quid particles, which are not easily removed, and with a tendency for desquamation and peeling. The underlying area assumes a wrinkled appearance. The lesion is usually localized and associated with the site of guid placement in the buccal cavity. The next effect seen on the oral mucosa of areca chewers is oral leukoplakia, [Fig 4] seen as a white plaque or patch, which is a potentially malignant disorder with transformation rates between 0.1 and 17.5% [22]. It can also cause oral sub mucous fibrosis (OSMF) a high risk potentially malignant condition with a malignant transformation of 7.6%. [23] It is also known as the crippling disease of the oral cavity. The individuals affected by this condition have inability to open their

Table 1. Chemical and metal constituents of areca nut

mouth due to formation of fibrous bands in the oral cavity [Fig 5]. Fibrosis and hyalinization of sub epithelial tissues account for most of the clinical features encountered in OSMF. Substantial amounts of copper released from areca nut induces lysyl oxidase activity up regulating collagen synthesis by fibroblasts, facilitating its cross linking and thereby inhibiting its degradation [24].

There is also historical evidence dating back nearly a century that shows that the areca nut chewing can lead to development of oral squamous cell carcinoma [25] [Fig 6]. It has been suggested that manganese, a metal constituent of areca, plays a role in the generation of Reactive oxygen species (ROS) that may result in neurotoxicity [26] More recent studies have provided evidence suggesting that oxidative stress induced by manganese exposure can trigger apoptosis of neural stem cells. ROS generated by arecoline, a key compound in areca nut, may be responsible for the higher incidence of tremor and skin lesions in betel quid chewers. Poor arsenic metabolism in female chewers may responsible for their greater arsenic induced skin. Nickel and chromium induce oxidative stress and are known to be genotoxic.[27] Chromium interacts directly with DNA, forming Cr-DNA adducts and causing DNA damage. Nickel cause damage to DNA through the inhibition of repair enzymes.

| Sl no | Parameter (ppm) | Sample A- commercial areca nut powder | Sample B – red areca nut |
|-------|-----------------|---------------------------------------|--------------------------|
| 1     | Copper          | 0.277                                 | 0.040                    |
| 2     | Iron            | 0.140                                 | BDL                      |
| 3     | Cadmium         | BDL                                   | BDL                      |
| 4     | Zinc            | 0.211                                 | 0.421                    |
| 5     | Nickel          | 0.266                                 | 0.232                    |
| 6     | Lead            | 0.317                                 | 0.033                    |
| 7     | Manganese       | 0.353                                 | 0.419                    |
| 8     | Magnesium       | 26.56                                 | 94.61                    |
| 9     | Chromium        | 0.032                                 | 0.043                    |
| 10    | Cobalt          | BDL                                   | 0.022                    |
| 11    | Mercury         | 1.178                                 | BDL                      |
| 12    | Arsenic         | 1.892                                 | 5.368                    |
| 13    | Potassium       | 364.4                                 | 149.64                   |
| 14    | Sodium          | 81.18                                 | 60.78                    |

Figure 1 .Worldwide cultivation of areca nut





Figure 3. Lichenoid reaction on the right buccal mucosa

Figure 5a. Blanching of the palate in OSMF



#### CONCLUSION

The habit of areca chewing is becoming prominent among the younger individuals due to impressive marketing strategies, ease of access and cost effectiveness. And the ill effects of the habit are also seen to be on the rise. Efforts to educate the community on the dangers of areca nut chewing, and encourage policy changes that regulate the use and sale of purified preserved betel nut preparations, is extremely important in decreasing the potential dangers of areca nut.

#### REFERENCES

- 1. Staples W G, Bevacqua F R. (2006). Species profiles for pacific island agro forestry. Areca catechu (betel nut palm).
- 2. Anonymous 1. Agro forest Data base. worldagroforestrycentre.org
- 3. Ahuja SC and Ahuja U. (2011). Betel Leaf and Betel Nut in India, History and Uses. Asian Agri-History, 15(1), 13-35
- 4. Anonymous 2.Plant cultures. Betel nut history. KEW.org
- 5. Khan S, Chatra L, Prashanth SK, Veena KM, Rao PK. (2012). Pathogenesis of oral submucous fibrosis. J of cancer research and therapeutics, 8(2), 199-203.
- 6. Nzegbule EC. (2003). Assessment of copper levels in the soil and vegetation following repeated application of Bordeaux mixture to a cocoa plantation in south eastern Nigeria. *Niger Agric J*, 34, 97-102
- 7. Kammardi T N P. (2012). Arecanut economy at cross roads. Report of Special Scheme on Cost of Cultivation of Arecanut in Karnataka, 1-95
- 8. Wang C K, Lee W H, Peng C H. (1997). Contents of phenolics and alkaloids in Areca catechu, Linn during maturation. *J Agric Food Chem*, 45(4), 1185-1188.
- 9. Wang CK, Su HY, Lii CK. (1999). Chemical composition and toxicity of Taiwanese betel quid extract. *Food Chem Toxicol*, 37(2-3), 135-144
- Wei-M Z, Jing W, Wen-xue C, Hai-D Z. (2011). The Chemical Composition and Phenolic Antioxidants of Areca (Areca catechu L) Seeds. International Conference on Agricultural and Biosystems Engineering, Advances in Biomedical Engineering, 1-2, 16-22
- 11. Betel quid and areca nut chewing, IARC Monographs Volume 85, 1-349.
- 12. Sivaramakrishnan VM. (2001). Text book of Tobacco and Areca-nut. 1<sup>st</sup> ed. Chennai, Orient Longman Ltd.
- 13. Lingappa A, Nappalli D, Sujatha G, Prasad S. (2011). Areca nut, To chew or not to chew?. *e-Journal of Dentistry*, 1(3), 46-49.
- 14. Benegal V, Rajkumar RP, Muralidharan K. (2008). Does areca nut use lead to dependence. Drug and Alcohol Dependence, 97, 114–121.



Figure 6. Squamous cell carcinoma on the gingival sulcus extending to retromolar pad area



- 15. Bhat SJ Blank MDBalster RL Nichter M (2010). Areca nut dependence among chewers in a South Indian community who do not also use tobacco. *Addiction*, 105(7), 1303-1310.
- 16. Inokuchi J, Okabe H, Yamauchi T, Nagamatsu A, Nonaka G, Nishioka I. (1986) Anti-hypertensive substance in seeds of areca catechu. *L Life Sci*, 38(15), 1375-1382.
- 17. Dasgupta R, Saha I, Pal S, Bhattacharya A, Sa G, Nag TC, Das T, Maiti BR. (2006). Immunosuppression, hepatotoxicity and depression of antioxidant status by arecoline in albino mice. *Toxicology*, 227(1-2), 94-104.
- 18. Rakhi MC, Manoj GC, Shivlal MR. (2013). Current concepts about areca nut chewing. *Journal of Contemporary Dentistry*, 3(2), 78-81.
- 19. Pickwell SM, Schimelpfening S, and Palinkas LA. (1994). 'Betelmania'-B Betel Quid Chewing by Cambodian Women in the United States and Its Potential Health Effects. *West J Med*, 160, 326-330.
- 20. Nelson SB, Heischober B. (1999). Betel Nut, A Common Drug Used by Naturalized Citizens From India, Far East Asia, and the South Pacific Islands. *Annals of Emergency Medicine*, 34(2), 238-243.
- 21. Trivedy CR, Craig G, Warnakulasuriya S. (2002). The oral health consequences of chewing areca nut. *Addict Biol*, 7, 115-125.
- 22. Nelson Anthikat RR, Michael A. (2009). Study on the areca nut for its antimicrobial properties. *J Young Pharmacists*, 1, 42-56.
- 23. Sudarshan R, Rajeshwari G Annigeri, Sree Vijayabala G. (2012). Pathogenesis of Oral Submucous Fibrosis, the Past and Current Concepts. *International Journal of Oral & Maxillofacial Pathology*, 3(2), 27-36.
- 24. Trivedi C, Baldwin D, Warnakulasuriya S, Johnson N, Peters T. (1997). Copper content in areca catechu products and oral submucous fibrosis. *Lancet*, 28, 246-251
- 25. Nitin Gupta, Susmita Saxena, Siddharth Gupta, Seema Gupta, Vishal Singh, Jyoti Yadav. (1997). Role of Copper in Oral Submucous Fibrosis, A Cytological Correlation. *Indian Journal of Dental Sciences*, 5(3), 29.
- 26. Al-Rmali S W, Jenkins O R, Haris I P. (2011). Betel quid chewing as a source of manganese exposure, total daily intake of manganese in a Bangladeshi population. *BMC Public Health*, 11, 85-86.
- 27. Vela D. Desai, M. V. Sunil Kumar, Renuka J. Bathi, Isha Gaurav, Rajeev Sharma. (2014). Molecular Analysis of Trace Elements in Oral Submucous Fibrosis and Future Perspectives. *Universal Research Journal of Dentistry*, 4(1), 27-32.