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ARECA CATECHU CONSUMPTION AND ITS MEDICINAL PROPERTIES - A COMPREHENSIVE REVIEW

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ABSTRACT
Areca catechu L is one of the most important medicinal plants grown in southeast asian countries and is shown to have both medicinal properties like improving concentration and having a relaxing effect apart from having cytotoxic effects. They also show anti-inflammatory, antiparasitic, anti-hypertensive, and antidepressant activities. They also have effectiveness in treating symptoms of Alzheimer's disease. In India, people consume areca nuts alone or in combination with tobacco and other products in the form of Pan masala or Gutka. Areca nut usage dates back to Harappan civilization and has a mention in our ancient vedic and sanskrit manuscripts. Chemically, Areca nuts are made up of flavonoids, alkaloids, tannins etc. Some of the important alkaloids include arecoline, arecaidine, guvacine etc. Arecoline is colourless, volatile and is an important component of Areca nut. It has been studied for its effects in both in vitro and in vivo studies. Though areca nut is popularly chewed in the Indian subcontinent and China its effect has not been investigated systematically in humans. When compared to modern medicine (allopathy), traditional medicines, especially the ones containing areca nut as an important ingredient, have not been researched much. In this review we have considered the medicinal properties of Areca nuts and their effectiveness against many human diseases. Fractions of Areca nuts are obtained through aqueous and organic solvent extraction techniques and have shown varied effects in the animal models used in research carried out across the world.

Keywords: betel nut, Areca catechu L, Arecoline, Betel leaf, Antiparasitic, Tobacco

INTRODUCTION
Areca nut is the seed of Areca catechu, which belongs to the family of palm trees. It is commonly known as betel nut and chewed with leaves of betel plant in many parts of the world [1]. Areca nut has been used in India for a very long time and it's a socio-cultural practice that is accepted widely by the society. This practice has been converted into a public health problem after European traders introduced tobacco some 400 years ago [2]. Areca nut is the fourth most commonly used psychoactive drug after Nicotine, Ethanol and Caffeine [3]. Areca nut use is associated with most ancient civilizations like Harappa and since then it has become an integral part of our tradition as "Thambula" [4].

Areca nut is native to South and Southeast Asia including India, Indonesia, Malaysia, Philippines, Cambodia etc., The fruit of Areca nut is harvested from November to December and the seeds are collected and dried in the sun.

Areca nut has a mention in Sanskrit Manuscripts and is used for religious purposes, Medicine, food and so on. It is mainly cultivated in India, Malaysia, Polynesia, Micronesia and most places of South pacific Islands [5]. Around 0.6 million tonnes of Areca nut are produced in the world currently and India produces almost 53% of it [6].

Areca nut has been used as Socio-economic practice in India. As per many reports areca nut is used with tobacco in the form of Pan masala or Gutka is increasing in the country and the ATS report suggests that Areca nut with tobacco is used by 7.5% men and 4.9% women. People of rural India use a lot of tobacco mixed Areca nut as compared to Urban people.

Chemical Composition
Different chemicals have been isolated from Areca nut plant in many countries for the last 150 years [7]. So far 59 compounds have been isolated and identified from areca nut plants. They have been characterised into Alkaloids, Tannins, Flavonoids, Triterpenes etc.,

There are four alkaloids present namely Arecoline, Arecaidine, Guvacine and Guvacoline of which Arecoline is the most important constituent [8].

Arecoline is a major alkaloid in areca nuts and has agonistic activity mainly at muscarinic acetylcholine receptors and stimulates the central and autonomic nervous system. This results in increased well-being, alertness and stamina in people who consume it regularly. Studies also suggest that areca nut extract improves

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concentration and relaxation, with other reported effects including lifting of mood, staying off hunger, aphrodisiac properties and as postprandial digestant. There is also the presence of cariostatic properties shown by areca nut [8,9]. Arecoline is a cholinomimetic and has a number of structural similarities to acetylcholine, a major neurotransmitter involved in central and autonomic nervous system signalling.

Chemically arecoline is a colourless, volatile and oily and its chemical formula is $C_8H_{13}NO_2$. The Taenifuge properties of the drug are probably due to nicotine like the principle of Arecoline. It mixes with water, Chloroform, Alcohol and Ethane. Chemical formula of arecaidine is $C_7H_{11}NO_2 + H_2O$ and it is non-poisonous and was discovered by Jahns in 1891. Guvacine has a chemical formula $C_6H_9NO_2$ and is the lower homologue of Arecaidine and is non-poisonous.

The tannins resemble catechu-tannic acid, is red and strikes green with ferric salts, quickly changing to brown and when alkali is added a violet colouration appears. It is not soluble either in hot water or cold water. It gives bitter and astringent taste to the areca nut [10,11].

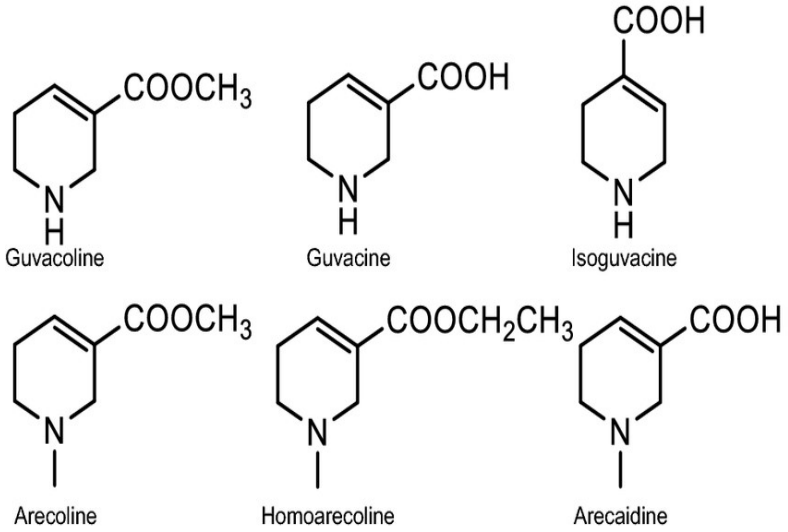

Fig.1: Structures of the components of Areca catechu L (Oliveira et. al., 2021)

Medicinal Properties of Areca Nut

Betel Nut or Areca nut is known to have Psychoactive properties in reducing tension, producing Euphoria or a sense of well-being, increasing the capacity to work and providing the means of social interactions and rituals [13, 14]. Parasympathomimetic properties are shown by Arecoline acting on both muscarinic and nicotinic receptors [15]. It induces an arousal response in animals and a cardio-acceleratory response in humans [16,17,18] Normally Areca nut is consumed with Betel leaf and quick lime and this mixture shows different reactions and interactions before the psychoactive compounds are released into the circulation [19]. Arecoline in the presence of lime is converted into arecaidine, which lack parasympathetic properties. Though areca nut is popularly chewed in the Indian subcontinent and China its effect has not been investigated systematically in humans. Arecoline and arecaidine from Areca nut are found to be stimulators of catecholamine release from chromaffin cells in-vitro [19]. Water extracts of Areca nut are known to kill tapeworms by paralytic effect [20,21]. 1% decoction of the areca nut effectively kills blood flukes by disrupting their nervous system [22]. Arecoline shows synergistic effect with pentachlorophenol sodium and esculentoside against Oncomelania, with mechanisms involving regulation of the smooth muscle contraction of the feet [23].

Effect on Digestive System

Studies on rabbits and mice reveal that water extract of Areca nut can significantly increase gastrointestinal motility at different concentrations and also improve gastrointestinal function of rats with functional dyspepsia [24]. Areca nut is also used in the treatment of diarrhea, constipation, ulcers and also gastrointestinal inflammation, dyspepsia and so on. Sympathetic nerves are shown to be stimulated by arecoline, one of the important components of Areca nut. It also stimulates Choline M receptors and promotes the secretion of human saliva, sweating and gastrointestinal peristalsis which helps digestive function in humans [25].

Wound Healing Properties

Traditional herbal formulas prepared by tribes and people in different countries are used in treating wounds, where they are known to exert antibacterial effects and are proven effective against Staphylococcus aureus. The

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studies showed that areca nut was one of the important constituents of such herbal formulations. Researchers also found that these formulations are effective against hydroxyl-free radicals as antioxidants [26].

Effect on Nervous System

Studies also suggest that Arecoline, an important component of areca nuts has acetylcholine like effect and experimental results tells us that it improved cognitive function in elderly rats after they were fed with 10mg/kg arecoline for six days without a break. This work explains the importance of areca nut in treating Alzheimer's disease as it improved some of the symptoms of the condition in rats. Further studies done in humans suggest that arecoline has an important pharmacological effect on improving the memory in patients suffering from Alzheimer's disease. [27,28].

Hypoglycemic Activity

Arecoline is reported to show hypoglycemic activity in many animal models of Diabetes. When the arecoline is injected subcutaneously in rabbits, they showed significant reduction of blood glucose level that lasted for 4-6 hours [29]. According to medical knowledge, α-glucosidase inhibitors are used for the treatment of diabetes. They work against postprandial hyperglycemia and reduce the blood glucose level. When arecoline was used as an alternative, it inhibited glucosidase activity thereby reducing the elevated levels of sugar in blood [30].

Anti-Hypertensive Activity

Anti-hypertensive activity was shown by fractions of areca nut extract containing tannins when administered in rats. 100 to 200 mg/kg concentration was introduced into hypertensice rats and the studies showed that there was a clear reduction in hypertension via inhibition of angiotensin converting enzymes. It is proposed through some studies that tannins present in areca nut extract possess blood pressure controlling effect [31].

Antidepressant Activity

Ethanolic extract of Areca catechu is known to have antidepressant effects in rats. When they were administered at a dose of 40-80 mg/kg, there was a reduction in the immobility time interval without reduction in the motor activity. This clearly indicates the antidepressant effect of areca nut. Aqueous extract of Areca catechu has an effect on Monoamine oxidase (MAO) in samples obtained from rat brains. Inhibition of MAO is very similar to some of the drugs used as antidepressants in humans [32,33]. This result is very significant as many people across the globe are suffering from depression and similar symptoms and are struggling to cope with it. If further research in this area can completely establish the antidepressant effect of areca nut seed extracts, this can-do wonders for people suffering with depression.

Anti-Inflammatory Activity

Areca catechu extracts prepared using ethanol as a solvent have proven to have anti-inflammatory activity in rats. For instance, a dose of 1 to 10 mg/kg/day for 5 days helped in the suppression of carrageenan-induced inflammatory edema and prostaglandin E2 levels. At higher doses there were dose dependent anti-inflammatory and analgesic effects reported in rats [34]. Both in vivo and in vitro assays carried out in rats and mice showed similar outcomes. There was a significant reduction in the edema that was induced in the animal models. Dose of the extract was an important factor in determining the effectiveness of areca nuts in reducing the inflammation.

Antiparasitic Effects

In traditional medicine, Areca nut is used in killing tapeworms, pinworms, nematodes etc. The investigations suggest that aqueous extracts of areca nuts are effective against tapeworm by causing paralysis. 1% decoction of areca nut can effectively kill blood flukes by affecting their nervous system [35].

CONCLUSION

Areca catechu L is one of the important economical as well as medicinal plants of southeast asian countries. India is one of the major producers and consumers of areca nut products. looking at the history, we understand that areca nut has been a part of our socio-cultural practices for a very long time. Large group of the Indian population are consumers of areca nut and its products. Even in religious practices of Hindus, the concept of "Thambula" refers to the combination of betel leaf and areca nut seed. Over the last 300-400 years, after the introduction of tobacco in India, people have been consuming a mixture of areca nut, tobacco and other products in the form of Pan masala. This has a negative impact on the health of consumers and many cases of Oral cancers are considered to be caused by the duo of areca nut and tobacco. Alternatively, Indian traditional medicine considers areca nut as one of the most important constituents in their formulations that plays a very important role in traditional medicine. Although there is sufficient evidence that indicates its importance as a medicinal compound, there is a lot of research work that suggests otherwise. Arecoline is a very important component of Areca nut extract and its role in medication has been proven beyond doubt through earlier works

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and literature. But Arecoline is also a major toxin that is responsible for Oral submucous fibrosis (OSF) and has cytotoxic effects on normal cells in humans that induces apoptosis [35]. In this review we have considered the general uses and medicinal properties of Areca nut. Both aqueous and organic solvent extracts have shown to have medicinal properties and animal studies have provided evidence for their effectiveness as anti-inflammatory, antiparasitic and so on. The review also suggested that Arecoline if injected in controlled doses can be effective against Alzheimer's disease as it is shown in rat models. We have gone through many original works during this review and it was found that many animal models have been established to study the effects of various doses of areca nut extracts in different conditions, but most of them have not spoken in large about the similar effects in humans. This opens up the possibility of further research in this area to understand how this compound can be effective in treating human ailments. There are excerpts from our Vedic literature that support the use of areca nuts in medicine, but much needs to be done in this regard to facilitate the research and find more evidence about the medicinal properties of areca nuts and its uses in treating a broad range of human diseases.

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