

A Comprehensive Review article On Therapeutic Qualities Of Poogi Phala (*Areca catechu* Linn. fruit) Correlating Its Physico-Chemical Analysis Study.

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ABSTRACT

Poogi Phala(Areca catechu Linn.) Fruit is known by most as addictive substance owing to the deleterious effects caused by it's over use. However, no plant on earth is devoid of medicinal qualities is as correctly said by the Indian sage Chanakya. Making an attempt to prove this fact and therein discover its therapeutic properties this study was conducted beginning with a Physicochemical analysis and a meta analysis on the various studies conducted till date on Areca nut. Sample of Areca catechu was authenticated and subjected to Physicochemical analysis and HPTLC fingerprinting to study its Physicochemical parameters. Later a thorough analysis was done on the studies available on Areca catechu. Based on this meta-analysis it is clear that Areca has a set of attributes on the myriad tissue systems of the human body. The right use of the plant proves it an asset for the health of humankind and its dose and duration dependant toxic effects render it a potential harm to its addicts ranging from being a broncho constrictor to a potent carcinogen.

Keywords: Areca catechu, Areca Nut, Pooga, Poogiphala, Physicochemical Analysis, Properties, HPTLC.

INTRODUCTION

Nature provides bountiful herbs which have a myriad of uses from being a magical spice to a wonder-acting remedy. *Poogi phala* (Sans., *Areca catechu* Linn. fruit) is one such drug which though is well known, is often defamed alone due to the deteriorating effect it creates on different parts of the body starting from the oral cavity. Areca nut (English; Taxonomical- *Areca catechu* Linn.) is a 40-60ft heighted tree. It is found mostly in East Africa, South Asia, and Pacific islands. It is commonly seen in coastal areas of India including the coastal belt of Karnataka, Maharashtra, Tamil Nadu, Assam and West Bengal. Its fruit is a monolocular, one-seeded berry, 3.8-5 cm long, smooth orange or scarlet when ripe, with a fibrous outer layer. Kernels of its green and mature fruits are chewed as an astringent and stimulant, often with the leaves or fruit of betel pepper (*Piper betle*). In South- East Asia every part of the arecanut tree finds its suitable use. From its stem being used as construction material for homes and for utilities like ladders, shelves and baskets, its inflorescence being used for ornamentation and ritual worship to its fruit's tannins being used for dyeing of clothes and tanning of leathers, almost every part of Areca serves a big deal in households.

Having a scientific rationale surpassing the contemporary evidence based science are the folklore practitioners of rural India. These Nature stalwarts use various herbs and minerals in their clinical practice to treat the faithful and obedient ill populace. Areca too is used by them for treating a spectrum of conditions including helminthiasis, gastric disorders, respiratory illness including bronchitis and asthma, obesity. In folklore medical practice across many parts of India Arecanut is used as a treatment for Migraine and is redeemed to be a panacea for the condition.

A Physico-chemical analysis of a sample of Areca catechu followed by high pressure thin layer chromatography for evaluating its chemical constituents. Later its chemical constituents were studied along with the properties of crude extract to explore the therapeutic and harmful effects and draw an inference from it. The study was neutral to either sides of the botanical entity aiming only at bringing out the true facts about it.

AIM & OBJECTIVES

To study in detail about the medicinal properties of Areca catechu fruit through extensive compilation and analysis

MATERIALS AND METHODS

- Physicochemical analysis and HPTLC fingerprinting for evaluation of chemical constituents
- Various textbooks, journals and research studies were referred to and scrutinized to form a meta-analysis on the topic of Medicinal properties of Areca catechu.

TAXONOMICAL DERIVATION

Kingdom : Plantae

Order : Arecales

Family : Arecaceae

Genus : Areca

Species : *Areca catechu* Linnaeus

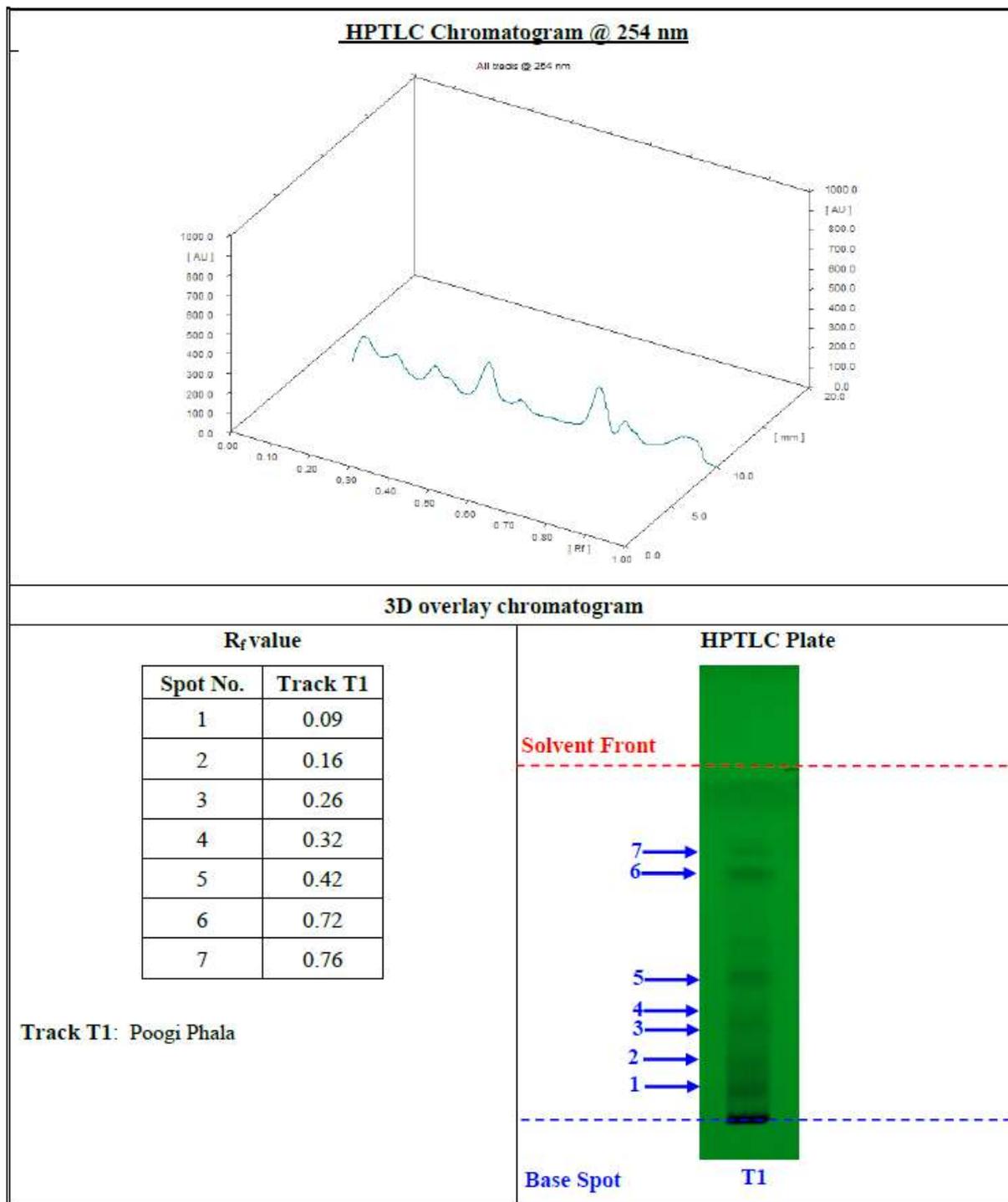
PHYSICOCHEMICAL ANALYSIS

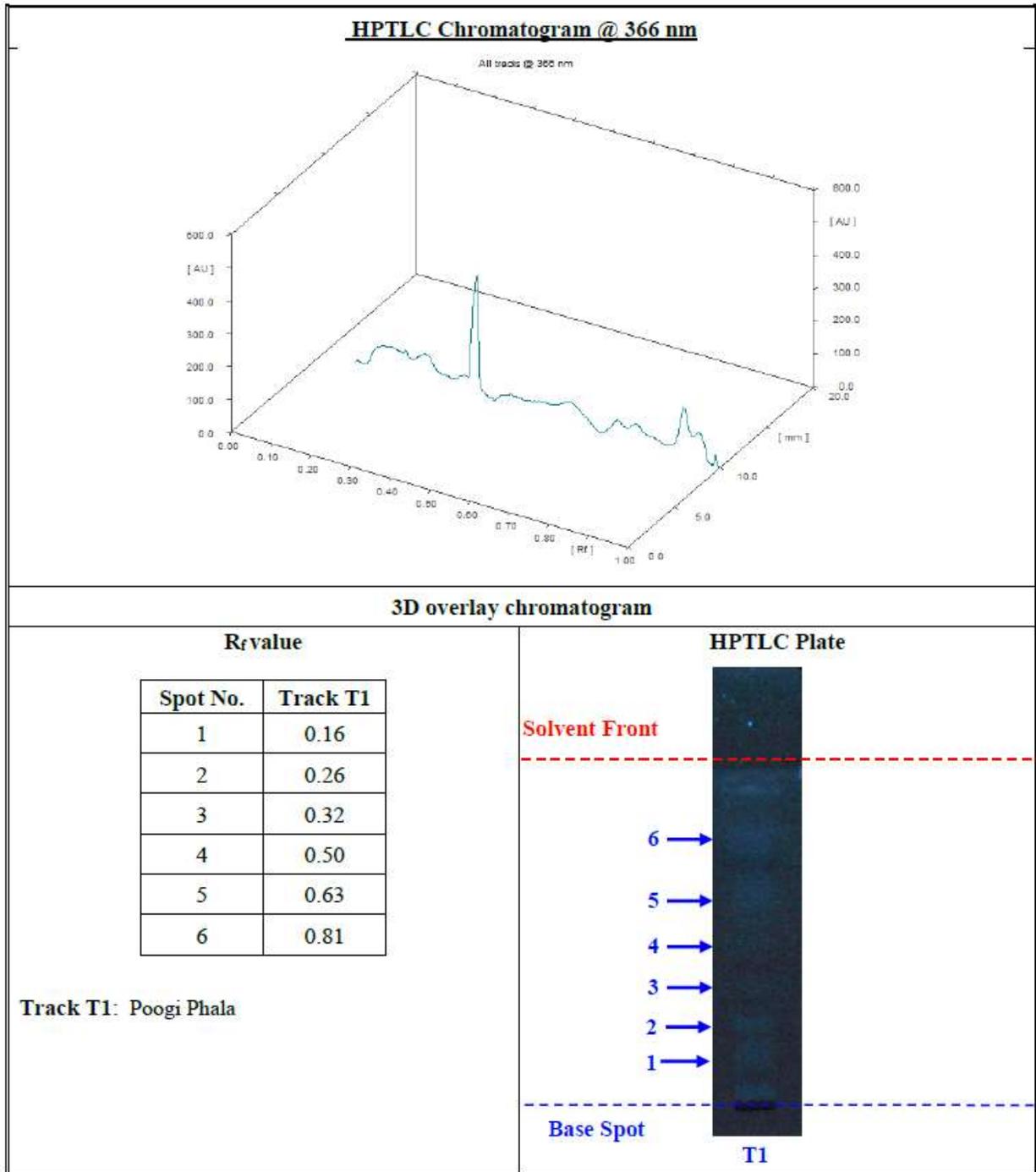
Sample of Areca catechu was collected from its most renowned habitat in India, the coastal belt of Mangalore, Karnataka. Following drug authentication the sample was subjected to Physicochemical analysis which yielded following report:

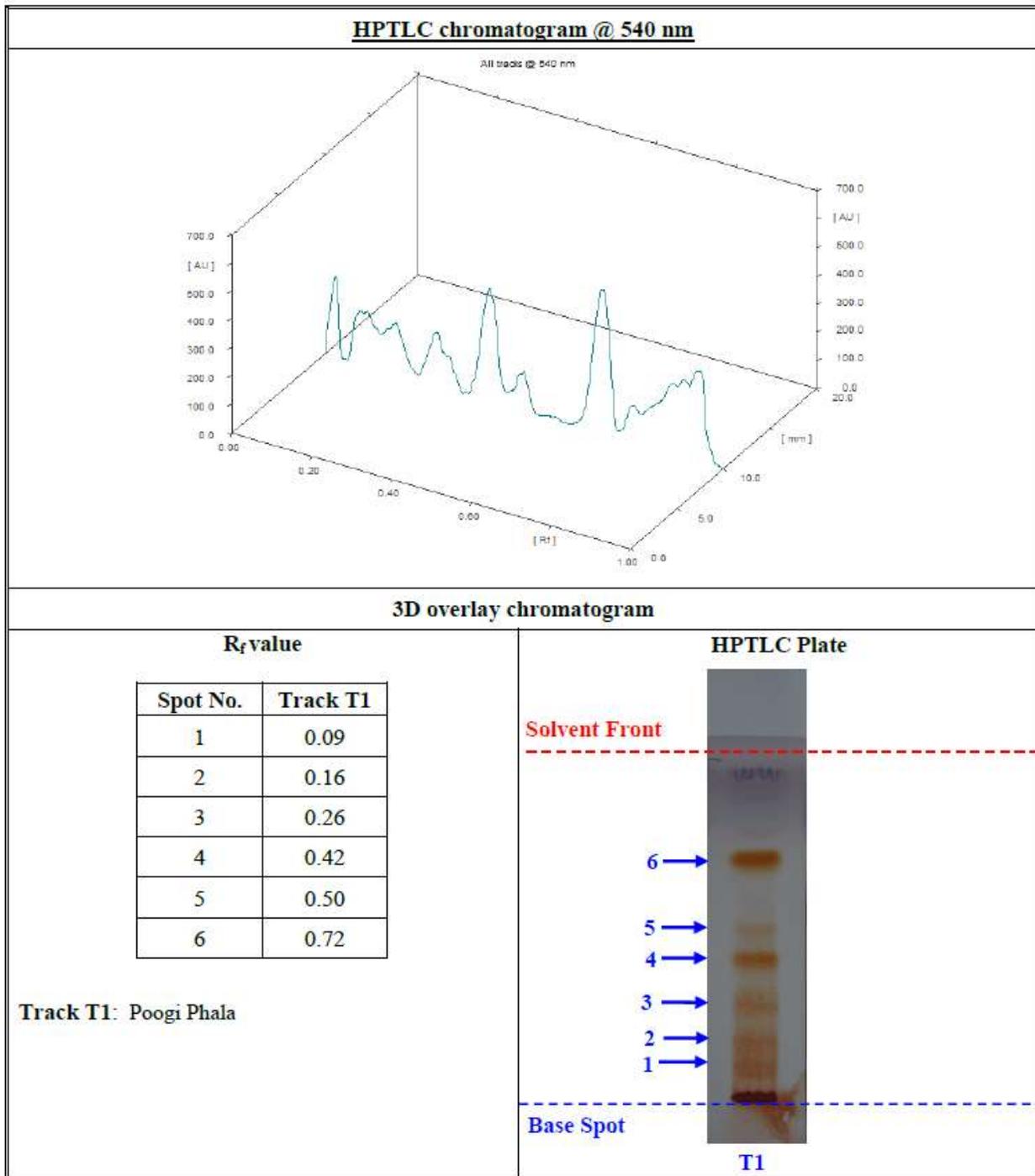
SL.NO.	PARAMETERS	VALUE
1.	DESCRIPTION	POWDER
1.a)	COLOUR	PALE BROWN
1.b)	ODOUR	PLEASANT
1.c)	TASTE	ASTRINGENT
1.d)	CONSISTIBILITY	COURSE POWDER
2.	Foreign Matter	Nil
3.	Limit Test for heavy metals	Non reactive
4.	Loss on drying at 110 ⁰ C (% w/w)	0.43%
5.	Total Ash Value	1.86%
6.	Acid insoluble ash	0.43%
7.	Alcohol soluble extractive	28%
8.	Water soluble extractive	16%

Table 1. Physico-Chemical Analysis Report of *Areca catechu* sample

Preparation of Test solutions: Weigh 2 g of sample in a conical flask and add 20 mL of methanol to it. Reflux for 15 hours on water bath. On completion of time filter with the help of Whatman filter paper No.1. Use the Test solution thus obtained for HPTLC fingerprinting.	
Preparation of Spray reagent [Anisaldehyde – sulphuric acid reagent]: 0.5 mL Anisaldehyde is mixed with 10 mL Glacial acetic acid, followed by 85 mL Methanol and 5 mL Sulphuric acid (98 %).	
Chromatographic Conditions:	
Application Mode	CAMAG Linomat 5 - Applicator
Filtering System	Whatman filter paper No. 1
Stationary Phase	MERCK - TLC / HPTLC Silica gel 60 F ₂₅₄ on Aluminum sheets
Application (Y axis) Start Position	10 mm
Development End Position	80 mm from plate base
Sample Application Volume	10.0 µL
Development Mode	CAMAG TLC Twin Trough Chamber
Chamber Saturation Time	30 minutes
Mobile Phase (MP)	Toluene : Ethyl Acetate : Methanol : Formic Acid (2.7 : 6.0 : 1.0 : 0.3)
Visualization	@ 254 nm, @ 366 nm and @ 540 nm (after derivatization)
Spray reagent	Anisaldehyde Sulphuric acid reagent
Derivatization mode	CAMAG – Dip tank for about 1 minute
Drying Mode, Temp. & Time	TLC Plate Heater Preheated at 100± 5 ⁰ C for 3 minutes
Table 2. HPTLC Fingerprinting Report (Methodology)	







A HPTLC based analysis by Dipti Dutta et al. proved varied arecoline content in different forms of Areca. It says that raw arecanut has 1.15% arecoline, while the pan masala arecanut has

around 0.94%, boiled arecanut has 0.79% and roasted arecanut has 0.75% of arecoline. Also it has been proved that the chemical composition of areca fruit changes with maturation.

CHEMICAL CONSTITUENTS

Areca has been studied now and again for exploring its active chemical components. A spectrum of results have shown up in different research studies, a compendium of which finds following constituents in Areca nut-

Polyphenols: These form the major chunk of its chemical matrix. They include mostly flavonols namely Catechin, Epicatechin, Tannin, Leucocyanidin and Gallic acid. Apart from these are some flavonoids in different degrees of polymerization.

Alkaloids: These form the second most important part of Areca's biochemical composition. Mainly 4 alkaloids are identified which include- Arecoline, Guavacoline, Arecaidine and Guavacine.

Fatty acids/ fats: They make up for 15-17.5% of dry weight of Areca fruit. The fatty acids present are lauric acid, myristic acid, palmitic acid, stearic acid, decanoic acid, oleic acid, dodecenoic acid, tetradecenoic acid and hexadecenoic acid.

Phytosterol: β -sitosterol is a natural plant sterol present in Areca. It is structurally similar to cholesterol and functionally a precursor to the anabolic steroid boldenone.

Minerals: Areca contains some minerals namely phosphorus, iron, calcium, Vitamin B₆ and Vitamin C.

RESEARCH PROVEN MEDICINAL PROPERTIES

<u>MEDICINAL ACTIVITY</u>	<u>RESEARCHER</u>	<u>RESPONSIBLE CONSTITUENT/S</u>
Anti-oxidant activity	Ohsugi et al.(1999), Lee et al. (2003) Thawatchai et al. (2009)	Methanolic extract of areca nut husk
Anti-helminthic activity	Alen et al. (2000), Orazaga MSI (2017)	Arecoline
Anti-inflammatory activity	Jeena Sharafudheen et al. (2018)	Arecoline, polyphenols
Hypolipidaemic activity	Byun S J et al. (2001)	Areca extract
Hypoglycaemic activity	B Chempakam et al (1993)	Arecoline
Anti-venom	Okuda et al.(1991), Mahanta and Mukharjee (2001). Pithayanukul et al. (2005)	Tannins (Catechin, epicatechin)

Vascular relaxant (vasoconstriction)	FC Kuo et al (2005)	Arecoline
Anti-microbial activity	Jeena Sharafudheen et al. (2018)	Arecoline, polyphenols
Anti-bacterial – against Helicobacter pylori	Wang and Huang (2005)	Ethanol extract of areca fruit
Anti-depressant	Ruckmani A et al. (2014)	Arecoline & Arecaidine (anxiolytic), dichloromethane (antidepressant)
Anti-nociceptive	Jeena Sharafudheen et al. (2018)	Arecoline, polyphenols
Platelet Aggregation inhibitory activity	Ghayur M N et al (2011)	Arecanut crude extract especially Catechin
Acetylcholinesterase inhibitory effect	Ghayur M N et al (2011)	Tannic acid, gallic acid, diosgenin and isoguvacine
Table 3. Pharmacological Activities of Areca based on Research		

Above are the pharmacological effects of Areca catechu proved through pharmaceutical research. In the ancient Ayurvedic text Bhava Prakasha Nighantu of Bhavamishra arecanut has been affiliated with therapeutic benefits in conditions of leucoderma, necrotizing skin diseases, anaemia, obesity and in helminthiasis. Current day research studies prove most of these words as true. From the results of the research studies we can know how Areca, as a whole, in a formulation or in extract form, could be a valuable medicine to treat various conditions including hepatic carcinoma, Alzheimer's disease, epilepsy, Obesity, indigestion, asthma, bronchitis, helminthiasis, migraine and even as an antidote to snake venom.

UNTOWARD/ TOXIC EFFECTS OF ARECA

The first and foremost toxic effect of areca is that for which it is most defamed, especially in the Indian subcontinent, is its carcinogenic effect on mouth. Based on studies it is known that arecanut has quite a many toxic effects based on its dose and duration of dosage. To begin with arecanut induces DNA damage and proves carcinogenic in oral cavity, pharynx, larynx, lungs, liver and uterus. Methylnitrosaminopropionitrile that presents on chewing of arecanut in the mouth is said to be the carcinogen responsible for oral cancer. Arecoline present in Areca has parasympathomimetic action on both muscarinic and nicotinic receptors owing to which consumption of areca can instantly bring about euphoria, alertness, increased body warmth (not pyrexia), increased salivation and also cause palpitation. It however has no effect on memory as is often mistaken. The alkaloids present in arecanut inhibit the uptake of GABA which cause the

euphoria as also trigger convulsions. An EEG based study proved that oral consumption of arecanut increased α and β activity while decreasing θ activity.

Long term usage of areca also predisposes one to coronary artery disease, arrhythmia and may even cause death due to myocardial infarction owing to the athero genesis it sets in by inhibiting the uptake of low density lipids by the liver. Researchers have also proven that arecoline inhibits insulin based glucose uptake and thereby increases the prevalence of Type II Diabetes and Hyperlipidaemia amongst areca nut chewers. Animal studies on Areca show that its nature of causing DNA damage in lower doses and apoptosis in higher doses brings about tissue injury, necrosis, liver cirrhosis and even carcinoma, rendering it hepatotoxic. Phospholipase C activation and mobilization of Calcium and Thromboxane-2 associated with platelet aggregation along with increased production of PGE-2 and 6-keto-PGF 1β from gingival keratinocytes, IL-1 and decreased intracellular glutathione, which promotes inflammation is seen in Arecanut chewers, which induces fibrogenesis in oral mucosa, making arecanut chewing the most important cause of oral submucous fibrosis. Arecoline has been also proven to reduce sperm motility and count and damage the local anti-oxidant system eventually causing male infertility. Habitual betel quid chewing in expectant mothers exposes the foetus to heavy metals and harmful carcinogens also affecting the birth weight and length of foetus and may also cause preterm births. Apart from the toxic effects of long term use areca nut has also acute toxic effects in the form of broncho constriction and reduced Forced Expiratory Volume (FEV) causing dyspnoea and tachypnoea, stress response in HPA axis and palpitation, tachycardia and hypotension owing to its effect on parasympathetic nervous system which may also lead to myocardial infarction in large doses.

DISCUSSION

In the ancient science of Ayurveda every substance of the body and nature is attributed to a building element called *Mahabhuta*. There are 5 great elements with individual attributes namely ether, air, fire, water and earth. A study by Kamla Moond et al. proves through pharmacognosy and pharmaceutical chemistry that Pooga phala (*Areca catechu* Linn) is a plant predominated by the earth element (Prithvi Mahabhuta). This can be understood on simplified grounds as the nature of a plant is highly influenced and predominated by the element predominant in its soil of growth. Areca is found to grow best in low altitudes and in low-shade areas. Such a habitat is said to be predominant of earth element and hence the earth dominated nature of areca can be logically derived. The pharmacological activities of areca are quite intriguing and hence any conclusion drawn should be well verified. For instance it is well known that arecoline is a cause of liver carcinoma however there are studies proving benefits of arecoline in hepatic cell carcinoma too. Chewing areca nut causes an instant increase in testosterone and was hence used in Indian tradition as an instant aphrodisiac, however studies prove that its long term usage ends in male infertility. Most studies prove the inflammatory process set inside the oral cavity, especially gingiva by areca, however there are studies showing that areca has an antimicrobial effect on the unwanted oral flora and hence could be a good dental formulation that helps to fight

plaque. Areca intake is studied to cause instant bronchoconstriction and reduced Forced Expiratory Volume but it is ironically used by folk clinicians to treat asthma successfully. While most studies talk about the negative/ toxic impacts of arecoline and catechin in areca, diligent Physicochemical analysis and clinical studies bring out a different picture as shown in the table below:

Chemical	Arecoline	Catechin
Molar mass	155.19 g/mol	290.26 g/mol
Formula	C ₈ H ₁₃ NO ₂	C ₁₅ H ₁₄ O ₆
Proved activity	anti- microbial, anti-depressant, improves cognitive action (In Alzheimer's), anti-thrombotic, inhibits atherogenesis, promotes digestion (through M receptor)	Anti-oxidant, anti-inflammatory, neuro-protective
Dose (Therapeutic)	5-20mg/day (short duration; not more than 45 days)	84- 386 mg/day
Toxic effects	Cytotoxic (on oral mucosal fibroblast-above 50 µg/ml, long duration), genotoxic(on peripheral blood lymphocyte- above 50 µg/ml, long duration)* *Cytotoxic and genotoxic effect is time-dependant and dose-dependant(Yi Juai Chen et al, 2002)	Hepatotoxic (above 750mg/kg)
Table 4. Physico-chemical attributes of Arecoline and Catechin of <i>Areca catechu</i>		

CONCLUSION

Areca is a drug that calls for stringent policies by the government for social welfare owing to its addiction and abuse, especially in India. India stands the biggest importer of areca in world trade while being the largest producer of the fruit in itself, marking the extent of abuse in the country. This abuse is what brings in the negative picture of deadly diseases like OSF, Oral and pulmonary carcinoma and even death. However if one steps in to use this drug judiciously, it is nothing less than a boon. This is rightly portrayed in the Charaka Samhita (ancient textbook of Ayurveda), efficacy of a substance stands in its use because a well planned use of poison too makes it a highly potent medicine and on the other hand a famous medicine if wrongly used can prove poisonous too. Similarly from this article we can know that when areca is judiciously used it bestows its own set of health benefits. It is used as a panacea for migraine which is proved by animal study too by Bhandare et al claiming NOS inhibition to be the reason for its anti-migraine action. Peng et al. concluded their study saying that areca could be a future anti-parasitic with arecoline being proved to inhibit gamma amino benzoic acid thereby paralyzing parasites. Ironically, Indians despite of engaging in unscrupulous consumption of areca have a globally lesser incidence of dental caries owing to the antibacterial action of areca. Also areca has been

proved to have significant anti-viral action against even Human Immunodeficiency Virus (HIV). Catechin present in Areca is proved to serve as chemo-preventive in tumour formation in animals. All in all, areca is a gift of nature that has been wrongly exploited by the human race rendering it an enemy for the health of mankind in many a population. However, the truth is that the substance in itself is not a harm, its man's deeds that has turned it against him. To conclude, its only upto human whether he decides to righteously use this boon called Areca and let it serve as a valuable medicine or whimsically chews on it until he reaches the door to disease/s which could in time prove fatal.

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