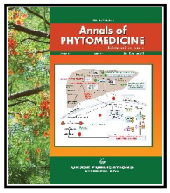
Annals of Phytomedicine 12(2): 180-185, 2023

DOI: http://dx.doi.org/10.54085/ap.2023.12.2.20

Annals of Phytomedicine: An International Journal
http://www.ukaazpublications.com/publications/index.php

Print ISSN : 2278-9839 Online ISSN : 2393-9885



Review Article : Open Access

A phytopharmacological review of the classical Ayurveda drug *Puga* (*Areca catechu* L.)

Ramakrishna Allam◆, Govardhan Sahani, Antony Stephen Raj and Faiz Mohammed
Sri Sairam Ayurveda Medical College and Research Centre, Chennai-600044, Tamilnadu, India

Article Info

Article history
Received 1 August 2023
Revised 16 September 2023
Accepted 17 September 2023
Published Online 30 December 2023

Keywords
Areca catechu L.
Ethnomedicine
Pharmacological
Phytochemical
Puga

Abstract

The Vedas are the epitome of knowledge and culture of a very high order and Ayurveda being a special branch of the Veda represents in full the achievement of ancient ages in the field of medicine and allied subjects. For thousands of years, plants have a vital role in maintaining human health and enhancing the quality of human life and have served humans as valuable components of medicines, beverages, cosmetics, and drugs. *Puga* (*Areca catechu* L.) is one of the drugs listed in Ayurvedic treatises and Nighantus (Ayurveda lexicons). Further, the herb is enumerated in other *Chikitsa grantha* (Medical books) for various pharmacodynamics attributes and diseases. This reflects that *Puga* (*A. catechu*) is a potential and beneficial herb in the management of various disorders in the form of *Aahara* (diet) and Aushdha (medicine). The Ayurvedic Pharmacopeia of India accepted *A. catechu* as a botanical source of *Puga*. According to ethnobotanical studies, the plant *Puga* (*A. catechu*) which is a member of the Arecaceae family, is used to treat a variety of conditions, including dyspepsia, abdominal distension, diarrhoea, and pain in the stomach. Pre-clinically, the plant is analyzed for antiparasitic, antihypertensive effects, antifungal effects, anti-inflammatory and analgesic effects, antiallergic effects, promotion of digestive functions, suppression of platelet aggregation, *etc*. An up-to-date assessment of this plant's phytochemistry and pharmacological advancements as well as its traditional uses are presented in the present study.

1. Introduction

The Vedas are the epitome of knowledge and culture of a very high order and Ayurveda being a special branch of the Veda represents in full the achievement of ancient ages in the field of medicine and allied subjects (Nagaiah, 2022). For thousands of years, plants have had a vital role in maintaining human health and enhancing the quality of human life and have served humans as valuable components of medicines, beverages, cosmetics, and drugs (Maroti *et al.,* 2022; Mehrotra, 2021). *Puga* (*Areca catechu* L.) is one of the drugs listed in Ayurvedic treatises and *Nighantus* (Ayurveda lexicons) is also referred to by the name *Kramuka* (*A. catechu*) in ancient Ayurvedic literature. Further, the herb is enumerated in other *Chikitsa grantha* (Medicinal books) for various ailments. *Nighantus* (Ayurveda lexicons) contributed to different synonyms, pharmacodynamics attributes, and properties of *Puga* (*A. catechu*). This reflects that *Puga* (*A. catechu*) is a potential and beneficial herb in the management of various disorders in the form of *Aahara* (diet) and *Aushdha* (medicine). The Ayurvedic Pharmacopeia of India accepted *A. catechu* as a botanical source of *Puga* (Anonymous, 1989).

According to reports, *A. catechu* spread widely over Southern and Southeast Asia, including China, India, Indonesia, Malaysia, the Philippines, and New Guinea, *etc*. It is commonly found along India's coastline, from Tamil Nadu and Kerala to Maharashtra. Additionally, it grows in the Andaman and Nicobar Islands, West Bengal, Assam, and the Deccan Plateau. Popular chewable items produced from *A. catechu* seeds are used in traditional herbal medicine. In tropical and subtropical nations like China, Chinese Taipei, South Asia, East Africa, *etc*., it is estimated that more than 400 million individuals chew betel quid (mainly containing areca nut, betel leaf, and lime) every day.

According to ethnobotanical studies, the plant *A. catechu* which is a member of the Arecaceae family is used to treat a variety of conditions like dyspepsia, abdominal distension, diarrhea, stomach pain, edema, jaundice, and parasitic diseases (Wei-Peng *et al*., 2015). Preclinically, the plant is analyzed for antiparasitic effects, antidepressive effects, antioxidant effects, antifatigue effects, antibacterial, antihypertensive effects, antifungal effects, anti-inflammatory and analgesic effects, antiallergic effects, promotion of digestive functions, suppression of platelet aggregation, regulatory effects on blood glucose and lipids, *etc*., but a comprehensive review on *A. catechu* is not available. Therefore, a thorough review of *A. catechu* is conducted. An up-to-date assessment of this plant's phytochemistry and pharmacological advancements as well as its traditional use are presented in the present study.

2. Phytochemistry of *A. catechu*

According to Shivasankar and Govindarajan (1963), *A. catechu* is a great source of polyphenols (20%), fat (15%), starch (20%) and

Corresponding author: Dr. A. Ramakrishna
Assistant Professor, Department of Dravyaguna Vijnana, Sri Sairam Ayurveda Medical College and Research Centre, Chennai-600044, Tamilnadu, India
E-mail: drarkrishna7812@gmail.com
Tel.: +91-9500176894

alkaloids (0.5%). According to Mathew and Govindarajan (1963), polyphenol, mostly contains flavonols, about 10% of the polyphenol is (+) catechin, 2.5% is (+) epicatechin, and 12% is (+) leucocyanidin. From the seeds of *A. catechu,* a series of dimeric, trimeric, and tetrameric procyanidins were isolated (Nonaka *et al*., 1981). Arecoline (7.5 mg/g weight), arecaidine (1.5 mg/g weight), guvacoline (2.0 mg/g weight), and guvacine (2.9 mg/g weight) are the four main alkaloids isolated from areca nut (Nai-Shin Chu, 2001). Chemically, all these alkaloids are related; arecoline is a colorless volatile substance that resembles nicotine. According to Pathak and Mathur (1954), fats contribute 15-17.7% of the total dry weight of areca nut. Areca nut fatty acid profile includes 5.4% dodecenoic acid, 0.3% tetradecenoic acid, 0.6% hexadecenoic acid, 12.7% palmitic acid, 1.6% stearic acid, 0.3% decanoic acid, 6.2% oleic acid, and 19.5% lauric acid. Calcium (0.05%), phosphorus (0.13%), and iron (1.5 mg/100 g) constitute the mineral matter of areca nut. Vitamin B6 (286.9 mg/100 g) and vitamin C (416.2 mg/100 g) are also present (Raghavan and Baruch, 1958; Gurumurthy *et al*., 2018).

Table 1: Phytochemical composition of *A. catechu*

S. No.	Phytochemical	Constituents	References
1.	Polyphenols	(+) catechin (10%), (+) epicatechin (2.5%) and (+) leucocyanidin (12%)	Mathew and Govindarajan, 1963
2.	Flavonoids	Isorhamnetin, quercetin, chrysoeriol, luteolin, 42, 52 -dihydroxy-32, 52,72 -trimethoxyflavone, 5,7,42-trihydroxy-32, 52-dimethoxyflavanone, liquiritigenin, and jacareubin	Yang *et al*., 2012; Zhang *et al*., 2009
3.	Fat	Fats contribute 15-17.7% of the total dry weight of areca nut. Areca nut fatty acid profile includes dodecenoic acid (5.4%), 0.3% tetradecenoic acid (0.3%), 0.6% hexadecenoic acid (0.6%), palmitic acid (12.7%), 1.6% stearic acid (1.6%0), decanoic acid (0.3%) 6.2% oleic acid (6.2%) and lauric acid (19.5%)	Pathak and Mathur, 1954
4.	Alkaloids	Arecoline (7.5 mg/g weight), arecaidine (1.5 mg/g weight), guvacoline (2.0 mg/g weight), and guvacine (2.9 mg/g weight)	Nai-Shin Chu, 2001
5.	Tannins	Proanthocyanidins like procyanidin B1, procyanidin A1, procyanidin B2, areca tannin B1, areca tannin A1, areca tannin A2, areca tannin C1, areca tannin B2, and areca tannin A3	Ma *et al*., 2014; Nonaka *et al*., 1981;
6.	Mineral	Calcium (0.05%), phosphorus (0.13%), and iron (1.5 mg/100 g)	Raghavan and Baruah, 1958; Gurumurthy *et al*., 2018
7.	Vitamins	Vitamin B6 (286.9 mg/100 g) and vitamin C (416.2 mg/100 g)	Raghavan and Baruah, 1958.

3. Pharmacological activities

3.1 Antioxidant activity

There was considerable antioxidant, free radical scavenging, and anti-hyaluronidase activity in the areca nut ethanolic extract. Similar to tocopherol and stronger than ascorbic acid, but antioxidative activity was less potent than butylated hydroxytoluene (Kim *et al*., 1997). Through, the application of the electron spin resonance (ESR) technology, areca nut extract exhibited scavenging activity against superoxide anion radical ($*O_2$) and 1, 1-diphenyl-2-picryl (DPPH) free radicals (Ohsugi *et al*., 1999; Koleva *et al*., 2002).

3.2 Anti-inflammatory/anti-melanogenesis effects

When it was applied topically, areca nut extract inhibited the activity of the enzyme hyaluronidase *in vivo* on delayed hypersensitivity and croton-oil-induced ear edema in mice. These findings strongly imply that areca nut extract can reduce the inflammatory and immune-regulatory effects on skin disorders. The areca nut extract showed an ability to reduce mushroom tyrosinase activity and melanin formation in B16 melanoma cells leading to skin-lightening actions. According to this study, areca nut extract is an excellent anti-inflammatory and anti-melanogenesis agent and can be used as a potential new cosmetic ingredient (Kook *et al*., 1999). The ethanolic extract of areca nut delays inflammatory (nitroglycerin-induced) responses in rats (Bhandare *et al*., 2011).

3.3 Skin ageing and cosmetics

Both *in vivo* and *in vitro* studies were done to examine the anti-ageing properties of *A. catechu* on the skin. Proline (13%), a free amino acid, is present in high concentrations in areca nut extract. On pig pancreatic elastase (PPE) and human leukocyte elastase (HLE), respectively, the areca nut extract showed 37-90% inhibition of elastase. With areca nut extract, the number of elastin fibers increased. In an *in vitro* test, the extract from areca nuts demonstrated the protection of elastic fiber from elastase enzyme breakdown. Compared to the control and standard ascorbic acid, the areca nut extract improved the proliferation of human fibroblast cells. The use of areca nut extract showed improvements in skin hydration, elasticity, and collagen synthesis, suggesting that areca nut extract may be useful as a new antiageing component for cosmetics (Lee and Choi, 1999). The elastase and hyaluronidase enzymes found in skin tissues were found to be inhibited by areca nut extract, which was isolated by solvent fractionation and found to be a phenolic compound that demonstrated competitive inhibition with the substrate. According to these findings, phenolic compounds isolated from *A. catechu* have an antiageing impact by safeguarding connective tissue (Kook *et al*., 2001).

3.4 Hypoglycemic activity

It has been discovered that arecoline when administered subcutaneously, exhibits hypoglycemic action in an animal model of

diabetes. An alkaloid fraction of *A. catechu* given subcutaneously to alloxanized rabbits exhibited a good hypoglycemic effect lasting for 4/6 h (Chempakam, 1993).

3.5 Hypolipidemic activity

In high-cholesterol-fed rats, areca extract was found to have a potent inhibitory effect on cholesterol absorption. In another study, rats were given a diet that included corn oil and areca nut extract as supplements. The supplementation of areca nut extract significantly reduced plasma lipid levels and triglyceride absorption (Byun *et al*., 2001). Areca nut extracts were discovered to have potent *in vitro* inhibitory effects against pancreatic cholesterol esterase (pCEase) and to reduce dietary cholesterol ester absorption (Jeon *et al*., 2000). Additionally, when provided a diet containing free cholesterol with the supplement of areca nut extract, both intestinal free cholesterol absorption and small intestine pCEase activity were markedly reduced (Park *et al*., 2002).

3.6 Alpha-glucosidase inhibitory and hypoglycemic activities

Hypoglycemic effect and α-glucosidase *in vitro* inhibitory activity by oral administration of areca nut ethanol extracts have been investigated in rats. The intestinal-glucosidase enzymes maltase and sucrose were shown to have *in vitro* inhibitory activity by areca nut extract, and their respective IC_{50} values were reported to be 12 g/ml and 30 g/ml. The postprandial elevation in levels of blood glucose at 30 and 60 min after oral administration of maltose with ethanol areca nut extracts (250 mg/kg and 500 mg/kg doses) showed a significant reduction compared to control group rats in blood glucose level. These findings suggested that the areca nut extract had strong α-glucosidase inhibitory effects and would be useful in reducing blood glucose levels in rats (Amudhan and Hazeena, 2008).

3.7 Antihypertensive effect

According to reports, areca nut fraction has a strong *in vitro* inhibitory effect on the angiotensin-converting enzyme (ACE). Oral administration of areca nut fraction spontaneously hypertensive rats (SHR) exhibited a long-lasting, dose-related antihypertensive effect and these results achieved with dosages of 100 and 200 mg/kg were comparable to 30 and 100 mg/kg doses of captopril. When areca nut fraction was administered intravenously to SHR at doses of 10 and 15 mg/kg, blood pressure dropped quickly and noticeably. At a 15 mg/kg intravenous dose, the highest antihypertensive impact of areca nut fraction was approximately 5 times greater than that of captopril at the same dose (Inokuchi *et al*., 1986). A constituent (Areca II-5-C) isolated from seeds of areca nut displayed the most effective *in vitro* ACE inhibitory action (Chung *et al*., 2007).

3.8 Vascular-relaxation effect

The human umbilical artery and vein rings were found to relax in a concentration-dependent manner in response to arecoline; the higher the concentration of arecoline, the greater the relaxation of the rings. This relaxation was reduced after the endothelium was removed or after pretreatment with L-NAME, a nitric oxide synthase inhibitor. Human umbilical arteries and veins cGMP levels were raised by arecoline in a dose-dependent manner. As a result, arecoline's relaxing actions on the umbilical artery and vein rings were dependent on the endothelium *via* the NO-cGMP systems (Kuo *et al*., 2005).

3.9 Antidepressant activity

Rodents were subjected to forced swimming and tail suspension experiments to measure antidepressant activity. The immobility period was significantly decreased by the ethanol extract (4-80 mg/kg), without affecting spontaneous motor activity. According to this finding, the ethanol extract has antidepressant properties (Dar and Khatoon, 2000). In morphine-dependent mice, the areca nut dichloromethane fraction from the nut exerts a suppressive effect on withdrawal symptoms. Compared to saline controls, a single intraperitoneal injection of dichloro-methane fraction considerably delayed the onset of withdrawal jumping behavior. During the withdrawal period, the dichloromethane fractions also drastically reduced jumping numbers and fecal and urine excretions (Kumarnsit *et al*., 2005).

3.10 Antimicrobial effect

Procyanidins and fatty acids (myristic and oleic acids) from the seed of *A. catechu* were found to have significant antibacterial properties against *Streptococcus mutans*, a primary cariogenic bacterium, and to have significant inhibitory activity against the glucosyltransferase from *S. mutans* (Sumitra *et al*., 2006). Areca nut extracts inhibited the growth of salivary organisms, such as *Streptococcus mutans*, *Streptococcus salivarius*, *Fusobacterium nucleatum*, and *Staphylococcus aureus* in a concentration-dependent manner, which were cultured from the saliva after chewing boiled areca nuts. Baked and boiled nuts were reported to be more potent than raw nuts. Based on some reports, hydrolysable tannins in the tannin fraction, which include tannic acid, may be the cause of the areca nut's antibacterial effects and extended intraoral contact with the nut may inhibit oral bacterial growth (De Miranda *et al*., 1996).

3.11 Wound healing profile

The combination of the arecoline alkaloid, and polyphenol of areca nut, increased the breaking strength in the incision wound model. On the 4th and 16th day, as well as during the period of epithelization, all extracts increased the wound's contraction. Only the areca alkaloid portion improved the tensile strength of granulation tissue in the dead space model. This study demonstrated that the polyphenols and alkaloids of areca can be utilized to speed up recovery from skin transplant surgery, leg ulcers, and burn wounds (Azeez *et al*., 2007; Verma *et al*., 2012)

3.12 Protective effect on ethanol-induced gastric mucosal lesions

The defatted ethanol extract of *A. catechu* was tested for its antiulcerogenic properties. Gastric mucosal malondialdehyde (MDA, a measure of lipid peroxidation), nitric oxide (NO) levels and activities of myeloperoxidase (MPx) and xanthine oxidase (XO) enzymes increased considerably after ethanol treatment. *A. catechu* pretreatment at doses of 250 mg/kg and 500 mg/kg, inhibited the production of stomach mucosal MDA, Nitric oxide contents, and MPx and XO activity. The levels of deoxyribonucleic acid (DNA), sialic acid, and glutathione (GSH) in the stomach mucosa were all significantly lowered by ethanol induction. The pretreatment with *A. catechu* kept the values of the parameters mentioned above within the level of normal control. These results imply that the protective benefits of both the 250 mg/kg and 500 mg/kg dosages of the plant extract against ethanol-induced gastric mucosa may be attributed to the antioxidant activity of areca nut (Amudhan and Hazeena, 2008).

3.13 Anticonvulsant activity

Arecaidine and guvacine, constituents of the *A. catechu* seeds, inhibited the uptake of GABA and α-alanine, but not that of glycine, by slices of the cat's spinal cord. Large doses of arecadine (1g/kg subcutaneous) slightly reduced the lethal effects of bicuculline in mice but did not show any anticonvulsant activity (Lodge *et al*., 1977).

3.14 Platelet aggregation inhibitory activity

The platelet aggregation brought on by arachidonic acid, adenosine phosphate, platelet-activating factor, adrenaline, and Ca^{+} ionophore was prevented by areca nut crude extract. ADP and Ca^{+} ionophore-induced aggregation was more effectively inhibited by areca nut crude extract. Significant acetylcholine esterase inhibition was seen in the crude areca nut extract (Ghayur *et al*., 2011).

3.15 Prevention of dental cavities

In the past, toothpaste with betel nut was used to prevent cavities. According to laboratory research, betel nuts may contain antibacterial properties that prevent the growth of cavities (Suresh Babu *et al*., 2005). Because of its astringent qualities, areca nut is used to make dentifrices which make the breath sweeter and strengthen the gums. Excellent dentifrices are made from the seed that has been turned into charcoal and ground (Kurian, 1995; Rashid *et al.,* 2015).

3.16 Central nervous system stimulant

Betel nuts may have euphoric and stimulating effects. As a result, it is occasionally employed for relaxation. An extremely aggressive skin response decreased when using arecoline as a transdermal delivery system to provide the cholinergic for treating neurological disorders in humans (Chopra *et al*., 1996).

3.17 Proteasome inhibitors

The proteasome hydrolyzes various cell cycle regulators, antigenic proteins, and transcription factors; it is a promising target for the development of drugs for different pathologies such as inflammation, cancer, immune diseases, and others (Kavita and Sanjay, 2002). The multi-catalytic protease complex (26S proteasome) plays a main role in intracellular protein degradation. Arecoline moiety has been considered as an important substrate for catalytic threonine which is present in the peptide portion derived from the protease (Orlowski, 1999). Proteasomes the catalytic site tripeptidic sequence of both N and C-terminal derivatives were found to bind with arecoline derivatives (Marastoni *et al*., 2004).

3.18 Molluscicidal activity

Arecoline, the active ingredient in areca nut greatly suppressed the activity of the enzymes acetyl-cholinesterase (AChE) and alkaline phosphatase (ACP/ALP), in both *in vivo* and *in vitro* experiments (Feng *et al*., 1999).

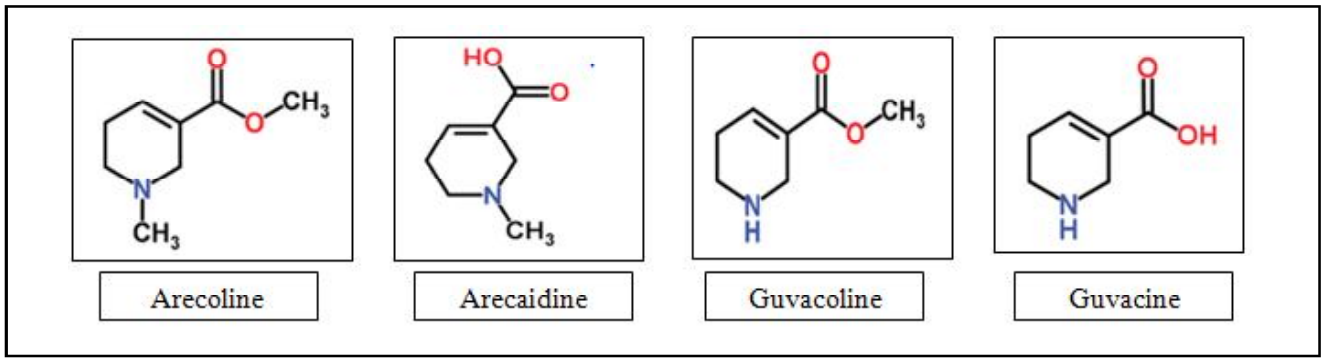


Figure 1: Chemical structures of the four most important alkaloids of *A. catechu*.

4. Conclusion

The pharmacological properties of plants have been recognized for a long time. Herbal remedies have been used for centuries by indigenous cultures around the world to treat a variety of ailments. *Puga* (*A. catechu*) is a classical drug found in various Ayurvedic books which were documented from 1000 BC to 1800 AD. Ethnomedicinally, the herb is used in the management of parasitic diseases, dyspepsia, abdominal distension, abdominal pain, diarrhoea, edema, jaundice, *etc.* In Ayurveda, the herb is enumerated as an external and internal remedy to manage *prameha (diabetes)*, raktapitta (bleeding disorders), *yonisrava* (vaginal discharge), and *upadamsa* (syphilis) in various dosages forms. The official Pharmacopeia of Ayurveda quoted *A. catechu* as the classical *Puga*. Pharmacodynamic attributes reflect *kasaya rasa* (astringent taste), *ruksha guna* (dry property), *sheeta veerya* (cold potency), *katu vipaka* (pungent biotransformation), and *kaphapittaghna* property (*kapha* and *pittadosha* pacifying effect).

The source plant *A. catechu* is also reported for its antioxidant, anti-inflammatory, anti-melanogenesis, skin ageing and cosmetics, hypoglycemic activity, hypolipidemic, α-glucosidase inhibitory and hypoglycemic activities, antihypertensive, vascular-relaxation, antidepressant, antimicrobial, wound healing, platelet aggregation inhibitory activity, anticonvulsant activity, central nervous system stimulant, proteasome inhibitors, and molluscicidal activity. Most of these studies are either *in vitro* or preclinical only.

Therefore, a review of the phytochemical and pharmacological profile of the classical Ayurveda drug *Puga* (*A. catechu*) showed encouraging results in classically indicated disorders such as diabetes and worm infections. However, there is a need to evaluate *A. catechu* for other classical Ayurveda indications based on pharmacological activities.

Puga (*A. catechu*) is widely mentioned in Ayurvedic classics but the therapeutic utilization of the drug is very limited. This article provides an overview of many characteristics of *Puga* (*A. catechu*) and its biochemical compounds which act on various disease conditions. To know the underlying mechanisms and type of biochemical compounds involved in these beneficial effects further studies are required with the utilization of modern medicine.

Data collection strategy

The data was collected with search keys like *Puga* (*A. catechu*), *A. catechu* + pharmacological activity, *A. catechu* + ethnomedicinal use, and *A. catechu* + botanical description. All the available pharmacognostic characteristics, phytochemicals, pharmacological activities, and clinical studies from Pubmed and Google Scholar databases were collected. The collected information was evaluated and systematically presented.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

References

Amudhan, M.S. and Hazeena Begum, V. (2008). Alpha-glucosidase inhibitory and hypoglycemic activities of *Areca catechu* extract. Pharmacognosy Magazine, **4**(15):223-227.

Amudhan, M.S. and Hazeena Begum, V. (2008). Protective effect of *Areca catechu* extract on ethanol-induced gastric mucosal lesions in rats. Pharmacologyonlin., **1**:97-106.

Anonymous, (1989). The Ayurvedic Pharmacopoeia of India, Part-I, vol.-I, first English ed., Government of India, Ministry of Health and Family Welfare, Department of Health, New Delhi, India, pp:124-125.

Azeez, S.; Amudhan, S.M.; Sachidananda A.; Namita, R; Nirmala, R. and Laxminarayana, U.A. (2007). Wound Healing profile of *Areca catechu* extracts on different wound models in Wistar rats. Kuwait Medical J., **39**:48-52.

Bhandare, A. M.; Kshirsagar, A. D.; Vyawahare, N. S.; Hadambar, A. A. and Thorve, V. S. (2010). Potential analgesic, anti-inflammatory and antioxidant activities of hydroalcoholic extract of *Areca catechu* L. nut. Food and Chemical Toxicology, **48**(12):3412-3417.

Bhandare, A.M.; Kshirsagar, A.; Vyawahare, N.; Sharma, P. and Mohite, R. (2011). Evaluation of anti-migraine potential of *Areca catechu* to prevent nitroglycerin-induced delayed inflammation in rat meninges: Possible involvement of NOS inhibition. Journal of Ethnopharmacology, **136**(1):267-270.

Byun, S.J.; Kim, H.S.; Jeon, S.M.; Park, Y.B. and Choi, M.S. (2001). Supplementation of *Areca catechu* L. extract alters triglyceride absorption and cholesterol metabolism in rats. Ann. Nutr. Metab., **45**(6):279-84.

Chempakam, B. (1993). Hypoglycemic activity of arecoline in betel nut *Areca catechu* L., Ind. J. of Exp. Biol., **31**(5):474-475.

Chopra, R.N.; Nayar, S.L. and Chopra, I.C. (1996). Glossary of Indian Medicinal Plants, 1st Ed., 4th reprint, National Institute of Science Communication, New Delhi. pp:23.

Chung, F., Shieh, T., Yang, Y., Chang, D. and Shin, S. (2007). The role of angiotensin-converting enzyme gene insertion/deletion polymorphism for blood pressure regulation in areca nut chewers. Translational Research, **150**(1):58-65

Dar, A. and Khatoon, S. (2000). Behavioral and biochemical studies of dichloromethane fraction from the *Areca catechu* nut. Pharmacol. Biochem. Behav., **65**(1):1-6.

De Miranda, C.M.; Van Wyk, C.W.; Van der Biji, P. and Basson, N.J. (1996). The effect of areca nut on salivary and selected oral microorganisms. Int. Dent. J., **46**(4):350-356.

Feng, Q.; Li, G.; Yang, Y. and Gao, J. (1999). Studies on the increasing-effect components for molluscicides in the nut of *Areca catechu*. Zhong Yao Cai, **22**(11):572-574.

Ghayur, M.N.; Kazim, S.F.; Rasheed, H.; Khalid, A.; Jumani, M.I.; Choudhary, M.I. and Gilani, A.H. (2011). Identification of antiplatelet and acetylcholinesterase inhibitory constituents in betel nut. Zhong Xi Yi Jie He Xue Bao, **9**(6):619-625.

Gurumurthy, B.R.; Akshatha, S. S.; Akshay, G. and Pavitra, S.K. (2018). Diversity of mineral contents in arecanut (*Areca catechu* L.) in different locations of Karnataka, India. Int. J. Curr. Microbiol. App. Sci., **7**(3):1527-1535

Chellammal, H. S. J. (2022). Fruits that heal: Biomolecules and novel therapeutic agents. Ann. Phytomed., **11**(1):7-14.

Inokuchi, J.; Okabe, H.; Yamauchi,T.; Nagamatsu, A.; Nonaka, G.I. and Nishioka, I. (1986). Antihypertensive substance in seeds of *Areca catechu* L., Life Sci., **38**(15):1375-1382.

Jeon, S.M.; Kim, H.S.; Lee, T.G.; Ryu, S.H.; Suh, P.G.; Byun, S.J.; Park, Y.B. and Choi, M.S. (2000). Lower absorption of cholesteryl oleate in rats supplemented with *Areca catechu* L. extract. Ann. Nutr. Metab., **44**(4):170-176.

Kavita V. and Sanjay G. (2002). Herbal medicines for sexually transmitted diseases and AIDS, Journal of Ethnopharmacol., **80**(1):49-66.

Kim, B.J.; Kim, J.H.; Kim, H.P. and Heo, M.Y. (1997) Biological screening of 100 plant extracts for cosmetic use (II): Antioxidative activity and free radical scavenging activity. Int. J. Cosmet. Sci., **19**(6):299-307.

Koleva, I.I.; Van Beek, T.A.; Linssen, J.P.H.; Groot, A. de. and Evstatieva, L.N. (2002). Screening of plant extracts for antioxidant activity: A comparative study on three testing methods. Phytochemical Analysis, **13**(1):8-17.

Kook, K.; Lee, J.J.; Cho, J.; Park and Choi, J.D. (1999). The effects of *Areca catechu* L. extract on anti-inflammation and antimelanogenesis. International Journal of Cosmetic Science, **21**(4):275.

Kook, K.; Lee, J.J.; Cho, J.; Park and Choi, J.D. (2001). Anti-elastase and anti-hyaluronidase of phenolic substance from *Areca catechu* as a new antiageing agent. International Journal of Cosmetic Science, **23**(6):341-346.

Kumarnsit, E.; Keawpradub, N.; Vongvatcharanon, U.; Sawangjaroen, K. and Govitrapong, P. (2005). Suppressive effects of dichloromethane fraction from the *Areca catechu* L. nut on naloxone-precipitated morphine withdrawal in mice. Fitoterapia, **76**(6):534-539.

Kurian, J.C. (1995). Plants That Heal, Oriental Watchman Publishing House, Printed and Published by E.B. Mathews, 7th Ed, Pune, pp:1-20.

Kuo, F.C.; Wu, D.C.; Yuan, S. S.; Hsiao, K.M.; Wang, Y.Y.; Yang, Y.C. and Lo, Y.C. (2005). Effects of arecoline in relaxing human umbilical vessels and inhibiting endothelial cell growth. J. Perinat. Med., **33**(5):399-405.

Lee, K.K. and Choi, J.D. (1999). The effects of *Areca catechu* L. extract on antiageing. Int. J. Cosmet. Sci., **21**(4):285-295.

Lodge, D.; Johnston, G.A.R.; Curtis, D.R. and Brand, S.J. (1977). Effects of the Areca nut constituents arecaidine and guvacine on the action of GABA in the cat central nervous system, Brain Research, **136** (3):513-522.

Mathew, A.G. and Govindarajan, V.S. (1963). Polyphenolic substances of areca nut II. Changes during maturation and ripening. Phytochemistry, **3**(6):657-665.

Ma, W., Guo, A., Zhang, Y., Wang, H., Liu, Y., and Li, H. (2014). A review on astringency and bitterness perception of tannins in wine. Trends in Food Science and Technology, **40**(1):6-19.

Marastoni, M.; Baldisserotto, A.; Canella, A.; Gavioli, R.;De Risi, C.; Pollini, G. P. and Tomatis, R. (2004). Arecoline tripeptide inhibitors of proteasome. J. Med. Chem., **47**(6):1587-1590.

Maroti, M.J.; Satish B. K.; Naheed, W. A. S. and Umesh, B. T. (2022). Cyperus rotundus L.: Phytochemistry and pharmacological activities. Ann. Phytomed., **11**(2):186-196.

Mehrotra, N. (2021). Herbs that heal: Natures pharmacy. Ann. Phytomed., **10**(1):6-22.

Nagaiah, K. (2022). AYUSH drugs need evidence based scientific research. Ann. Phytomed., **11**(2):1-6.

Nai-Shin, Chu. (2001). Effects of betel chewing on the central and autonomic nervous systems. J. Bio. Med. Sci., **8**(3):229-236.

Nonaka, G.I.; Hsu, F.L. and Nishioka, I. (1981). Structures of dimeric, trimeric and tetrameric procyanidins from *Areca catechu*. J. Chemical Soc. Chemical Commutations, **1**(15):781-783.

Ohsugi, M.; Fan, W.; Hase, K.; Xiong, Q.; Tezuka, Y.; Komatsu, K.; Namba, T.; Saitoh, T.; Tazawa, K. and Kadota, S. (1999). Active-oxygen scavenging activity of traditional nourishing tonic herbal medicines and active constituents of *Rhodiola sacra*. J. Ethnopharmacol., **67**(1):111-119.

Orlowski, R.Z. (1999). The role of the ubiquitin-proteasome pathway in apoptosis. Cell Death Differ., **6**(4):303-313.

Park, Y.B.; Jeon, S.M.; Byun, S.J.; Kim, H.S. and Choi, M.S. (2002). Absorption of intestinal free cholesterol is lowered by supplementation of *Areca catechu* L. extract in rats. Life Sci., **70**(16):1849-1859.

Pathak, S.P. and Mathur, S. S. (1954). The component acids and glycerides of areca-nut (*Areca catechu* L.) fat. Journal of the Science of Food and Agriculture, **5**(10):461-465.

Raghavan, V. and Baruch, H.K. (1958). Areca nut: Indian's popular masticatory. History, Chemistry and Utilization. Journal of Economic Botany, **12**:315-345.

Rashid, M., Shamsi, S., Zaman, R. and Ilahi, A. (2015). *Areca catechu*: Enfolding of historical and therapeutic traditional knowledge with modern update. International Journal of Pharmacognosy, **2**(5):221-228.

Shivasankar, S. and Govindarajan, V.S. (1963). Equilibrium relative humidity relationship of processed areca nut and whole dried areca nut, Food Sci., **12**(11):317-321.

Srinivasan, N. and Murali, R. (2022). An overview of the traditional importance, phytochemistry, and pharmacological properties of Sida acuta Burm.f.. Ann. Phytomed., **11**(2):245-254.

Sumitra H.; Nobuko K.; Masao H. and Tsuneo N. (2006). Identification of antibacterial principles against *Streptococcus mutans* and inhibitory principles against glucosyltransferase from the seed of *Areca catechu* L. Phytotherapy Research, **3**(4):140-144.

Suresh Babu, S. and Madhavi, M. (2005). Green Remedies: Healing Power of Herbs, Published by Pustak Mahal, pp:55-56.

Verma, D. K.; Bharat, M.; Nayak, D. R.; Shanbhag, T.; Shanbhag, V. and Rajput, R. S. (2012). *Areca catechu*: Effect of topical ethanolic extract on burn wound healing in albino rats. International Journal of Pharmacology and Clinical Sciences, **1**(2):74-78.

Wei-Peng; Yu-Jie, Liu; Na-Wu; Tao-Sun; Xiao-Yan He; Yong-Xiang Gao and Chun-Jie Wu. (2015). *Areca catechu* L. (Arecaceae): A review of its traditional uses, botany, phytochemistry, pharmacology and toxicology, J. Ethnopharmacol., **164**(22):340-356.

Yang, W.Q.; Wang; H.C., Wang, W.J.; Wang, Y.; Zhang, X.Q. and Ye, W.C. (2012). Chemical constituents from the fruits of *Areca catechu*. Journal of Chinese Medicinal Materials, **35**(3):400-403.

Zhang, X.; Mei, W.; Zeng, Y. and Liu, J. (2009). Phenolic constituents from the fruits of *Areca catechu* and their antibacterial activities. Journal of Tropical and Subtropical Botany, **17**(1):74-76.

Citation **Ramakrishna Allam, Govardhan Sahani, Antony Stephen Raj and Faiz Mohammed (2023). A phytopharmacological review of the classical Ayurveda drug *Puga* (*Areca catechu* L.). Ann. Phytomed., 12(2):180-185. http://dx.doi.org/10.54085/ap.2023.12.2.20**