सक्रिय कार्यशाला

सुपारी और मानव स्वास्थ्य

Interactive Workshop on

Arecanut and Human Health

24-25 July 2018

ABSTRACTS

भा कृ अनु प - केंद्रीय रोपण फसल अनुसंधान संस्थान
कासरगोड़ 671124 केरल

ICAR-CENTRAL PLANTATION CROPS RESEARCH INSTITUTE
KASARAGOD 671124 KERALA

(ISO 9001:2015)

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सुपारी और मानव स्वास्थ्य

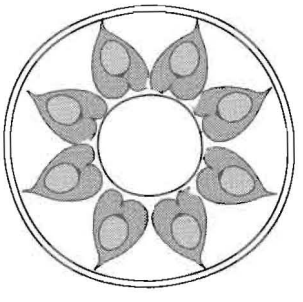
An Interactive Workshop on

Arecanut and Human Health

24 – 25 July, 2018

सारांश

ABSTRACTS



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ICAR-Central Plantation Crops Research Institute
Kasaragod – 671124, Kerala, India

Abstracts: An Interactive Workshop on Arecanut and Human Health, 24 – 25 July, 2018, ICAR-Central Plantation Crops Research Institute, Kasaragod – 671124, Kerala, India, p. 64.

Published by

Dr. P. Chowdappa
Director
ICAR-Central Plantation Crops Research Institute
KASARAGOD 671 124, Kerala, India
Phone : 04994 – 232893, 232894, 232895 & 232996;
Fax: 04994-232322
Email: directorcpcri@gmail.com, chowdappa.p@icar.gov.in
Website: http://www.cpcri.gov.in/

Compiled and edited by
K.B. Hebbar and
S.V. Ramesh

Cover design

K. Shyama Prasad

Layout Design

H. Muralikrishna

July, 2018

Printed at

M/s Digantha Mudrana Ltd.
Yeyyadi, Mangalore, Ph: 0824 2216551

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डॉ. आनंद कुमार सिंह
उप महानिदेशक (बाग. वि.)
कार्यकारी उप महानिदेशक (फसल वि.)
Dr. Anand Kumar Singh
Deputy Director General (Hort. Sci.)
I/C Deputy Director General (Crop. Sci.)

भाकृअनुप
ICAR

भारतीय कृषि अनुसंधान परिषद्
कृषि अनुसंधान भवन - II
पूसा, नई दिल्ली - 110012

INDIAN COUNCIL OF AGRICULTURAL RESEARCH
KRISHI ANUSANDHAN BHAWAN-II
PUSA, NEW DELHI-110 012

दूरभाष सं.:91-11-25842068, फैक्स सं.:91-11-25841976
Ph.: 91-11-25842068(O), Fax: 91-11-25841976
email: ddghort@gmail.com
aksingh36@yahoo.com

Message

Arecanut (*Areca catechu* L.) is a high value commercial crop of great economic importance and plays a vital role in the Indian economy. It forms an important component of the religious, social and cultural celebrations. In India, arecanut is cultivated in an area of 446 thousand ha, with an annual production of 608 thousand tones. Arecanut has been an ingredient of both ayurvedic as well as folk medicines since time immemorial. Notwithstanding numerous researches showcasing the benefits of arecanut in human health, it has been associated with the ill-effects. In this context, I am glad that ICAR-Central Plantation Crops Research Institute (ICAR-CPCRI) has conceptualized and taken a lead to conduct an "Interactive Workshop on Arecanut and Human Health" on 24 and 25 July, 2018. The basic premise of this workshop is to deliberate the scientific aspects and to reach a well-informed conclusion about the potential health benefits of arecanut. I am hopeful that the gathering of experts, from diverse backgrounds and possessing vast scientific expertise would facilitate delineating of appropriate research methodologies suitable for arecanut research in human health.

I wish the workshop a great success.

(Anand Kumar Singh)

भा कृ अनु प - केंद्रीय रोपण फसल अनुसंधान संस्थान
कासरगोड़ - 671124, केरल, भारत
ICAR-Central Plantation Crops Research Institute
Kasaragod - 671124, Kerala, India
(An ISO 9001:2015 Certified Institution)

Phone (Off): 04994 - 232333
Fax: 04994 - 232322
(EPABX): 04994 - 232893-95
04994 - 232090
04994 - 232996

E-mail: director.cpcri@icar.gov.in
directorcpcri@gmail.com
chowdappa.p@icar.gov.in
Website: http://www.cpcri.gov.in/

Dr. P. Chowdappa
Director

Preface

Arecanut (*Areca catechu* L.) is an important commercial crop cultivated in much of tropical Asia, Pacific and East Africa. India is the major producer and consumer of arecanut in the world. In India, arecanut is cultivated in an area of 446 thousand ha with an annual production of 608 thousand tonnes and around 10 million people are dependent on it, directly or indirectly, for their livelihood. Its cultivation can be traced back to the Vedic periods and it forms an important component of socio-religious lives of people in this regions. In addition, it has an important place in the ancient Indian system of medicine such as Ayurveda, Unani and Homeopathy. It possesses a plethora of medicinal properties *viz.*, anti-oxidant, anti-inflammatory and analgesic, anti-ulcer, hypolipidemic, anti-diabetic and neuro-protective. Sadly, despite these medicinal values, adverse human effects have been portrayed which has caused a lot of anxiety amongst areca growers, traders, consumers and other stakeholders in the commodity value chain. The situation necessitates concerted efforts on our part to unequivocally dispel the prevailing negative notions on arecanut and warrants systematic clinical research studies to understand the effects of arecanut products on human health, in addition to exploring its alternate uses. To scientifically address these issues, we have planned an "Interactive Workshop on Arecanut and Human Health" on 24-25 July, 2018, involving agricultural, chemical and clinical research scientists, human health specialists, traditional practitioners, growers, consumers, traders, policy makers and all those concerned with arecanut development to take stock of the current status, identity the gaps and develop a working network.

(P. Chowdappa)

Prologue

Arecanut Consumption and Human Health - Research Priorities

K.B. Hebbar*, S.V. Ramesh and P. Chowdappa
ICAR-Central Plantation Crops Research Institute, Kasaragod
*E-mail: balakbh64@gmail.com

Arecanut is a complex chemical mixture reported to contain different chemicals, including carbohydrates, lipids, nitrogenous compounds, vitamins, minerals, alkaloids and phenolic compounds. It is rich in alkaloids and amongst that arecoline plays a role in its popularity. The majority of studies on the health effects of arecanut consumption in humans are observational. Concerns about potential health risks of arecanut chewing and arecoline consumption raised by epidemiological research in the past were likely exacerbated by associations between arecanut chewing and other factors like chewing areca with tobacco, poor socio- economic status etc. Recent research has indicated, *A. catechu* has potential for the treatment of many diseases, especially parasitic diseases, digestive function disorders, and depression. However, in many cases, conflicting findings and concerns about methodological issues have made it difficult for health professionals and the public to interpret the available evidence on areca consumption and health. Meanwhile, there are few reports to show risk of cancer with areca consumption, but there is little conclusive evidence to show that areca chewing alone is a contributing factor. Thus more comprehensive epidemiological studies and in depth clinical trials are warranted to decipher the association between arecanut consumption and human health.

Prevalence of use

Areca catechu is an important commercial crop cultivated through tropical India, East Africa, Far East Asia, and South Pacific. India is the major producer and consumer of arecanut in the world. Arecanut production in India is the largest in the world, as per FAO statistics for 2016, accounting for 49.74 % of its world output, and is exported to many countries. Arecanut is grown in an area of 4.41 lakh ha with a production of 6.0 lakh tonnes of dry kernel in India. Almost entire production goes for chewing and a small portion for other commercial purposes.

Areca Preparations

Preparations and specific ingredients of arecanut vary by cultural group and individual user. A betel quid is defined as a substance, or mixture of substances, placed in the mouth, usually containing at least one of the two basic ingredients, areca nut, in raw or any manufactured or processed form with betel leaf and slaked lime, and may contain tobacco. If it contains tobacco and no betel leaf, the product is called gutkha or mawa. Other substances, particularly spices, including cardamom, saffron, cloves, aniseed, turmeric, mustard or sweeteners, are added according to local preferences. Catechu is an astringent, reddish-brown substance which is often smeared on the betel leaf used to wrap the ingredients of betel quid. Two main types of catechu may be used an extraction from the heartwood of *Acacia catechu*, or an aqueous extract prepared from the leaves and young shoots of *Uncaria gambir*, a climbing shrub.

Composition of the different types of areca-containing chewing substances

Betel quid:	Arecanut (fresh, unripe), alone or with lime Arecanut (dried, unripe), alone or with lime Arecanut (cured, ripe), alone or with lime Arecanut (fresh, unripe), with lime and betel leaf
Pan/paan :	Arecanut + betel leaf + slaked lime + with or without catechu + flavourings
Paan with tobacco:	Arecanut + betel leaf + slaked lime + with or without catechu + tobacco + flavourings
Gutka:	Arecanut + slaked lime + catechu + tobacco
Pan masala:	Arecanut (tender form) + slaked lime + catechu + flavourings
Mawa/kharra:	Arecanut (cured, ripe) + slaked lime + tobacco + flavourings

Compounds in arecanut that may affect human health

Many chemical compounds have been isolated and identified from *A. catechu* while pyridine-type alkaloids and condensed tannins have been identified as the characteristic constituents.

Alkaloids

Alkaloids possess notable biological activities and are considered to be the primary active ingredients in plant-derived medicines. It has been reported that *A. catechu* is the only

plant containing alkaloids of the Arecaceae family. Alkaloids are characteristic components of *A. catechu*, and the total alkaloid content of *A. catechu* is approximately 0.3–0.7%. Arecoline, with a content of 0.3–0.6%, is the main alkaloid in *A. catechu*. The predominant alkaloids are of the pyridine type and include arecoline, arecaidine, guavacoline, guavacine, arecolidine, ethyl N-methyl-l,2,5,6-tetrahy- dro-pyridine-3-carboxylate, methylnicotinate, ethylnicotinate, methyl N-methylpiperidine-3-carboxylate, ethyl N-methylpiperidine-3-carboxylate, nicotine isoguvacine), and homoarecoline.

Flavonoids

Flavonoids are common constituents of numerous plants world- wide. The flavonoids isolated from A. catechu include isorhamnetin, chrysoeriol, luteolin, quercetin, 40, 50-dihydroxy- 30, 50, 70-trimethoxyflavonone, 5,7,40-trihydroxy-30, 50- dimethoxyflavanone, liquiritigenin, and jacareubin.

Tannins

Tannins are another characteristic component of *A. catechu,* and the main types are condensed tannins (also called proanthocyanidins). Tannins are one of the main constituents that contribute to the perception of the taste of food (astringency and bitterness perception). The main classes of tannins in *A. catechu* are the catechuins and epicatechuins. The specific tannin compounds of *A. catechu* include procyanidin A1, procyanidin B1, procyanidin B2, arecatannin A1, arecatannin B1, arecatannin, arecatannin A2, arecatannin A3, and arecatannin B2.

Triterpenes and steroids

To date, six triterpenes and three steroids from *A. catechu* have been reported. In1993, ursolicacid and its derivative, 3β- acetyl ursolic acid were isolated from the leaves of *A. catechu*. Furthermore, arborinol, arborinolmethyl ether, fernenol, and arundoin were isolated from the pericarp of *A. catechu*. Later, a triterpenenamedcycloartenol and three steroids including 5,8-epidioxiergosta-6,22-dien-3β-ol, stigmasta-4- en-3-one, and β-sitosterol were identified from the seeds of *A. catechu*.

Potential health benefits of arecanut

Antiparasitic effects

Arecanut is a traditional medicine commonly used to kill parasites including tapeworms, lumbricus, and pinworms, etc. Investigations reported that the water extracts of areca nut (WEAN) can effectively kill tapeworms.

Effects on the digestive system

The water extract of arecanut can significantly increase gastrointestinal motility in rabbits (0.05, 0.25, and 0.5 μg/mL) and in mice (2.5 and 5 mg/kg) in in-vivo via stimulation of the M receptor and the verapamil- sensitive Ca_2 channel. It has been reported that the WEAN can also significantly improve the gastrointestinal function of rats with functional dyspepsia. Furthermore, ethanol extract significantly increases the contraction of gastric smooth muscle and muscle strips of the duodenum, ileum, and colon.

Effects on the nervous system

The hexane extracts of arecanut (HEAN) and the WEAN (HEAN at doses of 2.5, 5, 10 and13 mg/kg; WEAN at doses of 2.5, 5, 10, 13, 20 and 50 mg/kg) showed significant anti-depressive effects in mice and rats.

Antioxidant effect

Both WEAN and ETAN (ethanol extract of arecanut) found to have strong antioxidant activity on DPPH radicals. An investigation demonstrated that WEAN possess free radical scavenging activity against DPPH radicals with IC50 values of 5.34 μg/mL. Furthermore, in another investigation, the ETAN was reported to possess a powerful hydroxylradical-scavenging effect with an IC50 value of 83.14 μg/ mL.

Antibacterial and antifungal effects

MEAN (methanol extract of arecanut) and its sub-fractions (including ethylacetate, butanol and water fractions) possess notable anti-bacterial activities toward *S. aureus* with minimal inhibitory concentration (MIC) values of 125, 250, 62.5 and 250 μg/mL for the MEAN and its sub fractions respectively. In addition, arecoline isolated from the arecanuts was reported to be an active agent against *Bacillus proteus, Candida albicans, Bacillus anthracis,* with MIC values 0.8, 0.8, and 0.8mg/mL, respectively.

Anti-inflammatory and analgesic effects

The acetone extracts of the arecanut (AEAN), which contain abundant procyanidins, significantly down-regulate the expression of TPA-induced cyclooxygenase-2(COX-2) at lowdoses (0.1–1μg/mL) by inhibiting ERK phosphorylation in SAS cells. Furthermore, treatment of rats with AEAN (1 and 10 mg/kg/d, for 5days) clearly suppresses the carrageenan-induced inflammatory edema and PGE2 levels. ETAN was reported to be effective against nitroglycerin-induced delayed inflammatory migraines in rats.

Effects on the cardiovascular system

ETAN sub-fraction containing primarily arecoline and condensed tannin isolated from arecanut showed vasodilatory effect and relaxes the rat aorta containing intact endothelium. Furthermore, the MEAN significantly inhibits the platelet aggregation induced by arachidonicacid (AA), adenosine diphosphate (ADP), platelet-activating factor (PAF), epinephrine, or Ca_2-ionophore, with IC50 values of 1.59, 0.628, 1.902, 1.677, and 0.987 mg/mL, respectively.

Regulating effects on blood glucose and lipids

WEAN and water extracts of the pericarp of A. *catechu* (WEPA) significantly inhibit the phagocytic activity of neutrophils. Furthermore, it was shown that the WEAN could suppress the release of interleukin-2(IL-2) and interferon-γ (IFN-γ) with IC50 values of 42.8, and 38.17 μg/mL respectively, suggesting that the WEAN treatment can suppress T-cell activation and IFN-γ production by splenocytes.

Arecanut and cancer

Areca nuts are chewed for their stimulant effects in many Asian countries, and evidence links the practice to the development of oral and esophageal cancer. Recently the carcinogenesis of arecanut has aroused comprehensive investigation and attention. Several studies have reported that chewing of betel quid is closely associated with the occurrence of oral cancer. Furthermore the alkaloid arecoline found to induce apoptosis in human epithelial cell. But it all found to depend on the dose and how it was taken into the body. At normal or lower dose either areca nut extract or the arecoline is found to be safe. The harmful effect of areca nut and other chewing products containing areca nut might be due to their high doses or application in unusual manner like injection, direct exposure to cultured cells or due to several other factors such as contaminations and adulteration, the effect of other ingredients of betel quid or pan masala and the food habits of individuals etc. The majority of studies on the health effects of arecanut consumption in humans are observational. Concerns about potential health risks of arecanut chewing and arecoline consumption raised by epidemiological research in the past were likely exacerbated by associations between arecanut chewing and other factors like chewing areca with tobacco, poor socio- economic status etc. As much of the currently available information on the health effects of areca nuts is derived from epidemiological research, the study raises several issues regarding the exposure classification and potential co founders that should be considered when interpreting the results of epidemiological studies of areca nut consumption.

Exposure misclassification: areca nut consumption is often assessed using questionnaires that collect information regarding areca nut chewers and non chewers. As we are aware areca is consumed in various forms like areca alone (fresh/dry, ripe/unripe) with or without lime, betel leaf, catechu, tobacco, flavoring and other ingredients. In most of the studies irrespective of the way it is consumed, all are grouped under betel nut chewers and the data was collected and analyzed and inference was drawn. Secondly most of the epidemiological studies were conducted in urban areas where there is lot of heterogeneity amongst arecanut consumers. Lots of variation in the socio economic status and consumption of arecanut in various forms makes it difficult to get relatively homogenous sample of arecanut consumers only for the study.

Most of these studies were conducted with the presumption that arecanut contains lot of alkaloids which leads to nitrosation of the products and causes cancer in the animals. Extensive animal experiments have substantiated that nitrosamines are strong carcinogens. However, the response in *in vitro* as well as animal studies depends on the compound as well as the dose. Meat, most of the fast foods, tea, and coffee all are known to cause nitrosation at higher doses. Keshava Bhat *et al* 2017 very clearly showed that in most of the experiments where arecanut extract or arecoline is used were at higher concentration than consumption through mastication. Any substance when it is used at higher concentration bound to cause adverse effects both *in vitro* as well as animal studies. Therefore the inference from the above studies is to be viewed carefully. It is evident from the findings of a recent study by Fan et al (2016 Emory University School of Medicine, Atlanta, USA Published in reputed journal Molecular Cell Impact Factor >14) clearly demonstrated that when arecoline is administered in lower dose (0.1 micromolar) it inhibited phosphorylation of tetrameric ACAT1 (acetyl-CoA acetyltransferase 1), which is commonly upregulated in primary human leukemia cells and this could be a promising therapeutic strategy in the treatment of human cancer. It is very clear when it is at lower dose it inhibits the proliferation of tumor cells while at higher dose it may act reverse.

Cofounders: A frequent criticism of epidemiological research on areca nut is inadequate adjustment or cofounding factors that could influence the relationship between arecanut consumption and health outcome. From the previous survey reports it is clear that more than 65 per cent of areca nut chewer is habituated to mixing areca with tobacco and hence tobacco is often sighted as a potential cofounder. Under reporting the effect of tobacco, while accurately reporting areca nut effect could lead to over estimation of the effect of areca nut consumption on health outcome. Other life style factors may also compound association between arecanut

consumption and health outcome. For example people who chew areca nut are generally economically poor and malnourished. Therefore, the data on health effect in these population may be associated with malnourishment rather than areca consumption.

Conclusion: *A. catechu* has potential for the treatment of many diseases, especially parasitic diseases, digestive function disorders, anti microbial properties and depression. Many traditional uses of *A. catechu* have now been validated by current investigations. However, further research should be undertaken to investigate the clinical effects, toxic constituents, investigate the active molecular compounds and active constituents.

Future Research

- Phytochemistry for the identification of active nutraceuticals or functional molecules.
- Specific chemical mechanisms for the biological activities of the constituents.
- Epidemiological research which establishes the health effects of arecanut consumption must account for the issues regarding exposure classification and potential confounders while interpreting the results.
- Preclinical and clinical trials for the development and discovery of a new drug.
- Clinical studies to evaluate the possible therapeutic effects and toxicity.

Interactive Workshop on Arecanut and Human Health

24th and 25th July, 2018

Programme

Day-1 24-July-2018

10.00 AM to 11.30 AM **Inauguration**

Shri V.V. Bhat, IAS, Former Secretary to the Govt. of India & Member (Finance), Space Commission/Atomic Energy Commission/Earth Commission

Prof. Dr. Satheesh Kumar Bhandary, Vice Chancellor, NITTE, Mangalore

Dr. Manjunatha K. Naik, Vice Chancellor, University of Agricultural & Horticultural Sciences, Shivamogga

Dr. P. Chowdappa, Director, ICAR-CPCRI, Kasaragod

Convener: **Dr. K.B. Hebbar** **Rapporteur**: Dr. Ramesh S.V.

11.30 AM -11.45AM TEA

11.45 AM to 1.30 PM **Technical Session -I (Phytochemistry)**

Chairman: Dr. Jayarama Bhat Convener: Dr. Ravi Bhat

Rapporteur: Dr. Shameena Beegum

Identification and characterization of chemical constituents of Arecanut at its different stages - A case study-**Prof. J. Ishwara Bhat** and K. Sumalatha, Department of Chemistry, Mangalore University, Mangalore

Phytochemicals and therapeutic potential of Arecanut-**Dr. M. P. Sadashiva,** Department of Chemistry, University of Mysore

Arecanut- Anti-oxidant properties-**Dr. Laxmi Narayan Hegde,** Horticulture Research and Extension Centre, UHS, Bhagalkot

1.30PM -2.30 PM LUNCH

2.30 PM to 6.00 PM **Technical Session-II (Arecanut in Ayurvedic medicine and value addition)**

Chairman: Dr. Giridhara Kaje **Convener: Dr. Vinayaka Hegde**

Rapporteur: Dr. N. R. Nagaraja

Arecanut and Human Health - Challenges - **Dr. Sathyanarayana Bhat,** Ayurveda Consultant, Cancer Management Therapist, Writer, Columnist, Gold Medalist, Sahithya Academy awardee and Naturalist, Bangalore

Research on areca and cancer in colleges of Ayurveda – Approaches and incentives - **Shri V.V. Bhat, IAS,** Former Secretary to the Govt. of India & Member (Finance), Space Commission/Atomic Energy Commission/Earth Commission

Clinical evaluation of ***Dia Ketechu*** a compound herbal formulation in non-insulin dependent diabetes, **Dr. Jeddu Ganapathi Bhat,** Jeddu Ayurveda Specialty Hospital, Alike, Karnataka

Experimental evaluation of anti-diabetic activity of Areca tea on Wistar albino rats - Ravishankar B, **Dr. Naveen Chandra**, BhatSudhakar, Ravi M., SDM, College of Ayurveda, Udupi, Karnataka

Arecanut and Human Health: Some observations- **Dr. Jayarama Bhat,** Formerly, Professor of Botany, Goa University, Goa

Arecanut: Traditional Exploit and Scientific Rationale-**Dr. Hemand Aravind,** Consultant Scientist, Santhigiri Res. Foundation, Thiruvananthapuram

Pugaphala in traditional medicine of Tulunadu- **Dr. Subrahmanya Prasad K,** Nehru Arts & Science College, Kanhangad, Kerala

Arecanut, *Areca catechu* L., in folk medicine **Shri Shankar Bhat Badanaje**, Vitla

Day 2 25 July, 2018

9.30 AM to 11.00 AM: Technical Session-III

(Pharmacology I: Neuro-protective, hyperglycemic, wound healing effects etc.)

Chairman: Dr. Vijayalakshmi Deshmane **Convener: Dr. V. Niral**

Rapporteur: Shri Thava Prakash Pandian

Wound healing profile of *Areca catechu* extracts on different wound models in Wistar rats – Shameena Azeez, Senthil Amuthan, **Dr. Sachidananda Adiga**, Namitha Rao, Nirmala Rao, Laxminarayana A., Professor, Pharmacology, KSHEMA, Mangalore

Wound healing, anti-inflammatory and analgesic properties of Arecanut – **Dr. Sukesh Bhat** Department of Pharmacology, Kodagu Institute of Medical Sciences, Madikeri

Anti-ulcerogenic effects of Arecanut- **Dr. Reena R. Nelson**, P.S.G. College of Arts & Science, Coimbatore

Pharmacological Investigation of *Areca catechu* extracts for evaluation of learning, memory and behaviour in rats. **Prof. M. P. Joshi**, K.M. Gaonkar, I. James, Department of Pharmacology, Faculty of Pharmacy, Goa College of Pharmacy, Panaji Goa.

Arecanut husk and its protective effect on the tobacco induced cultured human oral mucosal cells- **Dr. Manjula Shantaram**, Dept. of Biochemistry, Mangalore University

Anti-hyperglycemic activity of *Areca catechu* flowers **Dr. Virupanagouda Patil**, Dept of Pharmacology, BLDEA'S College of Pharmacy, Bijapur

11.15 AM to 1.30 PM: Technical Session-IV (Pharmacology II: Anti-microbial properties)

Chairman: Dr. Ravichandra V **Convener: Dr. Murali Gopal**

Rapporteur: Dr. Neema M.

Arecanut a blessing or curse: **Dr. Malathi,** Vice Principal & Head, Department of Oral Pathology & Microbiology, Sri Ramachandra Medical College &Research Institute, Chennai

Arecanut: Potential Pharmacological Activities-**Dr. A. Ruckmani**, Professor and Head, Department of Pharmacology, Chettinad Hospital & Research Institute, Kelambakkam, Chennai

Pharmacological/alternative uses of arecanut: Antimicrobial and anticariogenic activities of arecanut. **Dr. Rekha Rai,** Prof. & Head, Dept. of Microbiology, KSHEMA, Mangalore

1.30PM -2.30 PM **LUNCH**

2.30 PM to 3.30PM **Technical Session –V (Epidemiology)**

Chairman: Dr. K. Satyamoorthy **Convener: Dr. Bhanu Prakash**

Rapporteur: Dr. V. H. Prathibha

An appraisal of the effect of arecanut consumption on human health – methodologies and limitations - **Dr. Ravichandra V.,** Associate Professor of Pharmacology, KSHEMA, Mangaluru

Consumption pattern and health issues of arecanut chewers in Karnataka -**Dr. C.T. Jose,** Principal Scientist and Head, ICAR-CPCRI, Vittal

Impacts of consuming arecanut and its by-product on human health- G.D. Narayana and **R. Devananda-** Bharthiar University, Coimbatore, Tamil Nadu

Arecanut (betel nut) is not carcinogenic to humans: Research results -**Dr. S. Keshava Bhat,** D. Ashwin and Sukesh Bhat -Arecanut Research and Development Foundation®, Mangaluru

3.30 PM to 5.00 PM Valedictory Session

3.30 PM to 5.00 PM: Concluding Session

Shri . K.N. Bhat, Senior Advocate, Supreme Court of India- Former Additional Solicitor General of India

Dr. Vijayalakshmi Deshmane, M.S., Former Professor and Head, Kidwai Memorial Institute of Oncology, Bangalore

Dr. K. Satyamoorthy, Director, School of Life Sciences, Manipal University, Manipal

Dr. P. Chowdappa, Director, ICAR-CPCRI, Kasaragod

Convener: **Dr. K.B. Hebbar** **Rapporteur**: Dr. Ramesh S.V.

ABSTRACTS

Identification and characterization of chemical constituents of Arecanut at its different stages – A case study

J. Ishwara Bhat* and K. Sumalatha

Department of Chemistry, Mangalore University, Mangalagangothri-574199, Mangalore, Karnataka
* E-mail: bhatij08@gmail.com

It is a well-accepted fact that arecanut is a rich source of several chemical constituents. It has obtained a prominent place in the field of religious, medicinal and economy of the country. Hence, we planned studies on the chemical constituents of arecanut at its various growth stages and to compare it with the mixed/adulterated arecanut (called *gutkha*) in the market.

In this paper we present the data obtained during our investigation on the extraction, identification and characterization of the chemical constituents at three stages, namely, tender, matured and dried arecanut samples. Arecanut seed was dried, crushed and powdered mechanically. Chemical constituents were extracted in methanol using sox let apparatus. Resultant extracts were subjected to characterization using Atomic Absorption Spectrophotometer (AAS), FTIR, TGA/DTA, XRD and GCMS. AAS indicated the presence of Fe, Zn, Cr, Na, K, Pb etc. in the extract. FTIR clearly showed the functional groups, such as, -NH, -OH, -C=C, aromatic ring, -C-N, -C-O, etc., present in the extract. TGA/DTA helped in the establishment of the stability or the decomposing nature of the constituents with respect to temperature. We identified 5 stages of decomposition. The initial decomposition temperature of the extract was found to be above 40^{0}C and the reaction appeared to be exothermic. X-ray analysis indicated the presence of the mixture of amorphous and crystalline substances in the system. It also identified that the majority of the constituents present in all the three samples are the same. Gas Chromatography-mass spectrometry (GCMS) separated and identified the various chemical constituents and also estimated the molecular mass of the separated constituents which helped in identifying the major chemical components of the areca extract. Moreover, it has been noticed that the component appeared at lower temperature range are of high melting point without any nitrogen in it.

We have also collected some samples of mixtures of arecanut, called *gutkha*, (RM, Vimal, Star, Siddu and Supari) from the market and subjected them for analysis. TGA/DTA clearly showed their decomposition starting from about 22 to 32^{0}C which is much less compared to the decomposition of the pure arecanut under consideration. This decrease in decomposition temperature could be most likely due to the formation of components with low melting point.

Key words: chemical constituents, arecanut, *gutkha*

Phytochemicals and therapeutic potential of arecanut

M.P. Sadashiva*

Department of Studies in Chemistry, Manasagangotri,
University of Mysore, Mysuru, Karnataka
*E-mail: mpsadashiva@yahoo.co.in, mpsadashiva@gmail.com

Areca catechu (Arecaceae) is widely distributed in southern and southeast Asian region including India, China, Indonesia, Malaysia, Philippines, etc. Arecanut seed has been used for medicinal properties more than 2000 years in south Asian countries. In fact, various pharmacological activities have been found in the arecanut seed extract or its constituents. Prevention of oxidative stress induced diseases is an urgent problem in all over the world. Traditional use of the plant for medicinal properties is to be documented for their possible use as future medicines or drugs. There is a need for identifying native natural plant sources to acquire to their recognized medicinal properties, which may widen them to use as new therapeutics for various diseases.

Key words: arecanut; oxidative stress; pharmacology; phytochemicals

Variation in anti-oxidant content in different types of areca nuts and processing methods

Laxminarayan Hegde* and Manju M. J.
Horticultural Research and Extension Center (UHS, Bagalkot),
P.B. No. 23, Banavasi Road, Sirsi-581401, UttaraKannada, Karnataka
* E-mail: hegdelax@gmail.com

Arecanut (*Areca catechu* L. Family: Palmaceae) is a tropical fruit, which is also called betel nut/*supari* and is widely distributed in different parts of the world. The arecanut contains many nutritional and functional components with different bioactivities. Since the 4th century A.D., humans have consumed the arecanut as food and medicine. Now, it is estimated that over 600 million individuals consume arecanut worldwide. Arecanut has main constituents like polyphenols, fat polysaccharides, fiber and protein. Besides these, nuts contain alkaloids, arecoline (0.1- 0.7%) and others in trace amounts such as arecadine, guvacoline and guvacine.

Fourteen different processed areca nut types from Uttara Kannada district from four selections/variety (Sirsi selection, Sagar type, Mohitnagar and Mangala variety) were evaluated for total anthocyanins, phenols, flavonoids, total anti-oxidant property (FRAP) and radical scavenging ability (DPPH). The mean of three replications showed that Sagar (Bette) type recorded maximum phenols (304.58mg/g dw), flavanoids (108.89mg/g dw) and DPPH (114.79mg/g dry wt.) while maximum FRAP of 103.65mg/g dry weight was in Sirsi *bette* type. The highest total anthocyanin content was recorded in Sagar *bette* (3.51mg/g) and Sagar *gotu* (3.50mg/g).The DPPH values were higher in ripe areca nut types compared to tender nuts. The estimated values were quite high compared to known plant sources of anti-oxidant property like tea and betel leaf. The results clearly showed that areca nut evaluated from different arecanut geographical locations and the processing types has significant effect on anti-oxidant properties available in areca nut. There is a great potential for areca nut to use as potential health product.

Key words: anti-oxidant potential; arecanut processing; FRAP

Arecanut and Human Health - challenges

Dr. Sathyanarayana Bhat*, MD (Ayurveda) PhD. (Botany)
Ayurveda consultant, cancer Management Therapist, Writer, Columnist, Gold Medalist, Sahithya Academy awardee and Naturalist

*E-mail: sathyanarayana.bhat@gmail.com

Do you think Areca nut is medicine?? No, its Food!!

Traditional use of medicines is recognized to learn about the potential of future medicines Arecanut was referred in many Indian ancient books, mythologies and classical Ayurvedic works. It is known as 'fruit of divine origin' in Hindu religious ceremonies and mentioned in many Ayurvedic classics for many diseases. The people from the Vedic times used the Arecanut along with betel leaves and some other condiments for its medicinal values. Arecanut has been in use for many purposes such as medicines, beautyaid, food coloring, disposable plates and cups etc.

Now the world is only concentrating towards adverse effect of Arecanut consumption, but the various pharmacological activities have been found in the areca seed extract or its constituents. It can be used as single drug formulation in Syphilis, intestinal worms, stomatitis etc. *Pugakhanda* is a popular formulation used for treating vomiting, gastritis, dyspepsia, abdominal colic pain, diabetes, obesity, and acts as natural aphrodisiac.

Arecanut is rich in several essential nutrients such ascalcium, phosphorus and vitamins. In fact, various pharmacological activities have been found in Areca seed and it requires proper clinical trials. Many large-scale industries have to encourage the cultivation of Areca tree in order to promote its alternate uses.

Clinical evaluation of Dia Ketechu **a compound herbal formulation in Non- insulin dependent diabetes**

Jeddu Ganapathi Bhat* and Manorama G. Bhat
Jeddu Ayurveda Specialty hospital
At & PO: Alike 574235 D.K. Dt. Karnataka.
* E-mail: dr.jeddu@gmail.com

Current research indicates that diabetes is a multifaceted health problem originated due to stress, metabolic dysfunction and life style imbalance, involving not just carbohydrate metabolism but more than that the lipid metabolism and hormonal functions.

In Ayurveda, Charaka states very particularly that "disorders like Prameha are due to deficiency of *Vikara Vighata Bhava* better known as factors responsible for prevention of diseases. Especially in case of *Prameha*, three things *viz: - Nidana, Dosha* and *Dushya* are assorted in such a way that it will damage or alter the Vikara Vighata Bhava (Cha. Ni.4/4).

Thus management of *Prameha* has three dimensions,

- First to recognize and avoid the Nidana or causative factors like sedentary life style and faulty food habits.
- Secondly to extricate Bahudrava Sleshma the special morbid factor (Dosha Vishesha) in the causation of *Prameha*.
- Finally to remove or repair the damaged body factors (Dushya Sangraha)*viz:- BahuMeda, AbaddhaMeda, Mamsa, Kleda, Shukra, Rakta, Vasa, Majja, Lasika, Rasa* and *Ojus*.

With these considerations, after a lone research of more than 15 years since 1996, Jeddu Ayurvedic Pharmaceuticals, pioneer in the field of Ayurvedic medical research and formulation, has developed a compound herbal formulation known as Dia Ketechu tablets consisting of 21 ingredients especially areca nut (*Areca catechu* Linn.).

Dia Ketechu an ideal combination of naturally tested ingredients having marked anti-diabetic action is totally free from iatrogenic effects like gastric irritation, constipations cramps etc, a purely herbal compound preparation consisting of time tested Ayurvedic medicinal plants having wider action as *Kapha-Medohara* and chiefly as *Pramehahara* action.

Therapeutic use: Effective in the management all verities of *Prameha* especially in non Insulin dependent Diabetes mellitus. Moreover, Dia Ketechu found to correct other associated health problems like obesity, renal dysfunction and indigestion etc. by correcting the functions of Dhatvagnis.

Diseases referred as of metabolic origin such as Prameha vis- a- vis Diabetes, and Medoroga Vis- a- vis Obesity are becoming rampant. According to Ayurveda both are of same origin requiring *Kaphahara - Medohara* type of management so as to correct *Agni Dosha* or metabolic dysfunction. In this context the ingredients of *Dia Ketechu* possess marked *Depana, Pachana, Kapha Hara, Medohara, Srotoshodhana, Rasayana* properties ultimately culminating in *Pramehagna* (Anti diabetic) activity. A detailed clinical evaluation of the product was carried out and results are presented in the paper.

Experimental evaluation of anti-diabetic activity of Areca tea on Wistar albino rats

Ravishankar B, ***Naveen Chandra****, Bhat Sudhakar, Ravi M
Sri Dharmasthala Manjunatheshwara College of Ayurveda and Hospital,
Kuthpady, Udupi-574118
* *E-mail:* naveenchandra.nh@gmail.com

Diabetes is one of the five leading causes of death in the world, with Type 2 diabetes occurring more frequently than Type 1. Management of diabetes without side effects is still a challenge and therefore new strategies need to be examined. Because of difficulties in human research, animal models of diabetes are useful research tools for this purpose and rodent models of Type 2 diabetes are the first choice. The aim of this study is an overview on one of the most frequently used models of Type 2 diabetes in rat, induced by streptozotocin and nicotinamide. Informal information from people consuming Areca tea especially those with diabetes indicated reduction in serum blood sugar level and improvement in diabetic related symptoms of degeneration. The present study was designed and carried out to ascertain whether any experimental basis could be provided for this observation.

Adult Wistar rats (180 ± 10 g) of either sex were obtained from the animal house attached to SDM Centre for Research in Ayruveda and Allied Sciences – Udupi. The study was initiated after obtaining the approval of the Institute's Animal Ethics Committee (SDMCRA/IAEC/GR-AD-01dated 14/03/2017). Diabetes was induced in overnight-fasted rats by administering single intraperitoneal (i.p.) injection of freshly prepared streptozotocin (STZ) 54 mg/kg b.w. followed by 60 mg/kg of nicotinamide (NIC) in 0.1 M citrate buffer (pH 4.5) in a volume of 0.5 ml/kg b.wt. (2). The induction of diabetes was confirmed by measuring fasting blood glucose levels after 48 h of induction. Rats with fasting blood glucose of more than 200 mg/dl were considered as diabetics and they were divided randomly into five different groups of six animals each as follows.

- Group I: Normal control
- Group II: Diabetic control
- Group III: Diabetic rats treated with Areca Tea Lower dose (200 mg/kg)
- Group IV: Diabetic rats treated with Areca Tea higher dose (400 mg/kg)

Acute toxicity study

The test formulation did not produce any mortality at the highest dose tested – 2000mg/kg. po. It also did not affect the behavioural parameters in a significant manner. Thus the LD 50 value seems to be much higher than 2000 mg/kg.

Anti diabetic activity

Test formulation at lower dose level produced only a marginal non-significant decrease in serum blood sugar level; whereas significant reduction was observed at higher dose level ($p<0.01$). Similarly highly significant decrease was observed in the reference standard Glibenclamide administered group also ($p<0.01$).

Test formulation at lower dose level produced moderate and statistically a non-significant decrease in serum Hb1 Ac level; whereas significant reduction was observed at higher dose level. Similar but highly significant decrease was observed in Glibenclamide administered group also.

The moderate to severe degenerative changes in the form of decrease in the number of islets, decrease in the size of islets, vacuolization of the islet cells and degranulation in STZ induced group had a significant reversal in Areca Tea treated group.

Conclusions

Analysis of the data indicates significant anti-diabetic activity in Areca tea in experimental diabetes. The activity profile of this formulation is similar to the activity profile of the reference standard- Glibenclamide which is a drug where as the test formulationis a health drinks. Areca tea can also provide protection to heart and to some extent to kidneys against DM induced degenerative changes. One of the significant findings is the observation that the cellularity and number of islet cells is increased by Areca tea indicating significant cytoprotection to pancreas. This opens up possibility of using it as preventive measure.

Arecanut and Human Health: Some Observations

D. Jayarama Bhat,* Ph.D., D.Sc.
Formerly, Professor of Botany, Goa University, Goa
* E-mail: bhatdj@gmail.com

Areca nut palm (*Areca catechu* L.) is cultivated extensively in many parts of India and S.E. Asian countries. For centuries, we depended on areca nut, primarily for chewing and secondarily in traditional medicines. As an ingredient of chewing pan, with betel leaves and slaked lime (calcium hydroxide), areca nut is used by more than 200-400 million people, mainly Indo-Asians and Chinese, both men and women, of all age groups, across the societies around the world. In India, areca has a long history of use and deeply ingrained in many of our socio-cultural and religious activities. Efforts were also made, in recent times, to see if areca nut can be used as a beverage, colourant, stimulant, etc. Two regional institutes, CPCRI, Vittal and CAMPCO Ltd., have done commendable work in enhancing areca production and further improving the trade.

From medical point of view, main concern is the presumed relation between areca nut use and development of mouth cancer (oral squamous cell carcinoma) and its precursor's leukoplakia and submucous fibrosis.

Perusing all available literature, sourced from around the world, scientists have compiled information on areca nut and its uses, in the form of review articles. These tell us that areca nut (paste or extract) has been used in ancient clinical practices for its laxative, digestive, carminative, anti-ulcer, anti-diarrhea, anti-helmintic, anti-malarial, anti-hypertension, diuretic, wound-healing, antibacterial, hypoglycaemic, anti-heart-burn activities. The main alkaloid in areca nut, arecoline, increases acetylcholine by inhibiting acetylcholine esterase activity in the brain and thereby decreases Alzeheimer's disease symptoms. Consumption of areca reduces plasma cholesterol and triglyceraldehyde by inhibiting their absorption in small intestine. Charred arecanut has cholesterol lowering effect and in obesity management.

Perusal of published reports indicates that, while highlighting the ill-effects of areca, conclusions were drawn hastily and the methods used for experiments lacked clarity. Several studies conducted were substandard. Therefore, correlating such results to chewing arecanut seems wrong as these processes are different from one another. Some researchers studied the effects of arecanut using very high doses and claimed arecanut is harmful. Some arrived

conclusion with very small sample size. In several papers, the quality of arecanut or its chewing products used for experiments were not of standard but simply blamed arecanut for all ill effects. In view of the complex compositions of herbal medicine of areca, it is felt that a coordinated international effort is needed to control the quality and establishing a standardized finger-print for *A. catechu*.

Areca Nut: Traditional exploit and scientific rationale

Hemand Aravind*
Consultant Scientist
Santhigiri Research Foundation,
Thiruvananthapuram-695 586
* E-mail: hemantharavind@gmail.com

Areca catechu L. (Palmaceae), commonly known as Areca nut in English, is a perennial tree cultivated in Indian subcontinent and traditionally used for several medicinal purposes. Almost the entire arecanut is maintained and harvested mainly for its seeds. The seeds are chiefly used along with betel chewing. About ten percentage of the world population are under the spell of this habituation. Arecanut is chiefly used, during older times, to cure oral ulcers, bleeding gums, inflammation of the gums, indigestion, constipation, fatigue etc. It is a powerful anthelmintic medicament, especially against tapeworms. Chewing arecanut together with the other ingredients such as betel chew (*Thaamboolam*) can render the body with a handful of other benefits. The present study evaluates the phytochemical contents of *A. catechu* nut using its methanol extract. The phytochemical analysis of *A. catechu* nut revealed the presence of quinines, sterols, tannins, carbohydrate, glycosides and phenols. Evaluation of nutritional values discovered that the methanol extract contains significant amount of carbohydrate, protein and crude fiber. Anti-inflammatory studies with *in vitro* models showed that areca nut posses considerable protein stabilization and HRBC membrane stabilization activity.

Key words: anti-inflammation; nutritional composition; phytochemical constituents

Pugaphala in traditional medicine of Tulunadu

Subrahmanya Prasad K*
Department of Botany, Nehru Arts & Science College, Kanhangad,
Kasaragod – 671 314, Kerala
* ***E-mail:*** prasadks83@gmail.com

Ancient cultures all over the world have exhibited a deep reverence for Nature. India has one of the oldest, richest and most diverse cultural traditions known as folk tradition associated with the use of plants. The long and intimate association of our ancestors with the flora and their dependence made them the kings of extensive knowledge. *Tulunadu*, the ancient heritage site situated along the west coast of India is not an exception. *Tulunadu* is the *Tulu* speaking area, lying along the Malabar Coast, consisting of Dakshina Kannada and Udupi districts of Karnataka and the northern parts of Kasaragod district of Kerala. *Tulunadu* is blessed with more than 1100 medicinal plants having diverse utility in the primary health care. One among them is the *Pugaphala* (*Areca catechu* L. - arecanut) which is the main ingredient of our traditional *tambula* – a healthy masticatory. Field visits, interviews and discussion with the knowledgeable persons were carried out in the nook and corner of *Tulunadu* to collect data about the use of arecanut in traditional medicine. This was carried out after convincing the local people about academic significance and bonafide intention of the study, both oral and written (Prior informed consent – PIC) consent were taken from them as per the CBD guidelines. Analysis of data makes it obvious that arecanut is an integral part of human life and culture in *Tulunadu*. Local people make use of this plant in their religious rituals, daily life and to alleviate different health problems. It is used for the treatment of 33 diseases through 26 herbal preparations of which only 6 are multi drug formulations. Among different plant parts, fruit (ripe and tender) is the most commonly used part followed by leaf, tender leaf, seed, inflorescence, root, fruit rind and bark. Medicine is administered usually either as extract or paste followed by decoction, powder and oil. This paper elucidates the ingredients of traditional *tambula*, its health benefits and traditional medicinal uses of betel nut palm. Detailed account of method of drug preparation, dosage, modes of drug administration and duration of treatment are also provided.

Key Words: *Tulunadu*, Folk medicine, *Pugaphala*, Traditional uses

Arecanut, *Areca catechu* L., in folk medicine

Shankara Bhat Badanaje*

Trustee, Arecanut Research and Development Foundation, Mangaluru: 575 001, DK, Karnataka.*Mobile: 9448081177

People introduced arecanut, *Areca catechu* L. along with the leaf of betel vine (*Piper betle*) for their medicinal values from vedic times. People also gave social sanctions and religious importance for these products in the Society. Ancient ayurvedic scholars such as Charaka, Sushruta, Vaghbhata, Chakradatta, Bhavamista and several others had long back recognized the use of arecanut or betel nut along with certain other herbs to cure several ailments. Medicinal use of arecanut in folk medicine is well known in villages since very long time. Some of them are presented in this paper.

- Arecanut is used as a good worm expeller both in humans and his livestock. Arecanut powder 2.5gms in equal quantity of fresh lime juice is given after 12-14 hrs of fasting. It acts as a good vermifuge against both round worms and tape worms.
- To stop bleeding of cut wounds village folk dust the arecanut powder which is astringent in its action.
- The decoction of arecanut is gargled for ulcerative stomatitis, sore throat, tooth ache and pharyngitis by village folk.
- Powders of activated charcoal of arecanut and turmeric 10-30 gms with buttermilk is given for the treatment of dysentery, heart burn and jaundice.
- Powders of activated charcoal of arecanut 1 teaspoon mixed with magnesium trisilicate 1 teaspoon, thrice daily an hour after food is used with gratifying results for gastric ulcer. It neutralizes the hyperacidity and absorbs the gases in gastrointestinal tract.
- Burnt arecanut powder along with turmeric is used as a tooth cleaner.
- Arecanut is found good to treat bowel complications in humans as well as in animals.
- Apart from these, arecanut is also used for treatment against diabetes, blood pressure, urinary stones, rheumatism, leprosy, seminal weakness, etc.
- Arecanut is known to regulate menstrual cycle in women.
- Extraction of young leaves is used for massaging and to relieve muscle pain.
- To treat ulcers and gangrene, village folk use the paste prepared by mixing arecanut powder with the juice of Bringaraj (*Eliptaalba*) for external application.
- For the treatment of Leucorrhoea there is a well known Unani Medicine called: majoon-e-supari.

Wound healing profile of *Areca catechu* extracts on different wound models in Wistar rats

Shameena Azeez, SenthilAmuthan , ***Sachidananda Adiga***[1]*, Namitha Rao, Nirmala Rao, Laxminarayana A.
[1] Professor, Pharmacology, K.S. Hegde Medical College, Mangalore
* E-mail: adigaiscool@yahoo.com

In this investigation the wound healing effects of different extracts of *Areca catechu* in an animal model was studied. Experimental study was done at department of Pharmacology, Kasturba Medical College Manipal. Male Wistar rats of 12 week old weighing 150-200g were chosen for the three wound models; incision, excision and dead space. Each model consisted of thirty animals to investigate the effect of alkaloid of areca, polyphenols of areca, combination of alkaloid and polyphenols, synthetic arecoline hydrobromide extracts along with one control group (six animals each). In the incision wound model, skin tensile strength was measured using the continuous water flow technique on the tenth day of experimentation. In the excision wound model, wound contraction and period of epithelization were measured. In the dead space wound model, the harvested granulation tissue was assessed or dry weight, tensile strength, hydroxyproline content and histopathological studies. The arecoline alkaloid, polyphenols of areca and the combined formulation enhanced the wound breaking strength in incision wound model. All the extracts increased the wound contraction on the day-4 and day-16 and period of epithelization. In the dead space model only areca alkaloid fraction enhanced the tensile strength of granulation tissue. Our study showed that alkaloid of areca and polyphenols of areca could be used to enhance the healing of burn wounds, leg ulcers and healing after skin graft surgery.

Wound healing, anti-inflammatory and analgesic properties of Arecanut

Sukesh Bhat*

Department of Pharmacology, Kodagu Institute of Medical Sciences, Madikeri
* E-mail: sukesh0148@gmail.com

Arecanut or betel nut (*Areca catechu* Linn.) is commonly used for skin ulcers in Indian traditional medicine. Arecanut oil is prepared and is applied topically for burn wound healing. However, scientific study has not been conducted so far. Hence, this study was aimed to evaluate burn wound healing activity of this nut.

Ethanolic extract of *A. catechu* kernel was prepared and an ointment was made with 2% of this extract. Burn wound was induced by standard procedure. Rats with burn wound model received vehicle, standard drug or test drug. Two other groups were injected with dexamethasone to delay the wound healing process. The dexamethasone treated groups received either vehicle or test drug topically. Wound contraction rate and period of epithelialization were measured and assessed to evaluate burn wound healing activity of arecanut. The collected data were subjected to statistical analysis.

The wound contraction rate was significantly increased inarecanut treated group in all the days compared to control. Period of epithelialization was faster in the drug treated group than control group. It was 15.67 days in the wounds treated with standard drug, Silver sulfadiazinine and 16.0 days in those treated with the arecanut extract. In the non treated control it was 24.33 days. In the dexamethasone treated group there was a significant delay in wound healing process when compared to control. Arecanut extract showed a significant reversal in wound contraction rate and epithelialization period in dexamethasone suppressed burn wound healing models also.

This study shows that arecanut has got good potential as wound healer. However, further study is required to know the compounds responsible for its wound healing property and to understand the mechanism of action.

Anti-ulcerogenic effects of *Areca catechu* L. in Sprague Dawley rats

Reena R. Nelson Anthikat*, A. Michael

P.S.G. College of Arts and Science, Coimbatore 641014.

* ***E-mail:*** reenarn@yahoo.com

The aim of this study was to evaluate the anti-ulcerogenic activity of aqueous extract of ***Areca catechu*** L in ethanol induced ulcer model in Sprague Dawley Rats. Possible mechanism of anti-ulcerogenic potential was investigated and the determination of ulcer index was done using the Merazzi-Uberti and Turba method. Also, an analytical method was used to test the 10% homogenate preparation of mucosa of the glandular stomach to study the protein content and glutathione level. The Sprague Dawley Rats were divided into five groups. Group I was maintained as the control (untreated); Group II was alcohol treated; Group III was treated with alcohol and administered the arecanut extract 1 g/kg.bwt; Group IV was the alcohol treated group and administered the arecanut extract 2g/kg.bwt; Group V was the alcohol treated group and protected using the positive control Ranitidine 50 mg/kg.bwt.In conclusion, aqueous extract of areca nut showed potential anti-ulcerogenic effect compared to Ranitidine, which is a standard gastric anti-secretory drug. This paper describes the rationale for using arecanut extract to protect the animals from ulcer formation.

Key words: anti-ulcerogenic; arecanut; anti-secretory drug; *Areca catechu*

Pharmacological investigation of *Areca catechu* extracts for evaluation of learning, memory and behaviour in rats

M.P.Joshi[1], K.M. Gaonkar[2], I. James[2]
[1]Department of Pharmacology, Faculty of Pharmacy, Goa College of Pharmacy, Panaji Goa -403001
[2]Department of Pharmacognosy, Faculty of Pharmacy, Goa College of Pharmacy, Panaji Goa-403001
* E-mail: joshimadhusudan@rediffmail.com

As human being evolves the life style continues to change. This change in life style is accompanied by changes in disease pattern. The major shift in the life style in India is seen in last two centuries when agrarian society was slowly changed to industrial society. The consumption of plant products was also affected. Betel nuts were consumed to large extent and also occupied an important place in rituals. The consumption of betel nut with betel leaf was a custom. The present study was done to evaluate learning and memory in rats using radial arm maze. The extract used for study was of two several types of *Areca catechu* namely, wet and dried *Areca catechu* extract. Three groups of rats each consisting of seven animals were taken. Test group were given 500mg/kg p.o of wet *Areca catechu* extract and dried *Areca catechu* extract respectively. It was noted that after continuous treatment with extract, group three which received wet *Areca catechu* extract showed greater reduction in latency to find feed, which was of statistical significance ($P<0.001$). Latency to reach feed recorded for control group of rats using Radial arm maze was found to be 4.249 ± 0.244minutes on day one and 2.293 ± 0.356minutes after 21 days It was observed that wet *Areca catechu* extract showed greater increase in spatial memory and learning in comparison to the control group of rats. Hence increase in spatial memory could be because of higher amount of arecoline present in wet *Areca catechu* extract.

Key-words - *Areca catechu*, radial arm maze, memory, and learning

Arecanut husk and its protective effect on the tobacco induced cytotoxicity in the cultured human oral mucosal cells

Maji Jose, Ipe Varghese, ***Manjula Shantaram****
Dept of Biochemistry, Mangalore University, Mangalore
* E-mail: manjula59@gmail.com

Arecanut husk used by the rural folk of Dakshina Kannada for oral health and hygiene has shown significant antimicrobial activity against oral pathogens. In addition, arecanut husk exhibits significant free radical scavenging and antioxidant properties. Tobacco causes oxidative stress in cells exposed to them; it produces genotoxicity and also triggers cytotoxic effects primarily by inducing apoptosis. Arecanut husk is capable of reducing the tobacco induced cytotoxic and genotoxic effect as well as oxidative stress. Various experiments conducted by our team confirm the aforesaid properties of areca nut husk. A detailed discussion with the valid data will be made during the presentation.

Key words: antioxidant activity; arecanut husk; genotoxic effect; free radical scavenging

Anti-hyperglycemic activity of *Areca catechu* flowers

Virupanagouda Police Patil*, Rupesh Ghate,Nanjappaiah Hanakunte Matha, Navanath Vishwanathappa Kalyane and ShivakumarHugar
P.G. Dept. of Pharmacology, BLDEA's College of Pharmacy,
BLDE University Campus,
Bijapur-586103, Karnataka
* E-mail: patllk183@gmail.com

This study was conducted with an objective ofevaluating the anti-diabetic effect of *Areca catechu* flower extracts in alloxan induced diabetic rats. Petroleum ether, ethanol and aqueous extracts of *A. catechu* flowers were administrated orally at the dose of 500 mg/kg for hypoglycemic effect in alloxan induced diabetic rats for 21 days. The anti-diabetic potential was ascertained through various biochemical parameters and body weight. Preliminary phytochemical investigation reveals high phenolic constituents in both the extracts. The results of anti-diabetic investigation revealed that, the ethanol and aqueous extracts of *A. catechu* flowers have shown a significant anti-diabetic efficacy in alloxan induced diabetic rats. Further, the anti-diabetic effect was confirmed by significant restoration of altered levels of biochemical parameters and improvement in body weight. The significant anti-hyperglycemic effect of ethanol and aqueous extracts in alloxan induced diabetic rats could be due to high phenolic constituents. Hence, the present research provides the scientific validation for the arecanuts in the management of diabetes.

Key words: anti-diabetic; alloxan; *Areca catechu;* phenolics

Arecanut – A Blessing or a Curse

Malathi N* and Aarthi
Dr. N. Malathi, Vice Principal & Head
Department of Oral Pathology & Microbiology
Faculty of Dental Sciences,
Sri Ramachandra Medical College & research Institute, Chennai
*E-mail: narasimhan.malathi@gmail.com

Indian culture and tradition hold areca nut and betel leaves in high esteem. In the Indian subcontinent the chewing of betel leaf and areca nut dates back to the pre-Vedic period of Harappan Empire. Arecanut consumption is primarily seen in Asian countries like India, China, Bangladesh and Pakistan. Arecanut consists of several constituents such proteins, lipids, carbohydrates and alkaloids, one such alkaloid is *'arecoline'* that leads to alertness, increased stamina, a sense of well-being and euphoria (Central nervous system stimulant).It is also known to stimulate salivation, thus aiding in digestion. Excess and routine consumption of arecanut leads to addiction and the development of potentially malignant disorders such as *'Oral Submucous fibrosis*. On the other hand, recent research has proven the effective antimicrobial property of arecanut extract against *enterococcus fecalis* and has been proposed as a root canal irrigant when compared to chlorhexidine. It has also been reported that areca nut extract exerts a direct antimicrobial effect against oral bacteria, including *Streptococcus mutans, Streptococcus salivarius, Candida albicans* and *fusiform nucleatum*. The questions now arises whether arecanut is a blessing or curse, whether the use of arecanut should be forbidden or should it be considered for its antimicrobial efficacy and utilized in the field of dentistry.

Arecanut: Potential Pharmacological Activities

Dr. A. Ruckmani*
Professor and Head, Department of Pharmacology,
Chettinad Hospital & Research Institute, Kelambakkam, Chennai.
**E-mail:* ruckmani.nirmal@gmail.com

The present paper will provide a short introduction to areca palm, a brief account of the documented pharmacological actions and an overview of the various research studies conducted in different countries including India on arecanut in the last ten years.

From the ancient Tamil Sangam literature we learn that the areca palm has been an integral part of Tamil culture. Therefore, it is no surprise that the people knew about its medical uses. Use of this plant is closely associated with cultural and religious practices in India and other countries.

The extracts of areca nut have been reported for their actions on the nervous, cardiovascular, gastrointestinal, respiratory, endocrine and genitourinary systems. The association between areca nut chewing and oral cancer as well as oral submucosal fibrosis and the molecular mechanism behind this association has been extensively evaluated. The maximum number of research studies in this area has been done in Taiwan and China. In India areca nut has been evaluated for the prevalence of oral cancerous and pre cancerous lesions, the behaviour and attitude of areca nut and betel quid chewing, the antiinflammatory, antidepressant, anxiolytic, organ toxic and inflammatory properties.

The details of these pharmacological activities will be presented in the conference.

Pharmacological/alternative uses of arecanut: Antimicrobial and anticariogenic activities of Arecanut

Rekha Rai*

Professor & Head, Dept. of Microbiology,

K.S. Hegde Medical Academy, Mangaluru, 575108, Karnataka

* E-mail: rairekharai@rediffmail.com

The objective of this study is to find out antimicrobial activity of arecanut against human pathogenic and oral cariogenic bacteria. This study was aimed at assessing the effects of areca nut extract against a series of pathogenic bacteria and cariogenic bacteria.

Extraction of areca nut was carried out by CPCRI Kasaragod. Testing of antibacterial and anticariogenic activity of the extract was carried out. The antibacterial activity of the extract of arecanut was tested individually on gram positive and gram negative ATCC bacterial strains. The purely isolated extract of arecanut was tested against these standard strains by the following methods

1. Antibacterial assay by agar diffusion method
2. Determination of MBC (Minimum bactericidal concentration) levels.

The arecanut extract was tested at various concentrations ranging from 25mgs/ml to 1000 mgs/ml for its antibacterial and Anticariogenic activities against standard strains. The study revealed that *Pseudomonas aeruginosa* and *Candida albicans* showed sensitivity to synthetic arecoline and *Staphylococcus aureus* and *Enterococcus faecalis* were sensitive to ethanol extract of arecoline at a very high concentration of 1000mg/ml. The oral Streptococci were resistant to the extract upto the concentration of 1000 mg/ml.

An appraisal of research work done on medicinal uses of arecanut, *Areca catechu* L.

Ravichandra V*
Associate Professor of Pharmacology,
K.S. Hegde Medical Academy, Mangaluru, 575108, Karnataka

* E-mail: ravi75chandra@yahoo.co.in

Arecanut, *Areca catechu* L. (betelnut or supari) chewing habit dates back to the period of Ramayan. Arecanut mixture taken after meals sweetens the breath producing energizing effect and euphoria. Major constituents of arecanut include polyphenols, tannins, fats and alkaloids. Of all the alkaloids, arecoline is the main active component with potent cholinergic activity resembling muscarine. Recent reports of harmful effects of chewing arecanut are produced mostly by incorrect evidences.

Arecanut is mainly used for mastication. Apart from that, it has considerable medicinal uses as well. Arecoline was incorporated into British Pharmacopeia and Indian Pharmacopeia due to its anthelmintic properties. Arecanut constituents have laxative and diuretic effect. Arecanut has astringent principles and prevents tooth decay. Though there is little clinical evidence to support the clinical use of arecanut, it might help those suffering from Alzheimer's disease and other psychological disorders such as schizophrenia and depression. Therefore, an explorative work on medicinal uses of arecanut as per three systems of medicine viz., Ayurveda, Yunani, Sidda and modern research work done on its medicinal properties is being evaluated.

Consumption pattern and health issues of arecanut chewers in Karnataka

C.T. Jose*, S. Keshava Bhat, K.P. Chandran and Ananda Gowda
ICAR- Central Plantation Crops research Institute Regional Station, Vittal-574 243
* E-mail: ctjos@yahoo.com

Arecanut chewing is an indigenous habit notably in Central, South, and Southeast Asia, and some South Pacific islands. World Health Organization estimated that about 600 million people use betel nut around the globe. It is an essential cultural and social tradition in several countries. It is perceived to have medicinal values; including oral hygiene, appetite as well as saliva production. It is a common practice to offer these products to guests in important social gatherings, weddings and other religious events. This habit is widely accepted among all strata of society, including women and children. A field survey was undertaken in three districts of Karnataka to study the pattern of arecanut chewing, perceptions about health benefit, risks and socio economic factors. Areca nut chewing with tobacco was common than without tobacco in these regions. Majority of the respondents thought that chewing had beneficial effects like increasing taste, digestion, pleasure and reducing tooth pain. The present study did not find any significant difference in health issues between arecanut chewers and non-chewers. The validity of the perceived benefits of chewing reported by the participants needs further study.

Impacts of consuming arecanut and its by-product on human health

(A medico sociological study-with special reference to Tarikere Taluk, Chickamagalur Dist, Karnataka state)

G.D. Narayana and ***R. Devananda****
Department of PG Studies and Research Sociology
Bharthiar University, Coimbatore Tamil Nadu
* E-mail: devanandar59@gmail.com

Arecanut is an important palm species in India and in some countries of South Asia. Arecanut plays an important role in Indian society socially, culturally, economically, and in religious activities also. In India arecanut is grown in 4,72,000 hectare area with approximately 7,36,000 tonnes of arecanut production. Karnataka state is a major grower of arecanut in India. Arecanut is being imported from Indonesia, Bangladesh, Myanmar, Thailand, Srilanka, etc. Arecanut is generally used for masticatory purpose and other forms of arecanut are also used. Arecanut has got various chemicals and has good medicinal values. The major constituents are polyphenols, fat, polysaccharides, fiber and protein. Alkaloid is present as a minor but significant constituent. Various types of arecanut are available; api, Saraku, Bette, Rashiedi, Gorabalu, White Chali, etc and by-products are Paanbeeda, Paan masala, sweet supari, arecanut wine, arecanut based soft drinks, arecanut based soaps, Paansupari nectar, areca tea and others. Due to modern systems of medicines and discovery of novel therapeutic molecules, the traditional knowledge and use of arecanut for medicinal purposes is decreasing day by day. Hence, objective of this study is to collect the information about arecanut and its by-products and to know the impacts of consuming arecanut and its by-products on human health. We propose a hypothesis that consuming arecanut and its by-products are also having positive impacts on human health. In this study, we used random sampling method on selected 20 respondents. We have used direct interview method for collection of information by respondents. And also used primary and secondary sources to collect the data.

Keywords: Arecanut, health, commercial crops, CFTRI, FSSAI, IIMS

Arecanut (betel nut) is not carcinogenic to humans: Research results

S. Keshava Bhat[1]*, D. Ashwin[2] and Sukesh Bhat[3]
[1]Arecanut Research and Development Foundation®, Mangaluru: 575 001, Karnataka
[2]Department of Pedodontics and Preventive Dentistry, Kannur Dental College, Kerala
[3] Department of Pharmacology, Kodagu Institute of Medical Sciences, Madikeri, Karnataka
* *E-mail:* ardf1998@gmail.com

Arecanut or betel nut is the endosperm or seed of an oriental, slender and tall palm, *Areca catechu* L. Since time immemorial, arecanut is being used for chewing or mastication throughout the world as it is believed to have a stimulating effect and helps in digestion apart from several medicinal uses. In India, the use of areca nut has been noticed as early as 1300 BC and the practice of its chewing from 650 BC. In other countries such as Vietnam, the antiquity of arecanut even goes back to Bronze Age. In several parts of the world, arecanut and betel leaf are considered as sacred and no ceremonial function is complete without them.

Arecanut has an important place in the ancient system of medicines in several countries such as India, China, Bangladesh, Philippines, etc. The World Health Organization has listed out as many as 25 beneficial effects of *A. catechu* and included areca palm in the list of medicinal plants of Papua New Guinea. Most of the folklore medicinal properties of arecanut are now validated with proper scientific evidences. It has antioxidant, anti-inflammatory and analgesic, anti-diabetic, hypolipidemic, antibacterial, anti-fungal, anti-malerial, anti-viral, anti-HIV, treatment for AIDS, anti-aging, treatment for Alzeimer's and Schizophrenic patients, wound healing, anti-ulcer, anti-migraine,antihypertensive, antidepressant, anti-allergic, anthelmintic, aphrodisiac, anti-venom, hepato-protective, cytoprotective, and so on. In China, as many as 30 medicines are prepared using arecanut as one of the ingredients are already available in the market for the treatment of several disorders. In India, certain Ayurvedic medicines with Arecanut as ingredient are now being prescribed by Ayurvedic doctors for the management of diabetes, cholesterol, cough and cold, etc.

However, there are several scientific reports which say that arecanut chewing is dangerous and even cause cancers. Contrary to this, there are more than 20 Research publications which say that arecanut chewing is not dangerous but is beneficial in human beings. Added to this, there are some scientific reports which even say that arecanut cures cancers. Such reports are collected and discussed in this paper. One such papers is that of Kumari *et al.* 1974, Inhibitory activity of *Areca catechu* on the development of mouse skin tumors induced by the chemical carcinogen 3.4,benzpyrene. *Journal of Plantation Crops*, 2(1):23-29. The irony is that most of these scientific reports are sidelined and not even cited or discussed properly by most of the research workers who say that arecanut is carcinogenic.

Arecanut and Cancer - A Lawyer's Perspective

Shri Khandige Narasimha Bhat*
Senior Advocate, Supreme Court of India- Former Additional Solicitor General of India
* *E-mail:* knbhat1@gmail.com

"The majority of cancers, some 90–95% of cases, are due to genetic mutations from environmental factors.[3] The remaining 5–10% are due to inherited genetics.[3] Environmental, as used by cancer researchers, means any cause that is not inherited genetically, such as lifestyle, economic and behavioral factors and not merely pollution.[32] Common environmental factors that contribute to cancer death include tobacco (25–30%), diet and obesity (30–35%), infections (15–20%), radiation (both ionizing and non-ionizing, up to 10%), stress, lack of physical activity and pollution.[3][33]

It is not generally possible to prove what caused a particular cancer because the various causes do not have specific fingerprints. For example, if a person who uses tobacco heavily develops lung cancer, then it was probably caused by the tobacco use, but since everyone has a small chance of developing lung cancer as a result of air pollution or radiation, the cancer may have developed for one of those reasons[34]"

The above is a reproduction from the Wikipedia on Cancer available in Google. It needs no explanation. Some 'hit and run' hired scientists in a hurry did a command performance by naming arecanut as carcinogens exposing crores of agriculturists and others depending on it to sure starvation. The government has to put its foot down and stamp out the Taliban type of efforts to kill the innocent agriculturists.

Arecanut and Carcinogenesis-An Oncologist's Viewpoint

Dr. Vijayalakshmi Deshmane*
Former Professor and Head, Kidwai Memorial Institute of Oncology, Bangalore
*E-mail: drdeshmane050@gmail.com

THE WHOLE WORLD IS IN SEARCH OF PEACE AND HAPPINESS
LIFE IS PRECIOUS
SURVIVAL IS IMPORTANT
I AM MY HABIT

It is high time that every individual, has to take up the responsibility of his/her own health.

In 1985 the International Agency for Research on Cancer concluded that there is limited evidence to conclude that areca chewing may directly lead to oral cancer.

Public health measures to quit areca use are recommended to control oral diseases.

Knowledge dissemination to help people adopt behaviour patterns to improve their health and decisions making process and to provide required public health education and training to promote lifestyle modifications are key to confronting the challenge.

An inreased risk for the development of oral malignancy in "ARECANUT only users" is reported.

Other conditions that have been associated with use of ARECANUT include

- Cardiovascular disease
- Diabetes mellitus
- Asthma

Aggressive counseling in tobacco cessation have to be implemented.

Alert for an epidemic of oral cancer due to use of the BETEL QUID substitute, GUTKHA and PAN MASALA

ORAL CANCER IS A MAJOR PROBLEM IN THE INDIA

The greatest threat of the oral cancer burden exists among the lower socioeconomic strata. Prevention through action against risk factors, especially tobacco will be key to reducing the burden amongst these groups.

Clean, healthy& nutritious, vegetarian diet keeps us healthy and active.

Health education is needed and health warning should be enacted including spitting.

Outright bans or restriction will probably prove to be counter-productive.

Further research is needed on the biomedical and psycho-social consequences of ARECA usage.

Need for the sustenance of research on Arecanut

K. Satyamoorthy*
School of Life Sciences, Manipal Academy of Higher Education, Manipal-576104
*E-mail: ksatyamoorthy@manipal.edu

Plantation crops such as areca nut is major economic product in such states as Karnataka, Assam and Kerala providing livelihood to thousands of people. The change in the scenario happened by design wherein to meet the demand, large scale cultivation of areca nut was encouraged by Government of India in early fifties and sixties of last century. This led to India being one of the largest producers of areca nut in the world. Now the areca nut use and misuse potentially leading to prevalent cancers in India such as in the oral cavity is popularly highlighted in general as well as scientific literature. While the discussion on various aspects effects and ill-effects of areca nut use are continuing, it is clear that there are opportunities to exploit the beneficial properties. Being a popular psychoactive substance next to nicotine, alcohol and caffeine, areca nut can be a treasure trove for substances of pharmacological interest. However, large scale research initiatives on various uses are sadly missing. Advances in knowledge and technologies have pervaded in to all aspects of research. For example, contemporary genomic technologies are sporadically being deployed to understand nature of the plant but are without vision or direction. Therefore, attempts are needed to focus on beneficial effects such as been described as for various biologically active contents such as tannins, polyphenols, flavonoids, carotenoids, their pathway analysis and application to conditions including effects on gastrointestinal function, obesity and diabetes.

Does pure arecanut chewing really cause oral and oropharyngeal malignancy? Findings of an epidemiological case history studies to revisit this question

Keshava H. Korse*
Director, Centre for Conservation Biology & Sustainable Development
Sirsi-581402 Karnataka
*E-mail: keshavakorse@gmail.com

India recorded about 3.9 million cancer cases in 2016, as per National Cancer Registry documented by National Centre for Disease Informatics and Research (NCDIR) of Indian Council of Medical Research (ICMR). More than 40% of them are of preventable kind, such as lung cancer and mouth cancers. Oral and oropharyngeal cancers are the commonest among such head and neck malignancies cases and oral cancer ranks first among cancer-related death in men in India Human papilloma virus, smoking, alcohol consumption and tobacco chewing are found to be the common etiological factors.

This paper deals with the findings of a short term epidemiological studies done in *Uttara Kannada* district, Karnataka India. It basically tried to revisit the question whether pure arecanut chewing is positively correlated to oral cancer manifestation. It is a short term pilot study done in a limited population. This retrospective study tried to determine the distribution of oral and oropharyngeal malignancies in terms of family occupation, sex, age and personal habits. 14 clinically and histo-pathologically confirmed oral and oropharyngeal malignancies patients were met and interviewed during 2015-16. Discussions were also held with their immediate family members in order to assess the possible causes that might have lead to the diseases manifestation.

Buccal mucosa was the commonest site of lesions among them. While more than 50% (8/14) of them had history of smoking, another 35 % (5/14) had history of smokeless tobacco consumption. Almost One-third of the patients had history of alcohol consumption. However, less than 10% patients had no addictions and she was a female (1/14). All patients who had the history of arecanut chewing were found to be users tobacco either in the form of commercially available *Ghutka* (4/14), or handmade *Mama*, prepared by rubbing Arecanut powder with tobacco (3/14) or tobacco–areca nut quid (3/14). That means they were neither pure areca nut chewers nor the consumers of traditional *Tamboola* (without tobacco).

Areca nut is declared to be the potential cancer causing agent by International Agency for Cancer Research (IACR) of WHO. As per the widely published papers in peer reviewed journals, alkaloid Arecolin present in areca nut is responsible for this. But this study indicates that there is huge lack of knowledge at epidemiological understanding, as patients with oral cancer studied are basically tobacco chewers, along with areca nut. And those arecanuts are also not farm fresh products, but commercially available packaged products, often added with colouring and fragrant agents. Interestingly, several normal men and women visited in this same study area, who have traditional arecanut chewing practise in *Tamboola* form (along with

lime and betel leaf, without tobacco) are found be very much healthy. Therefore, it indicated strong correlation to between *Tamboola* chewing (without tobacco) and good health in terms of strong bones, good digestion, mental alertness etc. So, this study strongly postulates that pure areca nut and *Tamboola* are not carcinogenic.

Therefore, there is an urgent need of looking at this inter-phase of cancer and arecanut afresh. While laboratory isolated Arecolin might have been carcinogenic when tested on cell lines or lab animals, the whole extract of areca nut which gets consumed in the form of traditional *Tamboola* (without tobacco), might not be cancerous at all. In fact, it could show much beneficial effects on health. So, arecanut needs to be further evaluated for its whole extract with a holistic approach. This is just a pilot study, which clearly indicates the need of taking up such a long term collaborated research works involving epidemiological, histo-pathological, *in-vitro* (cell line) and clinical studies.

NOTES

List of Organisations Corresponded

1. ICMR – National Institute of Cancer Prevention and Research
   Dist. Gautam Buddha Nagar, Uttar Pradesh – 201 301
2. Tata Institute of Fundamental Research, Mumbai 400005
3. Director, WHO FCTC Global Knowledge Hub on Smokeless Tobacco, Dist. Gautam Buddha Nagar, Uttar Pradesh – 201 301
4. National Centre for Biological Sciences, Tata Institute of Fundamental Research Bangalore 560065
5. Tata Institute of Fundamental Research, Hyderabad 500107
6. Indian Institute of Science (IISc), Bengaluru
7. CSIR-Centre for Cellular and Molecular Biology, Hyderabad 500007
8. General Secretary, Society for Indian Medical Anthropology, Mysore- 570026
9. NITTE, (Deemed to be University), Mangalore
10. K.S. Hegde Medical Academy, Deralakatte, Mangalore, Karnataka 575018
11. Kasturba Medical College, Manipal, Karnataka
12. AJ Institute of Medical Sciences and Research Centre, Mangalore
13. Mangalore UniversityMangalagangotri - 574 199 Mangalore
14. University of Mysore, K.G Koppal, Mysuru, Karnataka 570006
15. Kerala Agricultural University, Thrissur
16. Tamil Nadu Agricultural University, Coimbatore
17. University of Horticultural Sciences, (UHS), Bhagalkot
18. Main Horticultural Research and Extension Centre, Bagalkot
    E-mail: adre.uhsbagalkot@gmail.com
19. Regional Horticultural Research and Extension Centre, UHS Campus, GKVK (West), Bengaluru, E-mail: pgcgkvk@gmail.com
20. Regional Horticultural Research and Extension Centre, UHS Campus, Kumbapur, Dharwad, E-mail: specialofficerzhrec@yahoo.in
21. Regional Horticultural Research and Extension Centre, UHS Campus, Bengaluru, E-mail: rhrecb.gkvk@uhsbagalkot.edu.in
22. Horticultural Research Station, University of Horticultural Sciences, Tidagundi -586119, E-mail: hrsb_tid@rediffmail.com
23. College of Horticulture, Yelachanahalli Horticulture Farm, Yelwal Hobli,
    E-mail: Mysuruprakash.bg@uhsbagalkot.edu.in

24. Horticulture Research Station, University of Horticultural Sciences, Devihosur, E-mail: hrs_devihosur@rediffmail.com
25. Horticulture Research Station, Hassan, University of Horticultural Sciences, E-mail: hrshassan1@gmail.com
26. Horticulture Research Station, Hidkaldam University of Horticultural Sciences, E-mail: hrshidkaldam2010@gmail.com
27. Horticulture Research Station, Hogalagere, University of Horticultural Sciences, E-mail: hrshogalagere@gmail.com
28. Horticulture Research Station, Kanabargi, University of Horticultural Sciences, E-mail: hrskanabargi@gmail.com
29. Horticulture Research Station, Sirsi, University of Horticultural Sciences, E-mail: hrspepper@gmail.com
30. Horticulture Research Station, Tidagundi, University of Horticultural Sciences, E-mail: ars_tidagundi@rediffmail.com
31. Department of Crop Improvement and Biotechnology, College of Horticulture, University of Horticultural Sciences, Mysore-571130 Prakash Banavadi, prakash.banavadi@gmail.com
32. Alva's Centre for Post Graduate Studies and Research, Moodubidire Dakshina Kannada – 574227 Karnataka
33. Principal, University College, U.P. Malya Road, Mangaluru – 575001
34. The Chairman, Department of Applied Botany, Mangalore University, Mangalagangothri - 574 199, Mangalore
35. The Chairman, Department of Applied Zoology, Mangalore University, Mangalagangothri - 574 199, Mangalore
36. The Chairman, Department of Bioscience, Mangalore University, Mangalagangothri - 574 19, Mangalore
37. Sri Dharmasthala Manjunatheshwara College of Ayurveda & Hospital, Udupi: 574118

36. Kodagu Institute of Medical Sciences, Madikeri, 571201, Kodagu,
37. Alva's Ayurveda Medical Hospital, Sundari Ananda Alva Campus, Vidyagiri, Moodubidire – 574 227
38. Amrutha Ayurvedic Medical College and Hospital, Chitradurga - 577 501. Karnataka
39. Ashwini Ayurvedic Medical College Ring Road, Maralur, Tumkur - 572 105,

40. Atreya Ayurvedic Medical College, Hospital & Research Centre, Kakkali Road , Kodigehalli Post,Doddaballapura-561203, Bangalore.
41. BLDE Association's AVS Ayurveda Mahavidyalaya, Vidya Nagar Bagalkot Road, Bijapur-586 109. Dist. Bijapur.
42. Ayurved Seva Sangh's Ayurved Mahavidyalaya,Ganeshwadi, Panchavati, Nashik, Tal. Nashik, Dist. Nashik, Pin-422003
43. A.L.N. Rao Memorial Ayurvedic Medical College & P.G. Centre, Kachkal Road, Koppa, Chikmagalur Dist., Karnataka
44. Bapuji Ayurvedic Medical College and Hospital Sowlanga Road, Shimoga 577 204
45. Bhagwan Mahaveer Jain Ayurvedic Medical College State Highway 6, Gajendergarh, Gadag, Karnataka 582114
46. Shri C.B. Guttal Ayurvedic Medical College Shri R.F. Neeralakatti educational campus Garag road, Mummigatti, Dharwad 580011
47. Shikshana Prasaraka Samiti's Dhanvantari Ayurveda College Hospital and Research Centre Siddapur - 581 355
48. Dr. B.N.M. - BasavarajNagur Memorial - Rural Ayurved Medical College and Hospital, Bijapur, Karnataka
49. Taranath Govt. Ayurvedic Medical College Dr. Rajkumar Road, Bellary, Karnataka 583101
50. Grameen Ayurvedic Medical College, Hospital & Research Center, Gurukul Campus, Vidyagiri Terdal, Tq-Jamakhandi, District-Bagalkot, Karnataka-587315
51. SVVK Trust's Kalmathada Pujya Shri Virupaksha Shivacharya Ayurvedic Medical College and Hospital Manvi - 584 123
52. KVG Ayurveda Medical College & Hospital AmbateAdka, Sullia -574 327
53. Muniyal Ayurveda Manipal, Dr. U. Krishna Muniyal Memorial Trust (R), Manipal - 576 104
54. Shikshana Prasaraka Samiti's, Dhanvantari Ayurveda College Hospital and Research Centre, Siddapur - 581 355
55. Jeddu Ayurveda Specialty Hospital, Alike, Karnataka
56. Goa College of Pharmacy, Panaji, Goa: 403 001
57. Sri Ramachandra University, Chennai: 600 116
58. Chettinad Hospital and Research Institute, Kelambakkam, Chennai
59. Arecanut Research and Development Foundation®, Mangaluru: 575 001, Karnataka
60. The Hapcos Ltd. Shimogga

State-Directors of National Health Mission

1. Mission Director (NHM), State Health Society, Sheikhpura, Patna-800014, Bihar
2. Mission Director (NHM), National Health Mission,New Raipur Chhattisgarh- 492015
3. Mission Director (NHM), Department of Health & Family Welfare, Government of Jharkhand, Namkum, Ranchi- 834010.
4. Mission Director (NHM) Bhopal - 462004, Madhya Pradesh.
5. Secretary (FW) & Mission Director (NHM) Directorate of Medical and Health Services, Jaipur (Rajasthan.)-302001
6. Mission Director (NHM), Department of Health & Family Welfare, Government of Orissa, Bhubaneswar- 751012, Odisha
7. Mission Director (NHM), Government of Uttar Pradesh.
8. Mission Director (NHM), Government of Uttarakhand, Uttarakhand Health & Family Welfare Society, Directorate of Health & Family Welfare, Dehradun- 248 001, Uttarakhand
9. Mission Director (NHM), J&K, Regional Institute of Health & Family Welfare Jammu -181221, Jammu & Kashmir
10. Mission Director (NHM), Directorate of Health & Family Welfare, Govt of Himachal Pradesh, Shimla- 171009, Himachal Pradesh
11. Mission Director (NHM), Department of Health & Family Welfare, Office of Mission Director, National Health Mission, Guwahati -781 005, Assam
12. Mission Director (NHM), Government of Arunachal Pradesh, 791110, Arunachal Pradesh
13. Mission Director (NHM), Directorate Health Services, Imphal – 795 001 Manipur
14. Mission Director (NHM), Department of Health & Family Welfare, Shillong- 793 001, Meghalaya
15. Mission Director (NHM), Mizoram State Health Society, Govt. of Mizoram, Aizwal - 796001, Mizoram
16. Mission Director (NHM), Directorate of Health & Family Welfare, Govt. of Nagaland, Kohima Nagaland -797001
17. Mission Director (NHM), National Health Mission, Agartala - 799001 Tripura
18. Mission Director (NHM), Health Care, Human Service & FW Dept.Government of Sikkim, Gangtok - 737102 Sikkim.
19. Principal Secretary, Health Medical & Family Welfare Dept.,& Mission Director (NHM) Incharge ,Government of Andhra Pradesh, Amaravathi -522503 Andhra Pradesh

20. Mission Director (NHM), DM &HS Campus, Hyderabad- 500095, Telangana
21. Secretary (Health & FW), Government of Goa, Ministrial Block CM Office, Secretariat, Porvorim, Goa - 403521
22. Mission Director (NHM), Gandhinagar-Gujarat, 382010
23. Secretary (Health), Mission Director (NHM), Department of Health & Family Welfare, Government of Haryana, Panchkula, Haryana - 134109
24. Mission Director (NHM),Directorate of Health & FW Services, Bangalore- 560009, Karnataka
25. Mission Director (NHM), Department of Health & Family Welfare, Govt. of Kerala, Thiruvananthapuram- 695035 Kerala
26. Commissioner (Health), Mission Director (NHM), Mumbai-400 001, Maharashtra
27. Mission Director (NHM), Chandigarh - 160036, Punjab
28. Mission Director (NHM), State Health Society, Government of Tamil Nadu, Chennai-600 006, Tamil Nadu
29. Mission Director (NHM),Government of West Bengal, Department of Health & Family Welfare, Kolkata- 700091, West Bengal
30. Special Secretary (Health & Medical Education)& Mission Director (NHM) Andaman & Nicobar Administration, Secretariat, Port Blair- 7 44101 Andaman & Nicobar Island
31. Mission Director (NHM) U.T.,Community Health Center,
32. Mission Director (NHM), Secretariat UT Dadar & Nagar Haveli, Silvassa – 396230, Dadar& Nagar Haveli
33. Mission Director (NHM), Daman-396220
34. Mission Director (NHM), Delhi-110054
35. Mission Director, (NHM), Directorate of Medical & Health Services, Administrator of the UT of Lakshadweep, Kavaratti– 682555, Lakshadweep
36. Mission Director (NHM), Puducherry State Health Mission, Puducherry – 605 001

Health Secretaries of States and UTs

1. Principal Secretary (Health & FW), Department of Health, Government of Bihar, Patna – 800 015. Bihar
2. Principal Secretary (Health), Department of Health & Family Welfare, Government of Chhattisgarh, New Raipur -492002, Chhattisgarh

3. Principal Secretary, Department of Health & Family Welfare, Government of Jharkhand Doranda, Ranchi- 834002.Jharkhand.
4. Principal Secretary (Health& FW), Government of Madhya Pradesh, Bhopal-462 004, Madhya Pradesh
5. Addl. Chief Secretary (Health & FW), Department of Health & Family Welfare, Government of Rajasthan, Jaipur-302005, Rajasthan
6. Commissioner cum Secretary (Health & FW), Department of Health & Family Welfare, Government of Orissa, Bhubaneshwar -751 001, Odisha
7. Principal Secretary (Health & FW), Department of Health & Family Welfare, Government of Uttar Pradesh, Lucknow – 226 001, Uttar Pradesh
8. Secretary (Medical, Health & FW), Government of Uttarakhand, Dehradun, Uttarakhand-248001
9. Secretary (Health & Medical Education), Health & Medical Education Department, Govt. of Jammu & Kashmir, Srinagar -180001
10. Principal Secretary(Home, Health & FW & Medical Education), Department of Health & Family Welfare,Govt.of Himachal Pradesh,Shimla- 171002, Himachal Pradesh
11. Principal Secretary (H&FW), Health & Family Welfare Department, Govt. of Assam, Dispur, Guwahati, Assam - 781006
12. Commissioner (H&FW), Government of Arunachal Pradesh, District Papumpare, Ita Nagar-791111, Arunachal Pradesh
13. Principal Secretary (Health & FW), Department of Health & Family Welfare, Imphal – 795 001 Manipur
14. Addl. Chief Secretary, (Health& Family Welfare), Department of Health & Family Welfare, Shillong- 793 001, Meghalaya
15. Commissioner & Secretary (Health & FW), Department Health & FW, Government of Mizoram, Aizawl - 796001, Mizoram
16. Commissioner & Secretary (Health), Department of Health & Family Welfare, Government of Nagaland, Kohima- 797001, Nagaland
17. Secretary (Health & FW), Department of Health & Family Welfare, Government of Tripura, Agartala- 799006 , Tripura
18. Commissioner-cum-Secretary Health, Department of Health & Family Welfare, Government of Sikkim, Tashiling, Gangtok - 737101, Sikkim
19. Principal Secretary, Health Medical & Family Welfare Deptt.,& Mission Director

(NHM) incharge, Government of Andhra Pradesh, Amaravathi -522503 Andhra Pradesh

20. Principal Secretary (Health & MFW) Telangana Secretariat, Hyderabad-500022
21. Secretary (Health & FW), Government of Goa, Secretariat, Porvorim, Goa - 403521
22. Commissioner (Health) & Ex-Officio Secretary (Public Health & Family Welfare) Gandhinagar, Gujarat 382010
23. Addl. Chief Secretary (Health), Department of Health & Family Welfare, Government of Haryana, Chandigarh - 160001
24. Addl. Chief Secretary (H&FW), Health and FW Department, Bangalore-560001, Karnataka
25. Addl. Chief Secretary (Health), Department of Health & Family Welfare, Government of Kerala, Thiruvananthapuram-695001, Kerala
26. Principal Secretary,(Public Health Department), Government of Maharashtra , Mumbai – 400001, Maharashtra
27. Principal Secretary (Health & FW), Department of Health & Family Welfare Government of Punjab, Chandigarh, Punjab-160009
28. Principal Secretary (Health & FW), Department of Health & Family Welfare Government of Tamil Nadu, Chennai – 600 009,Tamil Nadu
29. Principal Secretary (H&FW), Department of Health & Family Welfare Government of West Bengal, Kolkata – 700091, West Bengal.
30. Principal Secretary (Health), Department of Health & Family Welfare, Andaman & Nicobar Administration, Secretariat, Port Blair- 744101 Andaman & Nicobar Island
31. Home Secretary-cum-Secretary, Health & Family Welfare, UT Secretariat, Chandigarh- 160017
32. Secretary HFW, Secretariat UT Dadar& Nagar Haveli, Silvassa – 396230, Dadar & Nagar Haveli.
33. Secretary HFW, Office of the Adviser to Administrator, Daman & Diu Administration, Daman & Diu- 396220.
34. Principal Secretary (Health & FW), Department of Health & Family Welfare, Government of NCT of Delhi, New Delhi – 110 002
35. Secretary (Health), UT of Lakshadweep, Kavaratti– 682555, Lakshadweep
36. Secretary (Health), Chief Secretariat, Government of Puducherry, Puducherry – 605 001

NOTES

Interactive Workshop on "Arecanut and Human Health" at ICAR-CPCRI, Kasaragod

24 and 25 July, 2018

I Organizing Committee

1. Dr. P. Chowdappa
2. Dr. Ravi Bhat
3. Dr. Vinayaka Hegde
4. Dr. (Mrs.) Anitha Karun
5. Dr. K. Muralidharan
6. Dr. C.T. Jose
7. Dr. K.B. Hebbar - Org. Secretary

II Programme/Publication Committee

1. Dr. K.B. Hebbar
2. Dr. S.V. Ramesh
3. Dr. H. Muralikrishna
4. Dr. Shyam Prasad
5. Mrs. Girija Chandran

III Invitation/Reception/Banner Committee

1. Dr. K. Bhanuprakash
2. Dr. Shameena Beegum
3. Mrs. Sugatha Padmanabhan
4. Mrs. Girija Chandran

IV Registration Committee

1. Dr. Anitha Karun
2. Dr. Neema
3. Dr. Sajini KK
4. Dr. Muralikrishna
5. Shri K.K. Nair

V Accommodation Committee

1. Dr. Rajkumar
2. Shri Neil Vincer
3. Shri V. Balakrishna
4. Shri K. Devadas

VI Hall arrangement Committee

1. Dr. M.R. Manikantan
2. Shri Sebastian George
3. Shri A. Sadanandan
4. Sri G.S. Hareesh
5. Shri A.O. Varghese
6. Shri K.A. Madhavan

VII VIP Reception Committee

1. Dr. Bhanuprakash
2. Dr. S.V. Ramesh
3. Dr. Shameena Beegum
4. Dr. Rajkumar

VIII Transportation Committee

1. Dr. Rajkumar
2. Shri Pandiselvam
3. Shri Sebastian George
4. Shri K. Devadas

IX Food and Refreshment Committee

1. Dr. Pandiselvam
2. Shri K. Devadas
3. Shri V. Balakrishna
4. Shri V. Sureshkumar
5. Shri Dinesh Kumar


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