ANTIDIABETIC POTENTIAL OF ARECANUT, *Areca catechu* L. AND CERTAIN ARECANUT FORMULATIONS AVAILABLE FOR TREATING DIABETES

S. Keshava Bhat[1], D. Ashwin[2] and S. Mythri[2]

ABSTRACT

Diabetes is a common human ailment affecting all age groups of people everywhere irrespective of their status. Several medicinal plants have been reported to possess antidiabetic properties. It is interesting to note that areca palm, *Areca catechu* L. which is widely distributed in several southern and southeast Asian countries including India is one among them. Almost all parts of this palm including its stem, flower, leaf and fruit are reported to be antidiabetic. The extracts of the nuts of areca palm showed significant suppression of blood glucose level at 250 mg/kg bw in albino rats. The extracts of the stem and leaf of areca palm were found to be even more potent and gave nearly 56% reduction in blood glucose level in rats at a dose of 100 mg/kg bw. The most efficient chemical compound responsible for the antidiabetic potential of areca palm may be identified and synthesized in large scale for its commercialization. Population based studies carried out by several researchers on betel quid or pan masala chewing people were inconclusive and one sided. They blamed only arecanut for the results they got without evaluating the role of other ingredients in betel quid or pan masala.

INTRODUCTION

Human diabetes is a chronic disorder primarily due to abnormal metabolism of glucose, fat and protein. Two types of diabetes are commonly noticed. The first one is called type 1 diabetes where the body cannot produce enough insulin mainly due to lack of functional beta cells in pancreas. Patients suffering from this type of disorder depend on exogenous source of insulin as curative measure. The second one is called type 2 diabetes where the body cannot respond or use insulin properly. Such disorders can be treated with proper medication coupled with dietary changes and exercise. Both these ailments are characterized by higher level of glucose in the blood. Such high level of glucose in blood leads to several health complications affecting the normal functioning of vital organs such as eyes, kidney, heart, blood vessels, nerves, etc., apart from delaying wound and wart healing leading to ulceration and infection culminating in the amputation of affected parts in severe cases. Type 2 diabetes is the most common type. The exact causes for its development are not clearly understood. However, certain risk factors like excess body weight, lack of exercise, imbalanced nutrition, old age, etc., aggravate the situation.

[1] Arecanut Research and Development Foundation, Varanashi Towers, Mission Street, Mangaluru- 575 001, Karnataka.
[2] Kannur Dental College, Anjarakkandy- 670 612, Kannur Dt., Kerala.

Diabetes is the eighth leading cause of death among male and fifth among the females (WHO, 2016). There are as many as 415 million people in the world suffering from diabetes (IDF, 2015). China, with 109.6 million identified diabetic patients took the first position during 2015 followed by India with 69.2 million and USA with 29.3 million diabetic patients. Antidiabetic chemical drugs are mostly used to manage these disorders. However, many side effects like low blood glucose level, weakness, gastrointestinal upset, lactic acid intoxication, liver toxicity, etc., have been reported in patients who practiced such medications. Alternative therapies having antihyperglycemic actions are good alternatives for this. In this line, herbal drugs which generally show less adverse effects and at the same time equally effective are ideal choice in the management of these disorders (Dey *et al.*, 2002).

Traditional medicines, mostly of plant origin are used by about 60% of the world's population and in rural India nearly 70% of the people depend on such medicines (Seth and Sharma, 2004). It is reported that plant polyphenols and polyphenol rich foods are effective in the management of type 2 diabetes (Kim *et al.*, 2016). Their action is by improving glucose homeostasis in the intestine, liver, muscle adipocytes and pancreatic β-cells, as well as through prebiotic effects in the digestive tract. They can also prevent several long term diabetic related complications like cardiovascular disease, neuropathy, nephropathy and retinopathy (Bahadoran *et al.*, 2013). Several experiments conducted on laboratory animals by using plant extracts having good antioxidant properties and rich in phytochemicals and polyphenols have confirmed their anti-diabetic activities (Chandra *et al.*, 2008; Khan *et al.*, 2012). Several other medicinal plants have been identified for having antidiabetic potentials (Grover *et al.*, 2002; Modak *et al.*, 2007). Certain medicinal plants in India were reported to have good pancreatic amylase inhibitory effects by reducing the rate of starch hydrolysis leading to lowered glucose levels (Ponnusamy *et al.*, 2011).

The areca palm, *Areca catechu* L. (family Palmaceae) is a tall (growing up to 30m height) and slender (about 50cm circumference) palm with an erect stem and a compact crown surrounded by 7-12 leaves at various stages of development (Ananda, 2004). The fruit of areca palm is commonly called as arecanut or *supari*. It is misnamed as betelnut by some people as it is commonly chewed along with the leaves of *Piper betle* L. Arecanut is known for its medicinal, phytochemical and pharmacological properties since time immemorial (Kirtikar *et al.*, 1918; Morton, 1976; Amudhan, 2005; Badanaje, 2008; WHO, 2009; Jaiswal, *et al.*, 2011; Amudhan, *et al.*, 2012).

Areca palm is widely distributed in several southern and southeast Asian countries including India, Indonesia, China, Malaysia, Philippines, Burma, Thailand, Sri Lanka, etc. (Balasimha and Rajagopal, 2004). India ranks first in both area (57%) and production (53%) of this crop and is mainly grown in the States of Karnataka, Kerala, Assam and Maharastra (Selvan, *et al.*, 2004). Total area under this crop in our country during 2013-14 was assessed to be around 4.5 lakh hectares with a production of 6.21 lakh tones (Cheriyan and Manojkumar, 2014). The leaves are pinnate and quite big (1.2 - 1.8m in length), with numerous confluent leaflets

(30-60cm length and 5.8-7cm breadth), often with several midribs attached to the rachis in a vertical line. On an average 6.3 such leaves are shed from each palm every year amounting to about 4kg dry matter of leaves from each palm (Bhat and Sujatha, 2011). One hectare of areca plantation in a normal spacing of 2.7m x 2.7m can accommodate about 1,300 palms (Bhat *et al.*, 1999). Preliminary phytochemical analysis of areca leaves revealed the presence of alkaloids, steroids, saponins, tannins, glycosides and carbohydrates (Mondal *et al.*, 2012; Sahane *et al.*, 2013).

The processed arecanut is rich in polyphenols 15-20%, polysaccharides 17.3-25.7%; proteins 6.2-9.4%; fats 8.1-15.1%; fibres 8.2-15.4%; alkaloids 0.11-0.24% and minerals 1.1-2.5% (Shivashankar *et al.*, 1969). The polyphenol content in arecanut is very high in tender nut stage (47.94%) and decreases to 29.44% in mature green nut, 26.40% in semi ripe nut and 17.81% in fully ripe nut (Mathew, *et al.*, 1964). Further, all the major chemical constituents in arecanut, including polyphenols were found to decrease significantly while drying and storing as whole nuts (Chempakam and Saraswathy, 1985), and also while roasting, soaking and boiling (Awang, 1988).

Most of the scientific studies on the antidiabetic activities of arecanut were carried out on experimental animals such as rats, mice and rabbits. Almost all parts of areca palm are reported to have antidiabetic properties. Some studies were also carried out on the hypoglycemic action of certain phytochemicals of arecanut such as arecoline. The works carried out by different researchers are reviewed in this paper.

Areca fruit/seed

The intestinal glycosidase enzymes are primarily responsible for the metabolism and absorption of dietary carbohydrates. The arecanut extract was reported to suppress the action of such enzymes in albino rats and thereby decrease the level of glucose in their blood. The IC_{50} values of the ethanolic extract of arecanut on the inhibitory activity of glycosidase enzymes such as maltase and sucrase were found to be 12 µg/ml and 30 µg/ml, respectively (Amudhan and Begum, 2008). Oral administration of arecanut extract at 250 mg/kg body weight after feeding maltose did not increase the blood glucose level but animals received only maltose showed very high level of blood glucose.

Anthikat *et al.* (2014) evaluated the antidiabetic property of aqueous extract of arecanut on Wister male albino rats in laboratory. In the test conducted on glucose tolerance it was noticed that arecanut extract at the dose of 250 and 500 mg/kg bw showed the maximum improvement in glucose tolerance when compared to that of the synthetic antidiabetic drug glibenclamide at 60 min and the decline reached its maximum at 120 min. In another experiment where the arecanut extract was administered for 21 days to diabetic induced rats by injecting streptozotocin *i.p.* it was noticed that both the doses of 250 and 500 mg/kg bw showed significant reduction in blood glucose levels when compared to that of diabetic rats.

The insulin levels in the blood of arecanut extract treated rats increased significantly when compared to those of diabetic induced control groups.

Arecanut powder when fed to Sprague dawley rats in water suspension at a dose of 20 mg and 30 mg/rat/day for 15 days reduced the serum glucose level from 92.7 to 85.7 and 82.6, respectively (Iqbal *et al.*, 2012). In another study, when arecanut powder was mixed with normal food at a very high dose (at 20% concentration) and given to adult CD1 mice for five days, no significant change in plasma glucose level was observed in such mice when compared to control (Boucher *et al.*, 1994). These results are in conformity with the observations of Chempakam (1993) wherein it was reported that neither the lower dose nor the higher dose of arecoline (< 0.20 mg and > 0.25 mg/kg bw) showed antidiabetic activity in rabbits. In this context it is to be remembered that the medicines are effective only if they are taken in the prescribed dose.

Areca flowers

The flowers of areca palm were also found to possess antidiabetic properties. Ghate *et al.* (2014) studied the antihyper-glycemic activities of three different extracts, *viz.*, petroleum ether, ethanol and aqueous extracts of areca flowers separately on alloxan induced diabetic male albino rats by orally administering the extract at 500 mg/kg bw. Both male and female flowers (got clarification from the author) were used for the extract. The treatment lasted for 21 days and observations on blood glucose levels were made in the beginning and after the end of the experimental period of 21 days. During the experiment, there was marked rise in fasting blood glucose level in diabetic induced rats. In ethanol and aqueous extract treated rats, there was significant reduction in the blood glucose levels when they were observed after 21 days. Rats treated with petroleum ether extract, though caused a reduction in blood glucose level, it was not significant. Similar results were observed in body weight also. Alloxan mediated body weight reduction was found to be reversed significantly in ethanol and aqueous extract treated rats but not in petroleum ether extract treated rats. Preliminary phytochemical examination revealed the presence of high level of phenolic constituents such as flavonoids, steroids, tannins, saponins in both these extracts.

Areca leaves

The leaves of areca palm were found to be more potent than that of its nuts as far as antidiabetic effects are concerned. Mondal *et al.* (2012) evaluated the antidiabetic effects of three extracts, *viz.*, petroleum ether, chloroform and methanol of the leaves of areca palm on Wister albino rats in the laboratory. The rats were induced diabetes by injecting streptozotocin *i.p.* The hyperglycemic rats were treated with all three extracts orally at a dose of 200 mg/kg bw daily for 15 days and observed at 5 days intervals. Glibenclamide was used as antidiabetic reference drug. The results showed that at this dose all the extracts exhibited antidiabetic activity significantly more when compared to those of the diabetic control groups and comparable to those results obtained with the reference drug. The treated rats started reducing blood sugar level after 5 days of treatment and reached to complete normal level after 15 days. The body weights were also restored to normal in the treated groups. Though there were no significant difference between the three extracts, the methanol extract was found to be most effective followed by chloroform and petroleum ether

extract. Only lacuna in this observation is that the authors tried only one dose of the extract. They should have tried the lower doses as well.

Sahane *et al.* (2013) studied the antidiabetic effects of ethanolic extract of the leaves of areca palm on streptozotocin induced diabetic Sprague dawley rats at two different doses, *viz.*, 100 and 200 mg/kg bw by oral feeding for 15 days and observed at 5 days intervals. The fasting blood glucose level in diabetic induced rats was more than 400 on all the days whereas it was 241, 172 and 97 on 5th, 10th and 15th days of treatment, respectively in 100 mg group and 264, 146 and 87, respectively in 200 mg group. The blood glucose level reached almost the same level to that of control group on the 15th day. The interesting observation is that the areca leaf extract did not induce any reduction in the blood glucose level in normal rats when they were given this extract.

In a study conducted on glucose tolerance test on Swiss albino mice it was found that the methanolic extract of areca leaves at 100, 200 and 400 mg/kg bw significantly lowered the level of serum glucose when compared to the control group which received only glucose (Akhter *et al.*, 2014). In mice which received only glucose, the blood serum level was 84.2, whereas it was 34.7, 32.9 and 28.9 (a reduction of 58.8%, 60.9% and 65.7%, respectively over control) in those groups of mice which received glucose with areca leaf extracts at 100, 200 and 400 mg/kg bw, respectively. However, in the reference control group which received glucose with the standard drug glibenclamide, the serum glucose level was 24.1 (71.4% reduction over control).

Areca stem

It is interesting to note that the areca stem extract is also effective in inducing anti-hyperglycemic action. Akhter *et al.* (2014) studied this aspect on Swiss albino mice. The areca stem (topmost part of the stem just below the leaves- got clarification from the author) extract was made with ethanol at a ratio of 1:3 (w/v). The preliminary phytochemical analysis revealed the presence of phenolic compounds, alkaloids, glycosides, and tannins. The anti-hyperglycemic activity was studied through glucose tolerance test wherein glucose (2 g/kg bw) was given orally one hour after feeding food containing the extract or standard drug, glibenclamide. Areca stem extract was tested at four different concentrations, *viz.*, 50,100, 200 and 400 mg/kg bw of the animal. The results showed a significant reduction in serum glucose level on all the concentrations as well as in the standard drug treated mice when compared to the control group which received only glucose. In the group treated with the standard drug the reduction was 71.4% when compared to control, whereas the figures for 50, 100, 200 and 400 mg/kg categories of the stem extract were 42.2%, 56.8%, 59.4% and 63.1%, respectively.

Arecoline

Arecoline is one of the major and most reactive chemical constituent of arecanut (Peng *et al.*, 2015). Chempakam (1993) studied the antidiabetic action of both synthetic and natural arecoline extracted from arecanut on male albino rabbits by administering different doses ranging from 0.05 to 0.50 mg/kg body weight in laboratory. Initially, diabetes was induced in

rabbits by a single *i.v.* injection of alloxan monohydrate in distilled water at the rate of 140 mg/kg bw. Extraction of arecoline from arecanut was done using alcohol. The extract was administered s.c. to both control as well as to alloxan induced diabetic rabbits. The results were also compared with that of synthetic arecoline treated rabbits. It was observed that in the treatments using 0.20 and 0.25 mg/kg bw there was a reduction of 52.1% and 49.7%, respectively in blood sugar levels when compared to control. The effect lasted for 4 to 6 hr after administration. Both synthetic and natural arecoline were found equally effective in reducing blood sugar levels. One interesting observation was that there was no reduction in blood glucose level either in the lower doses (< 0.20 mg/kg bw) or in the higher doses (>0.25 mg/kg bw) of arecoline.

Betel quid / pan masala

Most of the studies carried out on the prevalence of diabetes in people who chewed betel quid or pan masala were not direct studies, but based on the information the researchers / field staff collected from such people by circulating questionnaire. The studies were mostly on betel quid or pan masala chewing habits. The betel quid generally contains arecanut, betel (*Piper betle* L.) leaf or inflorescence or the stem of the vine, slaked lime, catechu, certain spices, sweeteners and certain essences (IARC, 2004). Pan masala also contains several ingredients such as arecanut, slaked lime, catechu, condiments and certain flavoring agents. Some preparations of betel quid or pan masala even contain tobacco in them, either in its leaf form or powder form. Ironically, most of the researchers did not take care to either reveal the ingredients of betel quid or pan masala in their paper or to discuss the role of such ingredients, but simply named arecanut as responsible for the entire results they got (Mannan *et al.*, 2000; Tung *et al.*, 2004; Tseng, 2010). Such vague conclusions may be avoided in research studies.

Certain antidiabetic formulations prepared from arecanut

Some of the ayurvedic formulations such as *'Dia areca'*, *'Pooga trim'*, *'Dia catechu'*, etc., with arecanut extract as the main ingredient are already available in the market with antidiabetic properties. *'Dia areca'* is a liquid preparation formulated by the Arecanut Research Station (University of Agricultural Sciences, Bengaluru), Navile Campus and marketed by Dia Enterprises, Bengaluru for treating diabetes in its initial stages. *'Pooga trim'* is a powder formulation prepared and marketed by SDM College of Ayurveda and Hospital, Udupi, Karnataka to reduce excess body fat as well as blood sugar level. *'Dia catechu'* is a tablet form of antidiabetic arecanut formulation invented and marketed by Jeddu Ayurveda Pharmacy, Alike, Dakshina Kannada Dt., Karnataka.

CONCLUSION

Though several chemical drugs are available for the treatment of diabetes, herbal preparations are preferred due to their low cost and lesser side effects. Until now, over 400 medicinal plants have been recorded to have antidiabetic principles. However, only very few plants have received scientific validation. *Areca catechu*, which is grown abundantly in several countries, including India is reported to be one of such plants with antidiabetic property.

Though all parts of areca palm showed antidiabetic potential, it is the leaves which showed the maximum activity. It is an added advantage that in areca palm, the leaves which are available in plenty and are presently not used for anything else other than making compost, could be exploited further for extracting antidiabetic principle. Researchers and pharmaceutical companies and laboratories may take active role in this work for the benefit of mankind.

REFERENCES

Akhter, S., Hassan, M., Rahman, S., Sultana, A., Shahreen, S., Banik, J., Jahan, R. and Rahmatullah, M. 2014. Anti-hyperglycemic activity studies on leaves and stems of *Areca catechu* L. (Arecaceae). *Ad.Nat. Appl. Sci.* 8: 233-236.

Amudhan, M.S. 2005. Pharmacological effects of arecanut. *Indian J. Arecanut & Med. Plants* 7: 10-11,14.

Amudhan, M.S. and Begum, V.H. 2008. Alpha-glucosidase inhibitory and hypoglycemic activities of *Areca catechu* extract. *Phcog Mag.* 4: 223-226.

Amudhan, M.S., Begum, V.H. and Hebbar, K.B. 2012. A review on Phytochemical and Pharmacological potential of *Areca catechu* L seed. *IJPSR* 3: 4151-4157.

Ananda, K.S. 2004. Botany. In: *Arecanut.* (Eds: D. Balasimha and V. Rajagopal). Central Plantation Crops Research Institute, Kasaragod:671 124, Kerala, India. pp7-50.

Anthikat, R.R., Michael, A., Vageesh, S., Balamurugan, R. and Ignacimuthu, S. 2014. The effect of *Areca catechu* L. extract on streptozotocin induced hyperglycemia in Wistar rats. *Int. J. of Pharma. Bio. Sci.* 5: 316-321.

Awang, M.N. 1988. Fate of betel nut chemical constituents following nut treatment prior to chewing and its reaction to oral precancerous & cancerous lesion. *Dental J. Malaysia* 10: 33-37.

Badanaje, S.B. 2008. *Arecanut - medicinal and alternative uses.* Arecanut Research and Development Foundation®, Varanashi Towers, Mission Street, Mangaluru: 575 001, India. 104p.

Bahadoran, Z., Mirmiran, P. and Azizi, F. 2013. Diatary polyphenols as potential nutraceuticals in management of diabetes: a review. *J. Dia. & Metabolic Disorders* 12: 43; doi: 10.1186/2251-6581-12-43.

Balasimha, D. and Rajagopal, V. 2004. Introduction. In: *Arecanut.* (Eds: D. Balasimha and V. Rajagopal). Central Plantation Crops Research Institute, Kasaragod: 671 124, Kerala, India. pp1-6.

Bhat, R., Reddy, V.M. and Khader, K.B.A. 1999. Areca based high density multispecies cropping system in coastal Karnataka. *J. Plant.* Crops 27: 22-26.

Bhat, R. and Sujatha, S. 2011. Organic matter recycling in arecanut based high density multispecies cropping systems. In: *Arecanut based cropping / farming* systems (Eds: G.V. Thomas; V. Krishnakumar; H.P. Maheswarappa; R. Bhat and D. Balasimha). Central Plantation Crops Research Institute, Kasaragod: 671 124, Kerala, India. pp63-76.

Boucher, B.J., Ewen, S.W.B. and Stowers, J.M. 1994. Betel nut (*Areca catechu*) consumption and the induction of glucose intolerance

in adult CD1 mice and in their F1 and F2 offspring. *Diabetologia* 37: 49-55.

Chandra, A., Mahdi, A.A., Singh, R.K., Mahdi, F. and Chander, R. 2008. Effect of Indian herbal hypoglycemic agents on antioxidant capacity and trace elements content in diabetic rats. *J. Med. food.* 11: 506-512.

Chempakam, B. 1993. Hypoglycaemic activity of arecoline in betel nut *Areca catechu* L. *Indian J. Expt. Biol.* 31: 474-475.

Chempakam, B. and Saraswathy, N. 1985. Biochemical changes during storage of arecanut (*Areca catechu* L.). In: *Arecanut Research and Development* (Eds: K.S. Bhat and C.P.R. Nair), Central Plantation Crops Research Institute, Kasaragod: 671124, Kerala, India. pp163-166.

Cheriyan, H. and Manojkumar, K. 2014. Arecanut production scenario in India. *Indian J. Arecanut, Spices and Med. plants* 16(4): 3-11.

Dey, L., Anoja, S.A. and Yuan, C.S. 2002. Alternative therapies for type 2 diabetes. *Alternative Medicine* Rev 7: 45-58.

Ghate, R., Patil, V.P., Hugar, S. and Kalyane, N.V. 2014. Antihyperglycemic activity of *Areca catechu* flowers. *Asian Pacific J. Trop. Diseases* 4: S148-S152.

Grover, J.K., Yadav, S. and Vats, V. 2002. Medicinal plants of India with anti-diabetic potential. *J . Ethnopharmacol* 81: 81-100.

IARC, 2004. *Monographs on the evaluation of carcinogenic risks to humans. Betel quid and arecanut chewing and some arecanut derived nitrosamines* 85, WHO, IARC, Lyon, France. P41-52.

IDF, 2015. *Diabetes Atlas*, Seventh edition, International Diabetes Federation, Brussels, Belgium. 144p.

Iqbal, M.P., Mehboobali, N., Haider, G., Pervez, S. and Azam, I. 2012. Effects of betel nut on cardiovascular risk factors in a rat model. *BMC Cardiovascular Disorders* 12: 94-98.

Jaiswal, P., Kumar, P., Singh, V.K. and Singh, D.K. 2011. *Areca catechu* L.: A valuable herbal medicine against different health problems. *Res. J. Med. Plants* 5: 145 - 152.

Khan, V., Najmi, A.K., Akhtar, M., Aqil, M., Mujeeb, M. and Pillai, K.K. 2012. A pharmacological appraisal of medicinal plants with antidiabetic potential. *J.Pharm. Bioallied Sci.* 4: 27-42.

Kim, Y., Keogh, J.B. and Clifton, P.M. 2016 Polyphenols and glycemic control. *Nutrients* 8, 17; doi:10.3390/nu8010017.

Kirtikar, K.R., Basu, B.D. and An, I.C.S. 1918. *Indian Medicinal Plants*, Vol IV. (Reprint 1975), M/S. Bishen Singh Mahendra Pal Singh, New Connaught Place, Dehra Dun, India. pp2547-2549.

Mannan, N., Boucher, B.J. and Evans, S.J.W. 2000. Increased waist size and weight in relation to consumption of *Areca catech* (betel-nut); a risk factor for increased glycaemia in Asian in East London. *Br. J. Nutrition* 83: 267-275.

Mathew, A.G., Venkataramu, S.D. and Govindarajan, V.S. 1964. Studies on arecanut: part 1. Changes in chemical composition and physical characteristics of nuts with maturity. *Indian J. Tech.* 2: 90 - 96.

Modak, M., Dixit, P., Londhe, J., Ghaskadbi, S. and Devasagayam, T.P.A. 2007. Indian herbs and herbal drugs used for the treatment of diabetes. *J. Clin. Biochem. Nutr.* 40: 163-173.

Mondal, S., Bhattacharya, S. and Biswas, M. 2012. Antidiabetic activity of Areca catechu leaf extracts against streptozotocin induced diabetic rats. *J. Adv. Pharm. Edu. Res.* 2: 10-17.

Morton, J.F. 1976. *Major medicinal plants: Botany, culture and Uses*. Charles C Thomas, Springfield, Illinois, USA. 359p.

Peng, W., Liu, Y.J., Zhao, C.B., Huang, X.S., Wu, N., Hu, M.B., Xie, D.S. and Wu, C.J. 2015. In *silico* assessment of drug-like properties of alkaloids from *Areca catechu* L nut. *Trop. J. Pharma. Res.* 14: 635-639.

Ponnusamy, S., Ravindran, R., Zinjarde, S., Bhargava, S. and Kumar, R.A. 2011. Evaluation of traditional Indian antidiabetic medicinal plants for human pancreatic amylase inhibitory effect in vitro. *Evid Based Complement Alternat Med.* 2011. Pii: 515647. Doi: 10.1155/2011/515647.

Sahane, R.S., Wankhade, V.M. and Nandi, P. 2013. Effect of *Areca catechu* L. leaf extract on type II diabetes in rats. *Int. J. of Bio. Pharmaceut. Res.* 4: 731-737.

Selvan, M.T., Sivaraman, K. and Manojkumar, K. 2004. Economics, marketing and development. In: *The Arecanut Palm.* (Eds: K.V.A. Bavappa, M.K. Nair and T.P. Kumar). Central Plantation Crops Research Institute, Kasaragod, Kerala, India. pp259-301.

Seth, S.D. and Sharma, B. 2004. Medicinal plants in India. *Indian J. Med. Res.* 120: 9-11.

Shivashankar, S., Dhanaraj, S., Mathew, A.G., Murthy, S.S., Vyasamurthy, M.N. and Govindarajan, V.S. 1969. Physical and chemical characteristics of processed arecanuts. *J. Food Sci. Tech.* 6: 113-116.

Tseng, C.H. 2010. Betel nut chewing and incidence of newly diagnosed type 2 diabetes mellitus in Taiwan. *BMC Res. Notes* 3: 228.

Tung, T.H., Chiu, Y.H., Chen, L.S., Wu, H.M., Boucher, B.J. and Chen, T.H.H. 2004. A population-based study of the association between arecanut chewing and type 2 diabetes mellitus in men (Keelung community-based integrated screening programme No.2) *Diabetologia* 47: 1776-1781.

WHO. 2009. *Areca catechu* L. pp 30-31. In: *Medicinal Plants of Papua New Guinea*, World Health Organization, 20 avenue Appia, 1211 Geneva 27, Switzerland, 302p.

WHO. 2016. *Global report on diabetes*, World Health Organization, 20 avenue Appia, 1211 Geneva 27, Switzerland, 86p.

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