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Effects of Arecanut (*Areca catechu* L) Chewing on Human Health: Misleading Titles Lead to Wrong Notions



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ABSTRACT

Arecanut is the fruit of a slender but tall palm, botanically called *Areca catechu* L. of Palmaceae family. It is mainly grown in south and southeast Asian countries. This nut is treated as very auspicious and medicinally important in several countries including India, Myanmar, Philippines, Indonesia, China, etc., since thousands of years. Apart from this, arecanut is also being used for chewing since time immemorial, either alone or in combination with several other materials as it is perceived to be of having several beneficial effects. During the last two to three decades certain dry, ready to use chewing products have entered the market in different trade names in small easy to carry sachets and are fast replacing the traditional forms of chewing areca nut. Simultaneously, it is also seen that the Scientific reports which say that arecanut chewing is deleterious to health have also substantially increased. While going through such papers it is seen that in most of them there is no clarity in nomenclature. The study was either carried out on betel quid or on certain packaged forms of chewing mixtures which contained, apart from areca nut, several other materials, both biological and chemical, but the authors blamed only arecanut for all the ill effects. Such ambiguity is highlighted in this report.

INTRODUCTION:

Arecanut is the fruit of an oriental palm called *Areca catechu* L. of the family Palmaceae. This palm is mostly grown in India and several other south and south east Asian countries including China, Bangladesh, Sri Lanka, Myanmar, Indonesia, Malaysia, etc. [1,2]. The endosperm or the inner nut of this fruit, called as arecanut, is widely used as a masticatory in India and several other countries[3]. In certain parts of the world, arecanut is also called as betel nut as it is generally chewed along with the leaf of a perennial evergreen vine called *Piper betle* (betel vine) of Piperaceae family[3]. Except for this combined usage, there is nothing common between these two plants. *A. catechu* is a slender, tall palm growing up to 30m height whereas *P. betle* is a creeper. In north India, arecanut is commonly called as *supari*, and betel leaf as *pan* (or *paan*). This nut is seldom chewed alone but chewed mostly along with several other ingredients such as the leaf or the inflorescence or even the tender stem of *P. betle*, slaked lime (calcium hydroxide), grades of dry coconut (*Cocos nucifera*), some condiments, sweeteners and sometimes with the leaf of tobacco (*Nicotiana tabacum*) either as fresh or as dry mixtures in different trade names[3].

The antiquity of arecanut dates back to few thousand years[4]. In India, its presence was quoted as early as 1300 BC as mentioned in Anjana Chaitra by Sisu Mayana[5]. But, in certain other countries such as Vietnam, the use of arecanut was even noticed during the bronze age of human civilization as evidenced by the presence of arecanut stained teeth still remaining intact in the dentition of human fossil remains of that period[6]. Arecanut or betel leaf chewing is a tradition, custom or ritual since time immemorial in south Asian and Pacific countries[7]. Offering arecanut and betel leaf together is a popular cultural activity in many Asian and Oceanic countries including India, Sri Lanka, Maldives, Myanmar, Solomon Islands, Thailand, Vietnam, etc. In India, both arecanut and betel leaf are treated as very auspicious since pre-vedic times and used in religious and other auspicious functions to honor priests, guests and others[7].

The famous ancient Ayurvedists like Charaka, Sushruta, Vagbhata, Chakradatta, Bhavamista, etc used arecanut for its ample medicinal qualities and areca preparations are still in practice in several Folk medicines[8]. These nuts are being used widely in several clinical practices in China and other south and southeast Asian countries [1,9-11]. WHO has listed out as many as 25 different beneficial effects of *A. catechu* on mankind[12]. Such medicinal qualities of arecanut

are now well validated by several Scientific works. It has antioxidant, anti-inflammatory and analgesic[13,14], anti-diabetic[15,16], hypolipidemic[17,18], antibacterial[19,20], anti-fungal[21,22], anti-malarial[23], anti-viral[24], anti-HIV[25], treatment for AIDS[26], anti-aging[27], treatment for Alzheimer's[28] as well as Schizophrenic patients[29], wound healing[30,31], anti-ulcer[32,33], anti-migraine[34], antihypertensive[35], antidepressant[36], anti-allergic[37], anthelmintic[38,39], aphrodisiac[40], anti-venom[41,42], hepatoprotective[43], cytoprotective[44], etc.

In spite of all the above useful properties of arecanut, several research and review papers highlight chewing arecanut as dangerous [3,45-47]. While going through such papers it was observed that most of the authors did not work on sole arecanut but on a mixture of products such as betel quid, pan masala, gutkha, etc. in which arecanut was one of the ingredients but blamed arecanut for all the ill effects. Such misleading statements without working on the actual product mentioned in the title should be avoided and the correct nomenclature of the target specimen or specimens be highlighted in all Scientific reports. Some of such ambiguous research papers are cited and discussed in this article.

ARECANUT AND BETEL LEAF:

Commercially, arecanut is the seed or endosperm of the fruit of areca palm. Areca fruit is a fibrous, ovoid to round drupe of the size of a hen's egg. It has a single central ruminant, hard and solid endosperm covered by pericarp (husk) which is green in color when unripe turns to orange-yellow when ripe[48]. When cut open, the endosperm shows several dark brown lines alternating with opal white portions giving a marbled appearance inside. The nut gives a characteristic astringent and slightly bitter taste[48]. Some minimum processing of areca fruit is done in most parts of India for its marketing[49]. One type of arecanut, called as 'red supari' is obtained from tender or unripe areca fruits. The tender fruits are harvested at different stages of maturity, dehusked, the inside nuts are boiled either as whole nuts (if they are semi mature ones) or sliced into two to three pieces and then boiled (if they are tender nuts), removed from boiling liquid, coated with *kali* (the concentrated liquid obtained after boiling unripe arecanut) and dried. Another type, called as 'white supari' is obtained from ripe areca fruits. Such ripe fruits are harvested, dried properly along with husk and dehusked just before marketing as whole arecanuts or as 'white supari'[49]. These arecanuts are one of the common ingredients of betel quid and

several other chewing products[3]. Betel leaf, the leaf of *P. betle* vine, is another common ingredient of betel quid. Some people use the inflorescence of *P. betle*, instead of its leaf, for the preparation of betel quid.

BETEL NUT AND BETEL

As arecanut is commonly chewed along with the leaf or the inflorescence of *P. betle* vine, several researchers misnamed arecanut as 'betel nut'. Hence as per the botanical terminology, the word 'betel nut' coined by such researchers for arecanut is not correct but confusing. The WHO in its Monograph 2004 has suggested to avoid such misleading nomenclature of arecanut as 'betelnut' in all scientific literature [3]. Certain other researchers even went to the extent of naming the chewing substance as only 'betel' in the title which is highly ambiguous. According to the Wikipedia, the word 'betel' is given to the vine of the family Piperaceae. But several researchers coined this word either to arecanut or betel quid and unless one reads the full paper it is not possible to know for sure the type of chewing substance considered for their study[50-53]. Hence, to avoid all such confusions it is suggested to give the actual name or the proper description of the chewing substance in all scientific literature.

CHEMICAL CONSTITUENTS OF ARECANUT

Arecanut is not the nut containing only one chemical compound, but is a combination of more than 35 phytochemicals and minerals. The major phytochemicals reported in arecanut on dry weight basis are polysaccharides 17.3-25.7%, polyphenols (including flavonoids and tannins) 11.1-29.8%, fibres 8.2-15.4%, fats 8.1-15.1%, proteins 6.2-9.4%, ash 1.1-2.5% and arecoline 0.11-0.24%[54]. Apart from arecoline, other alkaloid contents of arecanut are arecaidine, guvacine, guvacoline, isoguvacine, arecolidine and homoarecoline[55]. Arecanut also contains Vitamin B6 and Vit C[56]. Polyphenols decrease with maturity, whereas polysaccharides, alkaloids, fats and fibres increase with maturity of the nut[57]. All the major phytochemicals of arecanut, including arecoline, decrease significantly while drying and storing with husk as whole nuts compared to fresh mature nuts[58] and also while roasting, soaking and boiling[59]. Among the fatty acids, lauric (19.5%), myristic (46.2%) and palmitic (12.7%), oleic (6.2%), linoleic (5.4%) and hexadecenoic acids (7.2%) are the most prominent ones. Minor proportions of stearic, decanoic and monoethylenic C12 and C14 acids are also present[60]. Among the

proteins, peroxidases such as catechin, epicatechin and procyanidin B1 are the major ones[61]. As many as 36 different minerals are already recorded in arecanut[3]. Hence, by researching only on one single chemical compound of arecanut, whether it is arecoline or any other chemical, it is scientifically not correct to correlate the data for the whole nut.

CHEMICAL CONSTITUENTS OF BETEL LEAF AND ITS INFLORESCENCE

Betel leaf (the leaf of *P. betle*) is another common ingredient of betel quid[4]. Similar to areca nut, betel leaf also contains more than 35 chemicals in it. The major phytochemicals of this leaf are proteins (3-3.5%), carbohydrates (0.5-6.1%), minerals (2.3-3.3%), fat (0.4-1%), fibre (2.3%), essential oil (0.08-0.2%), tannin (0.1-1.3%) and alkaloid (arakene)[61]. The betel leaf also contains different vitamins like vitamin-C (0.005-0.01%), nicotinic acid (0.63-0.89mg/100gms), vitamin-A (1.9-2.9mg/100gms), thiamine (10-70µg/100gms), riboflavin (1.9-30µg/100gms). Beside these it contains minerals such as calcium (0.2-0.5%), iron (0.005-0.007), iodine (3.4µg/100gms), phosphorus (0.05-0.6%) and potassium (1.1- 4.6%). All the 36 minerals found in areca nut are recorded in betel leaf also [4]. These leaves further contain betel oil, a volatile liquid, which contains several phenols including eugenol, hydroxychavicol, betel phenol and chavicol[62]. The flower or the inflorescence of *P. betle* contains instead of hydroxychavicol, another important phenolic compound called safrole in fairly good amounts which is not reported in leaves[63].

SLAKED LIME

Slaked lime (calcium hydroxide) is another common ingredient of betel quid[4]. It is obtained either by heating the covering of molluscan shells (sea shells), corals or from lime stones. The slaked lime is used to enhance the stimulant effect of arecanut. It facilitates hydrolyses of arecoline of arecanut to produce the central nervous stimulant, arecaidine[64]. As many as 35 minerals are also recorded in slaked lime[3].

BETEL QUID

Betel quid is a popular wet type of chewing mixture containing several ingredients as per the local preferences [3,4]. This quid generally contains arecanut, betel leaf and slaked lime. Some people add catechu, colloquially known as *katha* which is a resinous extract from the bark of the

Acacia (*Acacia catechu*) tree. Several people also add a piece of tobacco leaf to this chewing mixture. Depending on the personal taste, certain other ingredients such as cardamom, clove, grated coconut (fresh or dried), ginger, sugar, etc are also added to such betel quids. In countries such as Taiwan, Papua New Guinea, etc, instead of the leaf of *P. betle*, its inflorescence or its tender stem is added to this chewing mixture[63]. They mostly used tender whole nuts (along with husk), instead of dried dehusked nuts. Tobacco is generally not added to the chewing mixture. In certain other countries such as Palau, Guam islands people also use the whole tender areca nuts (along with husk) but instead of betel inflorescence, they used betel leaves for preparing betel quids[3,4]. Hence, the properties or the actions of such chewing mixtures would vary from chewers to chewers depending on the ingredients used for such preparations. In India, the betel quid, colloquially called as 'pan', is generally prepared by taking a betel leaf, on the lower surface of which a little amount of slaked lime is smeared, pieces of areca nut (fresh or dried) are then placed on the leaf and folded before putting into the mouth for chewing. A piece of tobacco leaf is also added by several people.

PACKAGED FORMS OF CHEWING MIXTURES

Nowadays, in many countries, mass-produced sachets of several ready to use dry chewing products such as pan masala, gutkha, etc are readily available as proprietary mixtures[3]. Generally, pan masala is a packaged form of chewing mixture containing areca nut, lime, catechu, certain condiments, flavouring agents, artificial sweeteners, etc. but without tobacco. When tobacco is mixed with such chewing mixtures they are commonly called as gutkha, zharda, khaini, etc and marketed in different trade names depending on the manufacturers. Sweet supari is a form of the sweetened packaged chewing product containing arecanut[65]. However, in certain packaged chewing products the actual ingredients used and the quality of such ingredients are not properly disclosed[66]. There are reports that certain packaged chewing products are adulterated with some hazardous phytochemicals, toxic metals and even pesticides such as DDT and BHC isomers much above the permissible limit[67,68]. Several dangerous volatile aldehydes, such as formaldehyde, crotonaldehyde, propionaldehyde, isobutyraldehyde, etc., were also detected in some brands of pan masala[69]. Certain brands of chewing products were also reported to contain menthol and saccharin in much above the permissible level[70,71].

CHEWING HABITS AND OBSERVATIONS

Betel quid chewing: When there is such vast diversity in the preparation of betel quids, the effects of any individual substance will definitely vary depending on the synergistic actions of other ingredients mixed. For example, it is reported that when arecanut alone was mixed with human saliva the amylase activity was reduced by 800%, but when arecanut was mixed with betel leaf and lime (betel quid) the amylase activity was increased by 30% [72]. When catechu (*Acacia catechu*) was mixed with such chewing mixture, the amylase activity was again found to decrease by 100% [72]. All these data clearly show that the action of arecanut varies drastically depending on the ingredients used for the preparation of chewing mixture. Further, it was also reported that the chemical constituents of different parts of the same plant need not be the same. For example, in *P.betle*, the leaf contains good amount of hydroxichavicol, whereas its inflorescence contains, instead of hydroxichavicol, another phenolic compound by name safrole in fairly good quantity [63]. While the former is an anticarcinogen [73], the latter might have a carcinogenic effect [74]. Hence, while reporting any scientific observations, it is mandatory to disclose all the components used in such betel quids and discuss their synergistic actions rather than tagging a single ingredient to the overall effects of chewing such mixtures on human health. Ironically, in most of the research papers it is seldom done and the authors blamed only arecanut for all the ill effects.

There is a paper entitled Cardiac arrhythmia and betel nut chewing --- is there a causal effect? [75]. While going through that article it is observed that the study was not done on chewing sole betel nut (arecanut) but on chewing betel quid. One should know that the chemical compositions of betel nut and betel quid are not the same. There is another paper entitled hypercalcemia and metabolic alkaloids with betel nuts chewing [76]. In that study, the patient who was suffering from hypercalcemia was actually chewing betel nut along with lime (calcium hydroxide), but the authors projected as if it was due to betel nut chewing alone ignoring the effects of calcium hydroxide. Another paper is titled as Oral health consequences of chewing arecanut wherein the entire study was on chewing pan which contained betel leaf and lime in addition to arecanut [77]. While reading the title of that paper it gives an impression that the authors had worked on chewing sole arecanut. Unless one reads the whole paper it is difficult to know for certain on which subject they had worked. There are so many other publications with

such wrong terminologies [63,78-87]. Some researchers did not even disclose the actual chewing product properly but simply blamed arecanut. There is a research paper titled ‘Betel nut chewing ----- Taiwanese male adults’ where the actual chewing substance was not clearly defined but cited several research papers on betel quid chewing as betel nut chewing [88].

Certain other papers even failed to disclose the actual ingredients of betel quids used in their study. ‘Does arecanut use lead to dependence?’ is a paper wherein the study was done on three categories of chewers, viz., a) persons using arecanut preparations without tobacco additives, b) persons using arecanut preparations with tobacco as additives and c) non users[89]. The contents of arecanut preparations were neither disclosed nor discussed in that paper, but highlighted only arecanut in the title. Another interesting paper is titled as Prevalence of areca nut chewing among rural population in India[90]. The study was mainly on people chewing the mixtures in which arecanut was one of the ingredients. No study was made on sole areca nut chewing, but the title mentions only arecanut! “Different patterns of quid usage among subjects with Oral submucous fibrosis in Mangalore population” is a paper wherein the authors did not report any OSF case on lone arecanut chewing in a total of 250 cases of OSF recruited[91]. Still the first sentence in the abstract says ‘Oral submucous fibrosis (OSF) is a potentially malignant disorder associated with the usage of arecanut’. Further, the actual ingredients of the types of quids were not disclosed in that paper. Instead, it was mentioned ‘the type IV quid as processed arecanut and type V as processed arecanut and processed tobacco’. What is meant by processed arecanut and processed tobacco is not disclosed in that paper. The clarity in terminology is very much necessary in all research papers to avoid ambiguity.

Chewing packaged products: Almost similar reports are there in several research papers published on chewing packaged products as well, though ample number of ingredients, both biological and chemical, are used for such preparations. For example, in the paper entitled ‘Oral submucous fibrosis, areca nut and pan masala use: A case-control study’ data were collected from people who chewed pan masala, kharra, betel quid, etc, but not on sole arecanut users[92]. However, the word arecanut is prominently highlighted in its title. Probably, the authors thought that those packaged chewing products contain only arecanut and nothing else. In another paper also, though the title was entitled as ‘Prevalence of oral submucous fibrosis among betel nut chewers dental patients of Patna’ the subjects were not on betel nut chewers, but mostly on

chewers of gutkha and other related products[93]. There is a paper titled as ‘Screening of oral potentially malignant disorders among arecanut chewers in Guam and Saipan’[94]. In that paper also there were no data on sole arecanut chewers, but the data were on chewers of different mixtures containing arecanut as one of the ingredients. In another paper, though the objective was to evaluate the genotoxic and clastogenic potential of arecanut and tobacco, the study was on chewing mixtures containing these products and not solely on arecanut or tobacco [95].

In a paper entitled ‘Effect of arecanut chewing and maximal mouth opening in School going children in Ahmadabad’ wherein the objective was to find out the effect of areca nut chewing on mouth opening, a total of 40 students having the habit of eating areca nut for 6 months or more were selected for the study [96]. On enquiry with the first author it was revealed that the entire study was carried out on school children chewing sweet supari and not sole arecanut. The contents of such sweet supari were neither disclosed nor analysed. There is a research paper titled as ‘Prevalence of Arecanut Chewing Habit among High School Children in Kanpur- A Cross Sectional Study in North India’ where the entire study was carried out on School children who were chewing either sweet supari, pan masala, gutkha or mistee pan but titled as arecanut chewing habits [97]. Of the 3,513 students interviewed in the age group of 14-18 years from 16 high schools in Kanpur, UP, not a single individual was reported chewing only arecanut, but the title gives a wrong impression that the study was carried out only on arecanut chewing habit and not on gutkha, mistee, etc. Hence, there should have been more clarity while selecting the title.

Review papers and pamphlets: Even in several review papers and some of the pamphlets, similar observations are noticed. In a review paper entitled ‘Betel nut chewing and its deleterious effects on oral cavity’ the reference papers were mainly on chewing betel quid rather than betel nut but the title says betel nut chewing as if there is no difference between betel nut and betel quid [98]. ‘Multifaceted mechanisms of arecanuts in oral carcinogenesis--’ is a review paper wherein, again, the authors did not review any paper dealing with sole arecanut chewing, but reviewed several papers dealing with betel quid chewing [99]. Similarly, in the paper entitled ‘A review of the systemic adverse effects of areca nut or betel nut’ the authors had cited several papers on chewing betel quid but categorized them as arecanut chewing[45]. In another exhaustive review the authors had combined all chewing habits and titled the paper as ‘Areca nut use and cancer in India’ as if there is no difference between all such chewing mixtures and

arecanut![46]. In another paper, though the objective was to review the adverse effects of arecanut on human health, the authors mostly cited the papers on betel quid or commercial chewing products and titled the paper as Adverse effects of arecanut[47]. Similarly, there are several other review papers, the references were mainly made either on betel quid or packaged chewing products, but titled as arecanut or betel nut as if all chewing products and arecanut are same [100-102]. Javed et al combined both arecanut and betel quid chewing together by saying that 'since arecanut is an essential component in betel quid by weight they combined both arecanut and betel quid together' but titled the review paper as 'arecanut usage' as if other components of betel quid have no role at all[103]. The public awareness pamphlet compiled by Alok Lati et al [104] highlighted arecanut chewing as highly dangerous without citing any research work on lone arecanut chewing! It is sad to note that the authors in all such review papers failed to notice the difference between arecanut, betel quid, pan masala, gutkha, etc. and treated all such chewing products as arecanut.

CONCLUSION:

The antiquity of arecanut goes back to few thousand years without any major noticeable ill effects. Of late, several research and review papers have emerged highlighting arecanut chewing as dangerous. However, while going through such articles it was noticed that in most of them, though the title says arecanut, the data were not on sole arecanut but either on betel quid or on several other commercial chewing products where arecanut was one of the ingredients. The actions or the synergistic effects of other ingredients present in such betel quid or chewing mixtures were totally ignored by the researchers and projected only arecanut for the total ill effects as if other ingredients have no role at all. One should know that only arecanut can be called as arecanut. It is scientifically not correct to call betel quid or any other commercial chewing mixtures or products containing arecanut, as one of the ingredients, as arecanut. The researchers should look into this aspect very closely before coming into any conclusion on their observations. They are also urged to investigate the chewing mixtures properly and give unambiguous titles for their publications based on the real works carried out or reviewed by them so that the readers will get the correct scientific information on such studies.

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