

Areca nut use: an independent risk factor for oral cancer

The health problem is under-recognised

Areca nut is the seed of the fruit of the oriental palm, *Areca catechu*. It is the basic ingredient of a variety of widely used chewed products. Thin slices of the nut, either natural or processed, may be mixed with a variety of substances including slaked lime (calcium hydroxide) and spices such as cardamom, coconut, and saffron. Most significantly, they may be mixed with tobacco products or wrapped in the leaf of the piper betel plant. Hence the more common name betel nut. Areca nut is used by an estimated 200-400 million people, mainly IndoAsians and Chinese.¹ It is used by men and women—in some societies the latter predominate. All age groups and social classes use the product. Areca nut has a long history of use and is deeply ingrained in many sociocultural and religious activities.²

Of particular interest in the United Kingdom, and perhaps other developed countries, is that use of areca nut continues and is often enhanced following migration. Thus British Asians have brought the use of areca from India (some via East Africa), Pakistan, Bangladesh, and other countries in the region and its use is thus firmly culturally bound. From the medical point of view, the most important consideration is the relation between areca nut use and the development of mouth cancer (oral squamous cell carcinoma) and its precursors leukoplakia and submucous fibrosis.^{3,4}

An increased risk for the development of oral malignancy in “areca nut only users” is reported.^{5,6} Adding tobacco to the quid is indeed a confounder in many studies, but there are some populations such as Taiwanese who do not add tobacco to the betel and areca quid. The reported relative risk for oral cancer among those who chew areca only in the Taiwanese population is 58.4 (95% confidence interval 7.6 to 447.6).⁷ The admixture of tobacco products further increases the likelihood of developing oral malignancy.⁸ Both duration and daily frequency of areca use increase the risk of developing cancer, suggesting a dose response relation.⁷ Other conditions that have been associated with use of areca nut include cardiovascular disease, diabetes mellitus, and asthma, all conditions with a high prevalence in the Asian community in the United Kingdom.

Historically a betel quid (paan) was often formulated to an individual's wishes but in the United Kingdom and other countries readymade packets of these products are now available as a proprietary



Paan: small pieces of areca nut are mixed with several other ingredients, sometimes including tobacco, wrapped in a betel leaf and chewed

mixture known as paan masala. There is increasing evidence that areca products induce a true dependency syndrome. A recent study of Gujarati areca users in north west London assessed their degree of dependency as equivalent to that of cocaine users especially if there is tobacco in the paan masala.⁹ Patients describe typical dependency symptoms, with difficulty in abstaining, withdrawal symptoms including headache and sweating, and need for a morning paan to relieve these symptoms. Individuals report queuing outside the paan shops waiting for them to open and continuing sequential use, analogous to chain smoking.

The addictive components in the preparations have not been identified. Arecoline has been isolated from the basic nut¹⁰ and has major effects on various neurotransmitters particularly on cholinergic neurones, but there are a variety of other alkaloids—namely, arecaidine, guracine, guacine, and arecolidine, as well as unidentified peaks on chromatography of the extracts. The recent development of capillary electrophoresis techniques should facilitate the identification of further bioactive molecules including carcinogens as well as providing diagnostic and treatment monitoring aids.

The role of areca products in causing oral fibrosis and malignancy and possibly contributing to other diseases has raised important public health issues. These products are inadequately labelled. There are no health warning labels and no restrictions on its sale to children or consumption in public places. European Union regulations on the ban on chewing tobacco within Western Europe appear to be circumvented by



Taiwanese patient with oral cancer and a history of chewing betel nuts

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is needed and health warnings should be enacted, but outright bans or restriction will probably prove to be counterproductive. The identification of dependence should be more generally known and facilities for treatment and programmes to reduce harm are needed. In addition, further research, both clinical and experimental, is needed on the biomedical and psychosocial consequences of areca usage.

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The authors are trustees of Areca Concern a registered charity that aims to address some of the concerns listed above.

the availability of tobacco mixed with areca nut for oral use and its availability in the British paan shops.

Banning the import of areca nut products (they can readily be purchased on the internet) or repressive legislation will prove ineffective. Prohibition of alcohol sales in the United States was unsustainable and provided pump-priming funds for the Mafia. Similar widespread smuggling has impaired public health measures over cigarette smoking.

There are other important issues. Areca nut usage is culturally bound and is an integral aspect of several Indo-Asian customs and thus part of their identity. Casual use of small quantities of areca nut on a non-regular basis is widely prevalent in Asian communities. Although this practice is unlikely to have long term ill effects with time, some individuals may develop a dependency syndrome. Longitudinal studies involving young people are therefore important. In certain communities the preparation and sale of areca products makes a significant financial contribution to the local economy. Accurate labelling of the products, especially with respect to admixture with tobacco, should be an important requirement. Health education

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- 4 Thomas S, Kearsley J. Betel quid and oral cancer: a review. *Eur J Cancer B (Oral Oncology)* 1993;29B:251-5.
- 5 van Wyk CW, Stander I, Padayachee A, Grobler-Rabie AF. The areca nut chewing habit and oral squamous cell carcinoma in South African Indians. A retrospective study. *S Afr Med J* 1993;83:425-9.
- 6 Merchant A, Husain SS, Hosain M, Fikree FF, Pitiphat W, Siddiqui AR, et al. Paan without tobacco: an independent risk factor for oral cancer. *Int J Cancer* 2000;86:128-31.
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- 9 Winstock AR, Trivedy CR, Warnakulasuriya KAAS, Peters TJ. A dependency syndrome related to areca nut use: some medical and psychological aspects among areca nut users in the UK. *Addiction Biol* 2000;5:173-9.
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Murder by fake drugs

Time for international action

Until recently the most infamous internationally known example of fake drug dealing was Graham Greene's fictional account of a British fake penicillin peddler who was eliminated in the sewers of postwar Vienna in *The Third Man*.¹ Unfortunately, malevolent dealings in counterfeit drugs are very much a contemporary reality. Notorious recent real examples include neomycin eye drops and meningococcal vaccine made of tap water; paracetamol syrup made of industrial solvent; ampicillin consisting of turmeric; contraceptive pills made of wheat flour; and antimalarials, antibiotics, and snake antivenom containing no active ingredients.²⁻⁹

In a recent survey of pharmacies in the Philippines, 8% of drugs bought were fake (quoted by Wondemagegnehu²). A countrywide survey in Cambodia in

1999 showed that 60% of 133 drug vendors sampled sold, as the antimalarial mefloquine, tablets that contained the ineffective but much cheaper sulphadoxine-pyrimethamine, obtained from stocks that should have been destroyed, or fakes that contained no drug at all.^{3 4} In another recent survey, 38% of tablets sold in five countries in mainland South East Asia as the new antimalarial artesunate were fake.⁵ Artesunate is an extremely important antimalarial drug, and its rapid action and lack of side effects have created significant demand in endemic areas. These characteristics, along with a relatively high cost, make artesunate particularly attractive to counterfeiters, who have gone to great lengths to deceive patients, using small amounts of ineffectual bitter chloroquine, copying the blister pack design, and even providing

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