



'Dissolve flatulence and phlegm, ease hangover, facilitate digestion, eliminate toxins from overindulgence of fat and sweet foods, gourmet for everyone to enjoy.' [1]

'Many more studies now provide evidence for the carcinogenicity of betel quid without tobacco for oral cancer and for betel quid with tobacco for cancers of the oral cavity, pharynx and oesophagus.' [2]

In the late 19th to early 20th centuries, betel-quid (or betel nut) was popular among the nobles and the wealthy in Chinese society. They would carry the small, delicate betel-quid bags (or boxes) with them and gave away betelquid as a present on social occasions. Early Chinese medicine books and cookbooks [1] mention the many beneficial effects betel-quid has on health. For example, betel-quid can facilitate digestion and ease hangover.

However, when the eastern stimulant betel-quid is put under the scope of modern western addiction theory and methodology, the façade is peeled away. One notorious downside is that betel-quid is identified as a human carcinogen by the World Health Organization [2]. Another dark side that is, as yet, little known concerns the probable dependence symptoms that betel-quid chewers may develop in terms of DSM-IV and ICD-10 criteria [3–6].

Lee *et al.* [6] conducted a large-scale survey across six Asian countries to investigate betel-quid dependence symptoms and syndrome among betel-quid chewers. Three primary conclusions can be drawn from their study. First, betel-quid dependence prevalence among chewers varies largely across countries. Secondly, the amount and frequency of betel-quid consumption are critical factors that positively predict the risk of dependence. Thirdly, tobacco additives in betel-quid increase the risk of dependence in Sri Lankan chewers.

The research conducted by Lee *et al.* [6] has at least two advantages: (i) a large sample was recruited and (ii) various betel-quid types and ingredients were evaluated. A large sample size allowed the researchers to perform higher-level statistical analysis, facilitating the understanding of complicated relationships between dependence and chewing characteristics. Types and ingredients of betel-quid vary across countries. For example, tobacco is usually added by Nepalese and Indonesian chewers, while slaked lime and betel leaf are used by Taiwanese chewers. Because various ingredients and types of betelquid were included in Lee *et al.*'s study, they had the ability to investigate whether these ingredients and types, in addition to being solely tobacco-additive [3], affect the risk of dependence.

However, Lee *et al.* [6] may have overlooked the influence of tobacco smoking on betel-quid dependence. This influence was observed in a survey of chewers in Malaysia, Indonesia and Sri Lanka who chewed both tobaccoadded and tobacco-free betel-quids. Only in Sri Lankan chewers did tobacco additives increase the dependence risk. Why was this relationship between tobacco additive and dependence risk not observed in Malaysian and Indonesian chewers? The proportion of tobacco smokers in the tobacco-added and tobacco-free chewers may be a key issue, which was not investigated further by Lee and colleagues.

In Malaysian and Indonesian chewers, there was a larger (and significant) proportion of tobacco smokers among the tobacco-free chewers than the tobacco-added chewers. Conversely, in Sri Lankan chewers, the proportions of tobacco smokers in both types of betel-quid were equivalent. It is possible that the proportion of tobacco smokers among the chewers may affect betel-quid dependence. Specifically, not only is the tobacco additive in betelquid, but the tobacco smoked can affect betel-quid dependence. Betel-quid and tobacco are often used concurrently [7,8]. Neurologically, arecoline (one of the primary chemical ingredients of betel-quid) and nicotine have been shown to act on the muscarinic and nicotinic acetylcholine receptors [9,10]. Because of the concurrent use and similar neurological mechanisms of betel-quid and tobacco, the cross-substitutability of tobacco-added betel-quid and tobacco smoking should be taken into consideration when betel-quid dependence is assessed.

In addition to the large-scale epidemiological surveys, cognitive neuroscience provides important and intriguing theories and paradigms that can guide betel-quid researchers to investigate how betel-quid affects chewers' cognition and brain activity. While fruitful cognitive neuroscience studies on drugs and substances are familiar to the West, the same type of study on betel-quid is still very rare. Understanding chewers' cognition and brain activity can help medical practitioners understand why the chewers are addicted. For example, betel-quid chewing immediately concentrates visual attention [11,12], and heavy (not light) chewers) pay more attention to betelquid cues [13]. Betel-quid chewing may affect brain areas involving addiction, as shown in other substances (e.g. the amygdala-striatal and pre-frontal control systems) [14,15]. With knowledge of the neurological mechanisms of using betel nuts, more effective treatment plans can be developed.

When eastern betel-quid encounters western addiction theories, together they may bring new insights into betel-quid use. Researchers have come a long way in understanding betel-quid and addiction research, but there is a long way to go.

Declaration of interests

None.

Keywords Betel nut, betel-quid, cognitive neuroscience, dependence, epidemiological survey, tobacco.

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