

Betel leaf: Revisiting the benefits of an ancient Indian herb

In India, Betel leaf (BL) plays an important role since ancient culture. Its use in India dates back to 400 BC. As per ancient books of Ayurveda, Charaka, Sushruta Samhitas, and Kashyapa Bhojanakalpa, the practice of chewing BL after meals became common between 75 AD and 300 AD. Toward the 13th century, European traveler Marco Polo recorded betel chewing among kings and nobles in India.

Importance of BL has been described in ancient books of Ayurveda. Use of BL was known for centuries for its curative properties. In Chinese folk medicine betel leaves are used for the treatment of various disorders and claimed to have detoxification, antioxidation, and antimutation properties. There are number of research experiments on BL, where the leaf extract, fractions, and purified compounds are found to play a role in oral hygiene, and to have various properties including anti-diabetic, cardiovascular, anti-inflammatory/immunomodulatory, anti-ulcer, hepato-protective, anti-infective, etc., Patents were also awarded for some of the biological activities like anti-inflammatory, anti-cancer, and immunomodulatory associated with the leaf extracts and purified compounds.^[1]

There is archaeological evidence that the betel leaves have been chewed along with the areca nut since very ancient times. It is not known when these two different stimulant substances were first put together. Betel leaves are used as a stimulant, an antiseptic, and a breath-freshener, whereas areca nut was considered as aphrodisiac.

Chewing habits of people have changed over time. The betel leaves are chewed together in a wrapped package along with areca nut and mineral slaked lime. Catechu (kattha) and other flavoring substances and spices were also added subsequently. For many decades, tobacco has also been added to the BL package. The practice of chewing BL has been decreasing progressively and now the Quid comprising of tobacco, areca nut, and slaked lime (gutkha) is generally in practice.

Although use of BL was wide spread in ancient times, but there has not been strong evidence of incidence of oral cancer in ancient times.

Various experiments evaluating effects of BL suggested no harmful effect when consumed alone. Bhide *et al.*^[2] demonstrated effect of aqueous BL extract where administration of areca nut extracts in Swiss and C17 mice

developed different types of cancer while control group and mice fed with aqueous BL extract did not develop any tumors. Shirname *et al.*^[3] conducted experiments in which Swiss mice were given aqueous extracts of Betel Quid and its components by gavage. Mice fed with BL extracts alone had comparable tumor rates with those of controls. Rao *et al.*^[4] compared tumor development in Syrian golden hamsters which received topical applications of aqueous extracts of tobacco, areca nut, or BL. Animal treated with tobacco and areca nut had tumor development rate of 15 and 10%, respectively, whereas untreated animals, treated with BL alone, and treated with vehicle did not develop any tumors.

BL extract even showed beneficial effect in terms of reduced tumor growth rate in animal tumor models. Rao *et al.*^[5] demonstrated that the extract of betel leaves inhibited emergence of DMBA-induced mammary carcinogenesis in rats. However, it did not inhibit the growth in already induced mammary tumors. Chemopreventive effect of betel leaves was demonstrated by Bhide *et al.*^[6] where administration of BL extract lowered the benzo[a] pyrene induced fore-stomach papillomas in Swiss mice. Maximal inhibition of papilloma development was observed in mice receiving hydroxychavicol-a constituent of BL extract.

Thus, there is abundant evidence showing beneficial effects of BL alone in experimental animals, but its validation in humans is still lacking. There is no head to head comparison of incidence of oral cancer in Quid chewers with or without BL.

Shetty *et al.* in this issue of SAJC^[7] have nicely demonstrated the advantage of BL in maintaining salivary ascorbic acid levels in humans. Salivary ascorbic acid may help prevent carcinogenesis in the oral cavity, but the effects of quid/tobacco at other sites of body may still continue. At the same time, there is no long term follow up of study patients which could have given an insight into the development of oral cancer in Betel Quid v/s Quid chewers alone. Based on this study, we cannot recommend chewing of Quid even with BL as there is no long term follow up and more studies including epidemiological and basic science studies are warranted to clearly establish the role of BL in preventing carcinogenesis.

Rajendra Toprani, Daxesh Patel

Head and Neck Surgical Oncologist, Aastha Oncology Associates, HCG Cancer Centre, Sola-Science City Road, Ahmedabad, Gujarat, India

Correspondence to: Dr. Rajendra Toprani

E-mail: rajendratoprani@hotmail.com

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| Quick Response Code:  | Website: www.sajc.org |
| | DOI: 10.4103/2278-330X.114120 |

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How to cite this article: Toprani R, Patel D. Betel leaf: Revisiting the benefits of an ancient Indian herb. *South Asian J Cancer* 2013;2:140-1.
Source of Support: Nil. **Conflict of Interest:** None declared.

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Indian Cancer Congress 2013.
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For further details please contact Sonali Khurana, Secretariat Coordinator,
P: 011-42334196,
M: 9910777306 or visit www.indiancancercongress2013.org