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## Contents

- ▶ SEM evaluation of marginal sealing on composite restorations using different photoactivation and composite insertion methods
- ▶ Canal-centring ability of three rotary file systems in simulated curved canals: A comparative study
- ▶ Effect of a single-use toothbrush on plaque microflora
- ▶ Correlation of "in vivo" microcirculation and degeneration of the basal cells of the epithelium in lingual lichen planus
- ▶ A comparative study of inter-abutment distance of dies made from full arch dual-arch impression trays with those made from full arch stock trays: An *in vitro* study
- ▶ Evaluation of gastric tolerability, antinociceptive and antiinflammatory activity of combination NSAIDs in rats
- ▶ Community periodontal index of treatment needs index: An indicator of anaerobic periodontal infection
- ▶ Relationship between the size of patency file and apical extrusion of sodium hypochlorite
- ▶ Effect of water storage on resin-dentin bond strengths formed by different bonding approaches

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## Copper content of various constituents of betel quid

Sir,

Oral submucous fibrosis (OSF) is a chronic inflammatory condition leading to trismus and impairment of various oral functions. The malignant transformation rate of this premalignant condition is reported to be as high as 14%.<sup>[1]</sup>

OSF is prevalent in South East Asia. Various etiological factors have been implemented in the causation of this condition. Currently, the habit of chewing areca nut (*Areca catechu*) is recognized as the most important etiological agent in the pathogenesis of this condition, focusing at the high level of copper present in areca nut.<sup>[2]</sup> The chewing habit varies across

the country. With the introduction of various flavored areca nut products with or without tobacco, and other ingredients in the market, pure areca nut chewing habit has decreased.

The accumulation of copper in an organ may cause intracellular damage, ultimately expressing itself in cancerous lesions.<sup>[3]</sup> A substantial amount of copper is released into saliva while chewing areca nut. The high exposure to oral tissues during chewing could increase the local absorption and accumulation of copper. Copper reaches the connective tissue by transmucosal transport through the epithelial cells bound to metallothionein protein, by nonenzyme dependent diffusion.<sup>[2]</sup>

It has been demonstrated that copper chloride *in vitro*, significantly increases the production of collagen by fibroblast. Collagen deposition in the OSF tissue may be attributed to increase in the lysyl oxidase activity, which is a metalloenzyme of copper. Lysyl oxidase causes posttransitional modification of collagen fibers rendering them resistant to action of collagenase, the increase in the copper level in tissue is said to cause excessive cross-linking and accumulation of collagen.<sup>[4]</sup>

Many of the recent studies on OSF implicate copper as the causative factor in initiation of this disease. Keeping this in mind, we evaluated the copper content of various ingredients frequently mixed with areca nut to see whether these constituents may contribute to addition of copper content. Various ingredients were dried and powered and sent to Central Plantation Crops Research Institute (Vittal, India) for the estimation of the copper content using atomic absorption spectrometry.

The copper content reported is as follows: Red arecanut (18.3 ppm), white areca nut (14.9 ppm), betel leaf (18.5 ppm), gutkha (13.2 ppm), flavored areca nut (12.2 ppm), tobacco leaves (6.3 ppm). The above data shows that the betel leaf contains the highest amount of copper and tobacco contributes little to copper content. To our knowledge, the copper content of these products (except gutkha) has not been reported till date.

This shows the need to individually assess the effect of these ingredients on elevating the copper content in oral mucosa. We propose that two or more of these ingredients mixed with areca nut with high copper content can produce an additive effect thereby hastening the time for causing OSF.

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