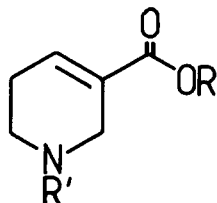


STIMULATION OF FIBROBLASTS BY ARECA ALKALOIDS AND THEIR RELATIONSHIP WITH ORAL SUBMUCOUS FIBROSIS

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The chewing of Betel nuts has been linked with the incidence of oral cancer and arecaidine has been postulated as a causative agent (Ashby et al 1979). It is possible that oral cancers develop subsequently to oral submucous fibrosis, which is a chronic disabling disease characterised in advanced cases by a gross fibrosis affecting the submucous tissues of the oral cavity. The fibrosis produces stiffness and eventual immobility of the tongue, lips, cheeks, soft palate and faucial pillars. Widespread epidemiological studies in India, South Africa and Taiwan have linked the disease with the chewing of "Betel chew" or "pan supari". The Betel Chew usually consists of a leaf of the Piper betel vine wrapped around fragments of the nut of the Areca catechu palm. The inside of the leaf is smeared with calcium hydroxide and various substances are added, the commonest of which is tobacco.



1. $R = R' = \text{CH}_3$
2. $R = \text{H}, R' = \text{CH}_3$
3. $R = \text{CH}_3, R' = \text{H}$

Recently (Canniff and Harvey 1982) it was found that arecoline (1), the major alkaloid of Areca catechu, stimulated DNA and collagen synthesis in human fibroblasts *in vitro*. The present work demonstrates that human buccal fibroblasts metabolise arecoline to arecaidine (2); 10^6 cells will convert over 50% of a 200 μg dose of arecoline in 7 days. It was found that arecaidine as well as guvacoline (3), nicotine and caffeine stimulated collagen synthesis by as much as 150% in these cells, in a dose dependant manner (0.1-100 $\mu\text{g ml}^{-1}$). Collagen synthesis was estimated by incorporation of ^3H -proline into native collagen and DNA synthesis was estimated by incorporation of ^3H -thymidine into the TCA insoluble fraction of the fibroblast. Thus stimulation of buccal fibroblasts by Areca alkaloids may be an important factor in oral submucous fibrosis. This effect is possibly mediated via the hydrolysis *in vivo* of arecoline to arecaidine.

Ashby, J. et al (1979) *The Lancet*: 112-113

Canniff, J. and Harvey, W. (1982) *Int. J. Oral Surg.* in press

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