PROCEEDINGS
– OF RESEARCH AND PRACTICE IN ALLIED AND ENVIRONMENTAL HEALTH –

Chasing the 'unusual suspects' underlying the procarcinogenic effects of *Areca catechu* nut

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Background: The high incidence of oral cancers in Asian countries is strongly linked to Areca nut mastication (*Areca catechu* L.). While areca alkaloids are recognized for their psychoactive effects, the precise cancer-inducing constituents remain unclear. Arecoline is often labeled as the main culprit, but the chemical complexity of *A. catechu* suggests the involvement of other compounds in carcinogenesis [1]. **Objective:** This study aims to further characterize the constituents in *A. catechu* that may contribute to carcinogenesis. **Methods:** Effects on matrix metalloproteinases were assessed through enzymatic assays (up to 200 µM), same applying to the impact on the activity of lipoxygenase 5 (LOX-5) and acetylcholinesterase. Effects on the cell viability of buccal mucosa cells were assessed in TR-146 cells via the MTT and NR assays, after exposure to the aqueous extract of *A. catechu* or its isolated phytochemicals (up to 1 mg/mL or 800 µM, respectively). **Results:** Significant inhibition of 5-LOX activity was observed, particularly with (+)-catechin and (-)-epicatechin (58% and 72%, respectively, $p < 0.001$) at 200 µM. Guvacoline and isoguvacine (28% and 35%, respectively, $p < 0.01$) also exhibited inhibition at concentrations higher than 100 µM. Guvacoline and isoguvacine significantly inhibited acetylcholinesterase (38%, $p < 0.05$), suggesting modulation of cholinergic neurotransmission, arecoline exhibiting the most potent effect (62%, $p < 0.001$) reinforcing its neuroactive role. Arecoline significantly reduced the viability of buccal mucosa cells at ≥400 µM ($p < 0.001$), with a marked reduction at 800 µM. Gallic and gallotannic acid exhibited cytotoxicity only at 800 µM ($p < 0.001$ and $p < 0.01$, respectively). *A. catechu* extract demonstrated high toxicity at 1 mg/mL ($p < 0.01$), suggesting a possible synergistic effect of its components. **Conclusions:** Flavonoids strongly inhibit 5-LOX, while alkaloids affect acetylcholinesterase and cause significant toxic effects upon TR-146 cells both at mitochondrial and lysosomal levels.

Keywords: Areca alkaloids; Carcinogenesis; Oral cancer

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References

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