

Khat induces G1-phase arrest and increased expression of stress-sensitive p53 and p16 proteins in normal human oral keratinocytes and fibroblasts

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Abstract:

Khat is a psychostimulant plant used by over 10 million people daily, mainly in eastern Africa and the Middle East. Previous studies have suggested an association between khat use and oral lesions such as hyperkeratosis and oral cancer. This study investigated the effects of an extract of khat on primary normal human oral keratinocytes (NOK) and normal human oral fibroblasts (NOF). Low (sublethal) concentrations of khat inhibited the proliferation of both cell types in a dose-dependent and time-dependent manner. Both NOK and NOF treated with khat accumulated in the G1-phase of the cell cycle and showed increased expression of the stress-sensitive p53 protein after 24 h. Normal human oral keratinocytes showed a profound increase in p16INK4A (p16) after 24 h and showed morphological changes suggesting cell differentiation. Normal human oral fibroblasts showed growth inhibition and increased expression of p21WAF1/CIP1 (p21) within 24 h. The concentrations of khat tested in this study were within the range of those found in the oral cavity of khat chewers. The results show that stress induced by khat modulates the cell cycle in oral keratinocytes and fibroblasts. It is further speculated whether khat could have similar effects *in vivo*, especially in keratinocytes.