

Abstract:

Khat chewing is a widespread habit that has a deep-rooted sociocultural tradition in Africa and the Middle East. The biological effects of khat are inadequately investigated and controversial. For the first time, we show that an organic extract of khat induces a selective type of cell death having all morphological and biochemical features of apoptotic cell death. Khat extract was shown to contain the major alkaloid compounds cathinone and cathine. The compounds alone and in combination also induced apoptosis. Khat-induced apoptosis occurred synchronously in various human cell lines (HL-60, NB4, Jurkat) within 8 h of exposure. It was partially reversed after removal of khat and the effect was dependent on de novo protein synthesis, as demonstrated by cotreatment with cycloheximide. The cell death was blocked by the pan-caspase inhibitor Z-VAD-fmk, and also by submicromolar concentrations of Z-YVAD-fmk and Z-IETD-fmk, inhibitors of caspase-1 and -8, respectively. The 50% inhibition constant (IC₅₀) for khat (200 µg ml⁻¹)-induced apoptosis by Z-VAD-fmk, Z-YVAD-fmk and Z-IETD-fmk was 8 × 10⁻⁷ M as compared to 2 × 10⁻⁸ M and 8 × 10⁻⁸ M, respectively. Western blot analysis showed a specific cleavage of procaspase-3 in apoptotic cells, which was inhibited by Z-VAD-fmk. The cell death by khat was more sensitively induced in leukaemia cell lines than in human peripheral blood leukocytes. It is concluded that khat induces a rather swift and sensitive cell death by apoptosis through mechanisms involving activation of caspase-1, -3 and -8.