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Comparative Lethality of Coca and Cocaine[1]

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BEDFORD, J. A., C. E. TURNER AND H. N. ELSOHLY. *Comparative lethality of coca and cocaine.* PHARMAC. BIOCHEM. BEHAV. **17**(5) 1087–1088, 1982.—The 24 hour lethal effects of cocaine were compared to those of a crude ethanol extract of the coca leaf (*Erthroxylon coca*) in male, Swiss mice. Various doses of cocaine HCl and coca leaf extracts suspended in a Tween 60, Arlacel 83, and distilled water vehicle were injected IP into groups of 10 mice. The LD_{50} for cocaine was 95.1 mg/kg. The LD_{50} for the coca extract was 3450 mg/kg. The LD_{50} of the extract based on its cocaine content was 31.4 mg/kg. The results clearly indicate that the coca leaf contains constituents other than cocaine that can contribute to a toxic effect of the plant.

Cocaine Coca Lethality Mice

PREVIOUS research [1] reported by our laboratory has indicated that the coca leaf contains constituents other than cocaine that are behaviorally active. We have reported anorexic activity in the absence of CNS stimulatory or depressant effects. We have also reported [6] that a cocaine free extract of the plant produces typical cocaine-like decreases in fixed-ratio food reinforced responding in rats. We have further shown that these same extracts, however, produce a decrease in fixed-interval responding while cocaine at moderate doses has been shown to increase fixed-interval responding. Finally, it has recently been reported [3] that a water soluble non-alkaloidal extract reduces oxygen utilization in mice and produced hyperglycemia, reduces heart rate and blood pressure in dogs. The present paper reports on the comparative lethality of a crude ethanol extract to that of cocaine in mice.

METHOD

Subjects

The subjects were male, Swiss mice obtained from Harlan Industries (Cumberland, IN). The subjects were housed individually in galvanized suspension cages with free access to water and chow (Purina rat chow). Ambient temperature was maintained at 20±2°C and the light/dark cycle was maintained at 12 hours on, 12 hours off.

Apparatus

Lethal dose testing was carried out in the subjects home cage.

Solution preparation. Coca leaves (*E. coca*) were powdered using a Wiley mill and then exhaustively extracted with 95% ethanol. Following solvent evaporation, various doses of the residue were suspended in sterile distilled water using 2 drops each of Tween 60 and Arlacel 83 per ml of water. Cocaine HCl doses were prepared in the same manner. Cocaine content of the extract was determined by a method developed in this laboratory [7].

Procedure

The subjects were deprived of food 18 hours prior to testing. On the day of testing, groups of 10 mice were injected (IP) with one of five doses of the ethanol extract of the coca leaf or one of five doses of cocaine HCl in identical vehicles. Injection volume was held constant at 10 ml/kg. The subjects were then observed for survival at the following times after dosing: 15 and 30 min, 1, 2, 4, 8, 12, 24 hours. The LD_{50} were obtained after the method of Litchfield and Wilcoxon [4].

RESULTS AND DISCUSSION

The obtained LD_{50} of the ethanol extract was 3450 mg/kg (95% CI 3100–3800). The LD_{50} of the extract based on its cocaine content was 31.4 mg/kg (95% CI 28.8–34.1). The LD_{50} obtained with cocaine alone was 95.1 mg/kg (95% CI 89.2–101.5). From these data it is quite clear that constituents other than cocaine, did, in some way, contribute to the lethal effects of the ethanol extract. To date there is no data to indicate any toxic effects associated with use of coca leaves. In fact, several investigators [2, 5, 8] have reported on the obvious lack of toxicity of the coca leaf, when compared to the primary alkaloid of the plant, cocaine. We have previously reported [1] a toxic effect with a non-alkaloidal, water soluble extract of the plant. The constituent responsible for this effect is unknown at the present time. The tremendous difference in the lethal dose of cocaine and that of

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the coca leaf reported here, however, indicated the coca leaf contains constituents other than cocaine which can, at the very least, contribute to its lethal effects. These results anticipate the isolation of the constituent or constituents responsible for the effects reported here.

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