Chapter 1
Plasma Cocaine Metabolite Levels and Liver CYP450 3A4 Isoenzyme Activity as Indicators of Cocaine Metabolism in Rats Treated With Salako Supplements

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ABSTRACT

The effects of Salako nutritional supplements on cocaine-dependent Sprague Dawley rats was investigated. Rats were made cocaine-dependent using conditioned place preference (CPP) where craving was analyzed regularly. Cocaine metabolite levels were determined from blood samples. CYP450 3A4 isoenzyme activities were obtained using liver homogenate. Statistical analysis was done using SPSS one-way ANOVA and Duncans multiple range test. Results show that when cocaine use was discontinued, the supplements reduced craving of cocaine significantly. Blood plasma results showed higher benzoylecgonine equilibrium possibly indicating that the supplements aided the removal of stored cocaine metabolites which may have contributed to better management of craving in the rats. CYP450 3A4 isoenzyme activity was further enhanced by the supplements and is indicative of increased cocaine metabolism. The results indicate that the Salako nutritional supplements reduce craving caused by chronic cocaine administration by increasing the liver CYP450 3A4 isoenzyme activity, resulting in better plasma clearance.

INTRODUCTION

Cocaine ($C_{17}H_{21}NO_4$), classified as a stimulant, is described as being the most potent, powerfully addictive stimulant of natural origin. The leaves of the Coca plant (*Erythroxylum coca*) can be harvested several times a year. The alkaloid, cocaine, is extracted from the leaves of the Coca plant, which originates in South America, and to a lesser extent, in Africa, Indonesia and India (UNODC, 2010). Cocaine is one of the oldest known psychoactive substances. Coca use has been traced as far back as around 5000 B.C. wherein the leaves of the plant were continually chewed in the mouth. Pure cocaine was isolated in the 1880's (National Institute on Drug Abuse, 2008). In the early 1900s, pure cocaine was the main active ingredient in numerous pharmaceutical and recreational formulations due to their properties that enhanced general activity and decreased fatigue.

Illicit cocaine from South America is produced normally as relatively pure hydrochloride salt (ranging from 80 – 95 percent) for export to the United States. Illicit cocaine is distributed ranging from a white crystalline powder (cocaine hydrochloride), to that of an off-white chunky material ("crack" or "rock" cocaine) (Drug Enforcement Agency, 2005). Street cocaine is usually adulterated with various substances such as mannitol, lactose and glucose, talc and flour. Due to the heat

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