PII-74

USE OF SALVIA DIVINORUM, AN UNSCHEDULED HALLUCINOGENIC PLANT: A WEB-BASED SURVEY OF 500 USERS. M. J. Baggott, BA, E. Erowid, F. Erowid, J. E. Mendelson, MD, California Pacific Medical Center Research Institute, Erowid.org, University of California, San Francisco, San Francisco, CA.

Salvia divinorum (SD) is a legal psychoactive plant that produces hallucinogen-like effects through a putative kappa opiate mechanism. We characterized the reasons, methods, and reported consequences of SD use in a sample of 500 users (92.6% male, 23.4±8.7, range 13-68 years) with an on-line questionnaire. They had used 13.3±22.9 (range 1–250) times, usually to explore altered consciousness or to have a spiritual/mystical experience. 80.6% probably or definitely would use SD again. 92.6% smoked SD with 61.4% using a concentrated extract and 37.3% using dried leaf; effects were estimated to last 14.1±12.8 minutes. Compared to other methods of altering consciousness, SD effects were felt to be unique. Common (>25%) after-effects of SD included feelings of increased insight (47%), improved mood (44.8%), calmness (42.2%), increased sense of connection with the universe or nature (39.8%), weird thoughts (36.4%), things seem unreal (32.4%), floating feeling (32%), increased sweating (28.2%) and body felt warm or hot (25.2%). 25.8% reported persisting (>24 hr) positive effects (usually an increased sense of well-being) on at least 1 occasion. 4.4% had persisting negative effects (most often anxiety). 0.6% had sought professional help for a SD-related problem. At some point, 0.6% felt addicted to or dependent upon SD; 1.2% reported strong cravings for SD; 0.4% endorsed three DSM-IV dependence criteria. We conclude that SD is commonly used and merits further study.

PII-75

ORAL KETAMINE AS A POSITIVE CONTROL IN ABUSE LIABILITY STUDIES. M. K. Romach, MSc, MD, E. M. Sellers, MD, PhD, H. L. Kaplan, PhD, L. C. Fernandes, MSc, J. Oldenhof, PhD, S. McDonald, PhD, Ventana Clinical Research Corporation, Forest Research Institute, Toronto, Canada.

Background. NMDA receptor antagonists are currently being developed for the treatment of several neurodegenerative disorders including Alzheimer's disease, Parkinson's disease and neuropathic pain conditions. Some high affinity NMDA receptor antagonists (e.g. phencyclidine and ketamine) have dissociative properties and are established agents of abuse. Other NMDA receptor antagonists such as memantine, amantadine or dextromethorphan do not exhibit significant potential for abuse. Therefore based on the pre-clinical and/or clinical pharmacological profiles, a clinical abuse potential evaluation may be required for a new NMDA receptor antagonist or a new formulation of an existing NMDA receptor antagonist. Positive (abused) control drugs such as ketamine are required in the conduct of human abuse liability studies. Most published studies have evaluated intravenous ketamine as a comparator drug.

Purpose. The present study was designed to assess the subjective effects of oral ketamine.

Methods. Twenty-nine healthy, experienced recreational drug users were given d-amphetamine (d-AMP) 20 mg p.o. in a single-blinded within-day qualifying day in which they could receive three doses of placebo and one dose of d-AMP. Sixteen subjects reliably reported liking d-AMP and 11 subjects (9 males, 2 females) entered a single-blind controlled dose escalating study in which they received ketamine 65 mg, 100 mg or 150 mg (intravenous formulation dissolved in juice) or placebo-juice orally. Subjective and physiologic measures were evaluated for up to 8 hours post-drug administration

Results. Graded dose related effects and differences from placebo were reported across a wide range of abuse measures (e.g. VAS feeling high, VAS liking, subjective price value, Cole ARCI euphoria). Pharmacologic effect characteristics of the class (e.g. floating, confusion) were also found. Ketamine 65 mg was readily distinguished from placebo on most measures. Doses of 150 mg were well tolerated in the 4 subjects who received this dose.

Conclusions. These pharmacological data suggest that oral doses of ketamine (60 -150 mg) can be used as positive controls for studies for NMDA receptor antagonist mediated effects.

PII-76

COMPARATIVE AMERICAN AND JAPANESE TOBACCO SMOKE UPTAKE PARAMETERS AFTER OVERNIGHT TOBACCO DEPRIVATION. E. F. Domino, MD, C. Kadoya, MD, PhD, S. Matsuoka, MD, L. Ni, MS, K. Fedewa, University of Michigan, University of Occupational and Environmental Health, Ann Arbor, MI.

Tyndale et al. (2002) reported that Japanese, among various ethnic groups, have a relatively high incidence of lower activity *CYP2A6* genotypes and are associated with decreased risk for tobacco smoking. Furthermore, a very large percentage of male Japanese smoke. American and Japanese overnight deprived tobacco smokers were phenotyped with respect to expired CO, plasma nicotine and cotinine, and red cell COHb. The participants were 51 American and 55 Japanese cigarette smokers of mixed gender who met similar strict criteria. American and Japanese female smokers had similar tobacco uptake parameters. American and Japanese male smokers differed; the latter had higher plasma nicotine and lower cotinine levels as well as calculated 24 hr dose of nicotine and lower exhaled CO. Japanese females and males were similar in all tobacco smoke uptake parameters. When the two racial groups were compared, irrespective of gender, the only statistically significant differences were lower mean exhaled CO levels and percent COHb in the Japanese. It is concluded that Japanese males inhale cigarettes in moderation compared to Americans.

PII-77

THE RELATION BETWEEN TOTAL AND FREE PLASMA CONCENTRATIONS OF NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS IN HIV-INFECTED CHILDREN. N. Y. Rakhmanina, MD, J. N. van den Anker, MD, PhD, J. Sever, MD, H. Spiegel, MD, PhD, S. Soldin, PhD, Children's National Medical Center, The George Washington University, Washington, DC.

Purpose: A significant relationship between the intracellular concentrations (ICC) of nucleoside reverse transcriptase inhibitors (NRTIs) metabolites and outcome parameters in HIV infection exists. Variability in free plasma concentrations of NRTIs may contribute to the variability in ICC of their triphosphate metabolites. To date no studies have investigated the relation between total and free plasma concentration of NRTIs. Our purpose was to determine the total and free concentrations of lamivudine (3TC), stavudine (d4T) and zidovudine (AZT) in plasma in HIV-infected children.

Methods: 22 pediatric patients (median age 8.9 years) were enrolled in the study. Unbound 3Tc, d4T, and AZT were separated by ultrafiltration. The drug plasma concentrations were determined by tandem-MS using Sciex APT-2000. Routine statistical methods were used.

Results: There was a highly significant relation between total and free plasma concentrations for all three NRTIs with a r-value of 0.995 for 3TC ($3TC_{freepl}=0.95\times 3TC_{totalpl}-36.51$, $p<0.0001$), a r-value of 0.924 for d4T ($d4T_{freepl}= 0.65\times d4T_{totalpl}-3.61$, $p<0.0001$), and a r-value of 0.907 for AZT ($AZT_{freepl}= 0.14\times AZT_{totalpl}+27.3$, $p<0.002$).

Conclusion: This pilot study showed a significant linear correlation between total and free plasma concentration of 3TC, d4T and AZT in pediatric HIV-infected children. Future studies need to investigate the relation between free plasma concentrations of NRTIs and ICC of their active metabolites.