# IMPLICATIONS OF RESEARCH FOR TREATMENT: *ROHYPNOL*

BY JANE C. MAXWELL, PH.D. THE CENTER FOR EXCELLENCE IN DRUG EPIDEMIOLOGY GULF COAST ADDICTION TECHNOLOGY TRANSFER CENTER U. T. CENTER FOR SOCIAL WORK RESEARCH

Rohypnol (flunitrazepam) is a benzodiazepine originally formulated for preoperative anesthesia or sedation and treatment of insomnia. At low doses, flunitrazepam acts as a muscle relaxant and a sedative-hypnotic. At higher doses, it can cause lack of muscle control and loss of consciousness. Flunitrazepam has had a long history of abuse by heroin and cocaine addicts, and because it was specifically formulated to produce anterograde amnesia, it has been used to commit sexual assault. In addition, it has gained popularity among youths as a "cheap drunk." Street names include roofies, la rocha, roche, R2, rope, FM2, forget-me pill, rowie, run-trip-and-fall, los dos, and Mexican valium [1].

### LATEST RESEARCH FINDINGS

In 1996, the U.S. government prohibited the importation of the drug into the country, but it remains available in other countries and continues to be illegally brought into the U.S. Since 2001, only the 1mg Roche tablet has been available, although generic products continue to be available in the 2mg strength [2], which has been the strength preferred for misuse, since street lore holds that the 2mg pill produces a quicker "high" than two 1mg pills. Although the generic pills may be white and round, Roche has reformulated the 1mg pill to be a gravish-green oval tablet. In an attempt to deter sexual assault, it now contains a dye which will turn the liquid blue. However, some sexual predators have been reported to serve blue punches and blue fruit drinks [3].

#### **Adverse Effects**

Adverse effects of flunitrazepam include hypotension, dizziness, confusion, visual disturbances, urinary retention, and in some users, aggressive behavior. Acute patient management of overdose is supportive care and attention to the possible ingestion of other CNS depressants [4]. The effect of flunitrazepam is confounded by the concurrent use of alcohol or other drugs. The drug is used non-medically because it reinforces the depressant effects of heroin and blunts the "crash" after use of cocaine [5]. Where available, it has been called the "most preferred" benzodiazepine among heroin users, but there are individuals who use the drug for its own effect to get high, rather than using it to enhance the effect of other drugs [6].

Studies of juvenile delinquent populations have found flunitrazepam use can lead to serious violent behavior in these groups ("unpredictable," "very aggressive," and "frightening") and in subjects characterized by vulnerable personality traits [7]. Of 60 non-psychotic young male forensic psychiatric patients in Sweden, 18 were flunitrazepam users. The frequency of previous admissions and actual sentences of these users deviated significantly from forensic patients who did not use flunitrazepam. Flunitrazepam abuse per se might be more responsible for their tendency to commit crimes characterized by danger and thrill-seeking than their personality traits. The most important conclusion was that an accurate assessment of flunitrazepam use is needed in forensic psychiatry [8].

Rohypnol has been found in cases of driving under the influence. In Norway, of 818 blood samples taken from suspected impaired drivers between 1987 and 1998, those who were actually impaired had significantly higher blood levels of diazepam, oxazepam, and flunitrazepam than those not impaired [9].

Interactions between flunitrazepam and the opioids are neither simple nor predictable. High-dose flunitrazepam augments lethality twofold in methadone-treated rats and six-fold in buprenorphrine-treated rats. Flunitrazepam administration appeared to have no significant effect on morphine lethality. However, time to death was altered in the buprenorphrine plus flunitrazepam group, suggesting differing mechanisms of death. The mechanisms for flunitrazepam-induced alteration of opioid toxicity remain to be seen [10]. The interaction between flunitrazepam and buprenorphrine could pose a significant problem in the U.S., given the continuing illegal importation of Rohypnol into border states and the recent implementation of buprenorphrine for treatment of opiate addiction in the U.S.

#### **TREATMENT IMPLICATIONS**

Patients who entered programs funded by the Texas Commission on Alcohol and Drug Abuse between 1996 and 2003 were young (average age 18), were predominately Hispanic, male, lived on the border, and had criminal justice or legal problems. Fortythree percent had a primary problem with marijuana. Others had problems with powder cocaine and heroin. Rohypnol clients were more likely to be admitted to outpatient services. If they received a DSM diagnosis, it was most often conduct disorder [11]. Other studies have reported on violent behavior among juvenile delinquent populations who were using flunitrazepam [7,8], and the characteristics of clients in Texas may be related to the high proportion of admissions who had criminal justice or legal problems and the conduct disorder diagnoses for this group of clients [12].

### TOXICOLOGY

While a standard component of most urine drug screens is testing for benzodiazepines, flunitrazepam is administered in such small amounts and distributed so rapidly that detection methods commonly fail. Flunitrazepam has an elimination half-life of about 3.5 hours. Samyn et al. [6] reported a method for onsite screening for flunitrazepam in oral fluids that could detect the drug within six hours of use, but the screen should be confirmed. Typical toxicological tests can only detect flunitrazepam in blood and urine for up to 72 hours after ingestion due to quick metabolism and elimination. ElSohly Laboratories had a contract from Roche to receive and test samples submitted by law enforcement agencies, and flunitrazepam was found in less than 1% of the 3,308 samples, as compared to 38% alcohol, 8% benzodiazepines other than flunitrazepam, 4% GHB, and 18% tetrahydrocannabinol. Negrusz and Gaensslen [12] found the electron ionization gas chromatographymass spectrometry method used by ElSohly did not provide enough sensitivity to detect flunitrazepam in urine after a single dose.

Drug-facilitated sexual assault cases require toxicological analysis in addition to the usual forensic biological examinations and DNA typing is routine in most sexual assault cases. Because persons who have been sexually assaulted may not report the crime for days or weeks, forensic hair testing can be used in the case of flunitrazepamfacilitated sexual assault [12].

## GLOSSARY

anterograde amnesia-loss of memory following an event.

buprenorphrine—an opiate drug used to relieve moderate to severe pain and also used as an opioid substitute in managing drug dependency.

half-life—the time required for half the amount of a substance (such as a drug or radioactive tracer) in a living system or ecosystem to be eliminated or disintegrated by natural processes.

#### REFERENCES

- 1 Maxwell, J.C. (2003) Response to club drug use. Current Opinion in Psychiatry. 16:279-289.
- 2 McGarry-Ross, C. (2002) More on Rohypnol. Can. Nurse. 98(6):6.
- 3 Maxwell, J.C. (2004) Substance abuse trends in Texas: December 2003. In: Epidemiologic Trends in Drug Abuse, Proceedings of the Community Epidemiology Work Group, Rockville, MD: National Institute on Drug Abuse.
- 4 Smith, K.M., Larive, L.L., Romanelli, F. (2002) Club drugs: Methylene dioxymethamphetaine, flunitrazepam, ketamine hydrochloride, and λ-hydroxybutyrate. Am. J. Health-Syst. Ph. 59(11):1067-1076.
- 5 Druid, H., Holmgren, P., Ahlner, J. (2001) Flunitrazepam: An evaluation of use, abuse, and toxicity. Journal of Forensic Science International. 122:136-141.
- 6 Samyn, N., De Boeck, G., Cirimele, V., Verstraete, A., Kintz, P. (2002) Detection of flunitrazepam and 7-aminoflunitrazepam in oral fluid after controlled administration of Rohypnol. J. Anal. Toxicol. 26(4):211-215.
- 7 Daderman, A.M., Fredriksson, B., Kristiansson, M., Nilsson, L.H, Lidberg, L. (2002) Violent behavior, impulsive decisionmaking and anterograde amnesia while intoxicated with flunitrazepam and alcohol or other drugs: A case study in forensic psychiatric patients. J. Am. Acad. Psychiatry Law. 30:328-351.
- 8 Daderman, A.M., Edman, G. (2001) Flunitrazepam abuse and personality characteristics in male forensic psychiatric patients. Psychiatry Research. 10:27-42.
- 9 Bramness, J.G, Skurtveit, S., Morland, J. (2002) Clinical impairment of benzodiazepines—relation between benzodiazepine concentrations and impairment in apprehended drivers. Drug and Alcohol Dependence. 68:131-141.
- 10 Borron, S.W, Monier, C., Risede, P., Baud, F. J. (2002) Flunitrazepam variably alters morphine, buprenorphrine, and methadone lethality in the rat. Human & Experimental Toxicology. 21: 599-605.
- 11 Maxwell, J.C., Spence, R.T. (2005) Profiles of club drug users in treatment. Substance Use and Misuse. (in press).
- 12 Negrusz, A., Gaensslen, R.E. (2003) Analytical developments in toxicological investigation of drug-facilitated sexual assault. Annal. Bioanal. Chem. 376:192-197.