

# Toxicology News

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## "Club" or "Rave" Drugs Offer Challenges to Laboratories

By Jimmie L. Valentine and Sarah Kerrigan

In many of the large metropolitan areas of the United States and Europe there are clubs where young adults go to listen to electronic or techno music, usually accompanied by pulsating lights. More recently, such clubs or staged events have become common in many smaller cities. To enhance the auditory and visual experience, participants may take drugs. Hence, the term "club drugs" has been coined to describe the drugs frequently taken for their psychedelic and euphoric effects.

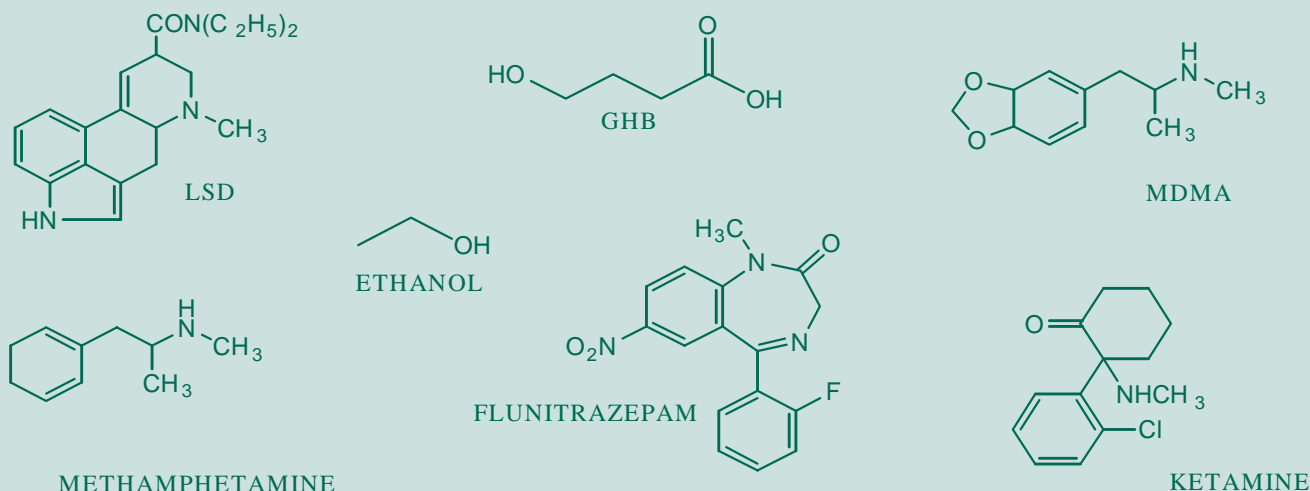
The term "club drugs" includes a number of illicit drugs that have become popular in nightclubs or large dance parties called "raves." The term normally applies to methamphetamine, lysergic acid diethylamide (LSD), methylenedioxyamphetamine (MDMA, Ecstasy), gamma-hydroxybutyrate (GHB), ketamine, and flunitrazepam (Rohypnol), but this review also includes ethanol, which is the most common recreational euphoriant (Figure 1).

Although the club-drug phenomenon is somewhat new, many of the drugs have been used recreationally for decades. The pharmacology and toxicology of these substances is relatively well understood but their incorporation into "club culture" and their subsequent influence on young people is a cause of growing concern to toxicologists, clinicians, and law enforcement. Statistics released by the Drug Abuse Warning Network (DAWN) show that the number of emergency department (ED) mentions involving GHB, ketamine, and MDMA increased significantly between 1994 and 1999, whereas MDMA and GHB mentions increased dramatically between 1997 and 1999 (Figure 2).

Young people are disproportionately represented in club-drug-related ED visits. Persons aged 18–25 years account for 67% of MDMA, 58% of ketamine, 50% of GHB, 46% of LSD, 32% of flunitrazepam, and 31% of methamphetamine visits. DAWN estimates that in 1999 there were more than 91,000 such ED visits; in 1998 there were more than 10,000 related fatalities. In response to this disturbing trend, in 1999 the National Institute on Drug Abuse announced a \$54 million initiative to combat the increasing use of club drugs.

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Figure 1. Structures of common club drugs



## January 1999 Workload

By Wayne R. Markus

In the AACC-CAP forensic urine drug testing survey (UDC-B) for 1999, a questionnaire was included to record workload for the month of January 1999. Ninety-six labs completed the questionnaire.

Some participants indicated that external blind proficiency testing specimens might be included, which would affect the numbers and percentages of

confirmed positives in a small way.

The aberration in the ethanol data, in which more than 100% of confirmations were positive, is probably caused by some participants including positive specimens in the "confirmed positive" column, but failing to include them as screen-positive specimens in the "number to confirmation" column.

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### Workload Questionnaire Results from 1999 UDC-B Proficiency Testing Survey

	Number of Specimens Screened	Number to Confirmation	Percent to Confirmation	Confirmed Positive Total	Percent of Confirmations Positive	Percent Confirmed Positive
Cannabinoids	941,333	35,887	3.812%	33,534	93.4%	3.562%
Ethanol	192,933	6,345	3.289%	2219	35.0%	1.150%
Benzoylcegonine	769,778	11,608	1.508%	11,007	94.8%	1.430%
Opiate Group	921,770	10,397	1.128%	4736	45.6%	0.514%
Codeine		8209		4128	50.3%	0.448%
Hydrocodone		8313		3951	47.5%	0.429%
Hydromorphone		2922		1473	50.4%	0.160%
6-MAM		3086		1255	40.7%	0.136%
Morphine		867		192	22.1%	0.021%
Oxycocone		785		21	2.7%	0.002%
Barbiturate Group	430,890	11,215	2.603%	2398	21.4%	0.557%
Amobarbital		1285		5	0.4%	0.001%
Butalbital		1895		1328	70.1%	0.308%
Pentobarbital		1721		27	1.6%	0.006%
Phenobarbital		1920		1014	52.8%	0.235%
Secobarbital		1775		22	1.2%	0.005%
Benzodiazepine Group	402,073	5640	1.403%	3020	53.5%	0.751%
Alprazolam metabolite		3685		806	21.9%	0.200%
Flurazepam metabolite		1344		36	2.7%	0.009%
Lorazepam metabolite		2995		119	4.0%	0.030%
Nordiazepam		3680		1804	49.0%	0.449%
Temazepam		2039		1027	50.4%	0.255%
Oxazepam		3808		2672	70.2%	0.665%
Triazolam		827		7	0.8%	0.002%
Amphetamine Group	835,916	7544	0.902%	3114	41.3%	0.373%
Amphetamine		6113		3189	52.2%	0.381%
Methamphetamine		6161		2940	47.7%	0.352%
Propoxyphene	309,658	3575	1.154%	2954	82.6%	0.954%
Methadone	338,719	1147	0.339%	992	86.5%	0.293%
Phencyclidine	882,785	995	0.113%	592	59.5%	0.067%
Methaqualone	248,945	42	0.017%	2	4.8%	0.001%
LSD	1,873	37	1.975%	1	2.7%	0.053%
All Drugs	6,276,673	94,432	1.504%			

### Club Drugs, Continued from page 1

Describing which drugs are typically used in these musical clubs is difficult. The tendency for club participants to experiment with various individ-

ual drugs or combinations of them constantly changes due, in part, to supply in a geographical area, urging from peers about new "must-try" drugs, and adverse outcomes associated with some drugs, so-called "bad trips." The scientific community gets

some insight into drug trends by investigating overdoses and adverse health effects. Periodically the U. S. Drug Enforcement Agency releases reports on the types of drugs being confiscated by its agents, which provides a window into the potential supply and availability. Another avenue of information comes through DAWN reports from emergency departments concerning presentations related to drug abuse along with medical examiners' or coroners' reports on deaths attributable to drug abuse. A recent DAWN report highlighted GHB, ketamine, LSD, MDMA, methamphetamine, and flunitrazepam as commonly used club drugs. However, this report also pointed out that such drugs are by no means used only individually but rather are predominantly used in combination with drugs such as alcohol, marijuana, amphetamines, cocaine, and heroin. Alcohol is often sold at clubs so the DAWN report verifies that it is most often found in combination with GHB, ketamine, LSD, MDMA, methamphetamine, and flunitrazepam. Marijuana and cocaine are also reported to be frequently combined with these drugs.

In this article, we will briefly review the pharmacology, toxicology, and methods of analysis for this emerging class of drugs.

### MDMA, Ecstasy

*My mood was light, happy, but with an underlying conviction that something significant was about to happen.... I felt that I could talk about deep or personal subjects with special clarity ... discoursing brilliantly and with particularly acute analytical powers.*

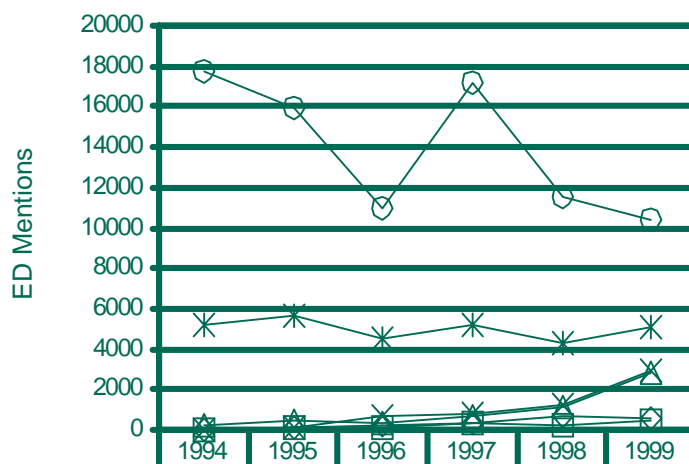
— An excerpt from PIHKAL. A Chemical Love Story, by Alexander and Ann Shulgin on [www.erowid.com](http://www.erowid.com).

MDMA was synthesized and patented as a chemical precursor by the pharmaceutical industry in the early 1900s, being initially evaluated and used as an adjunct to psychotherapy. Today, MDMA is a Schedule I drug under the Federal Controlled Substances Act. Structurally, MDMA is related to both methamphetamine and mescaline. As a result, the drug can produce stimulant and psychedelic effects. These properties have made the drug popular among young people as a means to improve their mood, enhance their "connectedness" with one another, and increase their energy, allowing them to dance or stay awake for prolonged periods of time. MDMA is often referred to as the "hug drug," because of its entactogenic effects. It reduces inhibitions, eliminates anxiety, and produces feelings of empathy and extreme relaxation.

Most frequently, MDMA is administered in tablet or capsule form in doses of 100–150 mg. Clandestine manufacturers of MDMA frequently use pill-presses and impregnate logos and icons onto the tablets, which sell for \$20–40. Tablets that are sold as MDMA frequently contain other drugs, such as caffeine, ephedrine, amphetamines, or dextromethorphan. In addition, methylenedioxyamphetamine (MDA), methylenedioxyethylamphetamine (MDE, Eve), p-methoxyamphetamine (PMA), and p-methoxymethamphetamine (PMMA), which are beyond the scope of this discussion, have been substituted for or combined with illicit MDMA. Most notably, the paramethoxy-amphetamine drugs have been associated with profound toxicity and life-threatening hyperpyrexia.

MDMA has a half-life of 7.6 hours and undergoes N-demethylation to the active metabolite, MDA. Following oral doses of 1.5 mg/kg (105 mg/70kg), peak MDMA plasma concentrations were 0.331 mg/L at 2 hours. The onset of action following an oral dose is 30–60 minutes. Peak MDA concentrations of 0.01–0.015 mg/L were measured at 2.5–6.3 hours. About 65% of the dose is eliminated in the urine as parent drug and 7% as MDA. Mono- and di-hydroxy metabolites of MDMA and MDA are excreted in the urine as conjugates.

**Figure 2. Number of ED mentions involving club drugs: 1994–1999. Source: Drug Abuse Warning Network.**



—◇— Flunitrazepam	13	111	217	293	624	540
—□— Ketamine	19	150	81	318	209	396
—△— MDMA	250	421	319	637	1143	2850
—×— GHB	55	145	638	762	1282	2973
—*— LSD	5158	5681	4569	5219	4282	5126
—◇— Methamphetamine	17696	15936	11002	17154	11491	10447

The sought-after effects of the drug last approximately 3–6 hours, but depression, anxiety, disruption of sleep, and paranoia have been reported to occur days or weeks after use. Post-MDMA depression or “hangover” is reported to take hold several days after drug use and may last up to five days. Symptoms of acute MDMA toxicity can include confusion, agitation, hallucinations, seizures, hyperpyrexia, coma, and hypotension. In large doses, MDMA can cause malignant hyperthermia, leading to muscle breakdown as well as kidney and cardiovascular failure. There is also evidence that MDMA is neurotoxic and causes depletion of serotonergic neurons in the brain, which may be irreversible. Following cessation of drug use, neurobehavioral disturbances have been reported.

MDMA, MDA, and related drugs can be analyzed by liquid chromatography (LC) or gas chromatography/mass spectrometry (GC/MS) of derivatized extracts. Both solid-phase extraction and solvent extraction techniques that are commonly utilized for the isolation of basic or alkaline drugs have been reported. Some immunoassay-based screening techniques that are directed against amphetamine-like drugs have proven useful, provided that they are sufficiently cross-reactive towards MDMA.

## GHB

*It is fairly soporific and highly relaxing with a time dilating effect similar to mushrooms but less profound. It is not at all psychedelic or entactogenic. It is easy to go to sleep at any time.*

— Posted on [www.hyperreal.com](http://www.hyperreal.com) by a user.

GHB is a relatively new recreational euphoriant that has grown in popularity since the early 1990s. It was formerly used as an anesthetic and hypnotic agent but was discontinued in the United States due to seizure-like effects and its lack of analgesia. However, GHB has been shown to decrease daytime sleepiness and episodes of cataplexy, sleep paralysis, and dream-like hallucinations in narcoleptic patients. The FDA recently approved a New Drug Application to explore GHB (Xyrem) as a treatment for narcolepsy. To date, there are no approved medicinal uses of the drug, and it is classified under Schedule I of the Controlled Substances Act.

GHB is claimed to provide a variety of beneficial and sought-after effects, including improved athletic performance, improved sleep, enhanced sexual prowess, relief from depression, and euphoria. DAWN statistics indicate a seemingly parallel trend in GHB and MDMA-related ED visits between 1994 and 1999 (Figure 2). Most ED visits involving club drugs involve multiple substances.

The second most common drug used in combi-

nation with GHB after ethanol is MDMA. Illicit doses are administered in “capfuls,” which may contain 2–3 g of GHB. One capful of GHB may sell for \$5–10. The drug is typically encountered as the dissolved sodium or potassium salt of GHB. Liquids with strong flavors, such as mouthwash, can be used to mask the unpleasant salty or solvent-like taste of the drug. The emergence of GHB alternatives and biological precursors has complicated many of the legislative and analytical approaches related to GHB. The pharmacological effects and toxicity of GHB precursors or prodrugs, such as gamma-butyrolactone (GBL) and 1,4-butanediol (BDL or BD), are identical to those of GHB.

Following oral administration, GHB is quickly absorbed and penetrates the blood–brain barrier, which accounts for its rapid onset of action, which can occur in as little as 15 minutes. GHB has a half-life of 0.3–1.0 hours and peak plasma concentrations occur 20–60 minutes after oral administration. Non-linear elimination kinetics in some studies indicate that GHB elimination is a capacity-limited process. At low doses, GHB causes relaxation, loss of inhibitions, and euphoria. Effects may last for as long as 4 hours. Higher doses can cause profound central nervous system depression, coma, and death. Adverse effects can include bradycardia, hypotension, loss of laryngeal reflex, disorientation, nausea, vomiting, tremors, hypothermia, and tonic-clonic jerking. Oral or intravenous doses of 10 mg/kg produce amnesia and hypotonia, 20–30 mg/kg can induce sleep, and doses above 50 mg/kg can produce anesthesia. Illicit doses of GHB are reported to be approximately 35 mg/kg, although the dose varies considerably among individuals, depending on experience with the drug, tolerance, and intended use. In one study, oral doses of 25 and 50 mg/kg GHB produced average peak plasma concentrations of 55 and 90 mg/L, respectively.

At present, there are no commercial immunoassays for GHB. Colorimetric screening tests have been reported but are not widely used. GHB is acidic in nature and can be extracted using solid-phase or solvent extraction techniques. GC/MS techniques for both GHB and GBL have been widely reported in the literature. GHB is a small, polar molecule that requires derivatization prior to GC/MS analysis. The interpretation of GHB test results must take into consideration the endogenous nature of the drug, artifactual production arising from preservation and storage issues, and post-mortem production of GHB.

## LSD

*My visual field was vibrating. Full of patterns. Things were getting pretty intense at this point....*

*Where there had been no tracers before, they were everywhere! When I moved, everything in my field of vision blurred off with tracers like looking between two mirrors.*

— Posted on [www.erowid.org](http://www.erowid.org) by a user.

The d-isomer of lysergic acid diethylamide is a potent hallucinogen of natural origin derived from ergot, a sugary excretion of *Claviceps purpurea*, which grows on rye grains. Knowledge of the medicinal properties of the ergot alkaloids dates back more than 400 years and their vasoconstrictive effects are utilized today for the treatment of migraine headaches. Recreational use of ergot alkaloids dates back more than 2,000 years to the ancient Greeks. In the United States, LSD was used as a psychotherapeutic agent until its use was strictly controlled in 1965. Today, LSD has no accepted medical uses and is classified under Schedule I of the Controlled Substances Act.

Illicit doses of LSD are typically 50–300 µg. The drug may be mixed with a binding agent and pressed into tiny pills (microdots), pressed into gelatin (window panes), or diluted and impregnated onto blotting paper (blotters) or sugar cubes. LSD blotters are often vividly colored or stamped with recognizable icons, characters, or logos. A dose typically costs \$3–5, and can produce a long-lasting pharmacological effect.

LSD can produce alterations in perception, cognition, and mood. Synesthesia, or a blending of the senses, is also reported. The drug has relatively low acute toxicity, and there have been only a few reports of LSD fatalities as a result of overdose. Symptoms of intoxication include lacrimation, tremor, ataxia, mydriasis, hypertension, tachycardia, and hyperthermia. Psychological signs include agitation, restlessness, anxiety, panic, paranoia, and perceptual distortions. Compared with other club drugs, the number of LSD-related ED visits remained relatively stable between 1994 and 1999 (Figure 2). In an emergency room, it can be difficult to distinguish LSD intoxication from other stimulant overdose or psychosis. Side effects of a psychiatric nature have included post-hallucinogen perception disorder, flashbacks, psychosis, and behavior-induced trauma.

LSD has a half-life of 3–4 hours and undergoes extensive biotransformation via N-demethylation, N-de-ethylation, hydroxylation, and conjugation to inactive metabolites. Peak effects may be observed in 30–90 minutes and may last 4–6 hours. Subjects who ingested a 160 µg dose produced peak plasma concentrations of 9 µg/L in the first 5 hours. In forensic settings, LSD is typically encountered in the low- to sub-µg/L concentration range, which poses a

significant analytical challenge.

LSD can be detected using enzymeimmunoassay, radioimmunoassay, and fluorescence polarization immunoassays, as well as thin-layer chromatography (TLC). Specific methods of analysis include LC and GC/MS. LSD is highly fluorescent under ultraviolet light, which facilitates detection by spectrofluorometry. However, care must be taken during storage of biological specimens because LSD is unstable under certain conditions of light and pH.

### **Ketamine**

*What I was feeling at this point: very disoriented, normal reality had just disappeared, physically dizzy and unable to walk without bumping against walls, a bit of paranoia that I was going to die ... mixed with periodic flashes wherein my surroundings would hang motionless and appear really beautiful and I felt totally painless.*

— Posted on [www.erowid.org](http://www.erowid.org) by a user.

This drug was originally developed as a human anesthetic agent but is not used in adults because it causes hallucinations; it is used mainly in children who do not experience the hallucinations. The drug is widely used in veterinarian practice for animal anesthesia and hence one of its street names is “cat valium.” Ketamine, a Schedule III drug, is structurally similar to phencyclidine (PCP); both are in the class of drugs known as dissociative anesthetics because of their ability to separate perception from sensation. In low doses, the dissociative effect produces reports of “floating” or “out-of-body” experiences. Higher doses may enhance these effects and abusers of the drug refer to this as a “K-hole” experience, where they have a near-death experience with the sensation of rising above their body. The higher doses are counter-productive for dancing because the person usually remains seated or lying down during the active effects of the drug. Reported mentions of this drug in emergency department visits increased from 19 in 1994 to 396 in 1999 (Figure 2).

Route of administration of the drug varies depending upon the form available to the user. Veterinarian forms of the drug are a liquid (hydrochloride salt placed in a physiological solution) and can be injected intramuscularly or taken orally. Evaporation of the water from the liquid formulation or extraction produces a powder that is administered by insufflation (snorting) or by adding to tobacco and smoking. The intramuscular, nasal, and smoking routes produce a pharmacological effect within 4–5 minutes, whereas, the oral route takes 20 minutes.

The major route of metabolism for ketamine is demethylation to norketamine. Immunoassays are

not available for detecting ketamine or norketamine in urine nor is there sufficient cross-reactivity to other tests like that for PCP. The chromatography techniques of TLC, GC, LC, and GC/MS have all been used to detect ketamine and norketamine.

### Methamphetamine

*I felt a great sense of well-being, and stimulation. I was full of energy I started doing my art work faster and better. I soon abandoned my work to further explore this substance.... I felt I could run miles and not get tired I felt I could take on the world.*

— Posted on [www.erowid.org](http://www.erowid.org) by a user.

This synthetic phenethylamine type drug (Figure 1) exists in optical forms. d-Methamphetamine, a Schedule II drug, is the form that is typically abused, but this form also has therapeutic uses as an appetite suppressant, for attention deficit disorder, and for narcolepsy. Because of its high potential for illicit diversion for abuse, most medical practitioners prescribe alternative drugs that are as effective. l-Methamphetamine is used as a nasal decongestant and it is important to identify in forensic applications because it is an over-the-counter drug. Methamphetamine is readily synthesized and clandestine laboratories regularly supply the drug in various degrees of purity.

Methamphetamine can be administered by a variety of routes, including oral, insufflation, intravenous, and smoking. The latter route is accomplished using the free base instead of the hydrochloride or sulfate salt, and the drug's nickname "ice" is derived from the crystalline-like appearance of the material. Smoking and intravenous use produce a "rush" that users describe as being pleasurable. Snorting and oral use produce a less intense high without the "rush" experienced by the other routes. The former routes produce their physiological effects almost immediately whereas there is a latency period of 5–15 minutes with the latter routes.

The pleasurable effect with the drug is short-lived and therefore users will often "binge" the drug, that is, use another dose in a short time period in an attempt to maintain the pleasurable experience. Reports from individuals who smoke methamphetamine suggest that this form provides a more prolonged pleasurable effect. Such reports also suggest that the effect is similar to cocaine but longer lasting. Thus, as interdiction has lessened the supply of cocaine from foreign countries, domestic methamphetamine has become more popular (Figure 2).

The mechanism of action for the pleasurable effects of methamphetamine has been well-characterized and is associated with enhanced release of dopamine in the nucleus accumbens and the

frontal cortex of the brain. Release of this powerful neurotransmitter also is responsible for methamphetamine being a powerful stimulant of the central nervous system; even small doses increase wakefulness and physical activity, and decrease appetite.

Methamphetamine is metabolized primarily via N-demethylation to give amphetamine. Since amphetamines are among the five classes of drugs designated for testing by Substance Abuse and Mental Health Services Administration regulations, commonly used immunoassay procedures will detect methamphetamine, amphetamine, or both, and some assays have considerable cross-reactivity with other sympathomimetic amines. To ensure that positive screening results for methamphetamine are not caused by ephedrine or other structurally similar sympathomimetic amines, workplace drug-testing accrediting agencies mandate at least 200 µg/L of amphetamine must be found in addition to 500 µg/L of methamphetamine in a GC/MS confirmation for a urine sample to be considered positive. Because amphetamine metabolite physiological concentration increases as methamphetamine concentration decreases, the ratio may give an indication of the time of use for the parent drug. Also, if a urine specimen is collected too soon after use, the amphetamine level may be below the arbitrary 200 µg/L cutoff, while the methamphetamine concentration may greatly exceed 500 µg/L.

### Flunitrazepam

*Rohypnol will calm you down quite like nothing you've ever experienced. The result is a warm, fuzzy, very comfortable feeling, free from anxiety, allowing you to drift away in a boat of bizarre and vivid dreams.*

— Posted on [www.erowid.com](http://www.erowid.com) by a user.

This drug is a benzodiazepine that is sold in Europe and Latin America under the tradename Rohypnol for use as a sedative-hypnotic and pre-anesthetic medication. The drug was never approved for marketing in the United States. Supposedly the street name of the drug "roofies" is related to some Mexican workers who did roof repairs bringing the drug into South Florida following Hurricane Andrew. This drug has been used for committing date rape because its hypnotic effect is enhanced if it is dissolved in an alcoholic drink. This synergism renders the victim helpless for sexual perpetration by the attacker and in addition the amnesic effect associated with the benzodiazepine class of drugs prevents the victim from remembering details of the crime. Highly publicized trials in various areas of the country brought this method of criminal activity to the public attention but the DAWN reports

(Figure 2) suggest that the problem may still be with us. Law enforcement officials are still interdicting large caches of this drug, many in the original manufacturers' unit dose packaging. More recently, the product has been reformulated with a dye so that attempts to adulterate a drink may result in a telltale sign.

Flunitrazepam is used orally but in addition to the synergism with alcohol discussed above it has reportedly been used with other drugs like heroin to achieve a greater high. When taken alone, flunitrazepam will in a dose-dependent manner produce within 30 minutes to 1 hour decreased blood pressure, drowsiness, memory impairment, and visual disturbances. Some drug users have reported that flunitrazepam is useful as a "parachute" drug, that is, to bring a person down gently following a high with another drug. The extent of its use for this purpose is unknown as related to the club scene.

The scheduling of flunitrazepam has been complicated by the illicit use of the drug, especially in date rape. Because it has not been approved by the U.S. Food and Drug Administration, it could be considered to have no medical use with a high potential for abuse and would, therefore, be a Schedule I drug. In fact, some states have taken this position and the U.S. Drug Enforcement Administration is considering similar action. Currently, the drug is in the federal Schedule IV classification.

Flunitrazepam is metabolized by reduction to 7-aminoflunitrazepam, which can be readily detected by HPLC and GC/MS. Since flunitrazepam is a benzodiazepine, a number of commercial immunoassays are capable of detecting it, but in the dosages encountered, the cutoff used is critical. From our collective experience, a cutoff of 50  $\mu\text{g/L}$  is necessary to achieve screening detection of flunitrazepam and metabolite. Since most immunoassays for benzodiazepines have diminished cross-reactivity with flunitrazepam and 7-aminoflunitrazepam, it is to be expected that use of this drug may go undetected with this screening technique. TLC, HPLC, or GC should be considered as the screening method for this drug.

## Ethanol

All the drugs discussed above are illicit or their use in a recreational manner represents an illegal diversion. Ethanol of course is different from these other drugs because it is legal in most jurisdictions and only used via the oral route. The major restriction to its use and possession is being of legal age. For these reasons, use of ethanol at dance clubs or dance events can almost be assured. Therefore, ethanol has a high probability of being used in conjunction with the club drugs.

*MacDuff: What three things does drink especially provoke?*

*Porter: Marry, sir, nose-painting, sleep, and urine. Lechery, sir, it provokes, and unprovokes; it provokes the desire, but it takes away the performance.*

This exchange between MacDuff and Porter in *Macbeth* illustrates many of the outwardly visible physiological effects of ethanol—flushing (vasodilation), somnolence, diuresis, and sexual desire but impotence (observed in chronic alcoholism). Ethanol exerts its action by depressing the central nervous system (CNS) through its effects on membrane fluidity. Most lay persons mistakenly believe that ethanol is a stimulant because at low levels, social inhibitions are reduced and giddiness and laughter are common. Blood levels of ethanol can be equated with the observed physiological effects because its water solubility permits uniform distribution throughout the body. Metabolism is exclusively via oxidation and is enzyme-mediated and therefore susceptible to saturation. The pharmacokinetics of ethanol obey zero-order kinetics due to the saturable nature of the metabolizing enzymes. The amount of ethanol metabolized per unit time is roughly proportional to body weight and on average is about 30 mL in 3 hours. Variations in this clearance rate are seen in males and females, tolerant and non-tolerant individuals, and in relationship to food in the gut during consumption.

The major oxidative metabolite of ethanol is acetaldehyde. Even though acetaldehyde has depressive actions on the CNS much like ethanol, it is rarely analyzed for correlation purposes with behavioral factors. Rather, legal precedent has been established specifying that ethanol concentration must be correlated to physiological effects, the so-called level of intoxication. Recent federal directives and subsequent action by most states have resulted in the adoption of 0.08 g/dL as the level for intoxication. Other regulatory bodies, such as the Federal Aviation Administration, have adopted 0.04 g/dL as the level of intoxication in recognition of the sensitive safety role of pilots. Although such legal levels are based upon average physiological effects, they may not be a true indicator of the extent of CNS depression occurring in a diverse population, such as young people attending club dances.

The adverse interactions between ethanol and many different drugs have been well-documented in countless case reports and death investigations. Synergism is expected between ethanol and any CNS depressant. Club drugs such as GHB and flunitrazepam, which are CNS depressants, have been shown from many reports to clearly have a synergistic effect with ethanol. The other club drugs discussed above are

CNS stimulants, so one would predict that synergism would not be an immediate concern during the early elimination phases of such combinations. Depending upon the dose of ethanol and club drug taken and their frequency of use in a specified time period, a period of simultaneous CNS depression will occur.

For forensic purposes, either blood ethanol levels or breath equated to blood levels is the current legal standard. Most breath collection devices are portable and use an integrated monitoring device to produce a level in breath that is then equated to a blood alcohol level. Blood specimens are usually processed in a laboratory using predominantly headspace GC. Enzyme assays are available that permit blood ethanol determinations, but should be regarded as a screening method for forensic needs. Enzyme assays can also be used to detect the presence of ethanol in urine and algorithms are available for correlations with blood levels. Case law is still being developed on urine ethanol so it may be some time before it will be in widespread use.

### Summary

Club drugs used to enhance dancing, auditory, and visual experiences include stimulants, depressants, and hallucinogenic substances. Adverse synergism between these drugs and ethanol or other neuropsychotropic drugs, like marijuana or cocaine, would be expected. Analytical detection of the club drugs is not standard in all laboratories because rapid screening techniques are not available for many of

them. Further, because of the lack of requests for tests for these drugs, many clinical laboratories are not equipped to provide helpful turnaround times. However, depending on the needs in a geographical area, it would be feasible to perform screening assays for most of the club drugs using chromatographic techniques, such as TLC, GC, or HPLC.

### Suggested Reading

1. Baselt RC. Disposition of toxic drugs and chemicals in man, 5th ed. Foster City, California: Chemical Toxicology Institute, 2000.
2. The DAWN report on club drugs, December 2000, Drug Abuse Warning Network, Office of Applied Statistics, Substance Abuse and Mental Health Services Administration. (<http://www.drugabusestatistics.samhsa.gov>)
3. Drug intelligence brief: an overview of club drugs, February 2000. Drug Enforcement Administration, Intelligence Division.

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