

CONTINUING EDUCATION



The University of Florida College of Pharmacy is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education

ACPE # 012-999-07-053-H01

This lesson is no longer valid for CE credit after 3/31/09.

**An ongoing CE program
of The University of Florida College of Pharmacy
and **DRUG TOPICS****

Drugs of abuse: A pharmacist's guide

To obtain immediate CE credit, take the test on-line at www.drugtopics.com. Just click on the "Continuing Education" box on the *Drug Topics* home page, which will take you to the CE site.

Log in, find and click on this lesson, and follow the three simple steps. Test results will be displayed immediately and you can print the certificate showing your earned CE credits.

Drugs of abuse: A pharmacist's guide

Ian R. Tebbett, Ph.D., Professor and Director, Forensic Science Program, College of Pharmacy
University of Florida, Gainesville



Photo: © PhotoDisc, Inc.

A staggering 10% of the U.S. adult population admits to drug abuse in the past 12 months. Although the majority use controlled substances such as cocaine, opiates, and marijuana illicitly, approximately 15 million per annum abuse prescription medications. Children as young as 10 years of age have been reported to regularly abuse drugs, which adds to the concern.

The Controlled Substances Act categorizes controlled substances into five distinct schedules. Drug placement is based on medical use, potential for abuse, and safety or dependence liability. A complete description of the Controlled Substances Act can be found at <http://www.usdoj.gov/dea/pubs/csa.html>. (See Table 1, page 69.)

Addiction

People expose themselves to harmful and potentially fatal substances for many reasons: peer pressure, to “feel good,” to escape from a stressful situation, or curiosity. Repeated exposure creates addiction to the substance(s), and breaking the habit is extremely difficult, even where the detrimental effects are obvious.

Drug abuse behavior does not follow “normal” patterns. Behavior can be described as compulsive, beyond voluntary control, and self-destructive. Normal behavior includes seeking experiences that are pleasurable and painless. Conversely, drug abusers spend inordinate amounts of time obtaining and administering the substance, despite harming their career, their family, and themselves.

Physical dependence describes the behavior of a user experiencing drug withdrawal symptoms. Drugs causing physical dependence are considered addictive. *Psychological dependence* describes the behavior of users who compulsively seek and administer drugs that have no physical withdrawal syndrome.

CONTINUING EDUCATION

GOAL

To provide pharmacists and technicians with knowledge about addiction, drugs of abuse, and recognizing the symptoms of drug abuse

CREDIT

This lesson provides two hours of CE credit and requires a passing grade of 70%.*

OBJECTIVES

Upon completion of this article, the pharmacist and technician should be able to:

- ✓ Recite the DEA classification of the major drugs of abuse
- ✓ Explain the physiology of addiction
- ✓ Explain the pharmacology of commonly abused substances
- ✓ Recognize the symptoms of drug abuse

*To receive credit you must score 70% or higher on the quiz and complete the evaluation. Upon successful completion, the University of Florida College of Pharmacy will mail Statements of Credit for written quizzes within 10 working days. Participants completing the program on-line may print a Statement of Credit after successfully completing the program.

Neurophysiology and neuroanatomy of addiction

Information transmission in the brain is mediated by release and detection of chemical neurotransmitters by neurons. Following an intracellular cas-

cade, neuronal communication may result in an alteration of the neuronal circuitry. Drugs of abuse may induce such neuronal changes, manifesting as drug tolerance, dependence, withdrawal, sensitization, and addiction. Drug reward circuitry chiefly involves the mesolimbic dopamine system, with involvement of the opioid, serotonin, and GABA (gamma-aminobutyric acid) systems.

Dopamine

The mesolimbic dopamine system plays a central role in drug addiction, particularly for psychomotor stimulant drugs such as cocaine and amphetamine. It has also been shown to play a role in the reinforcement of opiates, nicotine, and alcohol.

Opioids

Opioids are endogenous neurotransmitters that play a role in the positive reinforcement of opiates such as morphine. This system is also involved in the reinforcing effects of alcohol and nicotine.

Serotonin

Serotonin, or 5-hydroxytryptamine (5-HT), is a neurotransmitter involved in alcohol addiction. Increased serotonin at 5-HT synapses results in decreased alcohol consumption, and some 5-HT receptor subtypes may also be involved in cocaine positive reinforcement.

GABA

This major inhibitory neurotransmitter mediates the effects of sedative-hypnotic drugs such as alcohol and benzodiazepines. GABA systems in the central nucleus of the amygdala communicate with the basal forebrain, an area of the brain associated with emotion and stress and thought to be associated with the positive reinforcing effects of alcohol and benzodiazepines.

CONTINUING EDUCATION

Sedatives

Opium is a natural product obtained from the dried latex of the opium poppy *Papaver somniferum*. Crude opium is the source of the narcotic analgesics codeine and morphine. Although opium is still occasionally seen as a street drug, most illicit opiate use is associated with heroin (diacetylmorphine).

The opioids are a group of drugs with similar pharmacological effects to morphine. These include all natural and semi-synthetic alkaloid derivatives from opium, as well as the synthetic opiates, such as methadone. Commonly abused opiates include morphine and heroin.

Several synthetic drugs have pharmacologic properties similar to those of morphine. These include the phenylheptylamines (methadone and propoxyphene) and the phenylpiperidines (meperidine and fentanyl). Morphine antagonists naloxone and nalorphine, used to reverse the effects of morphine or heroin overdose, block their effects but have no pharmacological activity on their own.

Opioids can be administered orally, transdermally, or intravenously and are available as suppositories. Clinically, they are used in the treatment of pain, cough suppression, and diarrhea. Codeine and propoxyphene are used in the management of mild to moderate pain; morphine, methadone, oxycodone, and meperidine are used in the management of moderate to severe pain. The mood-elevating effects of opiates are useful in the management of the emotional distress commonly experienced by chronic pain patients. It is the euphoric effects of opioids that are sought after by abusers of opioids such as heroin.

Morphine and heroin may be used to treat pulmonary edema resulting from left-ventricle failure and in the treatment of neonatal respiratory distress. One side effect of opioids is

Table 1 Schedules of drugs or other substances		
Schedule	Criteria for substance inclusion	Examples of substances included in schedule
I	The drug or substance has high abuse potential; it has no currently accepted medical use in the United States; and there is a lack of accepted safety for use of the drug or substance under medical supervision.	Heroin, LSD, marijuana*, methaqualone
II	The drug or substance has high abuse potential; it has a currently accepted medical use in the United States, or a currently accepted medical use with severe restrictions; abuse of the drug or substance may lead to severe psychological or physical dependence.	Morphine, PCP, methadone, cocaine, methamphetamine
III	The drug or substance has less abuse potential than drugs or substances in Schedules I and II; it has a currently accepted medical use in the United States; abuse may lead to moderate or low physical dependence or high psychological dependence.	Anabolic steroids, codeine, and hydrocodone with aspirin or acetaminophen, some barbiturates
IV	The drug or substance has low abuse potential relative to Schedule III substances; it has a currently accepted medical use in the United States; abuse of the drug may lead to limited physical dependence or psychological dependence relative to Schedule III substances.	Propoxyphene, diazepam, alprazolam, pentazocine, meprobamate
V	The drug or substance has low potential for abuse relative to Schedule IV substances; it has a currently accepted medical use in the United States; abuse may lead to limited physical dependence or psychological dependence relative to Schedule IV substances.	Codeine-containing preparations

*Marijuana and its primary active ingredient, Δ^9 -tetrahydrocannabinol (THC), are currently listed by the DEA as Schedule I and cannot be prescribed by doctors. However, a synthetic THC in sesame oil in a gelatin capsule, dronabinol (marketed as Marinol), is available by prescription and is listed as Schedule III.

Most states follow federal guidelines regarding marijuana scheduling, but some have reassigned it to Schedule II. In these states doctors may still not prescribe marijuana since federal law supersedes state law.

A more complete list of the drugs included in each schedule can be found on the DEA Web site, <http://www.usdoj.gov/dea/pubs/scheduling.html>.

CONTINUING EDUCATION

constipation, an effect exploited by their use in the treatment of diarrhea. Diphenoxylate and codeine are also used in this way since they have minimal central nervous system (CNS) effects. Opioids can be used to supplement other anesthetics. Acting directly on the spinal cord, these drugs produce a regional block. Opioids with weak analgesic activity, such as pholcodine, dextromethorphan, and dihydrocodeine are commonly used as cough suppressants.

Clinically, opioids are safe and effective drugs, but excessive use produces predictable side effects: respiratory depression, nausea and vomiting, constipation, miosis, cardiovascular effects, pulmonary edema, and seizures.

Opiate binding sites are concentrated in areas known to affect pain transmission. Opioids cross the blood brain barrier rapidly, interacting with specific opiate receptor subtypes. Opioids bind with differing affinities to more than one receptor subtype to produce specific clinical effects. Mu receptors are responsible for the euphoric and respiratory depressive effects of opiates. Morphine is well absorbed from most routes of administration, including oral, sublingual and buccal, rectal, vaginal, spinal, intramuscular, intranasal, and transbronchial. Opioids have relatively short half-lives, with the half-life of morphine being only a few hours. Methadone is much longer acting, with a half-life of approximately 24 hours.

Accumulation of opioids in fatty tissue may be important, especially following long-term use of high doses of lipophilic opioids such as fentanyl, which are slowly metabolized. The opioids are metabolized to more polar metabolites easily excreted via the kidney. Morphine has free hydroxyl groups and so can be glucuronidated at the 3- and 6- positions to form morphine-6-glucuronide or morphine-3-glucuronide. Heroin is hydrolyzed first to monoacetyl morphine and then to morphine prior to glucuronidation.

Tolerance develops quickly to opiates. Within a short time, a larger dose will be required to achieve the same pharmacologic effect. After several months, tolerance develops to the extent that a user administers up

to 40 or 50 times the normal lethal dose. Cross-tolerance occurs with chemically similar opioids. On withdrawal, the receptors become super-sensitive and the system becomes overactive, causing physical withdrawal symptoms that include pain, anxiety, papillary dilation, yawning, sweating, vomiting, shivering, diarrhea, gooseflesh skin, and involuntary muscle spasms, leading to the colloquialisms *cold turkey* and *kicking the habit*. Withdrawal can persist for up to 48 hours and may be fatal.

Opioid withdrawal symptoms begin within 12 hours of the last administration of the drug, peak at 36-48 hours, and disappear within seven to 10 days. Drugs with short half-lives, e.g., heroin and morphine, have shorter-lasting but more severe periods of withdrawal; drugs with longer half-lives, such as methadone, have a longer-lasting but less severe withdrawal syndrome. In overdose cases, naloxone competes with the opioid agonist for the opioid receptors, thus reversing the overdose. Psychological dependence occurs significantly with opioid use, particularly with heroin, due to the euphoria it produces.

Heroin, a semi-synthetic compound produced by the reaction of morphine with acetic anhydride, is generally seen as a brown or white powder, or as a black, tar-like substance. Illicit heroin may be as little as 2% pure by the time it reaches the consumer. Other components are diluents such as sugar, starch, and even household cleanser and brick dust. Illicit heroin is also adulterated with other drugs such as strychnine and quinine.

Morphine and heroin are widely abused, and intermittent users generally snort it or administer it subcutaneously. Regular users tend to administer the drug intravenously to obtain the maximum euphoric effect, which often leads to infection and scar-tissue buildup. The 2003 National Survey on Drug Use and Health reported that approximately 3.1 million Americans age 12 or older had tried heroin at least once in their lifetime. Approximately 20% of eighth- to 12th-graders were reported as saying that heroin was “fairly” or “very” easy to obtain.

Paraphernalia associated with heroin use includes syringes, spoons, cotton, and aluminum foil. The syringes may have blood present, since the

CONTINUING EDUCATION

user tends to draw blood into the syringe prior to injection in an effort to ensure that the needle is in a vein. Heroin vapors can also be inhaled by placing the drug on aluminum foil and heating it with a cigarette lighter. The vapors produced are inhaled through a rolled-up dollar bill. Aluminum foil with a black stain present is a good indication that it has been used for this purpose.

Other sedative hypnotics

The sedative hypnotics are a class of drugs that have antianxiety and hypnotic effects, making them widely prescribed. Barbiturates have been popular in the past but have largely been replaced by the newer and safer benzodiazepines. These drugs are commonly used along with other drugs and, because of their behavior-modifying effects, are often involved in cases of violent crime, including assault, sexual abuse, and homicide.

Barbiturates

Generally, barbiturates suppress activity in all excitable tissues, including the CNS, peripheral nervous system (PNS), and cardiovascular (CV) system. In the CNS, barbiturates cause depression of neuronal excitability, facilitated by the effects of barbiturates on the binding of GABA to its postsynaptic receptor. Peripherally, barbiturates inhibit autonomic nicotinic receptors, causing hypotension and reduced cardiac function. Administered as an anesthetic, they may inhibit skeletal muscle nicotinic receptors, leading to suppression of neuromuscular transmission. In the CV system, inhibition of the autonomic nicotinic receptors results in hypotension—generally mild unless the patient already has congestive heart failure, dehydration, and hypovolemia. A barbiturate overdose may result in shock, renal failure, and death. Other CV effects include a decrease in cardiac output, decreased cerebral blood flow, and a decrease in myocardial contractility. Long-term use of barbiturates induces cytochrome P450 enzymes, increasing the metabolism of other drugs as well as barbiturates, ultimately decreasing circulating levels of the parent drug, and facilitating

the development of tolerance.

Barbiturates are administered orally or parenterally. Distribution depends largely on the lipophilicity of each drug. Barbiturate withdrawal syndrome occurs 12-20 hours after the last dose. Symptoms include anxiety, irritability, increased heart rate, increased respiration rate, muscle pain, nausea, tremors, hallucinations, confusion, and seizures.

Benzodiazepines

Benzodiazepines, widely prescribed for the treatment of anxiety and insomnia, are clinically used as anticonvulsants and antidepressants, as well as for treatment of acute alcohol withdrawal and for preoperative sedation. Benzodiazepines also act on the peripheral nervous system to cause muscle relaxation. The major effect of the benzodiazepines in the CNS is depression of neuronal excitability, facilitated by the effects of the drug on the binding of GABA to its postsynaptic receptor.

Benzodiazepines do not increase their own metabolism, but tolerance to the sedative effects of benzodiazepines develops readily, often within a week of treatment. If benzodiazepines are abused, tolerance may result in doses many times higher than the therapeutic dose being taken to achieve the desired effect. However, tolerance to the anxiolytic effects does not occur in short-term use.

Physical dependence can occur with benzodiazepine use and include withdrawal symptoms such as anxiety, dizziness, headache, insomnia, muscle stiffness, and sensitivity to light and sound. Severe symptoms include intense anxiety, nausea, vomiting, delirium, hallucinations, hyperthermia, sweating, panic attacks, paranoid psychoses, increased heart rate, increased blood pressure, and seizures. Short-acting and high-potency benzodiazepines are most likely to result in dependence, though long-term use is probably the biggest risk factor. Concern lies with the possibility of overprescribing, facilitating benzodiazepine abuse. Benzodiazepine abusers tend to abuse alcohol and other drugs. Sedative/hypnotic abusers tend to prefer barbiturates to benzodiazepines, but use benzodiazepines if

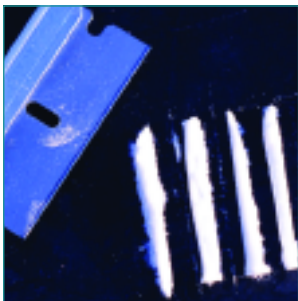
CONTINUING EDUCATION

they cannot obtain their drug of choice.

Large doses of diazepam increase the effect of opioids, a practice common with users on methadone maintenance. Benzodiazepines can be used with cocaine to offset the unwanted effects of cocaine as the user comes down from the high.

Diazepam and triazolam are more lipid-soluble than chlordiazepoxide and lorazepam and penetrate the CNS more rapidly, having a shorter onset of action. Benzodiazepines and other sedative hypnotics also have the potential to cross the placental barrier during pregnancy. There is potential for drug interactions via displacement of benzodiazepine from its plasma protein site, resulting in an increase in free drug and pharmacological effect.

Stimulants



The most significant drugs in this group are cocaine and amphetamine. Cocaine is a natural product present in the leaves of the coca bush, indigenous to the Andes region of South America. Cocaine is typically found in one of two forms: as cocaine HCl, a white powder usually snorted up the nose (insufflated) or injected; and crack cocaine, the free base, formed into rocks and smoked. Powder cocaine is often cut with local anesthetics such as lidocaine or procaine and a white

powder diluent such as sodium bicarbonate. Paraphernalia typically associated with cocaine use includes mirrors, razor blades, and some kind of tube for snorting the cocaine, or various pipes for smoking the crack form of the drug.

Cocaine stimulates central pleasure centers dependent on dopamine neurotransmission. It blocks the reuptake of

dopamine from the synapse, resulting in euphoria, increased motor activity, and psychotic symptoms. It is also a local anesthetic once used in dentistry. A potent vasoconstrictor and stimulant, it can create sudden changes in blood pressure, and cocaine-related deaths are often associated with cardiac failure or cerebral hemorrhage. See <http://www.usdoj.gov/dea/concern/cocaine.html>.

Amphetamines

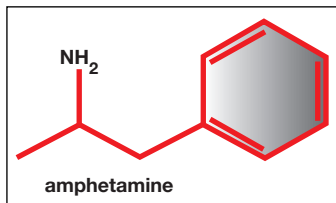
The chemical structure of amphetamine, shown below, is the base structure for the other amphetamines. Amphetamine can be chemically modified to create methamphetamine and methylenedioxymethamphetamine (MDMA, ecstasy). Similar in pharmacologic action to cocaine, amphetamines promote the release of dopamine and norepinephrine from presynaptic neurons and block the uptake of catecholamines. Like cocaine, amphetamines cause restlessness, stimulation, appetite suppression, paranoia, and psychosis. See <http://www.usdoj.gov/dea/concern/meth.html> and <http://www.usdoj.gov/dea/concern/mdma.html>.

Hallucinogens

The term *hallucinogen* refers to a drug that causes the user to have an altered perception of reality at doses at which there are few toxic effects. Other terms used to describe this group of drugs include *psychotomimetics*, *psychedelics*, *phantastants*, and *empathogenics*.

Serotonin-like hallucinogens

Lysergic acid diethylamide (LSD) is a semisynthetic substance produced from ergot alkaloids obtained from the *Claviceps purpurea* fungus originally developed as a possible treatment for schizophrenia. Its medical use was short-lived, due to its side effects. LSD is one of the most powerful mind-altering substances known; a typical dose of 50-



CONTINUING EDUCATION

100 mcg can produce effects that last several hours. It is thought to interact with serotonin in the brain, confusing the senses; music can be seen as vivid colors. Although LSD is considered impossible to overdose, death has been attributed to it as a result of accidents under its influence.

Flashbacks or the recurrence of hallucinogenic effects are also a symptom associated with LSD use. They may be explained by a small amount of the drug being sequestered in the brain and later released, causing a second hallucinogenic episode. LSD was most common in the 1960s but is still available. Taken orally, it is sold as blotters or sugar cubes; each hit contains around 100 mcg. Its effects include: dilated pupils, elevated blood sugar levels, tingling of extremities, drowsiness, nausea, vomiting, diarrhea, and abortion of fetus due to uterine muscle stimulation.

CNS effects of LSD include: altered time perception (time appears to pass very slowly); mood swings; distorted perception of size and shape of objects, movements, color, sound, touch and body image; and anxiety or depression. “Bad trips” may occur with LSD, resulting in feelings of panic and loss of control. Users may perform dangerous acts, resulting in injury or even death to themselves or others.

LSD is well absorbed orally and sublingually. Time to effect is generally 40-60 minutes, with the peak effect occurring after two to four hours and disappearing after six to eight hours. LSD has a half-life of approximately two to three hours in humans. LSD is distributed to all parts of the body, but only 1% of the dose reaches the brain. Tolerance occurs within a few days of repeated drug use. This tolerance is short-lived and disappears after several days of abstinence. Cross-tolerance is known to occur between LSD, psilocybin, and mescaline, suggesting that these drugs may have a common mechanism of action. Psychological dependence is known to occur with LSD, and users may develop intense cravings for the drug such that they believe they need it to function in their everyday lives. See <http://www.usdoj.gov/dea/concern/lsd.html>.

Psilocin and psilocybin are naturally occurring hallucinogens present in the *Psilocybe* genus of mushrooms known as “magic mushrooms.” Genera

of mushrooms containing psilocybin include *Psilocybe*, *Conocybe*, *Panaeolus*, and *Stropharia*.

Psilocybin abuse is popular among young people because of its availability on well-cultivated grasslands in the fall. LSD is around 100 times more potent than psilocybin but the effects are the same when dosage adjustments are made. After ingestion, psilocybin is converted to the active agent psilocin, considered responsible for the behavioral effects. Ten to 15 psilocybe mushrooms will induce hallucinogenic effects when taken orally. Psilocybe mushrooms are also dried and smoked with tobacco, and extracted with boiling water to produce infusions.

Norepinephrine-like hallucinogens

Mescaline. This hallucinogen is found in the peyote cactus. The top part of the cactus is cut into slices known as “mescal buttons,” which are dried in the sun and then chewed and swallowed. Use of mescaline was legalized by the U.S. Congress in 1970 due to its central use in Native American Church ceremonies; however, laws can still be passed against its use at the state level. The drug is readily absorbed when taken orally and the hallucinogenic effects are experienced within about an hour. Its effects are similar to those of LSD and last for several hours. However, LSD is approximately 2,000 times more potent than this drug.

Acetylcholine-like hallucinogens

Naturally occurring anticholinergic hallucinogens include atropine, scopolamine, and hyoscyamine. These alkaloids block acetylcholine receptors in the brain, resulting in delirium, loss of memory, and sleep. These drugs have been reported to give the user the sensation that he/she is flying. They also affect peripheral receptors, resulting in dilated pupils, tachycardia, and dry mouth. The alkaloids are obtained from several plants, including *Datura stramonium* and *Atropa belladonna*.

Datura, also known as jimsonweed or thorn apple, has been reported to have some medical use in the treatment of asthma, rheumatism, and men-

CONTINUING EDUCATION

strual pain. It has also been abused in the United States and smoked with tobacco or marijuana.

Atropa belladonna, also known as deadly nightshade, has a long history as a poison. The active alkaloid atropine has been isolated and has clinical use.

Other hallucinogens

Phencyclidine (PCP). A synthetic dissociative anesthetic once used as an animal anesthetic, PCP became available as a drug of abuse (known as angel dust, crystal, or hob) around 1965 but wasn't widely abused until the 1970s. The drug is still used illicitly, on its own or in combination with marijuana or cocaine. It can be smoked, snorted, or injected, but it doesn't produce hallucinations in the same way as LSD. It produces euphoria, and the user feels like he/she is floating. Symptoms appear rapidly and resemble those of schizophrenia. Euphoria, depression, agitation, violence, hallucinations, paranoia, panic, and suicidal tendencies are common effects. PCP users experience increased strength and a decreased sense of pain, making them extremely dangerous and difficult to control. Hypertension, tachycardia, coma and cardiac failure, and psychosis are adverse effects of this drug. Phencyclidine affects dopaminergic, cholinergic, and NMDA receptors, as well as noradrenergic and the serotonergic neurotransmitter systems.

PCP is absorbed well from a variety of administration routes. Oral administration provides onset of action within 30 minutes and peak effect within 90 minutes. The effects of PCP can last for up to eight hours owing to its rapid uptake into the brain and fatty tissue, where it is then slowly released.

As with LSD, tolerance to the effects of PCP occurs very rapidly and within a few days of repeated administration. While there have been very few reports of physical dependence associated with PCP use, they have reported a withdrawal syndrome consisting of anxiety, nervousness, and depression. (See <http://www.usdoj.gov/dea/concern/pcp.html>.)

Ketamine

Ketamine, an anesthetic used in children and animals, has a shorter duration of action than PCP. In recreational use it is known as *k*, or *special k*, and is used often as a date-rape drug. Ketamine is usually taken orally or intravenously.

Cannabis

Cannabis, or marijuana, is the most widely abused psychoactive substance in the United States. Dried plant material is mixed with tobacco and smoked. Cannabis is absorbed through the lungs and has a rapid onset of action, causing sedation and disruption of space and time perception. See <http://www.usdoj.gov/dea/concern/marijuana.html>.

The fruiting and flowering tops and the leaf material of the plant *Cannabis sativa* contain the highest concentrations of the active Δ^9 -tetrahydrocannabinol (THC). Over 60 individual cannabinoids have been identified, but only a few show any significant biological activity.

The constituents of cannabis may differ according to how the drug is administered: When cannabis is smoked, the burning process creates new cannabinoids with different potencies and effects. Users can still "get high" from smoking cannabis containing relatively little THC and high concentrations of cannabidiol since in the burning process, cannabidiol is converted to THC and some additional cannabinoids. The constituents of cannabis may also change with time or upon exposure to light.

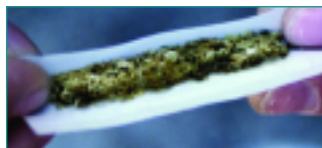
Marijuana refers to the dried leaves and flowers of the cannabis plant. It is usually smoked in a cigarette, cigar, or pipe, or may be baked in cookies or brownies. A hand-rolled cigarette with a cardboard filter is a good indication of cannabis use.

Bhang is dried leaves of female plants from which the resin has been removed. Bhang does not normally have a great deal of activity.

Ganja is made from the tops of female plants from which the resin has not been removed. This is three or four times more potent than bhang.

CONTINUING EDUCATION

Hashish refers to the dried resin from the fruiting and flowering tops of the female plant. This resin is pale yellow in color when harvested but turns almost black when dried. It is usually pressed into slabs and is crumbled and mixed with tobacco and smoked. It can also be baked in cookies or brownies. This preparation typically contains 6% to 10% cannabinoids.



Hash oil is a dark brown/black liquid produced by extracting marijuana with a solvent and concentrating the extract. It is a more concentrated version of hashish, made by boiling the hashish in a solvent such as alcohol, filtering the residue, and then allowing the solvent to evaporate. This oil can be dropped onto a regular cigarette and then smoked, or can be dropped onto hot aluminum foil, and the smoke inhaled.

Synthetic cannabinoids

Several synthetic derivatives of THC have been developed:

Dronabinol, a synthetic form of THC, and its analog nabilone are used clinically as antiemetics for cancer patients undergoing chemotherapy and to stimulate appetite in AIDS or cancer patients. Nabilone is marketed for these indications in the U.K., while dronabinol (Marinol) is marketed in the United States.

Anandamide (arachidonylethanolamide) acts to produce effects like those of THC. This drug, structurally related to the prostaglandins does not have a chemical structure similar to THC.

Cannabis has been shown to have legitimate clinical uses in the treatment of nausea and vomiting in cancer patients undergoing chemotherapy, and to stimulate appetite in AIDS and cancer patients. However, its use in AIDS patients is controversial, since cannabis may further suppress the immune system.

Cannabis may also have clinical uses in the treatment of glaucoma, functioning to decrease the intraocular pressure, and as an analgesic in chronic pain management, providing anti-inflammatory and anti-anxiety effects. Cannabis has also been shown to enhance the analgesic

effects of opioid drugs.

Despite the widespread belief that cannabis is a relatively harmless drug, it has a number of important physiological effects:

- Tachycardia—heart rate may increase by 20% to 50%
- Increased blood pressure
- Postural hypotension
- Decreased body temperature
- Dry mouth and throat
- Reddening of the conjunctivae of the eyes
- Decreased intraocular pressure
- Decreased pupil size
- Hunger

Cannabis also has behavioral effects that are dependent not only on the dose and form of cannabis taken, but also on the state of mind, mood, and expectations of the individual prior to use of the substance as well as the atmosphere and setting. At moderate doses these effects include:

- Euphoria
- Heightening of senses
- Altered sense of time (time appears to pass much more slowly)
- Short-term memory impairment

Cannabinoids have been shown to bind to cannabinoid receptors. Cannabinoid receptors are not found in the brain stem, which may explain the fact that even very high doses of cannabis are not life-threatening to humans, since respiratory functions are not affected.

Cannabinoids are very lipid soluble and are slowly absorbed from the stomach and small intestine. Absorption via this route can be increased by adding oil to the plant material prior to consumption, and a common way to do this is to bake the material in cookies or brownies. Significant first-pass metabolism occurs with oral ingestion of cannabis, and so a much larger dose must be taken in order to achieve the same effect as when the drug is inhaled. Oral bioavailability is estimated to be around

CONTINUING EDUCATION

6%. After an oral administration, the peak effect occurs one to three hours after ingestion and lasts up to five hours. Inhalation is the most efficient route of administration for cannabis. Via this route, it is estimated that 10% to 25% of the cannabinoids present enter the lungs, and all of this enters the body. Effects of the drug are noticed within a few minutes and peak after approximately 30 minutes.

Because of their high lipid solubility, cannabinoids distribute to all areas of the body with blood flow but tend to accumulate in the lungs, kidney, and bile. Approximately 1% of a dose will enter the brain. There is a delay between the peak plasma concentration of THC and the time taken for the behavioral effects to occur. This is due to the fact that cannabinoids partition slowly to the brain for up to several hours after the drug has been taken.

Tolerance to cannabis occurs and dissipates rapidly. Tolerance occurs as behavioral as well as some physiological effects, such as changes in heart rate and blood pressure. Fewer mood-altering effects are experienced by regular users of cannabis, and regular users have reported experiencing less of a “high” than naïve users.

A withdrawal syndrome has been seen in studies observing long-term cannabis users who suddenly stop using the drug. Symptoms include restlessness, irritability, mild agitation, insomnia, sleep disturbances, nausea, and cramps. Relatively few substance abusers seek treatment for cannabis addiction.

Psychological dependence related to cannabis use is common. Users feel

Table 2
Understanding the signs of drug abuse

Drug	Pupils	Nystagmus	Pulse	BP	Temp	Muscle tone	Injection sites
Depressants	normal	present	down	down	down	normal	not present
Stimulants	dilated	not present	up	up	up	rigid	possible
Hallucinogens	dilated	not present	up	up	up	rigid	not present
Phencyclidine	normal	present	up	up	up	rigid	not present
Opiates	constricted	not present	down	down	down	flaccid	possible
Cannabis	normal	not present	up	up	normal	normal	not present

they need the drug to function in their everyday life. Without the drug they feel that they cannot relax, unwind, or feel at ease in social situations.

Drug recognition experts

Law enforcement drug recognition experts (DREs) utilize a number of physical parameters to determine the possible use of CNS depressants, CNS stimulants, hallucinogens, phencyclidine, opiates, and cannabis. In the same way the DRE interacts with the public, the pharmacist may also be able to adopt a similar approach to determining drug use or abuse when interacting with patients. (See Table 2.)

For an explanation of the DRE unit and an overview of the DRE program, see <http://www.cityofla.org/LAPD/traffic/dre/drestuff.html>, by the Los Angeles Police Department.

Summary

Drugs have been abused throughout history, suggesting that efforts to eradicate drug abuse will never be completely successful. One only has to look at tobacco as an example of a drug that everyone knows is harmful

CONTINUING EDUCATION

and addictive, and yet millions still use it. However, the good news is that, through education, fewer young people are choosing to smoke than in previous generations, but the cost to society through health care is still enormous.

Similarly, attempts to legislate against drug use are not a solution. The prohibition of alcohol in the 1920s and '30s in the United States did little to prevent alcohol use and instead resulted in an increase in organized crime.

Only through understanding the causes of drug abuse, identifying the symptoms and consequences, and educating the public can we make an impact on the numbers of lives affected by drug misuse.

Pharmacists, tasked with filling prescriptions and counseling patients on drug use, are in an ideal position for identifying potential drug abuse and misuse, and as a resource as well for other healthcare professionals on the effects and dangers of drug misuse.

TEST QUESTIONS

Mark the most appropriate answer. The answer form follows the test questions.

- 1.** To which class of drugs do barbiturate substances belong?
 - a. Stimulants
 - b. Narcotics
 - c. Hallucinogens
 - d. Depressants
- 2.** Cocaine belongs to which class of drugs?
 - a. Stimulants
 - b. Narcotics
 - c. Hallucinogens
 - d. Depressants
- 3.** Mescaline is a naturally occurring hallucinogen that occurs in which substance?
 - a. PCP
 - b. LSD
 - c. Peyote cactus
 - d. Magic Mushrooms
- 4.** Which of the following substances was once used as an animal tranquilizer in the United States?
 - a. Heroin
 - b. Mescaline
 - c. PCP
 - d. LSD
- 5.** Something that is pleasurable, euphoric, or that produces some other positive effect is termed:
 - a. Positive reinforcement
 - b. Negative reinforcement
 - c. Habituation
 - d. Psychological addiction
- 6.** Which neurotransmitter system plays the major role in drug addiction, particularly cocaine and amphetamine addiction?
 - a. Serotonin
 - b. Dopamine
 - c. Opiate
 - d. GABA
- 7.** Which neurotransmitter system plays the major role in the positive reinforcement of sedative hypnotic drugs like alcohol and benzodiazepines?
 - a. Serotonin
 - b. Dopamine
 - c. Opiate
 - d. GABA
- 8.** The major inhibitory neurotransmitter of the CNS is:
 - a. Glutamate
 - b. GABA
 - c. Glutamine
 - d. Benzodiazepine
- 9.** Which of the following is not a cardiovascular effect of barbiturates?
 - a. Decreased cardiac output
 - b. Decreased cerebral blood flow
 - c. Increased myocardial contractility
 - d. All of the above
- 10.** A benzodiazepine with a half-life less than 24 hours is considered:
 - a. The best anxiolytic drug
 - b. A long-acting drug
 - c. A short-acting drug
 - d. Not useful as a preoperative anesthetic
- 11.** The muscle-relaxation effects of benzodiazepines are mediated through which system?
 - a. The peripheral nervous system
 - b. The central nervous system
 - c. The hepatic system
 - d. The cardiovascular system

TEST QUESTIONS

- 12.** Which one of the following statements is *false*?
- Heroin is more lipid-soluble than morphine.
 - Morphine is immediately metabolized to heroin in the body.
 - Heroin crosses the blood brain barrier faster than morphine.
 - Morphine is more hydrophilic than heroin.
- 13.** Which one of the following agents is a morphine antagonist only?
- Naloxone
 - Pentazocine
 - Buprenorphine
 - None of the above
- 14.** Which one of the following drug agents is commonly used for cough suppression?
- Methadone
 - Dextromethorphan
 - Naloxone
 - Oxycontin
- 15.** Which of the following is not a toxic effect of opiates?
- Diarrhea
 - Miosis
 - Pulmonary edema
 - Respiratory depression
- 16.** The opiate receptor subtype that is associated with morphine and its euphoric and respiratory depressive effects is:
- Kappa
 - Mu
 - Sigma
 - Delta
- 17.** The main active agent of cannabis is:
- Cannabinol
 - Tetrahydrocannabivanol
 - Tetrahydrocannabinol
 - Cannabidiol
- 18.** Smoking cannabis with a low concentration of tetrahydrocannabinol can still induce a “high,” since cannabidiol is converted to tetrahydrocannabinol in the smoking process.
- True
 - False
- 19.** The cannabis preparation that is made by boiling the hashish in a solvent such as alcohol, filtering the residue, and then allowing the solvent to evaporate is called:
- Bhang
 - Ganja
 - Hash oil
 - Marijuana
- 20.** Which one of the following synthetic cannabinoids is used in the United States as an antiemetic during cancer therapy?
- Dronabinol
 - THC
 - Anandamide
 - Nabilone

EVALUATION OF CE

Drug Topics is conducting an evaluation of this CE article. Please ✓ box that best reflects your opinion of the evaluation questions. Please keep this evaluation attached to your answer form.

	Strongly Agree	Agree	Disagree	Strongly Disagree
1. The program objectives were met.				
2. The program content was useful and relevant.				
3. The program was educational and not promotional.				
4. The program was fair, objective, balanced, and of scientific rigor.				
5. The program will help me in my practice.				

2006 CEU CREDIT REQUEST

To obtain immediate CE credit, take the test on-line at www.drugtopics.com. Just click on the "Continuing Education" box on the *Drug Topics* home page, which will take you to the CE site. Log in, find and click on this lesson, and follow the three simple steps. Test results will be displayed immediately and you can print the certificate showing your earned CE credits.

ANSWER FORM

Drugs of abuse: A pharmacist's guide

MARCH 19, 2007 ACPE # 012-999-07-053-H01

Test questions start on preceding page

- | | | | | |
|----------------|----------------|-----------------|-----------------|-----------------|
| 1. a. b. c. d. | 5. a. b. c. d. | 9. a. b. c. d. | 13. a. b. c. d. | 17. a. b. c. d. |
| 2. a. b. c. d. | 6. a. b. c. d. | 10. a. b. c. d. | 14. a. b. c. d. | 18. a. b. |
| 3. a. b. c. d. | 7. a. b. c. d. | 11. a. b. c. d. | 15. a. b. c. d. | 19. a. b. c. d. |
| 4. a. b. c. d. | 8. a. b. c. d. | 12. a. b. c. d. | 16. a. b. c. d. | 20. a. b. c. d. |

**Are you employed by a chain?
If so, which one?**

- Amount enclosed:** \$6.00 for this lesson
 \$54.00 for any 12 lessons you take over the next year, starting from the date you sign up
 Already series-enrolled for 2006

Submit your check (payable to The University of Florida) and form to:

University of Florida College of Pharmacy, P.O. Box 100482, Gainesville, FL 32610

E-mail address: continuinged@cop.ufl.edu

Fees not refundable or transferable

For questions concerning PRINT CEs, call (352) 273-6275.
For questions concerning ON-LINE CEs, call (866) 261-3558.

No longer valid for CE credit after 03/31/09

REGISTRANT INFORMATION

Name: _____
(Last) (First) (M.I.) Phone

Address: _____ **E-mail address:** _____
(Street)

City: _____ **State:** _____ **Zip:** _____

ATTENTION FLORIDA PHARMACISTS: The State of Florida has changed to a new record maintenance system for all continuing education, using a private company, **cebroker.com**. The University of Florida is registered with the Florida Board of Pharmacy as a Provider, and will report continuing education records for all pharmacists who are registered in Florida.

Please provide your license number _____