

## Amphetamines (Part 2)

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### Phentermine

This compound was widely used as an appetite suppressant. The combination of the phentermine with fenfluramine resulted in a popular diet drug, Phen-fen, which was released in 1990 but later taken off the market because of heart valve problems resulting from its use. Phentermine is known to function as an anorectic through its direct action on the adrenal glands resulting in the release of the catecholamines, epinephrine and norepinephrine. Epinephrine produces its weight loss by direct action on the cells triggering a break down in fats. In high doses phentermine can result in the release of dopamine, producing feelings of pleasure. Long term use can result both in physical and psychological addiction.

### Phenylpropanolamine

This drug is produced by substituting a hydroxyl group (-OH) for the hydrogen on the beta carbon of amphetamine. This group creates a second asymmetric center for this molecule. This simple addition changes the characteristics of the molecule. The two positions of asymmetry create four stereoisomers, which results in a change in pharmacological activity. Phenylpropanolamine does retain some of the stimulating and anorectic properties of amphetamine, however the conformational changes drastically reduces them. The primary use of this drug is to treat nasal congestion associated with the common cold, allergies and other respiratory conditions. Addiction poten-

tial is very low and adverse reactions are noted as dizziness, headaches, loss of appetite, nausea, and restlessness.

### Ephedrine/Pseudoephedrine

The addition of a beta hydroxyl group to methamphetamine produces the drug ephedrine and an isomer of ephedrine is called pseudoephedrine. This is the same as the above production of phenylpropanolamine by the beta addition of a hydroxyl group to amphetamine. Ephedrine is a stimulant that acts on the central nervous system. It is the primary active component in many dietary supplements taken for weight loss or energy enhancement. These substances use to be highly available over the counter; however, they have become much more regulated in their availability to the general population. The majority of side effects of this drug are associated with the cardiovascular system. These include hypertension, palpitation, arrhythmia, myocardial infarction, cardiac arrest, stroke, transient ischemic attack and seizures.

### Cathine, Cathinone, Methcathinone, and Khat

Cathine is one of the isomers of phenylpropanolamine and cathinone is the oxidation of the beta hydroxyl group to a ketone. Methcathinone is the formation of this same ketone from ephedrine. These compounds are listed as a schedule I controlled substance, however they are naturally occurring and can be obtained from the *Khat* (*Catha edulis*) plant. This substance is openly used and freely available in Somali, Ethiopian and Yemeni cultures. Khat

is not regulated in the United States, however cathine and cathinone are regulated as schedule I and V, respectively. Methylenedioxyrovalerone (MDPV) is a derivative of cathinone, and 4-methylmethcathinone is mephedrone, both of which are known as 'Bath Salts'. The physical effects are very similar to amphetamine and methamphetamine.

### MDA(3,4-methylenedioxyamphetamine)

### MDMA(3,4-

### methylenedioxymethamphetamine)

### Ecstasy or XTC

Both of these drugs are listed as schedule I drugs and are referred to by users as a 'party drug'. They are consumed as oral pills and the effect of the drug is typically felt within 20-60 minutes and lasts for hours. The effects of MDA and MDMA are listed as synthetic psychedelic stimulants. Since they elicit a feeling of 'connectedness' or empathy between people, they are classified as empathogens. There have been published studies, as well as controlled studies currently in progress, showing therapeutic efficacy in the treatment of 'end of life' anxiety and PTSD. The desired effects these drugs can produce are relaxation and the feeling of profound peace. The chronic use, however, can cause permanent brain damage to serotonin nerve terminals. Less severe effects include confusion, depression, paranoia, blurred vision and an inability to control body temperature leading to brain damage, liver, kidney and cardiovascular failure from hyperthermia.

Part 3 of this article will appear in the September issue of Toxicology Times

## ??? Did You Know ???

Mental and substance use disorders affect people from all walks of life and all age groups. These illnesses are common, recurrent, and often serious, but they are treatable and many people do recover. Learning about some of the most common mental and substance use disorders can help people recognize their signs and to seek help. According to SAMHSA's [2012 National Survey on Drug Use and Health \(NSDUH\)](#) an estimated 43.7 million (18.6%) Americans ages 18 and up experienced some form of mental illness. In the past year, 20.7 million adults (8.8%) had a substance use disorder. Of these, 8.4 million people had both a mental disorder and substance use disorder.

Source: SAMHSA

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## Question of the Month

**Question:** What if there is a large variance between the peak and trough values?

**Answer:** The peak value at three to four hours post-dose should be no more than twice the trough value. A large variation between peak and trough values would indicate rapid metabolism (early peaking) and excretion of the methadone by the patient. This would support a patient's claim of withdrawal.