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Amphetamine designer drugs - an overview and epidemiology

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Abstract

The methylenedioxy-derivatives of amphetamine and methamphetamine represent the largest group of designer drugs. The most frequently used compounds are 3,4-methylenedioxy-methamphetamine (MDMA-ecstasy) and 3,4-methylenedioxy-amphetamine (MDA), first synthesised in 1910 (MDA) and 1914 (MDMA), respectively, to be used as an appetite suppressant. At the end of the 1960s, non-medical (recreational) use appeared in the USA, and in the middle of the 1980s in Europe. In Norway, MDMA and related compounds have been detected in forensic samples since the early 1990s. In order to bypass the legal regulations and to produce more potent substances, a number of related compounds have been synthesised, including derivatives with one or more substituents (methoxy, methyl, halogen or sulphur), attached at different positions to the phenylring of amphetamine or methamphetamine. A report from 1998 shows that 0.5-3% of the adult European population, mainly young people, has used ecstasy.

Keywords: Ecstasy; Related compounds; Epidemiology

1. Historical background

The term ‘designer drugs’ includes compounds that have been chemically altered from federally controlled substances, to produce special effects and to bypass legal regulations. Designer drugs are mainly synthesised by so-called ‘underground’ laboratories. Addiction and numerous deaths have been reported as a result of designer drug use. The largest group, representing the most extensively studied, is the methylenedioxy-derivatives of amphetamine and methamphetamine. One well-known and probably the most used compound belonging to this group is 3,4-methylenedioxy-methamphetamine (MDMA), or mostly known as ecstasy (Fig. 1). MDMA was first synthesised and patented by Merck in 1914, with the purpose of being used for appetite control (Downing, 1986). However, the patent expired due to the lack of commercial interest and MDMA did not become available on the public market. Except for several toxicological animal studies with MDMA at the beginning of the 1950s, the compound remained relatively ignored until 1968, when non-medical use first appeared in the USA (Siegel, 1986). Around 1980, small doses of MDMA were

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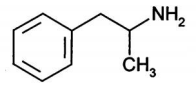
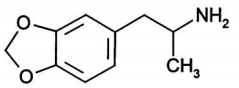
used legally as an adjunct to psychotherapy. During the 1970s, MDMA was widely abused throughout the USA under a variety of street names: XTC, Adam, MDM, M and M and several others. In the middle of the 1980s, a large number of clandestine laboratories provided the distribution of MDMA and other similar designer drugs to the US market. At this time, the European distribution was at its planning stage.

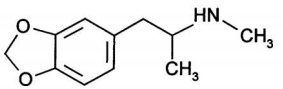
Another early known, and later frequently used, designer drug, is 3,4-methylenedioxyamphetamine (MDA), differing from MDMA by one methyl group. This compound was first synthesised in 1910 (Poklis et al., 1979) (Fig. 1). How-



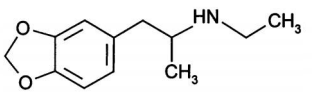
AMPHETAMINE



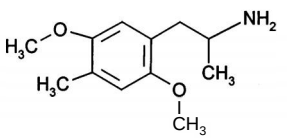
MDA (3,4-methylenedioxyamphetamine)



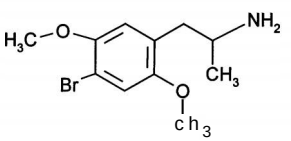
MDMA (3,4-methylenedioxy-N-methylamphetamine)



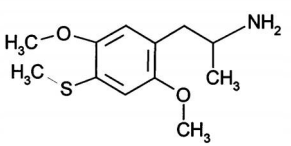
MDE A (3,4-methylenedioxy-N-ethylamphetamine)



DOM (2,5-dimetoxy-4-methylamphetamine)



2-CB (4-bromo-2,5 -dimetoxyphenylethylamine)



DOT (2,5-dimethoxy-4-methylthioamphetamine)

Fig. 1. Structures of amphetamine, MDMA, MDA and related substances.

ever, the first pharmacological studies demonstrating stimulatory properties, were not conducted until 1939 (Poklis et al., 1979). MDA was patented in 1940 as an antitussivum, in the beginning of the 1960s both as an ataractic and an anorexigenic drug. However, the drug has never been available commercially on the licit pharmaceutical market. Around 1970, widespread abuse of MDA started, followed by reports of several deaths from California and Canada. A common street name used for this drug is the 'love drug'.

Due to their addictive potential, in addition to extensive reports of misuse and overdoses, the US Department of Justice's Drug Enforcement Agency (DEA) placed MDMA and related derivatives with stimulant properties on the list of psychotropic substances under international control, schedule I. The necessity for this restriction was endorsed, but some disagreement appeared, connected to research and potential medical therapeutic prescription.

After 1986, a large number of derivatives from MDMA and MDA have been synthesised by clandestine laboratories, mainly to produce more potent drugs and to bypass these legal regulations. Up until these days, nearly 200 different derivatives have been synthesised and described, mainly by underground literature (Shulgin and Shulgin, 1995). Examples are derivatives with one or two methoxy groups connected to the phenyl-ring, with halogens, sulphur, methyl groups and phosphor, in addition to different substituents in the ethylamine side chain, attached at different positions against each other. Only a limited number of these derivatives are known from Europe, although both halogen- and sulphur-derivatives have been detected in confiscated tablets or biological samples. In Norway, six to seven different derivatives have been detected. Fig. 1 shows some examples of designer drugs with different substituents. The term ecstasy is also often used as a common name for several compounds belonging to this class of drugs.

2. Detection in biological samples

Due to the chemical relationship with amphetamine and methamphetamine, the presence of MDMA and related compounds can be detected in biological samples by immunogical methods designed for amphetamine/methamphetamine, depending on the concentrations and the type of the respective designer drugs. The assay sensitivity is mostly lower than the amphetamine/methamphetamine, and not all different drugs belonging to this class have been tested. To identify and confirm the type of drugs which have been used, and to separate similar chemical compounds, a specific analytical method (gas-chromatography/mass-spectrometry; GC/MS) has to be used.

3. Epidemiology

The real number of persons who have used amphetamine designer drugs at any time, or more regularly, is not known. The frequencies of such use are mainly known from anonymous questionnaire studies of drug use among large selected groups. Various estimates have been given, depending on the age group studies. The frequency of amphetamine-derived designer drugs detected in forensic samples, may also indicate the extent of such drug use compared to other illegal drugs. The use of amphetamine designer drugs has mostly been reported to occur among young people (15-25 years), in particular associated with clubs, raves and house parties. The 'rave scene' in particular appears to be responsible for the explosive growth of MDMA use in the UK, which has been described as developing into what many believe is the 'largest youth movement in British history' (Beck, 1993).

A study from the beginning of the 1980s, showed that 39% of the questioned students at Stanford University, USA, had used MDMA at least once (Peroutka, 1987). However, according to a 1993 National Institute on Drug Abuse survey, 2% of all US college students admitted having used MDMA in the previous 12 months (NIDA capsules, CAP 16, 1993). A questionnaire study among students (« = 3050) selected from 10 different universities in the UK, showed that 13% had used ecstasy once or regularly (Webb et al., 1996). However, the most frequently used drugs

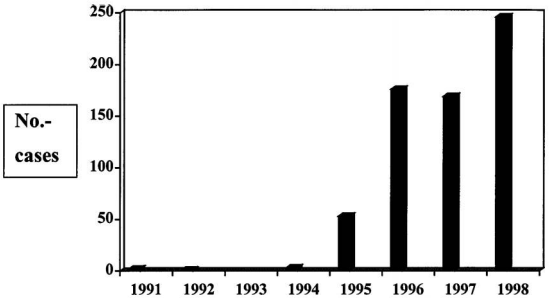


Fig. 2. Detections (n) of MDMA, MDA and derivatives from 1991 to 1998 in Norwegian forensic samples (blood or urine).

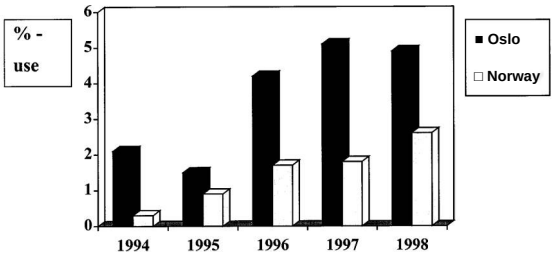


Fig. 3. Frequencies (%) of young people (15-20 years) in the capital Oslo and whole country (Norway) who say they have used ecstasy at some time (1994-1998).

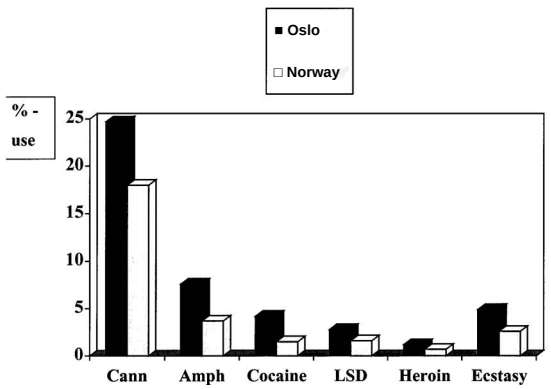


Fig. 4. Frequencies (%) of young people (15-20 years) in the capital Oslo (n = 822) and whole country (Norway) (n = 1636) who say they have used different drugs at some time (1998).

were cannabis (59%), amphetamines (19%), cocaine (18%) and LSD (18%). The frequencies of drug use were higher among males compared to females and were also dependent of the ethnic origin of the students.

Based on the 'Annual report on the state of the drug problems in the European Union', published by the European Monitoring Centre for Drugs and Drugs Addition (EMCDDA, 1998), 0.5-3% of the adult population within the EU has used ecstasy. The highest frequencies of ecstasy use among 15-16-year-old school students has been reported from Ireland (9%), the Netherlands (8.1%) and the UK (8%) (EMCDDA, 1998). In some countries, the use of ecstasy is reported to be increasing. Deaths caused by ecstasy are few in numbers compared to other drugs, e.g. to heroin. The use of amphetamine designer drugs is often combined with other drugs. The doses in tablets containing MDMA vary from 50 to 200 mg; most commonly they contain 100 mg. However, analyses of confiscated designer drug tablets have often documented a mixture with other drugs.

In Norway, MDMA and MDA and similar compounds have been detected in forensic samples since the early 1990s, increasing steadily up to 1998 (Fig. 2). The positive samples represent mainly cases of criminal offences connected to driving under the influence of drugs, illegal drug use, autopsy cases (without the drug being the main cause of death) and control of prison inmates. However, the number of designer drug detections is low, compared to other illegal drugs (e.g. cannabis, amphetamines, heroin). The frequency of designer drug detections in forensic cases may be non-representative compared to real use, due to the fact that such drugs are mainly used in closed parties and less in connection with criminal offences. A questionnaire study from 1998, performed by the National Institute of Alcohol and Drugs Research in Norway, showed that 4.8% of young people (15-20 years) from the capital Oslo had used ecstasy once or more, while the frequency from the whole country was 2.5% (Fig. 3) (Alcohol and Drugs in Norway, 1998). The use of ecstasy was significantly lower compared to cannabis (25% in Oslo) and also to amphetamine (8% in Oslo), but higher than cocaine, LSD and heroin (Fig. 4).

4. Conclusions

The use of amphetamine designer drugs seems to be increasing in some countries, mainly among young people. It may be expected that clandestine laboratories may produce new and more potent compounds, by introduction of 'new' chemical substituents in different positions of the molecules. This problem demands matter-of-fact warnings for the potential user groups, to avoid life-threatening complications and fatal intoxications.

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