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m-Chlorophenylpiperazine (mCPP)[1]

Introduction

A substantial amount of scientific literature exists on the pharmacological properties of m-chlorophenylpiperazine (mCPP). The following review focuses on those studies that are most relevant to its risk assessment as a drug of misuse. Although reports from Member States usually referred to mCPP (and this was confirmed in some cases by NMR spectroscopy), some illicit tablets contained the isomeric pCPP and, occasionally, other substituted piperazines. Much less information has been published on the properties of the positional isomers (i.e. oCPP and pCPP). Apart from these, mCPP is one of a family of aryl-substituted piperazines that includes, *inter alia*, benzylpiperazine (BZP), 1-(4-methoxyphenyl)-piperazine (MeOPP) and m-trifluoromethyl phenylpiperazine (TFMPP). Like mCPP itself (see later), many of them are metabolites of licensed medicines. Some piperazine derivatives were originally evaluated as potential anthelminthic agents for the treatment of roundworm infestations in humans and animals, but were never developed. However, the parent compound piperazine is still licensed for this purpose. Neither mCPP nor other piperazines are "synthesised from the pepper plant" nor can they accurately be described as belonging to the "same class as Viagra" (http://www.benzylpiperazine.com/bzp.html).

A: Review of the pharmacotoxicological data on mCPP

1. Chemical and pharmaceutical information

1.1 Chemical description

The chemical structure of mCPP is shown in Figure 1. The molecular formula is $C_{10}H_{13}ClN_2$ and the molecular weight of the free base is 196.68 Daltons. The Chemical Abstracts Service (CAS) registry number of the free base is 6640-24-0; the CAS number of the hydrochloride is 65369-76-8. Because mCPP is dibasic, it can form both mono- and dihydrochloride salts. The base and the hydrochloride salts are white powders. Other chemical names include meta-chlorophenylpiperazine, 1-(3-chlorophenyl)piperazine, 3CPP and 3Cl-PP. These abbreviations should be treated with caution since the term 'CPP' is also used for the unrelated herbicide 2-(4-chlorophenoxy)propionic acid. The mCPP molecule does not contain an asymmetric carbon atom, and therefore, unlike almost all of the more familiar substituted tryptamines and phenethylamines, it has no stereoisomers.

[1] This report was commissioned by the EMCDDA and written by L. A. King. No formal risk assessment of mCPP had been authorised within the terms of Article 6 of Council Decision 2005/387/JHA on information exchange, risk assessment and control of new psychoactive substances, nevertheless, this report follows the structure of Annexes A and B of the risk assessment guidelines (1999).

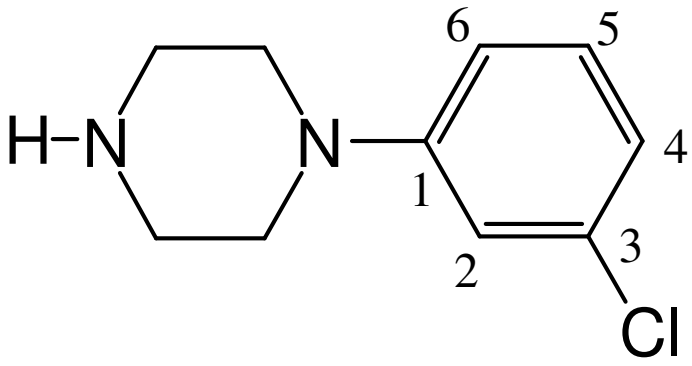

Figure 1. Structure of 1-(3-chlorophenyl) piperazine (mCPP) showing the numbering system in the phenyl ring.

1.2 Methods of synthesis and commercial availability

There are several routes to the synthesis of mCPP, the most common of which appears to be reaction of diethanolamine with 3-chloroaniline. Other methods involve the reaction of *m*-chloroaniline with bis(2-chloroethyl)amine or the reaction of piperazine with *m*-dichlorobenzene. The other two isomers of CPP could be made in a similar way. However, it is unlikely that the mCPP used in the various illicit products found in many EU countries has been synthesised in clandestine laboratories. The solid substance is available commercially as the base or as the hydrochloride at purities of 95% to 98%. Solutions of mCPP are also sold. Suppliers include Sigma-Aldrich (UK), LLB Chem (Germany), Maybridge (UK), Acros Organics (UK), Apollo Scientific Ltd (UK) Oakwood Products, Inc. (USA) and AB Chem Technologies LLC (Germany). Maybridge, for example, sell 50g of the free base for approximately €135.

1.3 Identification

There are no readily-available screening tests for mCPP; it does not react with Marquis, Nitroprusside or Scott's reagents. Analytical data (gas chromatography-mass spectrometry and infra red absorption) have been published by Aunan and Ely (1999) and Maurer (2004). In the mass spectrum, the principal ions (m/z) are 154 (base peak), 196, 156, 56 and 138. However, mass spectrometry does not distinguish mCPP from its isomers (oCPP and pCPP). Although studies on other substituted piperazines have shown that they react only weakly or not at all with amphetamine immunoassays (de Boer et al., 2001), no comparable results are available specifically for mCPP. However, it might be assumed that mCPP is unlikely to be detected in urine samples by common drug immunoassay screening systems. The quantification of mCPP and other piperazines in blood was described by Peters et al. (2003). They used solid-phase extraction, derivatisation with heptafluorobutyric anhydride and analysis by gas chromatography-mass spectrometry. The limit of detection was 5 micrograms per litre.

1.4 Legitimate uses of mCPP

A major use of mCPP is as an intermediate in the production of Trazodone[2] (Figure 2) and three related substances (Nefazodone[3], Etoperidone[4] and Mepiprazole[5]), which differ only in the substituent attached to the piperazinylpropyl moiety. The synthesis of Trazodone was also described by Baiocchi and Giannangeli (1974). As the most widely used of the four drugs, Trazodone is licensed in a number of Member States, e.g. as Trazolan® in Belgium, as Thombran® and Tombran® in Germany, as Pragmarel® and Pragmazone® in France, as Trittico® in Austria, the Czech Republic, Italy and Slovakia, as Tramensan® and Azona® in Finland, as Desyrel® in Italy and as Molipaxin® in the UK. Trazodone is thought to act by serotonin (5HT) reuptake inhibition. It is often prescribed with other antidepressants as a sleep-inducing agent because of its sedative side-effects, and is used in the treatment of depression and other disorders. Trazodone and related drugs are metabolised in the liver to form the active metabolite mCPP by *N*-dealkylation at the piperazinyl nitrogen (Odagaki et al., 2005; Maurer et al., 2004; Rotzinger et al., 1998a, 1998b). It has been suggested that mCPP may contribute to the antidepressant efficacy of Trazodone. As discussed later, a further use of mCPP is as a model reference compound in neurochemical studies of 5HT receptors.

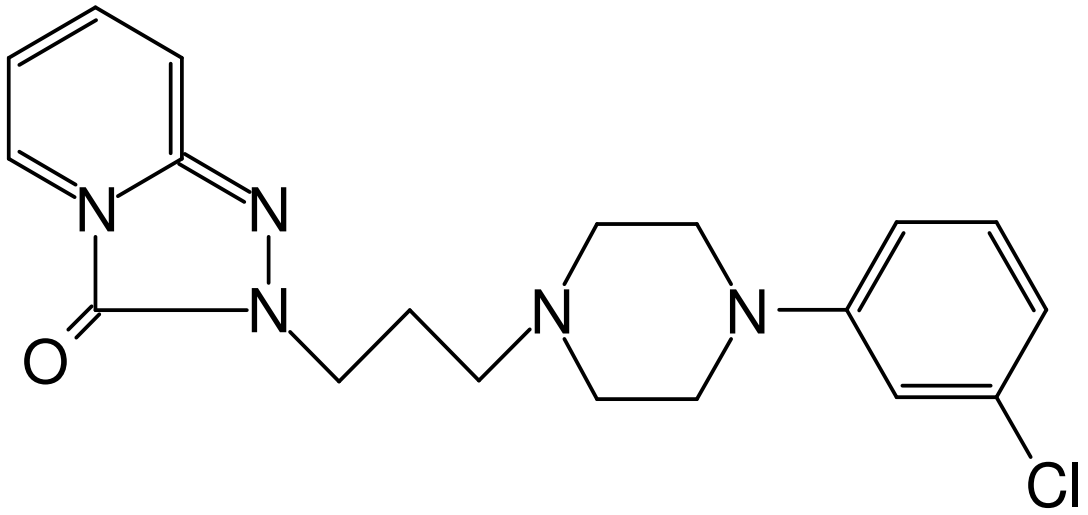

Figure 2. Structure of Trazodone: (2-[3-[4-(3-chlorophenyl)-1-piperazinyl]propyl]-1,2,4-triazolo[4,3-a]pyridine-3(2H)-one)

[2] US patent no. 3,381,009 of 30 April 1968.
[3] US patent no.4,338,317 of 6 July 1982.
[4] US patent no. 3,857,845 of 31 December 1974.
[5] US patent no. 3,491,097 of 20 January 1970.

1.5 Pharmaceutical form

There are no licensed medicinal uses of mCPP in the EU; it is not listed in the European Pharmacopoeia (2005). Apart from the less common powders and capsules, illicit tablets were often white/beige, either plain or marked with a logo and/or contain multi-coloured inclusions. Typical illicit dosage forms found in Member States in 2004 - 2005 are shown in Figure 3 (See Annex 2 for all mCPP encounters in 2006). Tablets have been known by a number of street names, e.g. 'X4' (Netherlands, Sweden), 'duhovka' (Hungary, Czech Republic), 'regenboogies' and 'arc-en-ciel' (Belgium), 'arlequin' (France), and 'rainbow' (Slovenia), many of which refer to the multi-coloured appearance of one of the tablets in Figure 1. Similar tablets were reported in Switzerland (http://www.eve-rave.net/abfahrer/download/eve-rave/dc117.pdf) where they are also known as 'Rolls Royce' and 'smarties'.

Figure 3. Illicit dosage forms containing mCPP

1.6 Routes of administration and dosage

In challenge tests of the serotonin system in psychiatry, mCPP is almost always used orally with doses typically up to 0.75 mg/kg, i.e. up to about 50mg for a 70kg person (Tancer and Johanson, 2001, 2003; Gijsman et al., 1998). Illicit mCPP is normally consumed orally, but some was seen in powdered form, so there is the possibility that it could also be snorted or injected. The amount of mCPP in illicit tablets was variable, and some contained other drugs as well. Nevertheless, the amounts of mCPP found in illicit tablets were broadly comparable to those used in clinical investigations. For example, of 16 samples quantified by the Dutch DIMS in 2004 and 2005, two contained 8mg mCPP or less and the remainder contained 22–46mg. Later samples examined by the DIMS in 2005 contained substantially higher amounts of mCPP (62, 72 and 80mg). The majority of the samples were tablets bought as 'Ecstasy', but two samples were powders sold as cocaine.

2. Pharmacology and toxicology in animals and humans

2.1 Metabolism and pharmacokinetics

Following oral administration of mCPP to healthy human male volunteers, the elimination half-life ranged from 2.6 to 6.1 hours (Feuchtl et al., 2004) with a wide range in peak blood levels and bioavailability. In rats, Staack and Maurer (2003) reported that mCPP was extensively metabolised by hydroxlation of the aromatic ring and, to a lesser extent, by degradation of the piperazine ring to produce hydroxy-mCPP (two isomers), *N*-(3-chlorophenyl)ethylenediamine, 3-chloroaniline and hydroxy-3-chloroaniline (two isomers). The hydroxy metabolites were partly excreted as the corresponding glucuronides and/or sulphates and the chloroanilines were partly excreted as the acetylated derivatives. Physiological and subjective effects reach their peak 1 to 2 hours after oral administration and can last 4 to 8 hours (Gijsman et al., 1998; Tancer and Johanson, 2001, 2003).

2.2 Toxicology

The negative effects of mCPP, often typical of a serotonin syndrome, include anxiety, dizziness, confusion, shivering, sensitivity to light and noise, fear of losing control, migraine and panic attacks (Gijsman et al., 1998; Tancer and Johanson, 2001, 2003; Feuchtl et al., 2004). A serotonin syndrome was found to occur in some psychiatric patients following oral dosing with mCPP (0.5mg/kg), but did not occur in normal volunteers at the same plasma concentrations (Klaassen et al., 1998). Unlike MDMA, mCPP lacks neurotoxic potential (Gobbi et al., 2002) and mCPP releases 5HT without causing long-term depletion (Ulrichsen et al., 1992; Baumann et al., 2001). This difference between MDMA and mCPP may be related to the ability of mCPP to release cytoplasmatic 5HT, whereas MDMA induces the release of both cytoplasmatic and vesicular 5HT (Gobbi et al., 2002). The main enzyme involved in hydroxylation of mCPP is CYP2D6, the activity of which is subject to considerable genetic variability (Bertilsson et al., 2002). Since this enzyme is involved with the metabolism of many other drugs, ‘slow-metabolisers’ are most at risk of drug interactions (Pritzker et al., 2002). Variability in CYP2D6 phenotype may partly explain the wide variation in the pharmacokinetics of mCPP as noted above.

No fatal poisonings from mCPP have been reported. Although Goeringer et al. (2000) and Martinez et al. (2005) gave details of a number of fatalities due to Trazodone, it is unclear what part the metabolite mCPP played in these deaths. Little is known about the mutagenic and carcinogenic potential of mCPP or its effects on other organ systems.

2.3 Neuropharmacology

As an agonist at the $5HT_{2C}$ receptor, and an antagonist at the $5HT_{2B}$ receptor, mCPP has been widely used as a probe of serotonin function in psychiatric research (Hamik and Peroutka, 1989; Thomas et al., 1996; Gijsman et al., 1998; Kahn and Wetzler, 1991). It has both pre- and postsynaptic effects on the serotonin system. It also induces a release of serotonin (5HT) dependent on the serotonin transporter (SERT) (Pettibone and Williams, 1984; Baumann et al., 1993, 2001; Eriksson et al., 1999; Gobbi et al., 2002). In this respect, mCPP is, to a certain extent, similar to MDMA, which also releases 5HT via a SERT-mediated process (Cole and Sumnall, 2003). As a consequence, the subjective effects of mCPP and MDMA are comparable (Tancer and Johanson, 2001, 2003). An important difference between mCPP and

MDMA and other substituted phenethylamines is that mCPP has little effect on the dopamine system (Baumann et al., 2001; Gobbi et al., 2002). As a consequence, mCPP does not display reinforcing effects (Tancer and Johanson, 2003), and is unlike the closely related piperazine BZP, which shows amphetamine-like (sympathomimetic) activity. This difference in receptor affinity was recently confirmed by Johanson et al., (2006), where it was found that humans could be trained to distinguish mCPP from d-amphetamine. However, half of the participants reported that MDMA was like amphetamine and half reported that it was like mCPP.

In alcoholics, mCPP causes a more intense 'high' feeling than in normal subjects (Buydens-Branchey et al., 1997a; Benkelfat et al., 1991). Similar results were found with cocaine addicts (Buydens-Branchey et al., 1997b) and with MDMA users (McCann et al., 1999). In a preliminary study of obsessive-compulsive patients, Erzegovesi et al. (2001) reported that low doses of mCPP (0.25mg/kg) induced a significant worsening of symptoms.

In addition to its serotonergic activity, mCPP also increases the levels of certain hormones (ACTH, cortisol and prolactin). Ghaziuddin et al. (2003) found gender differences in the neuro-endocrinal effects of mCPP, but noted that systolic and diastolic blood pressure, pulse rate and temperature were only mildly elevated. Using positron emission tomography, Hommer et al. (1997) found that mCPP significantly increased brain glucose metabolism. In rats, mCPP depressed spontaneous ambulatory activity (Lucki et al., 1989) and was associated with activation of certain 5HT receptors.

Squires et al., (1993) showed that, in rats, mCPP and other *N*-arylpiperazines also act as antagonists at γ-aminobutyric acid (GABA-A) receptors, but the implications of this do not appear to have been widely explored in more recent work.

There is no evidence to indicate that mCPP has the potential to produce dependence in humans, and as far as is known, it has no major effects on cognitive functions (Silverstone et al., 1994).

3. Clinical experience

3.1 Studies on street users

In Belgium, one of the CPP isomers (probably mCPP) was identified in urine samples taken from two intoxicated individuals. However, cocaine, MDMA, cannabinoids and GHB were also found, and the role of CPP is therefore unclear. Limited users' reports from Austria and the Netherlands reported negative or unpleasant effects. In France, users described the disorders that occurred following the ingestion of mCPP as ranging from 'light to severe'. These included nausea, vomiting, headaches and, occasionally, 'psychological discomfort' such as anxiety, depressive symptoms, feeling of being persecuted and aggressiveness. The French NFP reported that at the Dour music festival in Belgium near the French border some users suffered from hot flushes and a feeling of suffocation. Several users reported a 'quite long stimulation effect'. Two people who injected the substance reported face swelling, hot flushes and breathing difficulties.

4. Related substances

Apart from the large number of variously substituted piperazines, there are two positional isomers of mCPP, namely 1-(4-chlorophenyl)piperazine (also known as pCPP, para-CPP, 4CPP and 4Cl-PP) and 1-(2-chlorophenyl piperazine, (also known as oCPP, ortho-CPP, 2CPP and 2Cl-PP). Both are commercially available; their structures are shown in Figures 4 and 5 respectively.

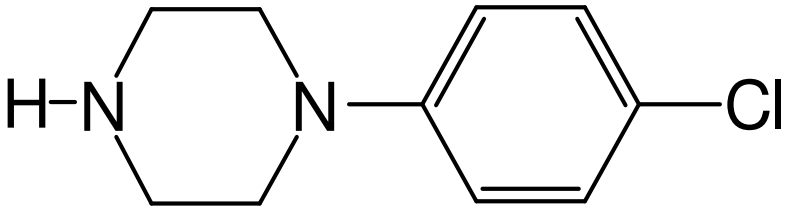

Figure 4. Structure of 1-(4-chlorophenyl)piperazine (pCPP)

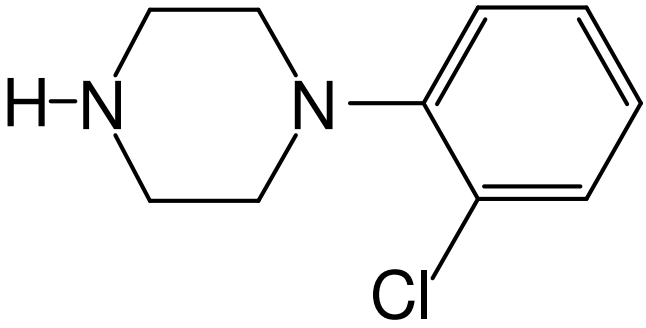

Figure 5. Structure of 1-(2-chlorophenyl)piperazine (oCPP)

As noted earlier, some illicit tablets contained pCPP. Compared to mCPP, neither pCPP nor oCPP have found significant use as probes of 5HT receptors. According to Fuller and Snoddy (1980), pCPP increases serotonin levels in rat brains but, unlike p-chloroamphetamine, caused no long-term depletion of 5-hydroxyindoleacetic acid. Verdonk et al., (1997) performed molecular mechanics calculations on several piperazines and showed that for optimum binding at the $5HT_{2C}$ receptor, the piperazine and phenyl rings should be co-planar. Furthermore, it was predicted that the ortho-isomer, unlike mCPP, would be an antagonist at this receptor. This was subsequently confirmed in both *in vitro* and *in vivo* tests. A structure search of the Merck Index (1996) shows that there are no medicinal products containing the pCPP or oCPP fragments in their structures.

B: Sociological and criminological evidence and public health risks of mCPP

Information in this section of the report is drawn largely from English language Internet searches, notifications to Europol by Europol National Units and to EMCDDA by Reitox National Focal Points in the 25 Member States and Norway, and the Europol–EMCDDA Joint Report (2005) on mCPP made in accordance with Article 5 of Council Decision 2005/387/JHA on information exchange, risk assessment and control of new psychoactive substances.

1. Sociological and criminological evidence

1.1 Legal status of mCPP

Control measures in the Member States under drug control or equivalent legislation[6]
In Greece, as of 20 January 2005, mCPP (shown as 'CPP') is listed under the terms of Law 1729/87 in Table A (13) and is, therefore, subject to the same control measures that apply to other psychotropic substances such as MDMA. In December 2005, Denmark decided to control mCPP along with four other piperazines. Furthermore, in 2006-2007 control measures were introduced in Belgium (22 October 2006), Hungary (1 January 2006), Lithuania (1 July 2006) and Germany (1 March 2007). At least two other Member States – Slovakia and Latvia – have informed EMCDDA that they are considering control measures.

Control measures in the Member States under medicines legislation
In Finland, mCPP is included in Annex 1 of the list of medicinal products covered by the Medicines Act (395/1987). Furthermore, in both the Netherlands and Spain, such possibility for control exists under medicines related laws.

Apart from the above nine Member States, mCPP is commercially available elsewhere without legal restriction.

According to the World Health Organisation mCPP is not currently under assessment for potential control by the United Nations 1971 Convention. In the USA, BZP was placed into Schedule I of the Controlled Substances Act in 2003, but mCPP remains uncontrolled.

1.2 Social consequences for the user

No crimes or violence have been directly linked to the use of mCPP. However, a Turkish Kurd was arrested on arrival in Finland from the Netherlands in possession of 25,300 tablets containing mCPP. As the substance is not under control in Finland, the courier was released shortly afterwards and subsequently seriously assaulted on returning to the Netherlands. No information was received on money laundering related to the production and/or trafficking of mCPP.

1.3 Wholesale production and distribution

[6] I.e. under the terms of the 1961 or 1971 UN drug control Conventions.

Because mCPP is legally available in most countries, there is no need, and indeed no evidence, for the involvement of organised crime in its manufacture. Most illicit tablets are thought to have been produced in Europe. Tabletting facilities were discovered in the Netherlands that had been involved in producing various tablets since early 2005; some of the mCPP had been sourced in India. It is clear that tablets and capsules are also being obtained via Internet sales. Some of these originated in New Zealand, where the use of piperazine-related drugs has been well described, e.g. http://www.benzylpiperazine.com/bzp.html, http://www.mindfuel.co.nz/euphoria.html and https://erowid.org/chemicals/bzp/bzp_info1.shtml. Although most countries reported seizures or other occurrences of mCPP, a few were particularly large.

However, there is no evidence yet that supply for mCPP is in decline. Evidence for this comes from the tenfold increase in the number of seizures in 2006 compared to 2005, as well as corresponding increases in the number of dosage units seized. (See Annex 2 for all mCPP encounters in 2006). Furthermore, as of October 2005 mCPP was identified in 18 Member States and Norway, whereas by the end of 2006 it had been identified in 26 Member states (all except Cyprus) and Norway.

2. Public health risks: epidemiological evidence

2.1 Availability and quality of product on the market

Tablets called X4 can be purchased from an Internet site (http://www.naturensdroger.nu/enter.html). They allegedly contain a total of 150mg of four different piperazines: mCPP, pCPP, MeOPP and TFMPP. However, the chemical name listed against mCPP is erroneously shown as 2-(2-Methyl-4-chlorophenoxy)propionic acid. Other Internet sites selling piperazines (mostly BZP and TFMPP) include http://www.mindfuel.co.nz/euphoria.html. As noted earlier, the amount of mCPP in tablets varied from 8 to 80mg. In 2 out of the 12 Hungarian seizures, tablets contained both mCPP and MDMA. In the UK, MDMA was also found mixed with mCPP in tablets, where it was estimated that the two substances were present in almost equal amounts. In the Netherlands, one sample of mCPP contained 1% cocaine. An analysis of the tablets sold by http://www.spiritualhigh.co.uk/ (Ramsey, 2006) showed that they did not contain mCPP. Apart from mixtures with other piperazines, mCPP was often found in illicit products in combination with MDMA. Since mCPP and MDMA are chemically unrelated compounds, their occurrence together is unlikely to represent accidental contamination; the deliberate addition of mCPP could be intended to potentiate or modify the effects of MDMA or vice versa.

2.2 Knowledge, perceptions and availability of information

Over the last year, in the majority of the Member States, mCPP-containing tablets, often designed to look like ecstasy, have increasingly been found in the context of various recreational activities (open-air dance/music festivals, dance clubs etc.), where they are almost always sold/bought as the popular drug ‘Ecstasy’. There seems to be little specific demand or market for mCPP in the European Union. Given the physical forms in which mCPP is available and the intended users, in the great majority of the cases the substance is taken orally. However, since mCPP in powder form is also available, it cannot be excluded that the substance is sometimes injected. So far, two cases of mCPP injection have been reported by the French

NFP, both involving users who normally inject ecstasy. In France, the tablets collected were bought as 'Ecstasy' or 'MDMA' (six cases), 'artisanal Ecstasy' (one case), one case involving MDMA mixed with either LSD or ketamine, and 'MDEA' (one case). Where reported, the price of mCPP-containing 'ecstasy' tablets varies considerably over time and across the Member States. The French NFP reported that at the end of 2004 the price of a tablet in Bayonne, South-West France, was €15, whereas in Hungary in the last three months the price of a mCPP-containing tablet was €5 (i.e. a little more expensive than an ordinary 'Ecstasy' tablet). In Lithuania, the price is reported to be €2.30 at wholesale and €3.20 at retail level. Very recent information from Slovenia mentions that the price is €6.25 per tablet. A 150-mg X4 tablet in Sweden is reportedly sold on the Internet for approximately €10 (99 SEK). In Austria, in 2006 and 2007 mCPP has been purchased as ecstasy for €10.

2.3 Prevalence and patterns of use

Tablets containing mCPP are usually bought and sold as 'Ecstasy'. Although mCPP was available in most countries in Europe, in comparison to illicit amphetamine and MDMA, the number of seizures and the amounts seized in the Member States are both relatively low.

2.4 Characteristics and behaviours of users

There have been no formal studies of the characteristics of mCPP users. However, it can be assumed that they are the same as those of the well-studied population of 'Ecstasy' users. This is typically associated with 15-to 24-year-olds, who frequent clubs, discos and dance events, with rates of drug use higher in males than in females and who are predominantly drawn from urban areas. For those users who are aware of the fact that they are consuming mCPP, it seems that this drug has no particular advantages over other drugs such as MDMA.

In a symposium devoted to 'club drugs', Tancer (http://www.aaap.org/meetings/2004am/symposia2004.pdf) noted that users of mCPP claimed that it acted as a stimulant at high doses and that it had similar spectrum to MDMA of both negative (dysphoria, anxiety) and positive (euphoria) effects. Some users' reports on the Internet, confirmed by information received from the French NFP, describe mCPP as a product of little recreational interest and a source of unpleasant effects such as anxiety, panic reactions, nausea, headaches and long-lasting hangover. A more positive reaction was described following ingestion of one 'rainbow' tablet, where the effect was claimed to be similar to MDMA (http://www.erowid.org/experiences/exp.php?ID=44771). Other accounts of mCPP are difficult to evaluate because it was ingested along with other drugs such as cannabis (http://www.erowid.org/experiences/exp.php?ID=44075) or other piperazines (http://www.erowid.org/experiences/exp.php?ID=2394).

Summary

- mCPP is a synthetic substance used in at least three Member States as an intermediate in the manufacture of Trazodone and several related antidepressant drugs. It also occurs as a metabolite of those drugs and is commercially available. There is no marketing authorisation for mCPP in the EU.

- Most illicit products containing mCPP were tablets, usually marked with logos typical of 'ecstasy' tablets; capsules and powders were less common. In illicit preparations, mCPP was sometimes mixed with other piperazines (e.g. TFMPP) or other drugs (e.g. MDMA), but the purpose of this is unclear.

- There was a tenfold increase in the number of seizures in 2006 compared to 2005, as well as a corresponding increase in the number of dosage units seized. Furthermore, by the end of 2006 mCPP had been identified in 26 Member states (all except Cyprus) and Norway.

- mCPP is widely used in experimental human pharmacology as a neurochemical probe of the serotonergic (5HT) system. It acts both as an agonist and antagonist at different 5HT receptors.

- Although mCPP may show weak amphetamine-like effects in some users (stimulation, loss of appetite), it does not interact with the dopaminergic system and has little impact on blood pressure or pulse rate. Unlike MDMA, it is not considered to be neurotoxic and would appear to have limited potential for producing dependence.

- The adverse effects of mCPP are more often seen in alcoholics, cocaine addicts and those who use drugs that also interact with 5HT receptors, such as MDMA. These side effects resemble those of the so-called serotonin syndrome, and include anxiety, panic attacks, dizziness, confusion, shivering, sensitivity to light and noise, and fear of losing control.

- No fatal poisonings with mCPP have been reported.

- There is no evidence to indicate that mCPP has the potential to produce dependence in humans, and as far as is known, it has no major effects on cognitive functions.

- The positional isomer, pCPP has also been reported in some illicit products, but only limited investigations have been made on the properties of pCPP and oCPP. Since the latter is an antagonist of the $5HT_{2C}$ receptor, then it is unlikely to produce similar effects to mCPP.

- It would appear that there is only a limited demand from users for mCPP. For many, it compares unfavourably with MDMA.

- Five Member States control mCPP as an illicit substance and three control it under medicinal legislation.

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