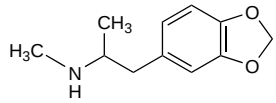
Methylenedioxymethamfetamine ⊗

MDMA; Methylenedioxymethamphetamine; 3,4-Methylenedioxymethamphetamine; Metilendioximetanfetamina. *N*,α-Dimethyl-1,3-benzodioxole-5-ethanamine.

$C_{11}H_{15}NO_2$ = 193.2.

CAS — 42542-10-9.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of methylenedioxymethamfetamine:
007s; 69s; Adam; Adam MTX; Anastasia; Apples; Baby slits; Bacalao; Batmans; B-bombs; Bean; Beans; Bens; Benzedrine; Bermuda triangles; Bibs; Bicho; Bickies; Bikkies; Biphetamine; Biscuits; Blue kisses; Blue lips; Blue nile; Booty juice; Bomber; Brownies; Burgers; Candies; Candy; Care bears; Cat in the hats; Charity; Chocolate chips; Chrystal methadrine; Clarity; Cloud nine; Clovers; Cowies; Cristal; Crowns; Dancing Shoes; Dead road; Debs; Decadence; Deccadence; Dennis the Menaces; Dex; Dexedrine; Diamonds; Diamond Whites; Disco biscuit; Disco biscuits; Doctor; Dollars; Dolls; Dolphins; Doobies; Dove; Doves; Drivers; E; EA1475; Eazy; Eazy E; E-ball; Ebeneezer; E-bomb; E-bombs; Eccies; Ecstacy; Ecstasy; Ecstasy Tablets; Eddie Bo; Egg Rolls; Egyptians; Ekies; Elaine; Elephants; Em; Empathy; Essence; Eve; Ex; Exiticity; Extasy; Fantasia; Fantasy; Fastin; Fizzle; Flipper; Flipping; Four leaf clover; Fuckstasy; Gaggler; Gary Ableths; Garys; Go; Googs; Green triangles; Greenies; Grey biscuits; Gum; Gurners; Gurns; GWM; Hamburger; Hamburgers; Happy drug; Happy pill; Herbal bliss; Hug drug; Hug-Drug; Huggers; Hydro; Hype; Iboga; Ice; Igloo; Illies; Jack and jills; Jellies; Jerry Garcias; Jiggas; Jills; Junnov; Khat; Kiks; Kleenex; Letter biscuits; Light meth; Lollies; Long lasting lollies; Louie Vuitton; Love-Bug; Love doctor; Love Doves; Love drug; Love drug of the '80s; Love drug of the '90s; Love Medicine; Love pill; Love potion #9; Lovers' special; Lover's speed; Lucky charmz; "M"; M25; Madman; Malcolm; Mandy; MAO; MDM; MDMA; Mercedes; Meth amps; Methedrine; Mini beans; Mitsibushis; Mitsies; Mitsu's; Mitsubishi; Mitsubishis; M&M; M&Ms; Mellow drug of America; Molly; Mollys; Monoamine oxidase; Morning shot; New Yorkers; Nineteen; Number 9; Orange bandits; Orbit; Pasti; Pillage; Pills; Pilules d'Amour; Pingers; Pink Calis; Pink panthers; Pink studs; Playboy bunnies; Playboys; Pollutants; Pressies; Rave energy; Red devils; Rhubarb & Custards; Rib; Ritual spirit; Road Runner; Roca; Roker's Barnet; Rolexes; Roll; Rolling; Rolls Royce; Running; Scooby snacks; Scum; Shabu; Skates; Slammin'; Slamming; Slits; Slows; Smartees; Smurfs; Speed for lovers; Spivias; Stars; Strawberry shortcake; Supermans; Swadger; Swans; Sweeties; Sweets; Tablets; Tabs; Tacha; Tachas; Tangos; Tens; The love drug; Thizz; Tom and Jerries; Triple crowns; Triple rolexes; Triple stacks; Tutus; Tweety Birds; Ultimate Xphoria; U.S.P.; Vitamin E; Vitamin X; Vowels; Wafers; Wee Boys; West Coast turnarounds; Wheels; Whiffledust; White diamonds; White dove; White doves; Whiz bombs; Wigits; Wingers; X; X-ing; X-Men; X-Men 2; X-Pills; XTC; Yips; Yokes; Yuppie psychedelic.

Profile

Methylenedioxymethamfetamine is a phenylethylamine compound structurally related to amfetamine and mescaline and is an analogue of tenamfetamine (p.2164). It is subject to abuse. Its toxicity is similar to that of dexamfetamine (see Abuse, below and under Dexamfetamine, p.2153) and may be treated similarly.

Abuse. Methylenedioxymethamfetamine may be ingested as tablets, capsules, or inhaled as a powder. It is often mixed with a combination of adulterants such as other amfetamines, caffeine, ephedrine, and pseudoephedrine.[1]

The toxicity associated with abuse of methylenedioxymethamfetamine has been the subject of a number of discussions.[2-7] Acute effects can be severe and symptoms have included cardiac arrhythmias, fulminant hyperthermia, convulsions, disseminated intravascular coagulation, rhabdomyolysis, and acute renal failure; fatalities may occur. Repeated use may cause hepatic damage. Psychiatric effects reported include psychosis[8-10] and depression.[9-11] Damage to central serotonergic nerves has been implicated[8-12] and hence there is some concern regarding the long-term effects of methylenedioxymethamfetamine abuse.[13,14] Hyponatraemia, inappropriate antidiuretic hormone secretion, and cerebral oedema have also been reported;[15-20] the severity may be increased by excessive fluid intake that is frequently advocated to prevent dehydration and hyperthermia.[18-22] Urinary retention has also been reported.[23]

Concern has been expressed regarding abuse during *pregnancy.* Twelve congenital malformations, including 2 cases of congenital heart disease, have been noted among 78 liveborn infants whose mothers had taken methylenedioxymethamfetamine, often with other drugs of abuse, during their pregnancies.[24]

For reviews of the properties of other phenylethylamine compounds, see under Tenamfetamine, p.2164.

1. Smith KM, *et al.* Club drugs: methylenedioxymethamphetamine, flunitrazepam, ketamine hydrochloride, and γ-hydroxybutyrate. *Am J Health-Syst Pharm* 2002; **59:** 1067–76.
2. Henry JA. Ecstasy and the dance of death. *BMJ* 1992; **305:** 5–6.
3. Henry JA, *et al.* Toxicity and deaths from 3,4-methylenedioxymethamphetamine ("ecstasy"). *Lancet* 1992; **340:** 384–7.
4. O'Connor B. Hazards associated with the recreational drug 'ecstasy'. *Br J Hosp Med* 1994; **52:** 507–14.
5. McCann UD, *et al.* Adverse reactions with 3,4-methylenedioxymethamphetamine (MDMA; 'Ecstasy'). *Drug Safety* 1996; **15:** 107–115.
6. Hall AP. Ecstasy and the anaesthetist. *Br J Anaesth* 1997; **79:** 697–8.
7. Schwartz RH, Miller NS. MDMA (ecstasy) and the rave: a review. *Pediatrics* 1997; **100:** 705–8.
8. McGuire P, Fahy T. Chronic paranoid psychosis after misuse of MDMA ("ecstasy"). *BMJ* 1991; **302:** 697.
9. Winstock AR. Chronic paranoid psychosis after misuse of MDMA. *BMJ* 1991; **302**: 1150–1.
10. Schifano F. Chronic atypical psychosis associated with MDMA ("ecstasy") abuse. *Lancet* 1991; **338:** 1335.
11. Benazzi F, Mazzoli M. Psychiatric illness associated with "ecstasy". *Lancet* 1991; **338:** 1520.
12. McCann UD, *et al.* Positron emission tomographic evidence of toxic effect of MDMA ("Ecstasy") on brain serotonin neurons in human beings. *Lancet* 1998; **352:** 1433–7.
13. Green AR, Goodwin GM. Ecstasy and neurodegeneration. *BMJ* 1996; **312:** 1493–4.
14. Bolla KI, *et al.* Memory impairment in abstinent MDMA ("Ecstasy") users. *Neurology* 1998; **51:** 1532–7.
15. Maxwell DL, *et al.* Hyponatraemia and catatonic stupor after taking "ecstasy". *BMJ* 1993; **307:** 1399.
16. Kessel B. Hyponatraemia after ingestion of "ecstasy". *BMJ* 1994; **308:** 414.
17. Satchell SC, Connaughton M. Inappropriate antidiuretic hormone secretion and extreme rises in serum creatinine kinase following MDMA ingestion. *Br J Hosp Med* 1994; **51:** 495.
18. Holden R, Jackson MA. Near-fatal hyponatraemic coma due to vasopressin over-secretion after ecstasy (3,4-MDMA). *Lancet* 1996; **347:** 1052.
19. Matthai SM, *et al.* Cerebral oedema after ingestion of MDMA (ecstasy) and unrestricted intake of water. *BMJ* 1996; **312:** 1359.
20. Parr MJA, *et al.* Hyponatraemia and death after ecstasy ingestion. *Med J Aust* 1997; **166:** 136–7.
21. Cook TM. Cerebral oedema after MDMA ('ecstasy') and unrestricted water intake. *BMJ* 1996; **313:** 689.
22. Henry JA, *et al.* Low-dose MDMA ("ecstasy") induces vasopressin secretion. *Lancet* 1998; **351:** 1784.
23. Bryden AA, *et al.* Urinary retention with misuse of 'ecstasy'. *BMJ* 1995; **310:** 504.
24. McElhatton PR, *et al.* Congenital anomalies after prenatal ecstasy exposure. *Lancet* 1999; **354:** 1441–2.

Interactions. A psychotic reaction has been reported in a patient who took methylenedioxymethamfetamine while receiving therapy with *citalopram.*[1]

A patient receiving *phenelzine* and lithium therapy experienced a serotonin syndrome (p.416) after ingesting methylenedioxymethamfetamine.[2] Symptoms included markedly increased muscle tension, tremulousness, abnormal posturing, limited pain response, tachycardia, hypertension, hyperthermia, increased white blood cell count, increased creatine phosphokinase concentration, respiratory acidosis, metabolic acidosis, delirium, and agitation. Within 15 minutes of methylenedioxymethamfetamine ingestion the patient was comatose; within 5 hours the patient was alert with a normal muscle tone. An interaction between phenelzine and methylenedioxymethamfetamine was suggested as the cause of the serotonin syndrome.

A fatal serotonergic reaction to methylenedioxymethamfetamine possibly due to an interaction with *ritonavir* has been described.[3] A prolonged and exaggerated effect from a small dose of methylenedioxymethamfetamine has been reported[4] in another patient also receiving ritonavir. Although this patient was also receiving saquinavir, the authors postulated that the mechanism may be ritonavir-induced inhibition of the cytochrome P450 isoenzyme CYP2D6.

1. Lauerma H, *et al.* Interaction of serotonin reuptake inhibitor and 3,4-methylenedioxymethamphetamine? *Biol Psychiatry* 1998; **43:** 923–8.
2. Kaskey GB. Possible interaction between an MAOI and "ecstasy". *Am J Psychiatry* 1992; **149:** 411–12.
3. Henry JA, Hill IR. Fatal interaction between ritonavir and MDMA. *Lancet* 1998; **352:** 1751–2.
4. Harrington RD, *et al.* Life-threatening interactions between HIV-1 protease inhibitors and the illicit drugs MDMA and γ-hydroxybutyrate. *Arch Intern Med* 1999; **159:** 2221–4.

Methylphenidate Hydrochloride *(BANM, rINNM)* ⊗

Hidrocloruro de metilfenidato; Methyl Phenidate Hydrochloride; Méthylphénidate, chlorhydrate de; Methylphenidati hydrochloridum; Metilfenidat Hidroklorür. Methyl α-phenyl-2-piperidylacetate hydrochloride.

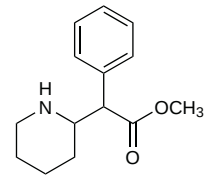
Метилфенидата Гидрохлорид

$C_{14}H_{19}NO_2$,HCl = 269.8.

CAS — 113-45-1 (methylphenidate); 298-59-9 (methylphenidate hydrochloride).

ATC — N06BA04.

ATC Vet — QN06BA04.



(methylphenidate)

NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of methylphenidate:
Rities; Vitamin R; West coast.

Pharmacopoeias. In *Chin., Swiss,* and *US.*

USP 31 (Methylphenidate Hydrochloride). A white, odourless, fine crystalline powder. Freely soluble in water and in methyl alcohol; soluble in alcohol; slightly soluble in acetone and in chloroform. Solutions are acid to litmus.

Adverse Effects, Treatment, and Precautions

As for Dexamfetamine Sulfate, p.2153. Hypersensitivity reactions have been reported. Skin reactions have included exfoliative dermatitis and erythema multiforme. Purpura, thrombocytopenia, and leucopenia have occurred. Blood counts should be monitored periodically during prolonged therapy.

◊ References.

1. Ahmann PA, *et al.* Placebo-controlled evaluation of Ritalin side effects. *Pediatrics* 1993; **91:** 1101–6.
2. Efron D, *et al.* Side effects of methylphenidate and dexamphetamine in children with attention deficit hyperactivity disorder: a double-blind, crossover trial. *Pediatrics* 1997; **100:** 662–6.
3. Rappley MD. Safety issues in the use of methylphenidate: an American perspective. *Drug Safety* 1997; **17:** 143–8.
4. Klein-Schwartz W. Abuse and toxicity of methylphenidate. *Curr Opin Pediatr* 2002; **14:** 219–23.
5. Leonard BE, *et al.* Methylphenidate: a review of its neuropharmacological, neuropsychological and adverse clinical effects. *Hum Psychopharmacol* 2004; **19:** 151–80.

Abuse. Reports of adverse effects after the abuse of methylphenidate by injecting solutions of crushed tablets.[1-3] Intravenous abuse of methylphenidate with pentazocine has also been reported.[4,5] In addition, there are also reports of intranasal methylphenidate abuse,[6-8] including fatalities.[8]

See also Effects on the Liver, below.

1. Wolf J, *et al.* Eosinophilic syndrome with methylphenidate abuse. *Ann Intern Med* 1978; **89:** 224–5.
2. Gunby P. Methylphenidate abuse produces retinopathy. *JAMA* 1979; **241:** 546.
3. Parran TV, Jasinski DR. Intravenous methylphenidate abuse: prototype for prescription drug abuse. *Arch Intern Med* 1991; **151:** 781–3.
4. Debooy VD, *et al.* Intravenous pentazocine and methylphenidate abuse during pregnancy: maternal lifestyle and infant outcome. *Am J Dis Child* 1993; **147:** 1062–5.
5. Carter HS, Watson WA. IV pentazocine/methylphenidate abuse—the clinical toxicity of another Ts and blues combination. *J Toxicol Clin Toxicol* 1994; **32:** 541–7.
6. Jaffe SL. Intranasal abuse of prescribed methylphenidate by an alcohol and drug abusing adolescent with ADHD. *J Am Acad Child Adolesc Psychiatry* 1991; **30:** 773–5.
7. Garland EJ. Intranasal abuse of prescribed methylphenidate. *J Am Acad Child Adolesc Psychiatry* 1998; **37:** 573–4.
8. Massello W, Carpenter DA. A fatality due to the intranasal abuse of methylphenidate (Ritalin). *J Forensic Sci* 1999; **44:** 220–1.

Breast feeding. No adverse effects were noted[1] in a 6-month-old breast-fed infant whose 26-year-old mother had been taking methylphenidate 40 mg twice daily for about 5 weeks. Despite the relatively high milk-to-plasma ratio of 2.7 the relative infant dose was low, at 0.2% of the maternal dose. Nonetheless the authors recommended caution when giving methylphenidate to breast-feeding mothers. Licensed product information also recommends that methylphenidate should be used with caution or avoided during breast feeding.

1. Hackett LP, *et al.* Methylphenidate and breast-feeding. *Ann Pharmacother* 2006; **40:** 1890–1.

Effects on the cardiovascular system. For mention of the adverse cardiovascular effects of stimulants, see under Dexamfetamine Sulfate, p.2153.

Effects on growth. Concern has been expressed about the effects of central stimulants such as methylphenidate on growth rate when used to treat hyperactivity in children. One study showed that methylphenidate produced decreases in weight percentiles after 1 year of therapy and progressive decrement in height percentiles that became significant after 2 years of use.[1] However, another suggested that moderate doses might have a lower risk for long-term height suppression than dexamfetamine.[2] There has also been a study which showed that, even when methylphenidate had an adverse effect on growth rate during active treatment, final height was not compromised and that a compensatory rebound of growth appeared to occur on stopping stimulant treatment.[3]

See also under Dexamfetamine Sulfate, p.2153.

1. Mattes JA, Gittelman R. Growth of hyperactive children on maintenance regimen of methylphenidate. *Arch Gen Psychiatry* 1983; **40:** 317–21.