[Template:Distinguish2](/wiki/Template:Distinguish2" \o "Template:Distinguish2) [Template:Pp-vandalism](/wiki/Template:Pp-vandalism) [Template:Use dmy dates](/wiki/Template:Use_dmy_dates) [Template:Drugbox](/wiki/Template:Drugbox) **3,4-Methylenedioxymethamphetamine (MDMA)**,[Template:#tag:ref](/wiki/Template:#tag:ref) commonly known as **ecstasy** (**E**), is a [psychoactive drug](/wiki/Psychoactive_drug) used primarily as a [recreational drug](/wiki/Recreational_drug_use). Desired effects of MDMA include increased [empathy](/wiki/Empathy), [euphoria](/wiki/Euphoria), and heightened sensations.[[1]](#cite_note-1)<ref name=Drugs2014/> When taken by mouth, effects begin after 30–45 minutes and last 3–6 hours.<ref name=Freye2009>[Template:Cite book](/wiki/Template:Cite_book)</ref><ref name=NIH2016/> It is also sometimes [snorted](/wiki/Snorted) or smoked.<ref name=Drugs2014>[Template:Cite web](/wiki/Template:Cite_web)</ref> [Template:As of](/wiki/Template:As_of), MDMA has no accepted medical uses.[[2]](#cite_note-2) Adverse effects of MDMA use include [addiction](/wiki/Addiction), memory problems, [paranoia](/wiki/Paranoia), difficulty sleeping, [teeth grinding](/wiki/Bruxism), blurred vision, sweating, and a [rapid heartbeat](/wiki/Tachycardia). Use may also lead to depression and fatigue. Deaths have been reported due to increased body temperature and dehydration.<ref name=Drugs2014/> MDMA [increases the release](/wiki/Serotonin-norepinephrine-dopamine_releasing_agent) and [slows the reuptake](/wiki/Serotonin–norepinephrine–dopamine_reuptake_inhibitor) of the [neurotransmitters](/wiki/Neurotransmitters) [serotonin](/wiki/Serotonin), [dopamine](/wiki/Dopamine), and [norepinephrine](/wiki/Norepinephrine) in parts of the brain. It has [stimulant](/wiki/Stimulant) and [psychedelic](/wiki/Psychedelic_drug) effects.<ref name=palmer/><ref name=nhtsa>[Template:Citation](/wiki/Template:Citation)</ref> The initial increase is followed by a short-term decrease in the neurotransmitters.<ref name=Drugs2014/><ref name=NIH2016>[Template:Cite web](/wiki/Template:Cite_web)</ref> MDMA belongs to the [substituted methylenedioxyphenethylamine](/wiki/Substituted_methylenedioxyphenethylamine) and [substituted amphetamine](/wiki/Substituted_amphetamine) [classes of drugs](/wiki/Chemical_classification).

MDMA was first made in 1912.<ref name=Drugs2014/> It was used to improve [psychotherapy](/wiki/Psychotherapy) beginning in the 1970s and became popular as a street drug in the 1980s.<ref name=Drugs2014/><ref name=NIH2016/>[[3]](#cite_note-3) MDMA is commonly associated with [dance parties](/wiki/Dance_party), [raves](/wiki/Rave_party), and [electronic dance music](/wiki/Electronic_dance_music).<ref name=WHO2004>[Template:Cite book](/wiki/Template:Cite_book)</ref> It is often sold mixed with other substances such as [ephedrine](/wiki/Ephedrine), [amphetamine](/wiki/Amphetamine), and [methamphetamine](/wiki/Methamphetamine).<ref name=Drugs2014/> In 2013, between 9 and 28 million people between the ages of 15 and 65 used ecstasy (0.2% to 0.6% of the world population). This was broadly similar to the percentage of people who use [cocaine](/wiki/Cocaine), [amphetamines](/wiki/Substituted_amphetamine), and [opioids](/wiki/Opioid), but fewer than for [cannabis](/wiki/Cannabis_(drug)).[[4]](#cite_note-4) In the United States, about 0.9 million people used ecstasy in 2010.<ref name=Drugs2014/>

MDMA is generally illegal in most countries. Limited exceptions are sometimes made for research. Researchers are investigating whether a few low doses of MDMA may assist in treating severe, treatment-resistant [posttraumatic stress disorder](/wiki/Posttraumatic_stress_disorder) (PTSD).<ref name=Current2013>[Template:Cite journal](/wiki/Template:Cite_journal)</ref><ref name=Pharm2014>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> More research is needed to determine if its usefulness outweighs the risk of harm.<ref name=Current2013/><ref name=Pharm2014/> [Template:TOC limit](/wiki/Template:TOC_limit)

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### Medical[[edit](/index.php?title=(none)&action=edit&section=2)]

[Template:See also](/wiki/Template:See_also) [Template:As of](/wiki/Template:As_of), MDMA has no accepted [medical indications](/wiki/Medical_indication).[[2]](#cite_note-2)[[5]](#cite_note-5) Before it was widely banned, it saw limited use in therapy.[[2]](#cite_note-2)[[6]](#cite_note-6)

### Alternative medicine[[edit](/index.php?title=(none)&action=edit&section=3)]

A small number of therapists continue to use MDMA in therapy despite its illegal status.[[7]](#cite_note-7)<ref name=Zarembo/>

### Recreational[[edit](/index.php?title=(none)&action=edit&section=4)]

MDMA is often considered the drug of choice within the [rave](/wiki/Rave) culture and is also used at clubs, festivals and [house parties](/wiki/House_party).[[8]](#cite_note-8) In the rave environment, the sensory effects from the music and lighting are often highly synergistic with the drug. The psychedelic amphetamine quality of MDMA offers multiple reasons for its appeal to users in the rave setting. Some users enjoy the feeling of mass communion from the inhibition-reducing effects of the drug, while others use it as party fuel because of the drug's stimulatory effects.[[9]](#cite_note-9) MDMA is sometimes taken in conjunction with other psychoactive drugs, such as [LSD](/wiki/LSD), [psilocybin mushrooms](/wiki/Psilocybin_mushroom), and [ketamine](/wiki/Ketamine). Users sometimes use [mentholated](/wiki/Menthol) products while taking MDMA for its cooling sensation.[[10]](#cite_note-10)

### Forms[[edit](/index.php?title=(none)&action=edit&section=5)]

[Template:Multiple image](/wiki/Template:Multiple_image) MDMA has become widely known as ecstasy (shortened "E", "X", or "XTC"), usually referring to its tablet form, although this term may also include the presence of possible [adulterants](/wiki/Adulterant) or dilutants. The UK term "mandy" and the US term "molly" colloquially refer to MDMA in a crystalline powder form that is thought to be free of adulterants.[[11]](#cite_note-11)<ref name=DrugFacts>[Template:Cite web](/wiki/Template:Cite_web)</ref>[[12]](#cite_note-12) However, in part due to the global supply shortage of [sassafras oil](/wiki/Sassafras_oil), substances that are sold as molly frequently contain no MDMA and instead contain [methylone](/wiki/Methylone), [ethylone](/wiki/Ethylone), [MDPV](/wiki/MDPV), [mephedrone](/wiki/Mephedrone), or any other of the group of compounds commonly known as [bath salts](/wiki/Bath_salts_(drug)).[[13]](#cite_note-13)[[12]](#cite_note-12)[[14]](#cite_note-14)[[15]](#cite_note-15) Powdered MDMA is typically 30–40% pure, due to bulking agents that are added to dilute the drug and increase profits (e.g., lactose) and binding agents.[[2]](#cite_note-2) Tablets sold as ecstasy sometimes only contain [3,4-methylenedioxyamphetamine](/wiki/3,4-methylenedioxyamphetamine) (MDA) instead of MDMA;[[16]](#cite_note-16)[[2]](#cite_note-2) the proportion of seized ecstasy tablets with MDMA-like impurities has varied annually and by country.[[2]](#cite_note-2) MDMA is also sold in the form of the hydrochloride salt, either as loose crystals or in [gelcaps](/wiki/Capsule_(pharmacy)).[[14]](#cite_note-14)[[15]](#cite_note-15)

## Effects[[edit](/index.php?title=(none)&action=edit&section=6)]

In general, MDMA users begin reporting subjective effects within 30 to 60 minutes of consumption, reaching the peak at about 75 to 120 minutes which plateaus for about 3.5 hours.[[17]](#cite_note-17) The desired short-term psychoactive effects of MDMA have been reported to include:

* [Euphoria](/wiki/Euphoria) – a sense of general [well-being](/wiki/Well-being) and happiness[[1]](#cite_note-1)\* Increased sociability and feelings of communication being easy or simple[[18]](#cite_note-18)[[1]](#cite_note-1)\* [Entactogenic](/wiki/Entactogen) effects – increased [empathy](/wiki/Empathy) or feelings of closeness with others[[18]](#cite_note-18)[[1]](#cite_note-1)\* A sense of inner peace[[1]](#cite_note-1)\* Mild hallucination[[1]](#cite_note-1)\* Enhanced sensation, perception, or sexuality[[18]](#cite_note-18)[[1]](#cite_note-1)\* Altered sense of time<ref name=NIH2016/>

## Adverse effects[[edit](/index.php?title=(none)&action=edit&section=7)]

### Short-term[[edit](/index.php?title=(none)&action=edit&section=8)]

The most serious short-term physical health risks of MDMA are [hyperthermia](/wiki/Hyperthermia) and [dehydration](/wiki/Dehydration).[[1]](#cite_note-1)[[19]](#cite_note-19) Cases of life-threatening or fatal [hyponatremia](/wiki/Hyponatremia) (excessively low sodium concentration in the blood) have developed in MDMA users attempting to prevent dehydration by consuming excessive amounts of water without replenishing [electrolytes](/wiki/Electrolytes).[[1]](#cite_note-1)[[19]](#cite_note-19)[[20]](#cite_note-20) The immediate adverse effects of MDMA use can include: [Template:Multicol-begin](/wiki/Template:Multicol-begin)

* [Dehydration](/wiki/Dehydration)[[8]](#cite_note-8)[[1]](#cite_note-1)[[19]](#cite_note-19)\* [Hyperthermia](/wiki/Hyperthermia)[[8]](#cite_note-8)[[1]](#cite_note-1)[[19]](#cite_note-19)\* [Bruxism](/wiki/Bruxism) (grinding and clenching of the teeth)[[8]](#cite_note-8)[[18]](#cite_note-18)[[1]](#cite_note-1)\* Increased wakefulness or [insomnia](/wiki/Insomnia)[[1]](#cite_note-1)\* Increased perspiration and sweating[[1]](#cite_note-1)[[19]](#cite_note-19)\* Increased [heart rate](/wiki/Heart_rate) and [blood pressure](/wiki/Blood_pressure)[[8]](#cite_note-8)[[1]](#cite_note-1)[[19]](#cite_note-19)[Template:Multicol-break](/wiki/Template:Multicol-break)
* Loss of [appetite](/wiki/Appetite)[[16]](#cite_note-16)\* Nausea and vomiting[[18]](#cite_note-18)\* [Diarrhea](/wiki/Diarrhea)[[1]](#cite_note-1)\* [Erectile dysfunction](/wiki/Erectile_dysfunction)[[21]](#cite_note-21)\* [Mydriasis](/wiki/Mydriasis)<ref name=pmid15228154/>

[Template:Multicol-end](/wiki/Template:Multicol-end)

### Intermediate-term[[edit](/index.php?title=(none)&action=edit&section=9)]

The adverse effects that last up to a week[[18]](#cite_note-18)[[22]](#cite_note-22) following cessation of moderate MDMA use include: {|table |- style="border-spacing: 2px; border: 0px solid white; vertical-align: top;" |**Physiological** | colspan="2" | **Psychological** |-style="vertical-align: top;" |

* [Trismus](/wiki/Trismus)[[18]](#cite_note-18)\* Loss of appetite[[22]](#cite_note-22)\* Insomnia[[22]](#cite_note-22)\* Tiredness or lethargy[[23]](#cite_note-23)[[24]](#cite_note-24)

|

* Anxiety or paranoia[[22]](#cite_note-22)\* Depression[[18]](#cite_note-18)[[22]](#cite_note-22)\* Irritability[[22]](#cite_note-22)\* Impulsiveness[[22]](#cite_note-22)|
* Restlessness[[22]](#cite_note-22)\* Memory impairment[[18]](#cite_note-18)\* [Anhedonia](/wiki/Anhedonia)[[22]](#cite_note-22)|}

### Long-term[[edit](/index.php?title=(none)&action=edit&section=10)]

[Template:As of](/wiki/Template:As_of), the long-term effects of MDMA on human brain structure and function have not been fully determined.[[25]](#cite_note-25) However, there is evidence of structural and functional deficits in MDMA users with a high lifetime exposure.[[25]](#cite_note-25)[[26]](#cite_note-26) In contrast, there is no evidence of structural or functional changes in MDMA users with only a moderate (<50 doses used and <100 tablets consumed) lifetime exposure.[[26]](#cite_note-26) MDMA use at high doses has been shown to produce [brain lesions](/wiki/Brain_damage), a form of brain damage, in the serotonergic neural pathways of humans and animals.[[27]](#cite_note-27)[[16]](#cite_note-16) It is unclear if typical MDMA users may develop neurotoxic brain lesions.[[28]](#cite_note-28) In addition, long-term exposure to MDMA in humans has been shown to produce marked [neurotoxicity](/wiki/Neurotoxicity) in [striatal](/wiki/Striatal), [hippocampal](/wiki/Hippocampal), [prefrontal](/wiki/Prefrontal_cortex), and [occipital](/wiki/Occipital_cortex) serotonergic [axon terminals](/wiki/Axon_terminal).[[25]](#cite_note-25)[[29]](#cite_note-29) Neurotoxic damage to axon terminals has been shown to persist for more than two years.[[29]](#cite_note-29) Brain temperature during MDMA use is positively correlated with MDMA-induced neurotoxicity.[[8]](#cite_note-8)[[25]](#cite_note-25) Adverse [neuroplastic](/wiki/Neuroplastic) changes to brain [microvasculature](/wiki/Microvasculature) and [white matter](/wiki/White_matter) also occur in humans using low doses of MDMA.[[8]](#cite_note-8)[[25]](#cite_note-25) Reduced [gray matter](/wiki/Gray_matter) density in certain brain structures has also been noted in human MDMA users.[[8]](#cite_note-8)[[25]](#cite_note-25) The effects established so far for recreational use of ecstasy lie in the range of moderate to large effects for SERT reduction.[[30]](#cite_note-30) MDMA also produces persistent cognitive impairments in humans.[[18]](#cite_note-18)[[31]](#cite_note-31)[[25]](#cite_note-25) Impairments in multiple aspects of cognition, including memory, visual processing, and sleep have been noted in humans;[[18]](#cite_note-18)[[31]](#cite_note-31)[[25]](#cite_note-25) the magnitude of these impairments is correlated with lifetime MDMA usage.[[18]](#cite_note-18)[[31]](#cite_note-31)[[25]](#cite_note-25) Memory is impacted by ecstasy use, which is associated with impairments in several forms of memory.[[18]](#cite_note-18)[[31]](#cite_note-31) Some studies indicate repeated recreational users of ecstasy have increased rates of depression and anxiety, even after quitting the drug.[[32]](#cite_note-32)[[33]](#cite_note-33)[[34]](#cite_note-34) However, these effects are typically considered small.[[35]](#cite_note-35)[[36]](#cite_note-36) At high doses, MDMA induces a [neuroimmune response](/wiki/Neuroimmune_system) which, through several mechanisms, increases the permeability of the [blood-brain barrier](/wiki/Blood-brain_barrier), thereby making the brain more susceptible to environmental toxins and [pathogens](/wiki/Pathogen).[[37]](#cite_note-37)[[38]](#cite_note-38)[Template:Page needed](/wiki/Template:Page_needed) In addition, MDMA has [immunosuppressive](/wiki/Immunosuppressive) effects in the [peripheral nervous system](/wiki/Peripheral_nervous_system) and pro-inflammatory effects in the [central nervous system](/wiki/Central_nervous_system).[[39]](#cite_note-39)

### During pregnancy[[edit](/index.php?title=(none)&action=edit&section=11)]

MDMA is a moderately [teratogenic drug](/wiki/Teratogenic_drug) (i.e., it is toxic to the fetus).<ref name=vorhees>[Template:Citation](/wiki/Template:Citation)</ref><ref name=meamar>[Template:Citation](/wiki/Template:Citation)</ref> [In utero](/wiki/In_utero) exposure to MDMA is associated with a [neuro](/wiki/Neurotoxicity)- and [cardiotoxicity](/wiki/Cardiotoxicity)<ref name=meamar/> and impaired motor functioning. Motor delays may be temporary during infancy or long-term. The severity of these developmental delays increases with heavier MDMA use.[[31]](#cite_note-31)<ref name=singer>[Template:Citation](/wiki/Template:Citation)</ref>

### Reinforcement disorders[[edit](/index.php?title=(none)&action=edit&section=12)]

[thumb|400px|In a 2011 survey of 292 clinical experts in Scotland, MDMA ranked 13th in personal harm and 16th in social harm out of 19 common recreational drugs.](/wiki/File:2011_Drug_Harms_Rankings.svg)[[40]](#cite_note-40) Approximately 60% of MDMA users experience [withdrawal](/wiki/Drug_withdrawal) symptoms when they stop taking MDMA.[[16]](#cite_note-16) Some of these symptoms include fatigue, loss of appetite, depression, and trouble concentrating.[[16]](#cite_note-16) [Tolerance](/wiki/Drug_tolerance) to some of the desired and adverse effects of MDMA is expected to occur with consistent MDMA use.[[16]](#cite_note-16) MDMA has been shown to induce [ΔFosB](/wiki/ΔFosB) in the [nucleus accumbens](/wiki/Nucleus_accumbens).[[41]](#cite_note-41) Since MDMA releases dopamine in the [striatum](/wiki/Striatum), the mechanisms by which it induces ΔFosB in the nucleus accumbens are analogous to other dopaminergic psychostimulants.[[41]](#cite_note-41)[[42]](#cite_note-42) Therefore, chronic use of MDMA at high doses can result in [altered brain structure](/wiki/Neuroplasticity) and [drug addiction](/wiki/Drug_addiction), which occur as a consequence of ΔFosB overexpression in the nucleus accumbens.[[42]](#cite_note-42)

### Harm assessment[[edit](/index.php?title=(none)&action=edit&section=13)]

Researchers such as [David Nutt](/wiki/David_Nutt) disagree with the legal categorization of MDMA with other more harmful drugs,[[43]](#cite_note-43) especially when compared to alcohol which ranked as the most harmful drug using a multicriteria approach.[[44]](#cite_note-44)[[45]](#cite_note-45) A 2010 UK study which took into account impairment of cognitive functioning placed MDMA at number 17 out of 20 recreational drugs.[[46]](#cite_note-46) In a 2011 survey of 292 clinical experts in Scotland, MDMA ranked 13th in personal harm and 16th in social harm out of 19 common recreational drugs.[[40]](#cite_note-40)[Template:Clear](/wiki/Template:Clear)

## Overdose[[edit](/index.php?title=(none)&action=edit&section=14)]

MDMA overdose symptoms vary widely due to the involvement of multiple organ systems. Some of the more overt overdose symptoms are listed in the table below.

|  |  |  |
| --- | --- | --- |
| Symptoms of overdose | | |
| **System** | **Minor or moderate overdose<ref name=pmid15228154/>** | **Severe overdose<ref name=pmid15228154/>** |
| [**Cardiovascular**](/wiki/Cardiovascular_system) |  | \* [Disseminated intravascular coagulation](/wiki/Disseminated_intravascular_coagulation)[[1]](#cite_note-1)\* [Intracranial hemorrhage](/wiki/Intracranial_hemorrhage)[[1]](#cite_note-1)\* Severe [hypertension](/wiki/Hypertension)[[1]](#cite_note-1)<ref name=oxford/> or [hypotension](/wiki/Hypotension)[[1]](#cite_note-1) |
| [**Central nervous system**](/wiki/Central_nervous_system) | \* [Abnormally fast reflexes](/wiki/Hyperreflexia)[[47]](#cite_note-47)\* [Agitation](/wiki/Agitation_(action))[[1]](#cite_note-1)<ref name=oxford/> \* [Mental confusion](/wiki/Mental_confusion)[[1]](#cite_note-1)\* [Paranoia](/wiki/Paranoia)[[1]](#cite_note-1)<ref name=oxford/> \* [Stimulant psychosis](/wiki/Stimulant_psychosis)[[8]](#cite_note-8) | \* [Cognitive and memory impairment](/wiki/Cognitive_deficit)[[1]](#cite_note-1) potentially to the point of [retrograde](/wiki/Retrograde_amnesia) or [anterograde amnesia](/wiki/Anterograde_amnesia)[[48]](#cite_note-48)\* Coma[[8]](#cite_note-8)<ref name=oxford>John; Gunn, Scott; Singer, Mervyn; Webb, Andrew Kellum. Oxford American Handbook of Critical Care. Oxford University Press (2007). ASIN: B002BJ4V1C. Page 464.</ref> \* [Convulsions](/wiki/Convulsion)[[1]](#cite_note-1)<ref name=oxford/> \* [Hallucinations](/wiki/Hallucination)[[1]](#cite_note-1)<ref name=oxford/> \* [Loss of consciousness](/wiki/Loss_of_consciousness)[[8]](#cite_note-8)\* [Serotonin syndrome](/wiki/Serotonin_syndrome)[[8]](#cite_note-8)[[1]](#cite_note-1)[[20]](#cite_note-20) |
| [**Musculoskeletal**](/wiki/Musculoskeletal_system) |  | \* Muscle rigidity[[1]](#cite_note-1)\* [Rhabdomyolysis](/wiki/Rhabdomyolysis) (i.e., rapid muscle breakdown)[[1]](#cite_note-1)[[20]](#cite_note-20) |
| [**Respiratory**](/wiki/Respiratory_system) |  | \* [Acute respiratory distress syndrome](/wiki/Acute_respiratory_distress_syndrome)[[1]](#cite_note-1) |
| [**Urinary**](/wiki/Urogenital_system) |  | \* [Renal failure](/wiki/Renal_failure)[[1]](#cite_note-1) |
| **Other** |  | \* [Cerebral edema](/wiki/Cerebral_edema)[[8]](#cite_note-8)\* [Hepatitis](/wiki/Hepatitis)[[1]](#cite_note-1)[[20]](#cite_note-20)\* [Hyperpyrexia](/wiki/Hyperpyrexia) (a life-threatening elevation of body temperature)[[1]](#cite_note-1)[[20]](#cite_note-20)\* [Hyponatremia](/wiki/Hyponatremia) ([Syndrome of inappropriate antidiuretic hormone](/wiki/Syndrome_of_inappropriate_antidiuretic_hormone))[[1]](#cite_note-1)[[19]](#cite_note-19)[[20]](#cite_note-20) |

## Interactions[[edit](/index.php?title=(none)&action=edit&section=15)]

A number of [drug interactions](/wiki/Drug_interactions) can occur between MDMA and other drugs, including [serotonergic](/wiki/Serotonergic) drugs.[[16]](#cite_note-16)[[49]](#cite_note-49) MDMA also interacts with drugs which inhibit [CYP450](/wiki/CYP450) enzymes, like [ritonavir](/wiki/Ritonavir) (Norvir), particularly [CYP2D6](/wiki/CYP2D6) inhibitors.[[16]](#cite_note-16) Concurrent use of MDMA with another serotonergic drug can result in a life-threatening condition called [serotonin syndrome](/wiki/Serotonin_syndrome).[[16]](#cite_note-16) Severe overdose resulting in death has also been reported in people who took MDMA in combination with certain [monoamine oxidase inhibitors](/wiki/Monoamine_oxidase_inhibitor),[[16]](#cite_note-16) such as [phenelzine](/wiki/Phenelzine) (Nardil), [tranylcypromine](/wiki/Tranylcypromine) (Parnate), or [moclobemide](/wiki/Moclobemide) (Aurorix, Manerix).[[50]](#cite_note-50)

## Pharmacology[[edit](/index.php?title=(none)&action=edit&section=16)]

### Pharmacodynamics[[edit](/index.php?title=(none)&action=edit&section=17)]

[Template:Multiple image](/wiki/Template:Multiple_image)

MDMA acts primarily as a presynaptic [releasing agent](/wiki/Releasing_agent) of [serotonin](/wiki/Serotonin), [norepinephrine](/wiki/Norepinephrine), and [dopamine](/wiki/Dopamine), which arises from its activity at [trace amine-associated receptor 1](/wiki/TAAR1) (TAAR1) and [vesicular monoamine transporter 2](/wiki/Vesicular_monoamine_transporter_2) (VMAT2).[[16]](#cite_note-16)[[51]](#cite_note-51)[[52]](#cite_note-52) MDMA is a [monoamine transporter](/wiki/Monoamine_transporter) substrate (i.e., a substrate for [DAT](/wiki/Dopamine_transporter), [NET](/wiki/Norepinephrine_transporter), and [SERT](/wiki/Serotonin_transporter)), so it enters [monoamine](/wiki/Monoamine) neurons via these neuronal [membrane transport proteins](/wiki/Membrane_transport_protein);[[51]](#cite_note-51) by acting as a [monoamine transporter](/wiki/Monoamine_transporter) substrate, MDMA produces competitive [reuptake inhibition](/wiki/Reuptake_inhibition) at the neuronal membrane transporters (i.e., it competes with endogenous monoamines for [reuptake](/wiki/Reuptake)).[[51]](#cite_note-51)[[53]](#cite_note-53) MDMA inhibits both [vesicular monoamine transporters](/wiki/Vesicular_monoamine_transporter) (VMATs), the second of which ([VMAT2](/wiki/VMAT2)) is highly expressed within monoamine neurons at [vesicular membranes](/wiki/Synaptic_vesicle).[[52]](#cite_note-52) Once inside a monoamine neuron, MDMA acts as a VMAT2 inhibitor and a [TAAR1 agonist](/wiki/TAAR1_agonist).[[51]](#cite_note-51)[[52]](#cite_note-52) Inhibition of [VMAT2](/wiki/VMAT2) by MDMA results in increased concentrations of the associated neurotransmitter (serotonin, norepinephrine, or dopamine) in the [cytosol](/wiki/Cytosol) of a monoamine neuron.[[52]](#cite_note-52)[[54]](#cite_note-54) Activation of TAAR1 by MDMA triggers [protein kinase A](/wiki/Protein_kinase_A) and [protein kinase C](/wiki/Protein_kinase_C) signaling events which then [phosphorylates](/wiki/Phosphorylation) the associated monoamine transporters – DAT, NET, or SERT – of the neuron.[[51]](#cite_note-51) In turn, these phosphorylated monoamine transporters either [reverse transport direction](/wiki/Transporter_reversal) – i.e., move neurotransmitters from the [cytosol](/wiki/Cytosol) to the [synaptic cleft](/wiki/Synaptic_cleft) – or [withdraw into the neuron](/wiki/Endocytosis), respectively producing neurotransmitter efflux and noncompetitive [reuptake inhibition](/wiki/Reuptake_inhibition) at the neuronal membrane transporters.[[51]](#cite_note-51) MDMA has ten times more affinity for uptake at serotonin transporters compared to dopamine and norepinephrine transporters and consequently has mainly serotonergic effects.[[55]](#cite_note-55)[Template:Rp](/wiki/Template:Rp)

In summary, MDMA enters monoamine neurons by acting as a monoamine transporter substrate.[[51]](#cite_note-51) MDMA activity at VMAT2 moves neurotransmitters out from synaptic vesicles and into the cytosol;[[52]](#cite_note-52) MDMA activity at TAAR1 moves neurotransmitters out of the cytosol and into the synaptic cleft.[[51]](#cite_note-51) MDMA also has weak agonist activity at postsynaptic serotonin receptors [5-HT1](/wiki/5-HT1_receptor) and [5-HT2 receptors](/wiki/5-HT2_receptor), and its more efficacious metabolite [MDA](/wiki/3,4-methylenedioxyamphetamine) likely augments this action.[[56]](#cite_note-56)[[57]](#cite_note-57)[[58]](#cite_note-58)[[59]](#cite_note-59) A [placebo-controlled](/wiki/Placebo-controlled) study in 15 human volunteers found 100 mg MDMA increased blood levels of oxytocin, and the amount of oxytocin increase was correlated with the subjective prosocial effects of MDMA.[[60]](#cite_note-60)(*S*)-MDMA is more effective in eliciting 5-HT, NE, and DA release, while (*D*)-MDMA is overall less effective, and more selective for 5-HT and NE release (having only a very faint efficacy on DA release).[[61]](#cite_note-61) MDMA is a ligand at both [sigma receptor](/wiki/Sigma_receptor) subtypes, though its efficacies at the receptors have not yet been elucidated.[[62]](#cite_note-62)

### Pharmacokinetics[[edit](/index.php?title=(none)&action=edit&section=18)]

[thumb|Diagram showing the sequence of MDMA metabolization.](/wiki/File:MDMA_en.pdf) MDMA reaches maximal [concentrations](/wiki/Concentration) in the [blood stream](/wiki/Blood_stream) between 1.5 and 3 hr after [ingestion](/wiki/Ingestion).[[63]](#cite_note-63) It is then slowly [metabolized](/wiki/Metabolism) and [excreted](/wiki/Excretion), with levels of MDMA and its metabolites decreasing to half their peak concentration over the next several hours.[[64]](#cite_note-64) [Metabolites](/wiki/Metabolite) of MDMA that have been identified in humans include [3,4-methylenedioxyamphetamine](/wiki/MDA_(drug)) (MDA), [4-hydroxy-3-methoxymethamphetamine](/wiki/4-hydroxy-3-methoxymethamphetamine) (HMMA), [4-hydroxy-3-methoxyamphetamine](/wiki/4-Hydroxy-3-methoxyamphetamine) (HMA), [3,4-dihydroxyamphetamine](/wiki/Alpha-Methyldopamine) (DHA) (also called alpha-methyldopamine (α-Me-DA)), [3,4-methylenedioxyphenylacetone](/wiki/MDP2P) (MDP2P), and [3,4-Methylenedioxy-N-hydroxyamphetamine](/wiki/Methylenedioxyhydroxyamphetamine) (MDOH). The contributions of these metabolites to the psychoactive and [toxic](/wiki/Toxic) effects of MDMA are an area of active research. 80% of MDMA is metabolised in the liver, and about 20% is excreted unchanged in the [urine](/wiki/Urine).[[8]](#cite_note-8) MDMA is known to be metabolized by two main [metabolic pathways](/wiki/Metabolic_pathway): (1) *O*-demethylenation followed by [catechol-*O*-methyltransferase](/wiki/Catechol-O-methyl_transferase) (COMT)-catalyzed methylation and/or glucuronide/sulfate conjugation; and (2) *N*-dealkylation, deamination, and oxidation to the corresponding [benzoic acid](/wiki/Benzoic_acid) derivatives conjugated with [glycine](/wiki/Glycine).<ref name=pmid15228154>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> The metabolism may be primarily by [cytochrome P450](/wiki/Cytochrome_P450_oxidase) (CYP450) [enzymes](/wiki/Enzyme) [CYP2D6](/wiki/CYP2D6) and [CYP3A4](/wiki/CYP3A4) and COMT. Complex, nonlinear [pharmacokinetics](/wiki/Pharmacokinetics) arise via autoinhibition of [CYP2D6](/wiki/CYP2D6) and CYP2D8, resulting in [zeroth order kinetics](/wiki/Rate_equation) at higher doses. It is thought that this can result in sustained and higher [concentrations](/wiki/Concentration) of MDMA if the user takes consecutive doses of the drug.[[65]](#cite_note-65)[Template:Npsn](/wiki/Template:Npsn)

MDMA and metabolites are primarily excreted as conjugates, such as sulfates and glucuronides.[[66]](#cite_note-66) MDMA is a [chiral](/wiki/Chirality_(chemistry)) compound and has been almost exclusively administered as a [racemate](/wiki/Racemic). However, the two enantiomers have been shown to exhibit different kinetics. The disposition of MDMA may also be stereoselective, with the S-enantiomer having a shorter elimination half-life and greater excretion than the R-enantiomer. Evidence suggests[[67]](#cite_note-67) that the area under the [blood plasma](/wiki/Blood_plasma) concentration versus time curve (AUC) was two to four times higher for the (*R*)-enantiomer than the (*S*)-enantiomer after a 40 mg oral dose in human volunteers. Likewise, the plasma half-life of (*R*)-MDMA was significantly longer than that of the (*S*)-enantiomer (5.8 ± 2.2 hours vs 3.6 ± 0.9 hours).[[16]](#cite_note-16) However, because MDMA excretion and metabolism have nonlinear kinetics,[[68]](#cite_note-68) the half-lives would be higher at more typical doses (100 mg is sometimes considered a typical dose[[63]](#cite_note-63)).

## Physical and chemical properties[[edit](/index.php?title=(none)&action=edit&section=19)]

[Template:Annotated image 4](/wiki/Template:Annotated_image_4) [Template:Multiple image](/wiki/Template:Multiple_image) MDMA is in the [substituted methylenedioxyphenethylamine](/wiki/Substituted_methylenedioxyphenethylamine) and [substituted amphetamine](/wiki/Substituted_amphetamine) [classes of chemicals](/wiki/Chemical_classification). As a [free base](/wiki/Free_base), MDMA is a colorless oil insoluble in water.[[2]](#cite_note-2) The most common salt of MDMA is the hydrochloride salt;[[2]](#cite_note-2) pure MDMA hydrochloride is water-soluble and appears as a white or off-white powder or crystal.[[2]](#cite_note-2)

### Synthesis[[edit](/index.php?title=(none)&action=edit&section=20)]

There are numerous methods available in the literature to synthesize MDMA via different intermediates.[[69]](#cite_note-69)[[70]](#cite_note-70)[[71]](#cite_note-71)[[72]](#cite_note-72) The original MDMA synthesis described in Merck's patent involves brominating safrole to 1-(3,4-methylenedioxyphenyl)-2-bromopropane and then reacting this adduct with methylamine.[[73]](#cite_note-73)[[74]](#cite_note-74) Most illicit MDMA is synthesized using [MDP2P](/wiki/MDP2P) (3,4-methylenedioxyphenyl-2-propanone) as a precursor. MDP2P in turn is generally synthesized from [piperonal](/wiki/Piperonal), [safrole](/wiki/Safrole) or [isosafrole](/wiki/Isosafrole).[[75]](#cite_note-75) One method is to [isomerize](/wiki/Isomerization) safrole to isosafrole in the presence of a strong base, and then oxidize [isosafrole](/wiki/Isosafrole) to MDP2P. Another method uses the [Wacker process](/wiki/Wacker_process) to oxidize safrole directly to the MDP2P intermediate with a [palladium](/wiki/Palladium) catalyst. Once the MDP2P intermediate has been prepared, a [reductive amination](/wiki/Reductive_amination) leads to [racemic](/wiki/Racemic) MDMA (an equal parts mixture of (*R*)-MDMA and (*S*)-MDMA).[Template:Citation needed](/wiki/Template:Citation_needed) Relatively small quantities of essential oil are required to make large amounts of MDMA. The essential oil of [*Ocotea cymbarum*](/wiki/Ocotea_cymbarum), for example, typically contains between 80 and 94% safrole. This allows 500 ml of the oil to produce between 150 and 340 grams of MDMA.[[76]](#cite_note-76) [Template:Multiple image](/wiki/Template:Multiple_image) [Template:-](/wiki/Template:-)

### Detection in body fluids[[edit](/index.php?title=(none)&action=edit&section=21)]

MDMA and MDA may be quantitated in blood, plasma or urine to monitor for use, confirm a diagnosis of poisoning or assist in the forensic investigation of a traffic or other criminal violation or a sudden death. Some drug abuse screening programs rely on hair, saliva, or sweat as specimens. Most commercial amphetamine immunoassay screening tests cross-react significantly with MDMA or its major metabolites, but chromatographic techniques can easily distinguish and separately measure each of these substances. The concentrations of MDA in the blood or urine of a person who has taken only MDMA are, in general, less than 10% those of the parent drug.[[77]](#cite_note-77)[[78]](#cite_note-78)[[79]](#cite_note-79)

## History[[edit](/index.php?title=(none)&action=edit&section=22)]

### Early research and use[[edit](/index.php?title=(none)&action=edit&section=23)]

[Template:Multiple image](/wiki/Template:Multiple_image) MDMA was first synthesized in 1912 by [Merck](/wiki/Merck_KGaA) chemist [Anton Köllisch](/wiki/Anton_Köllisch). At the time, Merck was interested in developing substances that stopped abnormal bleeding. Merck wanted to avoid an existing patent held by [Bayer](/wiki/Bayer) for one such compound: [hydrastinine](/wiki/Hydrastinine). Köllisch developed a preparation of a hydrastinine [analogue](/wiki/Chemical_analogue), methylhydrastinine, at the request of fellow lab members, Walther Beckh and Otto Wolfes. MDMA (called methylsafrylamin, safrylmethylamin or N-Methyl-a-Methylhomopiperonylamin in Merck laboratory reports) was an [intermediate compound](/wiki/Reaction_intermediate) in the synthesis of methylhydrastinine. Merck was not interested in MDMA itself at the time.[[80]](#cite_note-80) On 24 December 1912, Merck filed two patent applications that described the synthesis and some chemical properties of MDMA[[81]](#cite_note-81) and its subsequent conversion to methylhydrastinine.[[82]](#cite_note-82) Merck records indicate its researchers returned to the compound sporadically. A 1920 Merck patent describes a chemical modification to MDMA.[[83]](#cite_note-83) In 1927, Max Oberlin studied the pharmacology of MDMA while searching for substances with effects similar to [adrenaline](/wiki/Adrenaline) or [ephedrine](/wiki/Ephedrine), the latter being structurally similar to MDMA. Compared to ephedrine, Oberlin observed that it had similar effects on [vascular smooth muscle](/wiki/Vascular_smooth_muscle) tissue, stronger effects at the uterus, and no "local effect at the eye". MDMA was also found to have effects on [blood sugar](/wiki/Blood_sugar) levels comparable to high doses of ephedrine. Oberlin concluded that the effects of MDMA were not limited to the [sympathetic nervous system](/wiki/Sympathetic_nervous_system). Research was stopped "particularly due to a strong price increase of safrylmethylamine", which was still used as an intermediate in methylhydrastinine synthesis. Albert van Schoor performed simple toxicological tests with the drug in 1952, most likely while researching new stimulants or circulatory medications. After pharmacological studies, research on MDMA was not continued. In 1959, Wolfgang Fruhstorfer synthesized MDMA for pharmacological testing while researching stimulants. It is unclear if Fruhstorfer investigated the effects of MDMA in humans.[[80]](#cite_note-80) Outside of Merck, other researchers began to investigate MDMA. In 1953 and 1954, the [United States Army](/wiki/United_States_Army) commissioned a study of [toxicity](/wiki/Toxicity) and behavioral effects in animals injected with [mescaline](/wiki/Mescaline) and several analogues, including MDMA. Conducted at the [University of Michigan](/wiki/University_of_Michigan) in [Ann Arbor](/wiki/Ann_Arbor), these investigations were declassified in October 1969 and published in 1973.[[84]](#cite_note-84)<ref name=Shulgin/> A 1960 Polish paper by Biniecki and Krajewski describing the synthesis of MDMA as an intermediate was the first published scientific paper on the substance.[[80]](#cite_note-80)[[85]](#cite_note-85)[[86]](#cite_note-86) MDMA may have been in non-medical use in the western United States in 1968.[[87]](#cite_note-87) An August 1970 report at a meeting of crime laboratory chemists indicates MDMA was being used recreationally in the Chicago area by 1970.[[85]](#cite_note-85)[[88]](#cite_note-88) MDMA likely emerged as a substitute for its analog methylenedioxyamphetamine (MDA),[[89]](#cite_note-89) a drug at the time popular among users of psychedelics[[90]](#cite_note-90) which was made a Schedule 1 substance in the United States in 1970.[[91]](#cite_note-91)<ref name=exploration/>

### Shulgin's research and therapeutic use[[edit](/index.php?title=(none)&action=edit&section=24)]

[thumb|Alexander and Ann Shulgin in December 2011](/wiki/File:Shulgin_sasha_2011_hanna_jon.jpg)

American chemist and [psychopharmacologist](/wiki/Psychopharmacologist) [Alexander Shulgin](/wiki/Alexander_Shulgin) reported he synthesized MDMA in 1965 while researching methylenedioxy compounds at [Dow Chemical Company](/wiki/Dow_Chemical_Company), but did not test the psychoactivity of the compound at this time. Around 1970, Shulgin sent instructions for N-methylated MDA (MDMA) synthesis to the founder of a Los Angeles chemical company who had requested them. This individual later provided these instructions to a client in the Midwest.[[85]](#cite_note-85) Shulgin first heard of the psychoactive effects of N-methylated MDA around 1975 from a young student who reported "amphetamine-like content".[[85]](#cite_note-85) Around 30 May 1976, Shulgin again heard about the effects of N-methylated MDA,[[85]](#cite_note-85) this time from a graduate student in a medicinal chemistry group he advised at [San Francisco State University](/wiki/San_Francisco_State_University)[[90]](#cite_note-90)[[92]](#cite_note-92) who directed him to the University of Michigan study.<ref name=PiHKAL/> She and two close friends had consumed 100 mg of MDMA and reported positive emotional experiences.<ref name=Shulgin/> Following the self-trials of a colleague at the [University of San Francisco](/wiki/University_of_San_Francisco), Shulgin synthesized MDMA and tried it himself in September and October 1976.[[85]](#cite_note-85)[[90]](#cite_note-90) Shulgin first reported on MDMA in a presentation at a conference in Bethesda, Maryland in December 1976.[[85]](#cite_note-85) In 1978, he and [David E. Nichols](/wiki/David_E._Nichols) published a report on the drug's psychoactive effect in humans. They described MDMA as inducing "an easily controlled altered state of consciousness with emotional and sensual overtones" comparable "to marijuana, to [psilocybin](/wiki/Psilocybin) devoid of the hallucinatory component, or to low levels of MDA".[[93]](#cite_note-93) While not finding his own experiences with MDMA particularly powerful,[[94]](#cite_note-94) Shulgin was impressed with the drug's disinhibiting effects and thought it could be useful in therapy.[[94]](#cite_note-94) Believing MDMA allowed users to strip away habits and perceive the world clearly, Shulgin called the drug "window".[[95]](#cite_note-95) Shulgin took to occasionally using MDMA for relaxation, referring to it as "my low-calorie martini", and giving the drug to his friends, researchers, and others whom he thought could benefit from it.<ref name=PiHKAL>[Template:Cite book](/wiki/Template:Cite_book)</ref> One such person was [Leo Zeff](/wiki/Leo_Zeff), a psychotherapist who had been known to use psychedelic substances in his practice. When he tried the drug in 1977, Zeff was so impressed with the effects of MDMA that he came out of his semi-retirement to promote its use in therapy. Over the following years, Zeff traveled around the US and occasionally to Europe, eventually training an estimated four thousand psychotherapists in the therapeutic use of MDMA.[[94]](#cite_note-94)[[96]](#cite_note-96) Zeff named the drug "**Adam**", believing it put users in a state of primordial innocence.[[90]](#cite_note-90) Psychotherapists who used MDMA believed the drug eliminated the typical fear response and increased communication. Sessions were usually held in the home of the patient or the therapist. The role therapist was minimized in favor of patient self-discovery accompanied by MDMA induced feelings of empathy. Depression, substance abuse, relationship problems, premenstrual syndrome, and autism were among several psychiatric disorders MDMA assisted therapy was reported to treat.<ref name=exploration/> According to psychiatrist George Greer, therapists who used MDMA in their practice were impressed by the results. Anecdotally, MDMA was said to greatly accelerate therapy.[[94]](#cite_note-94)

### Rising recreational use[[edit](/index.php?title=(none)&action=edit&section=25)]

In the late seventies and early eighties, "Adam" spread through personal networks of psychotherapists, psychiatrists, users of psychedelics, and [yuppies](/wiki/Yuppies). Hoping MDMA could avoid criminalization like LSD and mescaline, psychotherapists and experimenters attempted to limit the spread of MDMA and information about it while conducting informal research.[[97]](#cite_note-97)<ref name=Eisner/> Early MDMA distributors were deterred from large scale operations by the threat of possible legislation.[[98]](#cite_note-98) Between the 1970s and the mid-1980s, this network of MDMA users consumed an estimated 500,000 doses.[[99]](#cite_note-99) A small recreational market for MDMA developed by the late 1970s,[[100]](#cite_note-100) consuming perhaps 10,000 doses in 1976.[[91]](#cite_note-91) By the early 1980s MDMA was being used in Boston and New York City nightclubs such as [Studio 54](/wiki/Studio_54) and [Paradise Garage](/wiki/Paradise_Garage).[[101]](#cite_note-101)[[102]](#cite_note-102) Into the early 1980s, as the recreational market slowly expanded, production of MDMA was dominated by a small group of therapeutically minded [Boston](/wiki/Boston) chemists. Having commenced production in 1976, this "Boston Group" did not keep up with growing demand and shortages frequently occurred.[[98]](#cite_note-98) Perceiving a business opportunity, Michael Clegg, the Southwest distributor for the Boston Group, started his own "Texas Group" backed financially by Texas friends.[[98]](#cite_note-98)[[103]](#cite_note-103) In 1981,[[98]](#cite_note-98) Clegg had coined "Ecstasy" as a slang term for MDMA to increase its marketability.<ref name=rising/><ref name=Eisner>[Template:Cite book](/wiki/Template:Cite_book)</ref> Starting in 1983,[[98]](#cite_note-98) the Texas Group mass-produced MDMA in a Texas lab<ref name=Eisner/> or imported it from California[[95]](#cite_note-95) and marketed tablets using pyramid sales structures and toll-free numbers.[[99]](#cite_note-99) MDMA could be purchased via credit card and taxes were paid on sales.[[98]](#cite_note-98) Under the brand name "Sassyfras", MDMA tablets were sold in brown bottles.<ref name=Eisner/> The Texas Group advertised "Ecstasy parties" at bars and discos, describing MDMA as a "fun drug" and "good to dance to".[[98]](#cite_note-98) MDMA was openly distributed in [Austin](/wiki/Austin) and [Dallas-Fort Worth](/wiki/Dallas-Fort_Worth) area bars and nightclubs, becoming popular with yuppies, college students, and gays.[[89]](#cite_note-89)[[98]](#cite_note-98)[[99]](#cite_note-99) Recreational use also increased after several cocaine dealers switched to distributing MDMA following experiences with the drug.[[99]](#cite_note-99) A California laboratory that analyzed confidentially submitted drug samples first detected MDMA in 1975. Over the following years the number of MDMA samples increased, eventually exceeding the number of MDA samples in the early 1980s.[[104]](#cite_note-104)[[105]](#cite_note-105) By the mid-1980s, MDMA use had spread to colleges around the United States.[[98]](#cite_note-98)[Template:Rp](/wiki/Template:Rp)

### Media attention and scheduling[[edit](/index.php?title=(none)&action=edit&section=26)]

#### United Kingdom[[edit](/index.php?title=(none)&action=edit&section=27)]

In the United Kingdom, MDMA was made illegal in 1977 by a modification order to the existing [Misuse of Drugs Act 1971](/wiki/Misuse_of_Drugs_Act_1971). Although MDMA was not named explicitly in this legislation, the order extended the definition of Class A drugs to include various ring-substituted phenethylamines.[[106]](#cite_note-106)[[107]](#cite_note-107)

#### United States[[edit](/index.php?title=(none)&action=edit&section=28)]

[thumb|27 July 1984 Federal Register notice of the proposed MDMA scheduling](/wiki/File:Federal_Register_notice_of_planned_MDMA_scheduling.pdf)

In an early media report on MDMA published in 1982, a [Drug Enforcement Administration](/wiki/Drug_Enforcement_Administration) (DEA) spokesman stated the agency would ban the drug if enough evidence for abuse could be found.[[98]](#cite_note-98) By mid-1984, MDMA use was becoming more noticed. Bill Mandel reported on "Adam" in a 10 June [San Francisco Chronicle](/wiki/San_Francisco_Chronicle) article, but misidentified the drug as [methyloxymethylenedioxyamphetamine](/wiki/MMDA_(drug)) (MMDA). In the next month, the World Health Organization identified MDMA as the only substance out of twenty phenethylamines to be seized a significant number of times.[[108]](#cite_note-108) After a year of planning and data collection, MDMA was proposed for [scheduling](/wiki/Controlled_Substances_Act) by the DEA on 27 July 1984 with a request for comments and objections.<ref name=Eisner/>[[109]](#cite_note-109) The DEA was surprised when a number of psychiatrists, psychotherapists, and researchers objected to the proposed scheduling and requested a hearing.[[97]](#cite_note-97) In a [Newsweek](/wiki/Newsweek) article published the next year, a DEA pharmacologist stated that the agency had been unaware of its use among psychiatrists.[[110]](#cite_note-110) An initial hearing was held on 1 February 1985 at the DEA offices in Washington, D.C. with administrative law judge Francis L. Young presiding.<ref name=Eisner/> It was decided there to hold three more hearings that year: Los Angeles on 10 June, Kansas City, Missouri on 10–11 July, and Washington, D.C. on 8–11 October.<ref name=exploration/><ref name=Eisner/>

Sensational media attention was given to the proposed criminalization and the reaction of MDMA proponents, effectively advertising the drug.<ref name=exploration/> In response to the proposed scheduling, the Texas Group increased production from 1985 estimates of 30,000 tablets a month to as many as 8,000 per day, potentially making two million ecstasy tablets in the months before MDMA was made illegal.<ref name=comprehensive>[Template:Cite book](/wiki/Template:Cite_book)</ref> By some estimates the Texas Group distributed 500,000 tablets per month in Dallas alone.<ref name=rising/> According to one participant in an [ethnographic](/wiki/Ethnographic) study, the Texas Group produced more MDMA in eighteen months than all other distribution networks combined across their entire histories.[[98]](#cite_note-98) By May 1985, MDMA use was widespread in California, Texas, southern Florida, and the northeastern United States.[[87]](#cite_note-87)[[111]](#cite_note-111) According to the DEA there was evidence of use in twenty-eight states[[112]](#cite_note-112) and Canada.[[87]](#cite_note-87) Urged by Senator [Lloyd Bentsen](/wiki/Lloyd_Bentsen), the DEA announced an [emergency Schedule I classification](/wiki/Comprehensive_Crime_Control_Act_of_1984) of MDMA on 31 May 1985. The agency cited increased distribution in Texas, escalating street use, and new evidence of MDA (an analog of MDMA) neurotoxicity as reasons for the emergency measure.[[111]](#cite_note-111)[[113]](#cite_note-113)[[114]](#cite_note-114) The ban took effect one month later on 1 July 1985<ref name=comprehensive/> in the midst of [Nancy Reagan's](/wiki/Nancy_Reagan) "[Just Say No](/wiki/Just_Say_No)" campaign.[[115]](#cite_note-115)[[116]](#cite_note-116) As a result of several expert witnesses testifying that MDMA had an accepted medical usage, the administrative law judge presiding over the hearings recommended that MDMA be classified as a [Schedule III](/wiki/Controlled_Substances_Act#Schedule_III_controlled_substances) substance. Despite this, DEA administrator [John C. Lawn](/wiki/John_C._Lawn) overruled and classified the drug as Schedule I.<ref name=exploration/><ref name=Harpers>[Template:Cite news](/wiki/Template:Cite_news) [Template:Open access](/wiki/Template:Open_access)</ref> Later Harvard psychiatrist [Lester Grinspoon](/wiki/Lester_Grinspoon) sued the DEA, claiming that the DEA had ignored the medical uses of MDMA, and the federal court sided with Grinspoon, calling Lawn's argument "strained" and "unpersuasive", and vacated MDMA's Schedule I status. Despite this, less than a month later Lawn reviewed the evidence and reclassified MDMA as Schedule I again, claiming that the expert testimony of several psychiatrists claiming over 200 cases where MDMA had been used in a therapeutic context with positive results could be dismissed because they weren't published in medical journals.<ref name=exploration/>[Template:Citation needed](/wiki/Template:Citation_needed) No double blind studies had yet been conducted as to the efficacy of MDMA for therapy.[Template:Citation needed](/wiki/Template:Citation_needed)

#### United Nations[[edit](/index.php?title=(none)&action=edit&section=29)]

While engaged in scheduling debates in the United States, the DEA also pushed for international scheduling.<ref name=comprehensive/> In 1985 the [World Health Organization's](/wiki/World_Health_Organization) Expert Committee on Drug Dependence recommended that MDMA be placed in Schedule I of the 1971 United Nations [Convention on Psychotropic Substances](/wiki/Convention_on_Psychotropic_Substances). The committee made this recommendation on the basis of the pharmacological similarity of MDMA to previously scheduled drugs, reports of illicit trafficking in Canada, drug seizures in the United States, and lack of well-defined therapeutic use. While intrigued by reports of psychotherapeutic uses for the drug, the committee viewed the studies as lacking appropriate methodological design and encouraged further research. Committee chairman [Paul Grof](/wiki/Paul_Grof) dissented, believing international control was not warranted at the time and a recommendation should await further therapeutic data.[[117]](#cite_note-117) The [Commission on Narcotic Drugs](/wiki/Commission_on_Narcotic_Drugs) added MDMA to Schedule I of the convention on 11 February 1986.[[118]](#cite_note-118)

### Post-scheduling[[edit](/index.php?title=(none)&action=edit&section=30)]

[thumb|A 1995 Vibe Tribe rave in](/wiki/File:1995-04-08_Vibe_Tribe_09_(10937582).jpg) [Erskineville, New South Wales](/wiki/Erskineville,_New_South_Wales), Australia being broken up by police. MDMA use spread globally along with rave culture. [thumb|A 2000](/wiki/File:Ecstasy_-_Is_it_Really_the_Dream_Drug.ogv) [United States Air Force](/wiki/United_States_Air_Force) video dramatizing the dangers of MDMA abuse. The use of MDMA in Texas clubs declined rapidly after criminalization, although by 1991 the drug remained popular among young middle-class whites and in nightclubs.[[98]](#cite_note-98)[Template:Rp](/wiki/Template:Rp) In 1985, MDMA use became associated with [Acid House](/wiki/Acid_House) on the Spanish island of Ibiza.[[98]](#cite_note-98)[Template:Rp](/wiki/Template:Rp)[[119]](#cite_note-119) Thereafter in the late 1980s, the drug spread alongside [rave culture](/wiki/Rave_culture) to the UK and then to other European and American cities.[[98]](#cite_note-98)[Template:Rp](/wiki/Template:Rp) Illicit MDMA use became increasingly widespread among young adults in universities and later, in high schools. Since the mid-1990s, MDMA has become the most widely used amphetamine-type drug by college students and teenagers.[[55]](#cite_note-55)[Template:Rp](/wiki/Template:Rp) MDMA became one of the four most widely used illicit drugs in the US, along with [cocaine](/wiki/Cocaine), [heroin](/wiki/Heroin), and [cannabis](/wiki/Cannabis_(drug)).<ref name=rising>[Template:Cite news](/wiki/Template:Cite_news)</ref> According to some estimates as of 2004, only marijuana attracts more first time users in the US.[[95]](#cite_note-95) After MDMA was criminalized, most medical use stopped, although some therapists continued to prescribe the drug illegally. Later,[Template:When](/wiki/Template:When) Charles Grob initiated an ascending-dose safety study in healthy volunteers. Subsequent legally-approved MDMA studies in humans have taken place in the US. in Detroit ([Wayne State University](/wiki/Wayne_State_University)), Chicago ([University of Chicago](/wiki/University_of_Chicago)), San Francisco (UCSF and [California Pacific Medical Center](/wiki/California_Pacific_Medical_Center)), [Baltimore](/wiki/Baltimore) ([NIDA](/wiki/National_Institute_on_Drug_Abuse)–[NIH](/wiki/NIH) Intramural Program), and [South Carolina](/wiki/South_Carolina), as well as in Switzerland (University Hospital of Psychiatry, [Zürich](/wiki/Zürich)), the Netherlands ([Maastricht University](/wiki/Maastricht_University)), and Spain ([Universitat Autònoma de Barcelona](/wiki/Universitat_Autònoma_de_Barcelona)).[[120]](#cite_note-120) "Molly", short for 'molecule', was recognized as a slang term for crystalline or powder MDMA in the 2000s.[[121]](#cite_note-121)[[122]](#cite_note-122) In 2010, the BBC reported that use of MDMA had decreased in the UK in previous years. This may be due to increased seizures during use and decreased production of the precursor chemicals used to manufacture MDMA. Unwitting substitution with other drugs, such as [mephedrone](/wiki/Mephedrone) and [methamphetamine](/wiki/Methamphetamine),[[123]](#cite_note-123) as well as legal alternatives to MDMA, such as [BZP](/wiki/Benzylpiperazine), [MDPV](/wiki/Methylenedioxypyrovalerone), and [methylone](/wiki/Methylone), are also thought to have contributed to its decrease in popularity.[[124]](#cite_note-124)[Template:Clear](/wiki/Template:Clear)

## Society and culture[[edit](/index.php?title=(none)&action=edit&section=31)]

[Template:Global estimates of illicit drug users](/wiki/Template:Global_estimates_of_illicit_drug_users)

### Legal status[[edit](/index.php?title=(none)&action=edit&section=32)]

MDMA is legally controlled in most of the world under the UN [Convention on Psychotropic Substances](/wiki/Convention_on_Psychotropic_Substances) and other international agreements, although exceptions exist for research and limited medical use. In general, the unlicensed use, sale or manufacture of MDMA are all criminal offences.

#### Australia[[edit](/index.php?title=(none)&action=edit&section=33)]

In Australia, MDMA was declared an illegal substance in 1986 because of its harmful effects and potential for abuse. It is classed as a [Schedule 9 Prohibited Substance](/wiki/Standard_for_the_Uniform_Scheduling_of_Medicines_and_Poisons) in the country, meaning it is available for scientific research purposes only. Any other type of sale, use or manufacture is strictly prohibited by law. Permits for research uses on humans must be approved by a recognized [ethics committee](/wiki/National_Health_and_Medical_Research_Council) on human research. In [Western Australia](/wiki/Western_Australia) under the [Misuse of Drugs Act 1981](/wiki/Misuse_of_Drugs_Act_1981) 4.0g of MDMA is the amount required determining a court of trial, 2.0g is considered a presumption with intent to sell or supply and 28.0g is considered trafficking under Australian law.[[125]](#cite_note-125) Some pills depict logos of products or shows popular with children, such as [Shaun the Sheep](/wiki/Shaun_the_Sheep).[[140]](#cite_note-140)

## Research[[edit](/index.php?title=(none)&action=edit&section=43)]

The [Multidisciplinary Association for Psychedelic Studies](/wiki/Multidisciplinary_Association_for_Psychedelic_Studies) (MAPS) is currently funding pilot studies or clinical trials investigating the use of MDMA in psychotherapy to treat [posttraumatic stress disorder](/wiki/Posttraumatic_stress_disorder) (PTSD),<ref name=Zarembo>[Template:Cite news](/wiki/Template:Cite_news)</ref> social anxiety in autistic adults,[[141]](#cite_note-141) and anxiety in terminal illness.[[142]](#cite_note-142)[[143]](#cite_note-143) MDMA has also been proposed as an adjunct to substance abuse treatment.[[144]](#cite_note-144) Contrary to ongoing treatment with approved psychiatric medications, MDMA is taken only a few times.[[145]](#cite_note-145) A review of the safety and efficacy of MDMA as a treatment for various disorders, particularly PTSD, indicated that MDMA has therapeutic efficacy in some patients;[[31]](#cite_note-31) however, it emphasized that issues regarding the control-ability of MDMA-induced experiences and neurochemical recovery must be addressed.<ref name=Pharm2014/> The author noted that [oxytocin](/wiki/Oxytocin) and [Template:Smallcaps all](/wiki/Template:Smallcaps_all)-cycloserine are potentially safer co-drugs in PTSD treatment, albeit with limited evidence of efficacy.[[31]](#cite_note-31) This review and a second corroborating review by a different author both concluded that, because of MDMA's demonstrated potential to cause lasting harm in humans (e.g., serotonergic neurotoxicity and persistent memory impairment), "considerably more research must be performed" on its efficacy in PTSD treatment to determine if the potential treatment benefits outweigh its potential to harm to a patient.[[18]](#cite_note-18)[[31]](#cite_note-31)[Template:Clear](/wiki/Template:Clear)

## Notes[[edit](/index.php?title=(none)&action=edit&section=44)]

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## References[[edit](/index.php?title=(none)&action=edit&section=45)]

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## External links[[edit](/index.php?title=(none)&action=edit&section=46)]

[Template:Commons](/wiki/Template:Commons) [Template:Commons category](/wiki/Template:Commons_category) [Template:Wiktionary](/wiki/Template:Wiktionary)

* [MDMA Facts and Statistics](https://www.drugabuse.gov/publications/drugfacts/mdma-ecstasymolly) National Institute on Drug Abuse
* [Methylenedioxymethamphetamine (MDMA or 'Ecstasy') drug profile](http://www.emcdda.europa.eu/publications/drug-profiles/mdma) European Monitoring Centre for Drugs and Drug Addiction
* [MDMA-Assisted Psychotherapy](http://www.maps.org/research/mdma) Multidisciplinary Association for Psychedelic Studies

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