

*Pharmacology of MDMA, Ketamine
and Methamphetamine*

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Pharmacology of MDMA, ketamine and methamphetamine :

1. Mechanism of action and pharmacokinetics
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MDMA

- Full name : 3,4-methylenedioxymethamphetamine
- Street names : Adam, E, Ecstasy, M&M, XTC, “Fing Tao” etc
- A “rave-party” drug
- Pharmacological classification : a phenylethylamine compound structurally related to amphetamine with CNS stimulation and hallucinogenic effects
- Legal classification in HK : Dangerous Drug

Pharmacology

- Major mechanism of action : by central stimulation and a rapid and brief liberation of noradrenaline from peripheral adrenergic terminals → sympathomimetic effects
- recent findings : mechanism of action could be related to a serotonin-depletion effect* → **“serotonin syndrome”**

* Fleckenstein, Gibb, Hanson, Eur J Pharmacol, 2000
Wallace, Gudelsky, Vorhees, Psychopharmacol, 2001

Pharmacology (cont'd)

- Pharmacokinetics :
 - absorption : oral
 - onset of action : 20 min
 - duration of effect : up to 8 hours or more
 - excretion : renal

Toxicity and Adverse Effects

- Class effects of the amphetamine group
 - acute and chronic
- MDMA-specific effects
 - acute and chronic

Toxicity and Adverse Effects

- General amphetamine effects :

- I. Acute :

- CNS : restlessness, dizziness, tremor, hyperactive reflexes, talkativeness, tenseness, irritability, weakness, insomnia, fever, euphoria (sometimes), fatigue and depression after stimulation

- psychotropic effects : paranoid hallucinations, panic states, suicidal or homicidal tendencies, aggressiveness, changes in libido, anxiety, delirium
- cardiovascular effects : pallor, flushing, palpitation, arrhythmias, anginal pain, hypertension, circulatory collapse

- GI : dry mouth, metallic taste,
anorexia, nausea & vomiting,
diarrhoea, abdominal cramps

- fatal poisoning → convulsions,
coma, cerebral haemorrhages,
cardiovascular collapse

II. Chronic effects :

- Weight loss, psychotic reaction with vivid hallucinations and paranoid delusions, incipient schizophrenia
- recovery usually rapid after discontinuation of drug

MDMA-specific Adverse Effects

1. “Serotonin Syndrome” :

- Diagnostic criteria : mental status changes (confusion, hypomania), agitation, myoclonus, hyperreflexia, diaphoresis, shivering, tremor, diarrhoea, incoordination, fever

“Serotonin Syndrome” (cont’d)

- Manifestations :

1. Cognitive and behavioral changes – disorientation, hallucinations, dizziness etc
2. Autonomic dysfunction – tachycardia, hypertension, flushing, salivation, hyperthermia etc
3. Neuromuscular effects : muscle rigidity, bruxism, trismus
4. Disseminated intravascular coagulopathy (DIC), rhabdomyolysis, renal failure, acute respiratory distress syndrome (ARDS) etc

MDMA-specific Adverse Effects (cont'd)

2. Acute symptomatic hyponatraemia with the syndrome of inappropriate antidiuretic-hormone secretion (SIADH)

- cause : MDMA-induced increased secretion of vasopressin \rightarrow \downarrow Na

- if fluid intake increased \rightarrow $\downarrow\downarrow$ Na \rightarrow hyponatraemic coma

MDMA-specific Adverse Effects (cont'd)

3. Others :

- “flashbacks”
- parkinsonism
- chronic paranoid psychosis
- jaundice
- subarachnoid haemorrhage
- cerebral infarction

4. Drug-drug interactions : with monoamine oxidase inhibitors, other anti-psychotic agents

Abuse of MDMA

- Forms : mostly as round tablets of various colours with different logos, less often powders and capsules
- Hallucinogenic dose : 50-150mg
- Adulterants : “Ice”, methaqualone, ketamine, phenobarbitone, caffeine, benzodiazepines, paracetamol
- Serious risk for uninformed users

Phenethylamine-type Stimulant Tablets



Ketamine

- Full name : Ketamine hydrochloride
- Street name : Special K, “K”
- Pharmacological classification : anaesthetic agent for minor human and veterinary surgical procedures
- Legal classification : Dangerous Drug

Pharmacology

- Mechanism of action : by blocking activation of non-competitive N-methyl-D-aspartate (NMDA) receptors → a state of “dissociative anaesthesia” → sensory loss, analgesia, amnesia but without actual loss of consciousness

Pharmacology (cont'd)

- Pharmacokinetics :
 - onset of action : IV – seconds
IM – 4 min
 - duration : 15-30 min
 - excretion : renally excreted after liver metabolism

Toxicity and Adverse Effects

- Emergence reactions : common during recovery, include unpleasant dreams, confusion, hallucinations and irrational behaviour (children less susceptible), reduced by prior administration of a benzodiazepine
- “out-of-body” state/experience : a psychological dissociation, “near death experience”
- “flashbacks”

Toxicity and Adverse Effects (cont'd)

- Hyper- and hypotension, arrhythmias, brady- or tachycardia
- Respiratory suppression, apnoea
- Long term effects : impaired memory, learning and attentional mechanisms; compulsive repeated use
- Drug-drug interactions : with other anti-psychotic agents

Abuse of Ketamine

- Forms : powder for snorting, injection for liquid
- Adulterants : often mixed with MDMA, “Ice”, benzodiazepines etc
- Hallucinogenic dose : 30mg po

Ketamine powder in paper packets



Ketamine Inhaling device



Methamphetamine

- Full name : methamphetamine/
methamphetamine hydrochloride
- Street names : crank, “Ice” for the high-purity crystalline smokeable form
- Pharmacological classification :
amphetamine-type CNS stimulant with
hallucinogenic effects
- Legal classification : Dangerous Drug

Pharmacology

- Mechanism of action : similar to MDMA
- Medical uses : appetite-suppressant, hyperactivity, narcolepsy
- Pharmacokinetics :
 - well absorbed orally and through mucous membrane of respiratory tract (inhalation)
 - instantaneous “high” after IV (a “rush”) or inhalation
 - duration of action : 8-24 hrs
 - excretion : renal excretion after hepatic metabolism

Toxicity and Adverse Effects

- Instant “rush” after inhalation or injection
- “crashing” after drug effect wears off :
profound sleep
- Depression and fatigue, sometimes suicidal
- Tendency to progress to compulsive use
- Tolerance after prolonged use

Toxicity and adverse effects (cont'd)

- Hyperthermia, hypertension, tachycardia, dysrhythmias
- CNS effects : insomnia, auditory hallucinations, confusion, delusions, paranoia, aggressive behaviour, suicidal
- High doses : extreme suspiciousness, overt paranoid psychosis → unpredictable violent behaviour
- Drug-drug interactions : with MAOIs, other anti-psychotic agents

Abuse of Methamphetamine

- Forms : by inhalation of the vapourized crystals , by IV injection
- Adulterants : often with MDMA, ketamine, or benzodiazepines
- Hallucinogenic dose : 20-25mg
- Tolerance develops after prolonged use

Methamphetamine

Fake (Alum)



Genuine



Hookahs



Summary

- MDMA, ketamine and methamphetamine have high potential for abuse
- Tolerance and dependence are common
- Combined use poses high risk of fatal poisoning