



OAS | CICAD



# DRUG MONITORING IN THE AMERICAS PROJECT

## Emerging Drugs, Synthetic Opioids, and Early Warning Systems

### Webinar

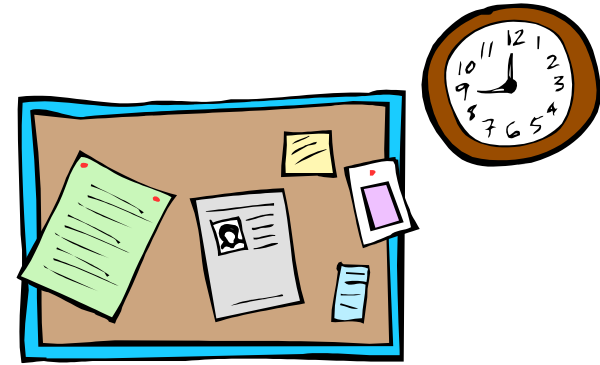
November 6-7, 2023

Panelist: Dr. Antonio Pascale, Medical Toxicologist

Organized by: Inter-American Observatory on Drugs (Spanish acronym, OID)

Inter-American Drug Abuse Control Commission (Spanish acronym, CICAD)

# Presentation (day 1)



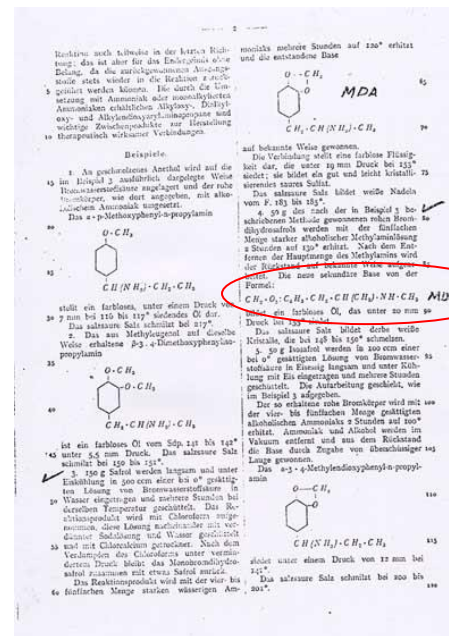
- Definitions. General concepts.
- Classification.
- Epidemiological aspects of NPS use in the Americas.
- Amphetamine-type stimulants (ATS).
- Synthetic opioids (part one).

# New Psychoactive Substances

- Known in the market by terms such as "synthetic drugs," "designer drugs," "emerging drugs," "legal highs," "herbal highs," and "bath salts."
- Wide variety of substances.
- Recently appeared on the market: are being incorporated into the International Conventions for their prohibition and recognition as legal drugs (emerging drugs).
- Predominance of Amphetamine-Type Stimulant drugs (ATS).

# SYNTHETIC DRUGS

- Recreational use linked to electronic music.
- Synthesized by the pharmaceutical industry since the beginning of the 20th century.
- Abandoned because they did not have the desired effects or were considered dangerous for the organism.
- Compounds analogous to so-called "classic" drugs.

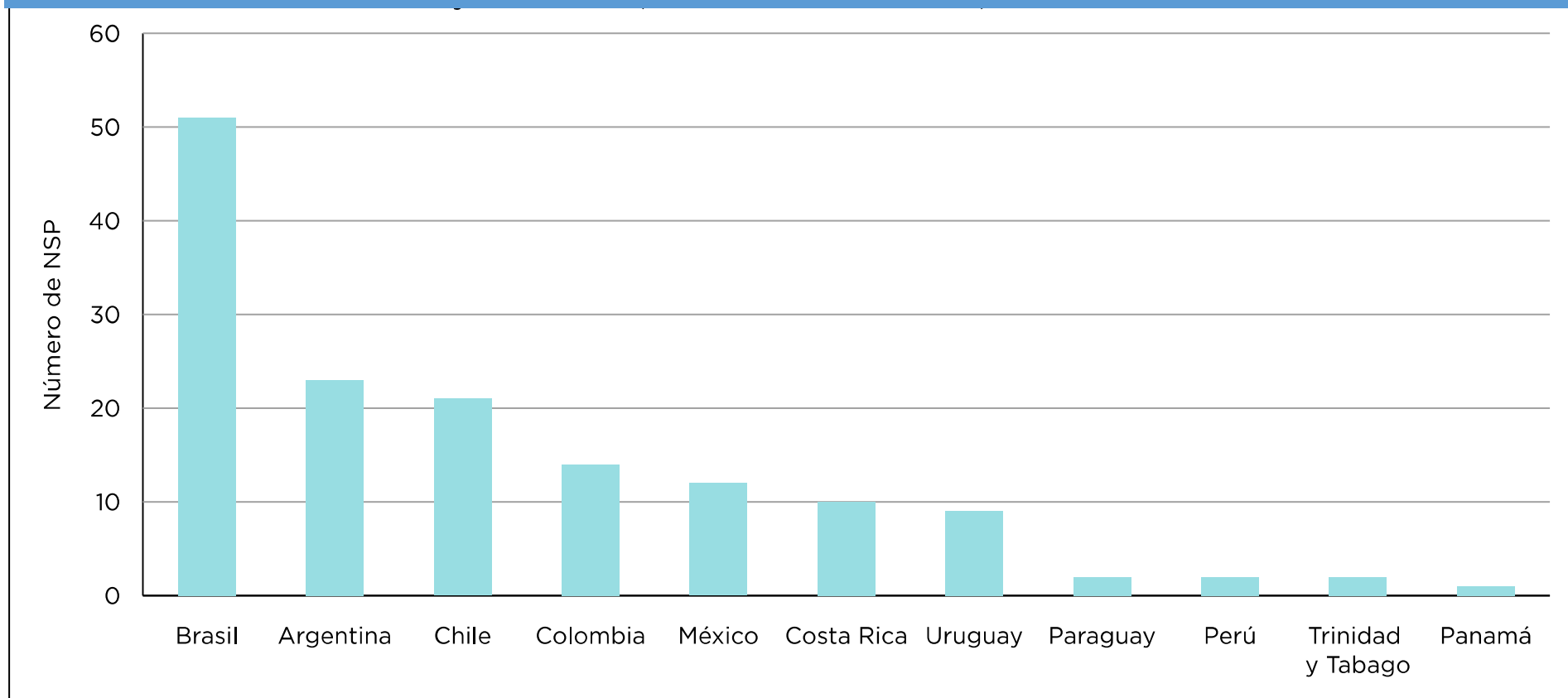


# NEW PSYCHOACTIVE SUBSTANCES

Types of NPS	
<u>Phenylethylamines and amphetamine derivatives</u>	Methamphetamine <u>Methylenedioxyamphetamines (MDMA - ecstasy)</u> <u>Methoxyamphetamines (PMA, PMMA)</u> Synthetic cathinones (mephedrone, MDVP) "2C" drugs
<u>Arylcyclohexylamines</u>	<u>Ketamine</u> , phencyclidine
<u>Piperazines</u>	Benzylpiperazine (BZP) and mCPP (m-Chlorophenylpiperazine)
<u>Synthetic cannabinoids</u>	JWH-018, CP 47497, JWH-073, and HU-210, indazoles (second generation).
<u>Synthetic opioids</u>	Fentanyl and analogues, benzimidazoles ('nitazenes'), AH-7921.
<u>Benzodiazepines</u>	Etizolam, flualprazolam

# Epidemiological aspects of NPS use in the Americas

*Figure 9: Number of new psychoactive substances with stimulant effects in the countries of Latin America and the Caribbean (as of December 2020)*



*Source: UNODC Global Smart Programme, 2021*

# Epidemiological aspects of NPS use in the Americas

Figure 6: Methamphetamine seizures reported in Latin America and the Caribbean, 2015 to 2019

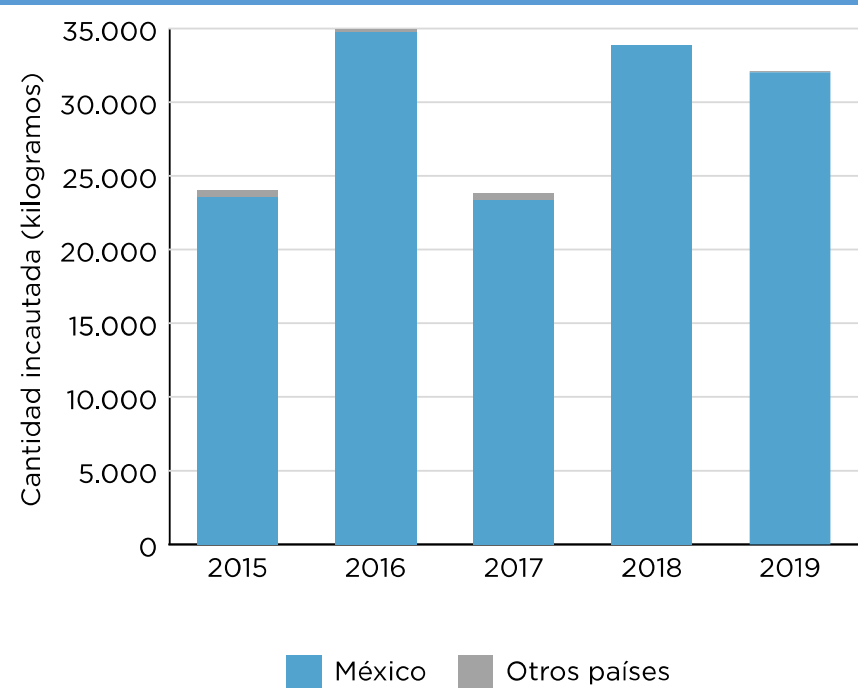
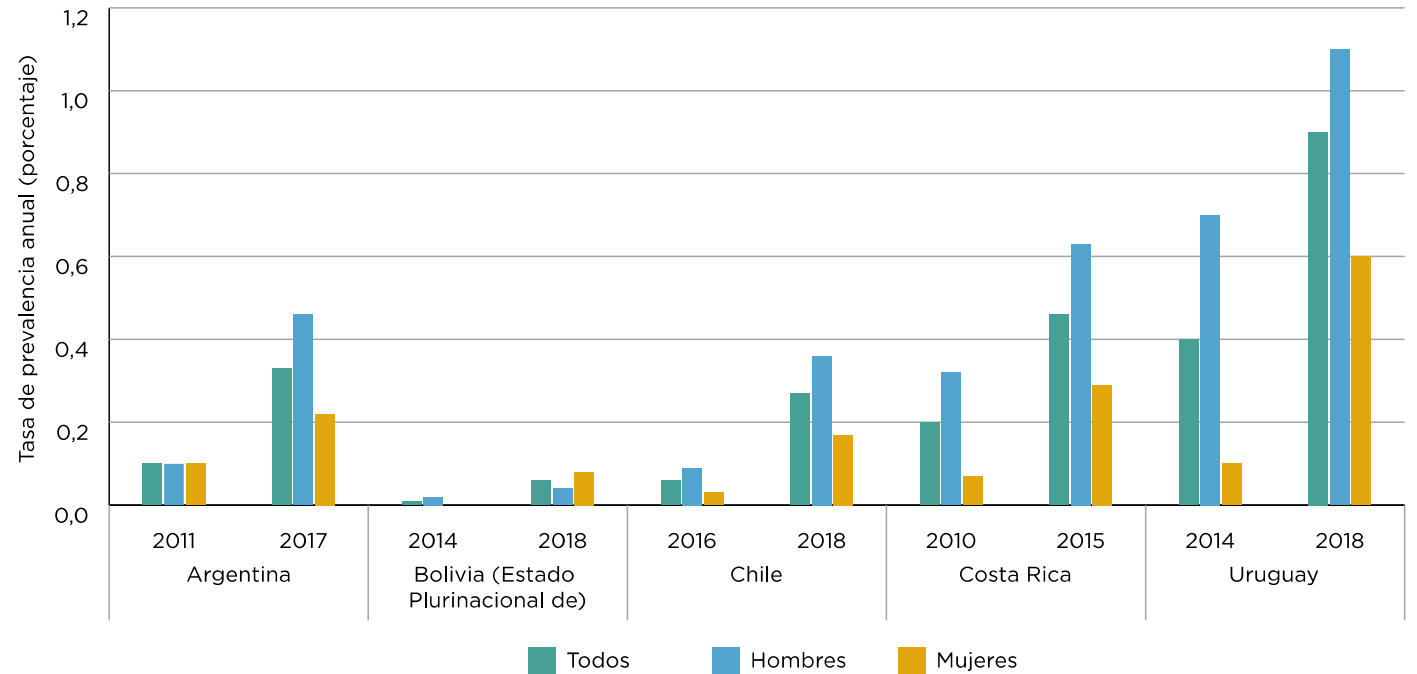


Figure 1: Annual prevalence of ecstasy use in the general population, selected countries in Latin America and the Caribbean, by sex and total, 2010 to 2018.



Fuente: UNODC, respuestas al cuestionario para los informes anuales.

Source: UNODC Global Smart Programme, 2021

# New psychoactive substances and adulterations

Emerging substances mimicking effects of "classic" internationally controlled drugs.

Availability: trafficking, synthesis (laboratories), internet.

Limited scientific evidence (e.g. potential for abuse or addiction).

Known toxic effects and adverse health consequences, including lethal intoxications.

Various consumption methods.

Unknown dose, adulterations, substitutions.

Polyconsumption.

Limitations in analytical detection capabilities at clinical laboratories

COVID-19 pandemic.



# CIRCUMSTANCES OF USE – AMPHETAMINE-TYPE STIMULANTS

- **Club drugs: MDMA and other synthetic amphetamines**
- **Occasional use at raves (club drugs)**
- **Dark web: illicit market over the internet.**
- **Potentially severe acute intoxications (dosage, adulterants, associations with other drugs)**
- **Tolerance**



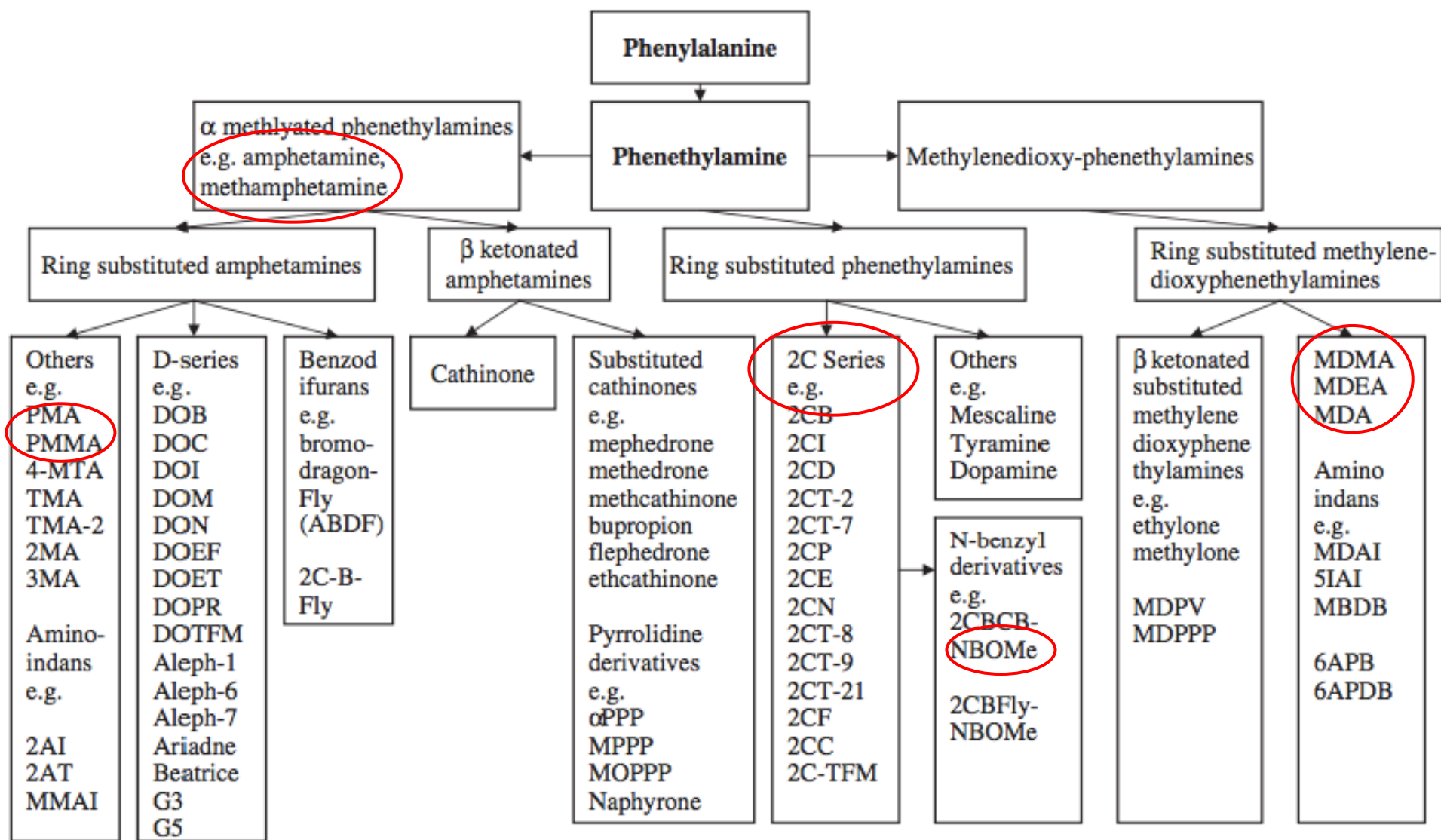
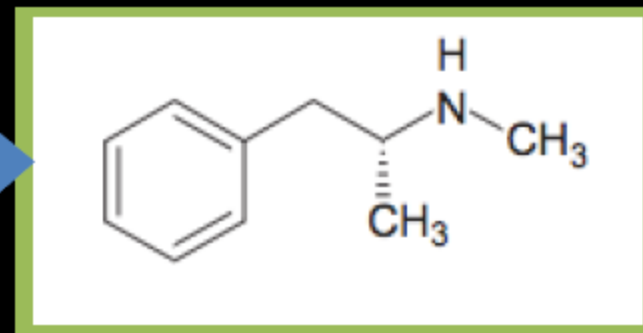
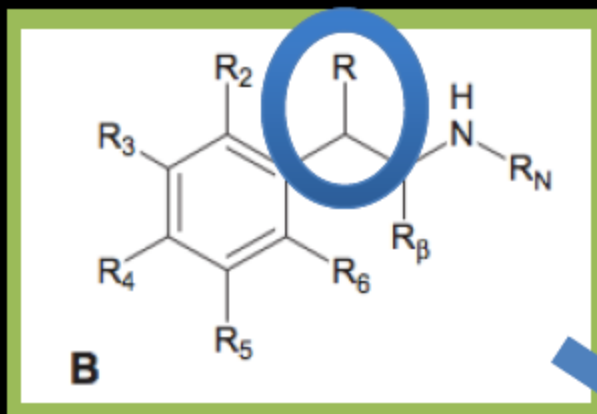
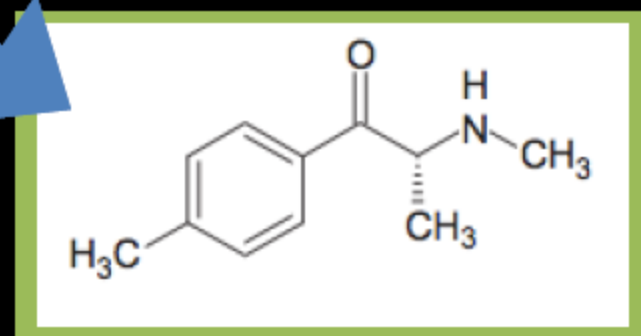


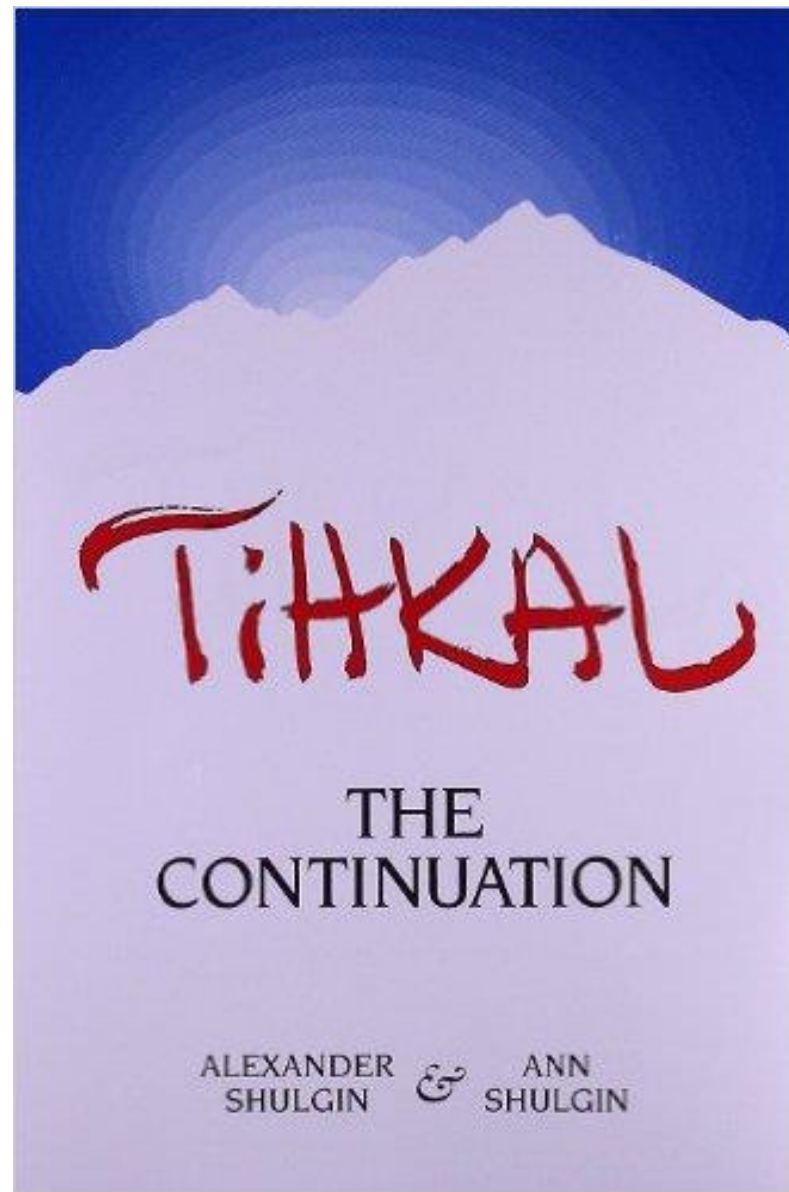
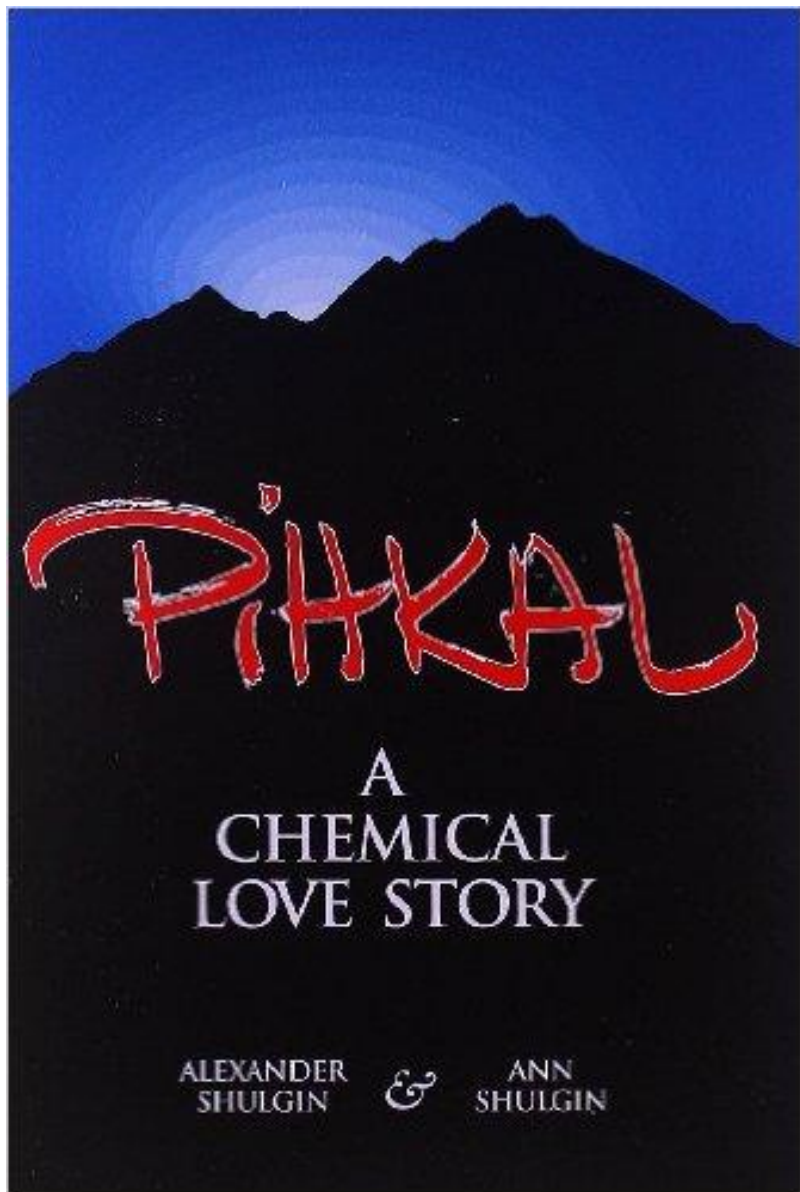
Fig. 4. Classification of the phenethylamines.



Methamphetamine



Mephedrone



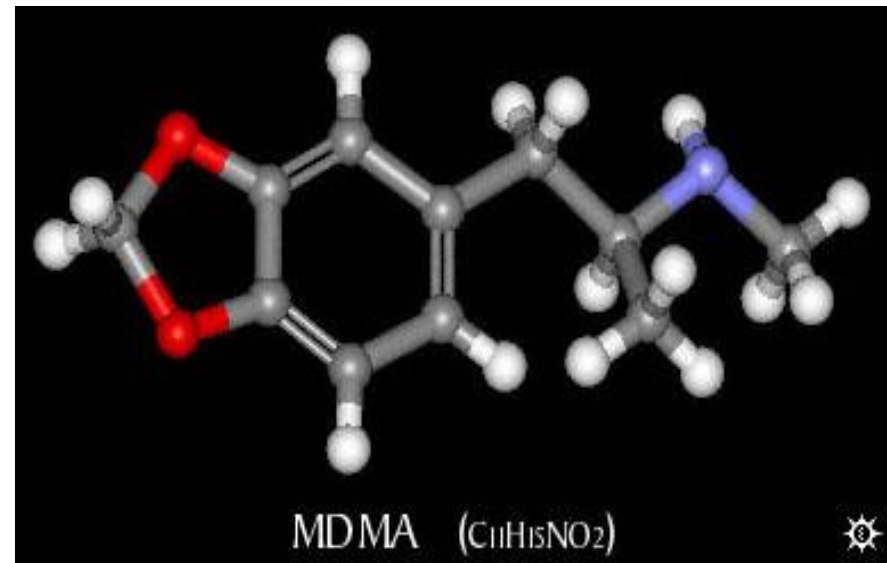
# MDMA (ecstasy)



# MDMA

---

- 3,4 - methylenedioxyamphetamine
- *Ecstasy, Adam, X, XTC...*
- Structurally related to the hallucinogen mescaline



# USE METHODS

- Oral Use: - tablets (pills)
  - Powder (crystals)
  - Capsules
- Other methods of use (rare):
  - Intravenous
  - Intranasal...
- Associated with:
  - Ethyl alcohol
  - Cocaine hydrochloride
  - Other synthetic drugs
- Intense and prolonged dancing
- Closed environments

# PRESENTATIONS - ADULTERATIONS

- Tablets: doses of 50 to 100 mg
- Varying in color, size, MDMA concentration, composition, price.
- Different designs
- **Adulterants:**
  - ASA, paracetamol
  - caffeine, ephedrine, cocaine
  - dextromethorphan
  - ketamine
  - MDA, MDEA, PMA...



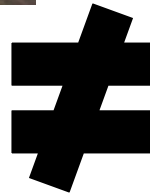
# USE METHODS: Crystals ("Molly")

- High toxicological risk:
  - ✓ Higher purity of MDMA
  - ✓ Risk of acute intoxication due to higher dosage consumed
  - ✓ Mixtures with MDMA (pills) and other abuse drugs
  - ✓ Adulterations (MDEA, PMA)





**Molly (MDMA)**



**Crystal meth  
(Methamphetamine)**

# TOXICOLOGICAL ASPECTS

- ✓ Clinical presentation
- ✓ Exposure circumstances - USE SCENARIO  
(raves, internet)
- ✓ Adulterations and substitutions
- ✓ POLYCONSUMPTION (diagnostic difficulties and multiplication of risks)
- ✓ Limitations of analytical toxicology (many of these substances are not detectable with conventional immunoassay techniques)

# PRESENTATIONS - ADULTERATIONS



# ACTION MECHANISM - MDMA

- Stimulates presynaptic release and blocks the presynaptic reuptake of dopamine, noradrenaline and serotonin.
- False neurotransmitter: direct sympathomimetic effect
- **Increased serotonergic action**
  - stimulates presynaptic release / inhibits presynaptic reuptake
  - MAO-A inhibition
  - 5 HT 2 receptor agonist

# MDMA - CLINICAL

- Onset of action after 20 to 30 minutes
  - Duration of action 4 to 6 hours. (75-150 mg)
  - **Rapid tolerance**
- 
- Positive symptoms (entactogenic)
  - Negative symptoms (acute intoxication/complications)
  - Post-consumption symptoms ("down" or "blues")

# LA NACION

Domingo 17 de abril de 2016 | lanacion.com

## DROGAS SINTÉTICAS Y TRAGEDIA EN COSTA SALGUERO



El dolor de la novia de uno de los chicos fallecidos frente al hospital Fernández, en Palermo. AGENCIADO NEGRO/LO

## Conmoción por la muerte de cinco jóvenes en una fiesta electrónica

**MADRUGADA DE TERROR.** Según el estudio toxicológico, las víctimas habían consumido drogas; investigan si fueron pastillas de éxtasis adulteradas; hay cinco internados en estado reservado

**Evangelina Himilitán**  
LA NACION

Así fue el final de la Time Warp, la fiesta electrónica que corrió a una multitud en Costa Salguero y terminó en tragedia: todavía estaba oscuro en la madrugada de ayer y en la puerta del complejo todo era desazón. Había jóvenes descompuestos sobre las veredas de pasto y los responsables de seguridad seguían trayendo chicos, duros como tablas, que vomitaban y sufrían convulsiones. Los médicos contratados para el evento no alcanzaban a atenderlos. Llamaron al SAME. Cuando llegaron las ambulancias, dos de ellos ya estaban muertos. Otros ocho fueron trasladados hasta los hospitales Fernández, Rivadavia y Argerich. Uno de ellos murió en el camino y otros dos, poco después de llegar al hospital.

Otros cinco jóvenes permanecen internados, en estado reservado.

Algunos de los que llegaron con vida al hospital tenían 42 grados de temperatura corporal.

Aunque hay que esperar los resultados de los análisis toxicológicos de las autopsias y los de laboratorio de las pastillas secuestradas en el predio, los investigadores del caso siguen dos pistas firmes: que las víctimas habían consumido pastillas de éxtasis adulteradas, el "falao éxtasis" y que por el horario en el que se descompusieron -el SAME recibió el pedido de ayuda a las 6.05- la droga se adquirieron dentro de la fiesta.

En un primer momento las autoridades sanitarias indicaron que las víctimas habían tomado éxtasis, cuyo principal componente es la metilendioximetilfetamina (MDMA), pero fuentes cercanas a la investigación sospechan que en realidad habían ingerido pastillas que contenían alta concentración de la letal paracetamolmetilfetamina (PMMA). Continúa en la página 26

**UBICACIÓN**



**La tragedia, en números**

**5**  
Muertos

**5**  
Internados

**10.900**  
Asistentes

**ADEMÁS**

"Se desvanecieron en la fiesta y nadie lo ayudó"  
Página 27

"La madre de Leandro lo encontró intubado, en terapia intensiva"  
Página 27

Drogas sintéticas, una amenaza que avanza  
Página 28

**OPINIÓN**

¿Por qué los padres estamos anestesiados?  
María Pía del Castillo. Página 27

El peligro de consumir pastillas desconocidas  
Mónica Nájoli. Página 28

Domingo 17 de Abril de 2016

HOY MAX 20° MIN 15°  
Probabilidad de lluvia

CHARLA EXCLUSIVA  
MARCO ANTONIO SOLÍS,  
CONFESSIONES DE UN ROMÁNTICO

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TRAGEDIA EN UNA FIESTA ELECTRÓNICA

**DEL ÉXTASIS  
A LA MUERTE**

Superman, una droga de moda y altamente tóxica, sería la responsable de las cinco víctimas fatales en Costa Salguero. Según testigos, las pastillas se conseguían a \$500 dentro del boliche. Toda la verdad sobre un flagelo que no distingue clases sociales  
Págs. 12-13-14

EL DOLOR DE LOS FAMILIARES DE UNO DE LOS FALLECIDOS

DESTROZOS Y PANICO  
**41 MUERTOS  
TRAS  
DEVASTADOR  
TERREMOTO  
EN ECUADOR**  
Pág. 10

ALCANZAN  
**MACRI PRESENTÓ  
PAQUETE DE  
MEDIDAS SOCIALES**  
Págs. 2-3

SEIS SON NIÑOS  
**FRANCISCO  
REGRESÓ A  
ROMA CON DOCE  
REFUGIADOS SIRIOS**  
Pág. 8

2-1 RAFAELA  
**LANÚS,  
PUNTERO  
INSACIABLE**  
EL LIBER DE LA ZONA 2  
GUARÓ SOBRE EL FINAL  
CON UN PUNTEO  
PENAL, QUE SAMO  
CAMBIÓ POR GOL  
El máximo artillero  
del torneo lo grita  
con todo.  
Págs. 10-11

4-1 ARTE ALDOSIVI  
**REMONTADA  
DEL BOCA  
MULETO**  
EL YENKIDZ ARRANCÓ FRENDO,  
PERO LOS SUPLENTE LO DEJON  
VUELTA A PURO FÚTBOL.  
Máx artillero de Chiver, autor de dos  
tetas y figura de la cancha  
Págs. 12-13

Argentine newspapers, April 2016

# ROLE of ADULTERANTS

- Pills sold as ecstasy contain low amounts of MDMA and some do not contain MDMA at all.
- Adulterants can potentiate the toxic effect of MDMA (by adrenergic/noradrenergic and/or serotonergic stimulation).
- - Some amphetamine derivatives do not have the same "desired" effects (entactogens).
- - They may have a later onset of effect.
- - PMMA: the stimulant effect is attained at the same time as the other unintended (toxic) effects

## INCREASED RISK OF ACUTE INTOXICATION



# 'Superman' pills linked to Telford man's death did contain dangerous ingredient, say police

Tests have found drugs with possible links to the deaths of four men did contain dangerous ingredient PMMA.



The distinctive 'Superman' tablet

*Shropshire Star, 2015*



SUFFOLK  
CONSTABULARY

**Police Warning**



## **Dangerous Drugs**

The ecstasy (MDMA) pill pictured is believed to be linked to the recent death of three people in the Ipswich area and is considered dangerous.

The following advice is issued:

**Do not take it**

Dispose of it safely by surrendering it to police by calling at your local police station or speaking to an officer, or hand it in to CRI, St Matthews Street, Ipswich, MVA Team, 70 - 74 St Helens Street, Ipswich or Fire Service, Princes Street, Ipswich, Ipswich A&E, Heath Road, West Suffolk Hospital A&E, Hardwick Lane, Bury St Edmunds.

**To report information to police contact 101**

For drugs information and advice visit the Talk To Frank website: [www.talktofrank.com](http://www.talktofrank.com).

There is also a 24/7 National Drugs Helpline on 0800 77 66 00

**If you have taken drugs and start to feel unwell call 999**

Call Suffolk Police on 101 or  
Crimestoppers anonymously  
on 0800 555 111

[www.suffolk.police.uk](http://www.suffolk.police.uk)

# CLINICAL PRESENTATION in OVERDOSES COCAINE AND AMPHETAMINE DERIVATIVES

## **SYMPATHOMIMETIC SYNDROME (MORE FREQUENT IN COCAINE)**

Psychomotor excitation, mydriasis, hyperthermia, tachycardia, arterial hypertension, chest pain (myocardial ischemia), tremors, convulsions.

## **SEROTONERGIC SYNDROME (MORE FREQUENT IN ATS)**

- Consciousness disorders: psychomotor agitation or excitation, drowsiness, confusion, coma.
- Neuromuscular activity disorders: hypertonia, clonus, trismus, tremors, convulsions (accompanied by hyperthermia).
- Dysautonomies.

# ACUTE COMPLICATIONS - ATS

- **Hyperthermia**

- Direct toxic effect
- Intense physical activity
- Closed environment with many people
- High temperatures, poor ventilation



- **Complications - Serotonergic syndrome:**

- Rhabdomyolysis, acute renal injury
- Cardiovascular collapse
- Respiratory distress and failure
- Disseminated intravascular coagulation

# ACUTE COMPLICATIONS - ATS

- **Hyponatremia (cerebral edema and convulsions):**
  - SIADH
  - Abundant water intake

Encefalopatía hiponatrémica y muerte cerebral en la intoxicación por éxtasis (3,4-metilendioximetanfetamina)

*Medicina Intensiva, 2010*

Hyponatremic encephalopathy and brain death in Ecstasy (3,4-methylenedioxymethamphetamine) intoxication

I. Aramendi y W. Manzanares\*

*Medicina Intensiva, Centro de Tratamiento Intensivo, Hospital de Clínicas, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay*

## Hiponatremia y muerte cerebral secundaria al consumo de éxtasis

B. AZKARATE<sup>a</sup>, P. MORRONDO<sup>a</sup>, G. CHOPERENA<sup>a</sup>, P. OLAIZOLA<sup>b</sup>, S. TRABANCO<sup>a</sup> Y R. SEBASTIÁN<sup>a</sup>

<sup>a</sup>Servicio de Medicina Intensiva. Edificio Aránzazu. Hospital Donostia. San Sebastián. <sup>b</sup>Coordinación de Trasplantes. Edificio Aránzazu. Hospital Donostia. San Sebastián. Guipúzcoa. España.

*Medicina Intensiva, 2003*

# PMA - PMMA

- Substituted amines with hallucinogenic and stimulant effect.
- Adulterant: lower cost precursors, could increase the desired effects of MDMA ("flooring")
- Effects at lower doses (50-80 mg)
- Increased latency in onset of action
- Increased serotonergic agonist action (5 - HT 2A)
- The desired effects are achieved almost simultaneously with the toxic effects (convulsions, QT prolongation, hypoglycemia, hyperkalemia)



# PMA and PMMA as ADULTERANTS

**Table 2.** Pills recently reported to have contained PMA (Source [www.pillsreport.com](http://www.pillsreport.com)).

Name	Country	Date	Description
Blue Dr. Death, Blue Cap	Australia	2001	Blue capsule, blue powder
Dr. Death, death	Australia	2001	Clear capsule, brown powder
Double Stacked Superman	USA	2001	Diamond/rounded tablet, off-white, with superman™ logo
Green Diamond	USA	2001	Round green tablet, with diamond log
Happy Face	Canada	2001	Light yellow, broad, round flat with logo “;-)”
Macintosh Green	USA	2001	Round green tablet, with Apple McIntosh™ logo
Mitsubishi Beige	Europe	2001	Round beige tablet with score on one side and Mitsubishi logo (3 diamonds) on the other
Mitsubishi Double-stack	USA	2001	White or tan with Mitsubishi logo (3 diamonds)
Purple TP	Canada	2001	White tablet, purple speckles, with logo “TP”
Snowball	USA	2001	White round tablet with no logo
Superman	Europe	2001	Round white tablet with Superman™ logo
Versace	Europe	2001	Round pure white with medusa head logo
White Rolex	Australia	2001	White tablet with Rolex™ symbol
White Cap	Australia	2001	White capsule
Green Sparkle	Australia	2001	Round dark green with a “*” logo

*Caldicott et al., Clin Toxicol. 2003.*

## Lethal 'Dr Death' ecstasy pills using Chupa Chups sweets logo flood Britain

ECSTASY pills carrying the name of a kiddies' treat are laced with a chemical dubbed Dr Death.

By **Patrick Williams, Exclusive** / Published 27th March 2016



TREAT: Ecstasy pills with the Chupa Chups logo could be laced with deadly chemicals

The tablets bearing the Chupa Chups lollies logo are flooding party venues across the UK, the Daily Star

Drugs

# Warning over fake ecstasy tablets after seven people die in Scotland

Police warn deaths may be linked to dangerous stimulants in green, white or yellow pills with Rolex, Mitsubishi or star logos



Some of the fake ecstasy tablets, which contain the dangerous stimulant PMA, are green and bear an imprint of the Rolex logo. Photograph: Police Scotland/PA

July 2013

T in the Park

# Warning after toxic green fake ecstasy pills found at T in the Park

Police say Rolex-stamped pills that were linked to several deaths in 2013 may be back in circulation



2015

# What causes the lethal cases?

- MDMA overdose (ATS)
  - + environmental conditions (use scenario)
  - + mixing with other drugs (alcohol, cocaine)
  - + adulterants
  - + increased MDMA purity in response to adulterations



## Amphetamine Derivative Fatalities in South Australia-Is "Ecstasy" the Culprit?

Byard, R. W.; Gilbert, J.; James, R.; Lokan, R. J.

- 6 deaths recorded from 1992 to 1998  
*(Am J Forensic Med Pathol 1998)*
- Adulterations and substitutions with PMA instead of MDMA.

## Severe paramethoxymethamphetamine (PMMA) and paramethoxyamphetamine (PMA) outbreak in Israel

Yael Lurie<sup>1</sup>, Asher Gopher<sup>2</sup>, Ophir Lavon<sup>1</sup>, Shlomo Almog<sup>2</sup>, Liron Suliman<sup>2</sup> & Yedidia Bentur<sup>1,3</sup>

*Clin Toxicol. 2011.*

- 108 lethal cases with screening + for amphetamines
- 32 positive in confirmatory tests
- 24 cases with PMA and PMMA detected.

# Dancing with “Death”: P-Methoxyamphetamine Overdose and Its Acute Management

David G. E. Caldicott, B.Sc.(Hons), N.U.I., M.B.B.S.,<sup>1,3,\*</sup>

Nicholas A. Edwards, M.B.B.S., F.R.A.C.P., F.F.I.C.A.N.Z.C.A.,<sup>2</sup>

Amanda Kruys,<sup>3</sup> K. Paul Kirkbride, Ph.D.,<sup>4</sup> D. Noel Sims, B.Sc.(Hons),<sup>4</sup> Roger W. Byard, M.B.B.S.,  
B.Med.Sci., M.Med.Sci., M.D., C.C.F.P., M.A.C.L.M., F.C.A.P., F.R.C.Path., F.R.C.P.C.,<sup>4</sup>

Michael Prior,<sup>5</sup> and Rod J. Irvine, Ph.D.<sup>3</sup>

*Clin Toxicol.* 2003.

- 32 lethal cases associated with PMA consumption (often instead of MDMA)
- 7 cases in 1973 (Ontario)
- Remaining deaths reported after 1995

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## PMA deaths in Ontario\*

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G. Cimbura,† M.SC.PHM., *Toronto*

CMA JOURNAL/JUNE 8, 1974/VOL. 110



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# Deaths from exposure to paramethoxymethamphetamine in Alberta and British Columbia, Canada: a case series

Jennifer J.E. Nicol MD, Mark C. Yarema MD, Graham R. Jones PhD, Walter Martz PhD, Roy A. Purssell MD, Judy C. MacDonald MD MCM, Ian Wishart MD, Monica Durigon MSc, Despina Tzemis MPH, Jane A. Buxton MBBS MHSc

Presented at the North American Congress of Clinical Toxicology, Sept. 1, 2013, Atlanta, GA

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**Nicol et al. CMAJ Open 2015.**

- 27 lethal cases associated with PMMA
- Average age 24 years (14 to 52 years old)
- 10 deaths prior to hospital admission
- 10 deaths in Emergency
- 7 deaths in IC
- 16 of the lethal cases that arrived at the hospital had serotonergic elements

**Table 2: Results of antemortem laboratory investigations for patients transported to hospital (n = 13/17)\***

Investigation	Level, median (range)	Normal range†
Peak potassium, mmol/L	7.0 (4.4–12.5)	3.5–5.1
Peak creatinine, mmol/L	214 (146–1127)	50–110
Peak AST, U/L	2944 (116–5124)	7–40
Peak creatinine kinase, U/L	8200 (1952–237 960)	38–215
Lowest recorded glucose, mmol/L	1.9 (0.4–17.1)	3.9–6.1

Note: AST = aspartate transaminase.

\*Data missing for 4 patients; they were pronounced dead shortly after arrival to the emergency department (no antemortem investigations).

†Normal values were obtained from the Royal College of Physicians and Surgeons of Canada.<sup>17</sup>

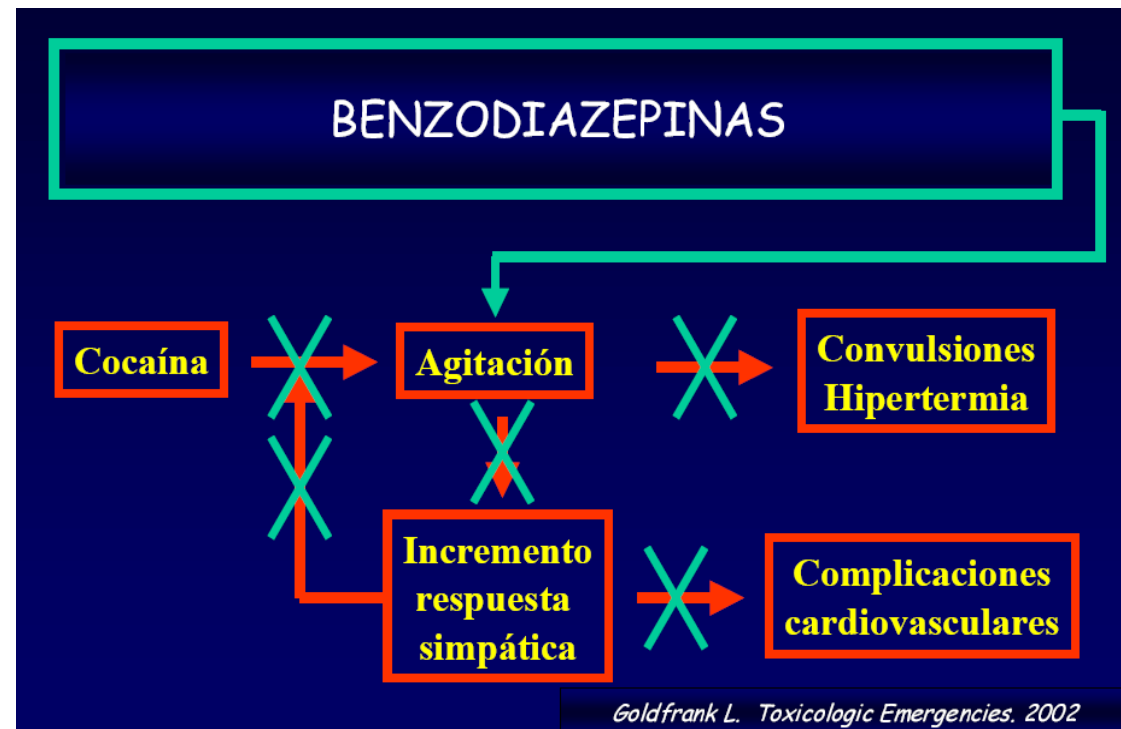
# ATS OVERDOSE TREATMENT

- Support of vital functions (A,B,C)
- Continuous ECG monitoring
- No antidote
- Caution with H-E repositioning (ionogram)
- Digestive decontamination? (late consultation...)
- Hemodialysis: ineffective as extrarenal depuration (in the presence of ARF or severe dysuria)
- Cardiovascular assessment - radbomyolysis - nephroprotection if needed
- Analytical toxicology (detection in urine by IC and/or GS/MS)

# BENZODIAZEPINES

- Anxiolytic and sedative effect
- Myorelaxant effect
- Anticonvulsant effect
- Myocardial protective effect
- Tachycardia and AHT control in most cases

**Neuroleptics and antipsychotics contraindicated**



# REDUCE DAMAGE AND RISKS...

## results

5 15 30 45 min.



VERY LOW MDMA CONTENT



LOW MDMA CONTENT



MEDIUM MDMA CONTENT



HIGH MDMA CONTENT

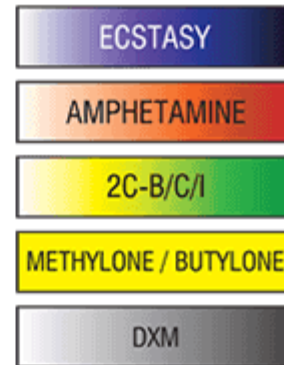


VERY HIGH MDMA CONTENT

THIS TEST WAS CALIBRATED ON A  
10 - 25 - 50 - 75 - 100 % PURE SAMPLE



## RESULTS



## MANDELIN

### SUBSTANCE

### Color Reactions

0 sec 30 - 60

KETAMINE	
MDMA/MDA/MDE	
PMA/PMMA	
HEROIN	
METHYLONE	
MESCALINE	
OXYCODONE	
CODEINE	
METHOXETAMINE	
AMPHETAMINE	
METHAMPHETAMINE	
RITALIN	
ASPIRIN	

No reaction: Morphine, DOB, DOI, MDPV, 2C-I, sugar & Others

# REDUCE DAMAGE AND RISKS...



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## Pill testing kits to be distributed at Melbourne University

Listen now Download audio

Wednesday 21 September 2016 6:43PM (view full episode)

The University of Melbourne's student union will be giving out free drug testing kits ahead of this year's summer festival season.




IMAGE: ECSTASY PILLS SIT ON A DESK. ('BOODOO' / SOURCE: FLICKR)

In what is reportedly an Australian first, the kits contain different kinds of fluid that change colour when reacting to party drugs such as MDMA and PMA.

The new program will be rolled out amid ongoing debate about the legalisation of pill testing.

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# SYNTHETIC CATHINONES

- Psychoactive substances sold as bath salts, stain removers, insect repellents.
- Legal high, legal cocaine (smart shops or internet)
- MDPV, mephedrone, methyldone...
- Consumption method: inhalation, oral, intravenous...
- Acute intoxications (sympathetic SN agonists, acute psychiatric conditions)
- **Not detectable by immunoassay**





# SYNTHETIC CATHINONES

**Table 4** Medical provider (including emergency department and poison center data) reported effects associated with use of synthetic cathinones [1, 13, 30, 35, 38, 70–72]

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Cardiovascular	Chest pain, hypertension, palpitations, myocarditis, tachycardia
ENT	Epistaxis, oral and pharyngeal effects, tongue disorder
Gastrointestinal	Abdominal pain, abnormal liver function tests, nausea, liver failure
Musculoskeletal	Elevated creatinine kinase, peripheral vasoconstriction, rhabdomyolysis
Neurologic	Agitation, aggression, altered mental status, collapse, confusion, dizziness, drowsiness, dystonia, headache, hyperreflexia, myoclonus, paraesthesias, seizures, tremor
Ophthalmologic	Abnormal vision, mydriasis
Pulmonary	Shortness of breath, tachypnea
Psychological	Anxiety, confusion, delusions, hallucinations, paranoia, psychosis
Renal	Abnormal renal function, acute renal failure
Other	Diaphoresis, fever, hyponatremia, rash

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It is possible that these effects are not all related to cathinone use as many users take these substance simultaneously with other drugs and ethanol. Additionally due to lack of reliability and consistency of products, users may not be aware of what drug they have actually taken. Please see text for more information

- Sympathetic stimulation +++
- Agitation, psychosis
- Some effects similar to acute MDMA toxicity

# PIPERAZINES

- Herbal highs, herbal tonics, herbal ecstasy or party pills (club drugs)
- Oral consumption in pill form or as an adulterant of MDMA
- Benzylpiperazines (BZP), phenylpiperazines
- Amphetamine-like effect (sympathomimetic syndrome and MDMA simile)
- **Not detectable by immunoassay**

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# Dissociative and Sympathomimetic Toxicity Associated with Recreational Use of 1-(3-Trifluoromethylphenyl) Piperazine (TFMPP) and 1-Benzylpiperzine (BZP)

*David M. Wood, MD<sup>a</sup>, Jenny Button, DipFMS<sup>b</sup>, Satnam Lidder, MD<sup>a</sup>, John Ramsey<sup>c</sup>,  
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JOURNAL OF MEDICAL TOXICOLOGY ■ VOLUME 4, NUMBER 4 ■ DECEMBER 2008



## 2 C - Phenethylamines

- Stimulant and hallucinogenic effects.
- Sympathetic stimulation ++
- Neuropsychiatric manifestations (agitation, convulsions).

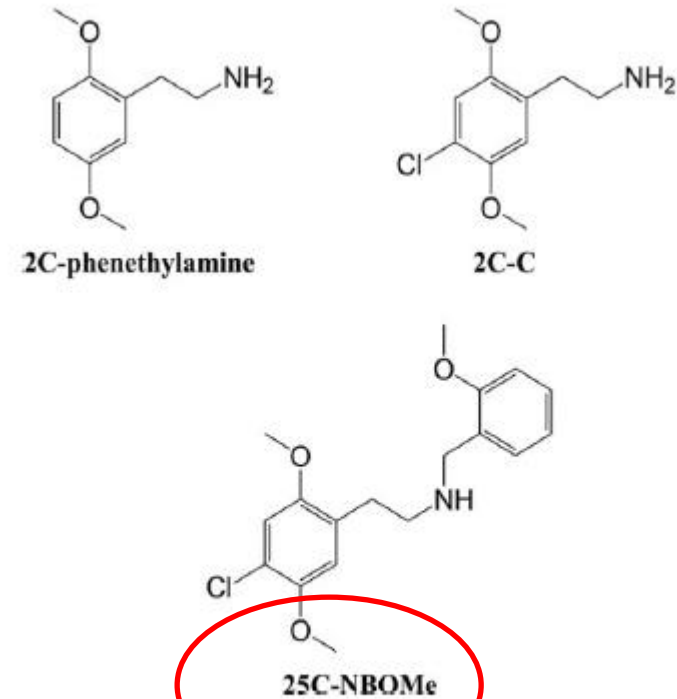


Figure 1: The chemical structures of 2C-phenethylamine, 2C-C and 25C-NBOMe

**LSD adulterant**

## Prevalence of use and acute toxicity associated with the use of NBOMe drugs

DAVID M. WOOD,<sup>1,2</sup> ROUMEN SEDEFOV,<sup>3</sup> ANDREW CUNNINGHAM,<sup>3</sup> and PAUL I. DARGAN<sup>1,2</sup>

- 29 published cases of acute toxicity associated with the use of substituted amines of the NBOMe type:
  - 25I-NBOMe - 23 cases
  - 25B-NBOMe - 3 cases
  - 25C-NBOMe - 3 cases.
- Reported clinical manifestations: tachycardia (96.6%), arterial hypertension (62.0%), agitation (48.2%), convulsions (37.9%) and hyperthermia (27.6%).
- Acute renal injury was reported in 5 cases.

# CONCLUSIONS - ATS

- The use of synthetic drugs can cause acute intoxication that depends on the substance(s) involved (associations/mixtures with "classic" drugs), adulterated presentations, and the context in which they are consumed (environment).
- Highly variable MDMA concentrations (in pills and crystals).
- New drugs in other contexts and consumption scenarios.
- Understanding proper emergency management can reduce morbidity and mortality associated with overdoses.
- Low risk perception: PREVENTION, at its three levels, is fundamental.

# OPIATES and OPIOIDS



# General considerations

- Opium-derived alkaloids.
- They act on opioid receptors in the CNS and peripheral sites.
- Classification

According to their origin:

- NATURAL: morphine, codeine, papaverine...
- SEMI-SYNTHETIC: heroin, buprenorphine, dextromethorphan, dextromethorphan
- SYNTHETIC: meperidine, fentanyl, methadone, tramadol, oxycodone...

According to their action:

- PURE AGONISTS: heroin, morphine, codeine, methadone, fentanyl, oxycodone...
- PURE ANTAGONISTS: naloxone, naltrexone
- AGONISTS - ANTAGONISTS: buprenorphine.

**\* Some of them are medicines, others are used only for RECREATIONAL purposes.**



- Uses:
  - Analgesia and/or sedation (morphine, meperidine, tramadol, fentanyl)
  - Antitussives (codeine, dextromethorphan)
  - Antidote (naloxone)
  - Detoxification (methadone, buprenorphine, naltrexone)
  
- Route of entry (according to type and presentation):
  - oral (tablets, syrup, drops)\*
  - intravenous, subcutaneous
  - transdermal (patches)
  - nasal (sniffed)
  - inhalatory (smoked)

\* body packers/body stuffers



Local and systemic complications: cellulitis, phlebitis, endocarditis, granulomas, HIV, hepatitis B and C virus.

**Tabla 1. Características de los receptores opioides (+/+++ = magnitud de la acción; - = no posee acción) <sup>12</sup>.**

Nomenclatura	Mu (μ, OP3, MOR)	Delta (δ, OP1, DOR)	Kappa (κ, OP2, KOR)	Nociceptina (N/OFQ,OP4, NOR)
Sistema efector	Proteína G	Proteína G	Proteína G	Proteína G
Ligando endógeno	β-endorfina, endomorfina	Enkefalinas (met y leu-enkefalina)	Dinorfina A	Nociceptina/orfanina FQ
Precursor	POMC (ACTH, MSH, β-lipotropina)	Proencefalina	Prodinorfina/	Pronociceptina/orfanina FQ
Analgesia:				
Supraespinal	+++	—	-/hiperalgesia	hiperalgesia
Espinal	++	++	+	+
Periférica	++	—	++	
Depr. respiratoria	+++	++	—	
Miosis	++	—	+	
Reduc. motilidad digestiva	++	++	+	
Sedación	++	—	++	
Euforia	+++	—	—	
Disforia	—	—	+++	
Dependencia	+++	—	+	
Agonista	Morfina	Morfina	Pentazocina	Ro 64-6198
Antagonista	Naloxona	Naloxona	Naloxona	

## Pharmacological action according to the type of receptor for which it has greater affinity (mu, delta, kappa, sigma, epsilon)

**Tabla 2. Acción de distintos fármacos opioides sobre los receptores opioides (Ag = agonista; An = antagonista; AP = agonista parcial; +/-+++ = magnitud de la acción; - = acción débil o nula) <sup>1,211</sup>.**

Fármaco/ Receptor	Mu	Delta	Kappa
Morfina	Ag +++	Ag +	Ag +
Petidina	Ag ++	Ag +	Ag +
Metadona	Ag +++	Ag+	-
Fentanilo	Ag +++	Ag +	-
Pentazocina	An+	Ag +	Ag ++
Butorfanol	An+	Ag+	Ag ++
Buprenorfina	AP+++	-	Ag ++
Naloxona	An+++	An+	An++
Naltrexona	An+++	An+	An+++

POMC = proopiomelanocortina; ACTH = corticotropina; MSH = melanotropina

# Opiate and opioid withdrawal syndromes

- cravings, anxiety
- lacrimation, runny nose
- muscle cramps
- arthromyalgias
- abdominal cramps
- headaches and general malaise
- nausea, vomiting and diarrhea
- heat followed by cold shivers
- piloerection
- profuse sweating
- hyperthermia
- palpitations
- suicidal ideation
- irritability, excitement, sleeplessness

# SYNTHETIC OPIOIDS

- *Growing public health problem*
- *Fentanyl and analogues, nitazenes, U series.*
- Adulterants or substitutes for prescription opioids, illicit use on the black market (high doses, alone or in combination with other classical drugs, NPS, oral use in pill form or as an adulterant of MDMA)
- Information sources: seizures, clinical cases admitted to hospitals, post-mortem cases, risk behaviors (road accidents - driving under the influence).
- **Not detectable by immunoassay (with the exception of fentanyl)**

# Synthetic opioids: depressants



GRACIAS



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