PHARMACOLOGY PROFILE OF METHAMPHETAMINE AND IT'S ASSOCIATION WITH PSYCHIATRIC SYMPTOMS IN METHAMPHETAMINE USE DISORDER

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ISSUP STIMULANT WEBINAR SERIES
23 JANUARY 2024, 11:00 AM WIB | 22 JANUARY, 2024 8:00 PM PST

OUTLINE

The situation of Stimulant Use in Indonesia

Profiling of Methamphetamine in Indonesia

Methamphetamine Pharmacology

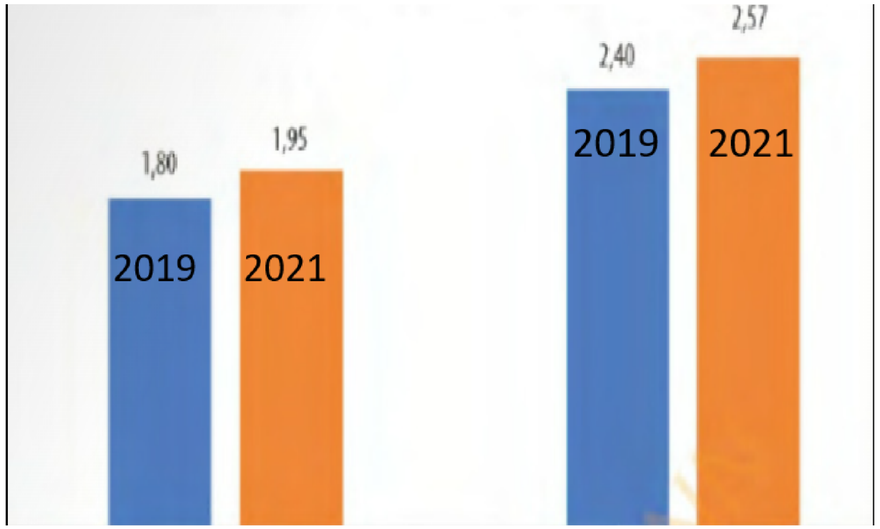
Methamphetamine use disorder and psychiatric disorders

IMPORTANT POINTS

THE SITUATION OF STIMULANT USE IN INDONESIA

SITUATION OF DRUG ABUSE IN INDONESIA

PREVALENCE OF DRUG ABUSE 2019 AND 2021 IN INDONESIA



PREVALENCE RATE OF DRUG USED IN THE PAST 12 MONTHS

PREVALENCE OF EVER-USE

- Prevalence rate of drug used in the past 12 months is increase 0.15% from 1.80% in 2019 to 1.95% in 2021
- In the same period, the prevalence rate of drug abuse of ever use, increased 0.17% from 2.4% in 2019 to 2.57% in 2021.
- In Indonesia amphetamine-type stimulants (ATS) is the second most consumed drug after marijuana at 41.4% and followed by methaphetamine at 25.7%
- People with methamphetamine use disorder was found to be female were quite dominant compared to male (56.9% and 34,9%).

NATIONAL SURVEY ON DRUG ABUSE IN 2021 : NATIONAL RESEARCH AND INNOVATION AGENCY, CENTRAL STATISTICS AGENCY AND BNN RESEARCH, DATA AND INFORMATION CENTER , INDONESIA 2022

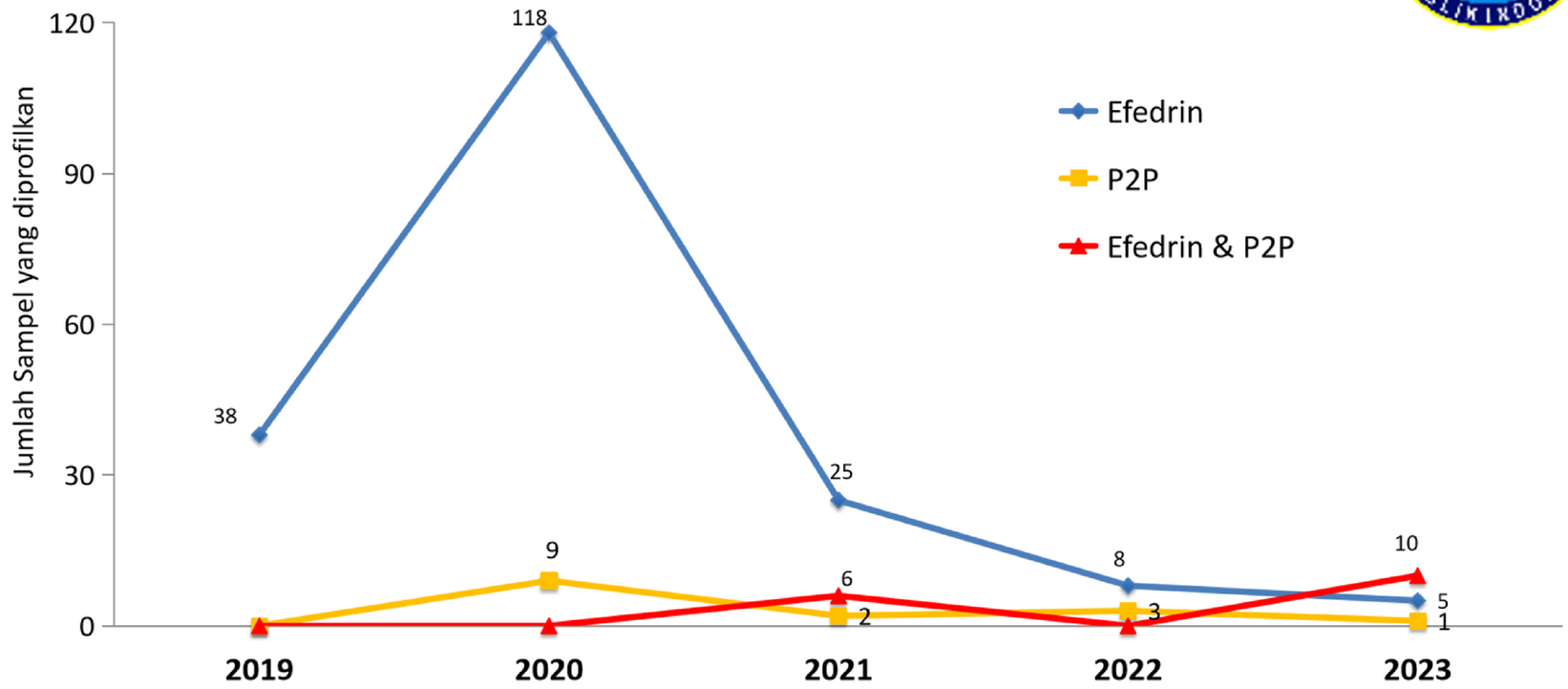
PROFILING OF METHAMPHETAMINE IN INDONESIA

METHAPHETAMINE PROFILING IN INDONESIA

- **Type crystal isomer of methamphetamine : dextro, levo or racemic**
- **Suspected Precusor type and Precusor source : natural, semisynthetic, synthetic**.

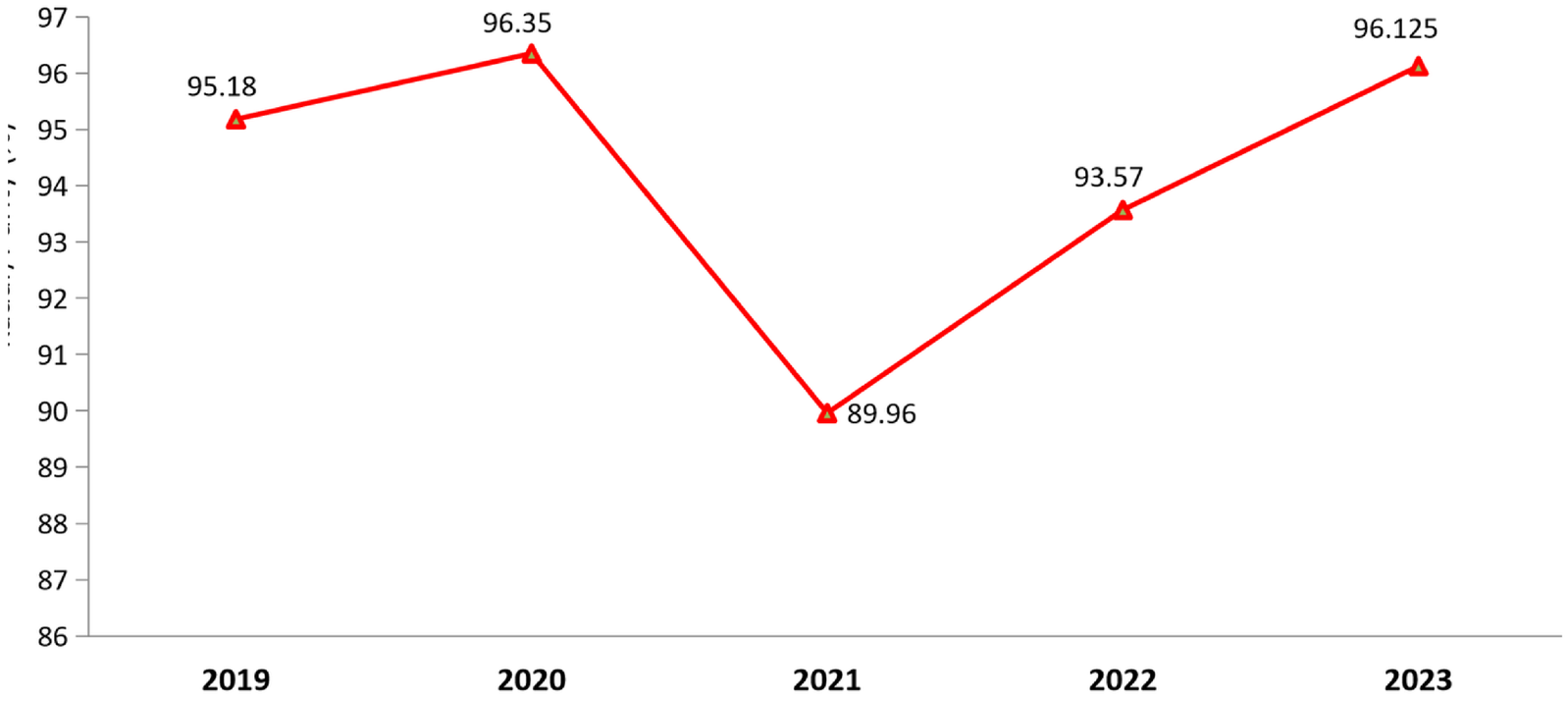
PROFILE OF PRECURSORS USED IN THE SYNTHESIS OF METHAMPHETAMINE IN INDONESIA

From 2019 - 2022, EFEDRIN was the most widely used type of precursor in the manufacturing of methamphetamine. However, in 2023 there was an increase in cases with the use of a mixture of 2 precursors (Ephedrine and P2P) in the manufacture of methamphetamine (Multi Compound).



PURITY OF METHAMPHETAMINE IN 2019 - 2023

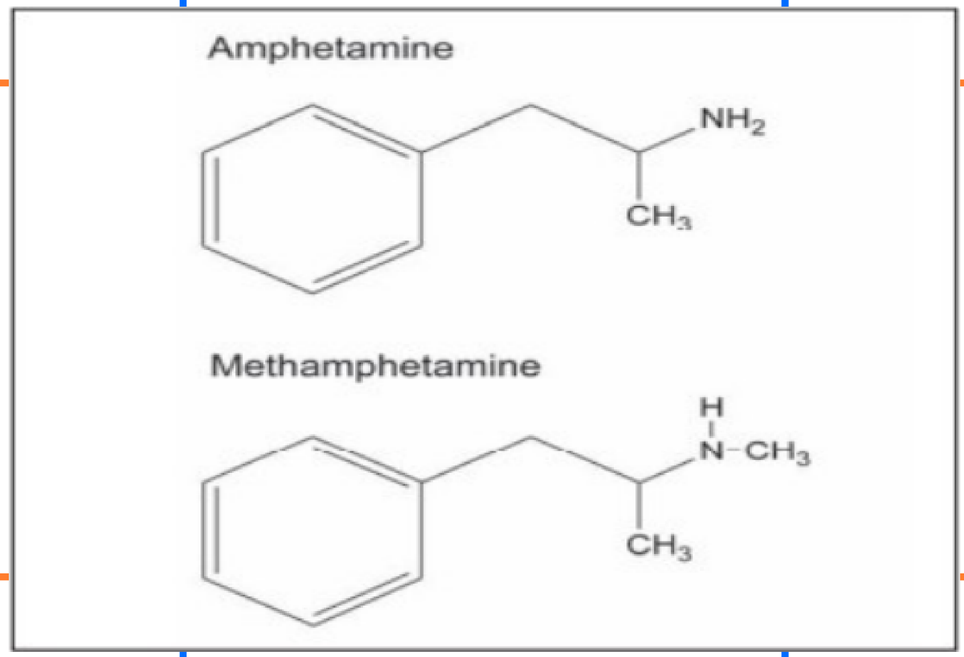
The average level of methamphetamine purity each year from 2019 to 2023 is above 90% except in 2021 where the average level of Methamphetamine HCl is lower at 89.96%.



PHARMACOLOGY OF METHAMPHETAMINE

PHARMACOLOGY OF METHAMPHETAMINE

- Amphetamine type stimulants (ATS) have a methyl group on one of the carbon arms of phenylethylamine
- The chemical structures of Methamphetamine and amphetamine are similar, both having a methyl group, which is attached to one of the carbon arms of phenylethylamine. The difference lies in the additional methyl group attached to the amine group. This causes Methamphetamine is very fat soluble so that it easily penetrates the brain barrier.



CRUICKSHANK CC, DYER KR. A REVIEW OF THE CLINICAL PHARMACOLOGY OF METHAMPHETAMINE. ADDICTION. 2009;104(7):1085–99.

PHARMACOLOGY OF METHAMPHETAMINE

METHAMPHETAMINE PHARMACOKINETICS

METHAMPHETAMINE PHARMACEUTICALS :
CRYSTAL, POWDERS, TABLETS AND LIQUIDS

METHAMPHETAMINE ABSORPTION IS RELATED
TO THE ROUTE OF ADMINISTRATION
(ORAL, INTRANASAL, SMOKED, INTRAVENOUS).

DISTRIBUTION THROUGHOUT THE BODY,
ESPECIALLY TO THE KIDNEYS, LUNGS,
LIVER, PANCREAS, HEART, AND BRAIN

METABOLIZED IN THE LIVER BY CYP2D6,
PLASMA HALF-LIFE 10 HOURS

EXCRETION THROUGH THE URINE
IS ABOUT 70%
IN THE FORM OF 30-50% METHAMPHETAMINE,
15% 4-HYDROXYMETHAMPHETAMINE,
AND ABOUT 10% AMPHETAMINE
WITH AN EXCRETION HALF-LIFE OF ABOUT 25 HOURS.

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PHARMACOLOGY OF METHAMPHETAMINE

METHAMPHETAMINE PHARMACOKINETICS

How to use	Dose	Bioavailability	Time to peak effect
Intravena	30 mg	100%	< 15 minutes
smoked	30 mg	90%±10%	18±2 minutes
Oral	30 mg	67%±3%	180 minutes
Nasal	50 mg	79%	≤ 15 minutes

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PHARMACOLOGY OF METHAMPHETAMINE

MECHANISM OF ACTION METHAMPHETAMINE

- Methamphetamine, also known as N-methylamphetamine or desoxyephedrine, is a class of Amphetamine type stimulants (ATS). Methamphetamine has two stereoisomers, namely d-methamphetamine which is 3-5 times stronger in activity against the central nervous system (CNS) compared to l-methamphetamine. Both stereoisomers affect the release of monoamine neurotransmitters, namely dopamine, norepineprin.
- Methamphetamine is an indirectly acting sympathomimetic amine. It releases dopamine (DA), serotonin, noradrenaline, and adrenaline from nerve terminals, thus increasing their neurotransmission. As a result of its high lipophilicity, methamphetamine easily crosses the blood-brain barrier.

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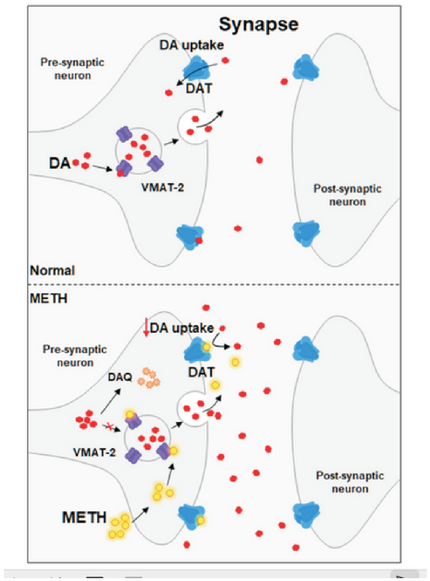
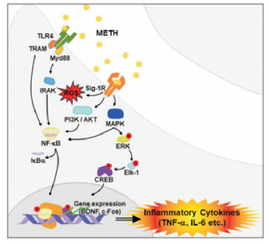
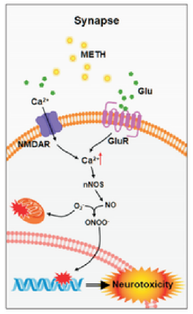
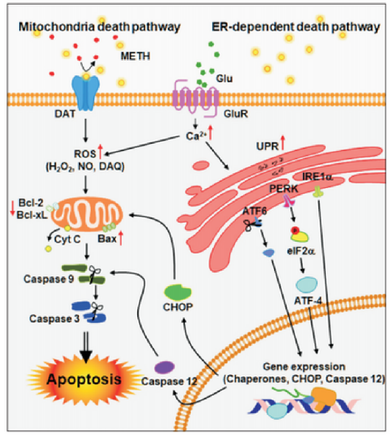


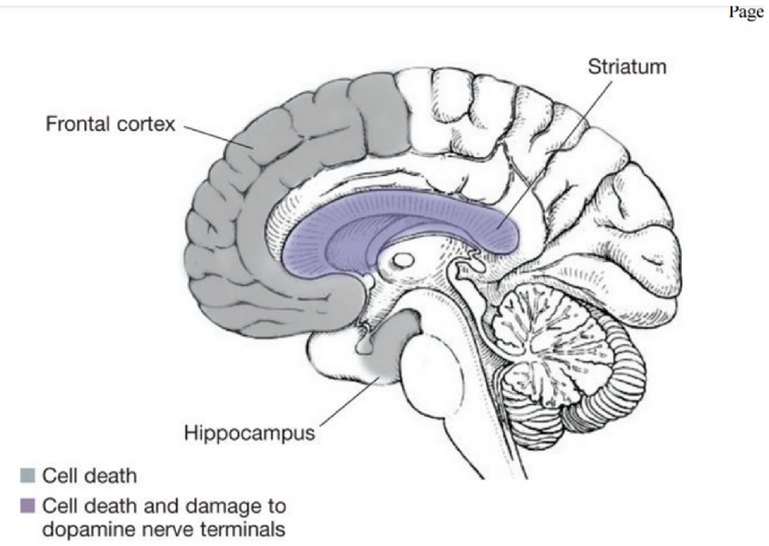
METH REGULATES DOPAMINE RELEASE







METH INDUCES MEDIATED NEUROTOXICITY. NEUROINFLAMMATION AND APOPTOSIS



METHAMPHETAMINE DAMAGES NEURONS IN SOME BRAIN AREAS

ANNA M , NEUROBIOLOGY AND CLINICAL MANIFESTATIONS OF METHAMPHETAMINE NEUROTOXICITY PSYCHIATR TIMES. 2016 SEPTEMBER ; 33(9): 16–18.

PHARMACOLOGY OF METHAMPHETAMINE

MOLECULAR MECHANISM METHAMPHETAMINE

Manifestation	Dose	Molecular mechanism
Anxiety, dysphoria	> 30 mg	Increased adrenergic α_1-receptor stimulation in the prefrontal cortex, 5-HT2 receptor, and DA receptor stimulation in the striatum
Elevated body temperature	> 30 mg	Increased DA, serotonin, and noradrenaline release in the hypothalamus
Talkativeness	> 50 mg	Activation of anterior cingulate cortex and ventral striatum
Paranoia	> 55 mg	Increased DA release in the striatum
Hallucinations (auditory, visual)	> 55 mg	Auditory: increased activation of thalamus and ventral striatum; visual: increased activation of paralimbic and primary motor cortices
Stereotypy (punding)	High	Imbalance between D1 and D2 receptor signaling in the dorsal striatum
Choreoathetosis, dyskinesia	High	Overstimulation of D2 receptors in the dorsal striatum

DA, dopamine.

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METHAMPHETAMINE USE DISORDER AND PSYCHIATRIC DISORDERS

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1842 METHAMPHETAMINE USE DISORDERS.

770 (41.8%) OF METHAMPHETAMINE USE DISORDERS ASSESSED WITH PSYCHIATRIC SYMPTOMS ACCORDING TO ASI.

DEPRESSION WAS THE MOST PREVALENT PSYCHIATRIC SYMPTOM (31.9%),

ANXIETY (24.5%), AND PSYCHOSIS (8.9%).

PSYCHOSIS (8.9%).

Psychiatric symptoms are health problems that often occur as a result of methamphetamine abuse.

ROHMANIKA ,ET ALL : PATTERNS OF METHAMPHETAMINE USE AND ITS ASSOCIATIONS WITH PSYCHIATRIC SYMPTOMS IN PATIENTS UPON ADMISSION AT THE NATIONAL REHABILITATION CENTER LIDO BOGOR, INDONESIA , 2022

METHAMPHETAMINE USE DISORDER AND PSYCHIATRIC DISORDERS

Psychiatric symptoms

Females, duration ≥ 5 years, smoking route of administration and use with other narcotics are more at risk for psychiatric symptoms in Methamphetamine use disorder

Psychosis

duration ≥ 5 years, smoking and co-administration with opiates are more likely to lead to psychosis in methamphetamine use disorder

anxiety

females, doses ≥0.2 grams, smoking and use with other narcotics are more at risk of causing anxiety in methamphetamine use disorder.

depression

females, duration ≥ 5 years, smoking, co-use of other narcotics, other ATS and transquilizers are more likely to cause depression in methamphetamine abusers.

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RESPONDING THE SITUATION OF PSYCHIATRIC DISORDERS DUE TO METHAMPHETAMINE USE DISORDER

IMPORTANT POINTS

- THE HIGH PREVALENCE OF METHAMPHETAMINE USE DISORDER AND THE HIGH LEVEL OF METHAMPHETAMINE PURITY WAS FOUND IN INDONESIA.
- METHAMPHETAMINE USE DISORDER CAUSES BRAIN DAMAGE
- THE ASSOCIATION BETWEEN PSYCHIATRIC SYMPTOMS AND GENDER, DURATION, DOSE, ROUTE OF ADMINISTRATION AND USE OF OTHER DRUGS SUGGEST THAT EARLY ASSESSMENT OF PSYCHIATRIC SYMPTOMS AND COMPREHENSIVE MANAGEMENT OF METHAMPHETAMINE USE DISORDER IS REQUIRED.

THANK YOU