

แอมเฟตามีน: นิติเวชปริทัศน์

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**Jumlongkul A. Amphetamines: A review of forensic medicine. Chula Med J 2016
July – Aug; 60(4): 399 - 412**

Amphetamine and its derivatives are drug abuse that can destroy world economy, society and human resources. Although Thailand has enforced suppressive and preventive of narcotic measures for a long time, these problems have persisted and difficult to be eradicated. Drug abusers are usually sent to hospitals in various statuses such as being a patient, suspected person, alleged offender, etc. In the cases of unnatural death that are suspected of drug overdose; autopsy will be done which includes investigation on amphetamine level. This article reviews history, types, physical and chemical properties, toxicokinetics and pharmacokinetics, toxicity, benefits for medication, specimen collection, laboratory analysis and relevant Thai legislation so that it would be benefits for forensic physicians and other medical specialties to apply the knowledge in their work.

Keywords: *Amphetamine, forensic doctor, narcotic cases.*

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Received for publication. March 20, 2016.

อานนท์ จำลองกุล. แอมเฟตามีน: นิติเวชปริทัศน์. จุฬาลงกรณ์เวชสาร 2559 ก.ค. – ส.ค.; 6(4): 399 - 412

แอมเฟตามีนและสารอนุพันธ์เป็นสารเสพติดที่สามารถก่อให้เกิดความเสียหายต่อเศรษฐกิจสังคม และทรัพยากรมนุษย์ในระดับโลก แม้ว่าประเทศไทยจะมีมาตรการปราบปรามและป้องกันมาเป็นเวลานาน แต่ปัญหาเหล่านี้ยังคงมีอยู่และยากที่จะกำจัดให้หมดไปได้ ผู้เสพยาเสพติดมักถูกส่งตัวมาโรงพยาบาลในหลายสถานะ เช่น ผู้ป่วย ผู้ต้องสงสัย และผู้ต้องหา เป็นต้น ส่วนศพที่ตายผิดธรรมชาติ และสงสัยเรื่องการใช้สารเสพติดเกินขนาด จะถูกนำมาผ่าชันสูตรและส่งตรวจหาระดับแอมเฟตามีน บทความนี้จึงมีเนื้อหาเกี่ยวกับประวัติความเป็นมา ประเภทของสารกลุ่มแอมเฟตามีน คุณสมบัติทางฟิสิกส์และเคมี พิษจลนศาสตร์และเภสัชจลนศาสตร์ ความเป็นพิษ ประโยชน์ในการรักษาโรค การเก็บสิ่งส่งตรวจ การตรวจวิเคราะห์ทางห้องปฏิบัติการ และกฎหมายที่เกี่ยวข้อง เพื่อประโยชน์สำหรับแพทย์นิติเวชและแพทย์สาขาอื่นในการนำไปประยุกต์ใช้กับการทำงาน

คำสำคัญ: แอมเฟตามีน, แพทย์นิติเวช, คดีสารเสพติด.

Amphetamine
 Amphetamines
 . . . 2014
 (UN Office
 on Drugs and Crime - UNODC)
 . . . 2012 Amphetamine-type
 stimulants ()
 13.94 - 54.81
 0.3 - 1.2 9.4 - 28.24
 0.2 - 0.6 (1)
 amphetamine 5,000
 (*Ephedra sinica*
 (Ma Huang)
 1
Catha edulis
 amphetamine^(2, 3)
 . . . 1887 Amphetamine
 Lazar Edeleanu 1920
 Amphetamine
 Ephedrine⁽⁴⁾
 . . . 1932 Amphetamine sulfate
 Amphetamine hydrochloride
 Gordon Alles⁽⁴⁾
 . . . 1933 Amphetamine
 Benzidrine Inhaler Smith, Kline
 and French (SKF) Oily
 Amphetamine 325
 Benzadrine Sulfate (narcolepsy),
 postencephalitic parkinsonism, attention deficit

hyperactivity disorder (ADHD),
 amphetamine psychosis^(5, 6)
 2 Amphetamine
 1960 Amphetamine
 Amphetamine derivatives Methylene-dioxyampheta-
 mine (MDA) *para*-Methoxy amphetamine
 John F. Kennady Amphetamine 15
 (5, 7)
 Amphetamine levo- isomer
 dextro- isomer
 (8)
 Methamphetamine
 . . . 1919 Akira Ogata
 Methamphetamine
 Ephedrine Pseudoephedrine
 drine Hydriodic Acid Yellow Phosphorus
 Crystal Methamphetamine
 reduction
 Ephedrine Hydriodic Acid Red
 Phosphorus⁽⁹⁾
 Methamphetamine
 " " Methamphetamine Hydrochloride
 " " (ice
 Crystal, Crank, Crystal Meth, Speed)
 100% (8, 10, 11)

Ring-substituted amphetamine (RSAs)

MDEA 13 . . 1987

MDMA, MDA, MDEA, MBDB

"Ecstasy"

RSAs

MDMA

(12)

Amphetamines⁽¹⁵⁾

Amphetamine-Type Stimulants

amphetamines 2

1. Amphetamine

(), Methamphetamine (), Methcathinone, Ecstasy Group (), MDA (), MDEA ()

2. Methylphenidate (MPH), Amphetamine Diethylpropione (DIE), Mazindol, Fenproporex (PPP)

1. MDMA⁽¹³⁾

3,4- Methylendioxyamphetamine (MDMA), Adam, Ecstasy . . 1912 Merck

2. MDA

3,4- Methylendioxyamphetamine (MDA), Love Drug, Tenamphetamine . . 1910 Mannich Jacobsohn . . 1939 . . 1941

parkinsonism

(8, 14)

1960 MDA

(ataraxia)

MDA

(hallucinogen)

MDA

Comprehensive

Drug Abuse Prevention and Control Act . . 1970⁽¹⁴⁾

Amphetamine

Amphetamine (IUPAC Name: 1-Phenylpropan- 2-amine) $C_9H_{13}N$ 135.20622 g/mol (boiling point) 200 - 203 °C 760 mmHg

(flash point) 26.6 °C (density) 0.913 g/mL 25 °C ethyl ether alcohol chloroform

Nitrogen Oxide ⁽⁸⁾

lethylamines β -pheny- Amphetamine

1

3. MDEA⁽¹²⁾

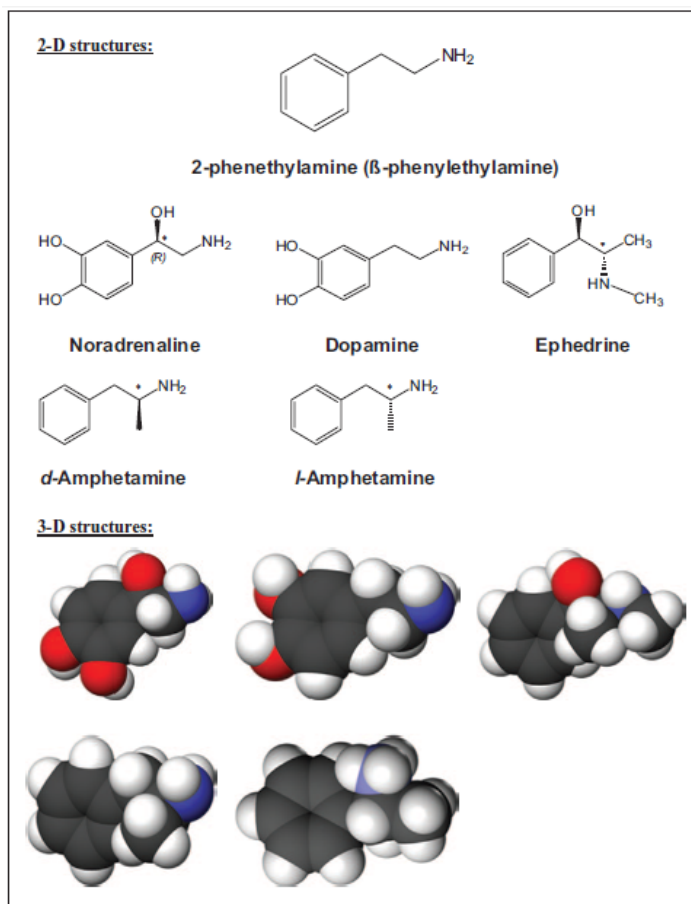
3,4- Methylendioxy-*N*-ethyl-amphetamine (MDEA), MDE, Eve, Intellect . . 1978 - 1980 1980

MDMA

Methamphetamine

Methamphetamine (IUPAC Name: (2S)-N-methyl-1-phenylpropan-2-amine) $C_{10}H_{15}N$ 149.2328 g/mol (boiling point) 212 °C 760 mmHg

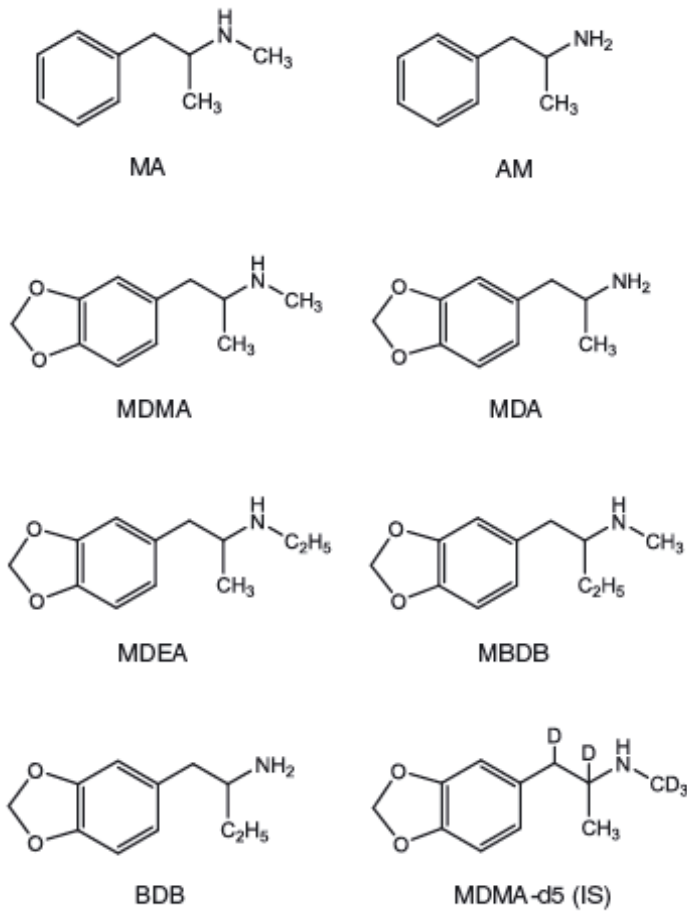
, Ethanol Ethyl Ether Geranium⁽⁸⁾



1. biological active β -phenylethylamines ⁽⁶⁾

* Chiral centre; ; ; ; ; ; ; ;

MDMA	179.21572 g/mol	(boiling point) 80-90 °C
3,4-Methylenedioxyamphetamine	0.2 mmHg	
MDMA (IUPAC Name: 1-(1,3-benzodioxol-5-yl)-N-methylpropan-2-amine)	⁽⁸⁾	
$C_{11}H_{15}NO_2$	(boiling point)	
193.2423 g/mol		
100 - 110 °C	0.4 mmHg	
⁽⁸⁾		
MDEA		
3,4-Methylenedioxy-N-ethyl-amphetamine		
MDEA (IUPAC Name: 1-(1,3-benzodioxol-5-yl)-N-ethylpropan-2-amine)		
$C_{12}H_{17}NO_2$		
207.26888 g/mol ⁽⁸⁾		
MDA		
3,4-Methylenedioxyamphetamine	MDA	
(IUPAC Name: 1-(1,3-benzodioxol-5-yl)propan-2-amine)		Amphetamines
$C_{10}H_{13}NO_2$		
	2	

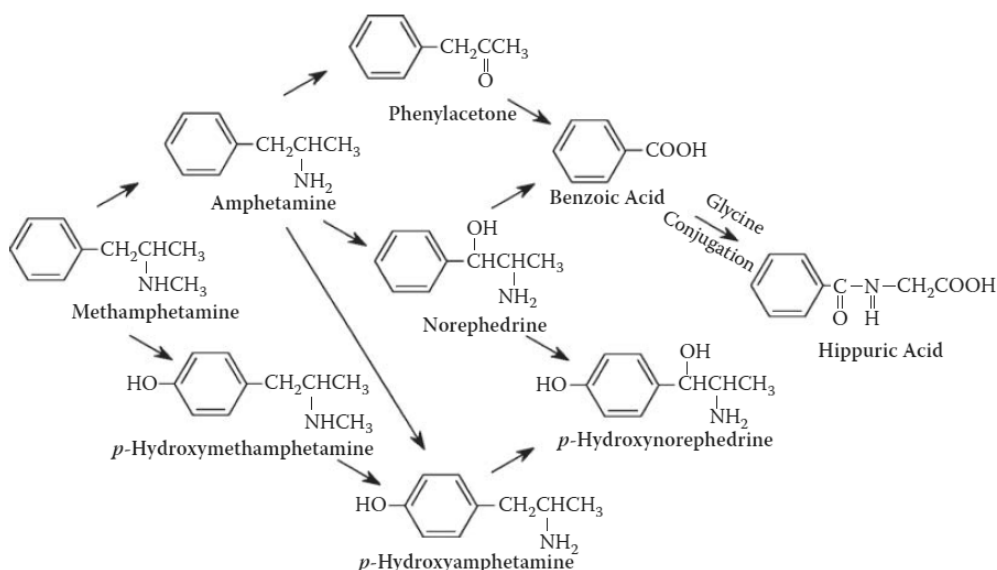


2. amphetamines

(: MA, methamphetamine; AM, amphetamine; MDMA, 3,4-Methylenedioxymethamphetamine; MDA, 3,4-Methylenedioxyamphetamine; MDEA, 3,4-Methylenedioxyethylamphetamine; MBDB, *N*-methyl-1-(3,4-methylenedioxyphenyl)-2-butanamine; BDB, 3,4-(methylenedioxyphenyl)-2-butanamine)⁽¹⁶⁾

Amphetamine	4	d-isomer
β -phenylethylamines	7 - 11	
Noradrenaline	d- l-isomer	pH
(Norepinephrine), Dopamine,	6.7	18 - 34 ⁽¹⁷⁻²⁰⁾
5-Hydroxytryptamine (5-HT; Serotonin)		
Racemic Amphetamine		
Ephedrine ⁽⁶⁾		
	10	8
1. (absorption)		(C _{max}) 1 - 2.5
Amphetamine		3
/		
(C _{max})	(bioavailability)	90% ⁽²⁰⁾

RSAs		RSAs	Amphetamine MDMA
	(12)		18
MDMA	30	30	(20)
60 - 90	4 - 6		
	160 mg MDEA	3.	(metabolism)
MDMA	MDA 3 - 5	Amphetamine	
8 - 12	(12, 20)	3	
		3.1 Deamination	
2.	(distribution)	metabolic pathway	Amphetamine
Amphetamine	Volume of distribution (Vd)	Cytochrome P450 2D6	<i>p</i> -
16 - 20 %	3.5 -	Hydroxyamphetamine	Phenylactone
Amphetamine	4.6 L/kg	Benzoic acid	
	6.1 L/kg	Hippuric acid	Glucuronide Conjugates ⁽¹⁸⁾
	(affinity)	3.2 Oxydation	Amphetamine
Amphetamine ⁽¹⁸⁾	Amphetamine	Norephedrine ⁽¹⁸⁾	
	2.86 : 1 ⁽¹⁹⁾	3.3 Hydroxylation	<i>o</i> -Hydroxynorephedrine (false neurotransmitter) ^(18, 21)
Methamphetamine			
Amphetamine			Amphetamine
(cortical, subcortical	CYP2D6 activity	
regions	white matter) ⁽²⁰⁾		CYP2D6 gene
		22 ^(7, 22)	



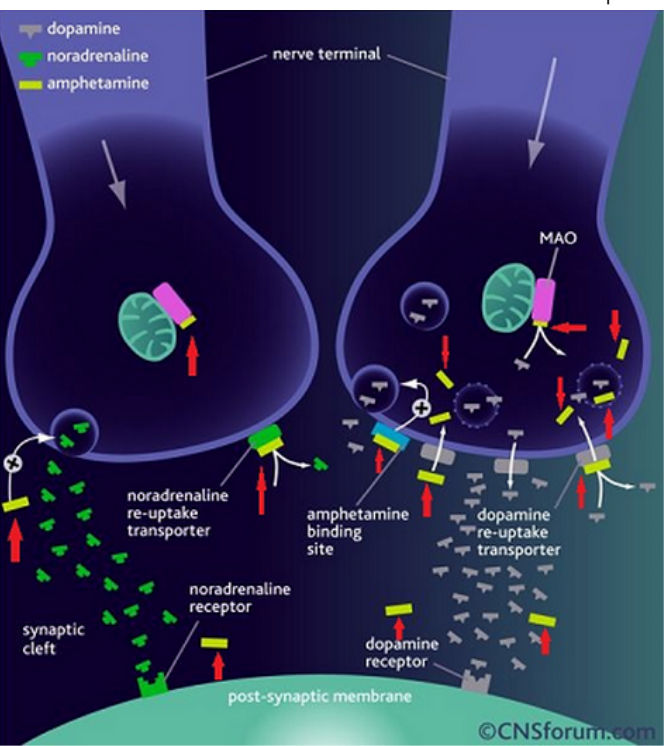
3. metabolic pathway (18)

Methamphetamine				50%, 4-Hydroxymetamphetamine
N-demethylation	Amphetamine	15%,	Amphetamine 10%	
CYP2D6	Metham-	25	(20)	
phetamine				
(20)				
MDMA			MDMA	
4 pathways			24	80%
1.) N-demethylation				20%
2.) O-dealkylation (Demethylenation)			MDMA	
3.) Deamination			6 - 9	(20)
4.) Methylation, Glucuronide, and Sulfate				
conjugation			Monoamine 1	2
	(affinity)		1	
CYP2D6			presynaptic terminal	monoamine
CYP1A2, CYP2B6,	CYP3A4		reuptake transporter	active transport
(20, 23)			terminal	nerve
				Na ⁺ /K ⁺ ATPase
4. (excretion)			2	
Amphetamine		1	(6)	
33% <i>d</i> -isomer	49%			Amphetamine
/isomer	30%			Catecholamines
(7, 18)				substrate monoamine reuptake transporters
Amphetamine				noradrenaline transporter, dopamine
; Hippuric Acid				transporter (DAT), 5-HT transporter (SERT)
16 - 28%, Benzoylglucuronide 4%, <i>p</i> -Hydroxyam-				presynaptic nerve terminals
phetamine 2 - 4%, Norephedrine 2%, Phenylactone				Catecholamines
1%, <i>p</i> -Hydroxynorephedrine				Dopamine
0.5% ⁽¹⁸⁾				
Methamphetamine			Amphetamine	
24	70%		monoamine oxidase	Dopamine
			synapse	Catecholamines
			(6, 7)	
				Amphetamines
				4

4

Amphetamine

(24)



adrenergic

(20, 25)

(paranoid form of schizophrenia)

(20)

Methamphetamine white matter
hypertrophy, hippocampus

matter⁽²⁰⁾

MDMA

(axon),

white matter,

(8, 20)

ruptured cerebral aneurysm

Methylphenedate

(15)

2.2

(15, 20)

Amphetamines

arrhythmia, coronary

spasm, ruptured coronary artery, stress cardiomy-

opathy (e.g. Takotsubo cardiomyopathy), myocardial

infarction/necrosis, heart failure, right ventricle

rupture ventricular hypertrophy

contraction band necrosis

Methamphetamine

myocarditis

MDMA

grey

2.3 (20) fatty changes, sinusoidal dilatation, cholestatic hepatitis, centrilobular necrosis, fulminant hepatic failure

2.4 (20) Amphetamines, muscle perfusion, rhabdomyolysis, myoglobin, fibrin-platelet complexes

2.5 (26, 27) Amphetamine, Methamphetamine, idiopathic pulmonary arterial hypertension, Methamphetamine, talc, interstitial pulmonary fibrosis

2.6 (15) Amphetamines, placental abruption, hypertension (28), Methamphetamine

Ecstasy (12, 28) malformations, Methamphetamine, visual motor integration, verbal memory, long term spatial memory, attention (28)

3. Amphetamine 200 (29) 2 - 3 ug/dL, 50 ug/dL, 200 ug/dL (30) (toxic level) Methamphetamine 0.2 - 5.0 µg/mL (fatal level) 10 µg/mL (31) MDMA 100 - 250 ng/mL 0.5 - 10 mg/L (32) MDA 500 (14)

1. Attention deficit/hyperactivity disorder (ADHD) (15) Methylphenidate ADHD Dopamine, Dopamine transporter, Dopamine 2. Obesity (15) Amphetamine Serotonin Catecholamines

(centers of satiety) Amphetamines Diethylpropion Fenproporex 3. Narcolepsy (33) Methylphenedate

Amphetamine				3. Thin layer chromatography (TLC)
Modafinil	Sodium oxybate			4. Gas chromatography flame ionization detector (GC/FID)
	(34, 35)			5. Fourier transform infrared (FTIR) spectroscopy
	Amphetamines			6. Gas chromatography-mass spectrometry (GC-MS)
				7. High-performance liquid chromatography (HPLC)
				8. ATS
				a. ¹ H-Nuclear magnetic resonance (NMR) techniques
		(36, 37)		b. Capillary electrophoresis (CE)
				c. Solid phase-micro extraction-gas chromatography (SPME-GC)
1.				d. Gas chromatography-fourier transform infrared spectroscopy (GC-FTIR)
a. Color tests				gold standard
i. Marquis test:	Amphetamine			Amphetamines liquid chromatography/mass spectrometry/mass spectrometry (LC/MS/MS) ⁽³⁸⁾
ii. Simon's test:	secondary amines			
Methamphetamine	secondary ring-			
substituted Amphetamines	MDMA MDE			
iii. Chen's test:	Ephedrine,			Amphetamines ⁽³⁹⁾
Pseudoephedrine, Norephedrine, Methcathinone				
Phenylpropanolamine	Amphetamine			
Methamphetamine				
iv. Gallic acid test:	MDMA, MDA			
MDEA Amphetamine	Methamphetamine			
b. Anion tests:				
		63	27	2522
		5		...
Silver nitrate test, Chloride, Bromide, Iodide, Sulphate,	(5)		2545
Phosphate, Sulphate salt test, Phosphate salt test		119	96	30 2545
c. Microcrystal tests:		-	7	
				1
	polarized light			
microscope		-	15	
2. Immunoassay				

- 1
- 15 (2)
375
15
1.5
- 65, 66, 67, 91, 93
65
1 15
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