Research Paper

Poisoned Streets: A Study on High-Purity Synthesis and Toxicological Profiling of Methamphetamine, MDMA, and Aminorex

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ABSTRACT

Background: This paper studies the toxicological assessment alongside high-purity synthesis of three psychoactive and degradative Methamphetamine, Aminorex, and MDMA.

Methods: Each of these compounds was synthesized using novel methodologies, with an emphasis on purity, cartridge yield, and stereoisomeric resolution, where applicable. Analytical-grade products that could undergo toxicological profiling due to meeting rigorous retention criteria were guaranteed to undergo multistep purification and recrystallization.

Results: The true pharmacological and toxicological, whether legal or illegal, is marked for each substance without the removal of contaminating impurities. Distinguished analytical capabilities, for instance, enabled the use of unparalleled analytical methods to correlate some articulated nuclei with their respective neurophysiological, as well as systemic, reactionary constructs. A toxicological and purification prerequisite comparison of the compounds revealed an inequality. Methamphetamine, Aminorex, and ecstasy posed the most neurotoxic potential, while Aminorex and ecstasy posed distinct risks of decomposition.

Conclusion: This sets the framework for synthesis evaluation in toxicological research and forensic analysis.

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Introduction

Methamphetamine, MDMA, and Aminorex are some examples of psychoactive stimulants and are a menace to public health due to their excessive misuse, unreliable pharmacological effects, and growing illegal availability. These compounds, particularly via actions at monoamine transporters, result in addiction and neurotoxicity as well as systemic toxicity. However, street formulations containing byproducts, stereoisomers, adulterants, and degradation products, and hence inconsistent purity, tend to obscure the real pharmacological and toxicological properties and complicate structure-activity relationship (SAR) analysis [1-3]. Impurities not only distort interpretations of a given mechanism but also pose their own toxicological threats. For instance, the methamphetamine that has been synthesized via the poorly done reductions would be expected to carry some traces of mercury, and MDMA would carry some safrole or chloramphetamine or any of the several byproducts termed to be associated with preliminary studies with some degree of hepatotoxicity, as well as false-positive screening. These studies are particularly relevant for MDMA, and for the sake of bias, poorly done studies tend to capture the risks of the compound, leading to misrepresentation of the drug [2].

For example, pure methamphetamine's dopaminergic neurotoxicity and the serotonergic and pulmonary profiles of MDMA and Aminorex show the intrinsic effects of a drug, and the isolating aspects of this method allow thorough comparative toxicology. Forensic identification, harm reduction, and evidence-based policymaking are readily available, thanks to the strong foundation provided by high-purity synthesis, along with analytical characterization (for example, mass spectrometry) and laboratory toxicology. For clinical research, along with diagnostics, to be safe and impurities to be removed, artifacts must be obtained, and regulatory actions must be focused and streamlined [3-10].

Materials and Methods

Methamphetamine Toxicology

Methamphetamine (METH) is well known as 'speed', 'glass', 'crank', 'go', and 'ice', for which it is commercially and clinically important. The WHO claims that over 35 million people worldwide use it. Its misuse has come to be recognized as one of the most pressing public health issues of our time. The toxic effects of METH go beyond the dopaminergic and serotonergic neurons to involve other types of brain and peripheral (To be used sparingly). METH (to be used sparingly) can be taken in through the nose and sublingually. It is known to be distributed throughout the body, including the brain, heart, lungs, liver, stomach, kidneys, eyes, hair, and even breast milk. It is most rapidly taken up in the lungs, heart, and kidneys. The liver and stomach have the slowest uptake, while the brain, liver, and stomach have the slowest drainage (or clearance) time among the organs. [2, 15-17].

The major metabolism of methamphetamine occurs in the liver via the CYP2D6 isoenzyme of cytochrome P450, yielding the p-hydroxymethamphetamine and amphetamine metabolites that are primarily further metabolized to norepinephrine before being excreted in urine. About 37-54% of the dose of the drug is recovered unchanged in the urine. The drug's strong potential for abuse is said to stem from the enhancement of subjective well-being, alertness, and energy monoaminergic empatholytic effects associated with 'pumping' dopamine, along with acute increases in blood pressure and heart rate [18-21].

The drug's high lipophilicity enables rapid diffusion across the blood-brain barrier and into the nerve terminals of the brain via monoaminergic transporters. Neurotoxic substances of methamphetamine induce the degeneration of terminals of dopamine and serotonin, apoptosis of the neurons, and the activation of the astrocytes and microglia, and, in general, the neuroinflammatory responses of the brain. The term 'neurotoxicity' in this context refers to the irreversible or reversible detrimental effects on neuronal structures, as well as permanent or reversible adverse effects on neuronal function, including the disruption of components, degeneration of neurons following injury, and evidence of abnormal behavior [22-24].

Users of METH are likely to develop heart disease, arrhythmias, heart attacks, cardiomyopathy, and heart failure, and do so much sooner than the average person who suffers from cardiovascular disease. They are known to suffer from high levels of reactive oxygen species, superoxide, and the lipid peroxidation product malondialdehyde. METH and the NOX2 oxidative burst theory are integral parts of these complications. In both animal and human models, prolonged use of METH has been shown to result in excess collagen fibrosis and cardiomyopathy, having been shown to induce cardiac fibrosis due to collagen fibrosis. METH also METH affects fibroblasts, which increase periostin, collagen, and smooth muscle actin, which all bind and weave into vastly expanded networks to form cardiac tissue gateways and connective tissue gardens. Cardiac and hydrogenated fat Mac fractures, alongside METH cardiomyopathy, result in the irreversible

breakdown of the connective and cardiac tissue due to the increased levels of periostin. METH also induces a form of apoptosis known as "the depriving death" due to the extreme lack of most cellular ingredients and hydrogenated fats. ELY directs oxygen onto each part of the Mac. Then the fields of cardiology. They lock onto the rest and coil around, forming gateways of tissue on exhale. Autopsy case studies on METH users show high levels of dysfunctional, increased cardiac muscle due to necrotic and excessive muscle, and connective tissue along the death zone. These spaces are veins and arteries that are very close to one another, and there is a massive overflow of hydrogenated fat. Along with the rest of the cardiac tissue, there are interstitial, perivascular, and varying levels of connective tissue between fields and muscle that also appear to be lacking. A weak form of these increased connective fields surrounds necrotic and dying tissue, as well as interwoven bands alongside atherosclerotic tubing [17-25].

The liver has been described as highly sensitive to METH toxicity with a spectrum of presentations ranging from trivial damage to fulminant hepatic failure. Pathological alterations include fibrosis, necrosis, centrilobular ballooning degeneration, hepatomegaly, and hepatitis, which are, in some instances, accompanied by cognitive and psychiatric symptoms. Assays of serum ALT, AST, ALP, and ammonia levels have consistently shown elevated levels in preclinical studies, indicating liver damage and increased membrane permeability. The ultimate mechanisms of METH-induced liver damage remain poorly elucidated. However, they are considered to be possibly associated with hyperthermia, disruption of the CYP1A2 pathway, oxidative metabolism of biogenic amines, hyperammonemia, mitochondrial dysfunction, apoptosis, suppression of cell proliferation, increased neurotransmitter efflux, and bile acid imbalance mediated by the gut microbiome [14-19].

Moreover, the increasing rate of METH consumption has brought forth grave problems concerning deaths associated with its simultaneous consumption of other drugs and suicide, which further emphasizes the necessity for comprehensive toxicological examination of this drug. In the present work, apart from synthesizing high-purity METH, we also conducted previously published toxicological studies, primarily assessing its effects on different tissues of the body, to create a scientific background for understanding the potential systemic actions of the compound synthesized here [17, 22].

Synthesis method for toxicology

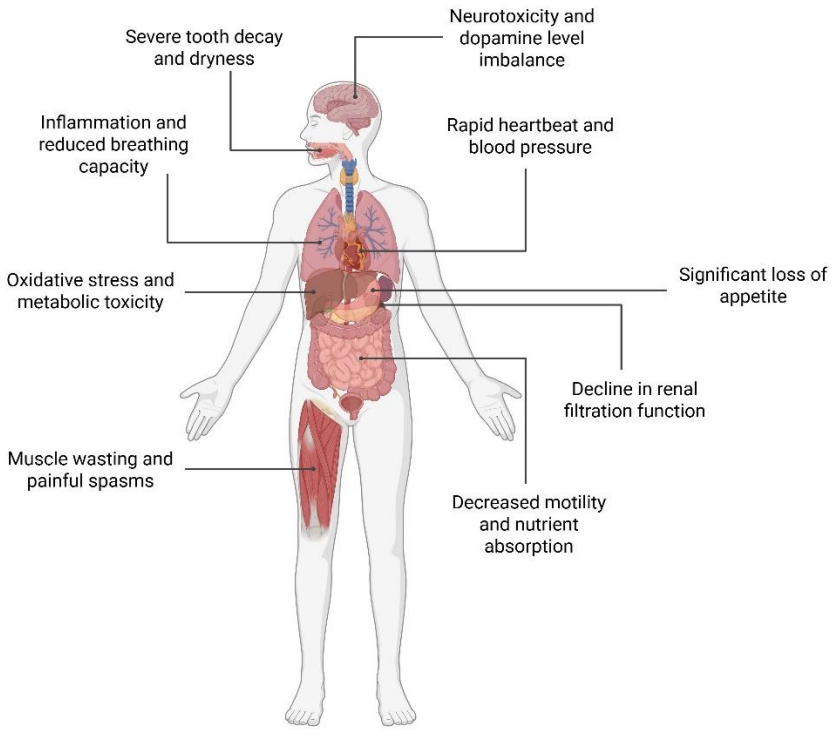

Figure 1. Methamphetamine-induced changes in key organ systems.

Synthesis of Methamphetamine

Phenylacetone (benzyl methyl ketone) was employed as the first precursor. The process of amination encompassed in situ production of methylamine under controlled conditions, and its condensation with the ketone to produce the respective imine intermediate. Reduction was carried out with an aluminium-based system to yield crude methamphetamine free base, which was obtained as oily residue following removal and extraction of solvent [5, 7, 11, 18, 22].

The crude free base was further converted into the hydrochloride salt by acidifying an alcoholic solution to form crystalline methamphetamine hydrochloride, suitable for subsequent treatment. To obtain the pharmacologically active enantiomer, the racemic mixture was resolved through chiral resolution via diastereomeric salt formation using L-(+)-tartaric acid, followed by selective crystallization and re-protonation. The procedure yielded dextro-methamphetamine hydrochloride of high stereochemical purity [4, 5, 11, 14, 22, 23].

The last purification step was achieved through recrystallization from binary solvent systems, resulting in pure crystals of d-methamphetamine hydrochloride suitable for toxicological and forensic analysis [11, 17].

MDMA

a. MDMA Toxicology

3,4-Methylenedioxymethamphetamine (MDMA), commonly referred to as ecstasy, is a synthetic psychoactive drug with a complicated neuropharmacological and toxicological profile. As an entactogen, MDMA's pharmacological profile is different from, yet also partially similar to, that of the classical hallucinogens and stimulants. Despite its Schedule I status in the majority of countries, MDMA remains widely abused, particularly by adolescents and young adults, and continues to receive much scientific and public attention due to its distinctive psychoactive effects and associated health risks. Mechanistically, MDMA is a potent indirect monoaminergic agonist, inducing non-exocytotic release and blocking reuptake of serotonin (5-HT), dopamine (DA), and norepinephrine (NE). These neurochemical actions underlie its hallmark effects, including euphoria, increased empathy, sociability, and sensory enhancement (Figure 3). However, these actions also underlie a wide variety of adverse effects, ranging from agitation, tachycardia, hyperthermia, serotonin syndrome, and serotonergic neurotoxicity. Exposure over the long term or in high doses has also been associated with oxidative stress, mitochondrial dysfunction, and excitotoxic injury, particularly to serotonergic circuits. Neuroimaging studies in chronic MDMA users have revealed reductions in gray matter volume and altered patterns of activation in the prefrontal, temporal, and occipital cortices [26-30].

Pharmacokinetically, MDMA displays nonlinear elimination kinetics, primarily because of autoinhibition of cytochrome P450 2D6 (CYP2D6), its major metabolic enzyme. The drug undergoes two predominant hepatic biotransformations: N-demethylation, which produces the active metabolite 3,4-methylenedioxyamphetamine (MDA), and O-demethylation, resulting in catechol derivatives 3,4-

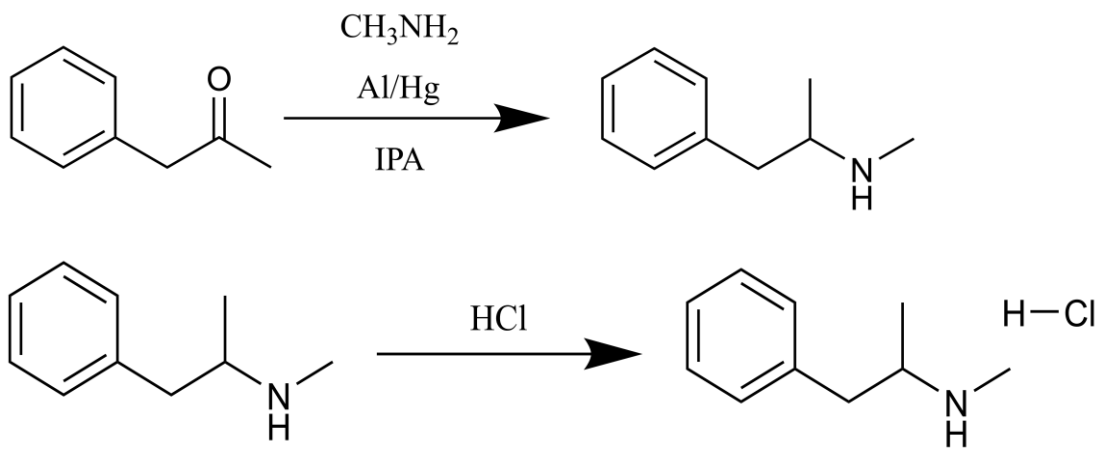

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Figure 2. Mechanism of synthesis and formation of methamphetamine.

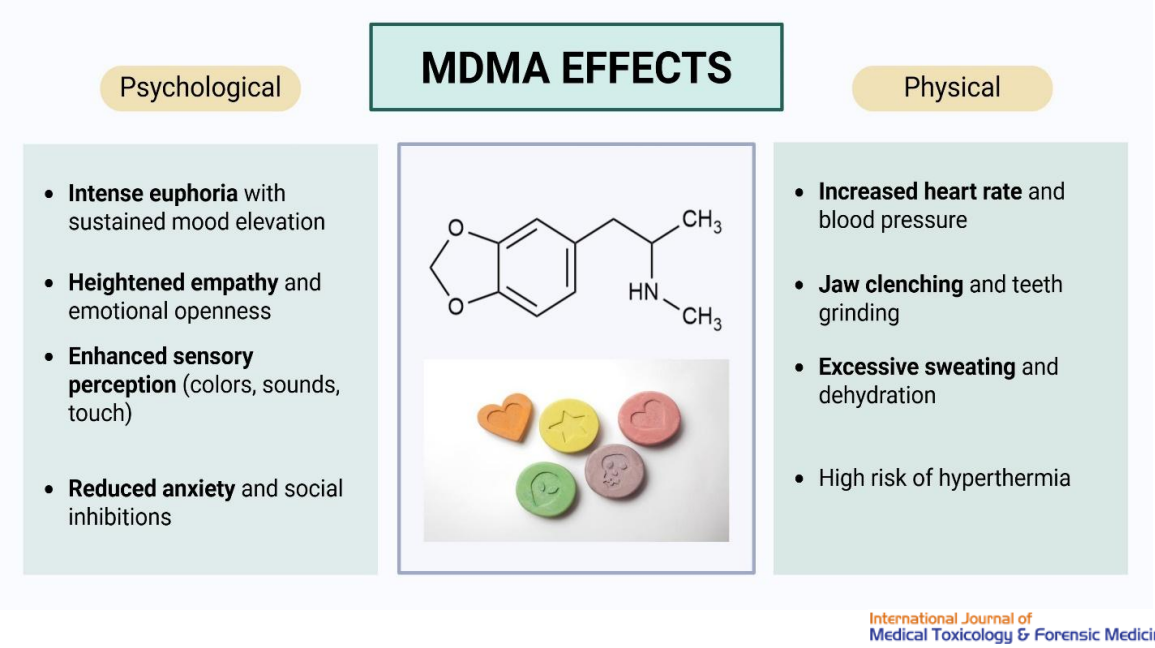


Figure 3. Overview of MDMA effects on the mind and body.

dihydroxy-1-(methylenedioxy)amphetamine (HHMA) and 3,4-dihydroxyamphetamine (HHA) [30-31].

These metabolites may then be conjugated or undergo redox cycling, processes that generate reactive oxygen species (ROS) and result in cellular damage [31].

Stereochemistry further complicates MDMA's pharmacology, as the drug exists in two enantiomeric forms: S-(+)-MDMA and R-(–)-MDMA. The S-enantiomer is more stimulant and empathogenic, and is also metabolized more rapidly due to its higher affinity for CYP2D6. Enantioselective metabolism is of paramount significance in determining individual susceptibility to the therapeutic and toxic actions of MDMA. Furthermore, genetic polymorphisms in CYP2D6 are a significant source of interindividual variability, classifying individuals as poor, intermediate, extensive, or ultrarapid metabolizers. Poor metabolizers represent approximately 5–10% of Caucasians, a phenotype that is associated with significantly higher plasma drug concentrations and longer pharmacodynamic responses [32-39].

The toxic effects of MDMA vary from mild sympathomimetic symptoms to severe, life-threatening events. Acute toxicity may involve hyperpyrexia, liver failure, cardiac arrhythmias, hyponatremia, and seizures. Deaths are usually multifactorial in character, frequently influenced by polydrug use, genetic susceptibility, and environmental stresses [39, 40].

MDMA also has a high potential for drug–drug interactions. It is a potent inhibitor of CYP2D6 and CYP3A4 but induces CYP1A1 and UGT1A1, thereby influencing the metabolism of numerous co-administered medications. Its concomitant use with selective serotonin reuptake inhibitors (SSRIs) can attenuate MDMA's desired psychoactive effects, potentially resulting in dose escalation. In contrast, co-administration with monoamine oxidase inhibitors (MAOIs) markedly increases the risk of serotonin syndrome [28, 33].

Aside from its well-documented neurotoxicity, hepatotoxicity, nephrotoxicity, and hyperthermia, recreational MDMA use has been linked with a broad array of cardiovascular complications. Clinical and case series evidence show that MDMA has the acute effect of raising heart rate and blood pressure and can be a precipitating cause of reversible cerebral vasoconstriction syndrome (RCVS). Chronic use has been associated with structural and histopathological cardiac changes, including myocardial hypertrophy, interstitial fibrosis, and microvascular injury [37].

Although such toxic effects are increasingly recognized, the precise underlying mechanisms, particularly those mediated by active or reactive metabolites, remain largely undefined. In summary, MDMA possesses a complex toxicological profile that is shaped by its stereochemistry, metabolism, and subject-related factors, including genetic polymorphisms and concomitant use of other drugs [38, 39].

b. Synthesis of MDMA

MDMA is also synthesized from 3,4-methylenedioxyphenylpropan-2-one (MDP2P) through several controlled laboratory processes. One such

process involves the production of an N-formyl intermediate from N-methylformamide and formic acid, followed by hydrolysis and transformation into the free base. This is subsequently transformed into crystalline MDMA hydrochloride and recrystallized for purification [33, 37, 39].

Another scalable process uses sodium borohydride reduction of an MDP2P methylamine imine. It yields MDMA free base after acid–base manipulation and distillation, which is further converted to MDMA hydrochloride crystals on acidification and recrystallization [22-38].

Other techniques are used to achieve analytical-grade purity. These include acetone washing for removing non-polar byproducts from crude material or from clandestine samples, and recrystallization using isopropanol, which cleans polar impurities and produces high-quality, large crystals [22-58].

Together, they supply MDMA hydrochloride of known stereochemistry, reproducibility, and purity that is appropriate for toxicological and forensic examination [20, 22, 38, 44-57].

Aminorex

a. Aminorex Toxicology

Aminorex, an amphetamine like compound, has been found in horses, dogs, and humans exposed to the levamisole cocaine adulterant. Levamisole is now one of the most common global adulterants in cocaine, having been identified in nearly 70% of tested samples [41-45].

Pharmacologically, aminorex is a monoamine transporter inhibitor, exhibiting greater inhibition at the NET and DAT compared to SERT. Cocaine-like in its potency, it has been variably characterized as a transporter substrate or inhibitor, which elevates extracellular dopamine and serotonin. Used initially as an appetite suppressant during the 1960s, it remains of toxicological interest [59-60].

Side effects of aminorex and its analogues are agitation, insomnia, panic attacks, psychosis, hallucinations, hyperthermia, tachycardia, nausea, jaw clenching, and sweating. Both aminorex and levamisole affect serotonin metabolism and have been linked to idiopathic pulmonary hypertension (IPH), a condition that can be fatal [61, 62].

Toxicological case reports also implicate aminorex derivatives, and more specifically 4,4′-DMAR, in some fatalities. Effects reported are cerebral edema, seizures, hyperthermia, respiratory and cardiac arrest, and internal bleeding, underlining the lethality of these drugs [63].

b. Synthesis Aminorex

The starting material 2-amino-1-(4-methylphenyl)propan-1-ol (4-methylnorephedrine) was prepared by stepwise bromination of 4-methylpropiophenone, conversion to sodium diformylamide, subsequent hydrolysis of the intermediate product, and reduction with sodium borohydride. The β-amino alcohol was thereby isolated as a solid, crystalline compound, ready for use in subsequent reactions [63-65].

Cyclization of the β-amino alcohol with cyanogen bromide in methanol and a basic work-up provided (±)-

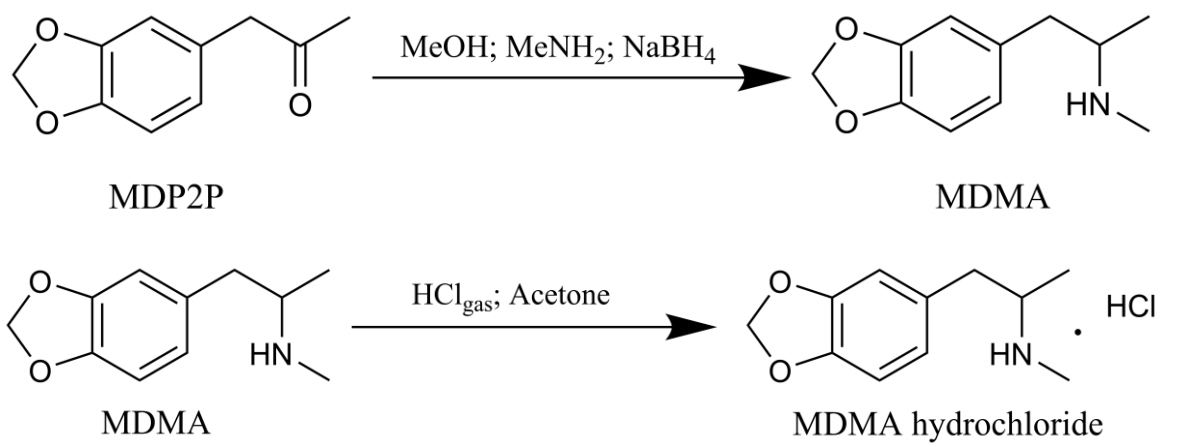


Figure 4. Mechanism of synthesis and formation of MDMA.

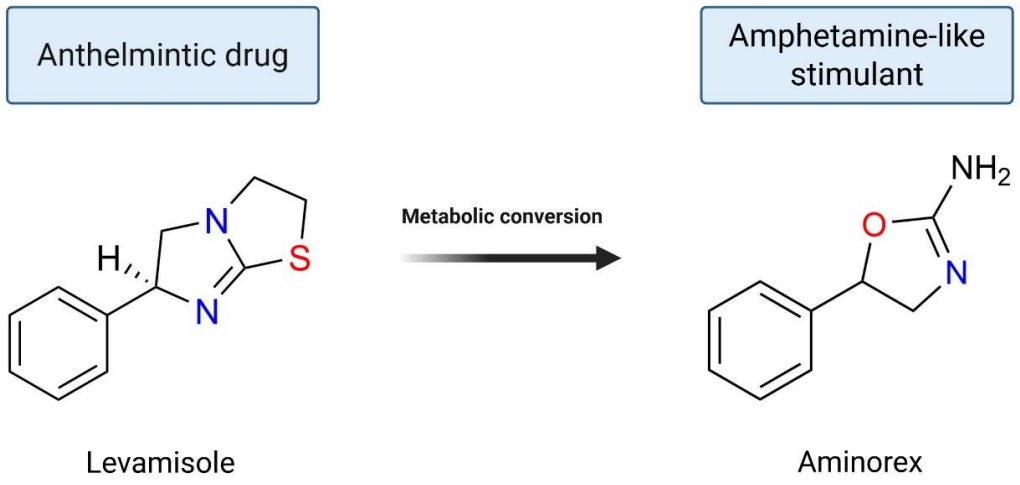


Figure 5. Metabolic conversion of levamisole to Aminorex.

cis-4-methyl-5-(4-methylphenyl)-4,5-dihydrooxazol-2-amine ((±)-cis-4,4-DMAR). The final crystalline powder was recovered after precipitation, filtration, and drying and was accessible to purification and analytical evaluation [66-71].

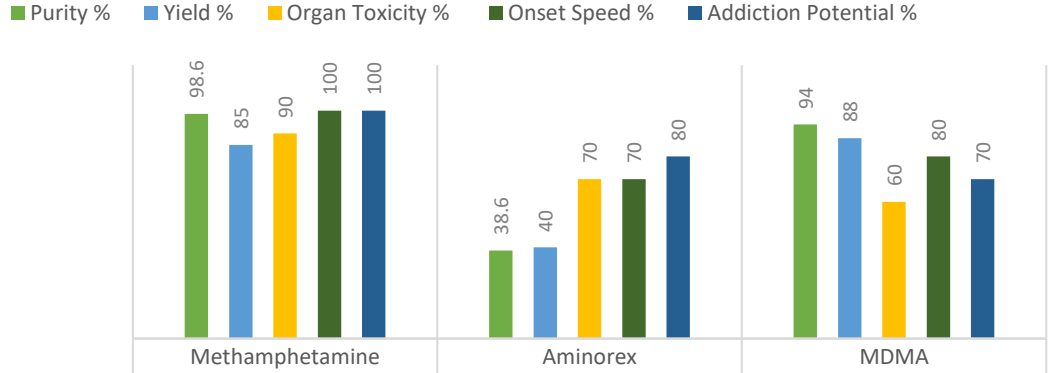
Results and Discussion

Reference quality, high-purity methamphetamine, MDMA, and aminorex samples were prepared through multistep purification and crystallinity analysis. Analytical confirmation was ensured through reproducible Mass spectrum profiles and compound-specific fragment ions for dependable identification. These preparations, in contrast to seized street samples that are often contaminated or stereochemically non-uniform, minimize confounding variables in toxicological studies.

Purity: The highest purities were obtained for substances with crystalline end products and distinctive analytical signatures. Ketamine and aminorex were characterized by halogen isotopic and heterocyclic signatures, which facilitated the elimination of co-eluting impurities. MDMA had to be strictly controlled upstream to prevent the formation of aromatic byproducts (Table 1) [8-60].

Yield: Yields ranged from moderate to high based on susceptibility to side reactions or rearrangements.

Table 1. Comparison of three psychoactive substances.



	Methamphetamine	Aminorex	MDMA
Purity %	98.6	38.6	94
Yield %	85	40	88
Organ Toxicity %	90	70	60
Onset Speed %	100	70	80
Addiction Potential %	100	80	70

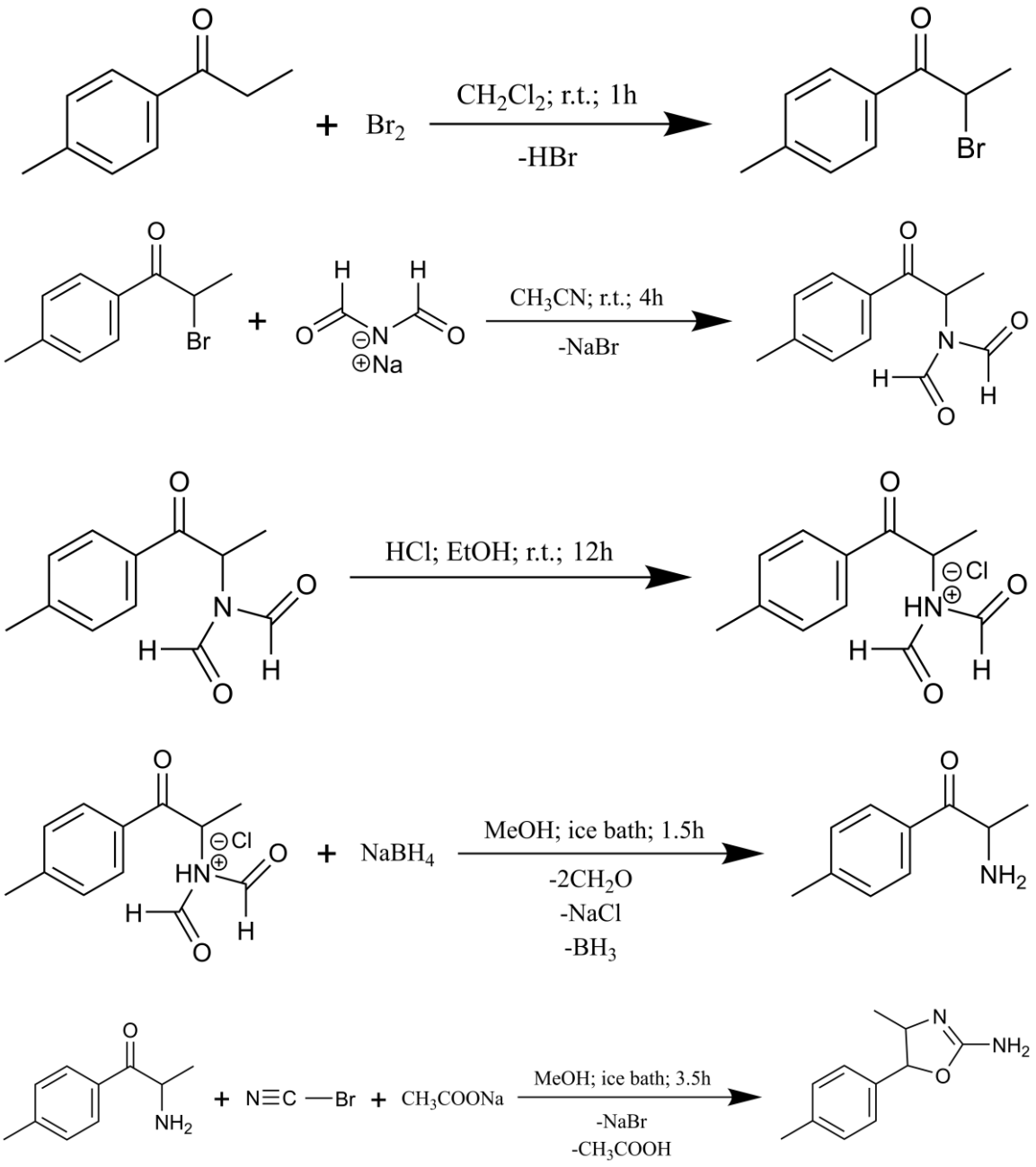


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Figure 6. Mechanism of synthesis and formation of DimethylAminorex.

Notably, purity rather than yield was given precedence to attain toxicological acceptability (Table 1) [19-45].

Onset & Duration

Pharmacokinetic profiles consistent with the literature: methamphetamine had a rapid onset, and MDMA had a retarded entactogenic profile. Pure samples reduced the variability of observations in onset time [13-22].

Addiction & Toxicity

Methamphetamine: Maximum for abuse liability, related to dopamine norepinephrine transporter activity, cardiovascular stress, and neurotoxicity. Destructive effects were evident even in pure samples, regardless of the presence of adulterants [1-30].

MDMA: Risks of toxicity centered on serotonergic and hyperthermic action. Purification of aromatic impurities determined hepatotoxicity to be partly a

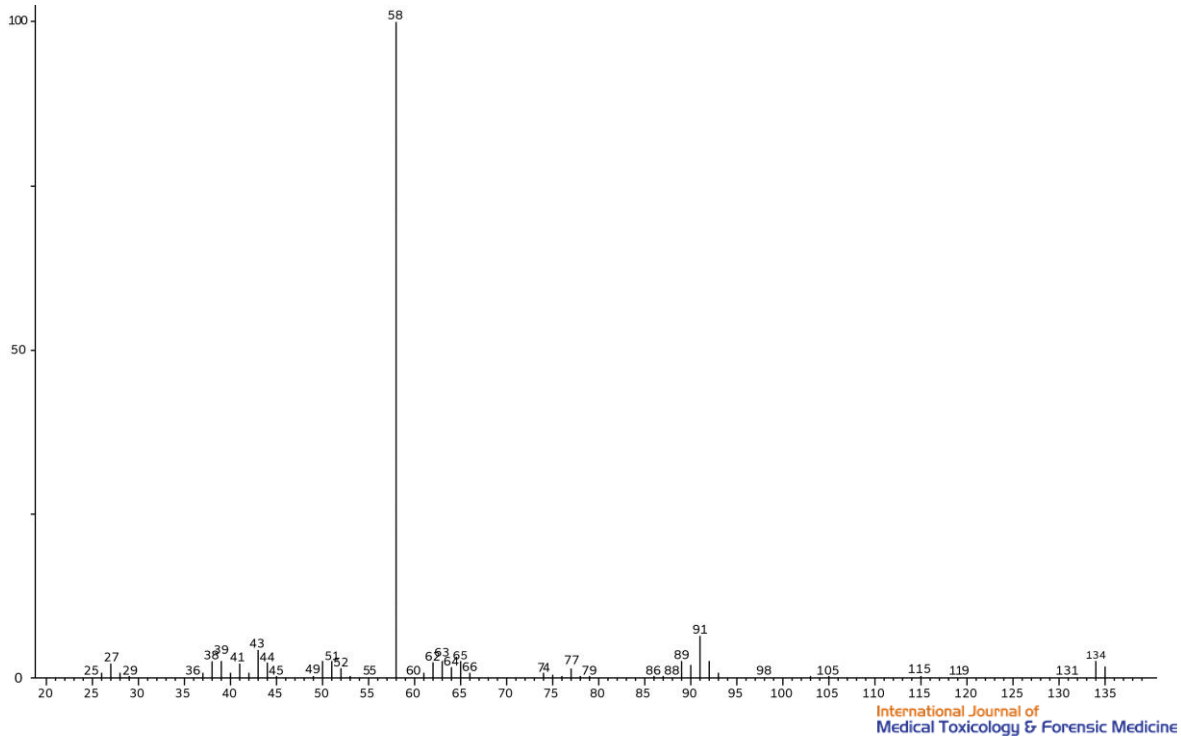

Figure 7. Mass spectrum of Methamphetamine.

Table 2. Mass spectrum Fragmentation Pattern of Methamphetamine.

m/z (Peak)	Likely Fragment / Marker	Interpretation & Forensic/Toxicological Note
58 (Base peak)	Isopropylamine fragment (–$CH(CH_3)_2$–NH_2^+)	Diagnostic ion; major marker for methamphetamine due to cleavage of the side chain.
91	Tropylium cation ($C_7H_7^+$)	Indicates aromatic ring structure; a well-known marker in phenethylamine-type drugs.
134	Molecular fragment related to the intact skeleton	Supports identification of methamphetamine; confirms phenylalkylamine framework.

consequence of impurities as opposed to the parent compound [25-55].

Dimethylaminorex (DMAR): Low-level stimulant toxicity, but linked with serious adverse effects; purified material highlights the mechanisms of its pulmonary vascular effect [59-70].

Impurity Profile & Methodological Value

Reference-grade materials enabled (1) exclusion of heavy metal halogen residues that would contaminate toxicity assays, (2) establishment of a clean spectral library for Mass spectrometry, and (3) enhanced metabolite mapping in biological samples with increased forensic attribution and reduced analytical errors.

Limitations

Experimental conditions (stoichiometry, scale) were not disclosed for safety. Toxicological interpretations relied on published literature rather than new human studies; variability and polydrug

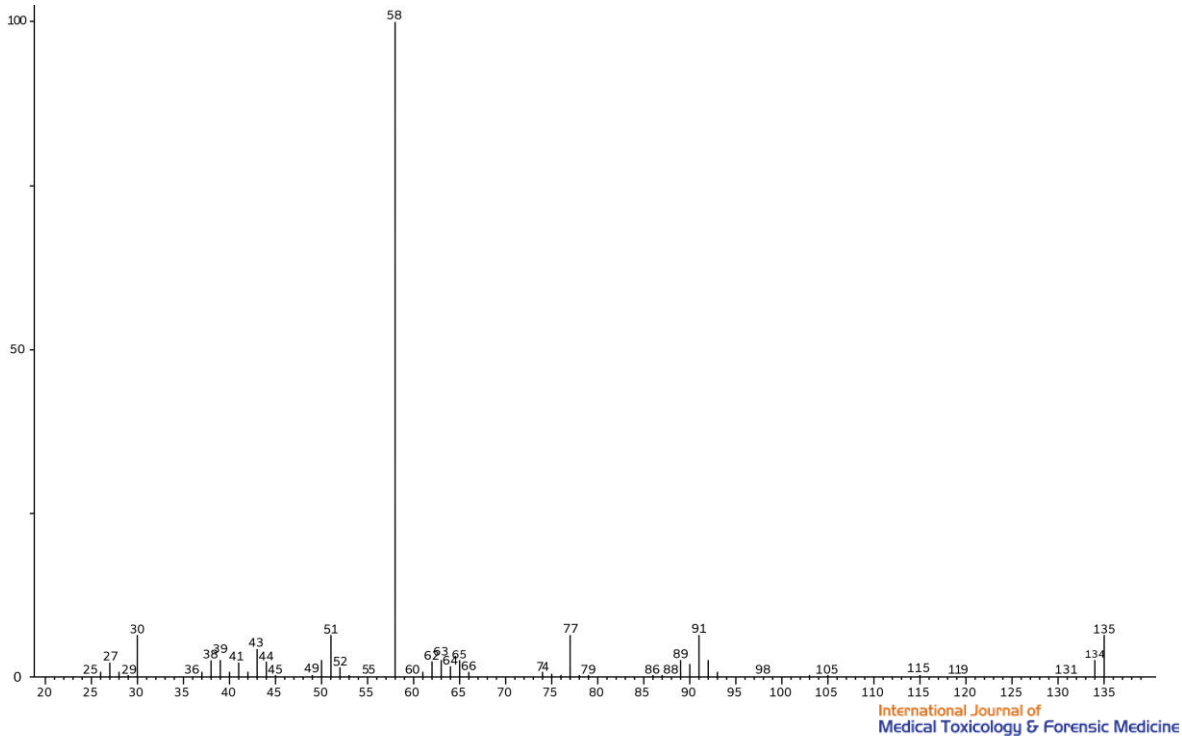

Figure 8. Mass spectrum of MDMA.

Table 3. Mass spectrum Fragmentation Pattern of MDMA (Ecstasy).

m/z (Peak)	Likely Fragment / Marker	Interpretation & Forensic/Toxicological Note
58 (Base peak)	Isopropylamine fragment (–$CH(CH_3)_2$–NH_2^+)	Major diagnostic ion of MDMA; common to methamphetamine derivatives due to side-chain cleavage.
135	Methylenedioxybenzyl cation ($C_8H_7O_2^+$)	Highly diagnostic marker for MDMA and related ring-substituted phenethylamines.
134	Aromatic fragment ion ($C_9H_{10}NO^+$)	Supports presence of substituted phenyl ring; confirms MDMA identity.
91	Tropylium ion ($C_7H_7^+$)	Indicates aromatic ring; shared with other amphetamine analogs but relevant in MDMA confirmation.
43,51,65,77	Small alkyl/aromatic fragments	Small alkyl/aromatic fragments Secondary cleavage ions; aid in differentiation from methamphetamine.

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interactions remain confounding factors.

Implications & Future Directions

Forensic science: Reference spectra of high purity contribute to the validity of drug confirmations and novel analog detection [18, 22, 38].

Toxicology: Pure molecules facilitate mechanistic studies of transporter selectivity, toxicity of metabolites, and cardiometabolic risks [17-22].

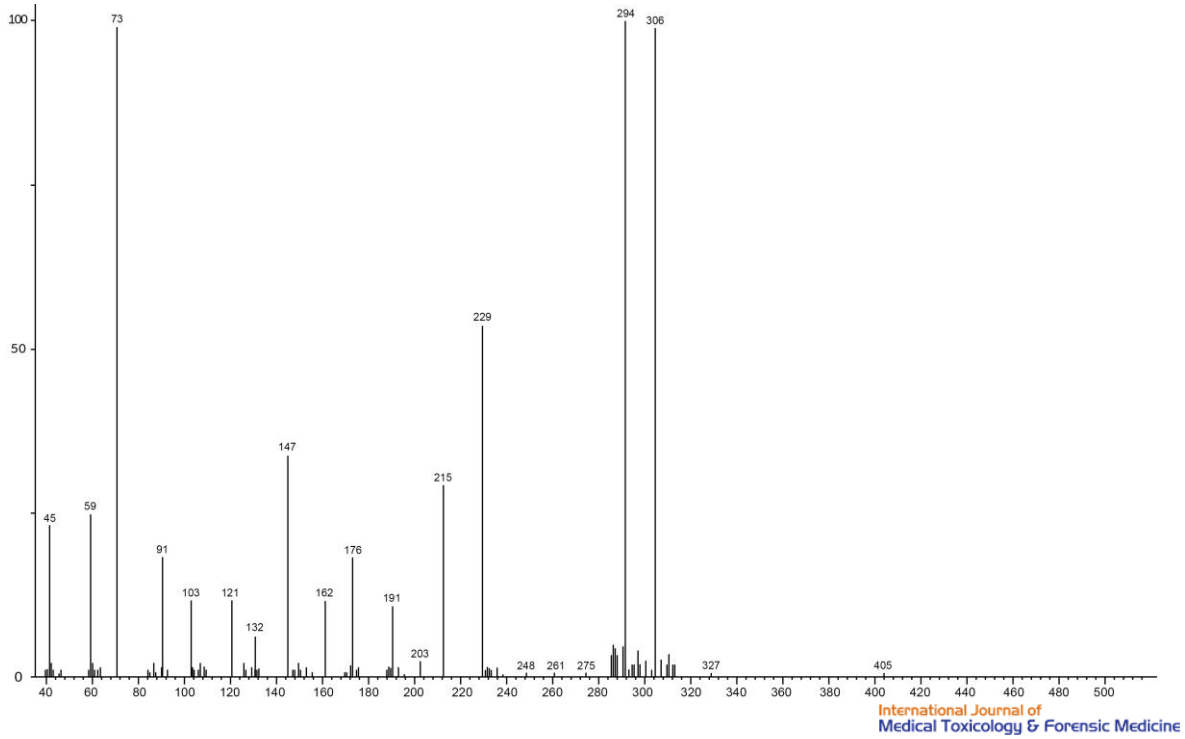

Figure 9. Mass spectrum of Aminorex.

Table 4. Mass spectrum Fragmentation Pattern of Aminorex.

m/z (Peak)	Likely Fragment / Marker	Interpretation & Forensic/Toxicological Note
45,59	$C_2H_5N^+$ / CHO^+	Small amine/oxime fragments; common low-mass ions.
73 (Base peak)	$C_3H_7N^+$ (fragment from amino group)	Major diagnostic ion; confirms presence of amine functionality.
91	Tropylium ion ($C_7H_7^+$)	Benzyl/phenyl-based fragmentation; strong aromatic contribution.
147	$C_9H_9NO^+$	Stable fragment including aromatic + N–O group.
176	$[C_9H_{10}NO_2]^+$	Key marker fragment of aminorex structure.
191	$[C_9H_9N_2O_2]^+$	Diagnostic fragment supporting aminorex
229	$[M–77]^+$ (Molecular ion – tropylium)	Strong secondary molecular-related fragment.
294,306 (Molecular ion region)	$[M]^+$ / adducts (derivative/residual)	Presence of molecular ion ~306 m/z consistent with aminorex derivative confirmation.

Public health & policy: Findings highlight that intrinsic risk is indeed present even in the absence of adulterants, vindicating the justification for regulation, surveillance, and harm-reduction strategies aimed at parent compounds per se [33-39].

Conclusion

We have thoroughly investigated three ideal psychoactive drugs, methamphetamine, MDMA, and aminorex, focusing on high-purity synthesis, analytical confirmation, and toxicological interpretation [14–28]. By maintaining purity at the reference level, we have

minimized confounding from impurities and clearly characterized the intrinsic pharmacological and toxicological signatures of the compounds.

Key findings are:

Analytical reliability: The mass spectrum identification of all compounds was invariably reproducible, yielding diagnostic fragmentation and high-quality reference spectra for forensic and clinical laboratories (Figures 7-9).

Purity as a measure of resolution: Removal of byproducts and impurities eliminated toxicological uncertainty, particularly in MDMA, where toxic effects were erroneously attributed to the parent drug rather than impurities.

Distinguishing addiction and toxicity: Comparative analysis verifies the elevated abuse potential of methamphetamine, highlighting the complex serotonergic risk profile of MDMA, and verifies the dual potential of aminorex for severe adverse effects, whereas its moderate stimulant potency (Table 1).

Public health implications: The findings confirm that intrinsic dangers exist even in pure substances. Therefore, harm reduction interventions, clinical surveillance, and regulatory plans must not only aim to cut agents but also specifically counter the pharmacological risks of the pure chemicals themselves.

This work contributes to the field by providing a comprehensive dataset for comparative studies between compounds, paving the way for further research on stereochemistry, metabolism, and semiodynamics over prolonged periods under rigorous analytical control. In the future, high-resolution orthogonal approaches, coordinated with targeted metabolomics studies, will become imperative to shed light on the mechanistic pathways of harm and thus inform public health policy and interventions. Finally, our findings send a **two-fold message:** clear science is enabled by purified synthesis, yet also refers to the unreduced dangers in these psychedelics. Forensic laboratories, clinicians, and policymakers alike can benefit from recognizing that while adulterations complicate toxicity, the underlying chemicals themselves remain potent drivers of public health issues.

Ethical Disclaimer

All synthetic methods described in this paper are intended for use in forensic, analytical chemistry, and toxicology applications only. No specific quantities, ratios, or complete operational procedures are disclosed to allow them to be duplicated for illicit purposes. The goal is to enhance analytical accuracy, facilitate the forensic identification of controlled substances, and support public health and law enforcement activities. All experiments were performed in licensed facilities under rigid regulatory and safety guidelines.

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None.

Conflicts of Interest

The authors report there are no competing interests to declare.

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