New and emerging psychoactive substances [1]

research chemicals, analogues, legal highs, herbal highs, synthetic drugs, designer drugs, novel psychoactive substances, bath salts

What are new and emerging psychoactive substances?

There are multiple terms in use globally that refer broadly to new, novel or emerging drugs. Terms such as ‘designer drugs’, ‘research chemicals’ and ‘emerging psychoactive substances’ are often used interchangeably
New Psychoactive Substances (NPS)
These are substances that are not controlled by the 1961 Convention on Narcotic Drugs [2] or the 1971 Convention of Psychotropic Substances [2], but which may pose a public health threat similar to drugs that are listed in these conventions.

Designer drugs
Designer drugs are manufactured to mimic the effects of a controlled substance. These close copies are referred to as ‘analogues’. The purpose of creating these analogues is to avoid detection or classification as ‘illegal’.

Emerging psychoactive substances (EPS)
This is a term used to describe psychoactive drugs that are relatively new to recreational drug markets. This term captures all NPS as well as drugs that may not be newly invented, but have recently experienced a resurgence, or increase in use.

Research chemicals
These are experimental chemicals not approved for human use; many of these chemicals were discovered in labs and examined in test-tubes (in vitro) or in low-level animal studies.

The terms ‘synthetic drugs’ and ‘legal highs’ can cause confusion when used to refer to NPS. This confusion stems from:

1. the fact that many ‘traditional’ illegal drugs, such as LSD, methamphetamine and MDMA (ecstasy), are also synthesised; and
2. many countries (including Australia) have moved to prohibit these substances, despite remaining ‘legal’ at the international level.

This section focuses on NPS as defined above; however, it also looks at some EPS (2C series, DMT).

The NPS market has grown rapidly over the past decade and currently encompasses hundreds of different substances, which can be classified into a number of different categories (outlined below). In Australia, synthetic cannabinoids have been the most widely used NPS, although stimulant and psychedelic NPS are also relatively common.

Synthetic cannabinoids
Synthetic cannabinoids (eg, Spice, K2, Kronic, Northern Lights, Kaos) are substances that are functionally similar to the primary substance responsible for the psychoactive effects of cannabis. They are generally sold in foil sachets and typically contain 1-3 grams of dried plant matter onto which the synthetic cannabinoid has been sprayed. More recently, liquid products containing synthetic cannabinoids have emerged for use with electronic cigarettes.

While the side effects of cannabis are well known, information on the health risks associated with synthetic cannabinoid use remains limited. Research to date suggests that the adverse effects of synthetic cannabinoid use may include:

- cardiovascular events
- acute kidney injury
- seizures
- psychiatric problems
Phenethylamines

Phenethylamines refer to a class of drugs with psychoactive and stimulant effects and includes amphetamine, methamphetamine and MDMA (ecstasy) — all of which are controlled under the 1971 Convention of Psychotropic Substances and are therefore not classified as NPS. Examples of phenethylamine NPS in Australia include the ‘2C series’, the NBOMe series, PMMA, and benzodifurans (Bromo-Dragonfly).

The 2C series are a group of psychedelic phenethylamines, with 2C-B being the most frequently reported ‘new’ phenethylamine. 2C-B has been described as a cross between LSD and ecstasy and is usually consumed in either powder or pill form. 2C-B first gained popularity internationally in the mid-1980s and was brought under international control in 2001, which means that it is no longer strictly classified as an NPS (as is the case with a number of the 2C series). However, in the Australian context, 2C-B is often still considered to be an ‘emerging’ psychoactive substance due to the fact that it is relatively new to the recreational drug scene.

The NBOMe series are a group of phenethylamines that contain an N-methoxybenzyl group. The most common of the NBOMe series are derivatives of the 2C-series (but more potent) and appeared on recreational markets in 2010. Compounds of the NBOMe series are not active when swallowed, and are usually taken by placing them under the tongue (sublingually). There have been reports of NBOMe being sold as LSD (when deposited on blotter paper LSD and NBOMe are virtually identical in appearance), which is concerning given that the effects of NBOMe are active at very low doses. Information on the health risks associated with use of these drugs is limited, however research suggests that the adverse effects of NBOMe toxicity may include:

- cardiovascular complications
- agitation
- seizures
- elevated body temperature (hyperthermia)
- imbalance of acids in the body (metabolic acidosis)
- abnormally fast heartbeat (tachycardia)
- organ failure
- death.

Synthetic cathinones

Synthetic cathinones are closely related to the phenethylamine family and typically have an amphetamine-type analogue. Examples of synthetic cathinones in Australia include Mephedrone (‘Meow Meow’, ‘M-CAT’); Methylone; MDPV (‘Ivory wave’); alpha-PVP (‘flakka’).

Synthetic cathinones first appeared in drug markets in the mid-2000s, with methylone the first to be reported. Mephedrone is perhaps the most well-known of the synthetic cathinones — it first appeared online as an NPS between 2007 and 2009 (although reported to have first been synthesised in 1929). Mephedrone became increasingly common in Europe; however, it never gained much prominence in Australia. Mephedrone is mostly available in powder form, although it can also be pressed into pill form, and is usually snorted or ingested. Research suggests that some of the health risks associated with the use of synthetic cathinones may include:

- anxiety
- agitation
- chest pain
- abnormal sensation, typically tingling or prickling of the skin (paraesthesia)
- heart palpitations
- seizures
- abnormally fast heartbeat (tachycardia)
- high blood pressure (hypertension)
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- dependence.

Tryptamines

Some tryptamines are natural neurotransmitters (brain chemicals), but most are psychoactive hallucinogens found in plants, fungi and animals. For information on natural tryptamines, see Natural hallucinogens [3].

DMT does not fall under the NPS definition mentioned above, but it could be classified as an emerging psychoactive substance in that it is relatively new to Australia’s recreational drug scene. 5-MeO-DMT is a powerful psychedelic that is found in a wide variety of plant species, and in the venom of the Bufo alvarius toad. It has been used by South American shamans for thousands of years, and was first synthesised in 1936. It is similar to DMT in effects, however it is substantially more potent and is usually smoked or snorted. Little is currently known about the short and long-term health effects of tryptamine use.

Piperazines

Piperazines have been described as ‘failed pharmaceuticals’, and are frequently sold as ecstasy due to their central nervous system stimulant properties. They are usually available in pill, capsule or powder form and are usually swallowed. Benzylpiperazine (BZP) is one of the most commonly reported piperazine NPS and was initially developed as a potential antidepressant drug. However, it was found to have similar properties to amphetamine and was therefore considered liable to abuse. BZP is often used in combination with trifluoromethylphenylpiperazine (TFMPP) to produce similar effects to ecstasy, however with less potency. Many of the piperazine NPS have limited information regarding the short and long term health effects of their use. Research suggests that some of the health harms associated with BZP and TFMPP use may include:

- headaches
- tremors
- poor concentration
- palpitations
- vomiting
- anxiety
- confusion
- increased body temperature (hyperthermia)
- destruction of muscle cells
- kidney failure
- seizures
- dizziness
- dilation of the pupils
- insomnia
- urine retention.

Novel benzodiazepines

Novel benzodiazepines are less well categorised and understood than other NPS; their interaction with the human body, as well as how similar they are to established agents, remain relatively unknown. Pyrazolam was the first novel benzodiazepine to appear as an NPS, having originally been a research trial drug that did not proceed to clinical use. Other novel benzodiazepines that have appeared online include:

- diclazepam
- fubromazepam
- clonazolam
- deschloroetizolam
- fubromazolam
- nifoxipam
- meclonazepam
- etizolam.
None of these have been approved for medicinal use in any country. Little is currently known about the short and long-term health effects associated with the use of novel benzodiazepines.

**Other NPS**

There are a range of other NPS categories including:

- aminoidanes (for example, MDAI)
- arylcyclohexylamines (for example, Methoxetamine); a class of compounds which typically produce dissociative anaesthesia, a form of anaesthesia that does not necessarily cause unconsciousness but produces other affects such as analgesia, catatonia and amnesia
- ketamine [4]; classified as a NPS since it is not controlled under UN conventions
- opioids (for example, fentanyl analogues)
- plant-based NPS (plants with psychoactive properties; for example, kratom, khat [5], Salvia divinorum [3]).

**How common is the use of synthetic drugs?**

The 2016 National Drug Strategy Household Survey found that 0.4% of Australians aged 14 and over have ever tried any type of emerging psychoactive substances (EPS), while 0.3% used EPS in the year preceding the survey. The 2013 Survey was the first to collect data on use of emerging psychoactive substances (EPS). EPS is a term used to describe drugs that are relatively new to the recreational drug market and have mind-altering effects similar to conventional illicit drugs (including those known as meow meow, kronic and BZP) (NDARC 2013).

**NPS and the law**

The laws surrounding NPS are complex and vary across jurisdictions. In 2011, Western Australia was the first government to ban individual synthetic cannabinoids. Most Australian jurisdictions followed suit shortly thereafter, and in July 2011 it became a federal offence to possess eight specific cannabinoid agonists. In 2012, the Therapeutic Goods Administration introduced a blanket ban on any type of synthetic cannabinoid that produces the same pharmacological effect as cannabis.

In order to deal with the rapid growth in the number of NPS, from 2013 onwards some Australian states (including Queensland, NSW, South Australia and Western Australia) introduced blanket bans on possessing or selling any substance that has a psychoactive effect (exempting alcohol, tobacco and food). In other Australian jurisdictions, specific NPS are banned with additional NPS regularly added to the list. Commonwealth laws are also in place that ban any substance with a psychoactive effect that is not otherwise covered by existing legislation. It is the importer’s responsibility to prove that a substance falls into an exemption category.

**Further reading**

- Synthetic drugs factsheet [6]- NSW Health
- New psychoactive substances [7]- Alcohol and Drug Foundation

**Effects**

There is currently limited information available on the short and long term health risks associated with NPS use, their addiction potential, interaction with other drugs and their impact upon driving behaviour. Some of the adverse effects of specific NPS are outlined in the sections above.

A difficulty of understanding the effects of these new substances is that they are not always consumed intentionally. For example, it was reported that the NPS 25I-NBOMe was being sold as LSD in Australia. Monitoring systems that do not include forensic analysis of drug samples or testing of bodily fluids will not be able to accurately match reported effects and adverse events with the substances consumed.

**NPS and pregnancy**
Little is known about the effects of NPS on an unborn child. However, many drugs and medications taken during pregnancy cross the placenta, or are present in breast milk. Therefore it is likely that NPS may be dangerous to pregnant women and their unborn babies.

It is generally considered risky to take any drug while pregnant or breastfeeding without medical advice.


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