

Episode 16: Synthetic Cathinones

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TRANSCRIPT

Hi everyone. Welcome back to The Tox Lab. I'm Rebecca.

I'm Rob.

What do plant food, bath salts, and monkey dust all have in common? They are all names that have been used for cathinones over the years.

This week we're going to be looking at the ACMD report that was recently published on cathinones in the UK. But before we get into that, what are cathinones?

Cathinones are a class of drug, and it's quite a broad class with a lot of different compounds in it. Their history is quite interesting. Cathinone itself is found in the khat plant. Khat is native to parts of Africa and the Arabian Peninsula, and for centuries it has been chewed because it has mild stimulant effects.

It's a bit like people in South America chewing coca leaves, or more broadly the way much of the world uses caffeine. The main psychoactive component in khat is cathinone, and chewing khat leaves produces mild stimulant effects such as euphoria, alertness, and sociability.

It has a history of use in social gatherings, business meetings, and among students trying to stay awake, that sort of thing. But while cathinone is a natural compound found in a plant, over the last few years we have seen a rise in synthetic cathinones, where chemists have altered the core cathinone structure to make new compounds.

One of the earliest and best-known examples is mephedrone. It was first synthesised back in 1929, then largely forgotten, before being rediscovered in the 2000s as a so-called legal high.

Mephedrone is essentially 4-methylmethcathinone. It first became popular in Israel, then spread across Europe, and became very big in the UK in the late 2000s. It was sold very freely in a lot of places under all sorts of names, including things like plant food and bath salts.

It became a major club drug, often used as an alternative to MDMA. In 2009 it was reportedly the fourth most popular drug in the UK after alcohol, cannabis, and cocaine, so it became a very widely used compound very quickly.

The timing also coincided with a global shortage of MDMA. There was a shortage of safrole, which is a precursor in MDMA production, and mephedrone very quickly filled that gap.

In April 2010 it was banned by the UK government and classified as a Class B drug. Its use dropped off quite quickly, but that didn't stop synthetic cathinones as a whole. It simply encouraged people making these compounds to start changing them, and that probably led to where we are now.

So I've set the scene. Rebecca, why don't you take us through some of the stats in the ACMD report?

It's quite a weighty document. It's about 125 pages long, so there's a lot in there. I'll just pick out some of the more interesting points.

Between March 2020 and March 2023, 71 different synthetic cathinones were detected in the UK, which is a lot. Mephedrone, which Rob mentioned earlier, is still the most commonly detected synthetic cathinone in the UK, followed by 4-CMC, MDPHP, which is often associated with the term monkey dust, alpha-PHP, and 3-MMC.

So CMC means chloromethcathinone, MMC means methylmethcathinone. In other words, there are a lot of different compounds, all representing slight variations on the same general cathinone structure.

And this more or less mirrors what has been seen in Europe. The EMCDDA has also reported on the types of cathinones seized across Europe, and compounds like 3-CMC, 4-CMC, 3-MMC, and alpha-PHP all feature prominently.

Since the mephedrone ban in 2010, overall reported use of cathinones has decreased quite a bit. In 2010 to 2011, among people aged 16 to 59, about 1.3 percent reported cathinone use. By 2023 to 2024, that had fallen to 0.1 percent.

So even though we are seeing a large number of different cathinones, they still make up a relatively small proportion of overall drug use.

Yes, but the market has also changed. Cathinones started out as club drugs sold as legal highs. Over time they seem to have become more associated with polydrug use and with more vulnerable populations. Some of the recent data in the report suggests cathinone use is now associated with areas of high deprivation and with homelessness.

So they have clearly changed in terms of who is most affected and where they are being detected.

There are also some strong regional differences, aren't there? One particular hotspot in the UK seems to be Stoke-on-Trent and the wider North Staffordshire area.

Yes, and in particular MDPHP, often referred to as monkey dust, seems to be one of the compounds most associated with that area.

A lot of that market appears to be driven by very low cost. The report describes doses being available for prices as low as about GBP1.50.

Looking at synthetic cathinone seizures in the EU, as reported by the EMCDDA, there has been a dramatic increase in the total quantity seized. In 2018, around 1,070 kilograms of synthetic cathinones were seized. By 2022, that had risen to about 26,500 kilograms.

It also seems that a lot of these powders originate in India. Supply appears to be increasing significantly, and that may be one reason prices are so low. That in turn may help explain why these drugs are being used more among vulnerable populations with very limited money.

So why don't we look at the pharmacology of these compounds? As we've already said, there isn't just one cathinone. The structures vary, and as a result the pharmacology is also quite variable.

Yes. Broadly speaking, cathinones act as stimulants and increase concentrations of monoamines in the brain, particularly dopamine, serotonin, and noradrenaline.

Different cathinones can do that in different ways. One mechanism is reuptake inhibition. They block transporters such as DAT, NET, and SERT, which normally move neurotransmitters back into the nerve terminal. Blocking those transporters increases the concentration of monoamines in the synapse.

Drugs such as alpha-PVP and MDPHP work largely in that way.

Other synthetic cathinones act more by promoting release of neurotransmitters. Mephedrone and methylone are examples more in that category.

So they all end up increasing monoamine concentrations in the synapse, but they do it through slightly different mechanisms.

And as a result, the subjective effects can vary, and the toxicity profiles can vary too. Some are more amphetamine-like, while others are a bit more MDMA-like and have more serotonergic effects.

The desired effects users often describe include euphoria, increased energy, increased alertness, empathy, and talkativeness. But negative effects can include headache, palpitations, nausea, cold extremities, hallucinations, paranoia, and panic attacks.

In some cases, serotonin syndrome has also been reported.

What about the broader psychological effects? There is a lot of discussion around paranoia and unusual behaviour.

Yes. There have been reports of severe paranoia and of formication or parasitosis, where people feel as though insects are crawling on or under their skin when they are not.

Fatalities involving cathinones have also been reported, often associated with hyperthermia, hypertension, cardiac arrest, and serotonin syndrome, so the kind of severe stimulant toxicity we also see with other stimulant-type drugs.

So clearly these drugs can be very harmful to an individual. But are there wider societal harms discussed in the report?

Yes. Synthetic cathinones, like other psychostimulants, can aggravate antisocial behaviour, increase aggression, and contribute to harms within families and communities. There is also an obvious knock-on effect for healthcare services dealing with people presenting to emergency departments under the influence of these drugs.

As we said earlier, there also seems to be a very uneven geographic distribution, especially the very high prevalence associated with North Staffordshire and Stoke-on-Trent. It's interesting that you can get what looks like a fairly concentrated local market around a drug like monkey dust.

I don't know whether that reflects particular supply chains, particular local demand patterns, or both. But it is quite striking.

The report also highlights particular compounds of concern, especially the pyrrolidino cathinones. This group includes alpha-PHP, alpha-PIHP, MDPHP, alpha-PVP, and MDPV.

The structural changes in these compounds make them more lipophilic, which raises concern that they may penetrate into the brain more readily and produce stronger effects. They also tend to show high potency at DAT and NET compared with some other cathinones.

So they may potentially be more harmful and produce more dangerous effects.

What we've really seen over the years is a progression from a natural plant compound, cathinone, to a relatively simple analogue like mephedrone, and then on to more heavily modified compounds that may be more potent, more lipophilic, and potentially more harmful.

And these pyrrolidino cathinones seem to have somewhat different effects from the earlier drugs like mephedrone. They have less of that serotonergic, entactogenic profile and are more strongly dopaminergic,

which makes them more similar in effect to drugs like methamphetamine than to MDMA.

So what was the outcome of the report? What did the ACMD recommend?

The ACMD did not recommend moving synthetic cathinones from Class B to Class A. Their view was that doing so would probably not have the effect people wanted and would risk further harming people who are already very vulnerable.

However, they did recommend changing the wording of the legislation so that it more clearly captures newer synthetic cathinones that may not fall neatly under the current generic definition.

It's a difficult balance, isn't it? If you tighten legislation further because a drug appears more harmful, you risk increasing criminalisation of possession among people who are already dependent and vulnerable.

Another recommendation in the report was to address homelessness and make sure affected populations are being directed toward appropriate health and social care support.

So the idea is not just to criminalise people who are already vulnerable, but to support them.

Exactly. From a toxicology point of view, one of the key issues, as with many drug classes, is making sure we are actually looking for these compounds analytically. The market keeps changing, and if we are not detecting them, then we are not reporting them, which means we may underestimate how much of a problem they are.

I think that is one of the biggest take-home points from the report: just how many cathinones are now being reported and detected across the UK and Europe.

So in conclusion, synthetic cathinones are still here and they look as though they are here to stay. They continue to evolve, we continue to see more potent variants emerging, and those variants may come with greater risks, not only for individuals but also in terms of wider social harms.

There is a case for reviewing how these drugs are controlled, but the ACMD's view is that simply increasing the severity of legal control may just encourage further evolution of the market and risk criminalising people who are already vulnerable and in need of support.

I think we're going to wrap it up there. I hope you've enjoyed listening this week.

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We'd love to hear from you, as always. Feel free to comment on any of our posts or send us a message if you have suggestions for future content.

Hope you've all had a wonderful week, and we'll see you next time. Bye.