

The Cathinone Hydra: Increased Cathinone and caffeine adulteration in the English MDMA market after Brexit and COVID-19 lockdowns

Drug Science, Policy and Law

Volume 8: 1–12

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DOI: 10.1177/20503245221099209

journals.sagepub.com/home/dsp

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Abstract

Adulteration poses additional unknown risks to the health of people who use illicit drugs. In this study, we sought to determine the extent and nature of adulteration of ‘MDMA’ in circulation at English summer music festivals in 2021, following Brexit, COVID-19 lockdowns and various regulatory changes overseas. At three festivals in 2019 and 2021, 1648 surrendered substances were analysed with Fourier-transform infrared spectroscopy and colourimetric reagents in a mobile laboratory as part of a harm reduction project. Form, mass, appearance and main psychoactive component were recorded. Analytical results were compared to a parallel self-report survey with 1124 attendees at the same events, as part of the annual *English Festival Study*. In 2019 and 2021, 417 and 377 samples strongly resembling MDMA (e.g. ecstasy tablets) were tested. Detection of MDMA in such samples decreased from 93% to 55% between the two years. Whilst virtually absent in 2019, synthetic cathinones and caffeine each constituted approximately one fifth of 2021 samples. 4-Chloromethcathinone (4-CMC), 3-methylmethcathinone (3-MMC) and *N*-ethylbutylone (eutylone) were the most prevalent cathinones detected. In both years, >35% of survey respondents reported use and/or intention to use MDMA on the fieldwork day; ≤1% reported cathinone or caffeine use, suggesting their consumption was predominantly unintentional. The sharp rise in synthetic cathinone prevalence in the summer 2021 UK market coincided with a unique combination of events including Brexit and the reopening of nightlife after 16 months of lockdowns, months ahead of other European nations. Echoing similar periods over the past decade, the cathinone hydra reared its head to satisfy the buoyant demand for MDMA at a time of scarcity, through substitution with substances legally obtainable in the Netherlands at the time of data collection. Alerts issued on social media led to >360,000 engagements, demonstrating extensive public engagement with illicit market monitoring and harm reduction advice.

Keywords

drugs, MDMA, cathinones, adulteration, festivals, England, drug checking

Introduction

The use of illicit psychoactive drugs at UK leisure events, as in wider society, is well established. In the most recent annual Crime Survey of England and Wales, significant numbers of 16–24-year-olds reported using cannabis (18.7%), cocaine (5.3%), MDMA (4.0%) and ketamine (3.2%) in the past year (Home Office, 2020). Compared to the general population, self-reported drug use is more prevalent amongst young adults attending licensed leisure venues such as nightclubs, bars and festivals (Hesse and Tutenges, 2012; Home Office, 2020; Measham et al., 2001). MDMA, ketamine and cocaine are currently the three most prevalent illicit drugs taken in leisure settings in the UK, with MDMA persisting as the most popular dance drug across the last three decades (Fisher and Measham, 2018).

MDMA is a phenylethylamine of the amphetamine class which acts as an indirect agonist of serotonin by binding to and blocking the 5-HT transporter (Hagino et al., 2011). Sought effects include euphoria, increased energy,

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increased musical appreciation and emotional closeness with others. Common adverse effects include restlessness, insomnia, muscular clenching, increased body temperature (hyperthermia), nausea and dry mouth. In rare cases, use of MDMA can lead to seizure, coma and death, primarily due to hyperthermia or hyponatraemia linked to water intoxication (Elkattawy et al., 2021). Whilst occurring less frequently than with other recreational drugs such as alcohol or cocaine, MDMA drug-related deaths in England and Wales escalated from a low point of 10 deaths in 2010 to a peak of 92 in 2018 (Office for National Statistics, 2021).

Illicit MDMA is diverse in appearance and is available in both crystalline and tablet forms. Crystalline MDMA appears in many shades of beige, from brown to off-white, and may be sold as whole crystals, crushed powder or prepared into capsules or “bombs” (cigarette paper wraps) for oral consumption. Contemporary ecstasy tablets are available in a wide range of shapes, colours and designs, imprinted with the logos of luxury brands, fictional characters and other cultural references. As with any unregulated substance, MDMA may be readily adulterated without the knowledge of those purchasing the product further along the supply chain. The diversity in the appearance of MDMA may increase opportunities for misrepresentation during sale (mis-selling), as users are already accustomed to receiving the substance in a wide variety of forms.

Synthetic cathinones (henceforth ‘cathinones’) are a class of new psychoactive substances (NPS) that first appeared in the UK illicit drug market in the late 2000s. Structurally related to amphetamines, cathinones are characterised by a ketone group at the β -carbon position (Zawilska and Wojcieszak, 2013). Cathinones are rich in substitutable regions and are readily modifiable (Figure 1), enhancing their ability to evade legislative controls. 4-Methylmethcathinone (4-MMC, ‘*mephedrone*’) emerged as a ‘legal high’ and grew rapidly in popularity in the UK from 2008 onwards (Measham et al., 2010). Numerous analogues have emerged in the UK since the prohibition of 4-MMC (Home Office, 2018) and attempts have been made to broadly categorise them by receptor activity and subjective effects; some appear block neurotransmitter reuptake, whilst others act as both blocking and releasing agents (Karila et al., 2015).

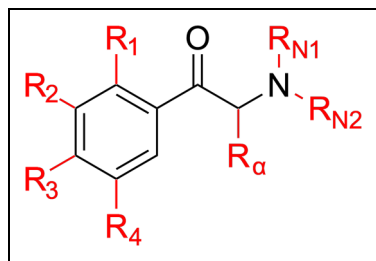


Figure 1. Structural overview of the cathinone pharmacophore with potential substitution sites labelled (R).

Whilst some cathinones seem to exhibit similar risk profiles to MDMA, toxicological information is often unknown upon emergence. Differences in time of onset and elimination half-life may affect redosing frequency, reinforcement behaviours and addictive potential (Vandewater et al., 2015; Papaseit et al., 2016). Methylenedioxypropylvalerone (MDPV), for example, produces similar reinforcement effects to methamphetamine in rodent models (Aarde et al., 2013). Whilst not within the cathinone class, other MDMA adulterants such as PMA/PMMA have a narrower therapeutic index and less potent psychotropic effects compared to MDMA, increasing risk of repeated redosing and adverse toxicological events (World Health Organisation, 2015). Numerous deaths were linked to these substances during a previous period of MDMA scarcity in the UK. The future emergence of another cathinone derivative of increased risk to users is plausible, given the rapid expansion of the class.

Within the last few years, there have been significant disruptions to illicit drug markets. In April 2019, the MDMA precursor PMK glycidate was listed under the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988. Events including COVID-19 pandemic lockdowns, associated closures of UK festivals and nightclubs for 16 months, and Brexit have together resulted in unprecedented disruptions to existing supply chains, including transnational movement of goods. Post-lockdown surveys indicated reduced availability of MDMA following the lifting of restrictions (Winstock et al., 2020; Aldridge et al., 2021) and drug checking organisations across Europe have identified a reduction in the MDMA content of ecstasy tablets, with fewer ‘super strength’ tablets in circulation (Trimbos Institute, 2021). It has yet to be determined whether this perfect storm of events precipitated a change in the supply and use of cathinones, as was observed during the previous decade (Blanco et al., 2021; Moore et al., 2013).

Study aims

This study sought to investigate post-lockdown changes in the UK illicit drug market by identifying drugs present in samples reasoned to have been purchased as MDMA (e.g. ecstasy tablets). Analytical drug surveillance data obtained at three English music festivals in 2019 and 2021 were compared with prevalence survey data collected at the same events. The study was part of a larger ongoing research project known as the *English Festival Study* (EFS), which includes the delivery of annual self-report surveys at English summer festivals conducted in parallel with chemical analysis of substances of concern in mobile laboratories located onsite at the same events (Turner and Measham 2019). The testing and surveys formed part of an interdisciplinary action research project with results used to inform an onsite harm reduction service at the

festivals, delivered by a nonprofit non-governmental organisation (NGO). For the purposes of this study summer 2019 (pre-COVID-19/Brexit) data were compared to summer 2021 (post-lockdown/Brexit) data.

Methods

Festival test sites

Data were collected by NGO staff testing substances of concern, conducting surveys and providing associated harm reduction services at three of the same English summer music festivals in 2019 and 2021, chosen as contrasting events in terms of their size, duration, attendee demographics, entertainment offerings and geographical locations.

Acquisition of substances of concern

Substances of concern were obtained predominantly through surrender to amnesty bins distributed at entrances and across the three festival sites and associated seizures and confiscations by police and security staff (95%); as well as through submissions directly to festival medical and welfare teams from attendees requesting support (5%). Upon delivery at the mobile laboratory, individual substances were photographed, weighed and catalogued according to source, form and visual appearance (e.g. colour, size, tablet design features). Due to the method of collection, purchase intent was obtained directly from buyers only for substances of concern submitted to medical and welfare services. Following analyses, remnants were collected by police for onward safe destruction.

In this study, samples were retrospectively categorised as known or reasoned to be MDMA based on several factors. Firstly, appearance was considered. For example, MDMA powder and crystal are visually distinct from cocaine and ketamine powder to the trained eye. Also, ecstasy tablets come in distinctive shapes, colours and brandings, many of which were known to be in circulation in Europe in summer 2021 sold as MDMA, through online reports such as those by testing and drug checking organisations. MDMA tablet sizes are distinct from tablets containing other psychoactive drugs of different usual dosage, such as 2C-B which has a smaller usual dose than MDMA and therefore distinctively smaller usual tablet size. Secondly, method of preparation and associated route of administration were considered. For example, capsules or 'bombs' prepared for oral ingestion typically contain MDMA powder or crystal. Other popular party drugs such as cocaine and ketamine are not typically consumed orally, either due to poor bioavailability (e.g. first pass metabolism) or due to users seeking rapid onset of effects. Thirdly, in the case of submissions to festival medical and welfare teams, attendees or their friends were

able to confirm the purchase intent directly to staff meaning that those samples were known to have been bought as MDMA. Fourthly, a small number of substances were surrendered to welfare amnesty bins alongside a note from support staff describing the substance, purchase intent and adverse effects experienced. Taken together, this information enabled MDMA purchase intent and instances of mis-selling to be reasonably or definitively inferred.

Substance identification

The contents of substances were determined through chemical analyses including attenuated total reflectance-Fourier transform infrared (ATR-FTIR) spectroscopy, using either Bruker Alpha or Shimadzu IRSpirit spectrometers. Spectra were recorded from 420–3500 cm^{-1} using 16 passes and matched to the Scientific Working Group for the Analysis of Seized Drugs (SWGDRUG), BCCSU and TICTAC Communications Ltd Drug Database libraries. Occasionally, spectral match confidence from tablet samples was low. In these instances, tablets were crushed and rinsed with methanol to extract the active substance from excipients. After evaporation of the methanol, extracts were again analysed by ATR-FTIR.

A selection of cathinones identified by FTIR ($n=12$) were also tested for trace MDxx content using colorimetric Marquis, Froehde and Liebermann reagent kits. These reagents produce a black colour change in the presence of MDxx compounds (limit of detection $<50 \mu\text{g}$; O'Neal *et al.*, 2000). An aliquot of each reagent was added to sectors of a white glazed tile and then a spatula of substance was added atop. Observed colour changes were recorded.

Annual prevalence survey of self-reported drug use

Short anonymous convenience sample surveys were conducted with the general festival population across each show day at each event, to identify patterns and prevalence of drug consumption at the same three festival sites. The survey was conducted parallel to but independent of laboratory testing. The survey formed part of the wider annual EFS, a mixed method, multidisciplinary research project operationalised through the same NGO (McCormack *et al.*, 2021). Ethical approval was provided by Durham University.

The self-report survey has been designed, reviewed and refined for use in nightlife settings across three decades, including bars (Measham and Brain, 2005), nightclubs (Measham *et al.*, 2001; Measham and Moore, 2009) and festivals (Turner and Measham, 2019). Surveys were conducted by demographically diverse teams of researchers between approximately 12pm and 6pm each show day, to maximise engagement whilst minimising the risk of respondent intoxication. Questions included respondent demographics, frequency, recency and quantities of

consumption of various legal and illicit drugs, and questions about policing and regulation of drugs in nightlife contexts. Researchers received a full day of training prior to conducting the surveys including regarding equality, diversity and consent issues. Respondents were signposted to further information, advice and support – both onsite at the festival and offsite through local services – at the end of the survey upon request

Survey questions related to drug taking behaviour included a comprehensive list of both established street drugs and NPS, reviewed and updated annually. An ‘other’ category allowed for reporting use of novel or obscure drugs. Data on drug taking behaviours of the wider festival population were compared with laboratory data, including scrutinising trends between years and between festivals. This facilitated identification of discrepancies between tested substances and self-reported drug use at group level at the same event.

Statistical analysis

Statistical analyses were performed in SPSS v27 for macOS. Where data were categorical, differences were compared using Fisher-Freeman-Halton exact tests. Post-hoc comparisons between specified data were made using adjusted standardised residuals. Bonferroni’s correction was applied to control for type I errors; α levels for each analysis is provided in the corresponding table.

Results

In 2019 and 2021 respectively, 846 and 802 substances were tested by the service in total. In 2019, 417 (49%) were known or suspected to have been sold as MDMA; in 2021, this number was 377 (47%). These proportions were consistent with previous years of testing. Between the two years, major shifts were observed in the contents of substances known or reasoned to have been bought as MDMA (Table 1). Between 2019 and 2021, MDMA detection decreased from 92.8% to 54.6% and detection of cathinones and caffeine rose substantially ($p < .0001$). Detection of other drugs and non-psychoactive substances was stable between years ($p .4479$).

Between 2019 and 2021, there was a significant fall in the number of samples where MDMA was detected, in both tablet and crystalline forms (Table 2; $p < .0001$). In 2019, MDMA detection in both tablet and crystalline samples was high and there were no significant differences in the drugs detected between sample form ($p .1312$). In 2021, significant differences were apparent in the classes of drug detected in both sample forms ($p < .0001$). Tablets were significantly more likely to contain MDMA than adulterants, whilst crystalline samples contained cathinones or caffeine more often than MDMA (Table 2).

Of the 73 samples in which cathinones were detected in 2021, over three quarters ($n = 56$, 76%) were in tablet form and otherwise visually indistinguishable from ecstasy tablets containing MDMA analysed by the service. 4-CMC was the most prevalent cathinone both overall and in tablets, whilst eutylone (*N*-ethylbutylone) was the most prevalent adulterant of crystalline samples (Table 3). Of the 12 substances identified to contain cathinones, only one produced a colour change indicative of the potential presence of an MDxx compound; the spectrum of this sample matched with that of 2-methyl-4’-(methylthio)-2-morpholinopropiophenone (MMMP).

The total number of respondents who completed the onsite general prevalence surveys at the three festivals was 600 in 2019 and 524 in 2021. In 2019, the average age of respondents was 25.7 years, 51.0% identified as female and 92.5% identified as White. In 2021, average age was 26.0 years, 51.1% identified as female and 90.1% identified as White.

Between 2019 and 2021, there were no significant changes in self-report of having taken and/or planning to take the drug on the fieldwork day, in relation to MDMA and cathinones ($p .4075$). In 2019 and 2021, 36.0% and 40.1% of survey respondents reported having taken and/or planning to take MDMA on the fieldwork day respectively. Reported use of 4-MMC was similar in both years, though overall prevalence was low ($\leq 1\%$). Notably, no survey respondents in either 2019 or 2021 reported having taken and/or planning to take any other cathinones, including 4-CMC, 3-MMC or eutylone.

Table 1. Total FTIR-identified major component of MDMA-suspected substances analysed at three festivals in 2019 and 2021. Bonferroni corrected $\alpha = .0125$.

	MDMA	Caffeine	Synthetic cathinone	Other/none
2019	387	4	1	25
(n = 417)	(92.8%)	(1.0%)	(0.2%)	(6.0%)
2021	206	80	73	18
(n = 377)	(54.6%)	(21.2%)	(19.4%)	(4.8%)
Adjusted residual	-12.350	9.269	9.256	-0.759
P	<.0001	<.0001	<.0001	.4479
2019–2021 trend	Decrease	Increase	Increase	No change

Table 2. Number and relative proportion of MDMA, caffeine and synthetic cathinones as the major component of ecstasy tablets and crystalline samples in 2019 and 2021. Bonferroni corrected $\alpha = .017$.

Year	Sample form	MDMA	Caffeine	Synthetic cathinones
2019 (n = 391)	Tablets	196 (89.9%)	0 (0.0%)	0 (0.0%)
	Crystals	191 (96.0%)	3 (1.5%)	1 (0.5%)
P		.1313	.2189	.6041
2021 (n = 359)	Tablets	145 (62.8%)	16 (6.9%)	56 (24.2%)
	Crystals	61 (42.1%)	64 (44.1%)	17 (11.8%)
p (incl. caffeine)		<.0001	<.0001	.0063
p (excl. caffeine)		.3009	-	.3009

Table 3. Number and relative proportion of synthetic cathinones detected in tablet (n = 56) and crystalline (n = 17) samples in 2021. Bonferroni adjusted $\alpha = .0125$.

	4-CMC	3-MMC	Eutylone	Other (including 4-MMC)
Total	41 (56.2%)	16 (21.9%)	13 (17.8%)	3 (4.1%)
Tablets	37 (66.1%)	15 (26.8%)	2 (3.6%)	2 (3.6%)
Crystals	4 (23.5%)	1 (5.8%)	11 (64.7%)	1 (5.9%)
Adjusted residual	3.096	1.825	-5.771	-0.420
P	.0224	.343	<.0001	.9813
Difference?	Borderline	No	Yes	No

Discussion

Overview

The data presented here suggests that there may have been a substantial shift in the UK drugs landscape between 2019 and 2021, particularly in the case of drugs reasoned or known to have been purchased as MDMA. In this study of substances in circulation at three English summer music festivals, MDMA detection decreased markedly, whilst the detection of both synthetic cathinones and caffeine rose substantially. Cathinones were identified as the primary component in 19.4% of samples, with 4-Chloromethcathinone (4-CMC) representing more than half of all cathinones detected.

Post-lockdown cathinone adulteration

In 2019, MDMA was detected in 92.8% of samples, with cathinones being identified in <1% of cases. In 2021, MDMA detection decreased to 54.8%, with cathinones

identified as the major component in 19.8% of cases (Table 1). Detection of MDMA and cathinones thus occurred in an approximate ratio of 3:1. Of the 73 substances identified as containing cathinones, over three quarters (Table 3) were indistinguishable from typical ecstasy tablets and many others were prepared in a manner consistent with oral consumption most usually associated with MDMA crystal (e.g. bombs/capsules). Oral bioavailability of other popular recreational drugs (cocaine and ketamine) is poor, making it unlikely that they would be prepared into bombs or capsules, and their forms differ substantially from MDMA and cathinones, further supporting our reasoning that many of these substances were purchased as MDMA.

Of the 524 respondents in the 2021 festival prevalence survey, 210 (40.1%) reported having taken and/or planning to take MDMA on the fieldwork day (Table 4). Taking the 3:1 detection ratio into account, if it is assumed that those in possession of cathinones knowingly purchased them as such, we would expect roughly 70 (13%) of survey respondents to have indicated this. Contrastingly, only three (0.6%) indicated intent to use cathinones when surveyed. In all three cases, self-reported cathinone use was for the longest established and most widely used cathinone in the UK (4-MMC, mephedrone) and no use of the more recent cathinones (4-CMC, 3-MMC and eutylone) was reported. On this basis, there is no evidence to suppose that the vast majority of cathinones identified in circulation at the three festivals in summer 2021 were intentionally purchased as such. Instead, there is every reason to believe that these cathinones were missold as another substance, with MDMA the prime suspect due to similarities in sample form and reported purchase intent to onsite medical and welfare services.

In 2021, 4-CMC was the cathinone detected most often across the three festival sites, constituting 56.2% of samples (Table 3), and was found more often in tablets than crystals (p .0224/ α .0125). Whilst scientific reports on 4-CMC are sparse, emerging evidence suggests a similar effects

Table 4. Self-report of planning and/or already having had MDMA and cathinones on the fieldwork day by festival attendees in 2019 and 2021. Bonferroni adjusted $\alpha = .01$.

	MDMA (any)	MDMA (tablets)	MDMA (crystals)	Synthetic cathinones (any)	4-MMC (mephedrone)
2019	216 (36.0%)	128 (21.3%)	158 (26.3%)	6 (1.0%)	6 (1.0%)
2021	210 (41.0%)	125 (23.9%)	131 (25.0%)	3 (0.6%)	3 (0.6%)
Adjusted residual	-0.782	-0.568	1.029	0.877	0.877
P	.9618	.9883	.9007	.9425	.9425
Difference?	No	No	No	No	No

profile to other stimulants (World Health Organisation, 2019), with some authors reporting methamphetamine-like properties due to preferential modulation of norepinephrine and dopamine systems (Majchrzak et al., 2018). 4-CMC fully substitutes for methamphetamine, cocaine and MDMA in drug discrimination models, though may exhibit an effects profile most like MDMA (Gatch, et al., 2019). Para-halogenation of methcathinone derivatives, particularly with chlorine, has been noted to increase their serotonergic toxicity (Luethi et al., 2019) and so use of 4-CMC may be higher risk than other cathinone derivatives. Anecdotal reports state typical 4-CMC dose ranges of 50–150 mg for insufflation and 100–300 mg for oral administration, with a similar duration of effects to MDMA (Griffell et al., 2017). Reported adverse effects for 4-CMC include hypertension, tachycardia, chest pain, agitation, psychoses and hallucinations (World Health Organisation, 2019).

Second to 4-CMC, 3-MMC was identified in 21.4% of cathinone samples. As its structural isomer, 3-MMC offers a similar effects profile to 4-MMC (Ferreira et al., 2019). Until its rescheduling in late 2021, use of 3-MMC increased in the Netherlands and was the most prevalent cathinone detected by Dutch drug checking services in 2017 (Hondebrink et al., 2020). In one study, 3-MMC was prevalent in wastewater collected in the Netherlands, Italy and Estonia over the 2019–2020 new year period (Bade et al., 2021). At the time of data collection, both 3-MMC and 4-CMC were legally available in the Netherlands and Class B controlled drugs in the UK (through 2010 generic legislation), placing them as convenient and lower risk substitutes for MDMA (a Class A controlled drug in the UK through 1977 generic legislation), in a period of exceptionally high demand combined with unprecedented disruption to supply chains in the UK.

Eutylone was detected in 3.4% of total MDMA-suspected samples in 2021, representing 17.8% of all cathinones detected, and was more likely to be encountered in crystalline samples rather than tablets (Table 3). As with 4-CMC, eutylone is poorly described in the literature. Adverse effects associated with eutylone include tachycardia, delirium, agitation, hyperthermia and cardiac arrest

(Chen *et al.*, 2021; World Health Organisation, 2021). *In vitro* assays indicate that the monoamine transporter inhibition profile of eutylone is similar to but more potent than pentylone; both primarily inhibit dopamine reuptake whilst acting as weak serotonin releasing agents (Glatfelter et al., 2021). Whilst the toxicity profile of eutylone is poorly described, weak serotonergic activity may encourage repeat dosing by individuals seeking but failing to obtain an MDMA-like empathic or euphoric experience along with its stimulant effects, increasing the risk of adverse events.

At the three festival sites in 2021, eutylone consumption was associated with several episodes of panic and psychosis brought to the attention of onsite medical, welfare and security services. Numerous individuals – experienced MDMA users – also reported severe and prolonged insomnia across the course of the festivals uncharacteristic of MDMA use, following consumption of substances later identified to contain eutylone. The mis-selling of cathinones including 3-MMC, 4-CMC and eutylone as MDMA, and their associated negative effects (excessive stimulation, paranoia, insomnia, nausea), was confirmed by festival attendees surrendering substances of concern alongside direct verbal reports of their effects to medical and welfare services; subsequent on-site analysis confirmed the identity of these substances, allowing direct comparison of the drug with the reported effects on a case-by-case basis.

Adulterants differ between sample forms

In 2019, when MDMA detection in samples was high, we did not observe differences in the substances detected in tablet or crystalline samples (Table 3). MDMA detection in both sample types fell significantly in 2021 and ecstasy tablets were observed to contain MDMA more often (62.8%) than crystalline samples (42.1%). Interestingly, crystalline samples were as likely to contain caffeine as MDMA upon analysis, whilst cathinones were twice as prevalent in ecstasy tablets than in crystalline samples (Table 3). The high prevalence of caffeine in crystalline samples appeared to be the primary driver of the observed differences between sample forms, as its removal from

statistical analyses resulted in a non-significant difference in MDMA/cathinone detection between tablets and crystals.

Caffeine crystals: A convincing counterfeit

A large increase in detection of caffeine in crystalline samples was a particularly notable observation in 2021. The sale of whole, large crystals of MDMA became increasingly prevalent 15 years ago as they were perceived to be less readily adulterated than tablets at that time and as a two tier market developed, with MDMA crystals sold as the higher priced, higher purity premium product (Smith et al., 2009; EMCDDA, 2016).

Caffeine was identified as the major component in <1% of 2019 samples, increasing to 21.2% overall in 2021 (Table 1). For crystalline samples specifically, caffeine detection was 44.1% (Table 2). Pure caffeine crystals are translucent whilst illicitly manufactured MDMA most often appears in various shades of beige and off-white due to the presence of contaminants such as precursor and intermediate compounds. In 2021, caffeine was identified as the active substance in many large beige and off-white crystalline samples extremely similar in visual appearance to MDMA (Figure 2). The consistency of appearance across different festival sites suggests that the counterfeit may have been produced by a limited number of manufacturers, likely above street level, with the express intent to mislead MDMA users. Caffeine was also a feature of the UK illicit drug market when NPS first emerged over ten years ago (Davies et al., 2012) and this recent innovation in form seems designed to capitalise on the latest period of MDMA scarcity.

Whilst caffeine is well tolerated at normal dietary intakes, excessive consumption may pose toxicity risks (Davies et al., 2012). Co-administration of caffeine and psychostimulants, including MDMA, amphetamine and cocaine, potentiates the latter's toxicity in animal models (Vanattou-Saïfoudine et al., 2012). Specifically, caffeine increases the risk of hyperthermia, seizure, cardiovascular events and reinforcement behaviours following consumption. Moreover, the antagonistic effects between caffeine and alcohol, which is often consumed alongside illicit drugs in festival and nightlife settings, can increase the risk of alcohol overconsumption and its associated consequences (Ferré and O'Brien, 2011).

Synthetic cathinones in the broader market

On a broader UK level, the Welsh Emerging Drugs and Identification of Novel Substances (WEDINOS) project recorded similar observations in 2021. WEDINOS test results are available on its website (WEDINOS, 2021) and include information on purchase intent and the identity of the sample upon analysis. Of the substances submitted to WEDINOS in 2021 in which MDMA was listed as the

intended purchase (n=273), 66.7% contained MDMA, 15.4% contained cathinones and 13.6% contained caffeine as the sole component. 4-CMC represented more than half of all cathinones mis-sold as MDMA. Of all 2021 substances in which 4-CMC was detected (n=29), 27 were purchased as MDMA, one was purchased as cocaine and one as amphetamine. None were purchased as 4-CMC or another synthetic cathinone (Josie Smith and Dean Acreman, 2021 - personal communication, 11 October 2021). Further afield, similar patterns of decreased MDMA and increased cathinone detection were noted in New Zealand, to the extent that their 2020/21 festival season was characterised as "the summer of cathinones" (KnowYourStuffNZ, 2020). In contrast to the UK, where 4-CMC was most prevalent cathinone, eutylone was the cathinone most often detected in both New Zealand (KnowYourStuffNZ, 2021) and the United States (Drug Enforcement Agency, 2021).

What is behind the new wave of cathinones?

Hypothesising the reasons behind illicit market trends is inherently challenging. Whilst the MDMA precursor PMK glycidate came under strict international legislative control in April 2019, the annual EFS observed minimal adulteration in the UK festival market that year. There was no onsite festival testing in the UK in 2020 because of the closure of all festivals due to COVID-19. Looking further afield to European drug checking results for that year, adulteration of MDMA was rarely detected by the Netherlands-based Drugs Information and Monitoring System (DIMS) in 2020 (Trimbos Institute, 2021). Our observations on the current state of the MDMA market appear to be specific to the UK, and seemingly unrelated to the control of PMK glycidate.

Events of significance which may have impacted on the illicit drugs market since 2019 include the global COVID-19 pandemic and the UK's secession from the European Union (Brexit). Like many other countries, the UK experienced prolonged periods of lockdown during the pandemic and most significantly, all nightclubs and festivals closed for 16 months from 20th March 2020 to 19th July 2021. This limited the opportunity for the types of social gatherings where drugs such as MDMA are more often consumed. The pandemic and its associated lockdowns were associated with a significant fall in the use of party drugs including MDMA (EMCDDA and Europol, 2020), with respondents to the COVID-19 Global Drugs Survey also reporting disrupted access to drugs (Winstock et al., 2020). In response to decreased demand, MDMA suppliers reportedly curtailed production (Tidy, 2021). Recent dismantling of crime networks, including Netherlands-based producers (Operation Parazonium) and UK-based suppliers (Operation Venetic), as well as dark web platforms (EncroChat), are also likely to have played

CAUTION: Caffeine crystal & powder found in circulation at Parklife 2021

Multiple samples presumably bought as MDMA were identified to be caffeine.

It is **visually similar to MDMA** crystal & powder.

Caffeine is a common legal stimulant found in many everyday hot & cold drinks which can **increase energy & decrease fatigue.**

Too much caffeine can result in headaches, insomnia & increased heart rate. **Caffeine overdose or fatality is rare but has occurred.**

If you think you have taken too much caffeine try and get some rest. Symptoms usually ease once you have slept. Seek medical help if unwell.

WE ARE THE LOOP @WeAreTheLoopUK @TheLoop_UK @WeAreTheLoopUK

Figure 2. Alert for caffeine crystals issued on 11th September 2021. In this example, several baggies were obtained from a single submission, indicating possible intent to supply at the festival site: <https://twitter.com/wearetheloopuk/status/1436771245132025862?lang=en-GB>.

a role in shaping the current UK drugs landscape through disruption to established supply chains (Australian Federal Police, 2019; Daly, 2020). Extensively documented supply chain issues experienced across the wider economy appear also to have affected drug supply chains including in the London area (Jones, 2021). As London is a major hub for UK drug distribution, disrupted supply to this area seems likely to affect the broader UK drug market. Additionally, Brexit-related changes in currency exchange values may have incentivised mis-selling, as substitute drugs can be sold at higher profit margins than MDMA (Tidy, 2021). Finally, cathinones may entail lower risk in terms of judicial punishment, if they are a lower level of classification than MDMA in the legislative controls of producer and consumer countries.

Since the emergence of 4-MMC in 2008, the appearance of cathinones in the UK drug market has been associated with fluctuations in the demand for and availability of established street drugs, particularly MDMA. In July 2021, UK nightclubs and festivals reopened after a 16-month blanket closure due to COVID-19, creating a sudden, very high demand for party drugs. During this time, continental Europe and notably the Netherlands continued with lockdowns and nightlife closures for several more months, leading commentators to surmise that Dutch MDMA manufacturers also may have remained closed (Tidy, 2021). Such gaps in supply during periods of high demand are readily filled by novel cathinone derivatives which may evade legislative control in producer and distributor countries outside UK jurisdiction. For example, both 4-CMC and 3-MMC were legal to supply and possess in the Netherlands until their control in October 2021. Previously, the EFS identified the

adulteration of UK MDMA with methylone in 2014–16, then pentylone and *N*-ethylpentylone in 2017–2018, in its annual summer festival testing programme (Measham and Jones, 2017). The United Nations Commission for Narcotic Drugs designated *N*-ethylpentylone as a Schedule II substance under the Convention on Psychotropic Substances 1971 in March 2019 and, whilst none was detected by the EFS in summer 2021, it was seemingly replaced by an array of alternatives, chiefly 4-CMC. Thus, whilst the legislative game of cat and mouse may have partly ended in the UK with the passing of the Psychoactive Substances Act, a new game of musical chairs appears to have begun.

Dissemination and communication outcomes

Test results and associated harm reduction advice from medical practitioners was cascaded to regional and national stakeholders including public health, police, event management and early warning systems to help inform service delivery (Linnell, 2021; NPoCC SIB, 2021). Where appropriate, analytical results and associated harm reduction advice were used to inform a number of alerts issued by the NGO on its social media platforms to a combined total number of followers of 120,000, demonstrating that social media can be a useful tool for communicating with diverse groups of interested parties including stakeholders, policy makers, practitioners and drug using communities.

An example of the turbulence of the UK illicit drug market in summer 2021 combined with the visually identical appearance of different drugs is illustrated in a social media alert issued by the NGO in September 2021. The alert – garnering over 96,000 impressions on Facebook,

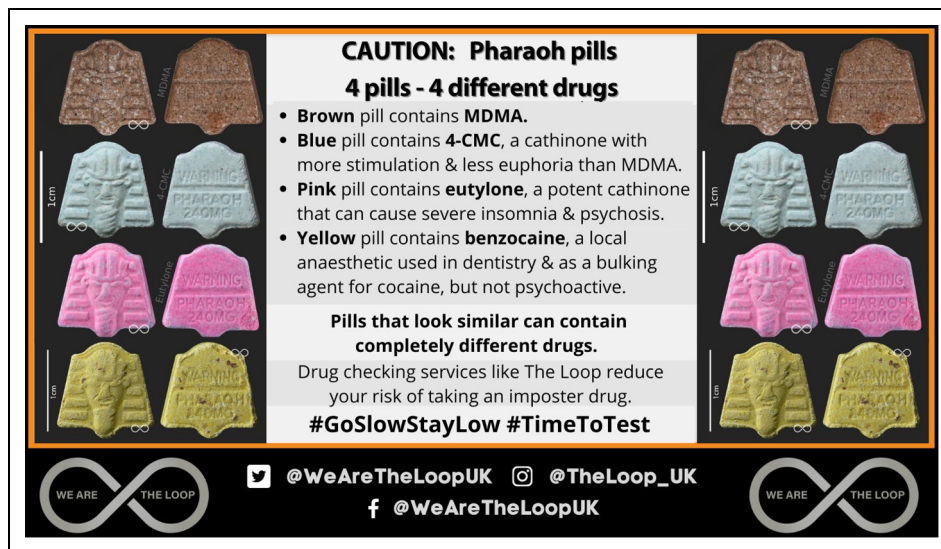


Figure 3. Alert issued on 16th September 2021 for four “Pharaoh” tablets identified as containing MDMA, 4-CMC, eutylone and benzocaine: <https://twitter.com/wearetheloopuk/status/1438534248206589953?lang=en-GB>.

54,000 on Twitter, 48,000 on TikTok and 33,000 on Instagram – featured four photographs of visually identical ecstasy tablets in the shape of a Pharaoh’s head in four different colours (Figure 3). All four tablets were analysed on the same day at the same festival, but testing revealed them to each contain distinct ingredients: only one contained MDMA, one 4-CMC, one eutylone and one benzocaine. A separate TikTok video about the four Pharaoh tablets alert was produced by a journalist and gained an additional 130,000 views (Griffin, 2021) and the four Pharaoh tablets alert was reported in the national press (e.g. Connolly, 2021; Hockaday, 2021), indicating a wider public interest in the results of onsite festival drug testing and broader market trends, as well as associated harm reduction advice. The authors were unable to find any replies or comments associated with this or any other alerts issued by the NGO in the summer of 2021 to contradict our reasoning that these substances were purchased as MDMA. An archive of past alerts from the NGO is available online at: <https://wearetheloop.org/drug-alerts>.

Limitations

Several limitations should be noted in this study. Firstly, substances were predominantly acquired through surrenders and welfare-related submissions. This may have introduced a sampling bias into the study, as samples may have been surrendered by individuals who experienced unexpected or unwelcome effects; this limitation is well recognised within the field (Yamamoto et al., 2013). Outside of analysing biological specimens of survey participants (Krotulski et al., 2018), these biases are difficult to address. Offering a publicly accessible drug checking service may allow purchase intent to be ascertained,

though may also introduce a self-selection bias for participants already concerned about the content of their drugs (Palamar et al., 2021). However, many substances were confiscated by security (i.e. not discarded) and, as the same collection methodology was used in both years, any resulting bias should not significantly affect comparisons between years in this study. Secondly, due to ongoing UK lockdown and associated restrictions, only three festival sites were attended in the second half of summer 2021, after festivals reopened. Whilst this may limit the generalisability of our findings, the concordant observations of WEDINOS, which receives samples from across the UK and continued to test intermittently during the pandemic, indicates this trend also occurred at a broader community level.

FTIR as the method of identification poorly discriminates between mixtures containing multiple substances at low concentrations (Daéid, 2005). Whilst FTIR can reliably detect substances comprising >10% of a sample (McCrae et al., 2020), it is insensitive to lower concentrations for some drugs. It is plausible that some of the substances tested contained additional drugs at concentrations below the reliable lower limit of detection. Nevertheless, 11 of the 12 cathinones tested using colorimetric reagents failed to produce colour changes consistent with the presence of trace MDxx compounds, indicating that these substances were not comprised of a mixture of cathinones and MDMA.

Without information direct from the consumer regarding purchase intent, some samples classified as “suspected MDMA” may not have been purchased as such. It is plausible that some of the substances tested were purchased as other stimulants, including cathinones. Except for three respondents reporting 4-MMC use, a drug with more than a decade of reported recreational use in the UK, there was

no evidence from onsite prevalence surveys or support services to suggest that attendees at these three events intended to consume either caffeine crystals or these emergent cathinones. This is supported by New Zealand festival drug checking services reporting a similar lack of purposeful consumption of these cathinones. However, we should note that our survey did not specifically ask about 4-CMC, 3-MMC or eutylone usage, as we were unaware prior to testing that these substances were in circulation in the UK in summer 2021, and this may have led to under-reporting of use. Offering a public drug checking service in the future would facilitate more accurate comparisons between purchase intent and sample content, to better assess the nature and extent of adulteration in drug markets.

Conclusion

This study highlights a period of unprecedented turbulence in the UK drug market in the summer of 2021 whereby a high proportion of drugs resembling and reasoned to have been sold as MDMA were found to contain cathinones or caffeine. Whilst caffeine poses relatively low risk to user health, there is limited toxicological information available for the cathinones identified (4-CMC, 3-MMC, eutylone). In the absence of any evidence to suggest a sudden surge in cathinone popularity, we suggest that the sharp rise in adulteration observed in summer 2021 may be due to the combination of buoyant post-lockdown demand for MDMA in the UK combined with supply side shortages. Given their contemporaneous occurrence, we suggest the shortage may be linked to Brexit-related disruptions to (legal and illicit) supply chains combined with the stalling of MDMA production in response to reduced demand during COVID-19 lockdowns spanning 2020 and 2021 and a brief period between announcing and implementing legislative control of these cathinones in Europe. This resulted in the cathinone hydra again rearing its head, echoing previous periods of MDMA scarcity across the last decade. Rapid onsite testing, dissemination of alerts, harm reduction information and associated risk communications through media and social media channels provides one way to inform interested parties – including practitioners, policy makers and drug using communities – of the apparent market disruption and maximises attempts to alleviate consequent drug-related harms.

Acknowledgements

Firstly, the authors would like to thank all volunteers of The Loop. Many volunteers offered their time and expertise to deliver the service and more broadly support the organisation, sometimes in challenging weather conditions not atypical of the English festival season. Secondly, we would like to extend our sincerest gratitude to all partners and stakeholders, including festival management, police and public health, for their continued support of this action research project.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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