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The identification of synthetic cannabinoids in English prisons

Mia Jane Abbott [*,1], Jodie Dunnett [2], John Wheeler [3], Alison Davidson [4]

Staffordshire University, Science Centre, Leek Road, Stoke-on-Trent ST4 2DF, United Kingdom

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ABSTRACT

Synthetic cannabinoids (SC) are extremely prevalent within the prison system and cause problems for prisoners, law enforcement and health services. SC are often soaked into paper then posted into prisons therefore one of the aims of this research is to collaborate with Rapiscan Systems Ltd. and local prisons in England to measure the effectiveness of trace detection methods for the indication of SC in prison post using the Itemiser 3E®. To ensure compounds did not go undetected, samples with Ion Trap Mobility Spectrometry™ peaks indicative of synthetic cannabinoids on the Itemiser 3E® were analysed using Gas Chromatography-Mass Spectrometry, Liquid Chromatography-Quadrupole Time-of-Flight Mass Spectrometry and Nuclear Magnetic Resonance Spectroscopy to identify chemical characteristics which allowed comparison to reference spectra. Sample data spanning three years from one prison's Itemiser 3E® were collated to identify trends in drug prevalence and the influence of library updates. To date, the method has identified four compounds: 5F-MDMB-PICA, MMB-4en-PICA, 4F-MDMB-BUTINACA and MDMB-4en-PINACA on prison post which were not already included on, or needed confirmatory analysis to update, the Itemiser 3E® library. As a result, the libraries on prison Itemiser 3E®s have been updated to ensure future detection of such compounds. Trends and influences from the processed Itemiser 3E® data were also reported back to the West Midlands Prison Group. This research directly benefitted both the West Midlands Prison Group and Rapiscan Systems Ltd. and it is anticipated that the continuation of this research could be expanded to a national scale.
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1. Introduction

Drugs have been a known problem in prisons for decades with use of "traditional" and prescription drugs plaguing the prison service prior to the increased popularity of synthetic cannabinoids in the UK in 2008. In recent years, synthetic cannabinoids have become one of the most popular drugs used within European prisons as 22 European countries reported NPS being used by their prisoners in 2020 [1]. In the UK, it is estimated by prison officials that 60% of the prison population use synthetic cannabinoids [2], however it is estimated by prisoners to be closer to 90% [3]. This use can lead to new addictions [2], physical and mental health issues [4], organised crime, debt and bullying, which all result in a stretched prison service [3].

The Psychoactive Substances Act 2016 [5] deemed it illegal to supply, possess with the intent to supply, produce, import, export, or possess within a custodial institution any psychoactive substances. NPS are classified by the Psychoactive Substances Act 2016 [5] as any substance that induces a psychoactive effect to an administered person. The resultant psychoactive effect may affect the person's mental or physical capacity through stimulation or depression of the central nervous system [5]. The structure of the 2016 Act was deliberately laid out to reduce the occurrence of waves of new generations of substances being produced to circumvent legislation and has been largely successful in achieving this aim compared to other countries with different legislation types where more variation is seen in the types of NPS [6,7]. However, even with 'blanket ban' style legislation, the number of NPS deaths in England and Wales has continued to increase, reaching a maximum of 258 deaths from NPS use in 2021 [8]. Two key drivers in the development of new NPS are the legislation in those countries where NPS are manufactured, particularly legislation dictating what can be produced and exported [9], and the use of novel structures to circumvent detection at ports, in prisons and in mandatory drugs tests [10,11].

One of the greatest appeals to the users of synthetic cannabinoids in prisons is that they are easy to access and are perceived as difficult to identify. Under the Prison Act 1952 [12], mandatory drug testing (MDT) through random urine samples can be undertaken to determine whether prisoners are under the influence of psychoactive substances. It is therefore important to ensure that the toxicology

* Corresponding author.
E-mail address: mia.abbott@staffs.ac.uk (M.J. Abbott).
[1] ORCHID ID: 0000-0001-8774-1116
[2] ORCHID ID: 0000-0003-3261-3314
[3] ORCHID ID: 0000-0003-4763-0555
[4] ORCHID ID: 0000-0003-3401-1368

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laboratories have the most up-to-date information to detect the most recent NPS substances and their metabolites [13-15,3,16]. To reduce the prevalence of synthetic cannabinoids being used in prisons, screening techniques can be employed to target the entry routes to intercept substances prior to them reaching the prisoners. The main entry routes are visitors, staff, 'over the wall', entering or returning prisoners and through the post [17].

Prison post soaked or sprayed with synthetic cannabinoid-laced solvents can be used as a method to smuggle synthetic cannabinoids into prisons by organised crime groups [10,18]. To ensure privacy for the recipient, legal correspondence between prisoners and their legal advisor by post is protected by Rule 39 of the Prison Rules 1999 [19] legislation. These rules state that legal correspondence, otherwise known as Rule 39 prison post, should not be stopped, opened or read by anyone other than the recipient unless the Governor suspects that the prison post is illegitimate and may contain harmful contents. Due to the fact staff do not regularly open Rule 39 prison post, this legislation can be exploited, with counterfeit legal correspondence being used for concealment of drugs [20].

Screening of post in prisons primarily relies on the use of desktop Ion Mobility Spectrometers from companies such as Rapiscan Systems Ltd. and Smiths Detection Ltd. [18,21] which can be used to swab paper (as well as individuals and their belongings if needed). The instruments are sensitive, easy to use and provide a quick result [22]. The instrument detects a substance from the time-of-flight characteristics and will indicate the presence of a previously defined substance through an alarm. If the library does not have a substance defined, it cannot identify what the sample is, resulting in an undefined peak. This is a problem with emerging synthetic cannabinoids that have not been added onto the library as the synthetic cannabinoid may be screened but not identified, therefore able to enter the prison. The effectiveness of portable screening techniques can be limited depending on the extent of their libraries, as also seen with bench-top NMR [23] and Raman spectrometry [24] and therefore continuous updates to these libraries need to be made through confirmatory analysis of synthetic cannabinoids to effectively detect these substances.

Although current screening techniques are proving popular for their ability to provide accurate results and adapt to the changing drugs market [25], they can only produce an indication of the presence of the substance and therefore must be used in conjunction with confirmatory analytical techniques [26]. Samples identified in prisons which need confirmatory testing for judicial purposes are submitted to a contracted private forensic provider: there is currently no scope for non-judicial samples to be tested through this process. In England, there is currently no national initiative focused on the confirmatory identification of synthetic cannabinoids from screened prison samples purely for intelligence purposes and independent research groups have increasingly taken on this role.

This research shows that a screening, confirmation and feedback cycle provided by the University for prisons in the West Midlands region, in collaboration with the West Midlands Prison Group and Rapiscan Systems Ltd., will successfully increase the amount of detected synthetic cannabinoids and potentially reduce the amount entering prisons.

2. Materials and methods

2.1. Materials

Acetone (HPLC grade), acetonitrile (LC-MS grade) and methanol (LC-MS grade) were purchased from Fisher Scientific, UK. Ammonium formate was purchased from Sigma Aldrich, USA. Formic acid was purchased from Optima Fisher Chemical, Belgium. Deuterated chloroform (99.8%) with 0.05% v/v tetramethylsilane (TMS) was purchased from Cambridge Isotope Laboratories Incorporated, USA.

2.2. Prison screening

Regular prison post (i.e. letters and cards) was opened upon arrival, read and checked by prison staff, then placed on a sterile surface for screening. In the prisons involved in this study, the screening was performed using Rapiscan Systems Ltd., Itemiser 3E® instruments which utilises Ion Trap Mobility Spectrometry™ (ITMS™). The instrument includes a "narcotics" library of flight time ranges for approximately 30 substances. At the start of this project, this included seven synthetic cannabinoids. The prison staff were required to wear disposable powder-free nitrile gloves and to check for contamination by swabbing the gloves and work area between each sample. In terms of daily use for drug screening, the Itemiser 3E® was set up using the "narcotics" positive ionisation mode, using ammonia as a chemical dopant for ionisation, a ^{63}Nickel ionisation source and thermal desorber temperature set to 235 °C. The instrument was calibrated once a day with cocaine-laced calibration traps provided by the vendor. Post was taken out of the envelope and swabbed front and back with a Teflon-coated trap, preferably pressing firmly and swabbed three times either side, then inserted into the Itemiser 3E® for 8 s. For Rule 39 post, a small slit was cut into the envelope to ensure that the contents could not be read while still allowing access for the trap to swab between the sheets of paper. This method was developed by Rapiscan Systems Ltd. for their training and later integrated into official guidelines: The Use of Narcotics Trace Detection Equipment on Correspondence Policy Framework [27]. This policy was created to ensure that the Prison Rules 1999 [19] were still met while the Rule 39 samples were still included in the screening process.

Once the trap had been desorbed in the Itemiser 3E®, the flight times for all positive ions desorbed from the trap were displayed on the plasmogram and in the corresponding table alongside the abundance (referred to as "strength"). If the flight time fell within the defined range for a substance in the library and surpassed the threshold strength value, then an alarm was triggered to indicate a match to a potential drug and the item would be seized and later destroyed. In addition to responding to alarms, Rapiscan Systems Ltd. trained their users to be alert to substances which did not alarm but had a flight time in the 9–10 ms region. These substances were treated as suspected new synthetic cannabinoids because testing by Rapiscan Systems Ltd. around 2018 indicated that the current synthetic cannabinoids had flight-times within that range. In these instances, during this study, prison staff were asked to place the post into an evidence bag, complete the corresponding evidence details on the bag and include the Itemiser 3E® print out so the item could be further investigated using confirmatory techniques.

Data spanning 33 months from June 2018 to February 2020 were collected from one Itemiser 3E® situated at a West Midlands prison to investigate trends and the effectiveness of definition changes in disrupting synthetic cannabinoids entering prisons. The data consisted of instrument alarms for the entire period but, due to a change in instrument settings, the flight times for samples which did not trigger an alarm were only available until June 2019. Using the flight time ranges supplied by Rapiscan Systems Ltd., the data were processed using Microsoft Excel 365 to identify, for each of the drugs in question, any sample which, prior to June 2019, had been screened but had not alarmed and, following changes in definition, any sample where these drugs did then produce an alarm.

2.3. Gas chromatography – mass spectrometry (GC-MS)

Items were received and logged, and observations made regarding appearance and odour. Samples of paper were prepared for

analysis using a hole punch to take 1 cm^2 from paper, with samples ideally taken from the corners, or if needed another clean (non-inked) area of the paper. Samples were sonicated for 20 min in 1 mL of LC-MS grade methanol or HPLC grade acetone. The solution was filtered using a 0.2 µm nylon syringe filter (Fisher Scientific, UK) and transferred to a clean autosampler vial labelled for GC-MS analysis. GC-MS operating parameters can be seen in the Supplementary Material.

Mass spectral interpretation used TurboMass Version 5.4 with the National Institute of Standards and Technology (NIST) Mass Spectral Search Program Version 2.0 2002, as well as online reference comparison through the Cayman Chemical GC-MS Drug Identification Tool [28], the Response Project Database [29], the SWGDRUG Drug Monograph table [30] and the NPS Discovery monographs produced by the Center for Forensic Research and Excellence [31].

2.3.1. Liquid chromatography – mass spectrometry (LC-MS)

For LC-MS analysis, a 1:20 dilution of the GC-MS methanol sample was transferred to a clean autosampler vial. LC-MS operating conditions can be seen in the Supplementary Material.

Data analysis was conducted using Agilent Qualitative Analysis 10.0 software alongside the Forensic Toxicology Personal Compound Database and Libraries B.07.01 and user defined libraries developed from ChemSpider .mol files.

2.4. Nuclear magnetic resonance spectroscopy (NMR)

For analysis by NMR, the GC-MS sample was evaporated to dryness under nitrogen and reconstituted with 1 mL of deuterated chloroform before being transferred to an NMR tube. NMR operating conditions can be seen in the Supplementary Material.

3. Results and discussion

In total, 47 paper samples were received from eleven English prisons over three years, including letters, cards and a diary. The results for eight of these samples are presented and discussed below because they show the importance of the screening, confirmation and feedback cycle. The analysis results of all 47 of the samples are summarised in the Supplementary Material provided.

3.1. 5F-MDMB-PICA

In Autumn 2018, two Halloween cards were posted to two different prisoners in the same prison. The cards appeared to be homemade and very similar in materials and style (Fig. 1). As it is highly unusual for cards to be exchanged for Halloween in England, both cards were tested in the post room.

The first card had an ITMS™ peak at 9.381 ms and the second card had a peak at 9.353 ms on the Itemiser 3E®. As these peaks fell in the 9–10 ms range, this indicated the possible presence of a synthetic cannabinoid, however there was no library match for those peaks to infer which synthetic cannabinoid could be present. The second card also had peaks which indicated the presence of cocaine and 5F-PB-22, a synthetic cannabinoid popular around 2014 and not encountered in other UK prison screening from 2018 onwards [18,32]. Accordingly, both cards were submitted for further analysis. As the trigger range for most Itemiser 3E® definitions are set by Rapiscan Systems Ltd. as ± 0.040 ms, it seemed likely that they were generated by the same chemical, potentially an unidentified synthetic cannabinoid. For more information regarding time-of-flight variation per synthetic cannabinoid, see Norman et al. [18].

Hole punches were taken from all four corners of the front page from each card. When analysed via GC-MS, good chromatography peaks were achieved for the acetone extracts of each sample, at very similar retention times (approximately 19.7 min). The NIST 2.0 library was unable to return a result with a high match statistic so an online search for synthetic cannabinoids with a *m/z* 232 base peak and relative molecular mass of 376 was conducted. A good match of the peak abundance values was eventually found with the Cayman Chemical spectrum of 5 F-MDMB-PICA. This synthetic cannabinoid was therefore presumptively noted as the likely main component of both samples.

Fig. 1. Halloween cards seized from a West Midlands prison.

LC-MS analysis of the Halloween cards was subsequently conducted to verify the identification of 5F-MDMB-PICA, by comparison with the accurate mass information on ChemSpider [33]. The accurate mass matched to four decimal places and the result had a 98.59% match score when compared to the user defined PCDL entry for 5F-MDMB-PICA, increasing the confidence in the identification. With confirmation by LC-MS, the previously collected GC-MS spectrum was therefore added to a user defined GC-MS library to aid identification in future samples.

To investigate the Itemiser 3E® indication of cocaine and 5F-PB-22 for these two samples, the smaller chromatographic peaks were investigated. Two small chromatographic peaks at 23 and 24 min featured in the samples of both Halloween cards, and had base peaks at *m/z* 232, which is indicative of both 5F-PB-22 and 5F-MDMB-PICA. However other significant *m/z* peaks in the spectra were not characteristic of 5F-PB-22, suggesting these peaks were due to thermal degradation or synthesis impurities of 5F-MDMB-PICA [18]. None of these peaks were consistent with the *m/z* values for cocaine [34], indicating that cocaine was either not present within the sample, was only present as surface level contamination from the sender [18] or was not extracted, perhaps because cocaine is only very slightly soluble in acetone [35]. Furthermore, both cocaine and 5F-PB-22 had entries in the NIST 2.0 library and The Forensic Toxicology PCDL (5F-PB-22 having been added to NIST 2.0 during a previous project) and neither were matched to spectra of these additional peaks. As the focus of the research was to investigate the potential synthetic cannabinoids present, this was not explored further.

3.2. 5F-MDMB-PICA and MMB-4en-PICA

5F-MDMB-PICA was also present in another sample analysed in November 2018: a homemade birthday postcard which featured a strong sweet odour and produced a peak at 9.155 ms on the Itemiser 3E®, indicating that the paper had been adulterated. When analysed using GC-MS, two peaks were featured in the chromatogram, a large peak at 18.89 min and a smaller one at 19.63 min, suggesting a mixture of compounds present. The spectrum associated with the large peak did not match any of the library spectra available at that

time but the mass spectrum for the small peak at 19.63 min produced a match to the spectrum of 5F-MDMB-PICA which had recently been added to the user defined library. Retention times were similar to those seen with the GC-MS analysis of the Halloween cards.

The larger peak at 18.89 min had *m/z* peaks at 212, 227, 41, 144, 43, 342, 228, 213, 130 and 116 (in order of abundance) but did not show any similarity to compounds featured in the NIST 2.0 library, the user defined library, online tools such as Cayman Chemical GC-MS Drug Identification Tool [28] or other reference spectra for compounds popular at the time of analysis. Therefore, focus was turned to the use of NMR for structural elucidation of the compound and Distortionless Enhancement by Polarisation Transfer (DEPT) experiments were used to enable assignment of the carbon peaks in the spectrum. The spectrum for the birthday postcard can be seen in the Supplementary Material.

At the same time as attempting to structurally elucidate the sample through NMR (February 2019), posts on Reddit.com by users and sellers of synthetic cannabinoids were investigated to determine the current synthetic cannabinoids on the market. MMB022 was included in a list of popular synthetic cannabinoid compounds on a post by a potential user. The compound name was then searched on the Cayman Chemical website [28] and their GC-MS reference spectrum was used to compare to the mass spectrum obtained for the GC-MS peak at 18.89 min. The spectra matched for 10 out of 10 peaks with the major peaks being of the same or similar abundance. The chemical structure provided by Cayman Chemical [28] is redrawn in the Supplementary Material along with the corresponding assignment labels and a table which depicts the structural inferences indicated through DEPT angle changes and interactions. This shows an alignment with the structure of MMB022, now formally known as MMB-4en-PICA. The presence of 5F-MDMB-PICA at low concentration did not appear to interfere with the identification of MMB-4en-PICA.

Thus, MMB-4en-PICA, was identified by GC-MS and NMR as the major compound present in the birthday postcard sample alongside what appeared to be 5F-MDMB-PICA at low levels. The identification of both compounds was further strengthened with the analysis of the sample using LC-MS, where the user defined PCDL spectra and sample spectra were compared with a 99.46% match to MMB-4en-PICA and 97.65% match to 5F-MDMB-PICA, plus good peak position within the predicted isotope distribution range was seen.

With confirmation by three analytical techniques, the presence of MMB-4en-PICA and 5F-MDMB-PICA within the birthday postcard sample was communicated to Rapiscan Systems Ltd. along with the identification of 5F-MDMB-PICA within the Halloween cards. Due to a perceived lack of prevalence at the time of reporting the substance, Rapiscan Systems Ltd. decided not to produce a library definition for MMB-4en-PICA. Although this highlights questions surrounding which compounds are included on the library, it shows the importance of the screening, confirmation and feedback cycle and ongoing reviews of the prevalence of drugs in prisons.

The 5F-MDMB-PICA identification did, however, result in the compound being added onto the Itemiser 3E® libraries in January 2019 following further testing by Rapiscan Systems Ltd. Therefore, the substance was expected to trigger an alarm if detected by the Itemiser 3E® on paper entering prisons.

3.3. 4F-MDMB-BUTINACA

In May and June 2019, two samples were submitted for analysis having been seized from within the prison, rather than having been identified and stopped by the screening of prison post. One sample was cut from an A4 piece of paper that had an Itemiser 3E® peak at 9.104 ms, and the other was a scrap of paper found during a prison cell search which had been tested with an Itemiser 3E® and had a peak at 9.099 ms.

When analysed by GC-MS, the chromatograms of the two samples each had one chromatographic peak, both of which had the same mass spectrum (top ten peaks being 219, 145, 131, 275, 307, 220, 304, 57, 232 and 41 *m/z*). Earlier that year, 4F-MDMB-BUTINACA had been raised as a potential emerging threat within the local area via discussions with forensic providers and the spectrum had therefore been researched online and recorded: this spectrum was then matched with the spectra seen for these two samples. Furthermore, the samples were analysed via LC-MS to confirm the identification, resulting in match scores with 4F-MDMB-BUTINACA of 98.94% and 99.18% for the two samples.

The identification of 4F-MDMB-BUTINACA was fed back to Rapiscan Systems Ltd. within four days of the submission to then urge Rapiscan Systems Ltd. to identify a time-of-flight definition for the compound on their Itemiser 3E®. The library definition for 4F-MDMB-BUTINACA was then added to the library in July 2019.

3.4. 5F-MDMB-PICA and MDMB-4en-PINACA

5F-MDMB-PICA was still proving to be popular in November 2019 when two other prisoner post samples were submitted that both featured 5F-MDMB-PICA, one piece of paper featuring orange smears and one piece of plain paper. The paper with orange smears had a peak at 9.190 ms which triggered an alarm for either 5F-ADB or MMB-FUBINACA on the Itemiser 3E® libraries. The flight-times of these two compounds overlap and therefore Rapiscan Systems Ltd. entered them onto the library as a single definition. The plain piece of paper had peaks at 9.165 ms, 9.675 ms (which triggered an alarm for 5F-AKB-48) and 9.959 ms. The presence of 5F-AKB-48 was questioned for this sample as although it was popular in 2015, it has rarely been seen since 2016 [32,18,6].

The GC-MS analysis resulted in multiple chromatograph peaks for both samples at very similar retention times. In both paper samples, the peak at 19.5 min was identified by the user defined library as 5F-MDMB-PICA. The spectrum associated with the peak at around 17.61 min in each sample featured top ten peaks of 213, 301, 145, 298, 171, 214, 357, 269, 185 and 131 *m/z*, and was identified using the Cayman Chemical GC-MS tool [28] as MDMB-4en-PINACA. Both samples were also analysed using LC-MS to further confirm the presence of MDMB-4en-PINACA and 5F-MDMB-PICA. Good chromatographic separation was achieved, and accurate mass values were obtained with match scores of 97% for the 5F-MDMB-PICA peak in each sample and 99.5% for the MDMB-4en-PINACA peak in each sample.

Furthermore, three of the GC peaks in each sample produced high match scores on the NIST 2.0 library to 1-hexadecanol and isopropyl palmitate, both used within detergents, and 1-heptadecanol, commonly used in flavourings. The presence of these compounds suggested that a household product had been added to the paper either as a solvent or to mask the synthetic cannabinoid.

Notably, although the 5F-MDMB-PICA library definition was already present on the Itemiser 3E® software, the samples did not trigger an alarm for that compound. This information was fed back to Rapiscan Systems Ltd. who identified an issue with the substance alarm parameters and amended and updated the definition for 5F-MDMB-PICA on Itemiser 3E® instruments in local prisons in January 2020.

Time of flight information for MDMB-4en-PINACA was also discussed with Rapiscan Systems Ltd. in February 2020 and, as this compound apparently has a very similar time-of-flight to that of 4F-MDMB-BUTINACA, they adjusted the parameters of the definition to encompass the flight times of both drugs, as also discussed by Norman et al. [18].

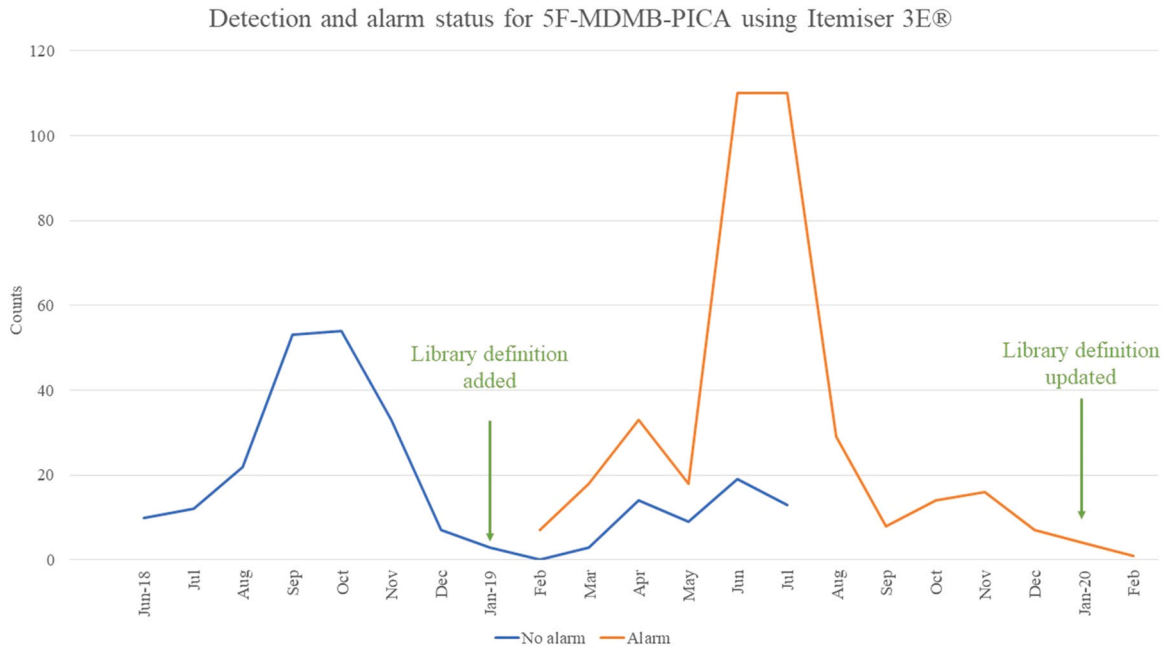

Fig. 2. Line graph for Itemiser 3E® data depicting 5F-MDMB-PICA detection and alarm trends.

3.5. MDMB-4en-PINACA or 4F-MDMB-BUTINACA

In March 2021, a sample was submitted consisting of 19 pages of stained, lined paper with a strong sweet smell. Five of these pages had been swabbed and had Itemiser 3E® peaks ranging from 9.153 ms to 9.191 ms, indicating the presence of 4F-MDMB-BUTINACA or MDMB-4en-PINACA (as both drugs were covered by the same library definition). The remaining 14 pages were not swabbed but included some pages soaked to the point of opacity.

GC-MS analysis determined that MDMB-4en-PINACA was present rather than 4F-MDMB-BUTINACA due to the top ten *m/z* peaks at 213, 301, 145, 298, 171, 214, 357, 269, 185 and 131. However, subsequent LC-MS analysis only achieved an 80% match score when compared to user defined libraries. Even though the correct accurate mass was determined, the library match only correlated with the ammonium adduct. This issue did not occur for the previous MDMB-4en-PINACA samples, resulting in a tentative identification for this sample and further analysis is planned alongside reference standards to confirm the identification.

3.6. Trends and observations

The data extracted from the Itemiser 3E® used at one of the prisons in this study enabled a retrospective investigation of the trends seen for each of the aforementioned drugs and an assessment of the effectiveness of the implementation of the time-of-flight definitions.

Fig. 2 shows the presence of 5F-MDMB-PICA in prison post from June 2018, when the study commenced, with an increased prevalence in Autumn 2018, when several samples were submitted (see Sections 3.1 and 3.2). The implementation of the first library definition for 5F-MDMB-PICA in January 2019 appears to have been very timely as there was a surge in the prevalence of this drug in May to September 2019. Fig. 2 shows that a significant number of samples containing 5F-MDMB-PICA would have entered the prison and caused significant harm and disruption had the definition not been added. Although the majority of the 5F-MDMB-PICA samples were identified by the first iteration of the definition, our investigation of the sample in November 2019 (Section 3.4) highlighted that some samples were not triggering alarms, leading to an update of the definition in January 2020 (see Fig. 2).

5F-MDMB-PICA was first registered by early warning systems in 2016 [36] and had noted popularity in Scottish and German prisons until the end of 2020 [6]. The drug was included in Schedule II of the 1971 Convention on Psychotropic Substances from November 2020, however it still featured in United States of America prevalence data in 2022 [37]. This shows that the popularity of 5F-MDMB-PICA allowed it to prevail in the wider environment over multiple years despite being controlled internationally.

The first samples containing 4F-MDMB-BUTINACA were received in May 2019 (Section 3.3) and the graph in Fig. 3 shows that samples had been entering the prison undetected since at least June 2018 (when the Itemiser 3E® was installed) and showed a dramatic increase in the prevalence of this drug in the first half of 2019. The implementation of the library definition update was after the apparent sudden decline of popularity of these drugs. A resurgence in popularity was seen in January 2020, but as these samples now triggered an alarm, they were prevented from reaching the prison population.

In February 2020, following our investigation of the sample described in Section 3.5, the Itemiser 3E® definition for 4F-MDMB-BUTINACA was expanded to include flight times for MDMB-4en-PINACA. However, our retrospective analysis of the alarm and signal data from the Itemiser 3E® shows that the original definition resulted in detection of MDMB-4en-PINACA and possibly another closely related compound. This is the subject of ongoing research as both drugs are still being reported as popular at the time of writing [37].

The collaboration between the prison, the University and Rapiscan Systems Ltd. proved very effective in identifying novel synthetic cannabinoids entering the prison. Although reference standards could not be used in this project, due to lack of availability and funding, there was generally a high level of confidence in the identifications as all samples were analysed using more than one Category A or B technique as classified by the SWGDRUG [26] guidelines.

This cycle is not currently being implemented on a national scale across the UK. There are, however, other research groups within the United Kingdom also providing confirmatory analysis services to

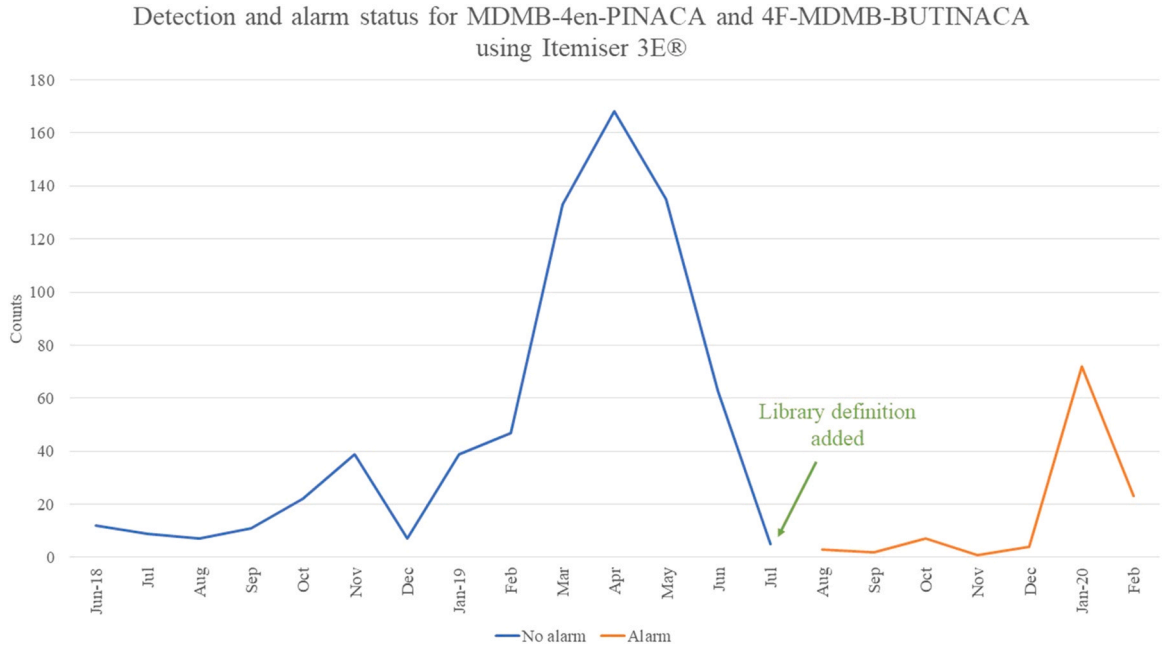

Fig. 3. Line graph for Itemiser 3E® data depicting MDMB-4en-PINACA and 4F-MDMB-BUTINACA detection and alarm trends.

their local prisons, such as the Leverhulme Research Centre for Forensic Science [38,18,6] and WEDINOS [6], plus private forensic companies conducting research, including TICTAC, LGC Group and Eurofins Forensic Services [25]. At the time of writing, further research is being conducted to investigate the processes being used internationally to determine best practice.

Samples which trigger an alarm on narcotics trace detection equipment may be sent for secondary testing under guidelines produced by the Ministry of Justice [27]. However, samples which do not trigger an alarm may still produce a signal, indicating that they contain an illicit substance that simply does not have a library definition yet. For example, on the Itemiser 3E®, signals with a flight-time range of 8.8–9.8 ms are considered likely to contain a synthetic cannabinoid [18]. Without confirmatory testing of these samples, synthetic cannabinoids may still enter prisons. The application of a screening, confirmation and feedback cycle presents a prime opportunity to identify emerging synthetic cannabinoids and disrupt the illicit drugs trade in prisons, and the organised crime groups which profit from it. Without this cycle, prisons will continue to be vulnerable to the next emerging drug threat.

4. Conclusion

During this project, 47 samples of prison post or related papers, were analysed. Using GC-MS, LC-MS and NMR, eight of these samples were identified as containing synthetic cannabinoids. Results for all samples, regardless of the outcome, were fed back to the West Midlands Prisons Group whilst only identifications which were strongly supported by the analytical results were fed back to Rapiscan Systems Ltd. This screening, confirmation and feedback cycle for the eight positive paper samples has resulted in the creation or update, by Rapiscan Systems Ltd., of synthetic cannabinoid library definitions on the Itemiser 3E® library.

The eight positive samples analysed during this project represent approximately 25 A4 sheets of paper which equates to 15,593 individual doses, where 1 cm^2 doses are typically used. Without this work, these samples could have entered prisons to be sold and smoked, ultimately resulting in adverse health effects and contributing to bullying and organised crime. This research has made it clear that, for screening in prisons to be effective, the Itemiser 3E® library must be continually updated as new drugs are identified by confirmatory testing. This feedback cycle has been proven to work in this study and in larger scale studies such as those outlined by Norman et al. [6]. Despite this, there is currently no country-wide system in England to allow this virtuous cycle to be available for all prisons.

Future work is needed to develop the screening, confirmation and feedback cycle on a larger scale to facilitate synthetic cannabinoid identification worldwide. The ready availability of reference standards at reasonable cost will further assist researchers working in this area. The aims of this work would be to reduce the number of synthetic cannabinoids entering prisons, to improve intelligence surrounding which synthetic cannabinoids people are attempting to smuggle into prisons, and to disrupt the knock-on effect of organised crime groups.

CRediT authorship contribution statement

Mia Jane Abbott: Conceptualization, Methodology, Formal Analysis, Investigation, Writing – original draft, Writing – review & editing, Visualization. **Jodie Dunnett:** Conceptualization, Formal analysis, Data curation, Writing – review & editing, Visualization, Supervision. **John Wheeler:** Writing – review & editing, Supervision. **Alison Davidson:** Conceptualization, Validation, Writing – review & editing, Supervision.

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Conflict of interest

The Itemiser 3E® instruments used in this study were owned by the West Midlands Prison Group, His Majesty's Prison and Probation Service (HMPPS) and used with their permission. Although technical

and operational matters were discussed, Rapiscan Systems Ltd. staff were not involved in the preparation of this manuscript.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.forsciint.2023.111613.

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