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REVIEW

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Air monitoring for illegal drugs including new psychoactive substances: A review of trends, techniques and thermal degradation products

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Abstract

The detection of illicit psychotropic substances in both indoor and outdoor air is a challenging analytical discipline, and the data from such investigation may provide intelligence in a variety of fields. Applications of drug monitoring in air include providing data on national and international drug consumption trends, as monitored by organisations such as the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) and the United Nations Office on Drugs and Crime (UNODC). Air monitoring enables mapping of illicit drug manufacturing, dealing or consumption in cities and the identification of emergent compounds including the recent proliferation of new psychoactive substances (NPS). The rapid spread of NPS has changed the global drug market with greater diversity and dynamic spread of such compounds over several nations. This review provides an up to date analysis of key thematic areas within this analytical discipline. The process of how illicit psychotropic substances spread from emission sources to the atmosphere is considered alongside the sampling and analytical procedures involved. Applications of the technique applied globally are reviewed with studies ranging from the analysis of individual dwellings through to major international air-monitoring campaigns providing evidence on global drug trends. Finally, we consider thermal breakdown products of illicit psychotropic substances including NPS that are released upon heating, combustion or vaping and related potential for exposure to these compounds in the air.

KEYWORDS
air monitoring, drugs of abuse, global drug trends, new psychoactive substances, thermal breakdown products

1 | INTRODUCTION

The presence of licit and illicit psychoactive substances in the environment has been investigated widely over the last 30 years in a range of investigative pursuits. For many years the analysis of drugs in wastewater has provided useful data on 'emerging pollutants' such as psychoactive substances but increasingly research in the field of air monitoring for such compounds is contributing valuable intelligence on drug trends and anthropogenic activity. These pursuits are encouraged by the diversity and growth of the illegal drug market globally. Traditional illicit drugs and new psychoactive substances (NPS) are growing as a global threat,[1] and so is the requirement to monitor

these compounds in the air, both indoor and outdoor. The importance of air monitoring in this context is the ability to provide useful drug monitoring data at two distinct levels: (i) drug levels in the ambient air of cities or rural areas can provide a wide-scale overview of drug distribution, consumption and dealing areas; (ii) drug levels in indoor air may provide valuable data at a local scale on secondary exposure risk. The presence of illicit drugs in ambient air, however, is often short lived and more variable than their presence in wastewater, and this can make the technique appear complex. It is beneficial, however, to view the application of air monitoring in such contexts as complementary to wastewater analysis rather than a rival technique. Both approaches offer very valuable data. Air monitoring for illicit drugs and NPS has shown useful strengths in a number of areas, including long term monitoring and mapping of drug trends, near real time information (dependent on sampling duration but often a window of hours), and anonymity. In addition, the choice of sampling sites for outdoor air monitoring are almost unlimited and the ability to target specific indoor sites at a local level with air sampling shows great promise.

The ability of analytical methods to cope with ever increasing numbers of analytes is crucial, and demand for multi-analyte methods in this field has been driven by the emergence of NPS. NPS are stated to be 'substances of abuse, either in pure form or preparation that are not controlled by the 1961 Single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic substances but which may pose a public health threat comparable to that posed by substances listed in these conventions'.[2,3]

The rapid proliferation of NPS abuse in recent times is of global concern, and as such we pay particular attention to these compounds regarding their determination in air in this review. NPS fit closely with their traditional drug counterpart that they are imitating or close to structurally.[4,5] Common stimulants are those in the cathinone family and are related to MDMA, cocaine and amphetamine like structures; mephedrone is an example of a popular NPS in this group.[6,7] Depressants include traditional opioids such as heroin/morphine or synthetic opioids like AH-7921; novel fentanyl derivatives (such as 2,5-dimethyl and 3,5-dimethyl- fentanyl) or benzodiazepine derivatives (such as diclazopam or flubromazepam) fall into this category as an NPS, due to their similar effects and structural similarities to their traditional counterparts.[7–10] Hallucinogens either traditional or the newer synthetic ones fall into the psychedelic category. A few of the known NPS that fall in this category are 5-MeO-DALT or the NBOMe series that have effects similar to traditional agents such as LSD or psilocybin.[7,9] Dissociative drugs form another category of the hallucinogens and include NPS such as methoxetamine and ketamine.[6,7,9] Lastly there are the cannabinoids; traditional cannabinoids stem from cannabis with tetrahydrocannabinol (THC) a principal component. Synthetic cannabinoids are known as synthetic cannabinoid receptor agonists (SCRAs) popularly referred to as 'Spice' or 'Black Mamba' which have similar cannabimimetic effects to THC.[7,11]

The choice of psychoactive substances to investigate in air samples reflects the increasing dynamicity of the global drug market with the significant growth of NPS alongside drug demand from regular users and those with drug disorders.[12–14] Traditional drugs (opium, heroin and cocaine) have also had a record increase in global production, manufacturing and seizures.[15] The largest market increase over the last two decades have been synthetic NPS, followed by amphetamine-type stimulants (ATS) and synthetic opioids.[1,16]

Monitoring techniques for air and water have been utilised by government bodies and researchers to determine the impact and potential consumption rate of these harmful compounds. Targeted actions by governmental bodies and organisations have often aimed to control the production and abuse based on prevalence and consumption data resulting from these monitoring campaigns.[17,18]

A multitude of monitoring techniques have been developed to improve detection capabilities of drugs of abuse (DoA) across many environments. There have been multiple types of monitoring studies (such as analysis of the air or analysis of wastewater) that are conducted to measure the concentration of a given drug in a specific population.[19,20] From this data researchers are able to calculate or at least estimate levels of drug consumption or disposal for that specific population, and from there determine socio-economic, geographic, environmental or temporal patterns that can be utilised to prevent the rising abuse levels.[21]

Air-monitoring approaches for DoA are the focus of this review paper; both new and traditional DoA have been detected in the air over the last several decades. Research has ranged from the detection of target parent drugs in ambient outdoor air in cities, to comparing indoor/outdoor pollutants, toxicants and DoA within singular establishments (establishments ranging in size from hospitals and schools to small cafes and dwellings).[22–26] In recent years the analysis of the smoke and associated drug paraphernalia to detect thermal transformation products of the parent drugs has grown in use; it offers a different perspective on the associated unknown potential risks that come from secondary exposure to new psychoactive substances.[27–29]

2 | THE MOVEMENT OF DRUGS OF ABUSE FROM PRODUCTION TO ENVIRONMENTAL CONTAMINATION OF THE AIR

Investigating the presence of DoA in the air requires an understanding of how the substance itself went from the point of production to being present in ambient air. Contaminants in the air can be linked to anthropogenic emission sources, typically they can be polycyclic aromatic hydrocarbons (PAHs) which are associated with vehicle sources, industrial sources as well as aerosols or fluorotelomer alcohols dispersed in surface waters.[21,23,30] DoA concentrations can depend on anything from the local areas meteo-climatic regime or the anthropogenic factors such as increased human social activity (recreational drug consumption and trafficking) or population size (or density).[31,32] Researchers have attempted to link target DoA prevalence to known drug-related criminal activity, based on higher DoA concentrations in certain districts; clinical or criminal records from the district of interest may be linked to concentrations that indicate related consumption, production, handling or transport.[33]

Investigating the different potential psychoactive emission sources in the atmosphere is vital to understand the population patterns (if any), especially to reveal further information about different backgrounds.[31] Drug movement in the atmosphere can differ based on source and the process involved. Cocaine can be present in the air via direct consumption or transported via intra-building air ventilation from peoples clothing and hair (from drug handling/contact).[26] Emission sources of production/handling can be specific to smuggling, trading and distribution of certain illicit drug groups which can result in direct disposal of the drug into the environment, whereas drug traces in the water and air from consumption have multiple administrationroutes. These can be through either solid ingestion (tablets/pills), intranasal (powder), intravenous injection or through combustion inhalation (i.e., smoking).[19,34] Consumption traces can be found via investigating the presence of metabolites and parent compound traces in the abusers urine in wastewater for example.[35] However, combustion/smoking is one of the more likely routes for DoA traces to contaminate the air during the act or previous to its metabolisation.[36]

Some traditional DoA such as heroin and cocaine are not typically smoked like cannabis, they can be placed on a surface or makeshift pipe, and heated using a lighter to inhale the vapours.[34,36] What can be detected in air afterwards often depends on the combustion temperature, and these products for cocaine and heroin have been researched previously in this context.[37] The parent compound (of either traditional or new psychoactive substances) may be detected in the air alone, alongside its thermal transformation products (i.e., thermal/pyrolytic degradants) or just the products alone depending on the thermal degradation route.[37,38] Smoking/combustion and intranasal ingestion are the likely emission sources for trace amounts of a DoA detected in the air.[39] Cannabis is almost always smoked and cocaine can be smoked or consumed via intranasal ingestion, so their levels in air can be relatively high compared to other traditional DoA detected due to their emission sources being potentially both consumption and handling/transport. Amphetamines, by contrast, are administered as pills, therefore are likely to have lower concentrations in the air as their emission sources directly relate to handling rather than consumption additionally.[39]

3 | SAMPLE PROCESSING AND INSTRUMENTAL TECHNIQUES FOR THE DETECTION OF TRADITIONAL AND EMERGING DRUGS OF ABUSE IN THE AIR

3.1 | Sample collection and storage

Targeted psychoactive substances in ambient air are typically present in particulate matter (PM) with the common grain sizes PM10 or PM2.5, that is, particles with an aerodynamic diameter finer than 10 or 2.5 μm, as these sizes are 'inhalable' and can affect our breathing if they enter our lungs.[31,40,41]

Investigating multiple substrates and particulate fractions allows for a better understanding of the true impact of substances on organisms. It is useful to understand which particulate fraction a certain drug accumulates in the most; cocaine accumulates in particulates with over 80% in PM2.5.[21] In a comparison between PM2.5 and PM10 inlets cocaine and its metabolite benzoylecgonine had similar distribution levels between the inlets.[31] The authors suggested that the aerodynamic diameter of particulates that cocaine was detected on were under 2.5 μm. Investigating one substrate, that is, PM10 or 2.5 singularly, as well as the presence of these compounds in the particulate phase is the common approach as there have been comparatively fewer studies that have investigated the vapour in the open atmosphere or distribution.[21]

Low, medium or high-volume samplers are chosen based on the intended sample size, the amount of air to be collected and the extent to which larger samplers may create an environmental disturbance. Low volume samplers may be chosen to minimise microenvironment perturbation inside a small establishment as opposed to the typical outdoor setting higher volume samplers are used in.[24] Low volume samplers have the ability to pump a large amount of air; however, it can be more time consuming, whereas, high-volume samplers can be noisy (due to strong air agitation) and large in size.[42] 'Active' samplers such as these pump air through a filter, whereas 'passive' samplers introduce molecular diffusion of contaminants through a diffusive surface on the adsorbent.[43] Although passive samples do not require a power supply (advantageous for monitoring inhospitable sites), they are not frequently used for emerging contaminants (including illicit drugs) in general.[43] The issue with passive SPME sampling (as opposed to dynamic SPME sampling) is that it only exposes the SPME fibre to a limited volume of air which can be impacted by uncontrolled air currents.[44] Dynamic SPME sampling allows for a higher volume of air to be sampled through the use of an air pump.

PM are typically collected on either PTFE membrane filters or quartz filters which act as an inert membrane for the PM to be collected on, thus they can be recovered effectively without interference.[21,45,46] Filter storage usually has a common approach regardless of type; PTFE or quartz filters are sealed after sampling, and typically wrapped in aluminium foil, stored at a low temperature (−20°C for example) and sometimes kept in the dark.[47–50] This type of storage helps to ensure there is no contamination from other particulates during transportation or handling, and to ensure minimal breakdown of the target compounds or PM from oxidation, thermal breakdown or photolysis.[46]

Daily air samples may be 'pooled' together into 'weekly pools' prior to the solvent extraction step to interpret weekly trends over the sampling campaign.[26,33,51] Cecinato et al.[25] pooled samples in 2- or 5-day pools to separate weekend and weekdays respectively to determine if there was a difference between them. The aim was to determine temporal patterns with certain compounds and outline if those compounds are abused more frequently on the weekend, that is, recreationally at social events, or if they are abused in everyday life.[52]

3.2 | Sample extraction

Among earlier ambient air DoA studies, organic solvent extraction was conducted using a Soxhlet apparatus followed by a column chromatography clean up step to ready the analytes for instrumental analysis.[25,30,32,51] If headspace analysis is conducted then typically solid phase microextraction will be used; Lai et al.[53] found that a 100 μm polydimethyl siloxane (PDMS) SPME fibre can be used in a headspace air sampling approach to extract and preconcentrate the targeted volatile markers of certain illicit compounds such as cocaine, MDMA and marijuana. This is supported by Ilias et al.[54] who established that SPME of several fibre types (PDMS, carboxen and divinylbenzene) could be used as a solvent-free sample preparation technique with high sensitivity and relatively low costs. Various SPME fibres may be used to extract a range of analytes based on the coating type; fibre sensitivity depends on molecular weight and polarity of the analytes to be extracted.[55] However, these studies were conducted within dwellings, a specific storage area or confined space of interest as opposed to outside and the ambient air.[44,54,56]

Other forms of extraction such as accelerated solvent extraction and ultrasonic baths are used less frequently in ambient air DoA monitoring; Postigo et al.[57] were able to analyse multiple illicit drugs in airborne particles using 'pressurised liquid extraction' (PLE). PLE has been used previously when analysing fine airborne PM to determine the presence of pesticides and PAHs.[58,59] Following PLE the extract can be directly injected into a liquid chromatography tandem mass spectrometry (LC-MS/MS) system without the need for further pre-treatment, lending the technique a degree of convenience. Although there has been little exploration regarding the optimisation or comparison of extraction techniques for illicit drugs in PM specifically, there have been studies comparing PLE, Soxhlet and sonication in the context of other substances such as PAHs and exhaust particulates.[60] Rynö et al.[60] compared these techniques and found that PLE showed an advantage over Soxhlet and sonication for extracting PAHs and exhaust particulates. Soxhlet can be a laborious process and sonication can sometimes unbind some of the filter material and detach collected particulates due to its vigorous extraction. PLE can be more efficient and the compounds extracted from the samples remain clear and can be directly injected into the LC system. In future studies the PLE technique may warrant consideration when determining the presence of illicit drugs in ambient air as it could offer further advantages.

3.3 | Instrumental analysis of target compounds

Detecting psychoactive substances in the air is a complex process as both air and airborne particles contain thousands of components, so a highly sensitive and selective method to reliably determine these compounds is needed. Instrumental analysis of DoA in air samples is dominated by mass spectrometry.[22,24,25,30,33,50,51,61] Comparably for PAH analysis for example in environmental samples GC is usually preferred over LC due to the greater selectivity, resolution, and sensitivity.[62,63] LC when applied in air-monitoring studies is typically coupled to a triple quadrupole mass spectrometric system; data acquisition will typically be performed in selected reaction monitoring mode that will involve recording the transitions between the precursor ion and the two most abundant product ions for each target analyte, usually two transitions per compound.[20,31,39,49,56,64]

There is a lack of published comparison between analytical instruments in this context specific to chromatographic separation; however, there have been investigations comparing GC/LC-MS systems to Ion Mobility Spectrometry (IMS) for air-monitoring applications.[65–67] The use of IMS in regard to air monitoring of illicit compounds ranges from investigations of the indoor environment (dwellings and laboratories) to being used in scanning shipments for traces of drug smuggling[53,66] as well as targeting volatile chemical signatures of illicit drugs and explosives.[67,68] Lai et al.[53] outlined the advantages that come with using IMS as opposed to the more traditional analytical systems, specifically in commercial realms. Commercial IMS and canines are common trace detection systems used in the US to detect particulates and vapours at checkpoints. Lai et al.[53] detail the coupling of SPME to an IMS analyser and its effectiveness as a detection technique for non-invasive headspace sampling of air. This process involves a SPME 100 μm PDMS fibre exposed to the container air, volatile/semi-volatile compounds are then extracted via adsorption onto a non-volatile polymeric coating or onto a solid sorbent phase (for extraction times of 2, 5, 10, 15 and 30 min). Following sampling, adsorbed compounds can be thermally desorbed into an IMS analyser. Cocaine HCl and free base, MDMA tablets and marijuana samples were successfully detected via this method. In turn, it is argued that SPME performs better with the traditionally chosen analytical systems as the IMS method suffers from interferences from other substances (such as nicotine) when trying to detect certain illicit substances such as methamphetamines.[44] It may be more reliable to use GC-MS as the analytical system especially if the procedure involves a SPME air sampler.

Guerra-Diaz et al.[68] tested a device that sampled large volumes of air through planar solid phase microextraction, which incorporated a high surface area for efficient absorption of the analytes onto a sol-gel polydimethylsiloxane (PDMS) coating for direct thermal desorption into an IMS. It sampled the headspace over MDMA, pentolite, low explosives, 2,4-dinitrotoluene (2,4-DNT) and diphenylamine (DPA), all of which were detected in the low ng range in a short time frame with low volume samples. Mohsen et al.[67] investigated the presence of THC and methamphetamines/amphetamines in air through the use of a field asymmetric IMS microchip sensor (FAIMS). The advantage of IMS may be its versatility with different forms of sample collection over GC/LC-MS/MS which may require more laborious sample preparation and experimental conditions, which is not desirable for field work that requires a fast, efficient, 'on-site' response. Mohsen et al.[67] was successful in detecting THC, methamphetamines, and amphetamines above the limit of detection using the FAIMS technique.

Outside of fieldwork, IMS has also been used to assess drug exposure in forensic laboratories as an occupational hazard. Armenta et al.[66] utilised the technique as an alternative to typical procedures used to control workplace air safety (GC-MS/LC-MS). Timing and

sample preparation impacts assessment, as it can take up to 2 weeks for a full analysis, by which point personnel could have been exposed to excessive amounts of an illicit substance. The authors tested the Smiths Detection IONSCAN-LS IMS analyser due to its simplicity, high sensitivity, high operational speed and its adaptability for sample collection. Cocaine was detected in air samples in the laboratory, reception and two vaults, and 4-MEC, MDMA and other amphetamines were detected in the reception area. The samples differed in concentration of cocaine over the days that there was no cocaine seizure and handling of seized cocaine. Cocaine concentrations in a day without large cocaine seizures were in the range of 100 ng m^{-3}, this increased as handling of cocaine seizures occurred with concentration levels reaching up to 10,000 ng m^{-3}. The concentrations without large seizures are considerably smaller than the occupational exposure limits (OELs) of pharmaceutical exposure in workplaces. However, there may be potential for chronic exposure from these low concentration surfaces; surface wipe and nasal samples revealed there could be hazardous amounts in their investigation.

Proton transfer reaction mass spectrometry (PTR-MS) has been applied to detect traces of explosives and illicit drugs in ambient air.[69] PTR-MS may have the potential of detecting traces of explosives and drugs that adhere to people or objects with a higher level of confidence than IMS technology. The technique involves measuring protonated parent signals through headspace sampling of small drug quantities without pre-treating, pre-concentration or thermal desorption. The higher sensitivity of PTR-MS allows identification of different compounds at low concentrations with little interference between background noise and the protonated parent drug peaks (for Certified Reference Materials [CRM]). 'Street' level drug samples are a more complex chemical environment due to the presence of adulterants/impurities. The authors showed that cocaine and ecstasy could be observed successfully, heroin did not show a second peak associated with the ^{13}C isotope; however, it could be identified on the spectra. 'Street' heroin was analysed to assess the adulterant impact, and it was demonstrated that heroin could be identified; however, caffeine and paracetamol (the adulterants) were the dominant ions. Although this technique shows promise, there is a lack of supporting research and DoA air studies are dominated by the prevalence of various GC-MS and LC-MS systems.

4 | AIR MONITORING FOR THE ASSESSMENT OF TRENDS IN DRUGS OF ABUSE

One of the key aims of DoA air monitoring is to demonstrate patterns in the data, whether they are temporal–spatial in their concentrations, or the way the compound breaks down during consumption routes. This information can further elaborate emission sources/types, provide links to crime statistics, geographic and socio-economic patterns. Such intelligence and data may increase the chance of successful drug seizures, mitigation and prevention of drug epidemics, ranging from distribution of abuse to their longer term physiological and eco-toxicological impact. Although air monitoring for DoA mainly has been used to detect drug usage patterns, it is argued that chronic exposure in contaminated areas may impact public health even in such low cumulative lifetime doses.[20,28,31,51,64,70–72] Table 1 presents an overview of drug analytes and concentrations detected in ambient air in various countries across the globe.

4.1 | Socio-economic and socio-environmental links to drug patterns

The spread and prevalence of illicit drugs can be monitored using air analysis to reveal key information and trends. Viana et al.[31] investigated potential socio-economic and socio-environmental links by comparing emission sources in various environments. They found an unexpected apparent decrease in drug use from night-time recreation locations in comparison to campus and residential areas. Cecinato et al.[47] conducted air sampling campaigns in 2006–2007 across urban regions separated by social, territorial, and meteo-climatic situations; they found a degree of proportionality between atmosphere cocaine concentrations and drug prevalence/seizures or crimes (in Rome, Milan and Taranto). Larger concentration differences in city districts could be due to youth meetings or music events being held there (with consideration of the meteo-climatic regime), suggesting an anthropogenic influence. Similarly, Cecinato et al.[33] compared drug concentrations in air to drug and non-drug-related crimes and found that airborne cocaine concentrations correlated with quantities of seized drugs (except heroin and marijuana) with some drug-related crime indicators.

Population size and density are factors that can link correlation between social backgrounds and drug concentrations (although this has only been outlined with cocaine for the majority). It has been suggested though that it is more effective to base population estimates on phone traffic coverage, cigarette or vehicle fuel consumption and urban refuse volumes.[23] DoA air concentrations may also vary based on different geographic regions due to weather conditions and the time of year.[73] Ilias et al.[51] investigated the geographic origins of cannabis samples by tracking their movement and distribution via headspace analysis. They tracked the individual principal components of the samples to different regions (Geneva and Zurich). This can link to transport-based patterns certainly; Viana et al.[31] believed that atmospheric patterns can impact targeted drug dilution rates and transport patterns 'at a local level'. Transporting and handling of goods could contribute to atmospheric contamination in addition to direct consumption, examples being large cargo movement and smuggling, to traces being transported from peoples clothing and hair to the atmosphere via intra-ventilation transport of drug traces indoors.[26,53,69] Farms on which plant-based drugs are found should not always be considered the source of drugs in the atmosphere, as air-monitoring studies are often conducted in places where coca and cannabis crops are not grown in large quantities.[21] They could therefore be removed as a potential source for atmospheric presence. Drug transportation or smuggling should be considered as another atmospheric source other than direct disposal or consumption.[53]

TABLE 1 Air-monitoring campaigns for illicit drugs

Year	Country	Air sampling technique	Analytical technique	Illicit drugs detected in ambient air	Concentration range (min and max) (pg m^{-3} or ng m^{-3})	Reference
2007	Italy	High-volume sampler on ultra-clean quartz microfibre filters 24 h sampling, with PM10 inlet.	Soxhlet extraction Gas chromatography coupled to high resolution mass spectrometry (GC-HRMS)	Cocaine	12 ± 10 to 98 ± 13 pg m^{-3}	Balducci and Cecinato[32]
2009	Spain	High-volume sampler on quartz microfibre filters 24 h sampling, with PM2.5 inlet.	Pressurised liquid extraction (PLE) Liquid chromatography-tandem mass spectrometry (LC-MS/MS).	Cocaine	204.03 ± 172.27 to 479.74 ± 275.68 pg m^{-3}	Postigo et al.[57]
				Benzoylecgonine	13.95 ± 6.09 to 29.07 ± 23.89 pg m^{-3}	
				Heroin	ND, 83.72 ± 52.74 pg m^{-3}	
				6-Acetylmorphine	ND, 22.80 ± 11.40 pg m^{-3}	
				3,4-Methylenedioxymethamphetamine	ND, 2.90 pg m^{-3}	
				Methamphetamine	<LOD, 3.49 pg m^{-3}	
				Amphetamine	1.42 ± 0.91 to 2.28 ± 1.18 pg m^{-3}	
				Δ9-Tetrahydrocannabinol	27.12 ± 42.38 to 43.70 ± 34.73 pg m^{-3}	
2009	Italy	High-volume sampler on ultra-clean quartz microfibre filters and PTFE membranes 24 h sampling, with PM10 inlet.	Soot extraction by ultrasonic bath Gas chromatography coupled with ion trap tandem mass spectrometry (GC-MS/MS)	Δ9-Tetrahydrocannabinol	<1 to 104 ± 61 pg m^{-3}	Balducci et al.[49]
				Cannabidiol	<1 to 6 ± 3 pg m^{-3}	
				Cannabinol	10 ± 2 to 70 ± 22 pg m^{-3}	
2009a	Italy, Portugal, Chile and Brazil	High-volume and low volume samplers on ultra-clean quartz microfibre filters sampling with PM10 and PM2.5 inlets (no data on collection hours)	Soxhlet extraction Gas chromatography mass spectrometry (GC-MS)	Cocaine	Italy = 7–470 pg m^{-3} Portugal = 37–304 pg m^{-3} Chile = 2200–3300 pg m^{-3} Brazil = 42–890 pg m^{-3}	Cecinato et al.[47]
2009b	Italy	High-volume sampler on PTFE membranes 24 h sampling, with PM10 inlet	Soxhlet extraction GC-HRMS	Cocaine	6–87 pg m^{-3}	Cecinato et al.[22]
2010	Italy	Medium volume samplers on ultra-clean quartz filters and Teflon filters 24 h sampling with PM10 and PM2.5 inlets	Soxhlet extraction GC-MS	Cocaine	ND, 0.116 ± 0.118 ng m^{-3}	Cecinato et al.[48]
				Total cannabinoid (cannabidiol + cannabinol + Δ9-tetrahydrocannabinol)	0.037 ± 0.022 to 0.537 ± 0.420 ng m^{-3}	
	Spain	High-volume sampler on quartz filters 24 h sampling with PM2.5 inlets	PLE (LC-MS/MS)	Cocaine	29–851 pg m^{-3}	Viana et al.[39]
				Benzoylecgonine	4–78 pg m^{-3}	

(Continues)

TABLE 1 (Continued)

Year	Country	Air sampling technique	Analytical technique	Illicit drugs detected in ambient air	Concentration range (min and max) (pg m^{-3} or ng m^{-3})	Reference
				Δ9-Tetrahydrocannabinol	3–156 pg m^{-3}	
				Heroin	<LOD, 143 pg m^{-3}	
				6-Acetylmorphine	<LOD, 30.9 pg m^{-3}	
				Amphetamine	0.5–5.2 pg m^{-3}	
				Methamphetamine	0.9–3.5 pg m^{-3} (only mean available)	
				3,4-Methylenedioxymethamphetamine	<LOD, 2.9 pg m^{-3} (only mean available)	
2011	Spain	High-volume samplers on quartz fibre filters 24 h sampling with PM10 and PM2.5 inlets	PLE LC-MS/MS	Cocaine	11–336 pg m^{-3} (only mean available)	Viana et al.[31]
				Heroin	5–90 pg m^{-3} (only mean available)	
				Amphetamine	<LOD, 15 pg m^{-3} (only mean available)	
				Δ9-Tetrahydrocannabinol	23–34 pg m^{-3} (only mean available)	
				6-Acetylmorphine	<LOD, 32 pg m^{-3} (only mean available)	
				Benzoylecgonine	<LOD, 54 pg m^{-3} (only mean available)	
				Ephedrine	3.1–4.4 pg m^{-3} (only mean available)	
2012	Italy	Medium volume samplers on quartz fibre filters 24 h sampling with PM10 and PM2.5 inlets	Soxhlet extraction GC-MS and GC-MS/MS	Cocaine	0.01 to 0.26 ± 0.11 ng m^{-3}	Cecinato et al.[51]
				Total cannabinoid (cannabidiol + cannabinol + Δ9-tetrahydrocannabinol)	ND, 4.2 ng m^{-3}	
2014	Italy	Medium and low volume samplers on PTFE filters 24 h sampling on PM2.5 inlets	Pressurised solvent extraction (PSE) GC-MS	Cocaine	0.03 ± 0.02 to 0.22 ± 0.16 ng m^{-3}	Cecinato et al.[25]
				Cannabidiol	<LOD, 0.93 ng m^{-3}	
				Cannabinol	0.05 ± 0.01 to 1.21 ± 0.17 ng m^{-3}	
				Δ9-Tetrahydrocannabinol	<LOD, 1.69 ± 1.82 ng m^{-3}	
	Italy	Low volume samplers on PTFE filters 24 h sampling on PM2.5 inlets	PSE GC-MS	Cocaine	0.07 ± 0.03 to 0.14 ± 0.06 ng m^{-3}	Cecinato et al.[24]
				Cannabidiol	0.01 ± 0.01 to 0.11 ± 0.11 ng m^{-3}	

TABLE 1 (Continued)

Year	Country	Air sampling technique	Analytical technique	Illicit drugs detected in ambient air	Concentration range (min and max) (pg m^{-3} or ng m^{-3})	Reference
				Cannabinol	0.05 ± 0.03 to 0.98 ± 0.89 ng m^{-3}	
				Δ9-Tetrahydrocannabinol	0.01 ± 0.01 to 2.52 ± 2.52 ng m^{-3}	
2015	Spain	High-volume samplers on quartz microfibre filters 24 h sampling on PM10 inlets	PLE LC-MS/MS	Cocaine	13–1848 pg m^{-3}	Mastroianni et al.[64]
				Benzoylecgonine	0.3–205 pg m^{-3}	
				Ephedrine	5–77 pg m^{-3}	
				Amphetamine	3–31 pg m^{-3}	
				Methamphetamine	0.7–610 pg m^{-3}	
				3,4-Methylenedioxymethamphetamine	0.2–7 pg m^{-3}	
				Heroin	2–49 pg m^{-3}	
				6-Acetylmorphine	3–32 pg m^{-3}	
				Methadone	0.6–28 pg m^{-3}	
				2-Ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine	0.4 pg m^{-3}	
				Cannabidiol	17–981 pg m^{-3}	
				Cannabinol	46–6020 pg m^{-3}	
				Δ9-Tetrahydrocannabinol	6–417 pg m^{-3}	
2016	United Kingdom, The Netherlands, and Sweden	Medium volume samplers on PTFE and quartz fibre filters 24 h sampling on PM10 and PM2.5 inlets	Sonication extraction GC-MS	Cocaine	The Netherlands = <LOD, 0.14 ng m^{-3} United Kingdom = 0.05 ± 0.03 to 0.23 ± 0.11 ng m^{-3} Sweden = <0.003 ng m^{-3}	Balducci et al.[50]
				Cannabinol	The Netherlands = <0.003 to 0.03 ± 0.03 ng m^{-3} United Kingdom = 0.01 ± 0.01 to 0.06 ± 0.02 ng m^{-3} Sweden = <0.01 to 0.02 ± 0.00 ng m^{-3}	

Note: Analytical approach and key findings from across the globe.
Abbreviations: ND, not detected. <LOD, below limit of dDetection.

4.2 | Impact of atmospheric conditions on temporal drug abuse patterns assessed via air analysis

Temporal patterns (seasonal and weekly) from air monitoring can be linked with illicit drug use. Weekly patterns of usage (based on concentration and consumption loads) showing higher 'drug use' on the weekend compared to weekdays is typically found (not always as shown by Mastrioanni et al.[64]), indicating 'recreational use' or illegal trade.[31,52] Higher weekend 'emissions' (i.e., concentrations) would support the sources likely being from consumption rather than transport/handling or smuggling.[21,24,31,39] Regarding seasonal patterns, Cecinato et al.[26] noted their target samples (nicotine, caffeine, cocaine, and cannabinol) occurred in all samples with a much lower concentration in the spring/summer period. Castiglioni et al.[21] outlines a lower summer concentration and higher winter concentrations may not be to do with less drug users existing in summer/spring periods, but more to do with influence of temperature, the boundary layer and oxidation capacity. There are lower concentrations in the summer due to an increase of dispersion and of atmospheric boundary layer (ABL) height during this period.[50] The ABL (also known as planetary boundary layer [PBL]) traps water vapour and pollutants (such as DoA) emitted from the earth's surface; a drop in height could be the result of a weaker turbulent transfer of heat and momentum.[74]

Anthropogenic emissions (pollutants and contaminants) are released in the form of plumes, which will be buoyant due to their higher temperature than the ambient air.[75,76] These conditions can influence the height they are raised to as well as the ABL/PBL, thus influencing the contaminant/pollutant distribution. Additionally, it can be inferred that the amount of solar radiation in autumn and winter months is less than the other seasons, therefore the ability to diffuse emissions and transport them to higher altitudes can be significantly inhibited.[75] The increase in pollutant/contaminant build up and winter concentrations is because they are not free to escape and dispense (weak thermal convection).[77,78] Stagnation and dispersion restriction can occur in the summer; however, the atmospheric oxidation capacity and photolytic degradation is greater, and most emitted atmospheric trace gases are removed by oxidising chemical reactions involving the ozone and hydroxyl free radicals.[79] The radical 'OH' is part of this atmospheric anthropogenic trace gas (fossil fuels, agriculture, vegetation, VOCs and more) 'removal mechanism'; OH sources can be decreased or 'turned off' by lowering ultraviolet radiation (in night-time and winter, increased cloudiness etc.), that is, influenced by solar radiation.[80,81] Local sources can overpower meteo-climatic regimes, however; this is why investigations have been conducted in different regions in similar climates.[50]

5 | DRUG TRANSFORMATION AND THERMAL DEGRADATION PRODUCTS

Air monitoring for DoA is not limited to the detection of parent compounds to demonstrate prevalence and concentration. There has been much focus on the relationship between drug transformation products (metabolites) and parent compounds to attempt to provide insight as to the emission source of the drug (handling, direct deposition or abuse).[27,31,64] Drug metabolites have been a focus of larger air-monitoring campaigns, but other products have also been targeted such as thermal degradation products (thermal degradants). Thermal degradants are created as a result of the parent drug being heated, volatilised, or combusted via the relatively common heating/smoking administration route.[28,82,83] The term 'pyrolytic products' specifically refer to products that result from a specific gas-phase thermal degradation reaction which can lead to the initiation of combustion and therefore are referred to differently than thermal degradants.[28]

Studies of the thermal breakdown (via smoking or heating) of drug compounds have been conducted since the late 80s where researchers investigated the thermolytic and pyrolytic breakdown of cocaine, heroin and amphetamines to determine how the drug itself may transform.[84–90] In recent years thermal degradation studies have investigated both traditional and new psychoactive substances to determine transformation products unique to the parent compound, that is, pyrolytic biomarkers aka 'pyromarkers'. The study of these transformation products can reveal further information about the parent drug itself, that is, what pathways it takes, how it fragments, thermal stability and how it could possibly affect the user.[91,92] In recent years synthetic cannabinoids and synthetic cathinones have been the subject of research focusing on pyrolysis and associated potential harm to the user's health.[27,29,93,94] Objectives of this work have been to: identify the thermal-based changes the parent compound undergoes; to ascertain if evidence of these changes can be found in the released vapour/smoke; and to determine if there is any associated toxic, carcinogenic, mutagenic risk associated with breathing in these products or being exposed to them in a close proximity.[28,72,82,84,95]

5.1 | Controlled studies and the sampling of drug thermal degradation products

The majority of drug thermal degradation studies to date have been conducted in controlled environments, combusting or heating drug compounds directly, rather than searching for drug degradation products in the ambient air in a city or a dwelling.[28,88,94] Drug thermal degradation experiments will need to consider the desired temperature range for the work; a suitable temperature range reflects the drug paraphernalia that drug users utilise which may range between: cigarettes, electronic cigarettes (E-cigs), aluminium foil, glass pipe/surface or a tube furnace. Different paraphernalia reach different temperatures; smoking for example (with a cigarette typically) can reach high temperatures up to 700–900°C and there are some toxic breakdown products that are not produced until approximately 200°C.[94,96] An 'e-cig' can have a very large temperature range; Chen et al.[97] investigated the heating coil temperature for e-cigarettes under different conditions (dry, wet-through-wick and full-wet) and found that it could range from 40–950°C. Other miscellaneous paraphernalia used for heating such as a glass bulb was found to reach over 300°C when heated with a disposable lighter to heat a powder until it turned

to tar.[27] Various studies have examined the temperature range for these different paraphernalia, as well as the 'optimal' temperature for an efficient combustion/heating of the product; for example, Nakahara et al.[85] investigated the pyrolysis of crack and cocaine hydrochloride and their degradation products produced at different temperatures. They investigated the correlation between the inhalation efficiency and the temperature and found that higher temperatures reduced the inhalation efficiency of cocaine and caused a greater production of methylecgonidine (thermal product of cocaine). Gostič et al.[89] studied the thermal degradation of adulterated cocaine samples under aerobic pyrolytic conditions and investigated the 'optimal' temperature for production (450°C approximately using their pyrolysis apparatus and 50 mg of sample) (Figure 1). Temperature monitoring of such experiments is often achieved using thermocouples, chosen for their efficient heat signature data collection and wide temperature range.[87,92,98] For effective heating of the compound a pyrolysis probe (pyroprobe/pyrolyzer) may be used as a more suitable device than simply a lighter or blowtorch. Such pyrolysis probes can avoid thermal reproducibility issues through heating the samples in a controlled environment (Figure 2).[82,88,99]

Research on drug thermal degradation products has focused on: sampling of the smoke/vapour itself; the burnt remnants/residue of the compound; the surrounding surface of the heated area; or different areas of the drug paraphernalia used. Proxy machines or chambers are used to 'simulate' smoking/combustion/heating of a compound prior to extraction of the smoke or the vapour; typically using a gas tight syringe to then be prepared for analysis.[29,82,88,94,95,98,100] When GC is used the sample is often injected directly into a GC port whereas if LC is used the vapour/smoke sample may undergo a dissolution process using a solvent to then be injected into the LC analytical system.[29,100] Some authors have also concentrated on the analysis of the drug paraphernalia and other parts of the apparatus used in these 'simulators'. Glass flasks, tubes, pipes and the apparatus surface are washed with a solvent to then be analysed in addition to the collected smoke/vapour to further determine the drugs ability to leave a notable trace.[27,87,101] Naqi et al.[94] created a smoke trap rig with 8 mm glass beads in two glass washing bottles in order to wash the beads to extract the condensed volatiles after synthetic cannabinoid cigarettes were ignited in a quartz chamber connecting them (Figure 3).

Klous et al.[102] investigated drug paraphernalia and drug trace detection via the volatilisation of pharmaceutical heroin for inhalation; they compared the composition of the vapours inhaled by the abusers to the residue found in the straws used for inhaling. These straw residues appeared to be representative of the vapour composition inhaled by the abusers, which provided insight to the drugs volatility and the difference in concentration between the combustion zone and the area beyond. The comparison of concentration and presence of drug traces in residues compared to direct smoke and vapour samples is important for this reason; circumstances could allow significant differences in concentrations and compositions between them as shown by Naqi et al.,[94] or similar compositions as found in Klous et al.[102]

Naqi et al demonstrated a specific phenomenon whereby the reaction/combustion zone (in this case wool in a quartz tube as

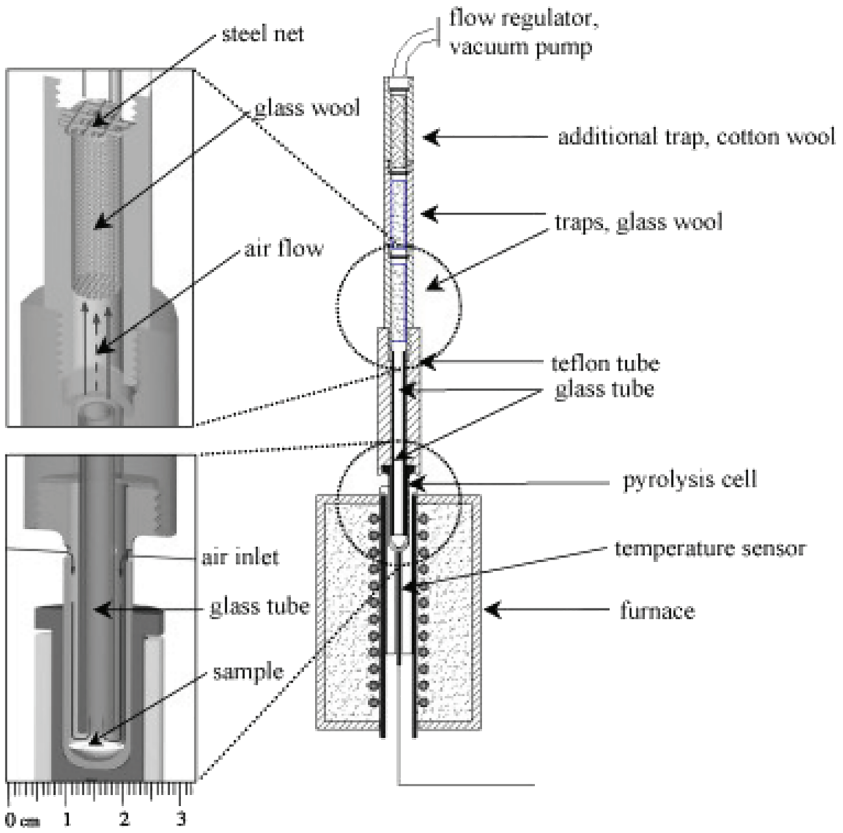

FIGURE 1 Schematic of pyrolysis apparatus used in Gostič et al.[84] to determine the pyrolysis behaviour of pure cocaine and the influence of included additives [Colour figure can be viewed at wileyonlinelibrary.com]

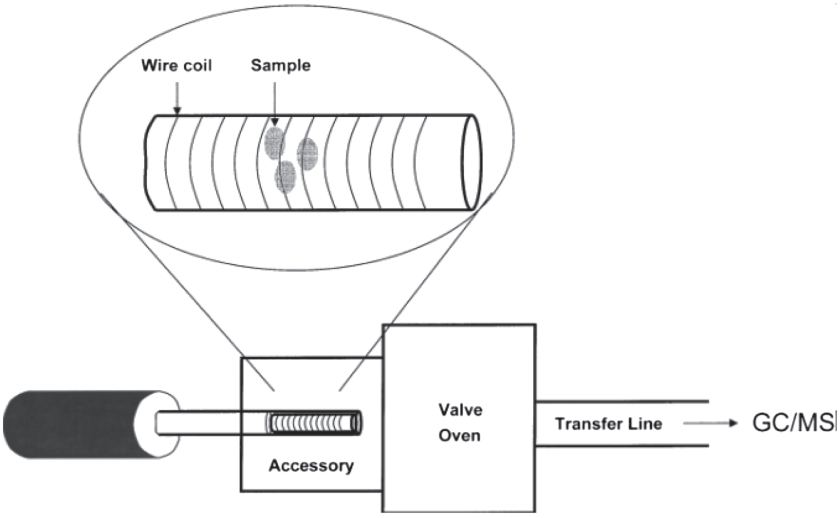

FIGURE 2 Schematic of a pyroprobe unit from Gayton-Ely et al.[88] used to simulate smoking by pyrolyzing the abused target drugs

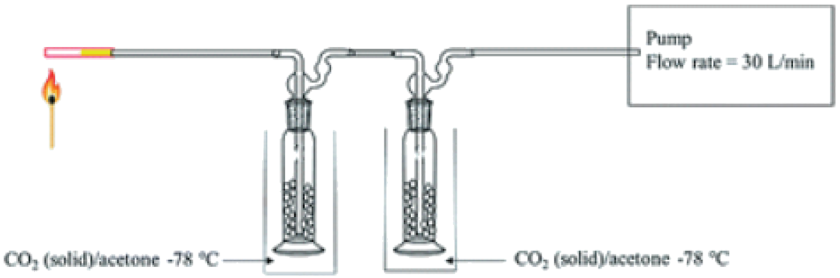

FIGURE 3 Schematic of the pyrolysis apparatus from Naqi et al.[94] used to simulate the smoking of synthetic cannabinoids and to trap the smoke, condensed volatiles and combustion products. (http://creativecommons.org/licenses/by/4.0/)

opposed to aluminium foil) had almost none of the targeted compounds (synthetic cannabinoids for Naqi et al.[94] compared to the smoke traps, that is, where the vapour was collected (similarly found by Nida[92]). If the combusted/heated compound is detected beyond the reaction/combustion zone with little left behind, there is a potential for harm as the compounds travel within inhaled smoke or the local atmosphere which may affect bystanders.[98] This phenomenon should be explored further as residues found on drug paraphernalia could provide a 'pyrolytic' fingerprint that supports the inference that the compound found as a residue was indeed smoked/vaporised.[27]

Quartz wool provides a useful bed for the drug compound to be ignited upon to facilitate detection of the thermal degradants.[71,88,92,98] Alternatively either sealed glass tubes or a sealed glass ampoule may be used, with heat applied to the compound from another source.[103] Guedes et al.[70] heated synthetic cannabinoids in a glass ampoule in a porcelain crucible at various temperatures in a muffle furnace. They demonstrated a decrease in synthetic cannabinoid concentration with an increase in temperature and detected seven synthetic cannabinoids across three herbal sources using GC-MS on their ashes.

5.2 | Thermal degradation pathways and affecting factors

As the number of functional groups present in a parent compound increases, so too does the number of potential degradation pathways, as well as the difficulty in predicting what products will be created. The typical reactions observed in thermal degradation are eliminations, fragmentations, and rearrangement. Oxidation/reduction reactions may also occur under specific conditions influenced by temperature, presence of oxygen and more.[104]

Understanding the products formed can be assisted by understanding the separation and cleavage of the bonds from the parent compounds. Texter et al.[101] investigated the NPS bk-2C-B and bc-2C-I and their thermal degradants; they found that most of the products of these NPS underwent homolytic cleavage of the C-N bond, with some C-C bond cleavage also (this fragmentation can be seen in Figure 4 which shows a schematic of bk-2C-B pyrolysis products). They compared these differences to other phenethylamines (such as methipropamine) and the ring-substituted cathinone mephedrone and found that the degradation pathways differed significantly. Largely, they found the breakdown involved oxidative degradation and mostly C-C or C-N bond cleavage often with halogenation. Cleavage at the C-N bond (often seen as the weakest bond) is relatively common for thermal decomposition to generate free radicals that form stable sterically favoured products.[28] Formation of product compounds may be predicted based on the relative stability of the products and bond strength influences initial cleavage which results in the free radicals that contribute to product stability.[28]

Thermal degradation of certain drug compounds can be inadvertently caused during the analysis itself. It has been suggested that the heat from a GC injection port can cause the thermal degradation of

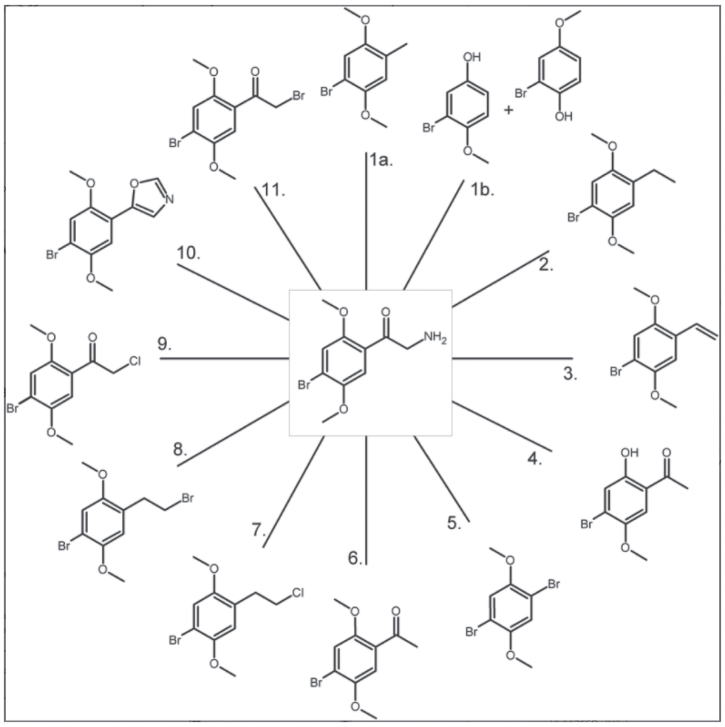

FIGURE 4 Schematic of bk-2C-B pyrolysis products outlined in Texter et al.[101]

specific functional groups, for example the cyclopropyl ring in NPS such as UR-144 and XLR-11.[105,106] The cyclopropyl ring is thermally labile and prone to opening when exposed to high temperatures, and as a result create new products[107]; therefore there might be interference in the GC-MS results from the GC injection port resulting in multiple peaks with similar fragments on the spectra. It may be optimal to analyse SC's with a cyclopropyl ring at a lower injection temperature to lessen the potential degradation and to. not to accidentally identify degradants caused by injection port temperature as actually being present in the ambient air being studied. LC is typically used in these thermal degradation and pyrolysis studies especially when the researchers are investigating drug trace residues on smoking/heating apparatus (usually in addition to using GC for the smoke/vapour).[27,83,90,94,103,108]

There are additional factors that may impact the thermal behaviour of DoA. Gostič et al.[89] found that certain mixtures of adulterants with cocaine can impact its thermal behaviour and the extent cocaine can be recovered and detected in its fumes. Cocaine was found to have an extremely low recovery (approximately 3%) from its fumes if paracetamol was introduced as one of the main adulterants as opposed to caffeine or phenacetin. The thermal degradants produced when heating DoA can also differ based on the composition of adulterant mixtures, some unique to the parent compound, some shared by multiple DoA.[88] Analysis of the mixtures both before and after heating/pyrolysis can reveal key information regarding the thermal stability of a compound. Thomas et al.[99] compared volatility and thermal stability for several NPS and found that thermal lability can differ based on the ring structures of the parent compounds; JWH-018 (naphthalene ring system) remained stable up to 800°C with a 90% recovery of the parent compound. Whereas PB-22

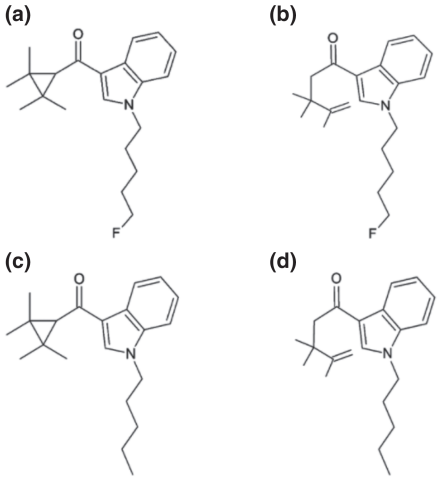

FIGURE 5 Chemical structures of XLR-11 (a), XLR-11 degradant (b), UR-144 (c) and UR-144 degradant (d) as discussed in Hataoka et al.[100] (http://creativecommons.org/licenses/by/4.0/)

(ester-linked quinolone ring system) is quicker to change under thermolytic and metabolic activity, as no parent compound was fully recovered when it was pyrolyzed. Certain synthetic cannabinoids such as UR-144 and XLR-11 (with the ketone-linked tetramethylcyclopropyl ring system) are sterically strained and prone to ring opening but not complete degradation (their degradant structures shown in Figure 5). Another system prone to ring-opening because of lower thermal stability is the cyclopropyl ring system commonly found in various synthetic cannabinoids[92,106,107]; comparing different ring systems among NPS especially is important in these thermal degradation and pyrolysis studies as it further outlines the likelihood of detecting certain breakdown products associated with targeted parent drugs.

5.3 | Potency, toxicity and effects of thermal degradants

A recent focus for DoA air-monitoring research has seen increased investigation of NPS, specifically synthetic cannabinoids, to examine whether they exhibit cannabimimetic effects when smoked and the potential for harm if inhaled by a user or via secondary exposure due to potency. Several studies have investigated these NPS and their effects once smoked by noting physiological changes to mice.[29,93,99,100] The specific physiological changes of interest were those that indicate the targeted drugs have exhibited a cannabimimetic effect, such as hypothermia, analgesia, impacted locomotive function, akinesia/catalepsy, hyperreflexic behaviour or hypomobility; all did not have to be present to establish the compound is cannabimimetic. In addition to this, if researchers observed these behavioural and physical changes, they investigated the human CB receptor (1 and 2) of the parent compounds and thermal degradants. Parent compounds and their degradants ranged from producing: a full profile of cannabimimetic effects; some of the effects; or no effects (in mice) at all nor produced an affinity for either human CB1 or CB2 receptors. XLR-11, UR-144, PB-22 and other synthetic cannabinoids were frequent targets in these studies.[29,93,99,100] Interestingly, some of the thermal degradants compared to the parent compounds that produced cannabimimetic effects, were found to be more potent than the parent compounds as well as have a greater affinity for either/both CB1 or CB2 human receptors.[29,100] The XLR-11, UR-144 and A-834735 degradants (unnamed) have been shown to have increased affinity and appeared to be more potent than THC.[99] Kaizaki-Mitsumoto et al. demonstrated that the CB1 agonistic activity for the UR-144 degradant was four times greater than the parent compound[29]; this is potentially because NPS are typically full agonists whereas their traditional counterparts may only be partial such as THC (linked to potency).[109,110] Although the physiology-based studies involved mice, not humans, the CB agonistic activity and affinity studies reflect the impacts of the fumes from these drugs on humans and these could be harmful. There have been investigations into the toxicity of these products to humans specifically as there is cause for concern based on incidences where several NPS (AMB-FUBINACA, MDMB-FUBINACA and NNEI) resulted in poisonings and toxic outbreaks in New York, Japan and Russia.[82]

In recent years there has been an interest in the harmful products formed when using terpenes/terpenoids as psychoactive enhancers when using vaporisers or dabbing. Cannabis and synthetic cannabinoids have been consumed in this manner creating toxic, carcinogenic and polluting products.[72,95,111,112] Meehan-Atrash et al.[72] investigated gas-phase thermal degradants of components from cannabis e-cigs and dabbing. Certain compounds are released when heated such as methacrolein and methyl vinyl ketone, which are highly toxic substances that can have an irritating effect on the mucous membranes. Kevin et al.[82] investigated this issue as relevant to NPS; a number of these degradation products such as naphthalene, 1-naphthylamine and toluene had toxic and carcinogenic effects. Cyanide was also found as a product thermally liberated from each of the target compounds (AMB-FUBINACA, MDMB-FUBINACA, and MN-18).

Ring structure changes caused by thermal breakdown is a key step in the fragmentation pathways from some parent NPS to their degradation products. Degradants unique to certain synthetic cannabinoids such as methylcyclohexanyl or naphthalene-based products have been outlined as reasonably harmful and toxic to humans if exposed.[98]

Some synthetic cannabinoid thermal degradants have a similar structure to serotonin (indole, 3-methoxyindazole, N-methylindole, 1H-indole-3-ethanol, N-pentylindole and 3-hydroxyindazole) and have recently been suspected to bind to the serotonin receptors (or have serotonin-like properties) which can lead to serotonin syndrome. This may manifest a triad of muscular abnormalities, autonomic hyperactivity and mental-status changes that are indeed harmful.[34,70,71]

Understanding the potential toxic effect of inhaling these different compounds/products as well as the potential risks for bystanders is as important as investigating the presence of illicit drugs in the ambient air. Air-monitoring research for DoA has the potential to make a significant contribution to our understanding of drug trends in a variety of environments and can present intelligence on potential health risks from direct and secondary toxic exposure. The conduct of large scale DoA air-monitoring sampling campaigns as well as specific focused analysis of the smoke/vapour components from the abused drugs that get introduced into the ambient air can be linked and have a potential to be mutually investigated in future studies.

6 | CONCLUSION

Air monitoring for DoA has evolved significantly over past decades in reflection of the changing drug market, habits of the human population and the advancement of laboratory instrumentation. Recent global drug trends, especially the proliferation of NPS on the market are not yet reflected in the number of studies conducted to monitor their presence in the ambient air in contrast to traditional illicit drugs and there is good potential for future study in this area. Monitoring illicit drugs in ambient air has allowed researchers to understand the associated anthropogenic activity of a specific population, and to investigate the movement of a target drug from production to emission in the atmosphere. Sampling techniques are well established for routine analytes as long as volume samplers and filters used are appropriate for the available area and sample size, but the detection of psychoactive substances in the air still presents a challenge analytically. Excellent sensitivity and selectivity are required to reliably determine the target compounds, especially if they are low in concentration. Research trends towards investigation of thermal breakdown products of DoA including NPS is important as the extent to which these are present in an environment may give an indication as to the extent a compound was thermally altered and further indicate the emission source (whether abuse, direct deposition or handling). Some of the thermal breakdown

products of illicit compounds are themselves toxic and more research is required here to better understand: the nature of compounds released during drug combustion, heating and vaping; the potential for secondary exposure to such compounds especially in indoor environments; and the associated potential for health risk. To date the majority of related research considering this has focused on the direct determination of breakdown products during controlled experiments and we recommend increased focus on the determination of such compounds in the air in a wide variety of environments to better understand the issue.

CONFLICT OF INTEREST

The authors have no competing interests to disclose.

AUTHOR CONTRIBUTIONS

Luke Gent: Conceptualization, Writing-Original Draft, Investigation. Richard Paul: Conceptualization, Writing-Original Draft, Writing-Review and Editing, Investigation, Supervision.

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