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CHANGING COMPOSITION OF STREET DRUG NYAOPE AND ITS IMPLICATIONS IN SOUTH AFRICA

Aye Aye Khine[1], Kebogile Elizabeth Mokwena[2], Joyce Mahlako Tsoka-Gwegweni[3]

[1]Department of Chemical Pathology, National Health Laboratory Service, Cape Town, South Africa
[2]NRF Research Chair in Substance Abuse and Population Mental Health, Sefako Makgatho Health Sciences University, South Africa
[3]Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa

ABSTRACT

Nyaope is a Novel Psychoactive Substance (NPS) that continues to bring major challenges to the health and social well-being of users and their communities in South Africa. The active ingredients that make up this cocktail drug Nyaope were first identified in 2015 using Time-of-flight mass spectrometry (TOF-MS) in the samples collected from the surrounding areas of the capital city Pretoria, and they were found to be variable across the samples. This variability had posed challenges to the treatment and rehabilitation programmes. The current study was conducted in 2020, and included significantly a larger number of Nyaope samples collected from two provinces: Gauteng and Kwa Zulu-Natal of South Africa. The analytical method applied was also an improved model of TOF-MS analyser with a larger library of various drugs and their metabolites for matching the ingredients. Strikingly, many non-addictive drugs that were found in the previous samples were not found in this study. The new trend of formulation has become more addictive and compact with major opiates and a few selected opioids, and with paracetamol and caffeine in different combinations. This study reports differences in the physical appearance and the chemical composition of street drug Nyaope across the 2 provinces of South Africa: Gauteng and KwaZulu Natal (KZN), and also compared with the previous findings of 2015 in the samples collected in Gauteng province. The drug appears to be widely consumed and has serious health consequences as per previous studies, and therefore, understanding the chemical substances used in the drug will be helpful in both treatment and rehabilitation efforts.

Keywords: Nyaope, Novel Psychoactive Substance, Time-of-flight mass spectrometry, Opiates

INTRODUCTION

It has been difficult for the healthcare programme managers and clinicians involved in the treatment and rehabilitation centres to predict the active ingredients present in street drugs in various countries as they have been changing over time, which may have implications on their pharmacological and toxicological effects on the users

Corresponding Author: Aye Aye Khine, Department of Chemical Pathology, Green Point Laboratory, National Health Laboratory Service, Cape Town, South Africa. Phone: +27 (0)21 417 9343 | ayeaye.khine@nhls.ac.za

(Zamengo et al., 2014). Due to a scarcity of resources and the high costs involved in analysing drug compounds, public health practitioners who focus on addiction behaviours, as well as clinicians in treatment centres, are in the dark about what the compositions are and how they may be changing from time to time or sourced from area to area (Ayres & Bond, 2012). Nyaope being a commonly used street drug in the northern parts of South Africa is a prime example.

In a previous study cohort of Nyaope samples collected in and around the capital city of South Africa, Pretoria, results showed a mixture of opiates and opioids (Khine et al., 2015). Opiates are chemical compounds that are extracted or refined from natural plant matter (poppy sap and fibres). Examples of opiates found in Nyaope are Morphine, Codeine, and Heroin. Opioids are chemical compounds that generally are not derived from natural plant matter, but they share a chemical structure with opiates and can bind the opiate receptors in the central nervous system. Most opioids are made in the pharmaceutical laboratory or synthesized. The same study reported other non-opiate compounds such as phenobarbitone, benzodiazepines, and bezitramide that are central nervous system suppressants, and stimulants such as amphetamines, pipradol and fenethyline (Khine et al., 2015).

Another study reported that drugs found in Nyaope share metabolic pathways and that probably leads to a longer plasma half-life of individual drugs with resultant synergistic effects. Khine and Mokwena, (2016) postulated that this synergistic effect may lead to higher levels of euphoria and that combined actions of drugs are probably causing the complex picture of withdrawal symptoms that seems to be unique to Nyaope.

The chronic use of Nyaope was found to be associated with organ dysfunctions (Khine et al., 2018) and compromised erectile dysfunction amongst male users was also reported (Moroatshehla et al., 2020). With even more serious health effects such as fronto-temporal cortical atrophy of the brain being reported (Ndlovu et al., 2021). Cortical and subcortical brain regions are involved in cognition, emotion regulation, decision-making, reward, and self-reference that may explain the high level of mental dysfunction among Nyaope users (Hammond et al., 2019). Other authors also propose that the nature of composition of these psychoactive substances needs to be monitored in order to understand their impact on the health of the users and social impact on the communities (Vandeputte et al., 2020).

The primary objective of this study was to analyse the current Nyaope samples to explore whether the compositions are different from the samples analysed previously. Secondly, it was to determine whether there are major differences in the samples between the Gauteng and Kwa Zulu Natal (KZN) provinces in terms of physical appearance and chemical compositions.

Ethical considerations

Ethics approval was received from Sefako

Makgatho Health Sciences University Research Ethics Committee (Reference SMUREC/H/28/2017: IR). Because the study involved drug samples, permission to collect the samples was obtained from the Medicines Control Council (Reference IN104108).

METHOD

This was a descriptive study reporting the physical appearance and chemical composition of 98 Nyaope (street drug mixture) samples. The procedure involved a simple dilution followed by analysis on an accurate quadrupole time-of-flight (qTOF) mass spectrometry system with confirmatory MS/MS detection at the International Standard Organisation accredited Food and Drug Assurance Laboratories® situated in Brooklyn, Pretoria.

Sample preparation procedure

Each sample was given a unique laboratory number and stored according to laboratory procedures. Sample characteristics such as appearance, weight, format and packing were recorded, as well as the geographical area where they were obtained. All the sample contents were weighed out (excluding capsule material and other packaging) and the weight was recorded to 5 decimal places with the contents being transferred into a 100 ml volumetric flask. Each flask was filled to the mark with distilled water, vortexed and sonicated for 30 minutes. Subsequently the flasks were allowed to stand at room temperature overnight. Samples were then filtered using a syringe filter and diluted in a vial to approximately 100 ppm (sample content) with 0.1% formic acid in water. The extracts were than analysed by ultra-liquid chromatogephay (µLC-qTOF).

Test methods employed

Accurate qTOF mass spectrometry with confirmatory MS/MS were used to detect the presence of specified drugs of abuse in capsule and powder samples. The system can detect up to 50 drugs and their metabolites. The accurate mass spectrometry instrument called ABSCIEX TripleTOF 4600 was manually calibrated on the day of analysis prior to the first sample injection and thereafter automatically calibrated by the instrument during the sample run. The automated calibration occurred after every 10 samples analysed. The qTOF-mass accuracy was verified and calibrated through the infusion of a standard positive-mode calibration solution (APCI Positive calibration solution). Similarly, the MS/MS product ion scan capabilities were calibrated with the same standard solution.

Method principle

Using µLC-qTOF a qualitative screening approach was used matching observed exact masses with libraries of known compounds. Additionally, the MS/MS product spectra were used to confirm that the fragment ions from the molecule were derived from a particular parent ion. Micro-capillary liquid chromatography (µLC) was performed on an Eksigent microLC system with PAL auto-sampler (20°C) with a column oven temperature set at 40°C. Chromatographic separations were performed on a 3Phenyl-120, 100

mm x 0.5 mm, 3.0 µm particle size column. Distilled water and acetonitrile:methanol (1:1) were used as the mobile phase, each containing 0.1 % (v/v) formic acid. A 10-minute chromatographic gradient elution programme was employed to effect separation. A neat standard of caffeine at 2 ppm was prepared in distilled water containing 0.1% formic acid from a Primary Caffeine standard of 100 ppm. This neat standard was analysed and used as a control to check the stability of the system.

Data analysis was done by automatic matching with the analyte molecular signature in the system library. A total of 50 analytes (drugs and their metabolites) were screened, 9 of which were not contained in the system library, thus matched with the web library. See table in Annexure 1.

RESULTS

Table 1: Description of physical appearances and demographics of collected Nyaope samples

Geographical area	No. of samples	Sample package appearance	Sample inside appearance
KZN Province			
Umlazi J and C-Sections	13	Smaller pink colour clear plastic capsule	Fine mixture of brown/grey powder
Umlazi F-Section	4	Small blue colour plastic bag closed with a knot	Fine brown powder in sand-like appearance
Umlazi H-Section	1	Smaller pink colour clear plastic capsule	Fine mixture of brown/grey powder
Umlazi Philani Valley	5	Smaller pink colour clear plastic capsule	Fine mixture of brown/grey powder
Durban Wentworth	10	Smaller pink colour clear plastic capsule	Fine mixture of brown/grey powder
Shallcross	1	Smaller pink colour clear plastic capsule	Fine mixture of brown/grey powder
Durban Cato-crest	6	Small blue colour plastic bag closed with knot	Yellowish white coarse powder
Gauteng Province			
Pretoria Central	1	Small brown knotted plastic	Fine yellowish white powder
Bloed	1	Small brown knotted plastic	Fine yellowish white powder

Sunnyside	1	Small brown knotted plastic	Fine yellowish white powder
Gezina (Pta)	1	Small brown knotted plastic	Fine yellowish white powder
Tembisa zones	7	Small clear knotted plastic	Fine yellowish white and brown powder
Thembisa	1	Small brown knotted plastic	Fine Brown Powder
Thembisa Winny	1	Small brown knotted plastic	Fine Cream Powder
Benoni & Daveyton	3	Small brown and blue knotted plastic	Fine Cream, grey, white Powder
Soweto	10	Small clear and black knotted	Granular cream powder
Murwa view M	1	Small brown knotted plastic	Fine Cream Powder
Mabopane C	1	Small brown knotted plastic	Fine Cream Powder
Mabopane Block B	1	Small brown knotted plastic	Fine White Powder
Bokohute	1	Small brown knotted plastic	Fine White Powder
Ga-Rankuwa zone 6	2	Small brown knotted plastic	Yellowish/Brown
Soshonguwe mix	10	Small brown knotted plastic	Granular off-white, fine white, brown and, creamy colour powder
Hammanskraal	16	Small brown and blue colour knotted plastic	Fine grey and creamy colour powder

Table 2: Drugs identified in Nyaope samples collected from various areas of KZN and Gauteng province in this study

Area	Morphine	Codeine/Hydrocodone	Heroin	Papaverine	Paracetamol	6- mono acetyl morphine	Caffeine	Meconin	Dextromethorphan	Normorphine	Oxycodone
KZN Province											
Umlazi-J	+	+	+	+	+	+	+	+			
Umlazi-C	+	+	+	+	+	+	+	+	+		
Umlazi-F	+	+	+	+	+	+	+	+	+		
Umlazi-Philani Valley	+	+	+	+	+	+	+	+	+		
Durban Wentworth	+	+	+	+	+	+	+	+	+		
Shallcross	+	+	+	+	+	+	+	+	+		
Durban Cato-Crest	+	+	+	+		+	+	+		+	+
Gauteng Province											
Pretoria Central	+	+	+	+		+	+	+			+
Bloed street (Pretoria)	+	+	+	+	+	+	+	+	+		

Table 2 Contd

Sunnyside (Pretoria)	+	+	+	+	+	+	+	+			+
Gezina (Pretoria)	+	+	+	+	+	+	+	+			+
Tembisa Zones	+	+	+	+	+	+	+	+	+	+	
Tembisa	+	+	+	+	+	+	+	+			
Tembisa Winny	+	+	+		+	+	+	+		+	+
Benoni and Daveyton	+	+	+	+	+	+	+			+	+
Soweto	+	+	+	+	+	+	+	+	+	+	+
Murwa View M	+	+	+	+		+	+			+	+
Mabopane Block C	+	+	+		+	+	+	+		+	+
Mabopane block B	+	+	+	+		+	+				+
Bokohute	+	+	+	+		+	+				
GaRankuwa zone 6	+	+	+	+		+	+	+		+	+
Soshanguwe mixed											
Hammanskraal	+	+	+	+		+	+	+		+	+

Table 3: Comparing the drugs constituents of Nyaope samples collected in Gauteng province in 2015 and 2020.

2015 Nyaope constituents (TOF -MS)	2020 Nyaope constituents (TOF -MS/MS)
Acetaminophen	Morphine
Meconin	Codeine/Hydrocodeine
Methadone.	Heroin
Papaverine,	Papaverine
Dimenoxitol	Paracetamol
Dextromethophan	6- mono acetyl morphine
Codeine/metabolites	Caffeine
Morphine /metabolites	Meconin
Heroine	Dextromethorphan
Amphetamine /meth - metabolites	Normorphine
Cathine (b OH amphetamine)	Oxycodone
Citroflex A	
Duracaine/lidocaine	
Anti -retroviral (zidovudine)	
Thiofentanyl	
Benzitramide (narcotics)	
Benzodiazepines	
Phenobarbitone	
Pipradol	
Moramide narcotics	
Fenethyline	

**Italics are the drugs not found in the current study yet were present in samples of 2015*

DISCUSSION

This study included a greater number of samples across Gauteng and KZN provinces of South Africa and revealed that the major contents are: opiates (morphine, codeine/hydrocodeine, heroin, and 6- mono acetyl morphine), papaverine (opioid), meconin (by-product of heroin or poppy or opium plant), cough suppressant dextromethorphan, normorphine (N-demethylated metabolite of morphine), oxycodone (semi-synthetic opioid medication), paracetamol and caffeine. The drugs which were found in the previous study in 2015 (Khine et al., 2015) and now lacking are dimenoxitol, amphetamine/meth-metabolites, cathine (b OH amphetamine), antibiotics citroflex A, duracaine/lidocaine, anti-retroviral (zidovudine), thiofentanyl, cenzitramide (narcotics), benzodiazepines, phenobarbitone, pipradol (dopamine reuptake inhibitor), moramide narcotics, and Fenethyline (Table 3).

The methodology used in the current study for analysing drugs was a much-improved method using µLC-Qtof mode of separation, and detection by tandem mass spectrometer (MS-MS) as compared to the method used in the 2015 study that was a direct sample application with TOF-MS with only one Mass Spectrometer (Allen & McWhinney, 2019). This confirms that missing drugs in the current study are not likely due to the analytical shortfall. In addition, the current method uses the library that was very comprehensive in matching the drug compounds with the spectrum from the Nyaope samples. (See Annexure 1)

Critically reflecting on these changes, Nyaope producers seem to have adjusted the constituents to be more focussed on opiates and opioids whilst removing others that are either difficult to obtain or costly, and perhaps because they provide less euphoria. Notably, the current combination does not contain the major stimulant Methamphetamine, but still has caffeine and papaverine that were specifically for improved erectile function (Table 3).

Looking closer at each of the locations where samples were collected, the trends in KZN province showed a similar pattern of constituents except Durban Cato-Crest area where an additional two drugs were found (normorphine and oxycodone) (Table 2). This may indicate that Nyaope in this province may have come from the same source except in Durban Cato-Crest area. This difference was also reflected in the trends of external appearance of the samples (Table 1) where the Nyaope powder appeared differently in Durban Cato-Crest area when compared to those collected from other areas of the province. The colour of packaging is also different in Durban Cato-Crest area compared to the other areas. It seems the sellers use different colour packing to differentiate between Nyaope that contains more drugs than the standard one. Prices of these samples were unfortunately not known.

Comparatively to KZN province, drugs constituents of Nyaope samples were also more variable amongst the areas

collected in Gauteng province (Table 2). Notably, amongst all the areas in Gauteng province, Soweto in Johannesburg and Soshanguve township in Pretoria showed all drugs listed when compared to other areas where one or the other drugs were missing (Table 2). These two townships also shared similarities in the appearance of Nyaope powder although external packaging looks different. These trends may shed some lights in how Nyaope is distributed within and across the provinces. Compared to Soweto and Soshanguve, Durban Cato-Crest area is missing two distinct drugs (paracetamol and dextromethorphen).

Individual drugs found in this study
Morphine, Codeine/Hydrocodeine, and Heroin are major opiates, but the 6-Monoacetylmorphine (6-MAM) is the major metabolite of Morphine which is also very addictive. It has a free 3-hydroxy group and shares the high lipid solubility of heroin, so it penetrates the brain just as quickly and does not need to be de-acetylated at the 6-position in order to be activated, and this makes 6-MAM somewhat more potent than heroin. 6-MAM is rarely encountered in an isolated form due to the difficulty in selectively acetylating morphine at the 6-position without also acetylating the 3-position. However, it is naturally found in significant amounts in black tar heroin along with heroin itself. The production of black tar heroin results in significant amounts of 6-MAM in the final product (Tasker et al., 1984).

Papaverine is an opium alkaloid antispasmodic drug and although it comes from opium, it is not narcotic, thus it has a limited neurological or addictive effect in the user. It is mainly used in clinical practice to improve blood flow in patients with circulation problems and works by relaxing the blood vessels so that blood can flow more easily to the heart and through the body. Papaverine is used primarily in the treatment of visceral spasm and vasospasm (especially those involving the intestines, heart, or brain), and occasionally in the treatment of erectile dysfunction. Its pharmacological actions are unclear, but it appears to be able to inhibit phosphodiesterases and may have direct effects. Papaverine 60 mg injections are used to treat erectile dysfunction in men and assist in the expansion of blood vessels and the increase in blood flow. Addiction by papaverine is not pronounced compared to opiates and its inclusion in Nyaope seems more likely targeted to erectile function (Mayo Clinic, 2024).

Normorphine is a metabolite of the illicit drug morphine and is metabolized by N-demethylation in the liver, by hepatic CYP3A4 and to a lesser extent by CYP2C8. Normorphine is an active metabolite of morphine, thus retains its addictive properties on the central nervous system. Other morphine metabolites include morphine-3-glucuronide (inactive) and morphine-6-glucuronide (active). A controlled clinical comparison of morphine and normorphine in 60 patients suffering from postoperative pain is reported. Normorphine was found to be approximately one-fourth as active as morphine. It appears unlikely that N-demethylation of morphine is necessary

for the analgesic effect of morphine in man (Lasagna & De Kornfeld, 1958). Normorphine is metabolised in the liver, thus it is not expected to be present in the Nyaope samples, but pharmacologically produced normorphine is available as an investigational compound for research (National Institutes of Health, 2023). It would be extremely difficult to source this compound from the market, and how it came into Nyaope samples remains a mystery.

Meconin is a lactone of meconinic acid extracted from opium. Meconin is a contaminating constituent from the poppy that is present in heroin. Therefore, as a metabolite of heroin, the presence of Meconin indicates the use of heroin and when found in the umbilical cord tissue indicates fetal exposure to heroin. The use of meconin as a useful adjunct in detecting illicit opiate use is recommended (Morley et al., 2007). The presence of meconin in Nyaope samples seems more likely to be coming from contamination of the poppy during the processing of heroin, and it does not have any addictive property on its own. This suggests that the Nyaope producer is sourcing the raw heroin.

The main reason for combining multiple classes of drugs was thought to be to enhance their effect of euphoria and thus the addictiveness is accentuated with each use of Nyaope. When opiate and their active metabolites are combined, they share the cytochrome P450 liver enzymes and inhibit the metabolism of each other leading to longer plasma half-life, and higher intensity of euphoria and addiction (Dean, 2006). Nyaope powder is wrapped in a Cannabis leaf to be consumed by inhalation. Synergy between opiates and cannabis was found in animal studies where cannabis up-regulates the opiate receptor proteins in the brain. This evidence provided the basis of better strategies in pain management of cancer patients (Cichewicz, 2004; Chimalakonda et al., 2012). Users experience of synergistic effects and their belief that acetaminophen (paracetamol) and caffeine had been added to combat the headache was found in a previous study (Mokwena & Huma, 2014). However, in the current study the omission of amphetamine and other CNS stimulants could be due to their high cost or difficulty to source. In addition, the presence of caffeine and paracetamol may have come from the common availability of over-the-counter pain medications that combine these two with codeine.

In 2020, concurrently to this study, the co-author of this article and her research group published a qualitative study describing the Focus group discussion data of 61 Nyaope users recruited from the various rehabilitation centres in the urban areas of Ga-Rankuwa, Soshanguve and Hammanskraal in Gauteng province (Fernandez & Mokwena, 2020). The centres were funded by registered and funded by the Gauteng Department of Social Development. The participants were chronic users and they reported experience of increasing addiction by Nyaope over the years. Nyaope was reported as being the only priority in

their lives, requiring to be consumed as the first thing in the morning, and otherwise they cannot function. Whilst one user reported Nyaope boosts his sexual performance, others reported that withdrawal symptoms were getting worse with continued use, which kept them going back to smoking more and more Nyaope. Although the areas involved in their study are also included in this changing composition study, unfortunately we cannot confirm if the users in the focus group discussion were consuming the new formula or not. Physical effects on health and behavioural changes were also reported, but not differentiating if they were getting worse over years of use or they were the same.

In summary, despite the changing composition of Nyaope from 2015 to 2020, the major constituent is still Heroin. Possibly due to the high cost, Ecstasy or Methamphetamine has dropped out of the list. Noteworthy is that morphine and its active metabolite 6-MAM, Codeine and its active compounds hydrocodone and oxycodone are also present across the current cohort samples. They are schedule 5 drugs requiring specialist's prescription and some are available only at the hospital pharmacies. Codeine in combination with paracetamol and caffeine as well as dextromethorphan are easily available as over the counter pain and cough medications. Normorphine is only available in the research field made by chemical pharmaceuticals. It is difficult to understand though how these schedule 5 drugs and research chemicals come into the Nyaope making process. Heroin seems to be sourced as black tar or as raw form from the poppy since Meconin which is a contaminant from its processing is also found in Nyaope. From this information, sources of changing Nyaope formula may be postulated.

Limitations

In 2015, we were not able to collect Nyaope samples outside Gauteng province due to difficulty in getting a permission, thus comparisons could not be made for Kwa Zulu Natal province. Another limitation is that as Nyaope users are a moving population, thus it was difficult to find the same cohort over time to document changes in their experience. The sources from whom we purchased the current samples were also users but did not give consent to be interviewed.

Conclusion

Ongoing changes in the constitution of Nyaope and other street drugs should be monitored for understanding of how ingredients are being sourced, how the changing composition affect the health and how this may implicate the treatment of withdrawal symptoms and rehabilitation programmes. This knowledge may also assist in tracking the sources and distribution of street drugs across provinces.

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Annexure 1

Drugs and metabolites (Analytes) screened by the uLC TOF-MSMS system in this study

	Analytes	Molecular Formula	See footnote*
	Anti-retrovirals		
1	Efavirenz	C14H9ClF3NO2	W
2	Tenofovir	C9H14N5O4P	W
3	Tenofovir Disoproxil	C19H30N5O10P	W
4	Emtricitabine	C8H10FN3O3S	W
5	Zidovudine	C10H13N5O4	W
	Potent skeletal muscle relaxants		
6	2-Amino-5-chlorobenzophenone	C13H10ClNO	Yes
7	2-Amino-5-nitrobenzophenone	C13H10N2O3	Yes
	CNS stimulants		
8	Amphetamine	C9H13N	Yes
9	Metamphetamine	C10H15N	Yes
10	3,4-Methylenedioxyamphetamine	C10H13NO2	Yes
11	3,4-Methylenedioxyethylamphetamine	C12H17NO2	Yes
12	3,4-Methylenedioxymethamphetamine	C11H15NO2	Yes
13	N-Ethyl-p-chloro-amphetamine	C11H16ClN	Yes
14	Pipradol	C18H21NO	W
15	Fenetylline	C18H23N5O2	Yes
	Benzodiazepines		
16	2-Hydroxyethylflurazepam	C17H14ClFN2O2	Yes
17	3-Hydroxybromazepam	C14H10BrN3O2	Yes
18	7-Aminoclonazepam	C15H12ClN3O	Yes
19	7-Aminodesmethylflunitrazepam	C15H12FN3O	Yes
20	7-Aminoflunitrazepam	C16H14FN3O	Yes
21	7-Aminonitrazepam	C15H13N3O	Yes
22	alpha-Hydroxyalprazolam	C17H13ClN4O	Yes
23	alpha-Hydroxymidazolam	C18H13ClFN3O	Yes
24	alpha-Hydroxytriazolam	C17H12Cl2N4O	Yes
25	Desmethylclobazam	C15H11ClN2O2	Yes
	Benzodiazepine antagonist/antidote		
26	Flumazenil	C15H14FN3O3	Yes
	Barbiturates		
27	Phenobarbital	C12H12N2O3	Yes
	Opiates		
28	Morphine	C17H19NO3	Yes

29	Apomorphine	C17H17NO2	Yes
30	Normorphine	C16H17NO3	Yes
31	Morphine-3-â-D-glucuronide	C23H27NO9	Yes
32	6-O-Monoacetylmorphine	C19H21NO4	Yes
33	Codeine / Hydrocodone	C18H21NO3	Yes
34	Dihydrocodeine	C18H23NO3	Yes
35	Heroin	C21H23NO5	Yes
36	Meconin	C10H10O4	W
37	Methadone	C21H27NO	Yes
38	Oxycodone	C18H21NO4	Yes
39	Papaverine	C20H21NO4	Yes
	Opioid analgesics		
40	Bezitramide	C31H32N4O2	W
41	Dextromoramide	C25H32N2O2	Yes
42	Thiofentanyl	C20H26N2OS	W
	Antibiotics		
43	Citroflex A	C20H34O8	W
	Cough suppressant and sedative		
44	Dextromethorphan	C18H25NO	Yes
	Local Anaesthetics		
45	Duracaine	C13H20N2O2	W
46	Lidocaine	C14H22N2O	Yes
	Miscellaneous		
47	Caffeine	C8H10N4O2	Yes
48	Paracetamol	C8H9NO2	Yes
	Neuroendocrine stimulants		
49	Norephedrine / Cathine	C9H13NO	Yes
50	Norepinephrine	C8H11NO3	Yes

*Matched with q-TOF library (Yes) or matched with web library (W)