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Qualitative Detection of Selected Designer Drugs and Relevant Metabolites in Environmental Water Samples

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QUALITATIVE DETECTION OF SELECTED DESIGNER DRUGS AND RELEVANT METABOLITES IN ENVIRONMENTAL WATER SAMPLES

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by

Marley Pruyn

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To: Dean Michael R. Heithaus
College of Arts, Sciences and Education

This thesis, written by Marley Pruyn, and entitled Qualitative Detection of Selected Designer Drugs and Relevant Metabolites in Environmental Water Samples, having been approved in respect to style and intellectual content, is referred to you for judgment.

We have read this thesis and recommend that it be approved.

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Piero Gardinali, Major Professor

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The thesis of Marley Pruyn is approved.

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Florida International University, 2016

ABSTRACT OF THE THESIS

QUALITATIVE DETECTION OF SELECTED DESIGNER DRUGS AND RELEVANT METABOLITES IN ENVIRONMENTAL WATER SAMPLES

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Florida International University, 2016

Miami, Florida

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Designer drugs are compounds which have been synthetically derived from illicit drugs. After consumption, drugs and their metabolites are introduced into the sewage water which is treated and disposed into the environment. A combined target, suspect and non-target workflow was created to detect designer drugs in environmental water samples. Multiple water samples were spiked with an unknown mixture of drugs and metabolites to assess the efficiency of the method. Samples were collected from sewage influent and effluent pipes, downstream from a sewage outfall and reclaimed water. Analysis was conducted with high resolution MS using the QExactive Orbitrap. Screening was performed using a database compiled in-house using TraceFinder EFS. Structure confirmation was achieved using MassFrontier. Target drugs and their metabolites were detected in sewage influent but not in sewage effluent, downstream of the effluent pipe, or in reclaimed water. The workflow was adequate to detect designer drugs in multiple water matrices at concentrations as low as 20ppt.

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4-MAR	2-methylaminorex
3,4-MDMA	3,4-methylenedioxymethamphetamine
3,4-DMMC	3,4-dimethylmethcathinone
$ddMS^2$	Data Dependent-MS^2
HESI	Heated Electrospray Ionization
HPLC	High Performance Liquid Chromatography
HRMS	High Resolution Mass Spectrometry
MDA	Methylenedioxyamphetamine
MDPV	Methylenedioxypyrovalerone
MMA	3-methoxy-4-methylamphetamine
SPE	Solid Phase Extraction
tMS^2	Target-MS^2
UNODC	United Nation Office on Drugs and Crime
UPLC	Ultra-High Performance Liquid Chromatography

1 INTRODUCTION

Designer drugs are defined as compounds which are synthetically derived analogs of drugs which are currently banned or controlled. The primary law for the regulation of drugs is known as the Controlled Substances Act. The act divides drugs into specific categories based on accepted medical uses and the potential for abuse, and regulates them accordingly. Laws regarding production and consumption of drugs are written to regulate specific chemical structures, thus modifications to the regulated structures allow drug manufacturers to circumvent current drug laws. The modifications of the parent structure can include the addition, modification or subtraction of a functional group. The resulting structure is not regulated under the Controlled Substances Act. As new drug laws are written to ban emerging designer drugs, newer compounds are created. In this manner, the production of designer drugs can stay ahead of regulations and the number of designer drugs available increases exponentially. In 2014, 69 new compounds were seen on the market for the first time, and were added to the United Nations Office on Drugs and Crime (UNODC) drug monitoring system. By the end of 2014, a total of 450 designer drugs were recorded in the UNODC system, which is more than triple the number of designer drugs recorded in 2009 (UNODC 2015).

Many designer drugs are produced overseas and sold online or smuggled into the United States to be sold on the streets, but some are produced domestically. In 2012, MDMA seizures were reported at 2 tons in East and South-East Asia but only 0.7 tons seized in the Americas (UNODC 2015.) Recipes to produce designer drugs are available online and in published literature, such as *PiHKAL* and *TiHKAL*, which means manufacturers have easy access to the information. In an attempt to restrict the manufacturing of illicit

and designer drugs, many precursors for the production of illicit drugs have been regulated under the Controlled Substances Act. In 2011 and 2012, enough MDMA precursors were seized worldwide to have produced approximately 44 tons of MDMA, while only 9 tons of MDMA itself were seized worldwide (UNODC 2015.) The creation of new designer drugs means that new precursors may be used for production, so manufacturers can avoid regulations and detection. Early warning systems have been implemented in several countries to monitor the use of illicit drugs and emergence of new drugs.

The numbers of designer drugs available on the market increases exponentially as new modifications are developed. For the purposes of this research, information on existing and newly developed designer drugs was gathered, not only from published, peer-reviewed articles, but also from government sources, such as the Drug Enforcement Administration and from user forums such as Erowid.org and Drugs-Forum.com. The large number of designer drugs on the market necessitates recognizable drug classifications. The compounds can be divided in the following categories: hallucinogens, empathogens, stimulants, opioids, sedatives, cannabinoids, and anabolic steroids. Drugs which fall into the hallucinogen classification includes psychedelics, lysergamides, and phenethylamines. The empathogen classification includes the group known as the MDxx family (i.e. MDMA) and piperazines. The stimulant classification includes amphetamines, cathinones, pyrollidines, and pyrrolidinophenones. The opioid group primarily consists of fentanyl derivatives. The sedative classification mainly includes GHB (gamma-hydroxybutyrate) derivatives. There are many sub-categories in the

cannabinoid group. They are commonly thought of as synthetic THC, but they can have a wide variety of pharmacological effects. The drugs in the anabolic steroid class are a relatively new group which contains primarily testosterone-derived performance enhancing compounds and "dietary supplements." A single drug or sub-category of drugs may be responsible for a variety of effects and may technically fit into multiple classifications but are typically sorted based on the primary effect seen when the drug is consumed. Of the new compounds reported in 2014, 39% were synthetic cannabinoids and 18% were phenethylamines, but new compounds were seen from each of the major classes of designer drugs (UNODC 2014.)

When structural modifications are performed, the original drug and the new compound typically share pharmacological effects. Due to these similarities, many of the drugs within a particular category share a common structural backbone. There is common backbone for the phenethylamine series, shown in Figure 1. There a several sub-classes within the phenethylamine group, and each group has its own common scaffold, to which further modifications can be made to produce new compounds. For example, the members of the 2C series, a phenethylamine sub-class, share a common dimethoxy-phenethylamine backbone. Each member of the 2C series has a different, additional substituent, such as a chlorine, a methyl group, an ethyl group, or an iodine. These additional functional groups are used in the naming system of the 2C series. 2C-E has an ethyl group, while 2C-I has an iodine, as shown in Figure 1 (Shulgin, 1991.)

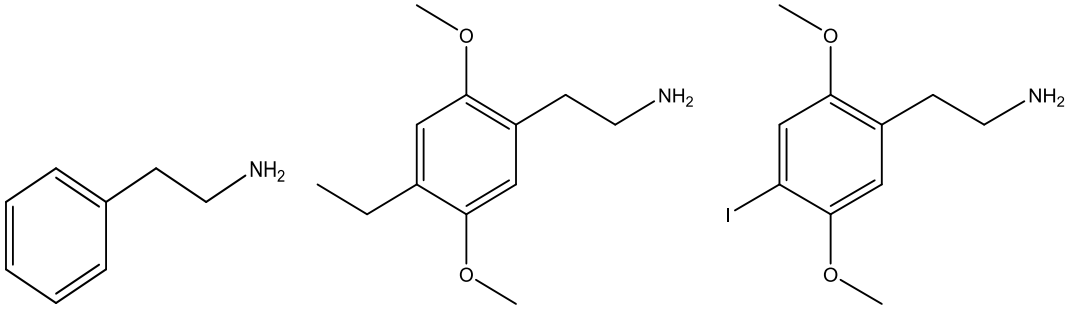


Figure 1. Comparison of phenethylamine (left), 2,5-dimethoxy-4-ethylphenethylamine aka 2C-E (center) and 2,5-dimethoxy-4-iodophenethylamine aka 2C-I (right)

Each sub-class of the phenethylamine group are classified in a similar manner. The members of the DOx series and the NBOMe series each share common structural features in addition to the common phenethylamine backbone. There are also common backbones shared within the tryptamines, cathinones, and many of other classifications.

When drugs are consumed, they are excreted as metabolites, the unchanged parent compound, or a combination of both. Once the drugs have been deposited into the sewage system, they are transported to the wastewater treatment plant. The wastewater undergoes three stages of treatment before being released into the environment. The primary treatment involves the removal of large waste items such as bottles, stick and other objects that may have been deposited into the sewers. The secondary stage of treatment removes up to 90% of the organic matter that is contained in wastewater through biological treatment with microbes. The tertiary stage of treatment is the chemical treatment stage, in which chemical additives are added to the wastewater causing pollutants to clump together, making them easier to remove by physical means (EPA, 2004.) Treatment protocols are developed to remove specific chemicals and contaminants which are regulated by law. Even the most sophisticated treatment protocols are not

capable of removing 100% of all contaminants present, some contaminants are released into the environment with the treated wastewater. Illicit drugs and their metabolites are among the compounds which survive the sewage treatment process (Heuett et. al., 2014.)

Public concern began to rise when it was observed that surface water contained trace amounts of pharmaceutical compounds and other personal care products. Researchers began to examine the level of exposure and the long-term health effects that these compounds may have on the ecosystem. Following the determination of the presence of standard pharmaceuticals, researchers began to examine the presence of illicit drugs, such as cocaine and THC, in surface water. It has been determined that many common illicit drugs will survive the sewage treatment process and be introduced into the environment via outfalls (Baker et. al., 2012; Castiglioni et. al., 2006; Chiaia et. al., 2008; Ostan et. al., 2014; Pal et. al., 2013; Senta et. al., 2014; Thomas et. al., 2012; Yargeau et. al., 2014). Concentrations of illicit drugs have been reported in influent and effluent streams, outfalls and surface water samples at levels as high as 27,500ng/L (Heuett et. al., 2014). These findings indicate that drugs can survive the sewage treatment process and will be deposited into the environment via treated effluent outfalls. MDMA and several of its derivatives have been detected in raw and treated wastewater and in water collected from rivers located throughout Europe (Bartelt-Hunt et. al., 2009; Postigo et. al., 2010; Valcartel et. al., 2012; Zuccato et. al., 2008b). Studies were conducted in the Ebro and Targus Rivers in Spain which detected MDMA in the ranges of 0.2 to 180.0ng/L (Postigo et. al., 2010) and 0.63 to 2.51ng/L (Valcarcel et. al., 2012), respectively. Prior to this

examination, no study has been conducted which searches for a comprehensive list of designer drugs in environmental water samples.

2 HYPOTHESIS AND OBJECTIVES OF RESEARCH

The hypothesis of this research was that a wide variety of designer drugs and their metabolites could be detected in sewage influent and effluents, and environmental water samples, allowing for the assessment of environmental prevalence. The intent of this research was to implement a single protocol for the detection of a wide variety of designer drugs and their metabolites to determine their prevalence in environmental water samples. The first aim of this study was to determine the efficacy of the method by identifying the components of a mixture of unknown parent drugs and metabolites. The second aim was to establish that designer drugs and their metabolites were present in raw sewage in detectable concentrations. The final aim was to determine if designer drugs were present in detectable concentrations in environmental water samples.

3 EXPERIMENTAL

The ThermoScientific QExactive Orbitrap was used to conduct this research paired with the EQuan Online SPE system. The online SPE system utilized a pair of pumps to push the sample through a pre-concentration column and an analytical column. The pre-concentration column retained the analyte compounds from the sample solution. The analytes were then washed out of the pre-concentration column by the mobile phases.

The mobile phases pushed the analyte through the rest of the online SPE system and carried the compounds to the analytical column where they were separated before being introduced into the HESI source (Ramirez et. al., 2014.) When the analyte molecules entered the HESI source, they were passed through a charged capillary tube. The analyte compounds in the mobile phase were sprayed out of the end of the capillary tube, where they became charged. The solvent portion of the droplets evaporated leaving only the charged analyte to move into the Orbitrap system. The newly formed ions were aimed into a quadrupole mass analyzer using a curved charged beam guide. The quadrupole is followed by an octopole. After passing through the quadrupole and the octopole, the ions reached the C-trap where they were held before they were introduced into the Orbitrap. The Orbitrap ion trap used a combination of radial and axial oscillations to create separate bands of ions moving tangentially around a curved electrode. Each ion had a specific rotational frequency which was recorded by the detector and translated into the spectrum displayed by the instrument. This system was run first as a full scan analysis, introducing all ions into the Orbitrap. During MS^2 analysis, the ions of the selected masses were sent into a collision cell to fragment the ions before they were moved into the C-Trap and into the Orbitrap.

One isolation and analysis protocol was developed and applied which was effective for all categories of designer drugs. The method was optimized in order to accommodate each of the target compounds and simultaneously conduct a screening for metabolites. The combined selectivity and sensitivity of the Orbitrap allowed for low concentrations of designer drugs to be detected with levels of confidence required for positive

identification (ThermoScientific, 2014). The Orbitrap has been shown to be capable of distinguishing between isotopes with an *m/z* difference as low as 0.0109 (Hu et. al., 2005) and has a mass accuracy capable of distinguishing between compounds within 2ppm routinely (Makarov et. al., 2006.) Previously conducted research indicates that the Orbitrap is capable of detecting compounds present in the ng/L range, which is sufficient to provide the environmental relevance required for this research (Heuett et. al., 2014.)

This study utilized MS^2 analysis. The first dimension of MS^2 analysis (full scan) was conducted by creating a spectrum of the ions produced in the HESI source. These ions are typically the $[M+H]^+$ peaks. The second dimension of the MS^2 analysis involved the selection of one or more ions which was then fragmented. These fragments were then recorded in a separate but linked spectrum. There are two methods for MS^2 analysis: target-MS^2 (tMS^2) and data dependent-MS^2 ($ddMS^2$). In this research, both methods were used. Analysis by tMS^2 involved creating a target ion inclusion list with known chemical structures, formulae and their accurate masses. Fragmentation occurred only when the instrument detects a $[M+H]^+$ peak with a mass specified in the inclusion list (de Hoffmann, 2007.) Analysis by $ddMS^2$ involved the fragmentation of the largest peaks detected during the full scan process. The number of peaks to be analyzed is set prior to analysis using the TOPN selection (de Hoffmann, 2007.) A preliminary scan was conducted to survey the masses present in the analyte sample. The selected number of precursor ions were selected from the results of this scan and underwent MS^2 analysis.

3.1 RESEARCH TASKS

This research was composed of four major tasks. The first task was the formation of a database of known designer drugs and the major metabolites associated with each of the drugs. The parent drugs and the associated metabolites were collected from published materials (Blachut et. al., 2012; Boatto et. al., 2005; Brandt et. al., 2010; Concheiro et. al., 2013; de Boer et. al., 2004; de Jager et. al., 2012; De Paoli et. al., 2013; Dean et. al., 2014; ElSohly et. al., 2014; Jankovics et. al., 2011; Lin et. al., 2004; Meyer et. al., 2010a; Meyer et. al., 2012; Meyer et. al., 2010b; Peters et. al., 2005; Sauer et. al., 2006; Seely et. al., 2013; Shulgin 1991; Shulgin 1997; Smolianitski et. al., 2014; Soblevsky et. al., 2012; Springer et. al., 2003; Springer et. al., 2002; Staack et. al., 2003; Swortwood 2013; Theoblad et. al., 2006; Uchiyama et. al., 2013; Wohlfarth et. al., 2014; Wohlfarth et. al., 2013; Zawilska et. al., 2013; Zuba et. al., 2013; Zuba et. al., 2012.) For drugs with no known metabolic pathways, the program MetWorks was used to predict the possible metabolites based on the parent structure. Each of the compounds was entered into the TraceFinder EFS software to create the database. The database contained parent drugs from each major class of designer drugs; a total of 179 parent compounds and 129 metabolites were included. Additionally, the exact masses, pKa values and predicted adducts were entered into the database. This database was used for the initial screening of full-scan data to create a list of target compounds for target-MS^2. The second task involved spiking an unknown mixture of designer drugs into environmental water samples to assess the performance of the method for separating, detecting and identifying designer drugs from different classes. The identification of the parent drugs and their metabolites was based on the parent $[M+H]^+$ peak and the fragmentation pattern

predicted *in silico* using the structural information in MassFrontier. The third task involved the analysis of authentic raw sewage samples to determine the presence of designer drugs in raw sewage samples which had been collected from the pumping station of a major university. The fourth task involved the analysis of environmental water samples, including reclaimed water and river water samples.

3.2 REAGENTS AND CHEMICALS

The mixture of unknown designer drugs was obtained from the laboratory of Dr. Anthony DeCaprio (Florida International University, Modesto A. Maidique Campus.) The mixture contained 10 compounds, each present at a nominal concentration of 1 ppm. No information regarding the identity of the compounds was given prior to analysis. The instrument used was the QExactive Orbitrap from ThermoScientific. The mobile phases consisted of Optima grade water, methanol, and acetonitrile, which are suitable for UPLC, were obtained from Fisher Scientific. 1mL ampules of Optima grade formic acid were purchased from Fisher Scientific. Sulfamethoxazole-D_4, used as an internal standard, was purchased from Fisher Scientific.

3.3 SAMPLE COLLECTION AND PREPARATION

3.3.1 UNKNOWN MIXTURE

The mixture of unknown designer drugs was prepared by another laboratory and provided for analysis. The mixture contained 10 compounds, at 1 ppm each in methanol. The mixture was stored in a glass vial, at -20°C in the dark. On the day of analysis, the mixture was removed from the freezer and allowed to reach room temperature. The

mixture was shaken for 10 seconds. A portion of the 1 ppm stock solution was used to create a 100 ppt working solution. Aliquots of the 100 ppt solution were used to create 20 ppt analyte samples. The 20 ppt solutions were prepared in deionized water, tap water, reclaimed water, and filtered raw sewage which was diluted 10 times with deionized water. Additional concentrations of 10 ppt, 5 ppt and 1 ppt were prepared in both deionized water and filtered sewage. The analytical method required a 5mL sample volume, so 10mL of each concentration was prepared to allow for both full scan analysis and MS^2.

3.3.2 SEWAGE INFLUENT

Raw sewage samples were collected from a pump station on the Modesto A. Maidique campus of Florida International University. After collection, the samples were filtered using a 1.0µm PreSep Prefilter glass filter, followed by 0.45µm PreSep Prefilter glass filter. The filtered raw sewage was then stored in polylethylene terephthalate bottles in the dark at -20°C. When analysis was conducted, the samples were thawed and then shaken for 10 seconds. The raw sewage was diluted 10 times with deionized water prior to analysis. The diluted sewage influent was spiked with an internal standard prior to analysis.

3.3.3 RECLAIMED WATER

Samples of reclaimed water were collected from reclaimed water taps located on Florida International University's Biscayne Bay Campus. Samples were collected twice a day, every day for two weeks. A selection of ten of these samples were analyzed. Samples

were chosen to represent both morning and afternoon collections, and early and late in the week. The reclaimed water line was allowed to run for several minutes before collection to minimize the presence of sediments in the water samples. The samples were collected and stored in polyethylene terephthalate bottles, in the dark at -20°C. At the time of analysis, the samples were thawed and then shaken for 10 seconds.

3.3.4 ENVIRONMENTAL SAMPLES

Samples were collected along a river system influenced by treated effluent releases in an undisclosed location and submitted for analysis as a representation of a typical outfall site. Samples were collected upstream from a wastewater treatment plant, as well as at the effluent point of the treatment plant. An additional sample was collected from the mixing zone, downstream of the treatment plant. Final samples were collected from the intake and output locations of a drinking water treatment plant located downstream from the wastewater treatment plant. A map of the collection locations is shown in Figure 2. The samples were stored in the dark at -20°C. The samples were thawed at the time of analysis and then shaken for 10 seconds.

Figure 2. Map of collection locations of environmental samples

3.4 MASS SPECTROMETRIC ANALYSIS

Analysis was conducted using the ThermoScientific QExactive Orbitrap high resolution mass spectrometer in full scan mode, target MS^2 (tMS^2) and data-dependent MS^2 ($ddMS^2$.) Pre-concentration of the samples was conducted using the EQuan online SPE system. The EQuan online SPE system utilized a pair of pumps to push the analyte and

mobile phases through a pre-concentration column and an analytical column, leading the analyte to the ionization source. Ionization was achieved using the heated electrospray ionization (HESI II) source in positive polarity mode. Positive ionization mode was selected because the majority of designer drugs will be positively ionized, including drugs in all the major categories. Analysis was conducted using Hypersil Gold PFP 50 x 2.1mm x 1.9µm (preconcentration) and Hypersep Retain PEP 20 x 2.1mm x 12µm (analytical) columns (both from ThermoScientific.) The Hypersil Gold PFP column was a reverse phase column with a C18 and pentafluorophenyl stationary phase. The Hypersep Retain PEP column was a reverse phase column, hydrophobic phase packed with polystyrene divinylbenzene with urea groups (ThermoScientific, 2011.) The hydrophobic column leads to non-polar non-polar interactions and Van der Waals interactions. The mobile phases used were Optima grade water, methanol, acetonitrile and 0.1% formic acid. Samples were spiked with sulfamethoxazole-D_4 as an internal standard, at a concentration of 20 ppt. This concentration was selected so that it was at the limit of detection, but not so high as to overwhelm the peaks of the target compounds. The settings for full-scan analysis are listed in Table 1.

Table 1. Source and full-scan operating conditions

Parameter	**Setting**
Ionization Source	HESI II
Ionization Mode	Positive
Run time (minutes)	15
Capillary temperature (°C)	300
Aux gas heater temperature (°C)	300
S-lens voltage	50
Source voltage (kV)	3
Sheath gas flow rate	35

Aux gas flow rate	30
Sweep gas flow rate	5
Full MS parameters	
Mass range (m/z)	80-1000
Resolution settings	70,000
AGC target	$1x10^6$
Max injection time (ms)	200

After the completion of the full-scan analysis, the raw data was screened using the database created in TraceFinder EFS. The database is shown in Appendix 1. TraceFinder EFS was used to search the full-scan spectra generated by the Orbitrap against a compiled database. The program indicated all possible matches between the spectra and the database, and the matches were assessed for consistency. The compounds were considered to be tentatively identified during screening based on the quality of the shape of the peak, the height of the peak and the scored isotopic pattern match. The peak shape had to be clean, without significant noise, and the peak height was required to be tall enough to be distinguishable from the background signal. As a general guideline, the height of the called peak was required to be at least five times the height of the background noise. The scored isotopic pattern was required to be 90% or higher. This value was based on the mass of the isotopes observed in the full scan data compared to the mass of the isotopes predicted from the chemical formula. The screened compounds were used to create the inclusion list for MS^2 analysis. The settings for the tMS^2 and $ddMS^2$ analyses are listed in Table 2.

Table 2. Target-MS^2 and data dependent-MS^2 operating conditions

Target-MS^2	
Resolution	17,500
NCE	35
Isolation window (*m/z*)	2.0

Data Dependent-MS^2	
Resolution	35,000
NCE	35
Isolation window (*m/z*)	2.0
TOPN	5

The UPLC operation was conducted using the gradient program detailed in Table 3. Pump 1 controlled the mobile phases which moved the analytes through the pre-concentration column. Pump 2 was responsible for the movement of the mobile phase and analyte compounds through the analytical column. Solvent A was water, solvent B was methanol, solvent C was acetonitrile and solvent D was 0.1% formic acid.

Table 3. HPLC gradient for pumps 1 and 2: solvent A (water), solvent B (methanol), solvent C (acetonitrile), solvent D (0.1% formic acid)

Pump 1					
Time	A%	B%	C%	D%	μL/min
0.00	0.0	97.0	0.0	3.0	500.0
1.50	0.0	97.0	0.0	3.0	500.0
4.50	94.0	3.0	0.0	3.0	500.0
8.30	94.0	3.0	0.0	3.0	500.0
8.80	37.0	60.0	0.0	3.0	500.0
9.30	22.0	75.0	0.0	3.0	500.0
9.80	12.0	85.0	0.0	3.0	500.0
10.30	7.0	90.0	0.0	3.0	500.0
10.80	3.0	94.0	0.0	3.0	500.0
11.30	1.0	96.0	0.0	3.0	500.0
11.80	0.0	97.0	0.0	3.0	500.0
12.00	0.0	97.0	0.0	3.0	500.0
12.50	0.0	97.0	0.0	3.0	600.0
15.00	0.0	97.0	0.0	3.0	700.0

	100.0	0.0	0.0	0.0	700.0
Pump 2					
Time	A%	B%	C%	D%	μL/min
0.00	100.0	0.0	0.0	0.0	1000.0
2.50	99.0	1.0	0.0	0.0	1000.0
3.00	94.0	3.0	0.0	3.0	1000.0
3.50	94.0	3.0	0.0	3.0	1000.0
5.00	0.0	100.0	0.0	0.0	1000.0
8.00	0.0	100.0	0.0	0.0	1000.0
8.10	0.0	100.0	0.0	0.0	2000.0
9.16	0.0	100.0	0.0	0.0	2000.0
9.17	0.0	100.0	0.0	0.0	1000.0
10.00	0.0	100.0	0.0	0.0	100.0
12.90	0.0	100.0	0.0	0.0	100.0
13.00	0.0	0.0	100.0	0.0	2000.0
13.50	0.0	0.0	100.0	0.0	2000.0
14.20	0.0	100.0	0.0	0.0	2000.0
14.50	100.0	0.0	0.0	0.0	2000.0
15.00	100.0	0.0	0.0	0.0	2000.0
	100.0	0.0	0.0	0.0	2000.0

Data processing was conducted using XCalibur. XCalibur is used to visualize the raw data generated by the instrumentation. Filters were applied to visualize specific masses within the spectrum. Once the desired mass was displayed, the individual MS^2 spectra containing that mass were scrolled through to identify the $[M+H]^+$ peak and the associated fragment peaks. The spectra generated by the Orbitrap was compared to the fragmentation patterns generated *in silico* in MassFrontier for structural confirmation. MassFrontier is capable of predicting the fragmentation pattern of a compound based on its structure. The structures of the compounds which had been tentatively identified through the screening process were entered into MassFrontier and the fragmentation pattern was generated based on the general fragmentation rules included in the program. The fragmentation pattern of the structure was then compared to the spectra generated by

the Orbitrap to determine if the observed spectrum was consistent with the *in silico* prediction of the fragmentation pattern.

4 RESULTS

4.1 CONFIRMATION OF UNKNOWN MIXTURE

Full scan and tMS^2 analyses were conducted on the samples spiked with the unknown mixture. The compounds were identified based on the consistency of the observed fragmentation pattern with the pattern predicted in MassFrontier. For the fragmentation pattern to be considered consistent, the presence of the parent $[M+H]^+$ ion peak was required, along with fragments which are consistent with the *in silico* prediction of the fragmentation pattern. The final step in confirmation was to determine the precision of the *m/z* of the parent ion. Identification was only considered to be confirmed if the *m/*z was within 5 ppm of the calculated mass of the chemical formula. This standard was met for all compounds in the unknown mixture. The full chromatogram of the unknown mixture in deionized water is shown in Figure 3. The ion chromatogram of each identified compound using its accurate mass is shown in Figure 4.

Figure 3. Full scan chromatogram of unknown mixture in deionized water at 20 ppt (positive ionization mode)

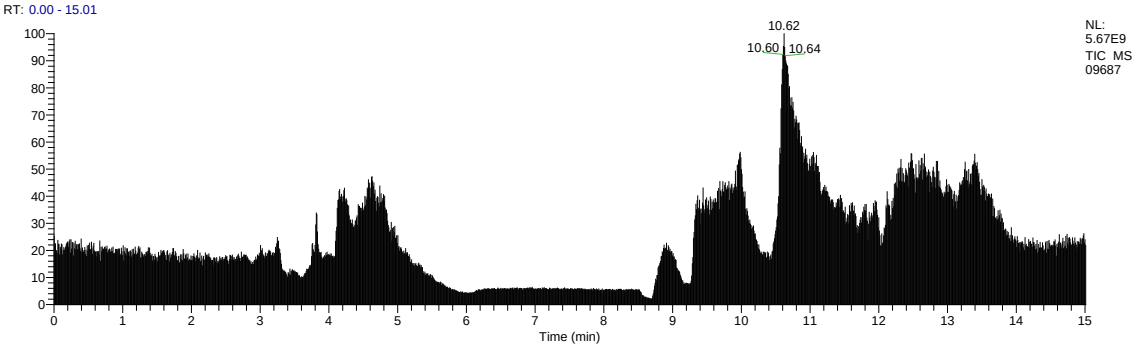
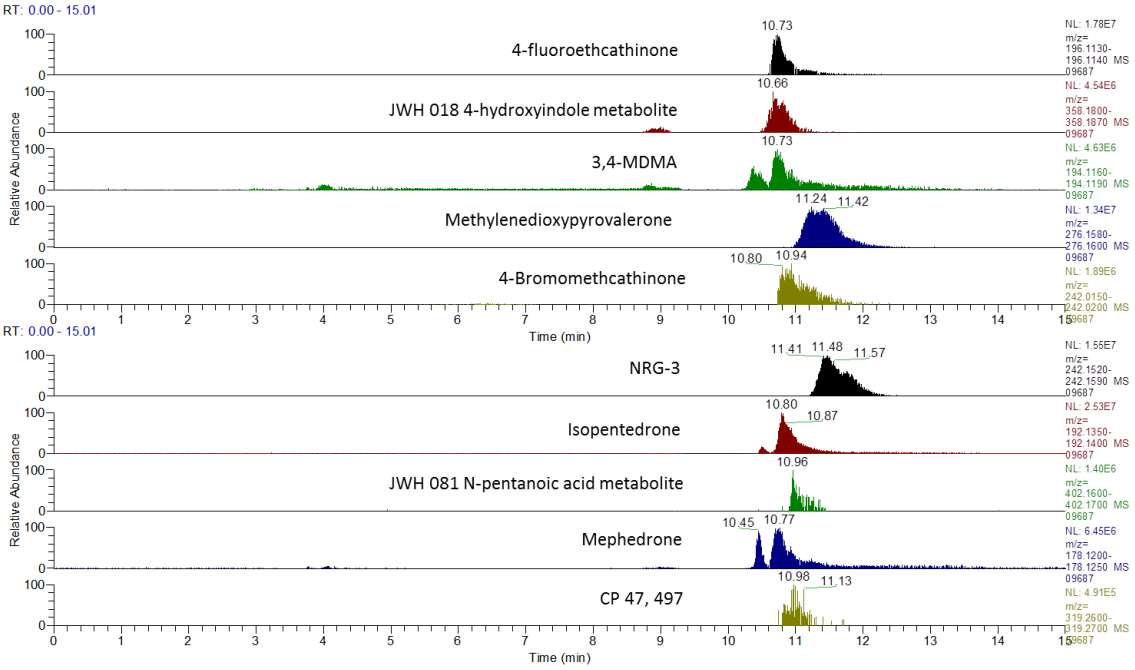


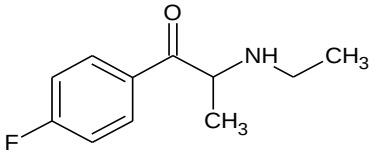
Figure 4. Full scan chromatogram of identified compounds in deionized water at 20 ppt (mass range m/z 80 to 1000)

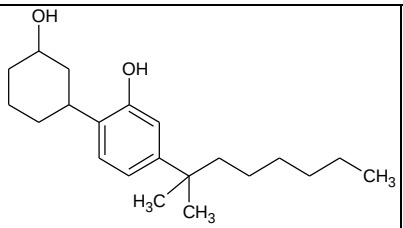
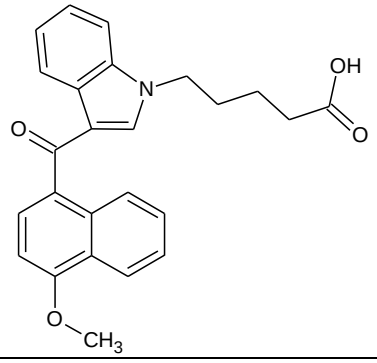
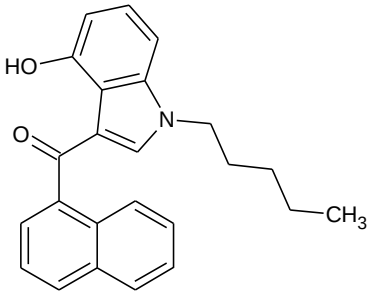
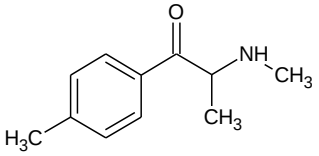
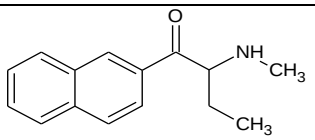
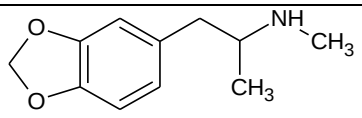


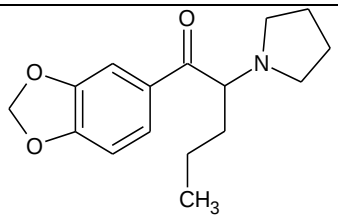
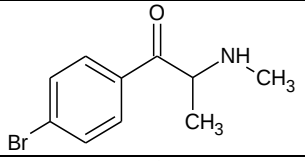
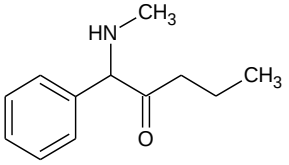
For some of the mass ranges shown in Figure 4, multiple peaks can be seen. This is due to additional compounds with the same mass being present in the sample when the mass filter is applied in XCalibur. The components of the unknown mixture and the additional compound can be easily distinguished when MS^2 analysis is conducted. The fragmentation patterns will be different for each compound.

After analysis, the list of compounds contained within the mixture was provided by the preparing laboratory and compared to the results obtained through analysis. The list of identified compounds was consistent with the list of compounds provided. The observed fragmentation patterns were consistent with the *in silico* prediction of fragmentation of the compounds in the list provided and the generated formula was within 2 ppm for the $[M+H]^+$ peaks all ten compounds. The mass errors of the observed fragments compared to the predicted fragments were all within 3.700 ppm. The accepted mass error threshold for identification is 5 ppm. The predicted fragmentation patterns are shown in Appendix 2. The MS^2 spectra associated with each component of the unknown mixture if shown in Figure 5. The fragments associated with each *m/*z peak are shown. All ten compounds were identified in the each of the water samples (deionized water, tap water, reclaimed water and filtered raw sewage.) The identified compounds, the structure of the compound and the major fragments observed are listed in Table 4.

Table 4. Compounds detected in MS^2 analysis of unknown spiked samples at 20 ppt

Analyte	**Structure**	**$[M+H]^+$**	**tMS^2 *(error*)***
4-fluoroethcathinone		196.11322	196.11322 *(0.006)* 178.10265 *(-0.024)* 150.07135 *(-0.027)* 123.06045 *(-0.041)*

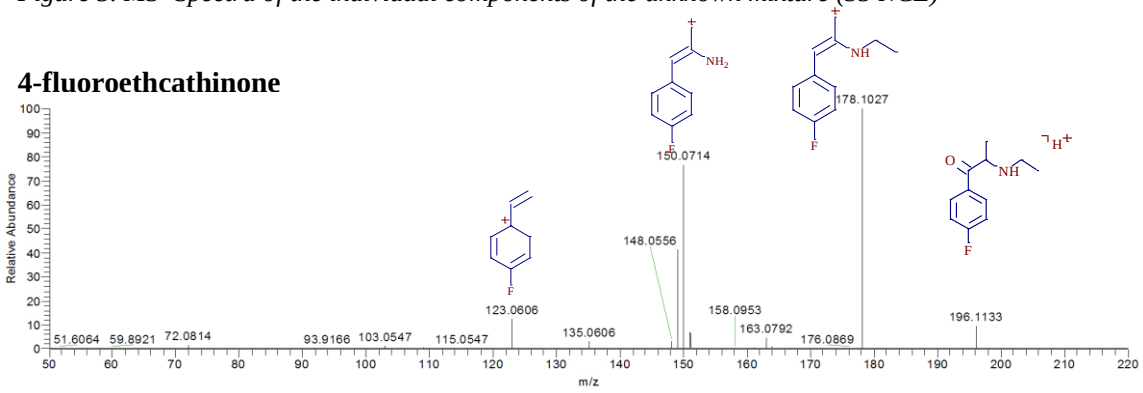
CP 47, 497		319.26316	319.26343 *(0.856)* 303.23116 *(-1.639)* 293.24732 *(-0.637)* 277.21578 *(-1.539)* 275.20052 *(-0.133)* 263.23635 *(-2.249)* 261.22143 *(0.528)* 249.22133 *(0.152)* 245.18958 *(-1.680)*
JWH 081 N-pentanoic acid metabolite		402.16998	402. 16953 *(-1.131)* 101.06008 *(3.700)*
JWH 018 4-hydroxyindole metabolite		358.18016	358.18016 *(0.013)* 230.11756 *(0.021)* 155.04914 *(-0.009)*
Mephedrone		178.12264	178.12247 (*-0.958)* 160.11193 *(-0.912)* 147.08031 *(-0.894)* 133.10118 *(0.023)* 121.06495 *(1.309)* 117.07006 *(1.5464)*
NRG-3		242.15394	242.15394 *(-0.003)* 224.14338 *(0.017)* 211.11174 *(-0.008)* 182.09643 *(0.022)* 141.06988 *(0.022)*
3,4-MDMA		194.11756	194.11765 *(0.488)* 163.07530 *(-0.344)* 133.06485 *(0.440)*

Methylenedioxy Pyrovalerone (MDPV)		276.15942	276.15942 *(0.000)* 205.08577 *(-0.735)* 175.07524 *(-0.663)* 149.02321 *(-0.742)* 135.04399 *(-0.489)* 126.12778 *(0.428)*
4-Bromomethcathinone		242.01750	242.01750 *(-0.013)* 224.00684 *(-0.440)* 210.97518 *(-0.588)*
Isopentedrone		192.13829	192.13829 *(-0.004)* 174.12773 *(0.023)* 161.09609 *(-0.010)* 132.08078 *(0.031)* 119.04914 *(-0.012)*

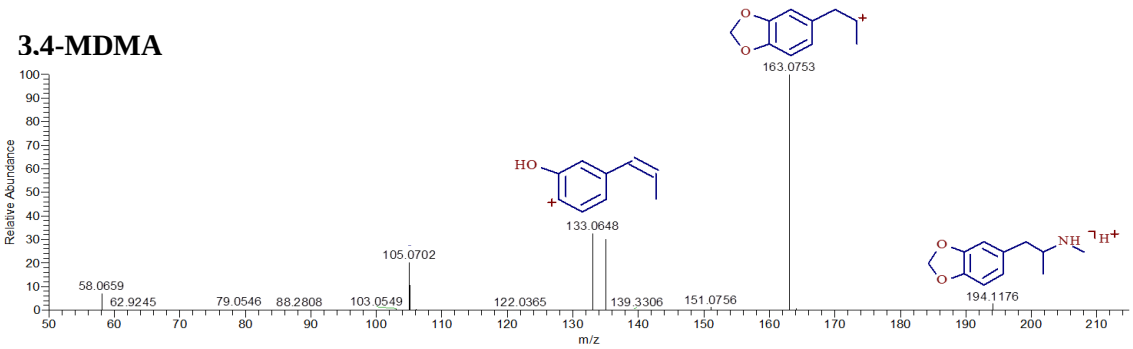
**Error in ppm based on the calculated mass of the chemical formula*

Figure 5. MS^2 Spectra of the individual components of the unknown mixture (35 NCE)

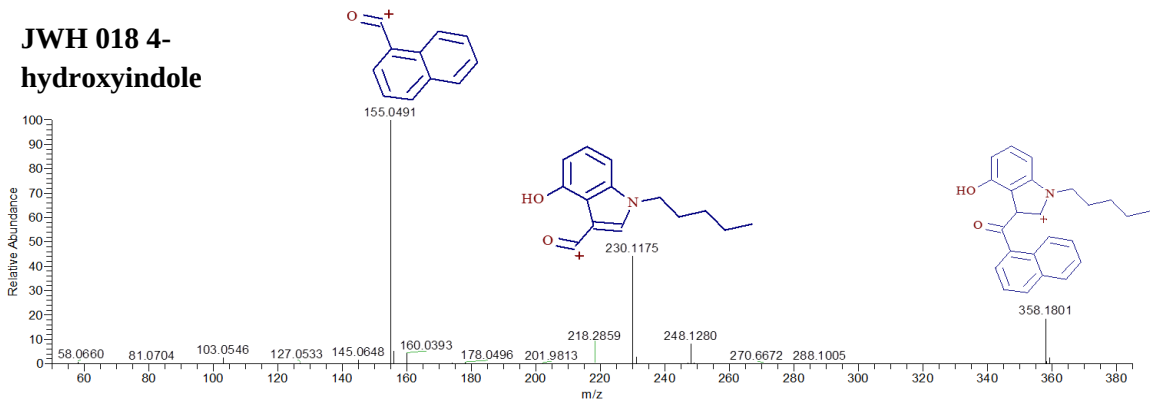
4-fluoroethcathinone



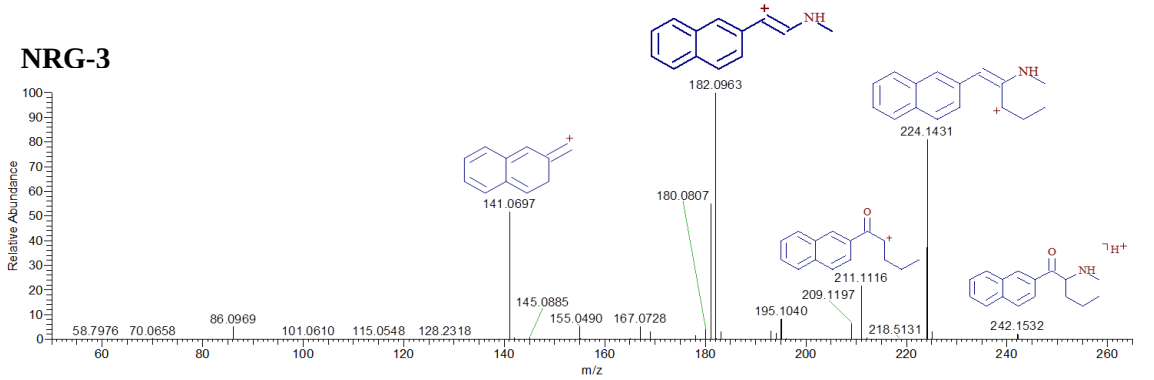
3.4-MDMA



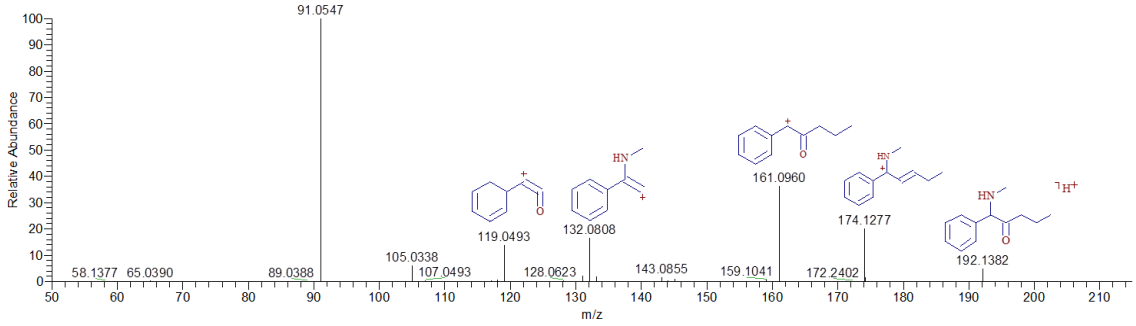
JWH 018 4-hydroxyindole



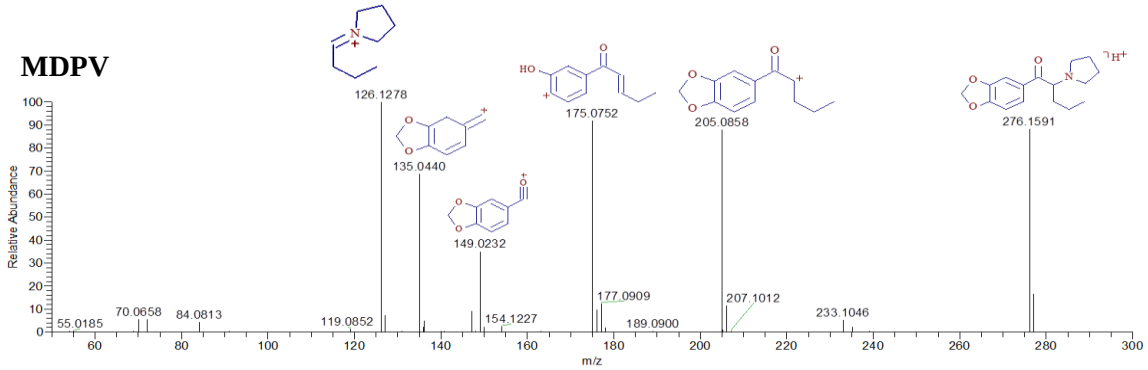
NRG-3



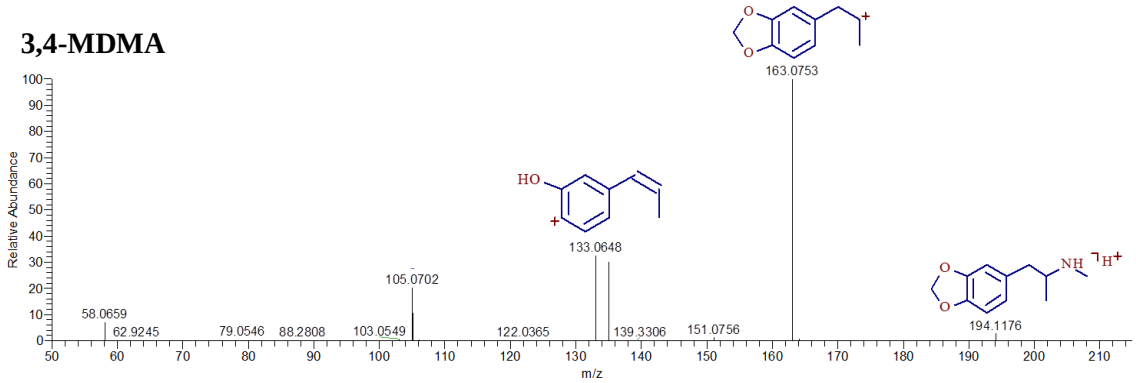
Isopentedrone

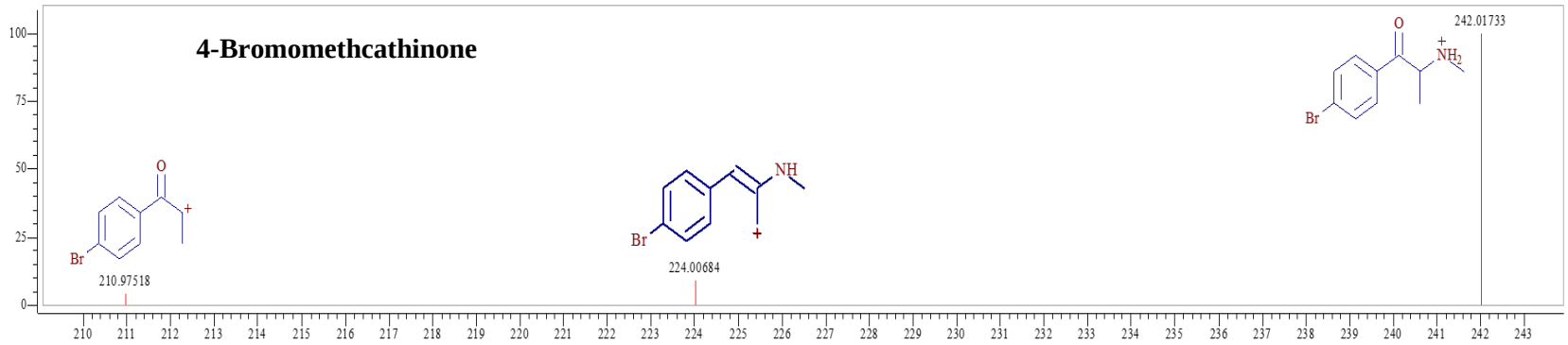


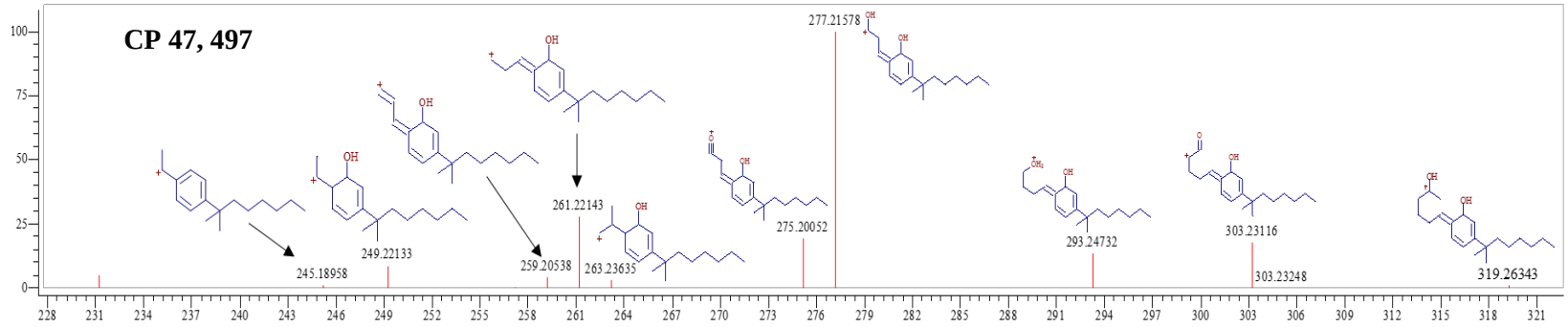
MDPV

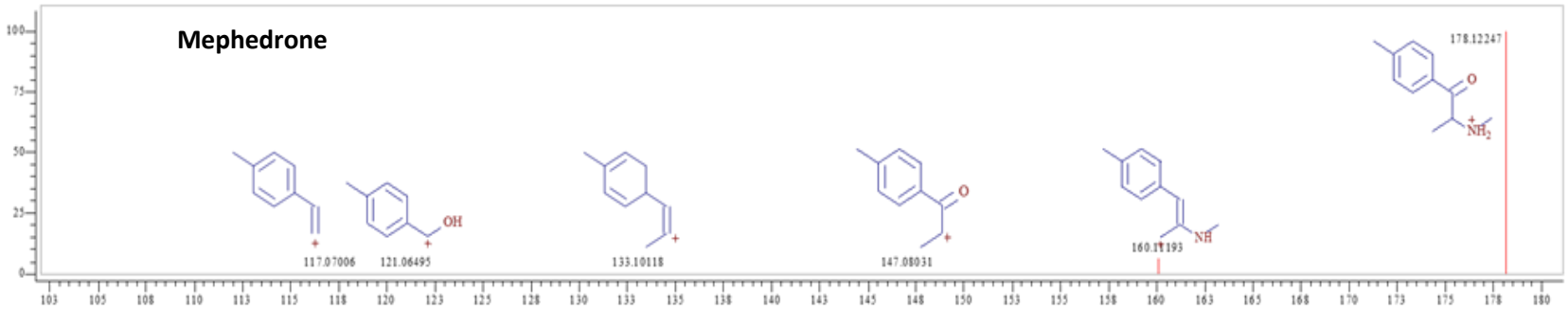


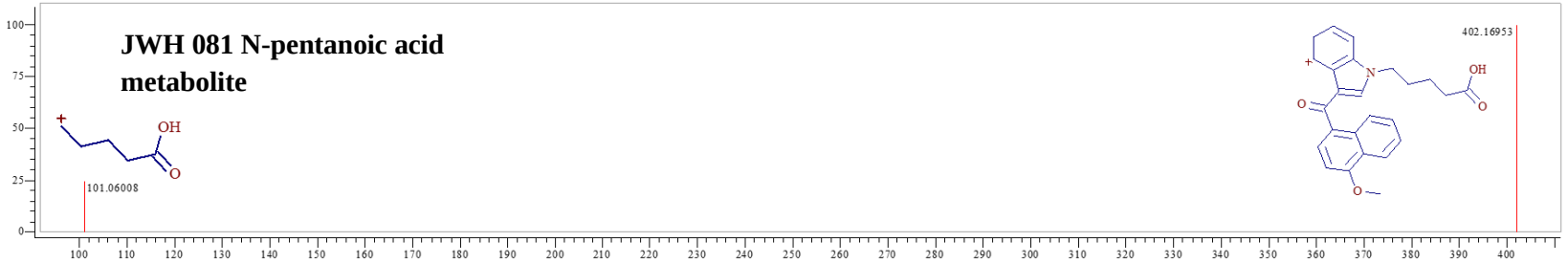
3,4-MDMA




4-Bromomethcathinone
210.97518
224.00684
242.01733


CP 47, 497
245.18958
249.22133
259.20538
261.22143
263.23635
275.20052
277.21578
293.24732
303.23116
303.23248
319.26343


Mephedrone
178.12247
117.07006
121.06495
133.10118
147.08031
160.11193

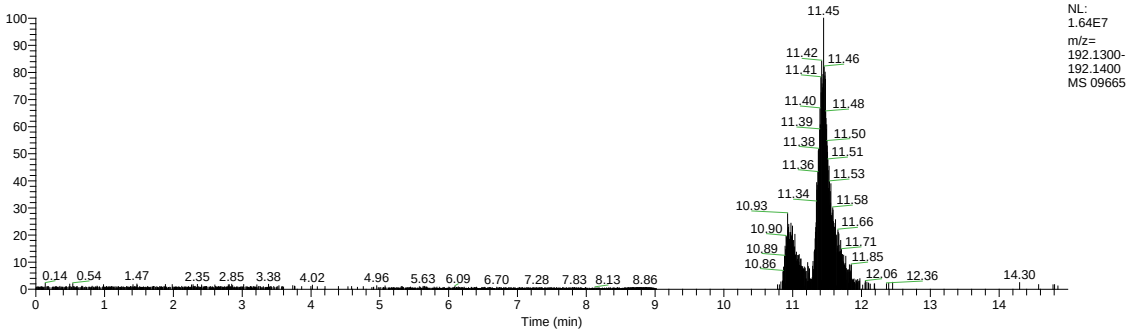

JWH 081 N-pentanoic acid metabolite
402.16953
101.06008

4.2 DETERMINATION OF LIMIT OF DETECTION

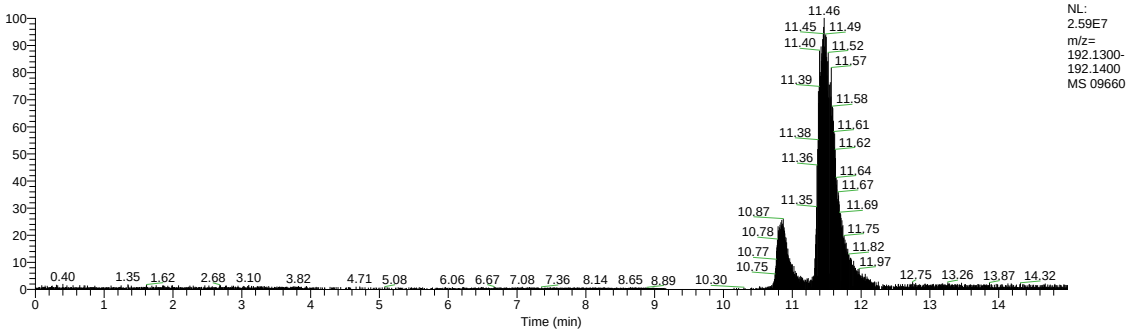
Limit of detection is traditionally determined by determining at what concentration the signal to noise ratio is above the accepted threshold (ie. 3:1 or 10:1). For the purposes of this research, limit of detection refers to the lowest detectable concentration (above 20 arbitrary intensity units) with environmental relevance independently of the signal to noise ratio. To assess the limits of detection for the method, the unknown mixture was spiked into deionized water at concentrations of 20 ppt, 10 ppt, 5 ppt and 1 ppt. All ten compounds were detected at 20 ppt. Seven compounds (4-fluoroethcathinone, isopentedrone, MDPV, mephedrone, NRG-3, JWH 018 N-pentanoic acid metabolite, and 4-bromomethcathinone) were detected at 10 ppt. Only one compound (isopentedrone) was detected at 5 ppt. The same compound was detected at 1ppt, but the background interference was greater in the lowest concentrations. A comparison of a compound detected at 20 ppt, 10 ppt, 5 ppt, and 1 ppt is shown in Figure 6. As the concentration decreased, the width of the peak increased. Based on these results, the limit of detection for this method was determined to be 20 ppt, due to the fact that all of the unknown compounds were detected and positively identified by HRMS and MS^2.

Figure 6. Comparison of MS^2spectra of isopentedrone detected at 20 ppt (top), 10 ppt (second), 5 ppt (third), and 1 ppt (bottom)

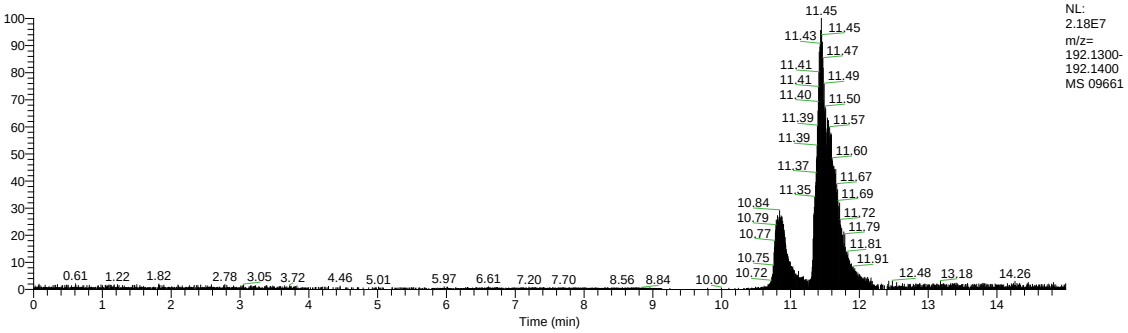
Isopentedrone at 20 ppt



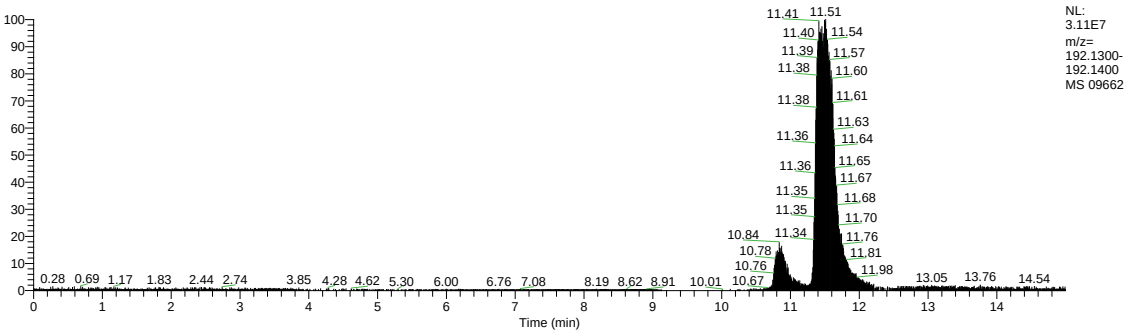
Isopentedrone at 10 ppt



Isopentedrone at 5 ppt



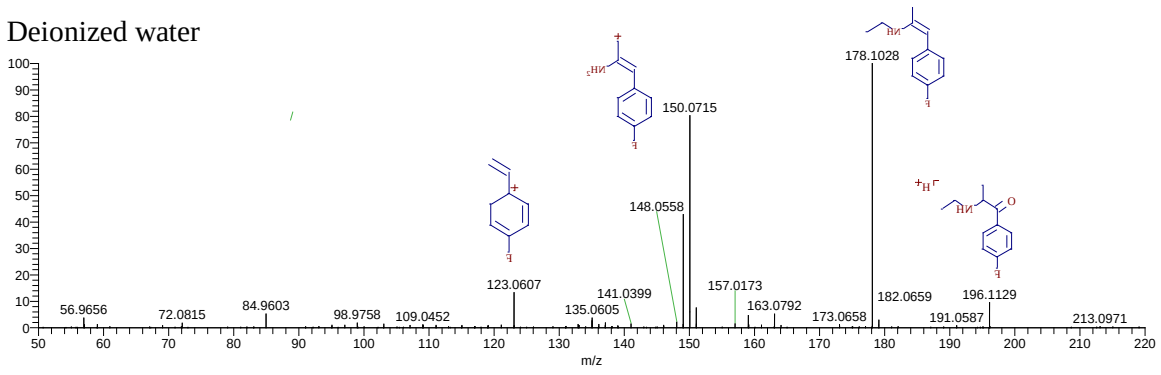
Isopentedrone at 1 ppt



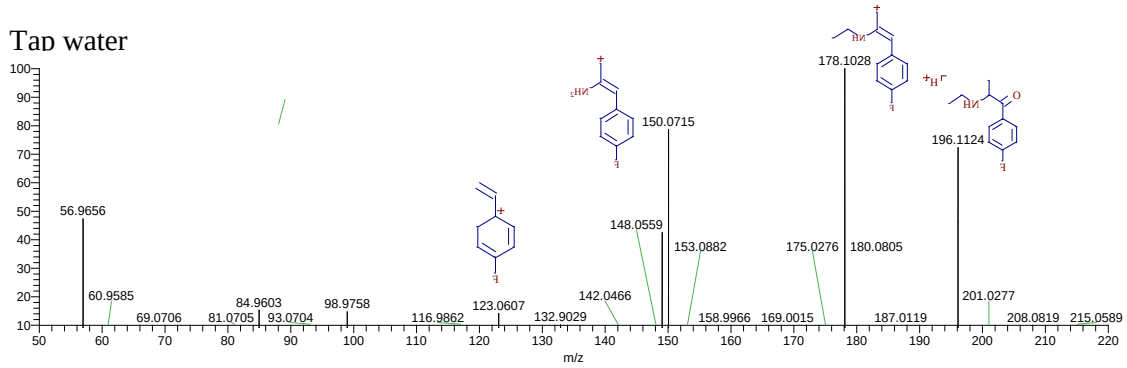
4.3 ASSESSMENT OF MATRIX EFFECTS

Matrix effects can be determined mathematically by comparing the peak height in the matrix to the peak height of the same analyte standard in the absence of the matrix. For the purposes of this research, matrix effects were assessed by comparing the peaks detected in the spectra in each matrix and examining the interference of the background signal. To assess the effects of the matrix on the detection of designer drugs, the unknown mixture was spiked into deionized water, tap water, reclaimed water and filtered raw sewage. The mixture was spiked at 20 ppt into each of the water samples. In each water sample, the ten compounds were identified and the major peaks listed in Table 3 were observed for each compounds. The background noise was more prominent in the raw sewage samples, but the $[M+H]^+$ and fragment peaks were identifiable in each sample. A comparison of the fragments observed in the detection of 4-fluoroethcathinone is shown in Figure 7.

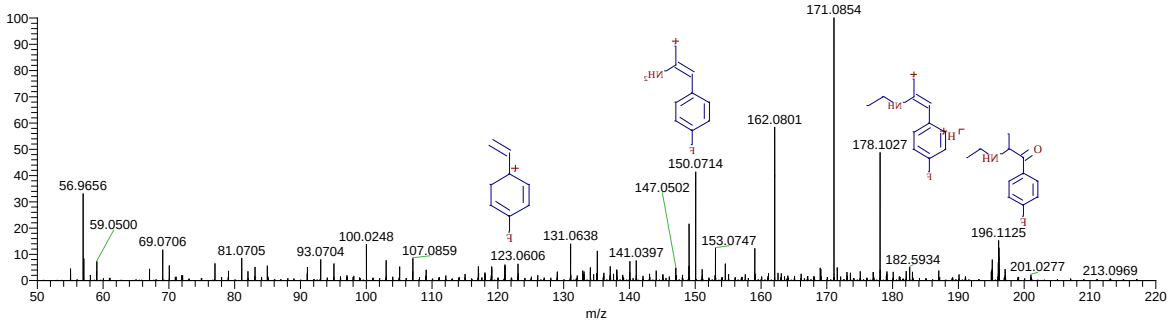
Figure 7. Comparison of 4-fluoroethcathinone in deionized water (top), tap water (second), reclaimed water (third), and filtered raw sewage (bottom)



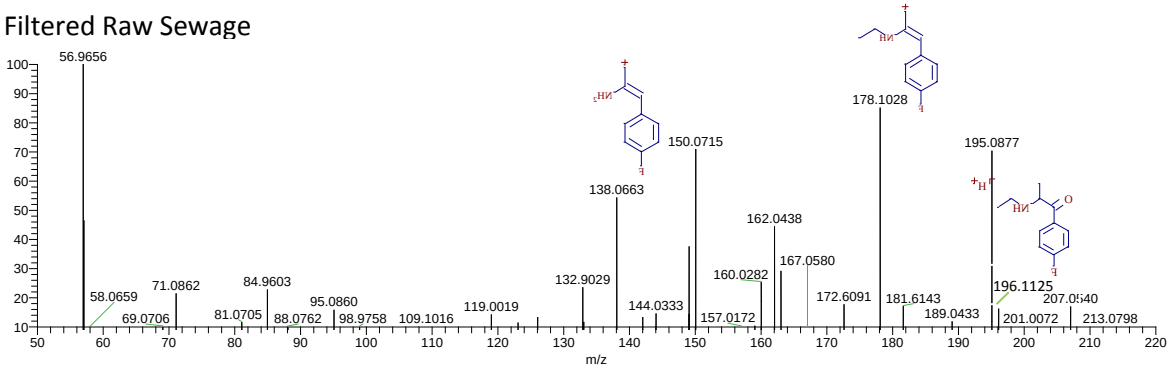
Tap water



Reclaimed water

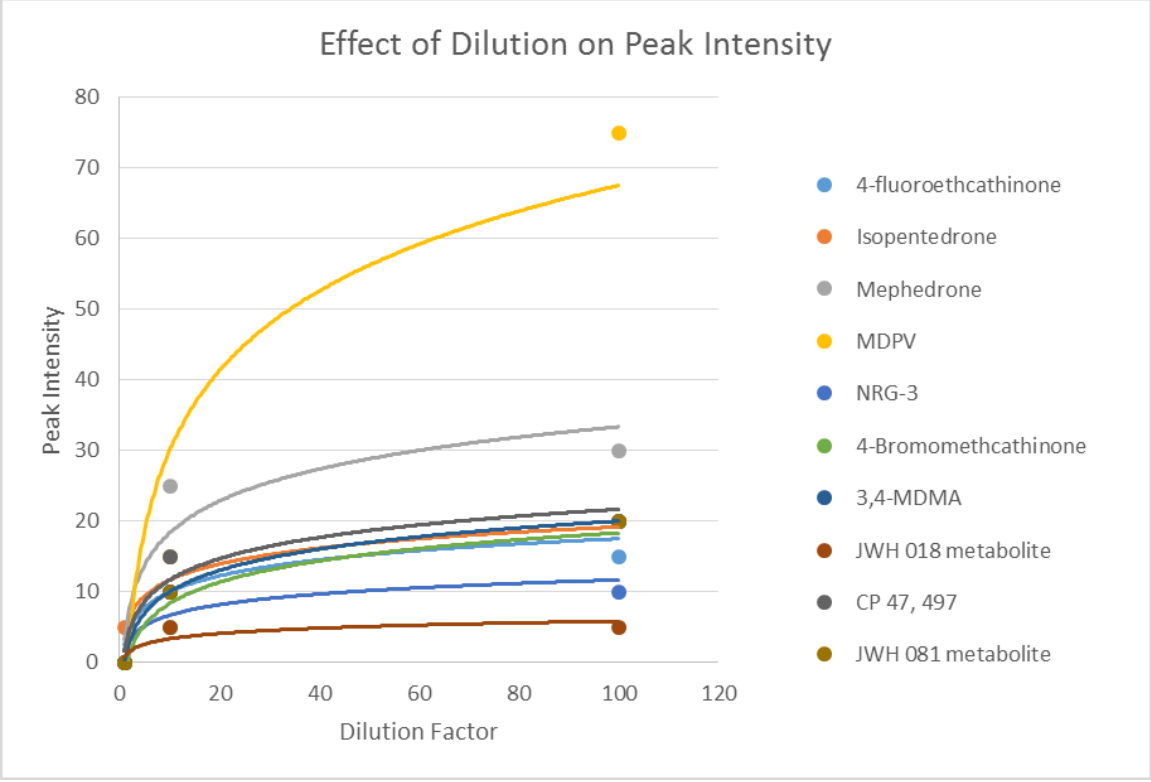


Filtered Raw Sewage



A further assessment of the effect of the matrix of the filtered raw sewage was conducted. The concentration of the unknown mixture was held constant at 20 ppt while the raw sewage was diluted to varying degrees (1x, 10x and 100x.) When the sewage was diluted 1 time (50:50 deionized water: filtered raw sewage), the background noise made the identification of each compound difficult. Only one compound, isopentedrone, could be identified. It was determined that there was no difference between the 10 and 100 dilution factors. A graph of the peak intensity versus the dilution factor of the raw sewage is shown in Figure 8. Because the concentration of the target compounds is expected to be low in sewage influent, it was decided to dilute the raw sewage by a factor of 10 to avoid over-dilution of the target compounds.

Figure 8. Graph of the effect of the dilution factor of raw sewage on the peak intensity of the $[M+H]^+$ peak for each component of the unknown mixture present at 20ppt

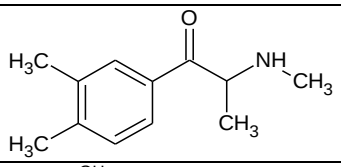
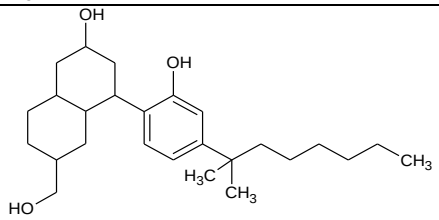
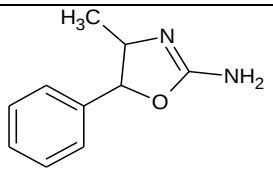
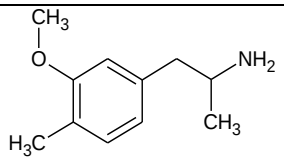
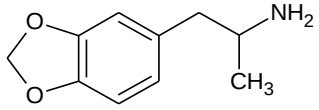


A second set of experiments was done by varying the concentration (20 ppt, 10 ppt, 5 ppt, and 1 ppt) of the unknown mixture while holding the dilution factor of the raw sewage constant at 10 times. All of the target compounds were detected at 20 ppt. The 10 ppt concentration allowed for the identification of five compounds in the mixture, but the background noise begins to obscure some of the major fragmentation peaks. At 1 ppt, only one compounds was detectable, with a considerable amount of background noise affecting the identification process. Based on these results, it was determined that the limit of detection in raw sewage was 20 ppt, which is consistent with the limit of detection determined in deionized water.

4.4 DETECTION OF PARENT COMPOUNDS AND METABOLITES IN INFLUENT SEWAGE

Parent compounds and major metabolites were considered confirmed via MS^2 when the parent ion was present, and the fragmentation pattern predicted *in silico* using MassFrontier was consistent with the fragmentation pattern observed in the data. The fragmentation patterns of the identified parent compounds and metabolites are shown in Appendix 2. The parent compounds detected and the observed fragments are listed in Table 5. The MS^2 spectra of each of the confirmed parent compounds are shown in Figure 9. The fragments associated with each peak have been overlaid to illustrate the confirmation process.

Table 5. Parent compounds detected in sewage influent and observed fragmentation

Compound Name	**Structure**	**$[M+H]^+$**	**tMS^2 *(error*)***
3,4-DMMC		192.13829	192.13823 *(-0.316)* 133.06485 *(0.440)* 105.07019 (*2.980)*
CP 55, 244		403.32067	403.32118 *(1.260)* 385.30974 *(-0.953)* 359.29429 *(-0.465)* 331.26274 *(-1.258)* 301.25221 *(-1.269)* 275.20036 *(-0.714)* 221.18977 *(-1.003)* 183.13788 *(-0.417)* 169.12219 *(-0.688)* 167.10655 *(-0.636)* 155.10652 *(-0.878)* 147.11672 *(-0.728)* 141.12728 *(-0.792)* 125.09617 *(0.627)* 113.09631 *(1.931)*
4-MAR		177.10224	177.10249 *(1.414)* 161.07084 *(-0.618)* 159.09154 *(-0.848)* 149.07090 *(-0.265)* 134.06002 *(-0.152)*
MMA		180.13829	180.13815 *(-0.781)* 164.10692 *(-0.430)* 163.11161 *(-0.807)* 149.09603 *(-0.413)* 121.06492 *(1.062)*
MDA		180.10191	180.10178 *(-0.695)* 163.07522 *(-0.835)* 137.05966 *(-0.336)* 133.06479 *(-0.011)* 121.06492 *(1.062)* 117.07005 *(1.479)* 107.04942 *(2.602)*

**Error in ppm based on the calculated mass of the chemical formula*

MMA and MDA have very similar $[M+H]^+$ masses. They can be distinguished based on the fragments which are unique to each of the structures. Additionally, the two different masses observed for the $[M+H]^+$ are within the mass errors threshold when compared to the respective masses based on the chemical formulae. MDA is a more commonly used designer drug than MMA. This corresponds with the fact that the MDA showed a peak that was approximately three times the size of the MMA in the raw sewage spectra. Several compounds were detected in sewage influent through the screening process, but were not confirmed through MS^2 analysis. These compounds are likely present in concentrations below the limit of detection of 20 ppt. The suspect compounds which were detected through screening but were not confirmed are listed in Table 6.

Table 6. Suspect compounds unconfirmed with MS^2

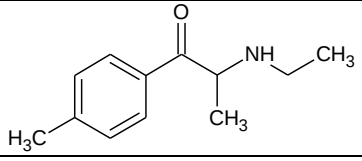
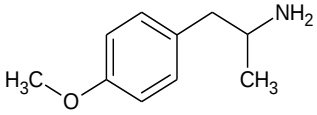
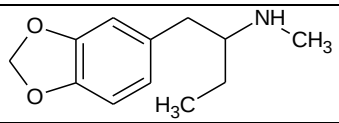
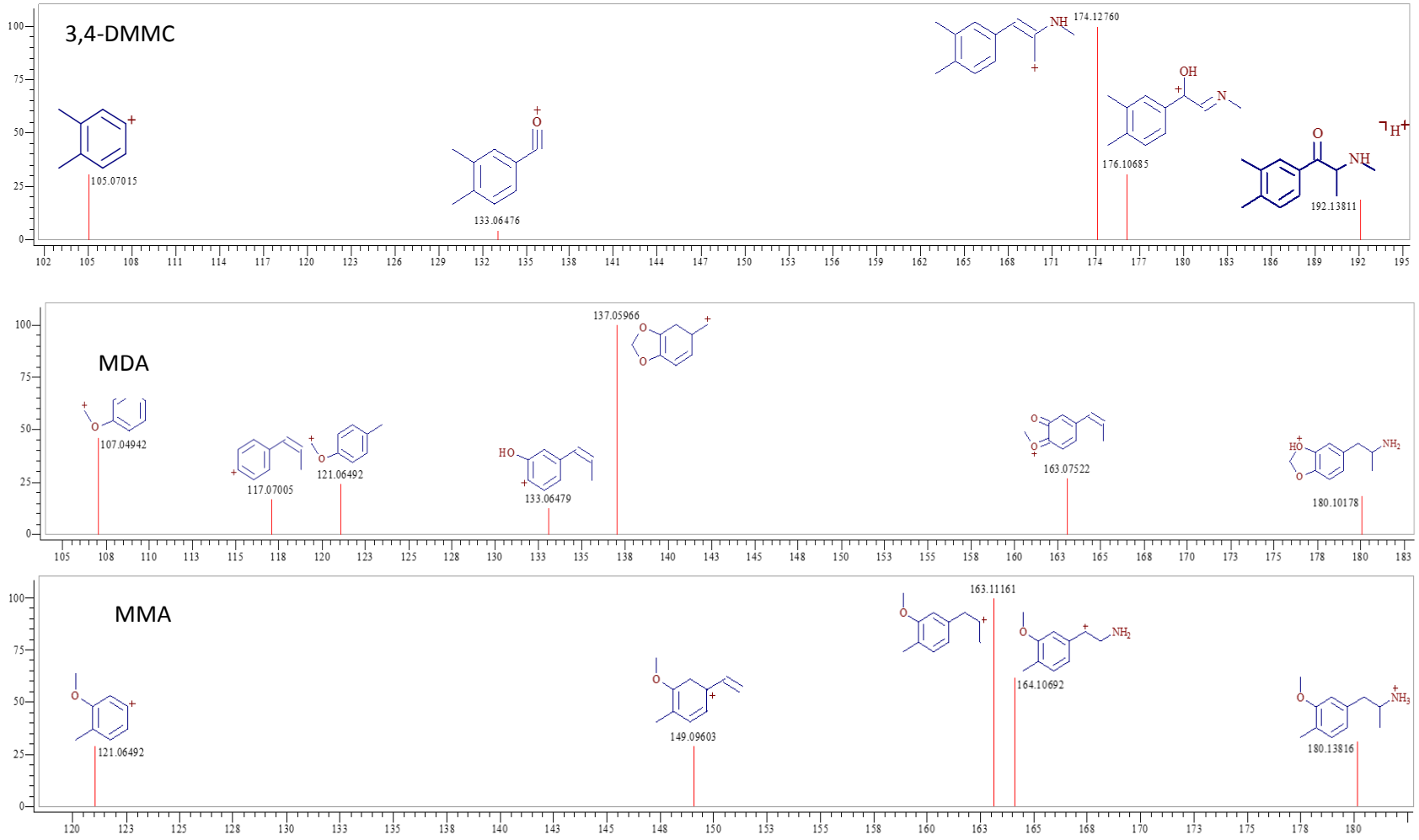
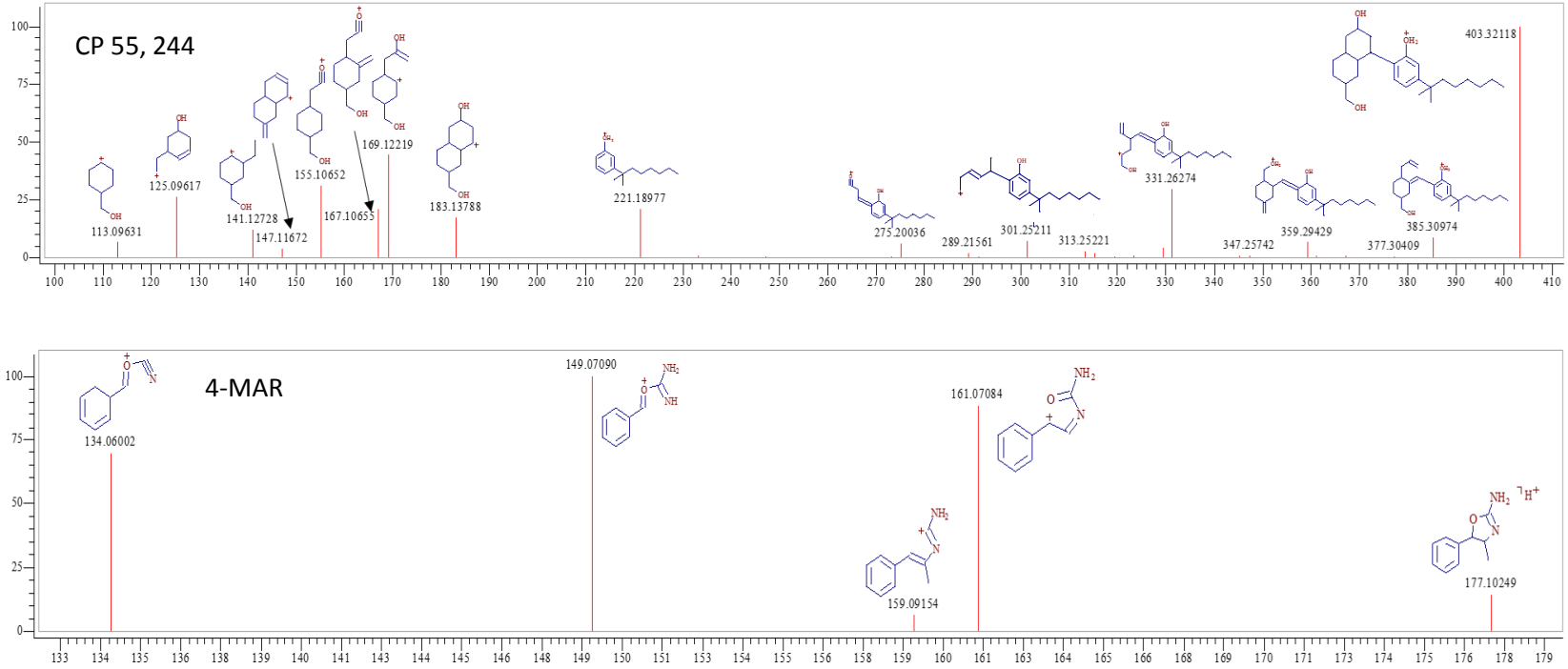
Compound	**Structure**	**$[M+H]^+$**
4- methylethcathinone		192.13829
Para-methoxyamphetamine		166.16224
Methylbenzodioxolylbutanamine		208.13321

Figure 9. Fragmentation spectra of confirmed suspect compounds in sewage influent

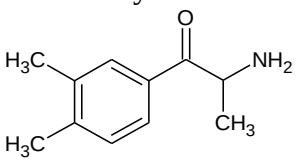


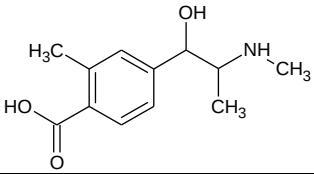
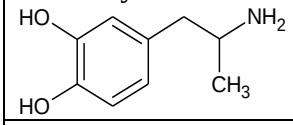
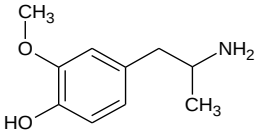

CP 55, 244
113.09631
125.09617
141.12728
147.11672
155.10652
167.10655
169.12219
183.13788
221.18977
275.20036
289.21561
301.25211
313.25221
331.26274
347.25742
359.29429
377.30409
385.30974
403.32118

4-MAR
134.06002
149.07090
159.09154
161.07084
177.10249

Parent drugs and their major metabolites which were observed and published in previous studies were included in the target screening list (Blachut et. al., 2012; Boatto et. al., 2005; Brandt et. al., 2010; Concheiro et. al., 2013; de Boer et. al., 2004; de Jager et. al., 2012; De Paoli et. al., 2013; Dean et. al., 2014; ElSohly et. al., 2014; Jankovics et. al., 2011; Lin et. al., 2004; Meyer et. al., 2010a; Meyer et. al., 2012; Meyer et. al., 2010b; Peters et. al., 2005; Sauer et. al., 2006; Seely et. al., 2013; Shulgin 1991; Shulgin 1997; Smolianitski et. al., 2014; Soblevsky et. al., 2012; Springer et. al., 2003; Springer et. al., 2002; Staack et. al., 2003; Swortwood 2013; Theoblad et. al., 2006; Uchiyama et. al., 2013; Wohlfarth et. al., 2014; Wohlfarth et. al., 2013; Zawilska et. al., 2013; Zuba et. al., 2013; Zuba et. al., 2012.) For the detected parent compounds which had no published metabolisms, metabolic products were predicted *in silico* using MetWorks. The major metabolites detected and the observed fragments are listed in Table 7. The MS^2 spectra of the identified metabolites are shown in Figure 10. The fragments associated with each peak are shown.

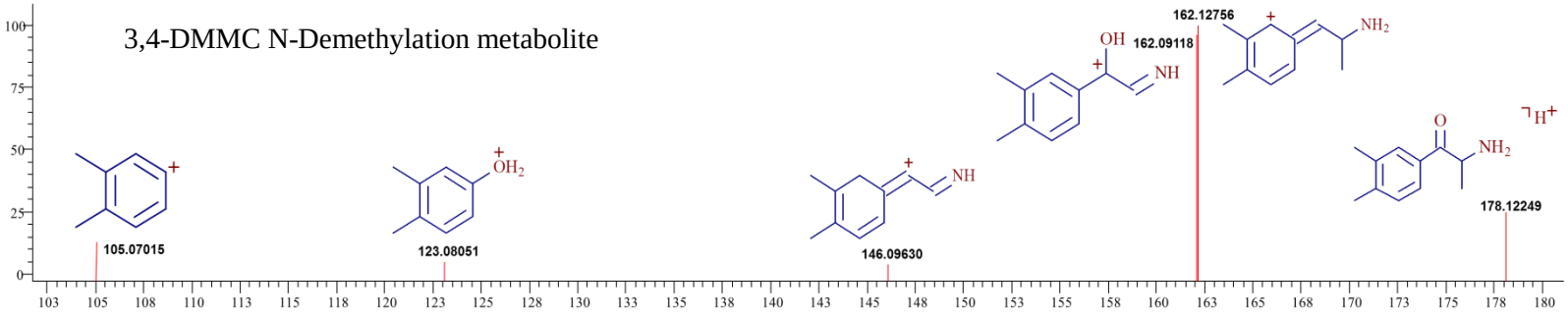
Table 7. Metabolites detected and observed fragmentation

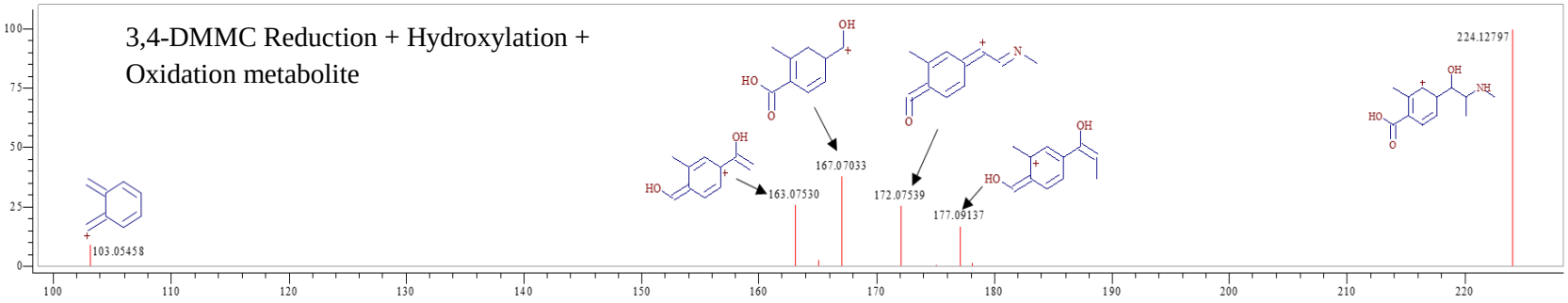
Parent Compound	**Metabolite**	**$[M+H]^+$**	**$ddMS^2$ *(error*)***
3,4-DMMC	N-demethylation 	178.1226	178.12249 *(-0.846)* 162.12756 *(-1.024)* 162.09118 *(-0.991)* 146.09630 *(-0.862)* 123.08051 *(0.556)* 105.07015 *(2.600)*

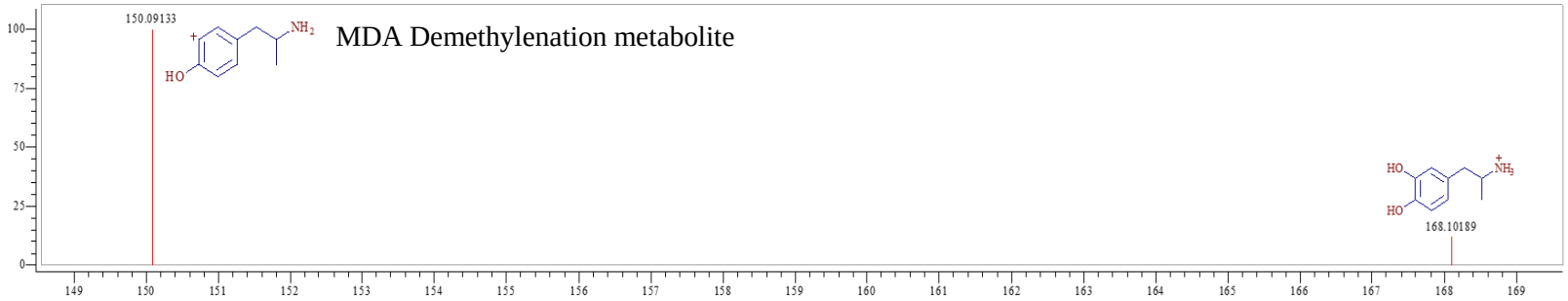
	Reduction + Hydroxylation+ Oxidation 	224.1281	224.12787 *(-1.115)* 208.09668 *(-0.672)* 192.10170 *(-1.068)* 174.09121 *(-0.750)*
MDA	Demethylenation 	168.10191	168.10189 *(-0.091)* 150.09133 *(-0.070)*
	Demethylation + o-methylation 	182.11756	182.11757 *(0.081)* 164.10698 *(-0.065)* 151.07534 *(-0.107)* 150.09133 *(-0.070)* 139.07533 *(-0.188)*

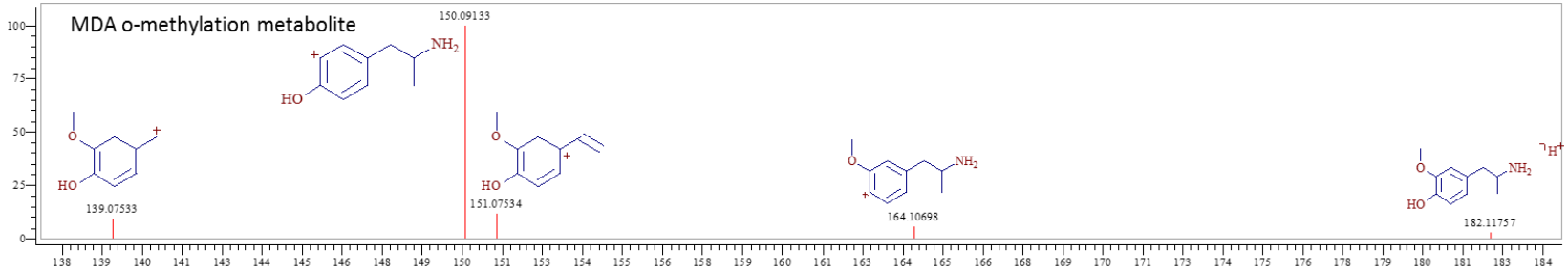
**Error in ppm based on the calculated mass of the chemical formula*

Figure 10. Fragmentation spectra of confirmed metabolites






MDA Demethylenation metabolite
150.09133
168.10189


MDA o-methylation metabolite
150.09133
139.07533
151.07534
164.10698
182.11757

4.5 COMPARISON OF ACQUISITION MODES

Both tMS^2 and $ddMS^2$ analyses were conducted to compare the methods. It was determined that tMS^2 was more effective at detecting the parent drugs. Fewer fragments were observed using $ddMS^2$ which made confirmation difficult. A comparison of the fragments observed in tMS^2 and $ddMS^2$ is shown in Table 7. A total of 5 parent compounds were confirmed using tMS^2 and only 2 were confirmed using $ddMS^2$. Analysis conducted by $ddMS^2$ was deemed to be more efficient in the detection of major metabolites due to the large number of metabolites that were determined through MetWorks.

Table 8. Comparison of target-MS^2 and data dependent-MS^2 analyses

Compound Name	**tMS^2 *(error)****	**$ddMS^2$ *(error)****
3,4-DMMC	192.13823 *(-0.316)* 133.06485 *(0.440)* 105.07019 *(2.980)*	192.13819 *(-0.524)*
MMA	180.13815 *(-0.781)* 121.06425 *(-4.473)*	180.13824 *(-0.282)* 121.06500 *(1.722)*

**Error in ppm based on the calculated mass of the chemical formula*

4.6 COMPARISON OF WATER SOURCES

Both parent compounds and major metabolites were detected in the analysis of sewage influents. A total of 5 parent compounds and 4 metabolites were detected in raw sewage, as shown in Tables 5 and 7. To date, no study has been conducted to detect a comprehensive list of designer drugs. Previous studies have detected illicit drugs and MDMA in wastewater in detectable concentrations (Baker et. al., 2012; Castiglioni et. al., 2006; Chiaia et. al., 2008; Ostman et. al., 2014; Pal et. al., 2013; Senta et. al., 2014;

Thomas et. al., 2012; Yargeau et. al., 2014). Analysis conducted on the samples collected from the effluent pipes determined that no designer drugs or metabolites were present in detectable concentrations. Analysis of samples collected upstream of the outfall pipe confirmed that designer drugs were not present in the river water prior to the addition of the treated wastewater. Samples collected from the downstream mixing zone, and the drinking water intake and output locations did not contain parent drugs or metabolites in detectable concentrations. In previous studies conducted on the sample set of samples, several pharmaceuticals and personal care products were tentatively identified (Heuett, 2015.) Additional studies have detected MDMA in surface water collected at varying distances downstream from sewage treatment facilities in concentrations ranging from 0.2 to 180 ppt (Bartelt-Hunt et. al., 2009; Postigo et. al., 2010; Valcarcel et. al., 2012; Zuccato et. al., 2008a; Zuccato et. al., 2008b). This indicates that a variety of compounds will survive the wastewater treatment process, but designer drugs are either removed by the treatment processes or are diluted beyond the limit of detection established in this method. The analysis of reclaimed water determined that no parent drugs or metabolites were present in detectable concentrations above 20 ppt. In previous studies of reclaimed water, pharmaceuticals and personal care products were detected, indicating that some of these products survive the entire wastewater treatment process, to be released into the environment with the use of reclaimed water in irrigation (Chen et. al., 2013).

5 DISCUSSION AND CONCLUSIONS

It was determined that the non-target screening and detection method developed was effective in the analysis of designer drugs and their associated metabolites. The parent

drugs and metabolites which were spiked into the samples were detected and identified in each of the investigated water samples, indicating that the method was effective for each water source, and matrix effects did not inhibit the detection of the target compounds. Compounds could be detected in each water source, including raw sewage at concentrations above 20 ppt. This represents the limit of environmental relevance. Additional compounds may be present at lower concentrations, however below 20 ppt those compounds are not likely to have an environmental effect. For optimum detection of compounds, the raw sewage was diluted ten times to minimize the background interference. As seen in the full scan chromatogram, not all compounds were separated by the column. Compounds which co-eluted were easily identified by comparing the observed fragmentation pattern to the predicted fragmentation. Isomers are distinguished using MS^2 because different fragmentation patterns will be observed in regions of structural differences. While two isomers have several fragment peaks in common, they differ in one or more fragments, which allows isomers to be distinguished from one another.

Designer drugs are excreted into the sewage system after consumption. Parent drugs, including 3,4-DMMC and CP 55,244, and metabolites, including the N-demethylation metabolite of 3,4-DMMC and the demethylation product of MDA, are present in detectable concentrations in sewage influent. It is interesting to note that the parent drugs detected in raw sewage were not as common as was expected. It was expected to detect drugs that were more commonly used, such as MDMA or MDPV, however those compounds were not detected. The wastewater proceeds through the sewage treatment protocols and is released into the environment via outfall pipes. Samples collected at this

point did not contain parent drugs or metabolites of designer drugs in detectable concentrations. These findings indicate that designer drugs are either removed by the sewage treatment process, or are so greatly diluted as to be no longer detectable by this method, which has an established limit of detection of 20 ppt. This trend continued in the samples collected downstream of the outfall pipe, indicating that there were no additional sources of designer drugs being added to the river water. The absence of designer drugs in the collected water samples indicates that designer drugs are not a significant source of environmental contamination at this time. Additional research should be done to determine if the compounds are present in the environment at lower concentrations, or if they are being effectively removed during the wastewater treatment process.

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APPENDICES

APPENDIX 1. DATABASE OF DESIGNER DRUGS AND METABOLITES

Systematic Name	**Common Name**	**Molecular Formula**	**Category**	**Molecular Weight**	**log Kow**	**$[M+H]^+$**
8-Quinolinyl 1-(5-fluoropentyl)-1H-indole-3-carboxylate	5F-PB-22	$C_{23}H_{21}FN_2O_2$	Parent	376.423401	5.71	377.16598
[1-[(tetrahydro-2H-pyran-4-yl)methyl]-1H-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone	A-834735	$C_{22}H_{29}NO_2$	Parent	339.471191	5.83	340.22711
(1s,3s)-adamantan-1-yl(1-pentyl-1H-indol-3-yl)methanone	AB-001, JWH-018 adamantyl analog	$C_{24}H_{31}NO$	Parent	349.509003	7.31	350.24784
{1-[(1-Methyl-2-piperidinyl)methyl]-1H-indol-3-yl}(2,2,3,3-tetramethylcyclopropyl)methanone	AB-005; AB-034	$C_{23}H_{32}N_2O$	Parent	352.513	5.81	353.25874
1-pentyl-N-tricyclo[3.3.1.13,7]dec-1-yl-1H-indazole-3-carboxamide	AKB48, APINACA	$C_{23}H_{31}N_3O$	Parent	365.52	6.67	366.25399
1-pentyl-N-tricyclo[3.3.1.13.7]dec-1-yl-1H-indole-3-carboxamide	APICA, LWH-018 adamantyl carboxamide	$C_{10}H_{12}NO_5P$	Parent	257.179688	-2.36	258.05259
(6aR,10aR)-3-(Adamantan-1-yl)-6,6,9-trimethyl-6a,7,10,10a-tetrahydro-6H-benzo[c]chromen-1-ol	AM-411	$C_{26}H_{34}O_2$	Parent	378.546997	8.7	379.26316
[6-iodo-2-methyl-1-(2-morpholinoethyl)indol-3-yl]-(4-methoxyphenyl)methanone	AM-630, 6-iodopravadoline	$C_{23}H_{25}IN_2O_3$	Parent	504.360687	4.86	505.09826
(2-iodophenyl)-(1-pentylindol-3-yl)methanone	AM-679	$C_{20}H_{20}INO$	Parent	417.28299	6.89	418.06623
[1-(5-fluoropentyl)-1H-indol-3-yl](2-iodophenyl)-methanone	AM-694	$C_{20}H_{19}FINO$	Parent	435.273804	6.83	436.05681
(6aR,9R,10aR)-3-[(1E)-1-Hepten-1-yl]-9-(hydroxymethyl)-6,6-dimethyl-	AM-906	$C_{23}H_{34}O_3$	Parent	358.514313	6.99	359.25807

6a,7,8,9,10,10a-hexahydro-6H-benzo[c]chromen-1-ol						
[1-[[(2R)-1-methyl-2-piperidyl]methyl]indol-3-yl]-(1-naphthyl)methanone	AM-1220	$C_{26}H_{26}N_2O$	Parent	382.497009	5.92	383.21179
[2-methyl-1-[(1-methyl-2-piperidyl)methyl]-6-nitro-indol-3-yl]-(1-naphthyl)methanone	AM-1221	$C_{27}H_{27}N_3O_3$	Parent	441.521606	6.28	442.21252
[1-(5-Fluoropentyl)-6-nitro-1H-indol-3-yl](1-naphthyl)methanone	AM-1235	$C_{24}H_{21}FN_2O_3$	Parent	404.433502	6.66	405.1609
(2-Iodo-5-nitrophenyl)[1-[(1-methyl-2-piperidinyl)methyl]-1H-indol-3-yl]methanone	AM-1241	$C_{22}H_{22}IN_3O_3$	Parent	503.332794	5.73	504.07786
Adamantan-1-yl[1-[(1-methyl-2-piperidinyl)methyl]-1H-indol-3-yl]methanone	AM-1248	$C_{26}H_{34}N_2O$	Parent	390.561005	6.33	391.27439
[1-(5-fluoropentyl)-1H-indol-3-yl](1-naphthyl)methanone	AM-2201	$C_{24}H_{22}FNO$	Parent	359.436005	6.84	360.17582
[1-(5-Fluoro-4-hydroxypentyl)-1H-indol-3-yl](1-naphthyl)methanone	4-hydroxypentyl AM2201	$C_{24}H_{22}FNO_2$	Metabolite	375.435394	5.3	376.17073
[1-(5-Fluoropentyl)-6-hydroxy-1H-indol-3-yl](1-naphthyl)methanone	6-hydroxyindole AM2201	$C_{24}H_{22}FNO_2$	Metabolite	375.435394	6.36	376.17073
5-[3-(1-Naphthoyl)-1H-indol-1-yl]pentanenitrile	AM-2232	$C_{24}H_{20}N_2O$	Parent	352.428406	5.43	353.16484
(2-Iodophenyl)[1-[(1-methyl-2-piperidinyl)methyl]-1H-indol-3-yl]methanone	AM-2233	$C_{22}H_{23}IN_2O$	Parent	458.335297	5.91	459.0927
(6S,6aR,9R,10aR)-9-(Hydroxymethyl)-6-[(1E)-3-hydroxy-1-propen-1-yl]-6-methyl-3-(2-methyl-	AM-4030	$C_{27}H_{42}O_4$	Parent	430.619995	7.78	431.31559

2-octanyl)-6a,7,8,9,10,10a-hexahydro-6H-benzo[c]chromen-1-ol						
3-{[(2R)-2-(Hydroxymethyl)-2,3-dihydro-1H-inden-4-yl]oxy}phenyl 4,4,4-trifluoro-1-butanesulfonate	BAY 38-7271	$C_{20}H_{21}F_3O_5S$	Parent	430.437897	4.88	431.11346
8-Quinolinyl 1-(cyclohexylmethyl)-1H-indole-3-carboxylate	BB-22; QUCHIC	$C_{25}H_{24}N_2O_2$	Parent	384.470306	6.56	385.19105
1-Naphthyl[4-(pentyloxy)-1-naphthyl]methanone	CB-13; CRA-13	$C_{26}H_{24}O_2$	Parent	368.46759	7.54	369.18491
N-Cyclopropyl-11-(3-hydroxy-5-pentylphenoxy)undecanamide	CB-25	$C_{25}H_{41}NO_3$	Parent	403.5979	7.79	404.31592
N-Cyclopropyl-11-(2-hexyl-5-hydroxyphenoxy)undecanamide	CB-52	$C_{26}H_{43}NO_3$	Parent	417.624512	8.28	418.33157
2-[(1S,3R)-3-Hydroxycyclohexyl]-5-(2-methyl-2-heptanyl)phenol	CP 47, 497 C6 homologue	$C_{20}H_{32}O_2$	Parent	304.466888	5.97	305.24751
2-[(1R,3S)-3-Hydroxycyclohexyl]-5-(2-methyl-2-octanyl)phenol	CP 47, 497 C8 homologue	$C_{22}H_{36}O_2$	Parent	332.519989	7.18	333.27881
2-[(1S,3R)-3-Hydroxycyclohexyl]-5-(2-methyl-2-decanyl)phenol	CP 47, 497 C9 homologue	$C_{23}H_{38}O_2$	Parent	346.5466	8.16	347.29446
(2S,4S,4aS,6R,8aR)-6-(Hydroxymethyl)-4-[2-hydroxy-4-(2-methyl-2-octanyl)phenyl]decahydro-2-naphthalenol	CP 55, 244	$C_{26}H_{42}O_3$	Parent	402.313385	7.54	403.32067
2-[(1R,2R,5R)-5-Hydroxy-2-(3-hydroxypropyl)cyclohexyl]-5-(2-methyl-2-octanyl)phenol	CP 55, 940	$C_{24}H_{40}O_3$	Parent	376.572601	6.13	377.30502
(4-Ethyl-1-naphthyl)[1-(5-fluoropentyl)-1H-indol-3-yl]methanone	EAM-2201	$C_{26}H_{26}FNO$	Parent	387.489105	7.88	388.20712

3-(1,1'-dimethylheptyl)-6aR,7,10, 10aR-tetrahydro-1-hydroxy-6,6-dimethyl-6H-dibenzo[b,d]pyran-9-methanol	HU-210	$C_{25}H_{38}O_3$	Parent	386.567413	7.44	387.28937
3-(1,1-dimethylheptyl)-6aS,7,10, 10aS-tetrahydro-1-hydroxy-6,6-dimethyl-6H-dibenzo[b,d]pyran-9-methanol	HU-211	$C_{25}H_{38}O_3$	Parent	386.567413	7.44	387.28937
[(1R,4S,5R)-4-[2,6-Dimethoxy-4-(2-methyl-2-octanyl)phenyl]-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl]methanol	HU-308	$C_{27}H_{42}O_3$	Parent	414.620605	8.96	415.32067
(2-Methyl-1-pentyl-1H-indol-3-yl)(1-naphthyl)methanone	JWH-007	$C_{25}H_{25}NO$	Parent	355.472107	7.44	356.20089
(2-Methyl-1-propyl-1H-indol-3-yl)(1-naphthyl)methanone	JWH-015	$C_{23}H_{21}NO$	Parent	327.418915	6.46	328.16959
1-Naphthyl(1-pentyl-1H-indol-3-yl)methanone	JWH-018	$C_{24}H_{23}NO$	Parent	341.445496	6.9	342.18524
[1-(5-Hydroxypentyl)-1H-indol-3-yl](1-naphthyl)methanone	5-hydroxypentyl JWH-018	$C_{24}H_{23}NO_2$	Metabolite	357.444885	5.43	358.18016
5-[3-(1-Naphthoyl)-1H-indol-1-yl]pentanoic acid	pentanoic acid JWH-018	$C_{24}H_{23}NO_3$	Metabolite	371.428406	5.66	374.17507
(5-Hydroxy-1-pentyl-1H-indol-3-yl)(1-naphthyl)methanone	hydroxyindole JWH-018	$C_{24}H_{23}NO_2$	Metabolite	357.444885	6.42	358.18016
(1-(5-chloropentyl)-1H-indol-3-yl)(naphthalen-1-yl)methanone	JHW-018 N-(5-chloropentyl) analog	$C_{24}H_{22}ClNO$	Parent	375.890594	7.15	376.14627
(1-Hexyl-1H-indol-3-yl)(1-naphthyl)methanone	JWH-019	$C_{25}H_{25}NO$	Parent	355.472107	7.39	357.20872
1-Naphthyl[1-(4-penten-1-yl)-1H-indol-3-yl]methanone	JWH-022	$C_{24}H_{21}NO$	Parent	339.429596	6.76	340.16959

(1-Butyl-1H-indol-3-yl)(1-naphthyl)methanone	JWH-073	$C_{23}H_{21}NO$	Parent	327.418915	6.41	328.16959
4-[3-(1-Naphthoyl)-1H-indol-1-yl]butanoic acid	N-butanoic acid JWH-073	$C_{23}H_{19}NO_3$	Metabolite	357.401886	5.17	358.14377
[1-(4-Hydroxybutyl)-1H-indol-3-yl](1-naphthyl)methanone	4-hydroxybutyl JWH-073	$C_{23}H_{21}NO_2$	Metabolite	343.418304		344.16451
(4-Methoxy-1-naphthyl)(1-pentyl-1H-indol-3-yl)methanone	JWH-081	$C_{25}H_{25}NO_2$	Parent	371.471497	6.98	373.20363
5-(3-(4-methoxy-1-naphthoyl)-1H-indol-1-yl)pentanoic acid	JWH-081 hydroxyindole metabolite	$C_{25}H_{23}NO_4$	Metabolite	401.1627	5.74	402.16998
(4-Methoxy-1-naphthyl)(2-methyl-1-pentyl-1H-indol-3-yl)methanone	JWH-098	$C_{26}H_{27}NO_2$	Parent	385.498108	7.52	386.21146
(2-Ethyl-1-pentyl-1H-indol-3-yl)(1-naphthyl)methanone	JWH-116	$C_{26}H_{27}NO$	Parent	369.498688	7.93	370.21654
(4-Methyl-1-naphthyl)(1-pentyl-1H-indol-3-yl)methanone	JWH-122	$C_{25}H_{25}NO$	Parent	355.472107	7.44	357.20872
[1-(5-Hydroxypentyl)-1H-indol-3-yl](4-methyl-1-naphthyl)methanone	5-hydroxypentyl JWH-122	$C_{25}H_{25}NO_2$	Metabolite	371.471497		372.19581
(4-methylnaphthalen-1-yl)(1-(pent-4-en-1-yl)-1H-indol-3-yl)methanone	JWH-122 N-(4-pentyl) analog, 4-methyl homologue of JWH-210	$C_{25}H_{23}NO$	Parent	353.456207	7.31	354.18524
(4-Methyl-1-naphthyl)(2-methyl-1-pentyl-1H-indol-3-yl)methanone	JWH-149	$C_{26}H_{27}NO$	Parent	369.498688	7.99	370.21654
1-(1-Pentyl-1H-indol-3-yl)-2-phenylethanone	JWH-167	$C_{21}H_{23}NO$	Parent	305.413391	5.95	306.18524
(1-Pentyl-1H-indol-3-yl)(4-propyl-1-naphthyl)methanone	JWH-182, 4-n-propyl homologue of JWH-120	$C_{27}H_{29}NO$	Parent	383.525299	8.43	385.24002
(4-Methyl-1-naphthyl){1-[2-(4-morpholinyl)ethyl]-1H-indol-3-yl}methanone	JWH-193	$C_{26}H_{26}N_2O_2$	Parent	398.496796	4.79	399.2067

(4-Methoxy-1-naphthyl){1-[2-(4-morpholinyl)ethyl]-1H-indol-3-yl}methanone	JWH-198	$C_{26}H_{26}N_2O_3$	Parent	414.496185	4.32	415.20162
{1-[2-(4-Morpholinyl)ethyl]-1H-indol-3-yl}(1-naphthyl)methanone	JWH-200	$C_{25}H_{24}N_2O_2$	Parent	384.470306	4.24	385.19105
[6-hydroxy-1-(2-morpholinoethyl)indol-3-yl]-(1-naphthyl)methanone	6-hydroxyindole JWH-200	$C_{25}H_{24}N_2O_3$	Metabolite	400.178693		401.18597
2-(3-Methoxyphenyl)-1-(1-pentyl-1H-indol-3-yl)ethanone	JWH-201; JWH-302	$C_{22}H_{25}NO_2$	Parent	335.439392	6.04	336.19581
2-(2-Chlorophenyl)-1-(1-pentyl-1H-indol-3-yl)ethanone	JWH-203	$C_{21}H_{22}ClNO$	Parent	339.85849	6.6	340.14627
(4-Ethyl-1-naphthyl)(1-pentyl-1H-indol-3-yl)methanone	JWH-210	$C_{26}H_{27}NO$	Parent	369.498688	7.93	370.21654
(4-Ethyl-1-naphthyl)[1-(5-hydroxypentyl)-1H-indol-3-yl]methanone	5-hydroxypentyl JWH-210	$C_{26}H_{27}NO_2$	Metabolite	385.498108		386.21146
(4-Ethyl-1-naphthyl)(5-hydroxy-1-pentyl-1H-indol-3-yl)methanone	5-hydroxyindole JWH-210	$C_{26}H_{27}NO_2$	Metabolite	385.498108		386.21146
2-(2-Methoxyphenyl)-1-(1-pentyl-1H-indol-3-yl)ethanone	JWH-250	$C_{22}H_{25}NO_2$	Parent	335.439392	6.04	336.19581
1-[1-(5-Hydroxypentyl)-1H-indol-3-yl]-2-(2-methoxyphenyl)ethanone	hydroxypentyl JWH-250	$C_{22}H_{25}NO_3$	Metabolite	351.438812		352.19072
5-{3-[(2-Methoxyphenyl)acetyl]-1H-indol-1-yl}pentanoic acid	pentanoic acid JWH-250	$C_{22}H_{23}NO_4$	Metabolite	365.422302		366.16998
1-(5-Hydroxy-1-pentyl-1H-indol-3-yl)-2-(2-methoxyphenyl)ethanone	5-hydroxyindole JWH-250	$C_{22}H_{25}NO_3$	Metabolite	351.438812		352.19072
2-(2-Methylphenyl)-1-(1-pentyl-1H-indol-3-yl)ethanone	JWH-251	$C_{22}H_{25}NO$	Parent	319.440002	6.5	320.20089

(4-Chloro-1-naphthyl)(1-pentyl-1H-indol-3-yl)methanone	JWH-398	$C_{24}H_{22}ClNO$	Parent	375.890594	7.54	377.15409
(8-Bromo-1-naphthyl)(1-pentyl-1H-indol-3-yl)methanone	JWH-424	$C_{24}H_{22}BrNO$	Parent	420.341614	7.79	420.09575
[1-(5-Fluoropentyl)-1H-indol-3-yl](4-methyl-1-naphthyl)methanone	MAM-2201	$C_{25}H_{24F}NO$	Parent	373.462585	7.38	374.19147
(4-Methoxyphenyl)(1-pentyl-1H-indol-3-yl)methanone	RCS-4	$C_{21}H_{23}NO_2$	Parent	321.412811	5.8	322.18016
1-[1-(2-Cyclohexylethyl)-1H-indol-3-yl]-2-(2-methoxyphenyl)ethanone	RCS-8	$C_{25}H_{29}NO_2$	Parent	375.503296	7.32	376.22711
(1-pentyl-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone	UR-144	$C_{21}H_{29}NO$	Parent	311.224915	6.79	312.23219
(1-(5-chloropentyl)-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone	UR-144 N-(5-chloropentyl) analog	$C_{21}H_{28}ClNO$	Parent	345.906097	7.04	346.19322
6-Methyl-2-[(4-methylphenyl)amino]-4H-3,1-benzoxazin-4-one	URB-754	$C_{16}H_{14}N_2O_2$	Parent	266.294586	2.22	267.1128
(1-(5-fluoropentyl)-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone	XLR-11, 5-fluoro UR-144	$C_{21}H_{28}FNO$	Parent	329.451508	6.73	330.22277
1-[1-(3-Methoxyphenyl)cyclohexyl]piperidine	3-MeO-PCP; 3-methoxyphencyclidine	$C_{18}H_{27}NO$	Parent	273.413086	4.97	274.21654
1-[1-(4-Methoxyphenyl)cyclohexyl]piperidine	4-MeO-PCP; 4-methoxyphencyclidine	$C_{18}H_{27}NO$	Parent	273.413086	4.97	274.21654
2-(3-methoxyphenyl)-2-(ethylamino)cyclohexane	3-MeO-PCE		Parent			
1-benzylpiperazine	BZP; A2	$C_{11}H_{16}N_2$	Parent	176.258102	1.12	177.13863
[5R, 10S]-(+)-5-methyl-10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5,10-imine	dizocilpine, MK-801	$C_{20}H_{19}NO_4$	Parent	337.369202	3.48	338.13868

N-ethyl-1-phenylcyclohexylamine	eticyclidine; PCE; Cl-400	$C_{14}H_{21}N$	Parent	203.323196	4.26	204.17468
2-(2-chlorophenyl)-2-(ethylamino)cyclohexanone	ethylketamine		Parent			
1-(3-chlorophenyl)piperazine	mCPP; meta-chlorophenylpiperazine	$C_{10}H_{13}ClN$	Parent	196.676605	2.11	183.08093
1-(4-methoxyphenyl)piperazine	MeOPP; para-methoxyphenylpiperazine	$C_{11}H_{16}N_2O$	Parent	192.257507	1.63	193.13354
2-(2-methoxyphenyl)-2-(methylamino)cyclohexanone	methoxyketamine; 2-MeO-ketamine	$C_{14}H_{19}NO_2$	Parent	233.306198	2.56	234.14886
1-Phenyl-N-propylcyclohexanamine	PCPr	$C_{15}H_{23}N$	Parent	217.349792	4.75	218.19033
N-(1-phencyclohexyl)-3-ethoxypropanamine	PCEPA	$C_{17}H_{27}NO$	Parent	261.402008		262.21654
	O-deethyl-PCEPA	$C_{17}H_{25}NO_2$	Metabolite	275.188529		276.19581
	O-deethyl-hydroxyphenyl-PCEPA	$C_{19}H_{27}NO_4$	Metabolite	333.194008		334.20128
	O-deethyl-4'-hydroxy-PCEPA isomer 1	$C_{19}H_{25}NO_4$	Metabolite	331.178358		332.18563
	O-deethyl-4'-hydroxy-PCEPA isomer 2	$C_{19}H_{25}NO_4$	Metabolite	331.178358		332.18563
	O-deethyl-3'-hydroxy-PCEPA	$C_{19}H_{25}NO_4$	Metabolite	331.178358		332.18563
	dehydrated O-deethyl-4'-hydroxy-PCEPA	$C_{17}H_{23}NO_2$	Metabolite	273.1728789		274.18016
	O-deethyl-3'-hydroxy-hydroxyphenyl-PCEPA	$C_{21}H_{28}NO_6$	Metabolite	390.191662		391.19894
	O-deethyl-4'-hydroxy-hydroxyphenyl-PCEPA	$C_{21}H_{28}NO_6$	Metabolite	390.191662		391.19894
	hydroxyphenyl-PCEPA	$C_{19}H_{28}NO_3$	Metabolite	318.206919		319.2142
	4'-hydroxy-PCEPA isomer 1	$C_{19}H_{28}NO_3$	Metabolite	318.206919		319.2142

	4'-hydroxy-PCEPA isomer 2	$C_{19}H_{28}NO_3$	Metabolite	318.206919		319.2142
	3'-hydroxy-PCEPA	$C_{19}H_{28}NO_3$	Metabolite	318.206919		319.2142
	dehydrated 4'-hydroxy-PCEPA	$C_{17}H_{25}NO$	Metabolite	259.193614		260.20089
	N-dealkyl-PCEPA	$C_{14}H_{19}NO$	Metabolite	217.146664		218.15394
	N-dealkyl-4'-hydroxy-PCEPA isomer 1	$C_{16}H_{20}NO_3$	Metabolite	274.144318		275.1516
	N-dealkyl-4'-hydroxy-PCEPA isomer 2	$C_{16}H_{20}NO_3$	Metabolite	274.144318		275.1516
	N-dealkyl-3'-hydroxy-PCEPA isomer 1	$C_{16}H_{20}NO_3$	Metabolite	274.144318		275.1516
	N-dealkyl-3'-hydroxy-PCEPA isomer 2	$C_{16}H_{20}NO_3$	Metabolite	274.144318		275.1516
	dehydrated N-dealkyl-4'-hydroxy-PCEPA	$C_{14}H_{17}NO$	Metabolite	215.131014		216.13829
	dehydrated carboxy-PCEPA	$C_{15}H_{19}NO$	Metabolite	229.146664		230.15394
	dehydrated carboxy-4'-hydroxy-PCEPA isomer 1	$C_{17}H_{19}NO_3$	Metabolite	285.136493		286.14377
	dehydrated carboxy-4'-hydroxy-PCEPA isomer 2	$C_{17}H_{19}NO_3$	Metabolite	285.136493		286.14377
	dehydrated carboxy-3'-hydroxy-PCEPA isomer 1	$C_{17}H_{19}NO_3$	Metabolite	285.136493		286.14377
	dehydrated carboxy-3'-hydroxy-PCEPA isomer 2	$C_{17}H_{19}NO_3$	Metabolite	285.136493		286.14377
	carboxy-PCEPA	$C_{18}H_{28}NO_2Si$	Metabolite	318.188931		319.19621
	carboxy-hydroxyphenyl-PCEPA	$C_{21}H_{37}NO_3Si_2$	Metabolite	407.231197		408.23847

	cis-carboxy-4'-hydroxy-PCEPA	$C_{21}H_{37}NO_3Si_2$	Metabolite	407.231197		408.23847
	trans-carboxy-4'-hydroxy-PCEPA	$C_{21}H_{37}NO_3Si_2$	Metabolite	407.231197		408.23847
	carboxy-3'-hydroxy-PCEPA	$C_{21}H_{35}NO_3Si_2$	Metabolite	405.215547		406.22282
	carboxy-4'-hydroxy-hydroxyphenyl-PCEPA	$C_{24}H_{45}NO_4Si_3$	Metabolite	495.265638		496.27291
	cis-O-deethyl-4'-hydroxy-PCEPA	$C_{21}H_{39}NO_2Si_2$	Metabolite	393.251932		394.25921
	trans-O-deethyl-4'-hydroxy-PCEPA	$C_{21}H_{39}NO_2Si_2$	Metabolite	393.251932		394.25921
1-(4-fluorophenyl)piperazine	pFPP	$C_{10}H_{13}FN_2$	Parent	180.222	1.28	181.11355
1-(1-phenylcyclohexyl)pyrrolidine	rolicyclidine, PCPy	$C_{16}H_{23}N$	Parent	229.360504	4.4	230.19033
1-(1-(2-thienyl)cyclohexyl)pyrrolidine	tenocyclidine, TCP	$C_{15}H_{23}NS$	Parent	249.414795	4.71	250.1624
1-[3-(Trifluoromethyl)phenyl]piperazine	TFMPP	$C_{11}H_{13}F_3N_2$	Parent	230.229507	2.43	231.11036
1-[4-(Methylsulfanyl)phenyl]-2-propanamine	4-MTA	$C_{10}H_{15}NS$	Parent	181.297806	2.36	182.0998
(RS)-1-(1,3-benzodioxol-5-yl)-N-methylpropan-2-amine	3,4-MDMA	$C_{11}H_{15}NO_2$	Parent	193.1103	2.28	194.11756
methylenedioxyamphetamine	MDA	$C_{10}H_{13}NO_2$	Parent	179.21572	1.82	180.10191
1-(7-Methyl-1,3-benzodioxol-5-yl)-2-propanamine	5-Me-MDA	$C_{11}H_{15}NO_2$	Parent	193.242294	2.36	193.10973
1-(1-Benzofuran-5-yl)-2-propanamine	5-APB	$C_{11}H_{13}NO$	Parent	175.227005	2.3	176.10699
1-(1-Benzofuran-6-yl)-2-propanamine	6-APB	$C_{11}H_{13}NO$	Parent	175.227005	2.3	176.10699
1-(1H-Indol-3-yl)-2-butanamine	AET; α-ethyltryptamine	$C_{12}H_{16}N_2$	Parent	188.268799	2.17	189.13863
1-(1,3-Benzodioxol-5-yl)-2-(methylamino)-1-butanone	butylone	$C_{12}H_{15}NO_3$	Parent	221.251999	2.4	222.11247

1-(1,3-Benzodioxol-5-yl)-2-(ethylamino)-1-propanone	ethylone	$C_{12}H_{15}NO_3$	Parent	221.251999	2.4	222.11247
1-(2,3-Dihydro-1H-inden-5-yl)-2-propanamine	IAP; 5-APDI	$C_{12}H_{17}N$	Parent	175.270096	3.23	176.14338
1-(1,3-Benzodioxol-5-yl)-N-methyl-2-butanamine	MBDB; methyl-J; Eden	$C_{12}H_{17}NO_2$	Parent	207.268906	2.77	208.13321
5,6,7,8-Tetrahydronaphtho[2,3-d][1,3]dioxol-6-amine	MDAT	$C_{11}H_{13}NO_2$	Parent	191.226395	2.25	192.10191
1-(1,3-Benzodioxol-5-yl)-N-ethyl-2-propanamine	MDEA	$C_{12}H_{17}NO_2$	Parent	207.268906	2.77	208.13321
1-(1,3-Benzodioxol-5-yl)-2-(methylamino)-1-propanone	methylone	$C_{11}H_{13}NO_3$	Parent	207.2258	1.91	208.09682
1-(3-Methoxy-4-methylphenyl)-2-propanamine	MMA	$C_{11}H_{17}NO$	Parent	179.258804	2.38	180.13829
1-(4-Methoxyphenyl)-2-propanamine	PMA; para-methoxyamphetamine; Death; Dr. Death	$C_{10}H_{15}NO$	Parent	165.232193	1.77	166.12264
1-(4-Methoxyphenyl)-N-methyl-2-propanamine	PMMA; 4-methoxymethamphetamine	$C_{11}H_{17}NO$	Parent	179.258804	1.91	180.13829
	PMMA (AC)	$C_{13}H_{19}NO_2$	Metabolite	221.141579		222.14886
p-hydroxymethamphetamine	Pholedrine (2AC)	$C_{14}H_{19}NO_3$	Metabolite	249.136493		250.14377
1-hydroxypholedrine	Oxilofrine (3AC)	$C_{16}H_{21}NO_5$	Metabolite	307.141973		308.14925
1-hydroxypholedrine	O-demethyl-HO-alkyl-PMMA (3AC)	$C_{16}H_{21}NO_5$	Metabolite	307.141973		308.14925
p-methoxyamphetamine	nor-PMMA (AC); PMA (AC)	$C_{12}H_{17}NO_2$	Metabolite	207.125929		208.13321
p-hydroxyamphetamine	bis-demethyl-PMMA (2AC)	$C_{13}H_{17}NO_3$	Metabolite	235.120843		236.12812
3',4'-dihydroxymethamphetamine	O-demethyl-HO-aryl-PMMA; di-HO-MA	$C_{16}H_{21}NO_5$	Metabolite	307.141973		308.14925

4'-hydroxy-3'-methoxymethamphetamine	O-demethyl-methoxy-PMMA isomer 1 (2AC)	$C_{14}H_{19}NO_4$	Metabolite	265.131408		266.13868
3'-hydroxy-4'-methoxyamphetamine	O-demethyl-methoxy-PMMA isomer 2 (2AC)	$C_{14}H_{19}NO_4$	Metabolite	265.131408		266.13868
4'-hydroxy-3'-methoxyamphetamine	bis-desmethyl-methoxy-PMMA (2AC)	$C_{14}H_{19}NO_4$	Metabolite	265.131408		266.13868
N-Ethyl-1-(4-methoxyphenyl)-2-propanamine	PMEA	$C_{12}H_{19}NO$	Parent	193.2854	2.79	194.15394
N-Phenyl-N-[1-(1-phenyl-2-propanyl)-4-piperidinyl]propanamide	α-methylfentanyl; China White	$C_{23}H_{30}N_2O$	Parent	350.497101	4.31	351.24309
N-(4-Fluorophenyl)-N-[1-(2-phenylethyl)-4-piperidinyl]propanamide	para-fluorofentanyl	$C_{22}H_{27}FN_2O$	Parent	354.460999	4.09	355.21802
1-Methyl-4-phenyl-4-piperidinyl propionate	MPPP (opiod)	$C_{15}H_{21}NO_2$	Parent	247.332703	3.03	248.16451
6,7-Dimethoxy-2-methyl-1-[2-(4-nitrophenyl)ethyl]-1,2,3,4-tetrahydroisoquinoline	4'-nitromethopholine	$C_{20}H_{24}N_2O_4$	Parent	356.415588	4.04	357.18088
3-{2-[(Dimethylamino)methyl]-1-hydroxycyclohexyl}phenol	o-desmethyltramadol	$C_{15}H_{23}NO_2$	Parent	249.348602	2.45	250.18016
4,4-diphenyl-6-(pyrlidin-1-yl)-heptan-3-one		$C_{23}H_{29}NO$	Parent	335.482513	5.11	
2-(methylamino)-1-(naphthalene-2-yl)pentan-1-one	NRG-3	$C_{16}H_{19}NO$	Parent	241.1467	4.01	242.15394
2-(4-Bromo-2,5-dimethoxyphenyl)ethanamine	2C-B	$C_{10}H_{14}BrNO_2$	Parent	260.127686	2.39	260.02807
2-(4-Chloro-2,5-dimethoxyphenyl)ethanamine	2C-C	$C_{10}H_{14}ClNO_2$	Parent	215.676697	2.14	216.07858
2-(2,5-Dimethoxy-4-methylphenyl)ethanamine	2C-D	$C_{11}H_{17}NO_2$	Parent	195.258194	2.05	196.13321

2-(4-Ethyl-2,5-dimethoxyphenyl)ethanamine	2C-E	$C_{12}H_{19}NO_2$	Parent	209.284805	2.54	210.14886
3,4-dimethyl-2,5-dimethoxyphenethylamine	2C-G	$C_{12}H_{19}NO_2$	Parent	209.284805	2.59	210.14886
2-(2,5-Dimethoxyphenyl)ethanamine	2C-H	$C_{10}H_{15}NO_2$	Parent	181.231598	1.5	182.11756
2-(4-Iodo-2,5-dimethoxyphenyl)ethanamine	2C-I	$C_{10}H_{14}INO_2$	Parent	307.128113	2.67	308.0142
N-acetyl-2-(4-Iodo-2,5-dimethoxyphenyl)ethanamine	2C-I (AC)	$C_{12}H_{16}INO_3$	Metabolite	349.017486		350.02476
N-acetyl-acetoxy-4-iodo-methoxy-β-phenethylamine isomer 1	O-desmethyl-N-acetyl-2C-I isomer 1 (AC)	$C_{13}H_{16}INO_4$	Metabolite	377.012401		378.01968
N-acetyl-acetoxy-4-iodo-methoxy-β-phenethylamine isomer 2	O-desmethyl-N-acetyl-2C-I isomer 2 (AC)	$C_{13}H_{16}INO_4$	Metabolite	377.012401		378.01968
2-(4-iodo-2,5-dimethoxyphenyl) ethyl acetate	desamino-HO-2C-I (AC)	$C_{12}H_{16}IO_4$	Metabolite	351.009327		352.0166
2-(acetoxy-4-iodo-2,5-dimethoxyphenyl) ethyl acetate isomer 1	desamino-HO-O-desmethyl-2C-I isomer 1 (2AC)	$C_{13}H_{16}IO_5$	Metabolite	379.004241		380.01152
2-(acetoxy-4-iodo-2,5-dimethoxyphenyl) ethyl acetate isomer 2	desamino-HO-O-desmethyl-2C-I isomer 2 (2AC)	$C_{13}H_{16}IO_5$	Metabolite	379.004241		380.01152
2-acetoxy-2-(acetoxy-4-iodo-methoxyphenyl) ethyl acetate	desamino-di-HO-O-desmethyl-2C-I (3AC)	$C_{14}H_{16}IO_6$	Metabolite	406.999156		408.00643
2-(acetoxy-4-iodo-methoxyphenyl)-2-oxo-ethyl acetate	desamino-HO-O-desmethyl-oxo-2C-I (2AC)	$C_{13}H_{13}IO_6$	Metabolite	391.975681		392.98296
N-acetyl-hydroxy-4-iodo-methoxy-β-phenethylamine isomer 1	O-desmethyl-N-acetyl-2C-I isomer 1	$C_{11}H_{14}NIO_2$	Metabolite	319.006922		320.0142
N-acetyl-hydroxy-4-iodo-methoxy-β-phenethylamine isomer 2	O-desmethyl-N-acetyl-2C-I isomer 2	$C_{11}H_{14}NIO_2$	Metabolite	319.006922		320.0142

N-trifluoroacetyl-2-(4-Iodo-2,5-dimethoxyphenyl)ethanamine	2C-I (TFA)	$C_{12}H_{13}NIO_3F_3$	Metabolite	402.989221		403.9965
N-trifluoroacetyl-trifluoroacetoxy-4-iodo-methoxy-β-phenethylamine isomer 1	O-desmethyl-2C-I isomer 1 (2TFA)	$C_{12}H_{10}NIO_4F_6$	Metabolite	472.955869		473.96315
N-trifluoroacetyl-trifluoroacetoxy-4-iodo-methoxy-β-phenethylamine isomer 2	O-desmethyl-2C-I isomer 2 (2TFA)	$C_{12}H_{10}NIO_4F_6$	Metabolite	472.955869		473.96315
methyl-4-iodo-2,5-dimethoxy-β-phenylacetate	desamino-HOOC-2C-I (ME)	$C_{11}H_{13}IO_4$	Metabolite	335.985852		336.99313
methyl-trifluoroacetoxy-4-iodo-methoxy-β-phenylacetate	desamino-HOOC-O-desmethyl-2C-I (METFA)	$C_{12}H_{10}IO_5F_3$	Metabolite	417.952501		418.95978
6-iodo-5-methoxy-1-benzofuran-2(3H)-one	desamino-HOOC-O-desmethyl-2C-I (H_2O)	$C_9H_7IO_3$	Metabolite	289.943987		290.95126
2-[2,5-Dimethoxy-4-(methylsulfanyl)phenyl]ethanamine	2C-T	$C_{11}H_{17}NO_2S$	Parent	227.323196	1.81	228.10528
2-[4-(Ethylsulfanyl)-2,5-dimethoxyphenyl]ethanamine	2C-T-2; Rosy	$C_{12}H_{19}NO_2S$	Parent	241.349792	2.59	242.12093
2,5-dimethoxy-4-(n)-propylthiophenethylamine	2C-T-7; Blue Mystic	$C_{13}H_{21}NO_2S$	Parent	255.376297	3.08	256.13658
2-{4-[(2-Fluoroethyl)sulfanyl]-2,5-dimethoxyphenyl}ethanamine	2C-T-21	$C_{12}H_{18}FNO_2S$	Parent	259.34021	2.53	260.1115
2-(2,5-Dimethoxy-4-nitrophenyl)ethanamine	2C-N	$C_{10}H_{14}N_2O_4$	Parent	226.229202	1.32	227.10263
2-(8-Bromo-2,3,6,7-tetrahydrofuro[2,3-f][1]benzofuran-4-yl)ethanamine	2CB-FLY	$C_{12}H_{14}BrNO_2$	Parent	284.149109	3.26	284.02807
3-[2-(Diisopropylamino)ethyl]-1H-indol-4-yl acetate	4-acetoxy-DiPT	$C_{18}H_{26}N_2O_2$	Parent	302.411011	3.36	303.2067
4-acetoxy-dimethyltryptamine	4-acetoxy-DMT	$C_{14}H_{18}N_2O_2$	Parent	246.304993	1.54	247.1441

3-{2-[Ethyl(methyl)amino]ethyl}-1H-indol-4-o	4-HO-MET	$C_{13}H_{18}N_2O$	Parent	218.2948	1.95	219.14919
3-{2-[Isopropyl(methyl)amino]ethyl}-1H-indol-4-ol	4-HO-MiPT	$C_{14}H_{20}N_2O$	Parent	232.321396	2.37	233.16484
1-(5-Methoxy-1H-indol-3-yl)-2-propanamine	5-MeO-AMT	$C_{12}H_{16}N_2O$	Parent	204.126266	1.76	205.13354
N-allyl-N-[2-(5-methoxy-1H-indol-3-yl)ethyl]prop-2-en-1-amine	5-MeO-DALT	$C_{17}H_{22}N_2O$	Parent	270.368988	3.72	271.18049
N-Isopropyl-N-[2-(5-methoxy-1H-indol-3-yl)ethyl]-2-propanamine	5-MeO-DiPT, Foxy, Foxy Methoxy	$C_{17}H_{26}N_2O$	Parent	274.401093	3.84	275.21179
N-[2-(5-Methoxy-1H-indol-3-yl)ethyl]-N-methyl-2-propanamine	5-MeO-MiPT	$C_{15}H_{22}N_2O$	Parent	246.348007	2.93	247.18049
(8β)-6-Allyl-N,N-diethyl-9,10-didehydroergoline-8-carboxamide	AL-LAD	$C_{22}H_{27}N_3O$	Parent	349.469299	3.11	350.22269
(8β)-1-Acetyl-N,N-diethyl-6-methyl-9,10-didehydroergoline-8-carboxamide	ALD-52	$C_{22}H_{27}N_3O_2$	Parent	365.468689	1.95	366.2176
(2R)-1-(8-Bromofuro[2,3-f][1]benzofuran-4-yl)-2-propanamine	Bromodragonfly	$C_{13}H_{12}BrNO_2$	Parent	294.14389	3.74	294.01242
N-[2-(1H-Indol-3-yl)ethyl]-N-isopropyl-2-propanamine	DiPT	$C_{16}H_{24}N_2$	Parent	244.375198	3.76	245.20123
1-(4-Bromo-2,5-dimethoxyphenyl)-2-propanamine	DOB	$C_{11}H_{16}BrNO_2$	Parent	274.154205	2.58	274.04372
1-(4-Chloro-2,5-dimethoxyphenyl)-2-propanamine	DOC	$C_{11}H_{16}ClNO_2$	Parent	229.703201	2.56	230.09423
1-(4-Iodo-2,5-dimethoxyphenyl)-2-propanamine	DOI	$C_{11}H_{16}INO_2$	Parent	321.154694	3.08	322.02985
1-(2,5-Dimethoxy-4-methylphenyl)-2-propanamine	DOM	$C_{12}H_{19}NO_2$	Parent	209.141586	2.46	210.14886

N-[2-(1H-Indol-3-yl)ethyl]-N-propyl-1-propanamine	DPT	$C_{16}H_{24}N_2$	Parent	244.375198	3.91	245.20123
[(2S,4S)-2,4-Dimethyl-1-azetidinyl][(8β)-6-methyl-9,10-didehydroergolin-8-yl]methanone	LSZ	$C_{21}H_{25}N_3O$	Parent	335.442688	2.5	336.20704
1-(2,4,5-Trimethoxyphenyl)-2-propanamine	TMA-2	$C_{12}H_{19}NO_3$	Parent	225.284195	1.74	226.14377
1-(2,4,6-Trimethoxyphenyl)-2-propanamine	TMA-6	$C_{12}H_{19}NO_3$	Parent	225.284195	1.57	226.14377
2-(4-chloro-2,5-dimethoxyphenyl)-N-(2-methoxybenzyl)ethanamine	25C-NBOMe, NBOMe-2C-C, Pandora	$C_{18}H_{22}ClNO_3$	Parent	335.825195	4.4	336.1361
4-iodo-2,5-dimethoxy-N-[(2-methoxyphenyl)methyl]-benzeneethanamine	25I-NBOMe, NBOMe-2C-I, Solaris	$C_{18}H_{22}INO_3$	Parent	427.276611	4.92	428.07171
3-(2,4-Dimethylphenyl)-2-methyl-4(3H)-quinazolinone	methylmethaqualone	$C_{17}H_{16}N_2O$	Parent	264.321686	4.88	265.13354
3-(2-Bromophenyl)-2-methyl-4(3H)-quinazolinone	GBL; mebroqualone	$C_{15}H_{11}BrN_2O$	Parent	315.164612	4.67	315.01275
5-Benzyl-5-butyl-2,4,6(1H,3H,5H)-pyrimidinetrione	GHV; benzylbarbiturate	$C_{15}H_{18}N_2O_3$	Parent	274.315002	2.8	275.13902
7-Bromo-5-(2-chlorophenyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one	GHL; phenazepam	$C_{15}H_{10}BrClN_2O$	Parent	349.609711	3.2	348.97378
6,7-Dimethyl-5-phenyl-3,7-dihydropyrrolo[3,4-e][1,4]diazepin-2(1H)-one	premazepam	$C_{15}H_{15}N_3O$	Parent	253.299103	2.21	254.12879
4-(2-Chlorophenyl)-2-ethyl-9-methyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine	etizolam	$C_{17}H_{15}ClN_4S$	Parent	342.845795	4.17	343.07787

1-Phenyl-2-(1-pyrrolidinyl)-1-propanone	α-pyrrolidinopropiophenone; PPP	$C_{13}H_{17}NO$	Parent	203.280197	2.93	204.13829
1-(2-Fluorophenyl)-2-propanamine	2-fluoroamphetamine	$C_9H_{12}FN$	Parent	153.196701	1.96	154.10265
1-(3-Fluorophenyl)-2-propanamine	3-fluoroamphetamine	$C_9H_{12}FN$	Parent	153.196701	1.96	154.10265
1-(4-Fluorophenyl)-2-(methylamino)-1-propanone	2-FMC, fluoromethcathinone; flephedrone	$C_{10}H_{12}FNO$	Parent	181.206802	2.05	182.09757
1-(3,4-dimethylphenyl)-2-(methylamino)propan-1-one	3,4-DMMC	$C_{12}H_{17}NO$	Parent	191.270004	2.94	192.13829
(RS)-1-(3-fluorophenyl)-2-(methylamino)propan-1-one	3-fluoromethcathinone; 3-FMC	$C_{10}H_{12}FNO$	Parent			
1-(1,3-Benzodioxol-5-yl)-2-(1-pyrrolidinyl)-1-propanone	MDPPP	$C_{14}H_{17}NO_3$	Parent	247.289703	2.99	248.12812
1-(4-Fluorophenyl)-2-propanamine	4-fluoroamphetamine	$C_9H_{12}FN$	Parent	153.196701	1.96	154.10265
1-(4-Fluorophenyl)-2-(methylamino)-1-propanone	4-fluoromethcathinone; 4-FMC	$C_{10}H_{12}FNO$	Parent	181.206802	2.05	182.09757
(RS)-1-(4-fluoropheny)-2-methylaminopropan-1-one	4-flurorethcathinone; 4-FEC	$C_{11}H_{14}FNO$	Parent	195.1059	2.05	196.11322
1-(4-bromophenyl)-2-(methylamino)-1-propanone	4-bromomethcathinone	$C_{10}H_{12}BrNO$	Parent	241.0102	2.74	242.01750
4-Methyl-5-phenyl-4,5-dihydro-1,3-oxazol-2-amine	4-MAR	$C_{10}H_{12}N_2O$	Parent	176.215103	1.56	177.10224
2-(ethylamino)-1-(p-tolyl)propan-1-one	4-MEC	$C_{12}H_{17}NO$	Parent	191.270004	2.89	192.13829
1-(4-Methylphenyl)-2-(1-pyrrolidinyl)-1-propanone	4-MePPP	$C_{14}H_{19}NO$	Parent	217.306793	3.48	218.15394
2-methylamino-1-(4-methylphenyl)-1-propanone	4-MMC, 4-methylmethcathinone; mephedrone	$C_{11}H_{15}NO$	Parent	177.242905	2.39	178.12264

	mephedrone (AC)	$C_{13}H_{17}NO_2$	Metabolite	219.125928		220.13321
	nor-mephedrone (AC)	$C_{12}H_{14}NO_2$	Metabolite	204.102453		205.10973
	nor-dihydro-mephedrone isomer 1 (2AC)	$C_{14}H_{18}NO_3$	Metabolite	248.128668		249.13594
	nor-dihydro-mephedrone isomer 2 (2AC)	$C_{14}H_{18}NO_3$	Metabolite	248.128668		249.13594
	carboxytolyl-dihydro-mephedrone (2AC)	$C_{16}H_{21}NO_4$	Metabolite	291.147058		292.15433
	nor-HO-tolyl-mephedrone (2AC)	$C_{14}H_{17}NO_4$	Metabolite	263.115758		264.12303
	HO-tolyl-mephedrone (2AC)	$C_{15}H_{19}NO_4$	Metabolite	277.131407		278.13868
1-Phenyl-2-(1-pyrrolidinyl)-1-propanone	α-PPP	$C_{13}H_{17}NO$	Parent	203.280197	2.93	204.13829
1-phenyl-2-(1-pyrrolidinyl)-1-pentanone	α-PVP	$C_{15}H_{21}NO$	Parent	231.333298	3.91	232.16959
1-(1,3-benzodioxol-5-yl)-2-(methylamino)-1-butanone	butylone; bk-MBDB	$C_{12}H_{15}NO_3$	Parent	221.251999	2.4	222.11247
	butylone (AC)	$C_{14}H_{17}NO_4$	Metabolite	263.115758		264.12303
	nor-butylone (AC)	$C_{13}H_{15}NO_4$	Metabolite	249.100108		250.10738
	demethylenyl-methyl-butylone (2AC)	$C_{16}H_{23}NO_4$	Metabolite	293.162708		294.16998
	dihydro-butylone (2AC)	$C_{16}H_{21}NO_5$	Metabolite	307.141973		308.14925
2-(methylamino)-1-phenyl-butan-1-one	buphedrone	$C_{11}H_{15}NO$	Parent	177.242905	2.34	178.12264
N-Methyl-3-phenylbicyclo[2.2.1]heptan-2-amine	camfetamine	$C_{14}H_{19}N$	Parent	201.307404	3.4	202.15903
2-(Diphenylmethyl)piperidine	desoxypipradrol	$C_{18}H_{21}N$	Parent	251.365997	4.43	252.17468

Diphenyl[(2S)-2-pyrrolidinyl]methanol	diphenylprolinol	$C_{17}H_{19}NO$	Parent	253.338898	2.95	254.15394
2-(Ethylamino)-1-phenyl-1-propanone	ethcathinone	$C_{11}H_{15}NO$	Parent	177.242905	2.34	178.12264
Ethyl phenyl(2-piperidinyl)acetate	ethylphenidate	$C_{15}H_{21}NO_2$	Parent	247.332703	3.27	248.16451
N-Methyl-1-(2-thienyl)-2-propanamine	methiopropamine	$C_8H_{13}NS$	Parent	155.260498	2.26	156.08415
1-(1,3-benzodioxol-5-yl)-2-(1-pyrrolidinyl)-1-pentanone	MDPV, bathsalts, maphyrone	$C_{16}H_{21}NO_3$	Parent	275.342804	3.97	276.15942
	oxo-MDPV	$C_{16}H_{19}NO_4$	Metabolite	289.131407		290.13868
	demethylenyl-methyl-MDPV (AC)	$C_{18}H_{24}NO_4$	Metabolite	318.170533		319.17781
	demethylenyl-N,N-bisdealkyl-MDPV (2AC)	$C_{16}H_{19}NO_5$	Metabolite	305.126322		306.1336
	demethylenyl-MDPV (2AC)	$C_{19}H_{24}NO_5$	Metabolite	346.165447		347.17272
	demethylenyl-methyl-oxo-MDPV (AC)	$C_{18}H_{22}NO_5$	Metabolite	332.149797		333.15707
	demethylenyl-methyl-HO-MDPV (2AC)	$C_{19}H_{23}NO_6$	Metabolite	361.152537		362.15981
	demethylenyl-methyl-oxo-carboxy-MDPV isomer 1 (2AC)	$C_{20}H_{26}NO_7$	Metabolite	392.170927		393.1782
	demethylenyl-methyl-oxo-carboxy-MDPV isomer 2 (2AC)	$C_{20}H_{26}NO_7$	Metabolite	392.170927		393.1782
	oxo-carboxy-MDPV (AC)	$C_{18}H_{22}NO_6$	Metabolite	348.144712		349.15199
	demethylenyl-methyl-N,N-bisdealkyl-MDPV (2TMS)	$C_{18}H_{32}NO_3Si_2$	Metabolite	366.192072		367.19935

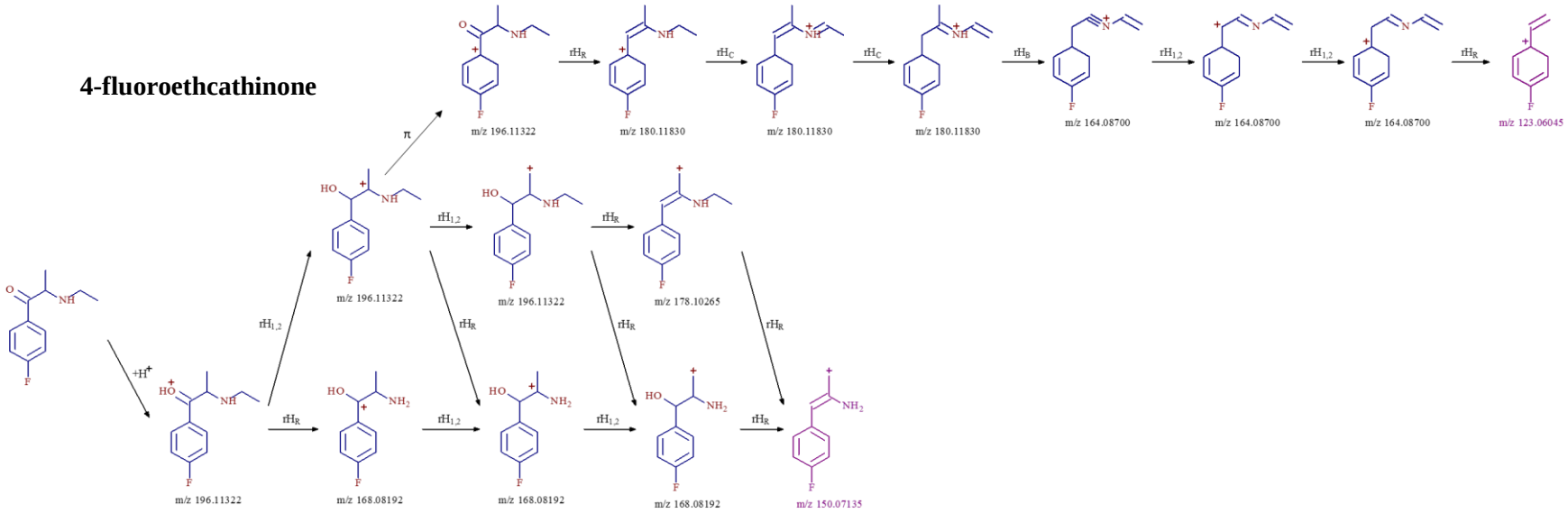
	demethylenyl-N,N-bisdealkyl-MDPV (3TMS)	$C_{20}H_{38}NO_3Si_3$	Metabolite	424.215948		425.22323
	demethylenyl-methyl-MDPV (TMS)	$C_{19}H_{30}NO_3Si$	Metabolite	348.199495		349.20677
	demethylenyl-MDPV (2TMS)	$C_{22}H_{36}NO_3Si_2$	Metabolite	418.223372		419.23065
	demethylenyl-methyl-HO-phenyl-MDPV (TMS)	$C_{22}H_{38}NO_4Si_2$	Metabolite	436.233936		437.24121
	demethylenyl-methyl-oxo-MDPV (TMS)	$C_{19}H_{28}NO_4Si$	Metabolite	362.178759		363.18604
	demethylenyl-methyl-HO-MDPV (2TMS)	$C_{22}H_{37}NO_4Si_2$	Metabolite	435.226112		436.23339
	demethylenyl-oxo-MDPV (2TMS)	$C_{21}H_{34}NO_4Si_2$	Metabolite	420.202636		421.20991
	demethylenyl-HO-MDPV (3TMS)	$C_{24}H_{43}NO_4Si_3$	Metabolite	493.249988		494.25726
1-(4-Methoxyphenyl)-2-(methylamino)-1-propanone	methedrone	$C_{11}H_{15}NO_2$	Parent	193.242294	1.93	194.11756
1-(1,3-benzodioxol-5-yl)-2-(methyamino)-1-propanone	methylone	$C_{11}H_{13}NO_3$	Parent	207.089543	1.91	208.09682
	methylone (AC)	$C_{13}H_{15}NO_4$	Metabolite	249.100108		250.10738
	nor-methylone (AC)	$C_{12}H_{13}NO_4$	Metabolite	235.0844578		236.09173
	nor-demethylenyl-methyl-methylone (2AC)	$C_{14}H_{17}NO_5$	Metabolite	279.1106725		280.11795
	demethylenyl-methyl-methylone (2AC)	$C_{15}H_{19}NO_5$	Metabolite	293.126323		294.1336
1-(methylamino)-1-phenylpentan-2-one	isopentedrone	$C_{12}H_{17}NO$	Parent	191.131	2.14	192.13829
1-phenyl-2-(1-pyrrolidinyl)-1-butanone	MPBP	$C_{15}H_{21}NO$	Parent	231.162314		231.16177

2-(methylamino)-1-phenyl-1-pentanone	carboxy-desamino-oxo-MPBP (ME)	$C_{12}H_{12}O_4$	Metabolite	220.0735588		221.08084
1-(1,3-benzodioxol-5-yl)-2-(methylamino)-1-pentanone	oxo-MPBP	$C_{15}H_{19}NO_2$	Metabolite	245.141578		246.14886
	carboxy-MPBP (ME)	$C_{16}H_{21}NO_3$	Metabolite	275.152143		276.15942
	carboxy-oxo-MPBP (ME)	$C_{16}H_{19}NO_4$	Metabolite	289.131408		290.13868
	carboxy-oxo-dihydro-MPBP (ME)	$C_{16}H_{20}NO_4$	Metabolite	290.139233		291.14651
	carboxy-dihydro-MPBP (2TMS)	$C_{21}H_{37}NO_3Si_2$	Metabolite	407.231197		408.23847
	HO-MPBP (TMS)	$C_{18}H_{29}NO_2Si$	Metabolite	319.196756		320.20403
	carboxy-MPBP (TMS)	$C_{18}H_{27}NO_3Si$	Metabolite	333.17602		334.1833
	carboxy-oxo-MPBP (TMS)	$C_{18}H_{25}NO_4Si$	Metabolite	347.155284		348.16256
	carboxy-oxo-dihydro-MPBP (2TMS)	$C_{18}H_{35}NO_4Si_2$	Metabolite	385.210461		386.21774
4'-methyl-α-pyrrolidinohexanophenone	MPHP	$C_{13}H_{25}NO$	Parent	211.193614		212.20089
	HO-tolyl-MPHP (AC)	$C_{19}H_{27}NO_3$	Metabolite	317.199094		318.20637
	carboxy-MPHP (ET)	$C_{19}H_{27}NO_3$	Metabolite	317.199093		318.20637
	oxo-carboxy-MPHP (ET)	$C_{19}H_{25}NO_4$	Metabolite	331.178358		332.18563
	oxo-MPHP	$C_{17}H_{23}NO_2$	Metabolite	273.172879		274.18016
	oxo-HO-tolyl-MPHP (AC)	$C_{19}H_{25}NO_4$	Metabolite	331.178358		332.18563
	oxo-carboxy-dihydro-MPHP (ET)	$C_{19}H_{26}NO_4$	Metabolite	332.186183		333.19346
	carboxy-MPHP (TMS)	$C_{20}H_{31}NO_3Si$	Metabolite	361.20732		362.2146
	dihydro-MPHP (TMS)	$C_{17}H_{25}NOSi$	Metabolite	287.170541		288.17782
4'-methyl-α-pyrrolidinopropiophenone	MPPP (stimulant)	$C_{14}H_{19}NO$	Parent	217.146664		218.15394

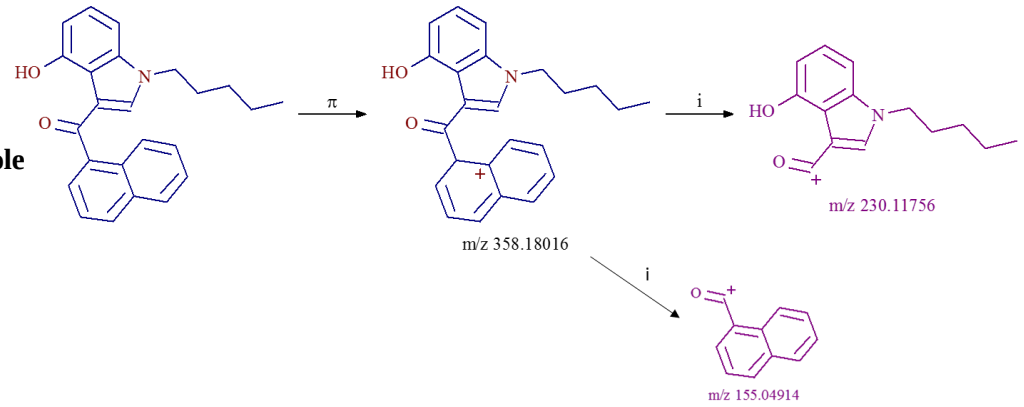
	4'-carboxy-PPP	$C_{16}H_{21}NO_3$	Metabolite	275.152143		276.15942
	2-oxo-4'-carboxypropiophenone	$C_{12}H_{12}O_4$	Metabolite	220.073558		221.08084
	4'-carboxybenzoic acid	$C_{12}H_{14}O_4$	Metabolite	222.089209		223.09649
	2''-oxo-MPPP	$C_{14}H_{17}NO_2$	Metabolite	231.125929		232.13321
	2''-oxo-4'-carboxy-PPP	$C_{16}H_{19}NO_4$	Metabolite	289.131408		290.13868

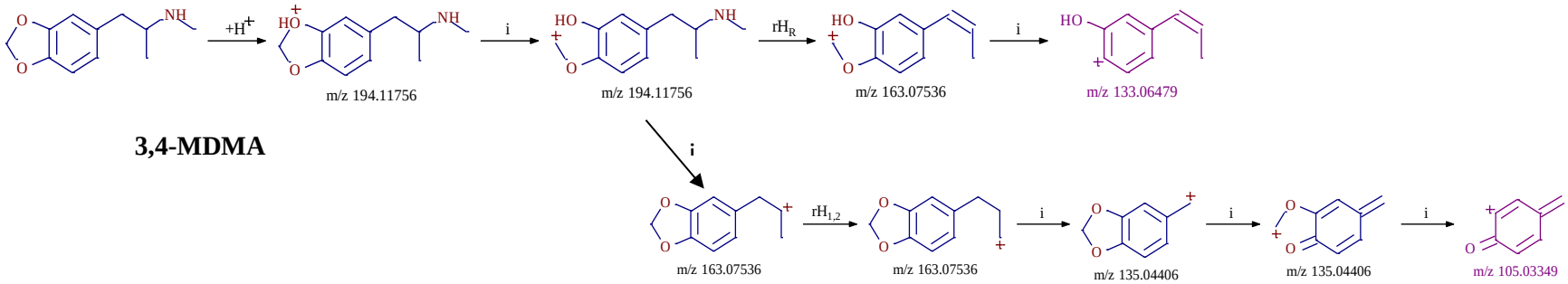
APPENDIX 2. IN SILICO PREDICTION OF FRAGMENTATON PATTERNS OF INDIVIDUAL COMPONENTS OF UNKNOWN MIXTURE

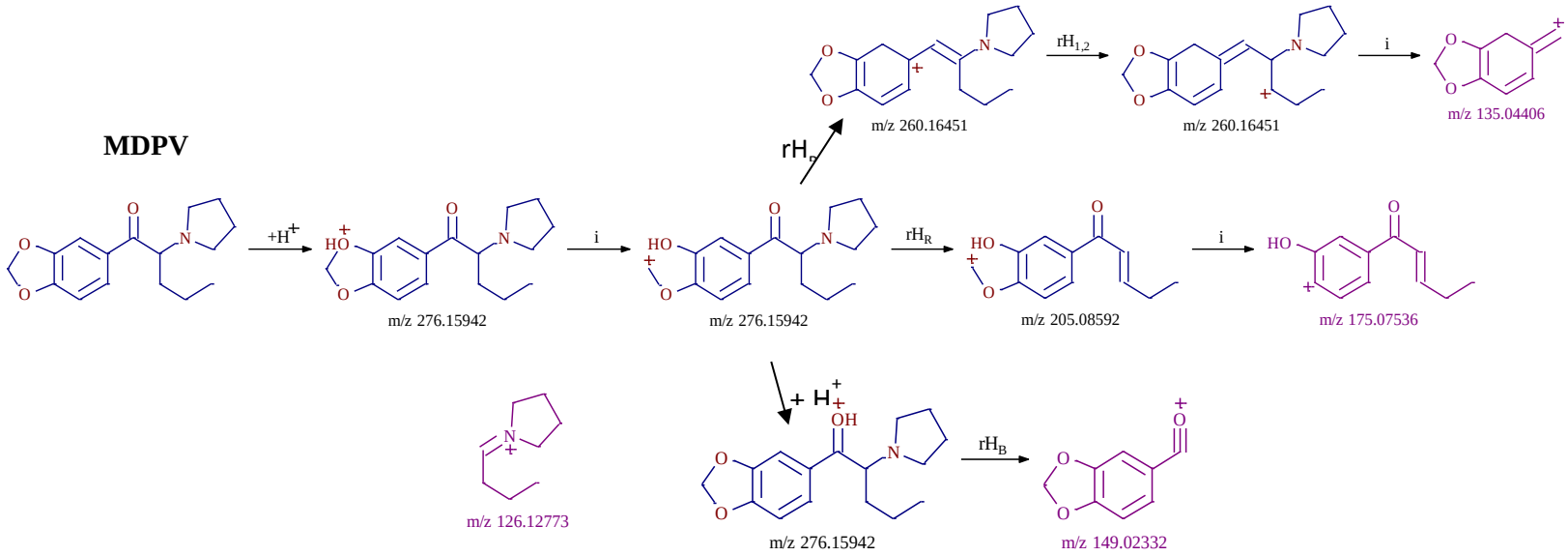
4-fluoroethcathinone



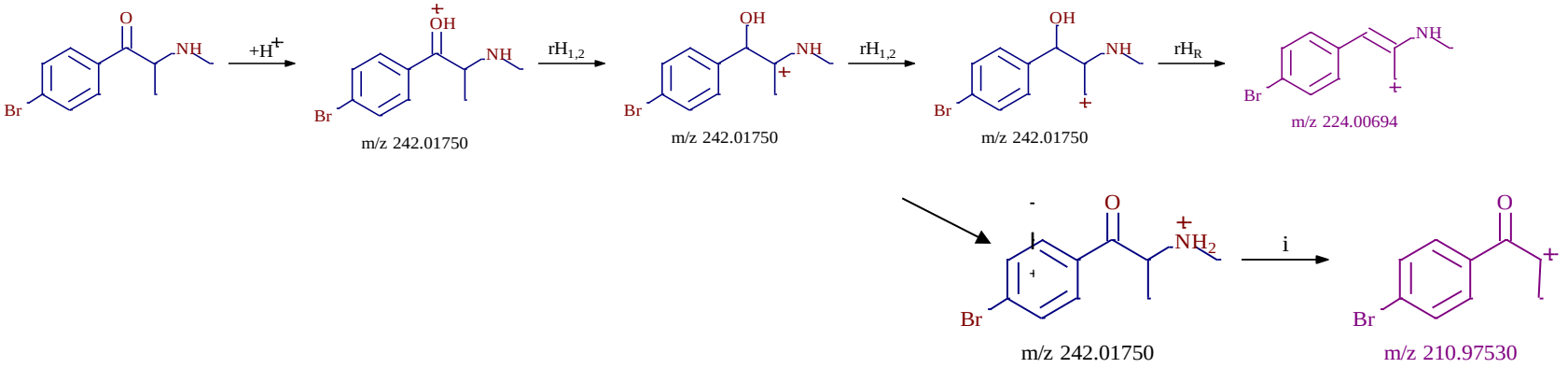
JWH 018 4-hydroxyindole metabolite



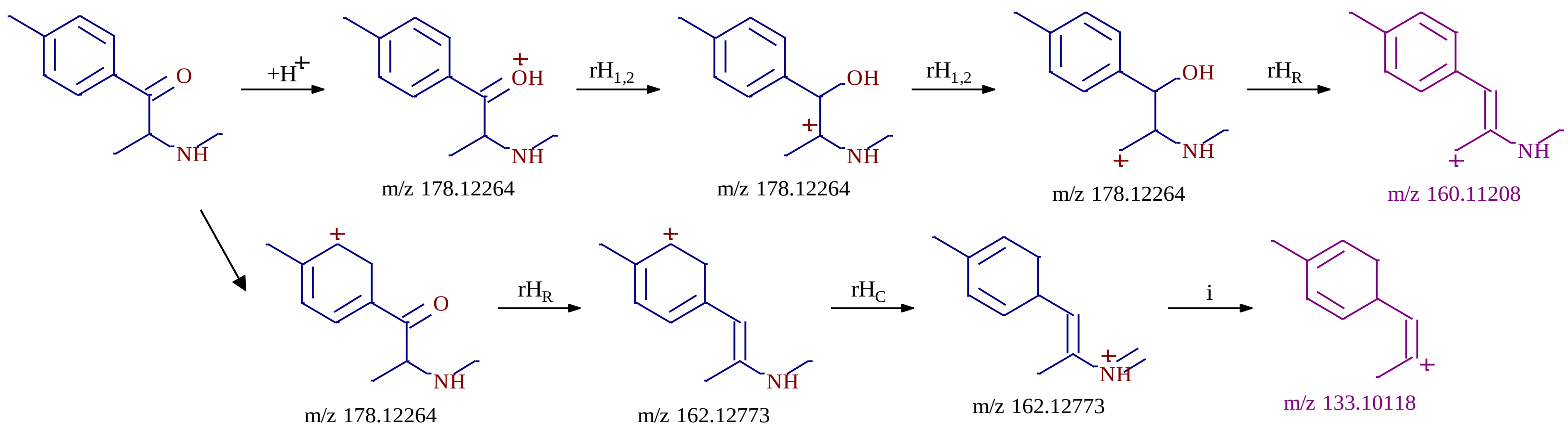

+H+
i
rHR
i
m/z 194.11756
m/z 194.11756
m/z 163.07536
m/z 133.06479
3,4-MDMA
i
rH1,2
i
i
i
m/z 163.07536
m/z 163.07536
m/z 135.04406
m/z 135.04406
m/z 105.03349


MDPV
+H+
m/z 276.15942
i
m/z 276.15942
rHn
m/z 260.16451
rH1,2
m/z 260.16451
i
m/z 135.04406
rHR
m/z 205.08592
i
m/z 175.07536
+ H+
m/z 126.12773
m/z 276.15942
rHB
m/z 149.02332

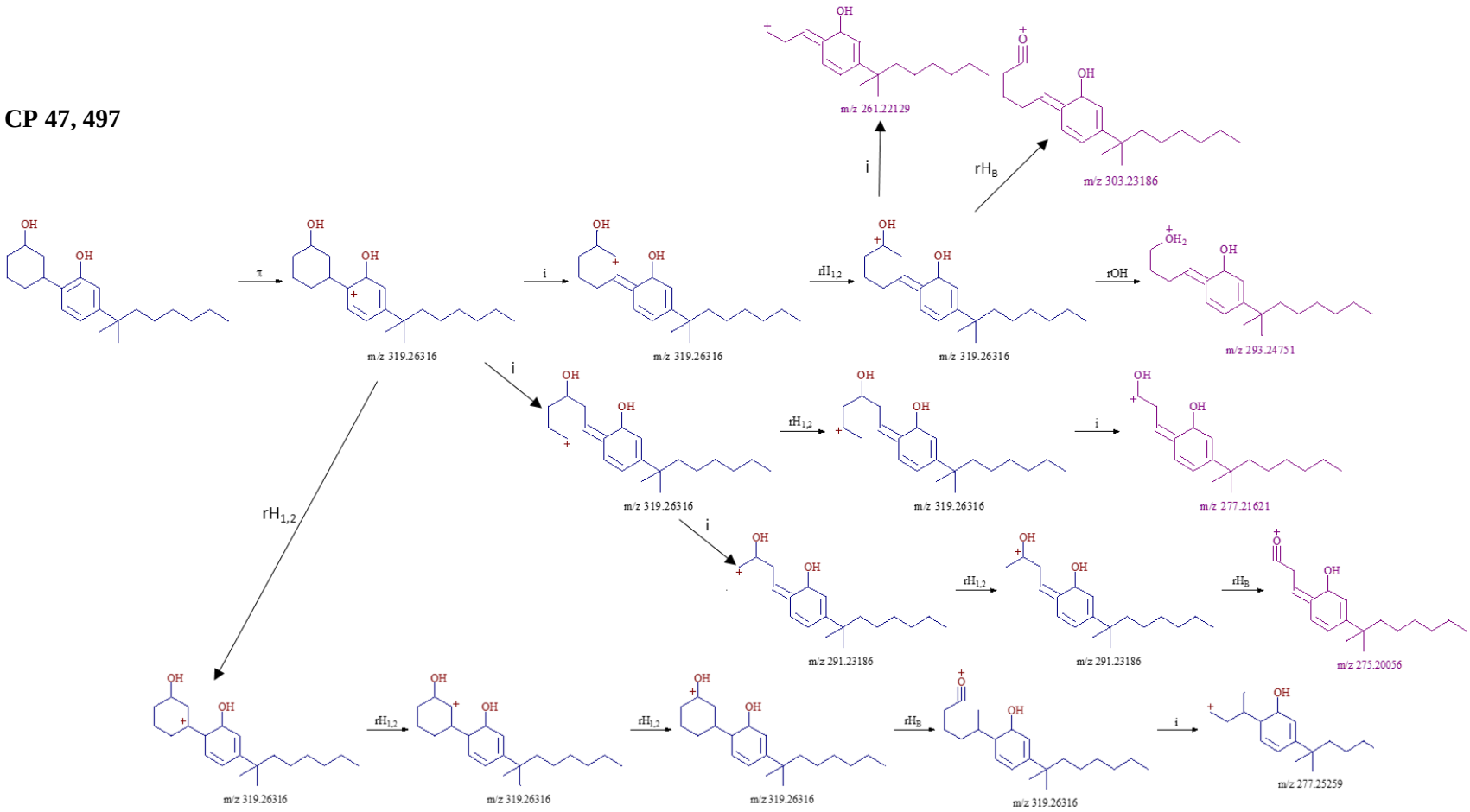
4-Bromomethcathinone



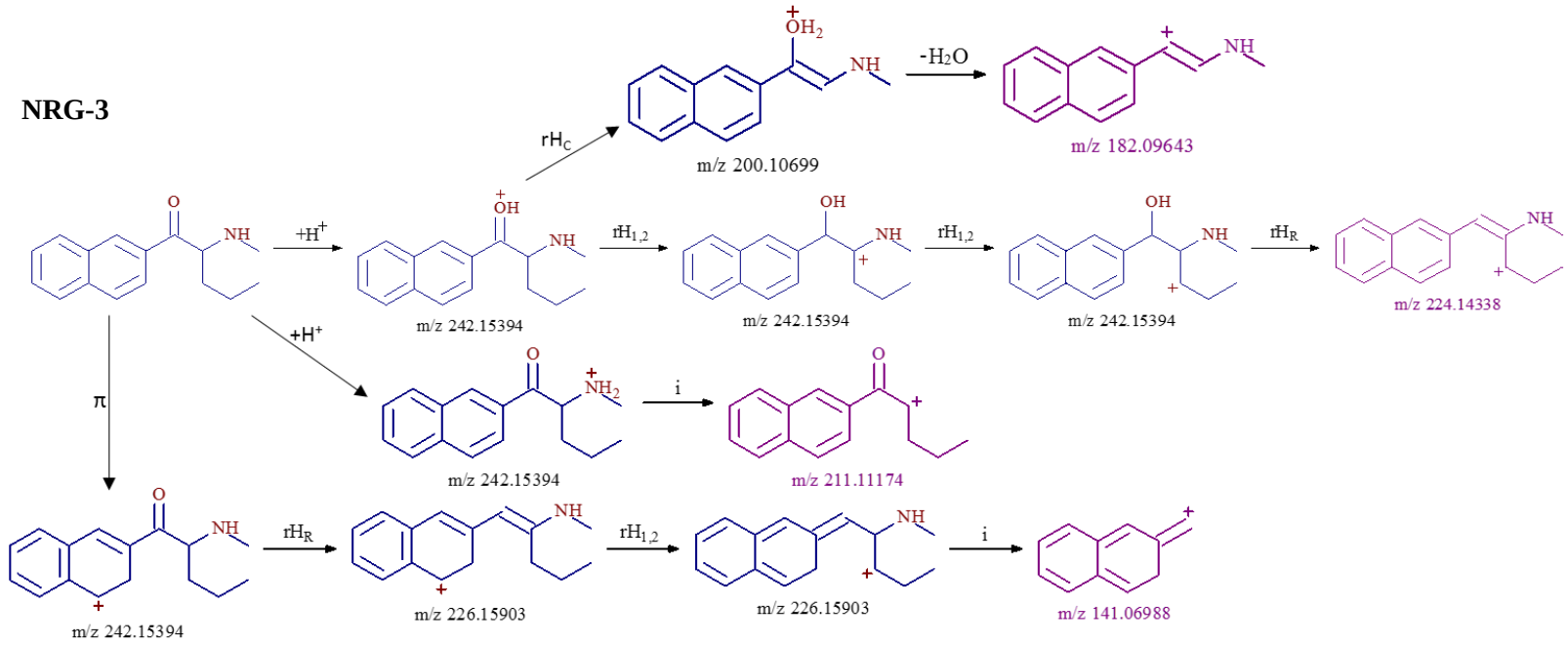
Mephedrone


O
+H+
+OH
m/z 178.12264
rH1,2
OH
NH
m/z 178.12264
rH1,2
OH
m/z 178.12264
rHR
m/z 160.11208
rHR
m/z 178.12264
m/z 162.12773
rHC
m/z 162.12773
i
m/z 133.10118

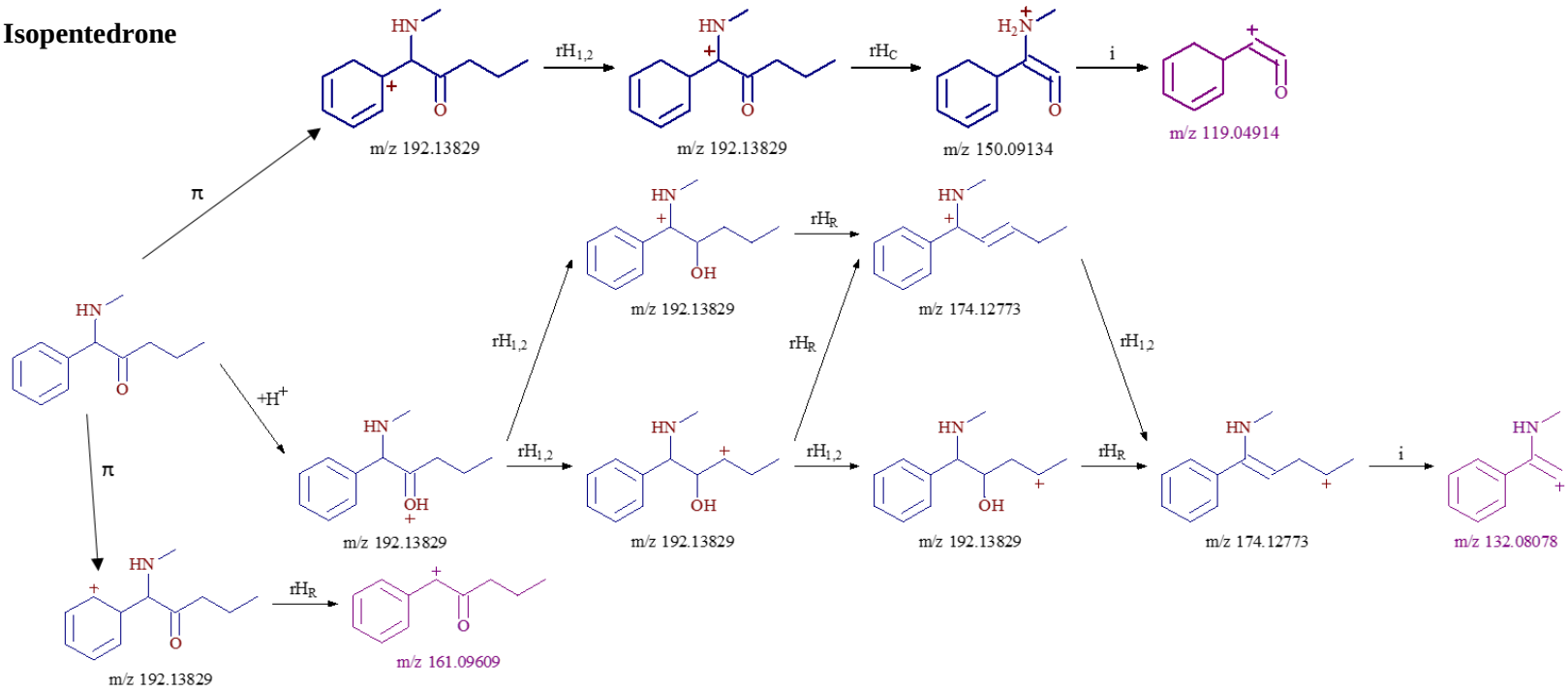
CP 47, 497


m/z 261.22129
m/z 303.23186
m/z 319.26316
m/z 293.24751
m/z 277.21621
m/z 291.23186
m/z 275.20056
m/z 277.25259

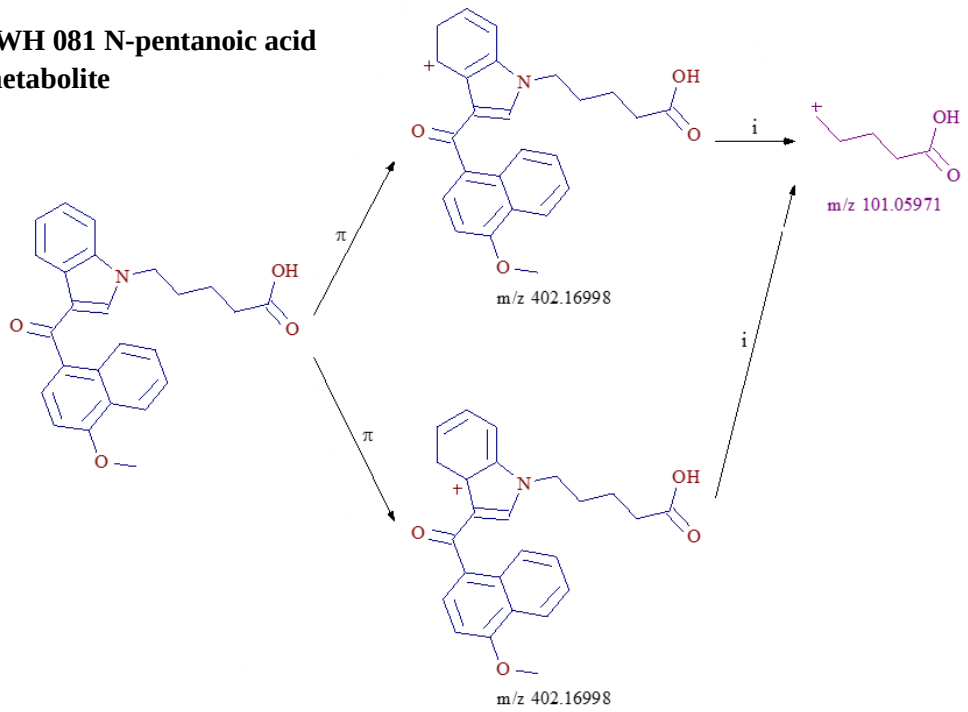
NRG-3

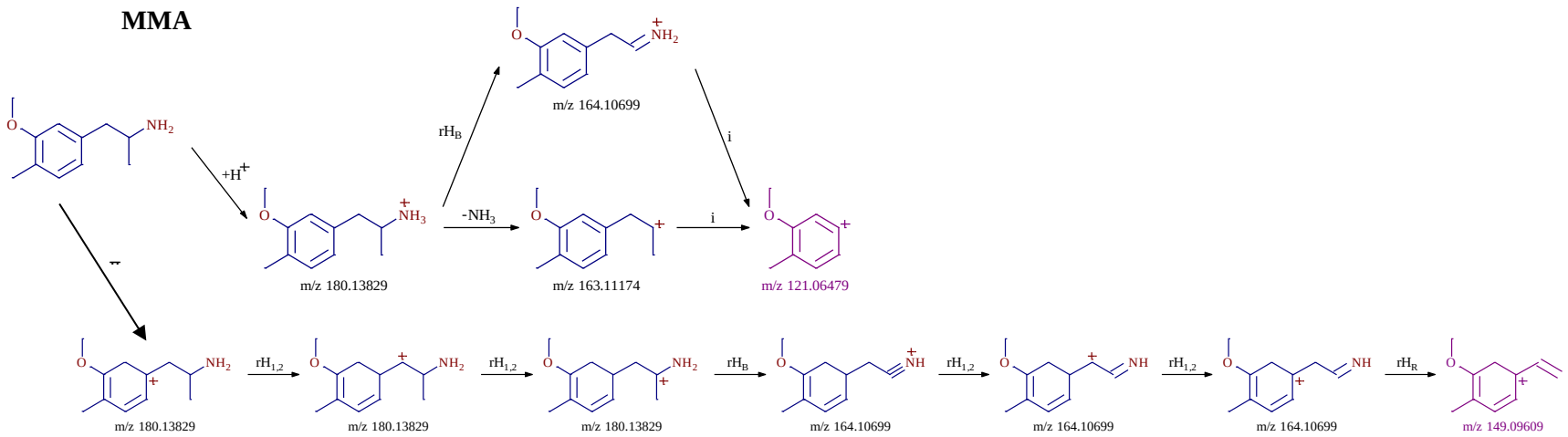

+H+
rHC
m/z 200.10699
-H2O
m/z 182.09643
rH1,2
m/z 242.15394
rH1,2
m/z 242.15394
rHR
m/z 224.14338
+H+
m/z 242.15394
i
m/z 211.11174
π
rHR
m/z 242.15394
rH1,2
m/z 226.15903
i
m/z 226.15903
m/z 141.06988

Isopentedrone

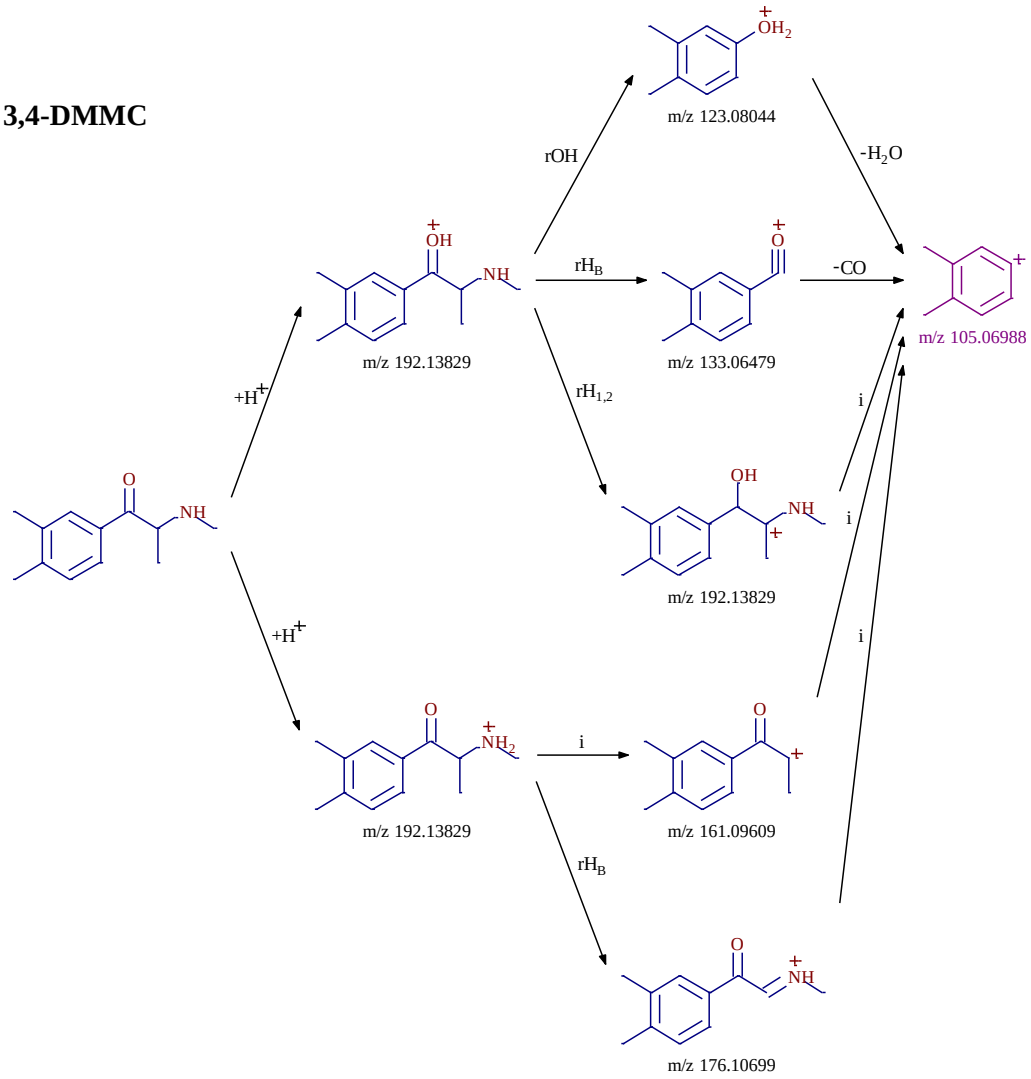


JWH 081 N-pentanoic acid metabolite

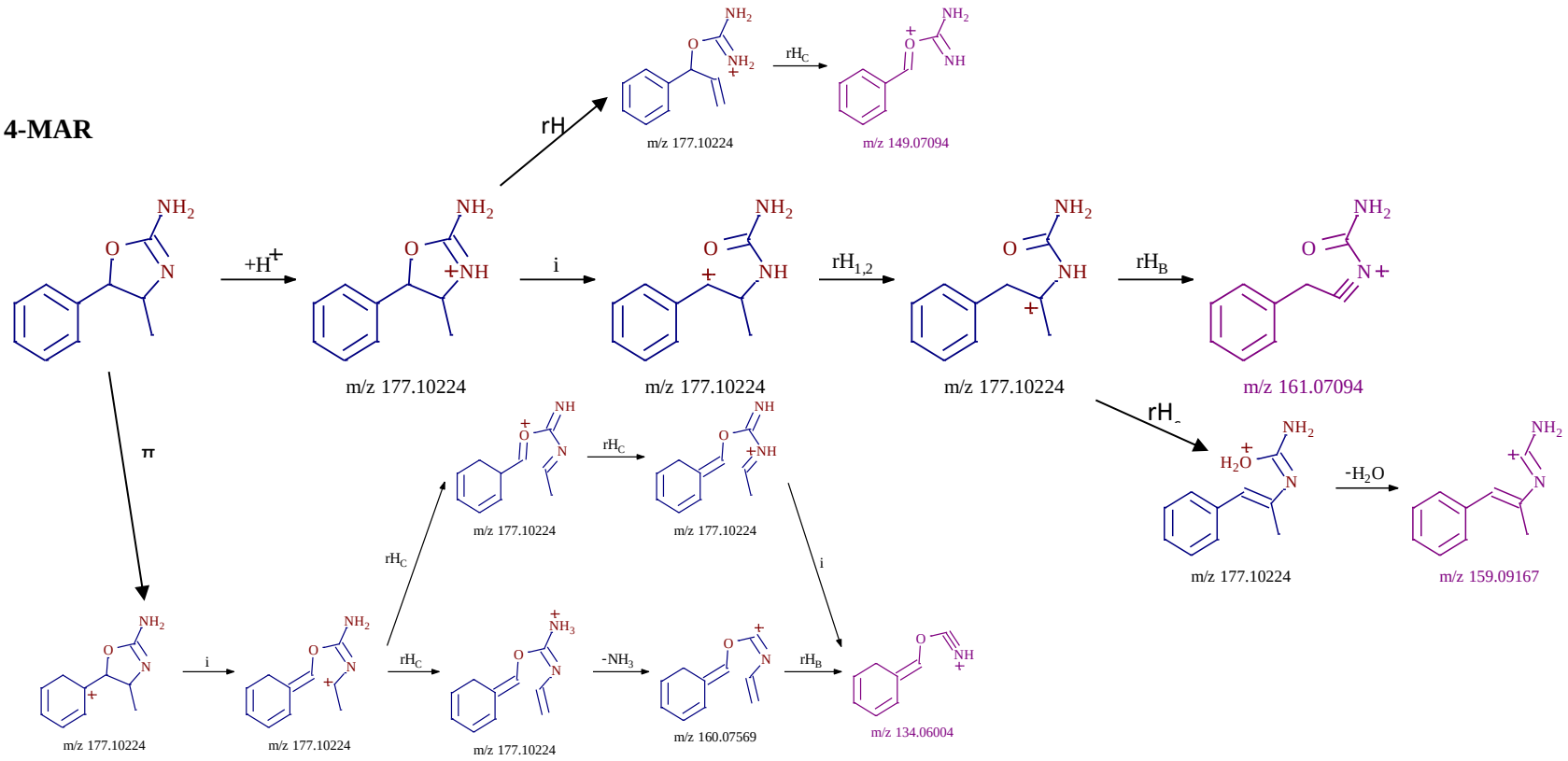



MMA
+H+
rHB
m/z 164.10699
i
-NH3
m/z 180.13829
m/z 163.11174
m/z 121.06479
rH1,2
rH1,2
rHB
rH1,2
rH1,2
rHR
m/z 180.13829
m/z 180.13829
m/z 180.13829
m/z 164.10699
m/z 164.10699
m/z 164.10699
m/z 149.09609

3,4-DMMC


m/z 123.08044
rOH
-H2O
m/z 192.13829
rHB
m/z 133.06479
-CO
m/z 105.06988
+H+
rH1,2
i
m/z 192.13829
i
+H+
m/z 192.13829
i
m/z 161.09609
rHB
m/z 176.10699

4-MAR


rH
rH_C
m/z 177.10224
m/z 149.07094
+H+
i
rH_1,2
rH_B
m/z 177.10224
m/z 177.10224
m/z 177.10224
m/z 161.07094
π
rH_C
rH_C
i
m/z 177.10224
m/z 177.10224
m/z 177.10224
m/z 177.10224
m/z 177.10224
-H2O
m/z 177.10224
m/z 159.09167
i
rH_C
-NH3
rH_B
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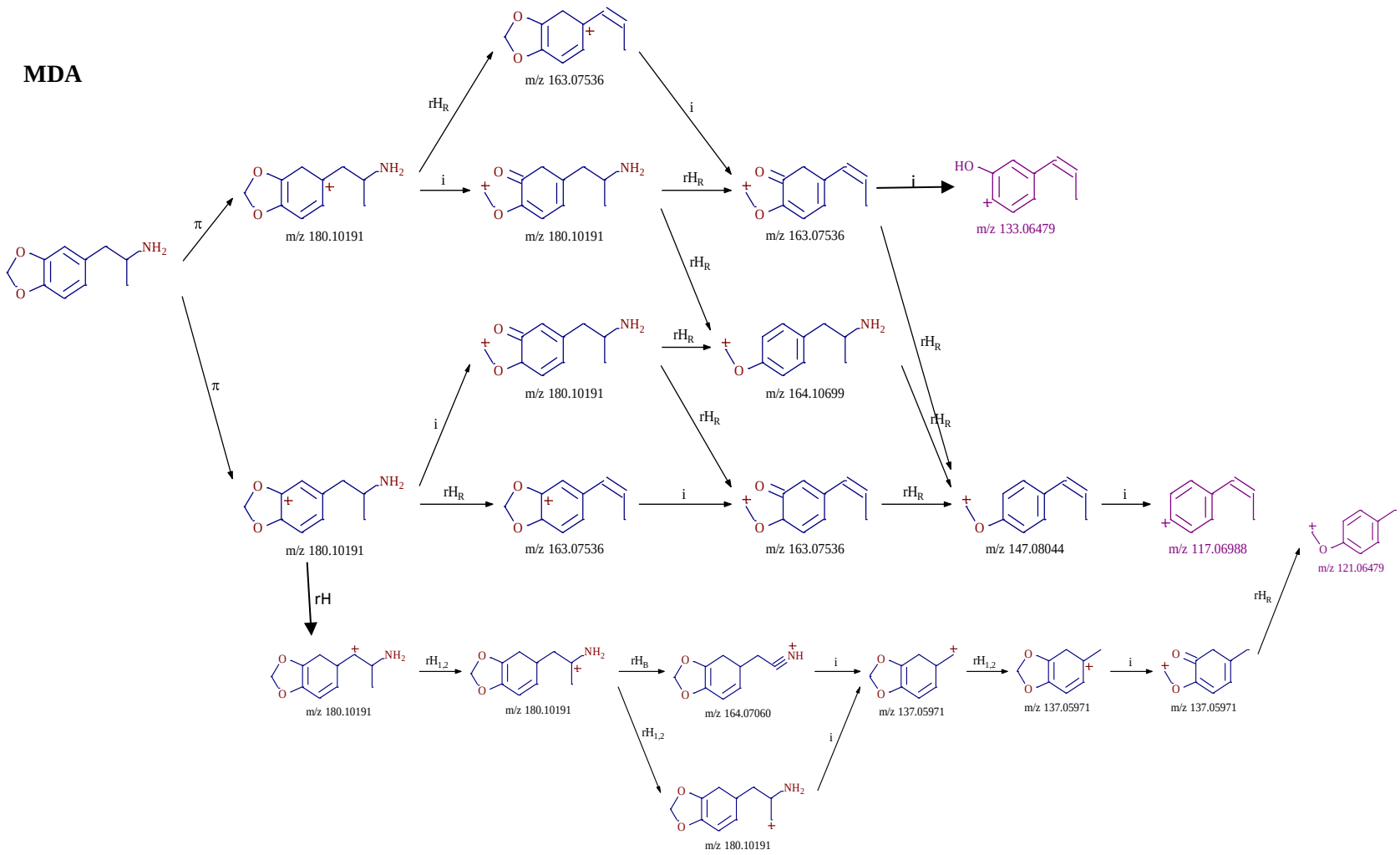
m/z 177.10224
m/z 160.07569
m/z 134.06004

MDA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m/z 180.10191
m/z 180.10191
m/z 163.07536
m/z 133.06479
m/z 180.10191
m/z 164.10699
m/z 180.10191
m/z 163.07536
m/z 163.07536
m/z 147.08044
m/z 117.06988
m/z 121.06479
m/z 180.10191
m/z 180.10191
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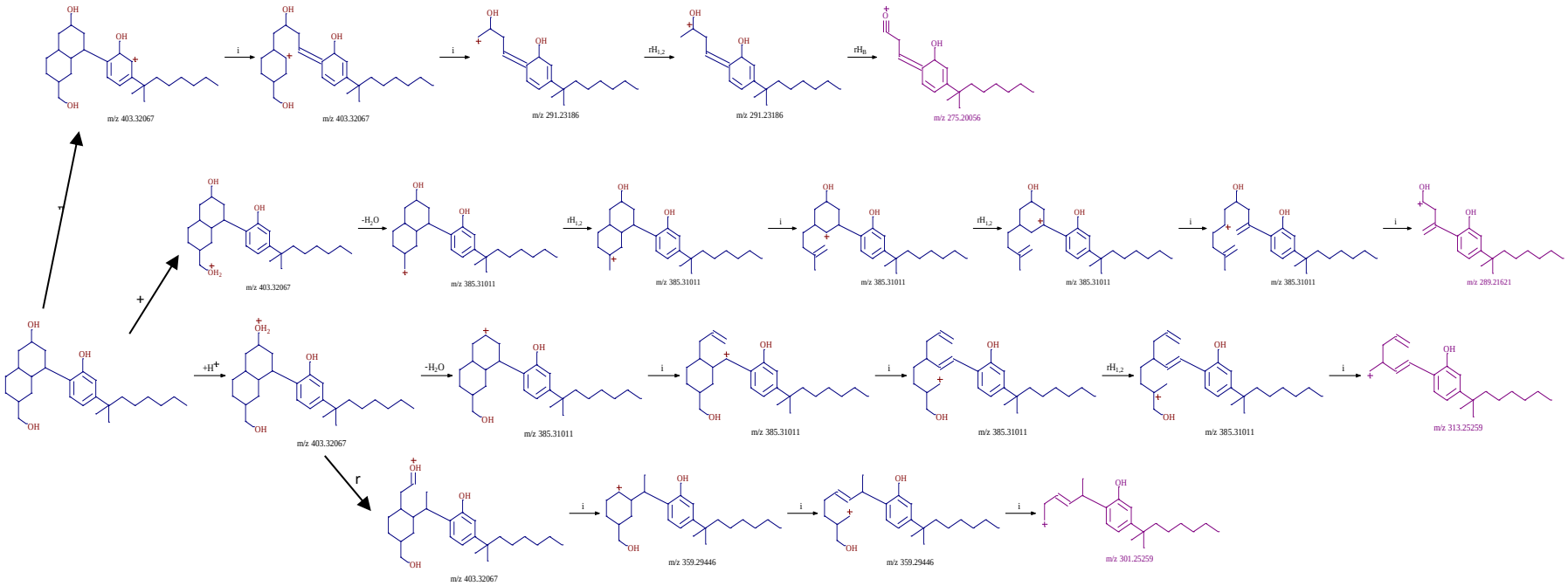
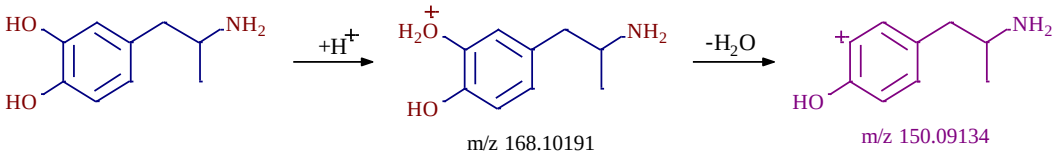
m/z 137.05971
m/z 137.05971
m/z 180.10191

CP 55, 244


m/z 403.32067
m/z 403.32067
m/z 291.23186
m/z 291.23186
m/z 275.20056
m/z 403.32067
m/z 385.31011
m/z 385.31011
m/z 385.31011
m/z 385.31011
m/z 385.31011
m/z 289.21621
m/z 403.32067
m/z 385.31011
m/z 385.31011
m/z 385.31011
m/z 385.31011
m/z 313.25259
m/z 403.32067
m/z 359.29446
m/z 359.29446
m/z 301.25259

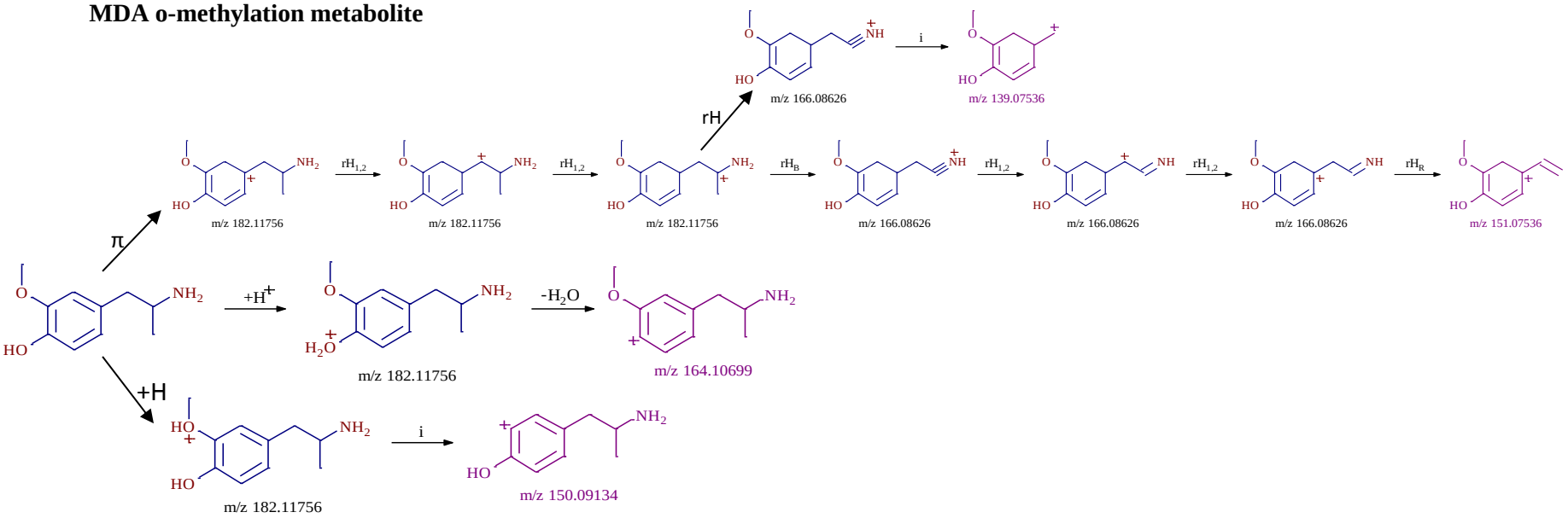
MDA demethylation metabolite



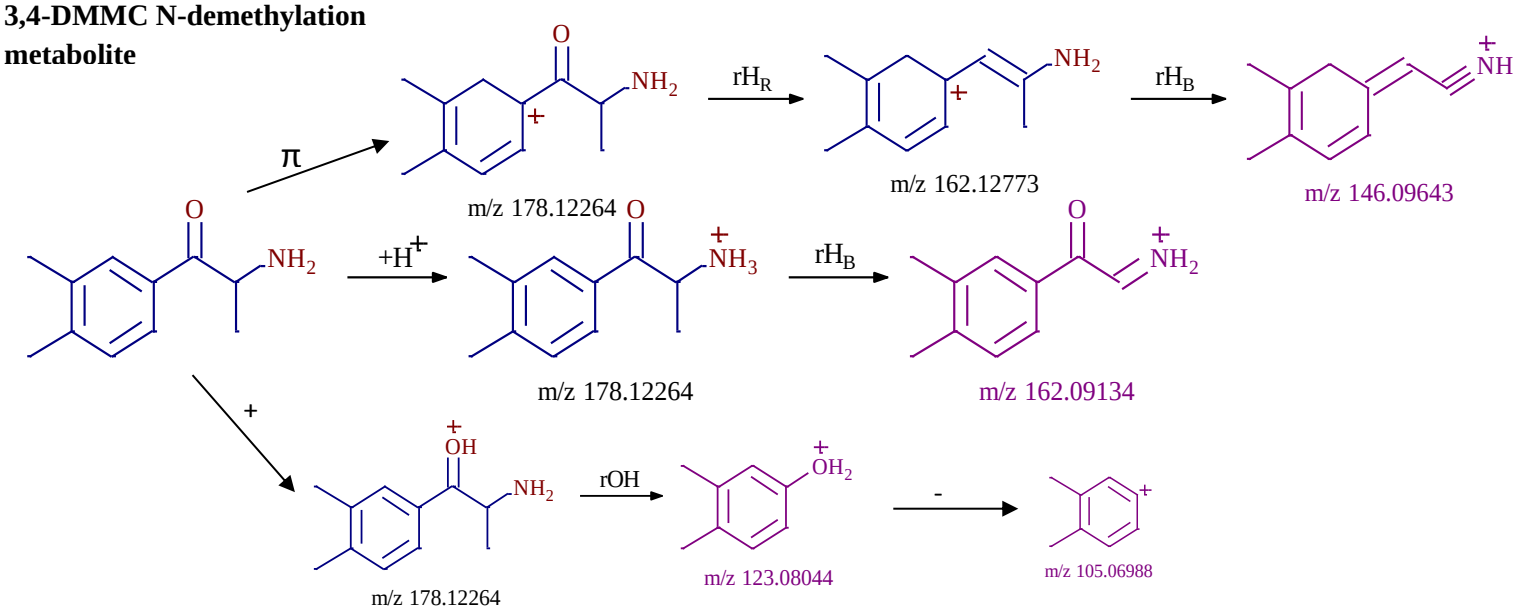
m/z 168.10191

m/z 150.09134

MDA o-methylation metabolite



3,4-DMMC N-demethylation metabolite



3,4-DMMC reduction + hydroxylation + oxidation