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PHARMACEUTICAL DRUG DISPOSAL SYSTEM - RX DESTROYER™ ALL-PURPOSE

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Revision Details

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Executive Summary

C2R Global Manufacturing Inc. contracted HRL Technology Group Pty Ltd to evaluate the efficacy of a pharmaceutical drug disposal system, called the 'Rx Destroyer All-Purpose.'

This report examined a combination of Activated Carbon and a proprietary liquid agent, "Rx Destroyer™," to safely dissolve, deactivate, and adsorb pharmaceutical drugs.

The Rx Destroyer™ All-Purpose is an effective device to deactivate API's. Most API's were completely (at least > 98 %, typically > 99.7 %) adsorbed within the first 24 hours.

The adsorption curves all indicate typical first-order reaction kinetics following the standard first-order reaction half-life decay equation.

All the API's were adsorbed by the Rx-Destroyer™ All-Purpose, mostly within the first day; some API's required longer absorption periods. The Rx-Destroyer™ All-Purpose is an excellent tool for disposing of pharmaceuticals, ensuring that the active ingredients will not be retrievable by common means available to the general public, and nor will the ingredients easily land up in the environment.

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1 Introduction

C2R Global Manufacturing Inc. (hereafter referred to as C2R) contracted HRL Technology Group Pty Ltd (hereafter referred to as HRL) to evaluate the efficacy of a pharmaceutical drug disposal system, called the 'Rx Destroyer All-Purpose.'

The pharmaceutical drug disposal system is based on the principle that activated carbon adsorbs a large variety of chemicals on its surface; activated carbon usually has a huge surface area, often in excess of one thousand square metres per gram.

There are several specific applications of pharmaceutical drug disposal systems:

1. Reduce the environmental and biological impact of pharmaceutical drugs
2. Reduce the illicit use of pharmaceutical drugs
3. Reduce the availability of illicit pharmaceutical drugs
4. Reduce the inadvertent intake of pharmaceutical drugs by children, mentally handicapped persons, or other people with other frailties or disabilities
5. Safe disposal at various facilities, including
    a. pharmacies (drug stores),
    b. aged care facilities,
    c. care facilities for frail or handicapped persons,
    d. police stations,
    e. hospitals,
    f. clinics,
    g. and various other facilities where pharmaceutical drugs need disposal

This report examined a combination of Activated Carbon and a proprietary liquid agent, "Rx Destroyer™" to safely dissolve, deactivate, and adsorb pharmaceutical drugs.

Please note that in some literature the terms 'Activated Charcoal,' 'Activated Carbon,' and 'Active Carbon' are used interchangeably.

2 Overview

This study focused on the following areas of interest:

1. Previous Literature reviews
2. The time to deactivate several model Active Pharmaceutical Ingredients (API's)

3 Literature Review

The literature overview focused on the traditional use of Activated Carbon, and how it supports the use of Activated Carbon as an adsorbent of pharmaceutical drugs, as well as other, similar compounds.

3.1 Book: Activated Carbon by Harry Marsh & Francisco Rodríguez Reinoso

ISBN: 9780080455969, 0080455964
Page count: 554
Published: 12 July 2006
Format: E-book
Publisher: Elsevier Science
Language: English
Author: Harry Marsh, Francisco Rodríguez Reinoso
Editor: Francisco Rodríguez Reinoso

This book refers to Activated Carbon as being 'as old as history itself and would be known to Hippocrates, the father of medicine. The earliest recorded applications include their use as a medicine to relieve digestion problems which continue today in the removal of overdoses of drugs from stomachs.'

This book also indicates that the 'most dramatic application of charcoal was in World War I with its use in gas masks for the protection of soldiers against chlorine, phosgene, and mustard gas in trench warfare… It was reported at that time that these respirators were more effective against chlorine (Cl_2) and phosgene ($COCl_2$) than with mustard gas (1,1-thiobis(2-chloroethane)) … because of its size and shape, would be adsorbed more slowly than the smaller molecules of chlorine and phosgene.'

The authors describe some tests that are generally used to determine the suitability of Activated Carbon for its intended use. Test methods have been developed and approved by various organisations and the methods are freely available. These organisations include:

- American Society for Testing Materials (ASTM)
- The American Water Works Association (AWWA)
- The International Organization for Standardization (ISO)
- The Deutches Institut für Normung (DIN)

Some of the tests include:

- Physical Characterisation
  - Bulk Density
  - Real Density
  - Apparent Density
  - Particle Size Distribution

    - Mechanical Strength
- Chemical Characterisation
    - Moisture Content
    - Ash Content
    - Ignition Temperature (kindling point)
    - Self-Ignition Test
    - pH Value
    - Water-Soluble Content
- Adsorption Characterisation
    - Carbon Tetrachloride Activity
    - Benzene Adsorption
    - Iodine Adsorption
    - Methylene Blue Adsorption
    - Phenol Adsorption
    - Molasses Decolourisation
    - Butane Adsorption
    - Phenazone Adsorption
    - Specific Surface Area (BET Test, i.e., Brunauer–Emmett–Teller theory)

3.2 Book: Activated Carbon Adsorption by Roop Chand Bansal & Meenakshi Goyal

ISBN: 9781420028812, 1420028812
Page count: 520
Published: 24 May 2005
Format: E-book
Publisher: Taylor & Francis
Language: English
Author: Roop Chand Bansal, Meenakshi Goyal

The authors of this book list some of the following areas as typical liquid-phase applications:

- Food processing
- Preparation of Alcoholic Beverages
- Decolourising of Oils and Fats
- Sugar Industry
- Pharmaceutical Industry
- Recovery of Gold
- Purification of Electrolytic Baths
- Purification of Liquid Fuels

Some more specific applications are listed in Chapter 7 of the book, under the heading of ‘Activated Carbon Adsorption and Environment: Adsorptive Removal of Organics from Water’

- Activated Carbon Adsorption of Halogenated Organic Compounds
- Activated Carbon Adsorption of Natural Organic Matter (NOM)
- Activated Carbon Adsorption of Phenolic Compounds
- Adsorption of Nitro and Amino Compounds
- Adsorption of Pesticides
- Adsorption of Dyes
- Activated Carbon Adsorption of Drugs and Toxins
- Adsorption of Miscellaneous Organic Compounds

Once again, the authors mention that 'The activated carbon adsorption of synthetic drugs have been studied with a view to removing them from the human body when taken in excess…'

3.3 Book: Activated Carbon Surfaces in Environmental Remediation by Teresa J. Bandosz

ISBN: 9780080455952, 0080455956
Page count: 588
Published: 27 February 2006
Format: E-book
Publisher: Elsevier Science
Language: English
Author: Teresa J. Bandosz
Editor: Teresa J. Bandosz

The author discusses the use of Activated Carbons as Medical Adsorbents in more detail than the previous authors and mentions that 'Activated Carbons have been used in medicine since ancient times.' The author refers to another book (described in paragraph 3.4 in this report), 'Activated Charcoal in Medical Applications' by David O. Cooney which details activated charcoal's great effectiveness in treating drug overdoses and poisonings in both humans and animals, as well as activated charcoal's ability to reduce the systemic absorption of a vast array of drugs, chemicals, and biochemical substances-including analgesics, antipyretics, sedatives, alkaloids, snake venoms, and bacterial and fungal toxins.

The authors list a table (page 536, Table 1) titled 'Toxic Organic Substances and Drugs Adsorbed by Activated Carbon' and list some of the following types of poisons which can be adsorbed (specifically in humans, but also in animals): strychnine, aspirin, acetaminophen, propoxyphene, phenobarbital, barbital, zolpidem, carbamazepine, mefenamic acid, piroxicam, phenylbutazone, indomethacin, imipramine, desipramine, nortriptyline, doxepin, furosemide, and many more.

3.4 Book: Activated Charcoal in Medical Applications by David O. Cooney

ISBN: 9780367401917, 0367401916
Page count: 608
Published: 23 September 2019
Format: Paperback
Publisher's Press LLC
Language: English
Author: David O. Cooney

The publisher of this book describes it as highlighting activated charcoal's great effectiveness in treating drug overdoses and poisonings in both humans and animals, and this comprehensive, single-source reference brings together vital information from every significant study on the use of activated charcoal for medical purposes – describing all available charcoal products and their characteristics.

The book details activated charcoal's ability to reduce the systemic absorption of a vast array of drugs, chemicals, and biochemical substances – including analgesics, antipyretics, sedatives, alkaloids, snake venoms, and bacterial and fungal toxins.

3.5 Book: Activated Charcoal Antidote, Remedy and Health Aid by David O. Cooney

ISBN: 9781479603367, 1479603368
Page count: 102
Published: 6 October 2016
Publisher: TEACH Services, Inc.
Language: English
Author: David O. Cooney

In this book, the author gives an overview of the medical applications of Activated Carbon. The author lists proven applications of Activated Carbon in Chapter 5 under the heading 'Effects of Activated Charcoal on Various Types of Drugs and Poisons.' The list includes the following and some other chemicals:

- Common Household Chemicals
- Alkaloids
- Aspirin and Other Salicylates
- Acetaminophen
- Hypnotics and Sedatives
- Tricyclic Antidepressants
- Cardiac Glycosides

The author describes more details regarding research done on hypnotics and sedatives, specifically works done by Anderson in 1948, Picchioni's research group in 1966, and later works done by Picchioni, Chin, and Laird in 1974. Other works are listed. The research works indicate, in general, that 'It is clear than the charcoal, …, was effective in lowering blood drug levels.'

3.6 Scientific Publication: Management of Acute Poisoning with Activated Charcoal by Donald G. Corby & Walter J. Decker

Publication: Pediatrics
Authors: Donald G. Corby & Walter J. Decker
Date: September 1974
Volume: 54 (3)
Pages: 324-329

In this publication, the authors found that 100 % adsorption of 10 capsules and 85 % adsorption of 20 capsules (each capsule = 32 mg propoxyphene) after only 20 minutes in a 150 mL solution of simulated gastric juice to which 5 grammes of activated charcoal had been added.

3.7 Scientific Publication: Activated Carbon-Based System for the Disposal of Psychoactive Medications by Song et al

Publication: Pharmaceutics
Authors: Song Y, Manian M, Fowler W, Korey A, Kumar Banga A
Date Published: 07 November 2016
Volume: 2016; 8(4):31
doi: 10.3390/pharmaceutics8040031

(This Scientific Paper is Published by MDPI AG, St. Alban-Anlage 66, CH-4052 Basel, Switzerland)

The authors mention that 'Activated carbon is obtained by thermal decomposition of carbon-based materials such as coal, coconut, or wood. The purpose of this activation procedure is to achieve a high internal surface area which is good for the adsorption of the drug from the formulation to the activated carbon. This large surface area is due to the presence of small, low volume pores on the charcoal where the pore size distribution contributes to the efficiency of the activated carbon in the drug adsorption. Activated carbon has numerous micropores in comparison to charcoal which provides maximum bonding surface area for drug binding. This granular activated carbon is already being used in water treatment processes for removal of micropollutants including pharmaceuticals and endocrine disruptors.'

The authors concluded their study by saying that 'The effectiveness of the activated carbon-based drug disposal system was examined using three model psychoactive medications. The deactivation system successfully adsorbed and deactivated about 70 % of the psychoactive medications by 8 h and more than 99 % within 28 days and did not release adsorbed drug substances when exposed to large volumes of water or 30 % ethanol. Thus, this unique system is simple, safe, and user-friendly for patients who can deactivate unused or expired psychoactive medications from the comfort of their homes.'

The authors proved that the drugs are irreversibly adsorbed onto the Activated Carbon and cannot be removed by means generally available to the general public.

3.8 Summary of Literature Review

It is evident from the literature study that a wide range of pharmaceutical drugs, and many other organic and inorganic chemicals, can be adsorbed onto Activated Carbon. Activated Carbon is commonly used in medical fields to adsorb various chemicals to reduce toxicity (e.g., after an overdose).

Activated Carbon has been proven to adsorb large amounts of pharmaceuticals from aqueous media (e.g., simulated gastric juice) with small amounts of Activated Carbon in a matter of minutes.

Pharmaceutical drugs that have been adsorbed onto Activated Carbon are not easily removed by solvents like water or ethanol.

The use of Activated Carbon seems to be a natural choice in the use of Pharmaceutical Drug Disposal systems.

4 Materials used in this Study

4.1 Activate Carbon

The Activated Carbon used in this study was supplied by Calgon Carbon, A Kuraray Company. The specific product was VGAC 1000 12X40. The Safety Data Sheet (SDS) is available.

The specification sheet is shown below in Figure 1:

Figure 1: VGAC 1000 12X40 Specification Sheet

CalgonCarbon

SALES SPECIFICATION SHEET

VGAC 1000 12X40

Granular Activated Carbon

Test	Specification Min	Specification Max	Calgon Carbon Test Method
IODINE NUMBER, mg/g	1000	-	TM-4,ASTM D4607
MOISTURE (AS PACKAGED), wt%	-	5	TM-1,ASTM D2867
12 US MESH [1.70 mm], wt%	-	5	TM-8,ASTM D2862
< 40 US MESH [0.425 mm] (PAN), wt%	-	5	TM-8,ASTM D2862

Typical Properties:

This product complies with the requirements for activated carbon as defined by the Food Chemicals Codex (FCC) (Latest Edition) published by the U.S. Pharmacopeia.

This product is produced under supervision of the Islamic Food and Nutrition Council of America (IFANCA).

This product is prepared under the supervision of the Kashruth Division of the Orthodox Union and is Kosher.

Only products bearing the NSF Mark are Certified to NSF/ANSI 61 - Drinking Water System Components - Health Effects standard. Certified Products will bear the NSF Mark on packing or documentation shipped with the product.

Calgon Carbon Corporation's activated carbon products are continuously being improved and changes may have taken place since this publication went to press. (11333-06/07/2017)

4.2 Rx Destroyer Proprietary Solution

The Rx Destroyer solution was supplied by C2R. The solution is described in the Safety Data Sheet (SDS) as a mixture consisting of non-regulated materials.

4.3 Active Pharmaceutical Ingredients

A range of highly scheduled API's, mainly opioids, was selected to cover the typical field of application of this device. The following API's were investigated:

- Morphine
- Dilaudid (Hydromorphone)
- Oxycodone
- Fentanyl
- Propofol

Opioids are a group of medicines that may be prescribed to treat pain. Opioids reduce feelings of pain by interrupting the way nerves signal pain between the brain and the body. Sometimes opioids are taken after being obtained illegally for non-prescribed use.

Opioids work by interacting with the opioid receptors in your brain. This can have several effects, including altering how you feel pain.

4.3.1 Morphine

Morphine is used to relieve severe pain, such as pain caused by a major trauma or surgery, labour pain in childbirth or cancer pain.

Morphine should only be used where other forms of pain relief have not been successful in managing pain or are not tolerated.

Morphine works directly on opioid receptors in the central nervous system and reduces feelings of pain by interrupting the way nerves signal pain between the brain and the body.

It is available in tablet, capsule, granule, oral liquid, and injection formulations.

4.3.2 Dilaudid (Hydromorphone)

Hydromorphone is used for the short-term relief of severe pain, whereas other pain medicines have been ineffective or cannot be used. It is more potent than morphine and should only be used under specialist medical supervision.

Hydromorphone should also be used only when other forms of pain relief have not been successful in managing pain.

Hydromorphone works directly on opioid receptors in the central nervous system and reduces feelings of pain by interrupting the way nerves signal pain between the brain and the body.

It is available as tablets, an oral liquid, or injections.

Hydromorphone should only be used in limited circumstances under specialist medical care.

4.3.3 Oxycodone

Oxycodone is used to relieve moderate to severe pain. It should only be used when other forms of non-opioid pain relief have not been successful in managing pain or are not tolerated.

Oxycodone is not usually recommended for the treatment of chronic pain.

Oxycodone works directly on opioid receptors in the central nervous system and reduces feelings of pain by interrupting the way nerves signal pain between the brain and the body.

It is available in tablet and injection formulations.

4.3.4 Fentanyl

Fentanyl is used to treat acute pain caused by major trauma or surgery, as well as chronic pain caused by cancer.

How long you need to take fentanyl will depend on why it has been prescribed. For example, fentanyl patches for cancer pain or in people receiving palliative care are approved for life-long use, while fentanyl used in acute pain or anaesthesia will be used only for a short time.

Fentanyl works directly on opioid receptors in the central nervous system and reduces feelings of pain by interrupting the way nerves signal pain between the brain and the body.

It is available in several formulations in different strengths, including patches, lozenges, tablets that disintegrate in your mouth and sublingual tablets. Fentanyl is also given by injection for severe acute pain or as part of anaesthesia before surgery.

4.3.5 Propofol

- Induction of General Anaesthesia in Children and Adults
    - Propofol is a short-acting intravenous anaesthetic agent suitable for induction of general anaesthesia in adults and children aged one month and older
- Maintenance of General Anaesthesia in Children and Adults
    - Propofol is a short-acting intravenous anaesthetic agent suitable for maintenance of general anaesthesia in adults and children aged 3 years and older. Propofol may also be used for maintenance of general anaesthesia in children aged from one month to 3 years for procedures not exceeding 60 minutes unless alternative anaesthetic agents should be avoided.
- Propofol has no analgesic properties.
- Use for Sedation During Intensive Care in Adults
    - Propofol may also be used in patients >16 years for sedation of ventilated patients receiving intensive care.
- Conscious Sedation for Surgical and diagnostic Procedures
    - Propofol may also be used for monitored conscious sedation for surgical and diagnostic procedures in adults and children aged one month and older

This medication is administered intravenously. It appears as a milky white, oil-in-water emulsion, in a colourless glass ampule.

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5 Experimental Setup

5.1 Components and Specified Ratios

C2R prescribed the components and their specific proportionate ratios. C2R prescribed the following for the Rx Destroyer™ All-Purpose; the exact proportionate ratios were used to scale down to an experimental level.

The Activated Carbon, Rx Destroyer™ Liquid, and API's were weighed into 50 mL Cell Culture Flasks. The reasoning behind using cell culture flasks as a reaction vessel was to easily observe the actions in the flask, and to allow for enough area to operate as the device may usually do.

The actual amounts of Activated Carbon, Rx Destroyer™ Liquid, and the API's are listed in Table 1 below, while the amounts of API's are listed in Table 2.

Table 1: Proportions of Activated Carbo, Rx Destroyer™ Liquid, and API's

Ingredient	Given Amount	Calculated Portion	Experi-mental Level	Actual Mass	Actual Portion
Activated Carbon	46.0 g	12.15 %	4.792 g	4.7945 g	12.13 %
Rx Destroyer ™ Liquid	236.5 g	62.48 %	24.637 g	24.6380 g	62.35 %
API	96.0 g	25.36 %	10.001 g	10.0846 g	25.52 %
TOTAL	378.5 g		39.430 g	39.5171 g	

Table 2: Amounts of API's added to the Reaction Vessel

Ingredient	Amount of Medication Loaded	Active Ingredient Concentration	Amount API
Morphine	2.1947 g	10 mg/g	21.947 mg
Dilaudid (Hydromorphone)	2.2750 g	10 mg/g	22.750 mg
Oxycodone	1.0276 g	50 mg/g	51.38 mg
Fentanyl	2.0766 g	0.1 mg/g	0.20766 mg
Propofol	2.5107 g	10 mg/g	25.107 mg

The various materials were weighed out separately and added together promptly. We noted the starting time.

5.2 Sampling at Specified Intervals

The API's were left in contact with the Activated Carbon and Rx Destroyer™ Liquid for predetermined periods and very small subsamples (approximately 0.1000 g) were extracted at the appropriate time intervals.

The time intervals were designed to determine the reaction kinetics – that is the rate at which the API's adsorb onto the Activated Carbon. The time intervals were 1 hour, 2 hours, 4, 8, 24, 48, 96, and 168 hours. The amount of material adsorbed onto could be determined by analysing the concentration of the active ingredients in the retrieved subsample. The subsamples were placed into an HPLC liquid vial and diluted with water to approximately 1.0000 g; the vials were tightly closed and stored until analysis.

The actual time, the amount of subsample, and the dilution factor of the subsample are listed below in Table 3.

Table 3: Sampling Times, Subsample Weight, Dilution Factor

Sampling Time (hh:mm)	Subsample Weight	Final Diluted Weight	Dilution Factor
01:05	0.0990 g	0.9821 g	9.92
02:27	0.1001 g	0.9964 g	9.95
04:03	0.0964 g	1.0259 g	10.64
07:59	0.1030 g	1.0346 g	10.04
24:10	0.0978 g	1.0404 g	10.64
48:40	0.1035 g	1.0364 g	10.01
121:02	0.0979 g	1.0206 g	10.42
168:16	0.1024 g	0.9957 g	9.72

5.3 Agitation

C2R requested that the samples should be agitated regularly; the samples were agitated right before the sampling event, and then lightly agitated again immediately afterwards (to ensure the material is settled in an even layer).

6 Analytical Methods

6.1 Reference Material for Calibration

The laboratory personnel calibrated the instruments using various dilutions of the original Pharmaceuticals, as they were purchased from the supplier.

6.2 Instrumentation

Two types of instruments were used for the analyses of these samples, depending on the concentration levels, and the type of API.

6.2.1 HPLC

Morphine, Dilaudid, Propofol, and Oxycodone were determined using High-Performance Liquid Chromatography (HPLC) with Ultraviolet Spectrometric (UV) detection.

The column was a C18 column, 250 mm long, 4.6 mm diameter, and 5 µm bead size.

The mobile phase (eluent) was a mixture of water (H_2O), acetonitrile (ACN), phosphoric acid (H_3PO_4), and sodium dodecyl sulphate (SDS).

A gradient elution was used to achieve effective separation, sharp and symmetrical peaks, and complete evacuation of the column.

The composition of the eluents is listed in Table 4, the Gradient programme in Table 5, and the operating parameters in Table 6 below.

Table 4: Composition of the Eluents for HPLC

Ingredient	Eluent A	Eluant B
Water	900.0 mL	180.0 mL
Acetonitrile	90.0 mL	810.0 mL
Phosphoric Acid	0.900 mL	0.900 mL
Sodium Dodecyl Sulphate	1.300 g	1.300 g

Table 5: Gradient Programme for HPLC

Time	% Eluent A	% Eluent B
0	50.0 %	50.0 %
3	20.0 %	80.0 %
4	0.0 %	100.0 %
10	0.0 %	100.0 %
11	50.0 %	50.0 %
20	50.0 %	50.0 %

Table 6: Operating Parameters

Parameter	Value
Eluent Flow Rate	1.50 mL/min
Oven Temperature	45.0 °C
Injection Volume	10.0 µL
Detection Wavelength	220.0 nm

6.2.2 LC-MS/MS

Fentanyl was determined using Liquid Chromatography with Tandem Mass Spectrometry detection (LC-MS/MS) because of the complexity and very low concentration range.

The column was a C18 column, 250 mm long, 2.0 mm diameter, and 5 µm bead size.

The mobile phase (eluent) was a mixture of water (H_2O), acetonitrile (ACN), and formic acid (FA).

A gradient elution was used to effectively separation, sharp and symmetrical peaks, and complete evacuation of the column.

The composition of the eluents is listed in Table 7, the Gradient programme in Table 8, and the operating parameters in Table 9 below.

Table 7: Composition of the Eluents for HPLC

Ingredient	Eluent A	Eluant B
Water	250.0 mL	0.0 mL
Acetonitrile	0.0 mL	250.0 mL
Phosphoric Acid	0.25 mL	0.25 mL

Table 8: Gradient Programme for HPLC

Time	% Eluent A	% Eluent B
0	90.0 %	10.0 %
1	90.0 %	10.0 %
5	10.0 %	90.0 %
9	10.0 %	90.0 %
10	90.0 %	10.0 %
15	90.0 %	10.0 %

Table 9: Operating Parameters

Parameter	Value
Eluent Flow Rate	0.30 mL/min
Oven Temperature	25.0 °C
Injection Volume	2.0 µL
Selection / Detection Mass	337 → 188 m/z

6.3 Sample Preparation

All samples, including the reference solutions, were thoroughly shaken and subsequently centrifuged (3,600 revs.min^{-1} for 10 minutes at 24 °C). the supernatant from each solution was filtered (through a 0.45 µm PTFE filter). The reference standard solutions were suitably diluted with 50 % Acetonitrile in Water to create sets of calibration standards. The samples were analysed as received (see Table 3 and Paragraph 5.2).

6.4 Calibration and Analysis

Ten microlitres of each calibration standard and sample were injected for HPLC analysis, while 2.0 µL of each calibration standard and sample were injected for LC-MS/MS analysis. The chromatograms were interrogated and the resultant peak area for each calibration standard and sample was noted for calibration or quantification of the relevant API's.

6.5 Chromatograms

Example chromatograms are shown for the various methods; one blank, one high calibration standard, and one sample are included for comparison. Full details are included in Appendices A and B.

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Single Injection Report

Sample name:	S0		
Data file:	S002.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-01 16:38:17+02:00
Inj. volume:	10.000	**Location:**	21
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	Blank
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	
		Sample amount:	0.00
Manually modified:	Manual Integration		

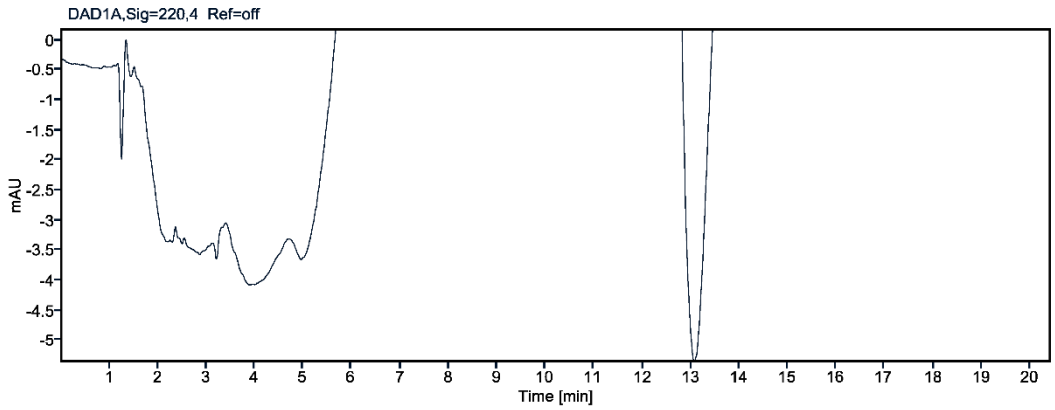

Figure 2: Chromatogram – HPLC Analysis – Blank (S0)

hrl:

Single Injection Report

Sample name:	S6 FRD		
Data file:	S6 FRD01.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-01 16:17:13+02:00
Inj. volume:	10.000	**Location:**	27
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	SystemSuitability
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	
		Sample amount:	0.00
Manually modified:	Manual Integration		

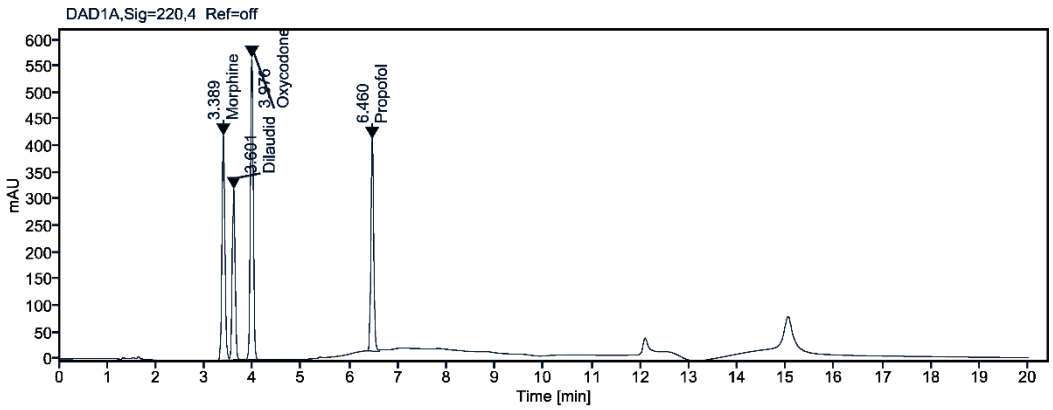

Figure 3: Chromatogram – HPLC Analysis – High Standard (S6)

Single Injection Report

Sample name:	Sample 1		
Data file:	Sample 110.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-01 19:26:56+02:00
Inj. volume:	10.000	**Location:**	1
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	Sample
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	
		Sample amount:	0.00
Manually modified:	Manual Integration		

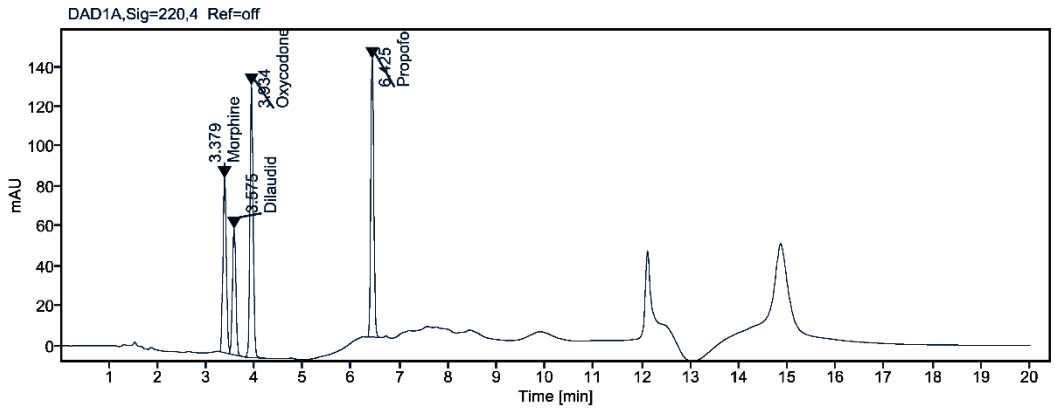

Figure 4: Chromatogram – HPLC Analysis – Sample

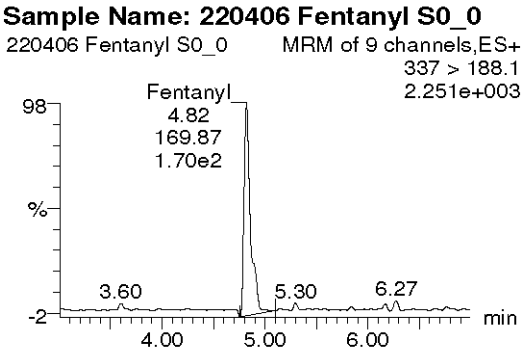

Figure 5: Chromatogram - LC-MS/MS Analysis - Blank (S0)

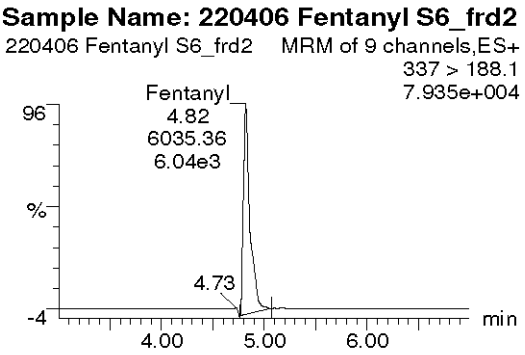

Figure 6: Chromatogram - LC-MS/MS Analysis - High Standard (S6)

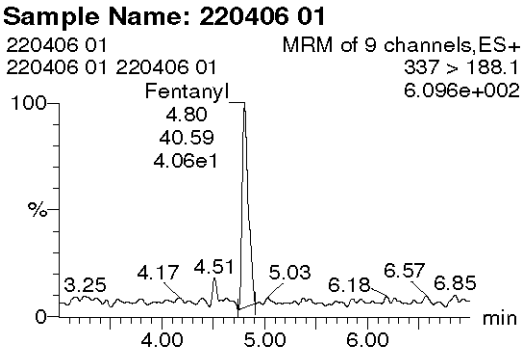

Figure 7: Chromatogram - LC-MS/MS Analysis - Sample

6.6 Calibration Data

The HPLC and the LC-MS/MS were calibrated using various dilutions of the pharmaceuticals, as supplied. Table 10, below, shows the various concentrations used for calibration of each API.

Table 10: Standards used for Calibration of Instruments

Analyte / Calibration Standard	Morphine [µg/g]	Dilaudid [µg/g]	Oxycodone [µg/g]	Fentanyl [µg/g]	Propofol [µg/g]
Retention Time	3.4 Min	3.6 Min	4.0 Min	4.81 Min	6.5 Min
S0	0.0	0.0	0.0	0.000	0.0
S1	8.8	8.8	14.4	0.100	8.8
S2	22.0	22.0	36.0	0.250	22.0
S3	44.0	44.0	72.0	0.750	44.0
S4	66.0	66.0	108.0	---	66.0
S5	110.0	110.0	180.0	---	110.0

The calibration graphs are shown below; the calibration data are shown in Table 11, below. A second-order calibration in the form of $y = a + bx + cx^2$ was used. The correlation coefficients (r) were excellent, with no calibration below 0.999956 (please note that $r = \sqrt{R^2}$). LOR: Limit of Reporting.

Table 11: Summary of Calibration Data

Analyte / Statistical Parameter	Morphine	Dilaudid	Oxycodone	Fentanyl	Propofol
Retention Time	3.4 Min	3.6 Min	4.0 Min	4.81 Min	6.5 Min
a	3.387E-02	4.768E-02	2.011E-01	-1.190E-04	9.959E-02
b	5.782E-02	8.097E-02	7.562E-02	4.761E-04	6.640E-02
c	9.690E-07	1.438E-06	6.457E-07	1.284E-07	1.148E-06
r	0.999991	0.999988	0.999956	0.999997	0.999974
LOR in Test Solution	0.20 µg/g	0.20 µg/g	0.20 µg/g	0.010 µg/g	0.20 µg/g

6.7 Calibration Graphs

Below are the calibration graphs obtained for each API.

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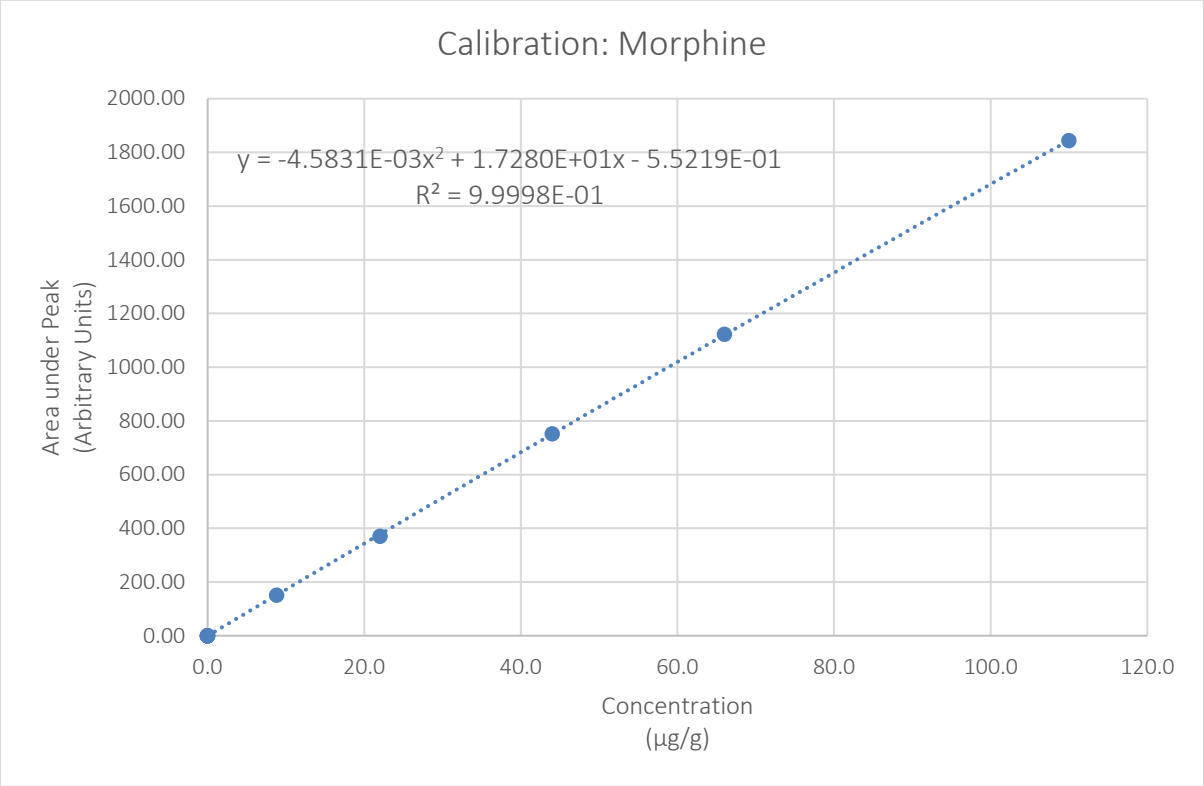

Figure 8: Calibration Graph – Morphine

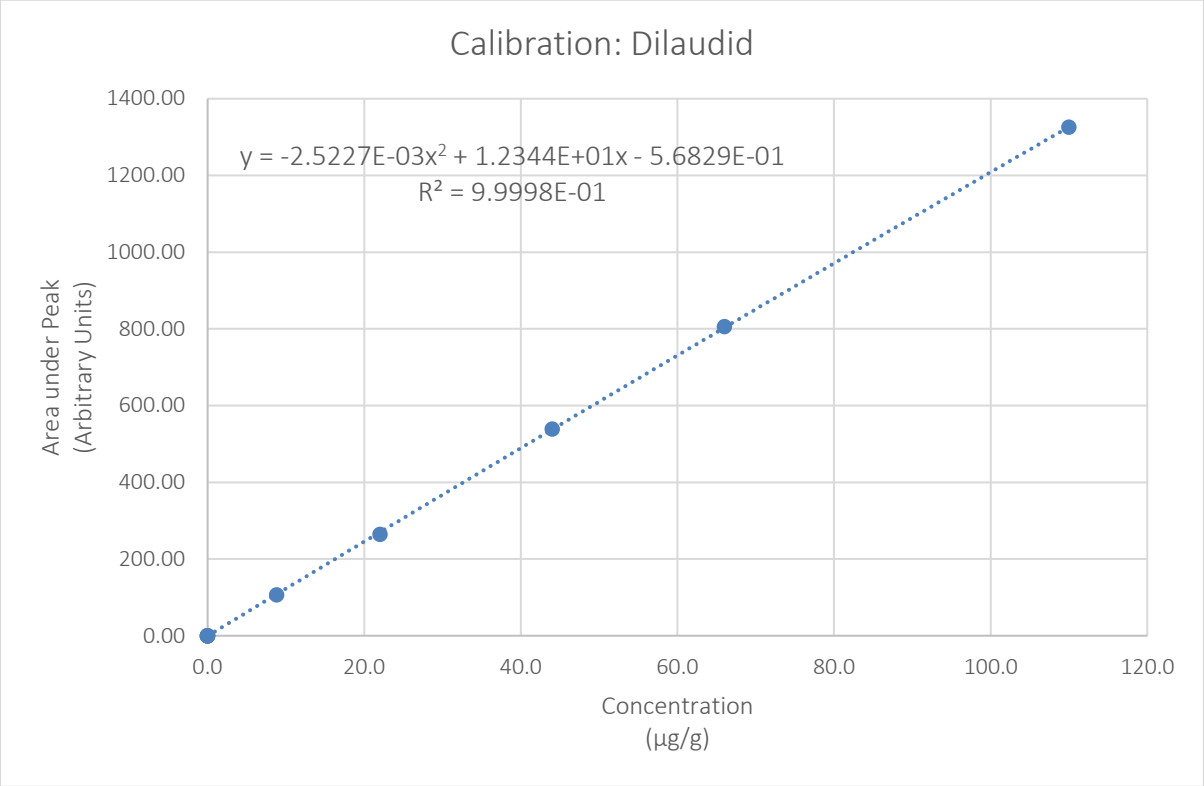

Figure 9: Calibration Graph – Dilaudid

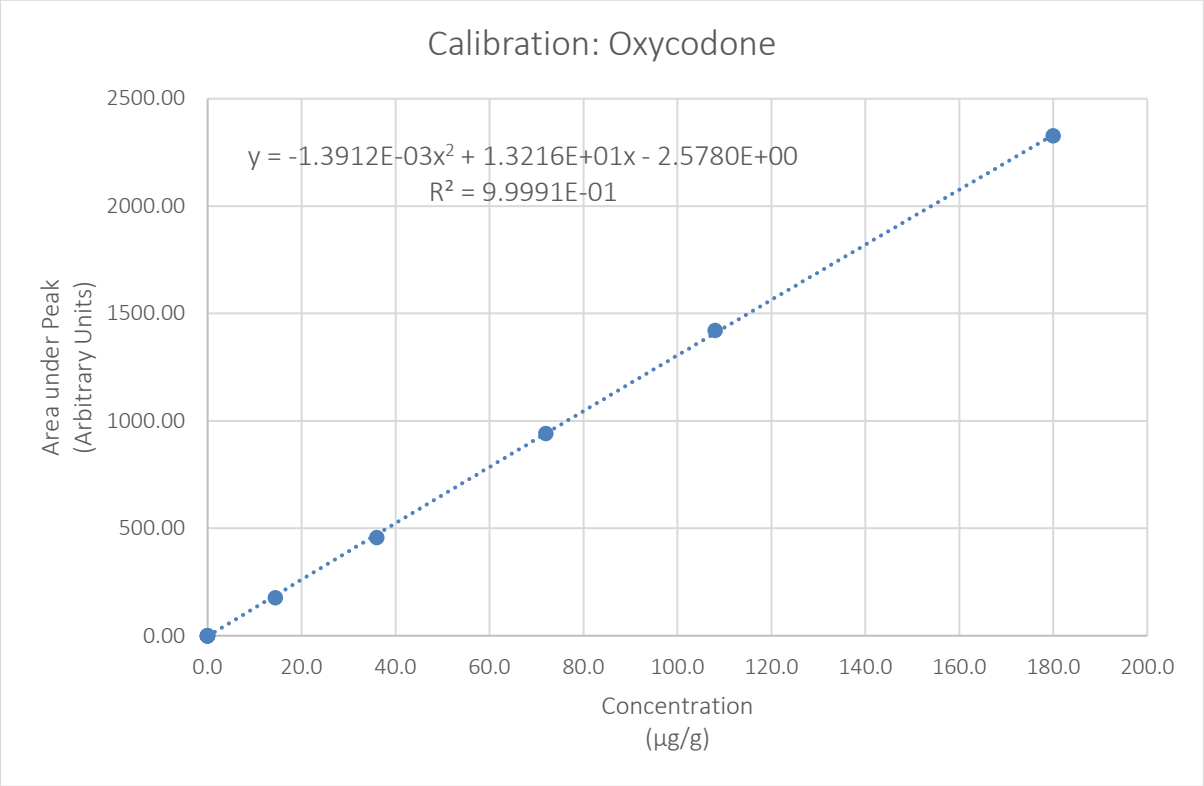

Figure 10: Calibration Graph – Oxycodone

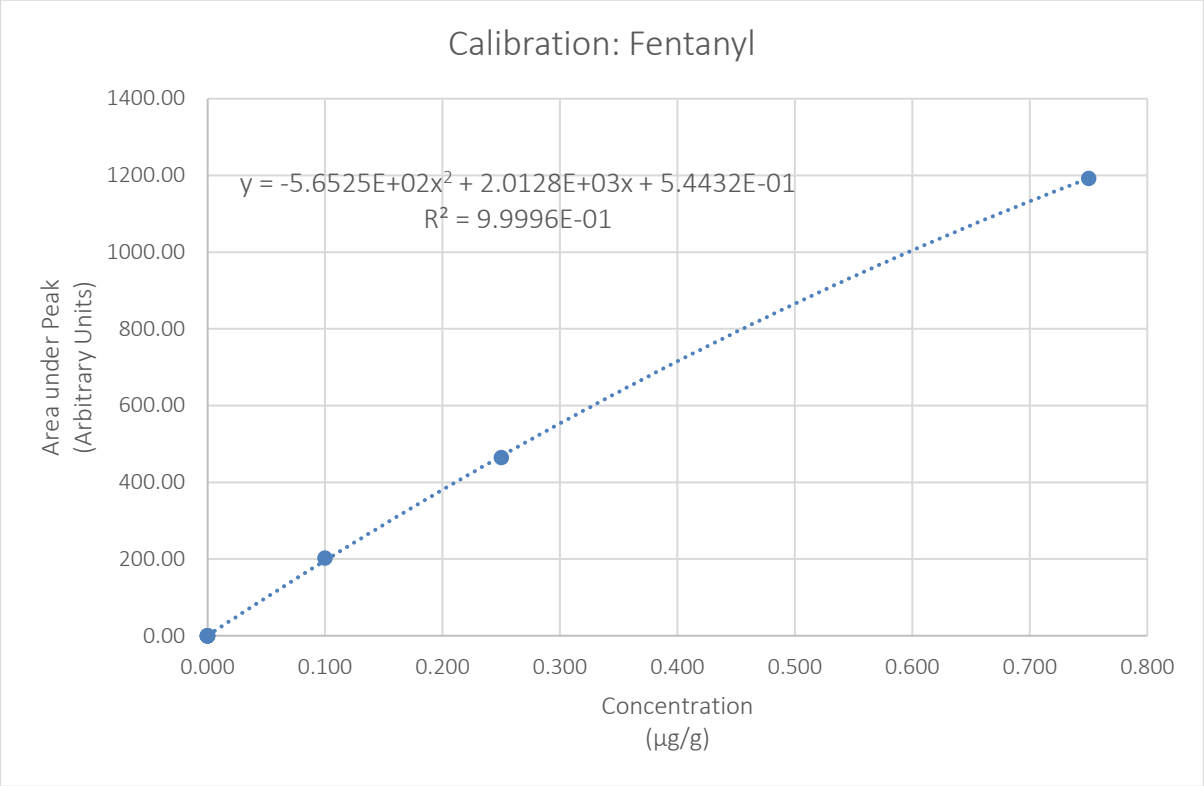

Figure 11: Calibration Graph – Fentanyl

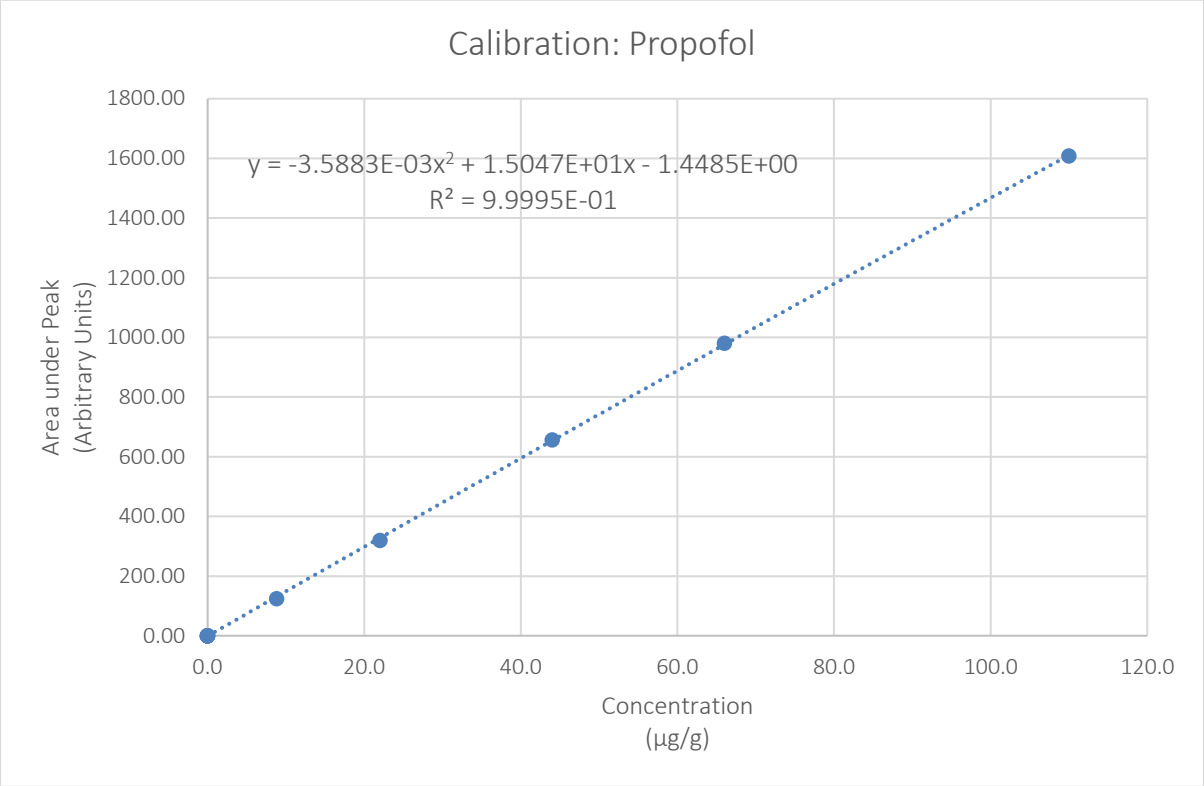

Figure 12: Calibration Graph – Propofol

7 Analysis Results

7.1 Numerical Results

Table 12, below, shows the starting concentrations for each API, as well as the residual concentrations of the API's after the respective contact times.

Table 12: Starting Concentrations of API's and after Respective Contact Times

Analyte / Contact Time (hh:mm)	Morphine	Dilaudid	Oxycodone	Fentanyl	Propofol
00:00 (Start Time)	651 µg/g	675 µg/g	1484 µg/g	6.2 µg/g	745 µg/g
01:05	253 µg/g	248 µg/g	482 µg/g	0.19 µg/g	394 µg/g
02:27	140 µg/g	132 µg/g	257 µg/g	0.11 µg/g	284 µg/g
04:03	73.4 µg/g	66.1 µg/g	129 µg/g	< 0.10 µg/g	187 µg/g
07:59	36.2 µg/g	30.3 µg/g	59.0 µg/g	< 0.10 µg/g	125 µg/g
24:10	2.17 µg/g	3.69 µg/g	< 2.0 µg/g	< 0.10 µg/g	58.7 µg/g
48:40	< 2.0 µg/g	< 2.0 µg/g	< 2.0 µg/g	< 0.10 µg/g	32.7 µg/g
121:02	< 2.0 µg/g	< 2.0 µg/g	< 2.0 µg/g	< 0.10 µg/g	13.2 µg/g
168:16	< 2.0 µg/g	< 2.0 µg/g	< 2.0 µg/g	< 0.10 µg/g	< 2.0 µg/g

Table 13, below, shows the amount of material adsorbed relative to the starting concentrations (starting concentrations are set to 0 % adsorbed).

Table 13: Amount of API's Adsorbed after Respective Contact Times

Analyte / Contact Time (hh:mm)	Morphine	Dilaudid	Oxycodone	Fentanyl	Propofol
00:00 (Start Time)	0.0 %	0.0 %	0.0 %	0.0 %	0.0 %
01:05	61.2 %	63.3 %	67.5 %	97 %	47.1 %
02:27	78.5 %	80.5 %	82.7 %	98 %	61.8 %

Analyte / Contact Time (hh:mm)	Morphine	Dilaudid	Oxycodone	Fentanyl	Propofol
04:03	88.7 %	90.2 %	91.3 %	> 98 %	74.9 %
07:59	94.4 %	95.5 %	96.0 %	> 98 %	83.2 %
24:10	> 99.7 %	99.5 %	> 99.9 %	> 98 %	92.1 %
48:40	> 99.7 %	> 99.7 %	> 99.9 %	> 98 %	95.6 %
121:02	> 99.7 %	> 99.7 %	> 99.9 %	> 98 %	98.2 %
168:16	> 99.7 %	> 99.7 %	> 99.9 %	> 98 %	> 99.7 %

7.2 Graphical Results

Figure 13, below, shows the amount of adsorption of the API's against the contact time.

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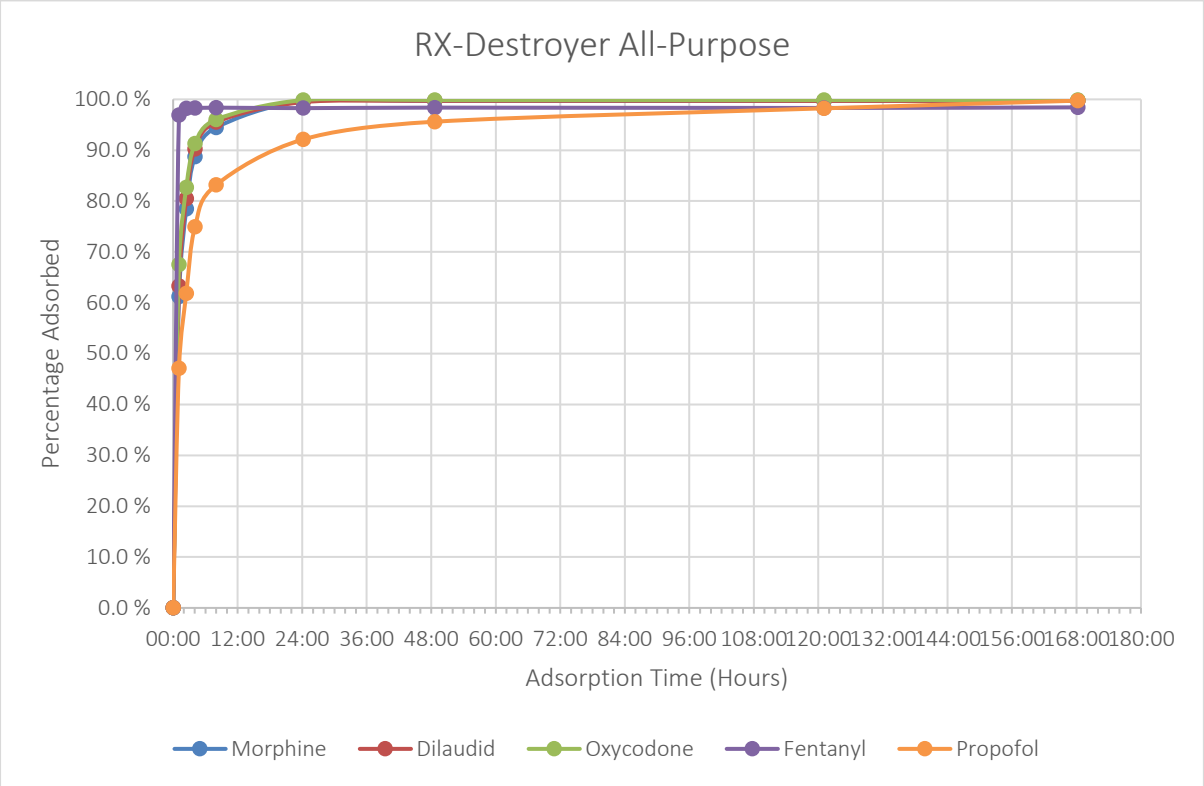

Figure 13: Adsorption of API's vs Contact Time

8 General Discussion

The Rx Destroyer™ All-Purpose is an effective device to deactivate API's. It is evident from the graph in Figure 12 (above) that most API's are completely (at least > 98 %, typically > 99.7 %) adsorbed within the first 24 hours. The only API that required a longer adsorption time was the Propofol, which required more than 120 hours (5 days) to adsorb completely (> 99.7 %).

8.1 Reaction Kinetics

The adsorption curves all indicate a typical first-order reaction kinetics following the standard first-order reaction half-life decay equation:

$$N_{(t)} = N_0 e^{-\lambda t}$$

Equation 1: First-order Reaction Half-Life Equation

Where: N_0 is the initial quantity
N_t is the remaining quantity after time, t
$t_{½}$ is the half-life
λ is the decay constant

The approximate decay constants for the various API's are shown in Table 14, below.

Table 14: Amount of API's Adsorbed after Respective Contact Times

Analyte	Morphine	Dilaudid	Oxycodone	Fentanyl	Propofol
Approximate Decay Constant	0.60	0.60	0.60	3.0	0.35

The higher the decay constant, the faster the compound adsorbs onto the activated carbon.

Propofol has a low decay constant, meaning it takes a long time to adsorb completely onto the activated carbon; this may be attributed to the size or shape of the molecule, but it may also be that propofol is well complexed by the original emulsion (soybean oil, egg phospholipids, and glycerol).

8.2 Conclusion

In short: all the API's were adsorbed by the Rx-Destroyer™ All-Purpose, mostly within the first day; some API's required longer absorption periods. The Rx-Destroyer™ All-Purpose is an excellent tool for disposing of pharmaceuticals, ensuring that the active ingredients will not be retrievable by common means available to the general public, and nor will the ingredients easily land up in the environment.

9 Appendix A – HPLC Chromatograms

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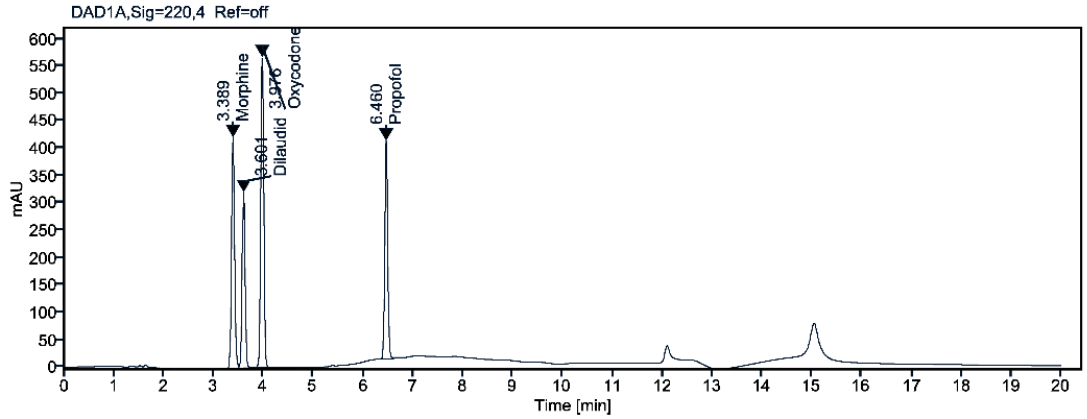
Figure 14: HPLC Chromatogram - High Standard

Single Injection Report

Sample name:	S6 FRD		
Data file:	S6 FRD01.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-01 16:17:13+02:00
Inj. volume:	10.000	**Location:**	27
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	SystemSuitability
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	
		Sample amount:	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=220,4 Ref=off

Name	RT [min]	RF	Area	Sample Multipliers	Sample Dilution Factors	Amount [mg/L]	Concentration [mg/L]
Morphine	3.39	16.812	1835.096	1;1;1;1;1	1;1;1;1;1	109.154	109.154
Dilaudid	3.60	12.083	1315.444	1;1;1;1;1	1;1;1;1;1	108.865	108.865
Oxycodone	3.98	12.959	2315.079	1;1;1;1;1	1;1;1;1;1	178.653	178.653
Propofol	6.46	14.680	1640.142	1;1;1;1;1	1;1;1;1;1	111.726	111.726
					Sum	508.398	

Figure 15:: HPLC Chromatogram - Blank Standard

Single Injection Report

Sample name:	S0		
Data file:	S002.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-01 16:38:17+02:00
Inj. volume:	10.000	**Location:**	21
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	Blank
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	
		Sample amount:	0.00
Manually modified:	Manual Integration		

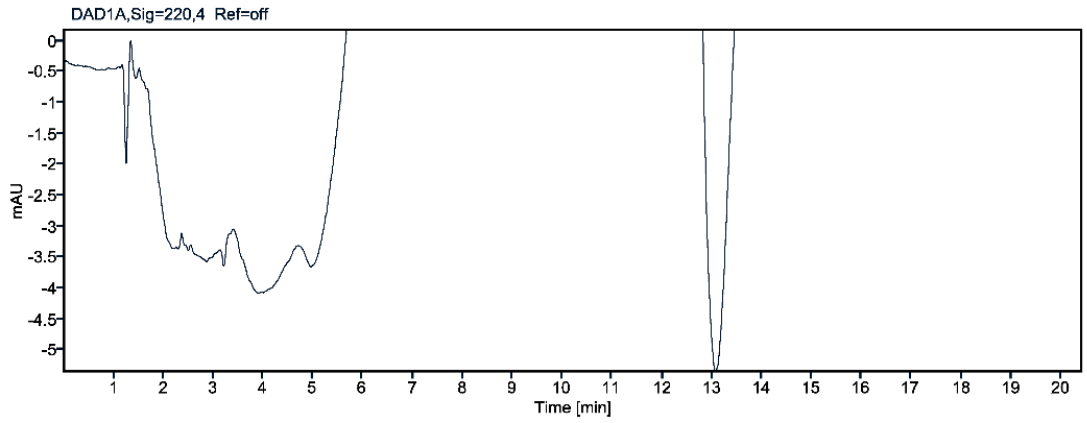
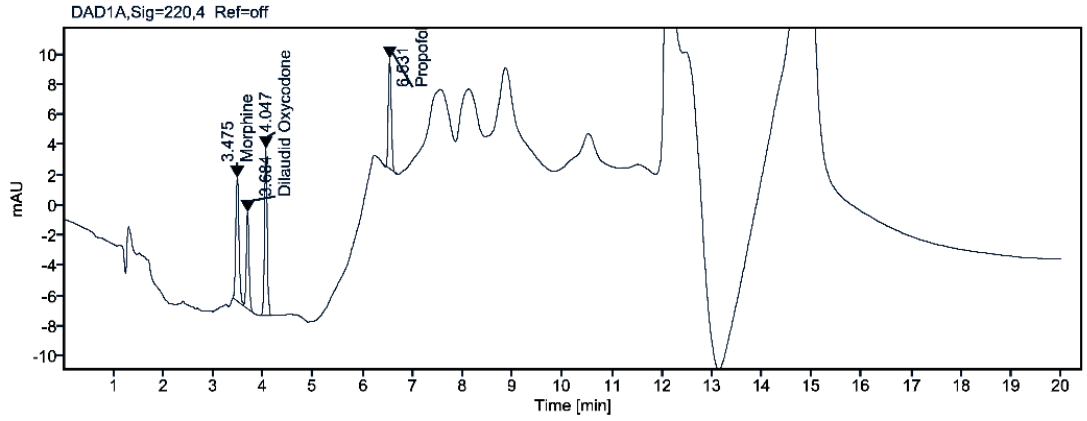


Figure 16: HPLC Chromatogram - Calibration Standard 1

Single Injection Report

Sample name:	S1		
Data file:	S103.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-01 16:59:21+02:00
Inj. volume:	10.000	**Location:**	22
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	Calibration
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	1
		Sample amount:	0.00
Manually modified:	Manual Integration		



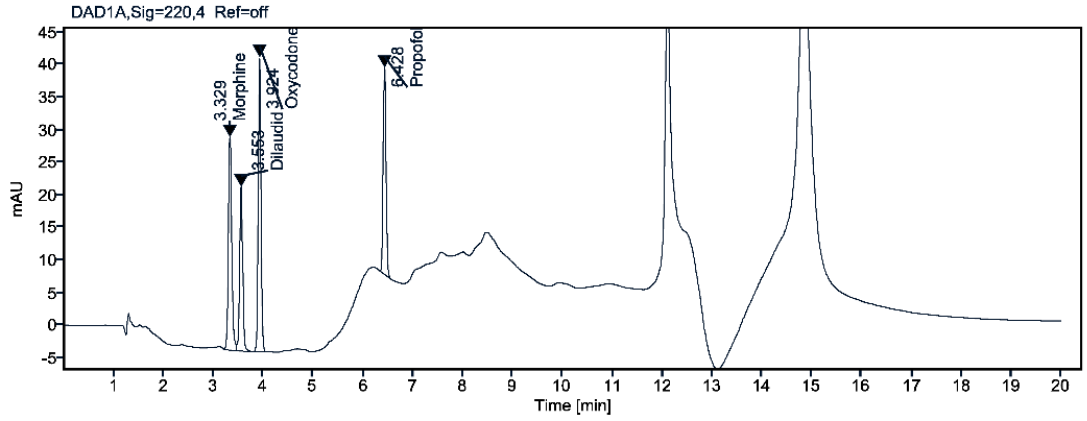
Signal: DAD1A,Sig=220,4 Ref=off

Name	RT [min]	RF	Area	Sample Multipliers	Sample Dilution Factors	Amount [mg/L]	Concentration [mg/L]
Morphine	3.47	24.413	36.261	1;1;1;1;1	1;1;1;1;1	1.485	1.485
Dilaudid	3.68	16.011	24.751	1;1;1;1;1	1;1;1;1;1	1.546	1.546
Oxycodone	4.05	14.470	42.739	1;1;1;1;1	1;1;1;1;1	2.954	2.954
Propofol	6.53	18.221	29.157	1;1;1;1;1	1;1;1;1;1	1.600	1.600
					Sum	7.585	

Figure 17: HPLC Chromatogram - Calibration Standard 2

Single Injection Report

Sample name:	S2		
Data file:	S204.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-01 17:20:25+02:00
Inj. volume:	10.000	**Location:**	23
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	Calibration
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	2
		Sample amount:	0.00
Manually modified:	Manual Integration		



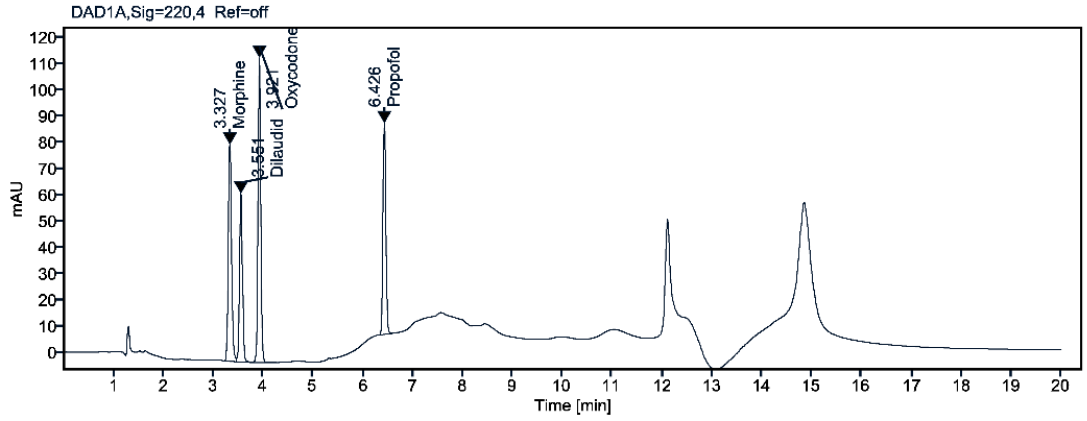
Signal: DAD1A,Sig=220,4 Ref=off

Name	RT [min]	RF	Area	Sample Multipliers	Sample Dilution Factors	Amount [mg/L]	Concentration [mg/L]
Morphine	3.33	18.073	151.435	1;1;1;1;1	1;1;1;1;1	8.379	8.379
Dilaudid	3.55	12.761	107.020	1;1;1;1;1	1;1;1;1;1	8.386	8.386
Oxycodone	3.92	13.272	177.856	1;1;1;1;1	1;1;1;1;1	13.401	13.401
Propofol	6.43	15.336	124.597	1;1;1;1;1	1;1;1;1;1	8.124	8.124
					Sum	38.291	

Figure 18: HPLC Chromatogram - Calibration Standard 3

Single Injection Report

Sample name:	S3		
Data file:	S305.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-01 17:41:32+02:00
Inj. volume:	10.000	**Location:**	24
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	Calibration
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	3
		Sample amount:	0.00
Manually modified:	Manual Integration		



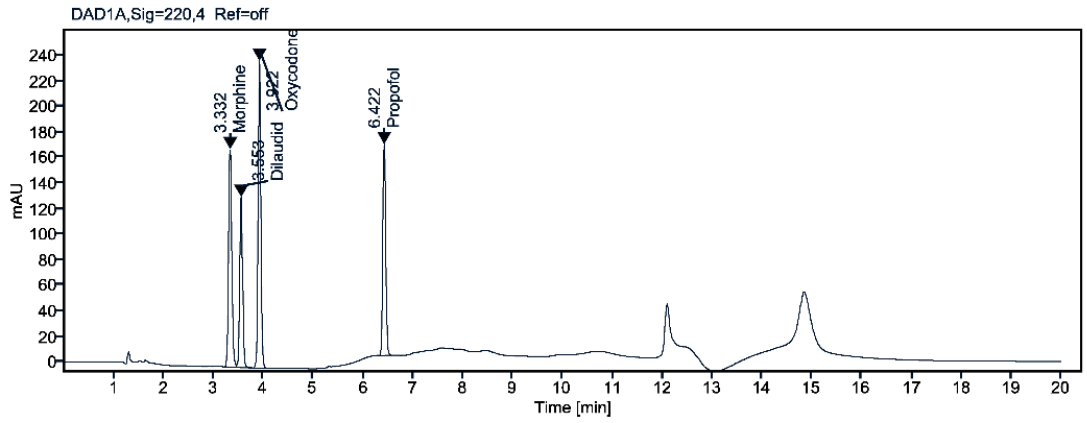
Signal: DAD1A,Sig=220,4 Ref=off

Name	RT [min]	RF	Area	Sample Multipliers	Sample Dilution Factors	Amount [mg/L]	Concentration [mg/L]
Morphine	3.33	17.240	370.249	1;1;1;1;1	1;1;1;1;1	21.476	21.476
Dilaudid	3.55	12.314	264.093	1;1;1;1;1	1;1;1;1;1	21.447	21.447
Oxycodone	3.92	13.063	456.933	1;1;1;1;1	1;1;1;1;1	34.979	34.979
Propofol	6.43	14.896	319.619	1;1;1;1;1	1;1;1;1;1	21.456	21.456
					Sum	99.358	

Figure 19: HPLC Chromatogram - Calibration Standard 4

Single Injection Report

Sample name:	S4		
Data file:	S406.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-01 18:02:37+02:00
Inj. volume:	10.000	**Location:**	25
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	Calibration
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	4
		Sample amount:	0.00
Manually modified:	Manual Integration		



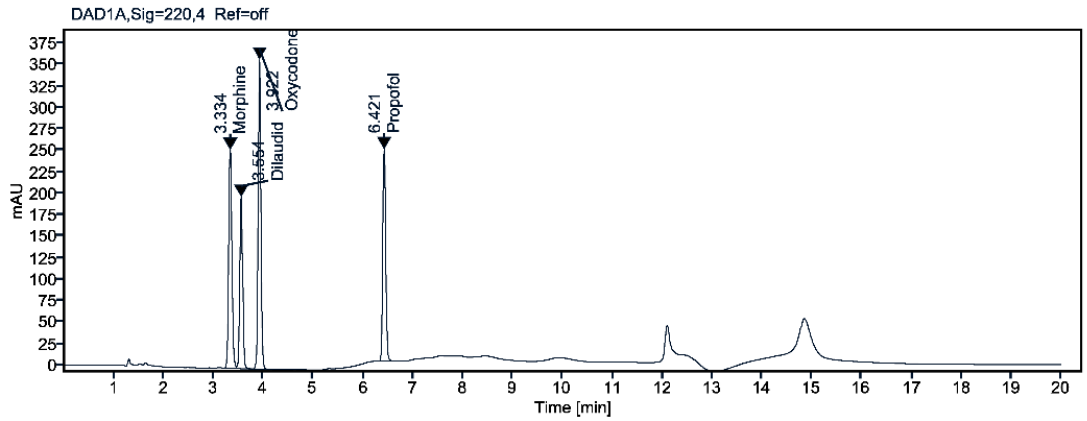
Signal: DAD1A,Sig=220,4 Ref=off

Name	RT [min]	RF	Area	Sample Multipliers	Sample Dilution Factors	Amount [mg/L]	Concentration [mg/L]
Morphine	3.33	16.965	752.288	1;1;1;1;1	1;1;1;1;1	44.343	44.343
Dilaudid	3.55	12.166	539.119	1;1;1;1;1	1;1;1;1;1	44.315	44.315
Oxycodone	3.92	12.996	941.279	1;1;1;1;1	1;1;1;1;1	72.430	72.430
Propofol	6.42	14.758	656.969	1;1;1;1;1	1;1;1;1;1	44.517	44.517
					Sum	205.604	

Figure 20: HPLC Chromatogram - Calibration Standard 5

Single Injection Report

Sample name:	S5		
Data file:	S507.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-01 18:23:45+02:00
Inj. volume:	10.000	**Location:**	26
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	Calibration
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	5
		Sample amount:	0.00
Manually modified:	Manual Integration		



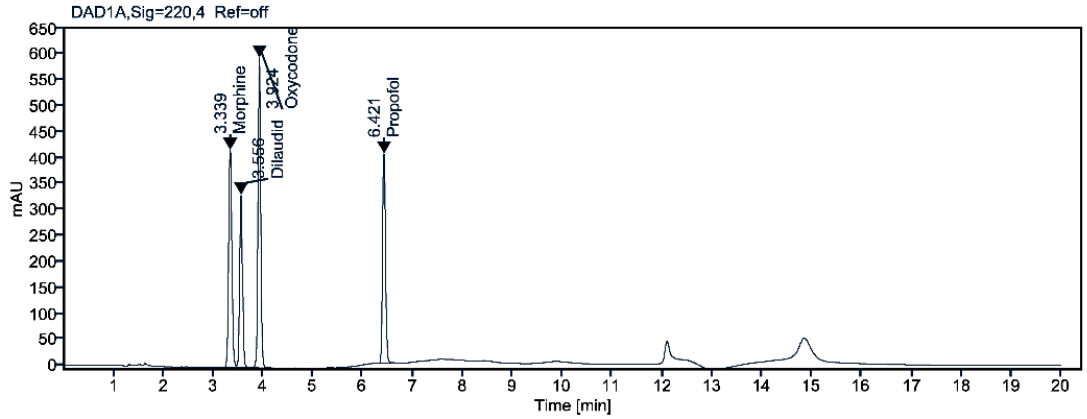
Signal: DAD1A,Sig=220,4 Ref=off

Name	RT [min]	RF	Area	Sample Multipliers	Sample Dilution Factors	Amount [mg/L]	Concentration [mg/L]
Morphine	3.33	16.879	1123.270	1;1;1;1;1	1;1;1;1;1	66.548	66.548
Dilaudid	3.55	12.119	805.723	1;1;1;1;1	1;1;1;1;1	66.482	66.482
Oxycodone	3.92	12.975	1412.165	1;1;1;1;1	1;1;1;1;1	108.839	108.839
Propofol	6.42	14.715	980.419	1;1;1;1;1	1;1;1;1;1	66.628	66.628
					Sum	308.497	

Figure 21: HPLC Chromatogram - Calibration Standard 6

Single Injection Report

Sample name:	S6		
Data file:	S608.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-01 18:44:49+02:00
Inj. volume:	10.000	**Location:**	27
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	Calibration
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	6
		Sample amount:	0.00
Manually modified:	Manual Integration		



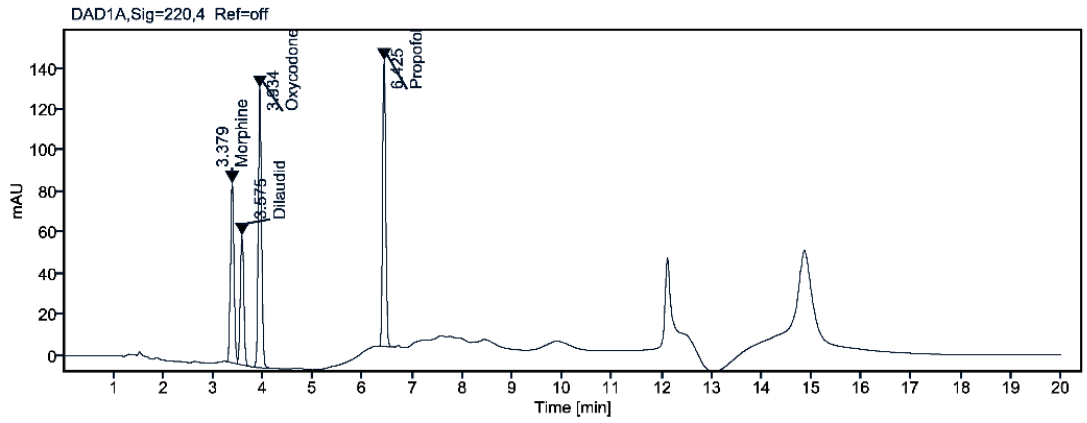
Signal: DAD1A,Sig=220,4 Ref=off

Name	RT [min]	RF	Area	Sample Multipliers	Sample Dilution Factors	Amount [mg/L]	Concentration [mg/L]
Morphine	3.34	16.811	1843.693	1;1;1;1;1	1;1;1;1;1	109.669	109.669
Dilaudid	3.56	12.083	1325.781	1;1;1;1;1	1;1;1;1;1	109.724	109.724
Oxycodone	3.92	12.958	2327.288	1;1;1;1;1	1;1;1;1;1	179.597	179.597
Propofol	6.42	14.681	1608.661	1;1;1;1;1	1;1;1;1;1	109.574	109.574
					Sum	508.564	

Figure 22: HPLC Chromatogram - Sample after 01:05

Single Injection Report

Sample name:	Sample 1		
Data file:	Sample 110.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-01 19:26:56+02:00
Inj. volume:	10.000	**Location:**	1
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	Sample
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	
		Sample amount:	0.00
Manually modified:	Manual Integration		



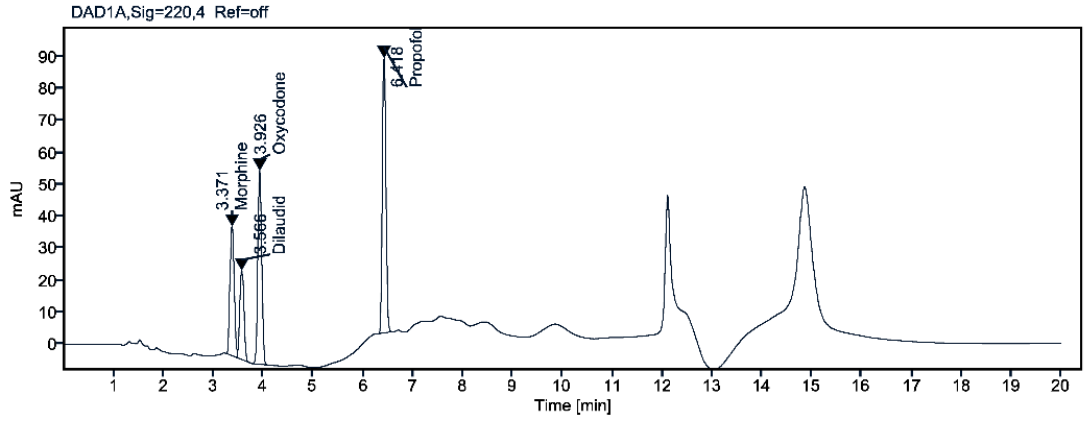
Signal: DAD1A,Sig=220,4 Ref=off

Name	RT [min]	RF	Area	Sample Multipliers	Sample Dilution Factors	Amount [mg/L]	Concentration [mg/L]
Morphine	3.38	17.157	436.747	1;1;1;1;1	1;1;1;1;1	25.456	25.456
Dilaudid	3.57	12.274	306.210	1;1;1;1;1	1;1;1;1;1	24.949	24.949
Oxycodone	3.93	13.026	637.033	1;1;1;1;1	1;1;1;1;1	48.905	48.905
Propofol	6.43	14.772	590.708	1;1;1;1;1	1;1;1;1;1	39.988	39.988
					Sum	139.298	

Figure 23: HPLC Chromatogram - Sample after 02:27

Single Injection Report

Sample name:	Sample 3		
Data file:	Sample 312.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-01 20:09:04+02:00
Inj. volume:	10.000	**Location:**	3
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	Sample
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	
		Sample amount:	0.00
Manually modified:	Manual Integration		



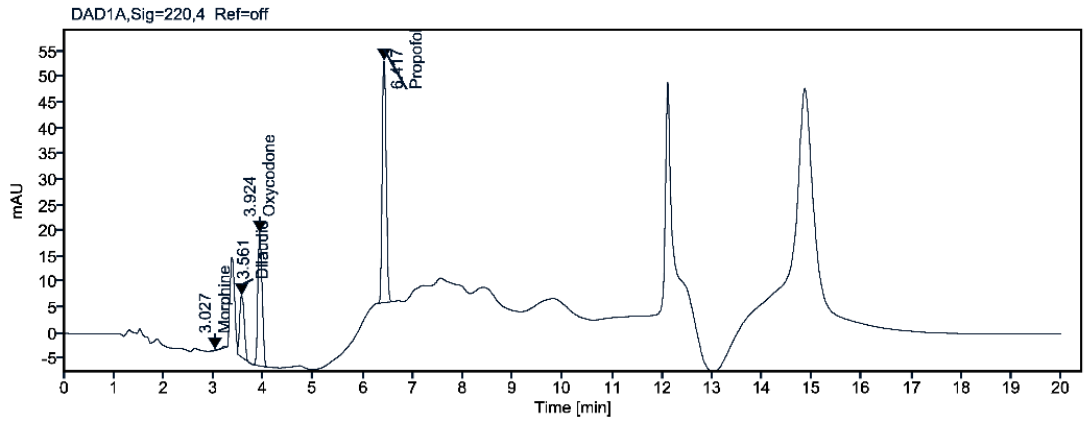
Signal: DAD1A,Sig=220,4 Ref=off

Name	RT [min]	RF	Area	Sample Multipliers	Sample Dilution Factors	Amount [mg/L]	Concentration [mg/L]
Morphine	3.37	17.535	242.308	1;1;1;1;1	1;1;1;1;1	13.818	13.818
Dilaudid	3.57	12.500	162.528	1;1;1;1;1	1;1;1;1;1	13.002	13.002
Oxycodone	3.93	13.109	338.209	1;1;1;1;1	1;1;1;1;1	25.800	25.800
Propofol	6.42	14.829	425.782	1;1;1;1;1	1;1;1;1;1	28.713	28.713
					Sum	81.333	

Figure 24: HPLC Chromatogram - Sample after 04:03

Single Injection Report

Sample name:	Sample 5		
Data file:	Sample 515.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-01 21:12:21+02:00
Inj. volume:	10.000	**Location:**	5
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	Sample
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	
		Sample amount:	0.00
Manually modified:	Manual Integration		



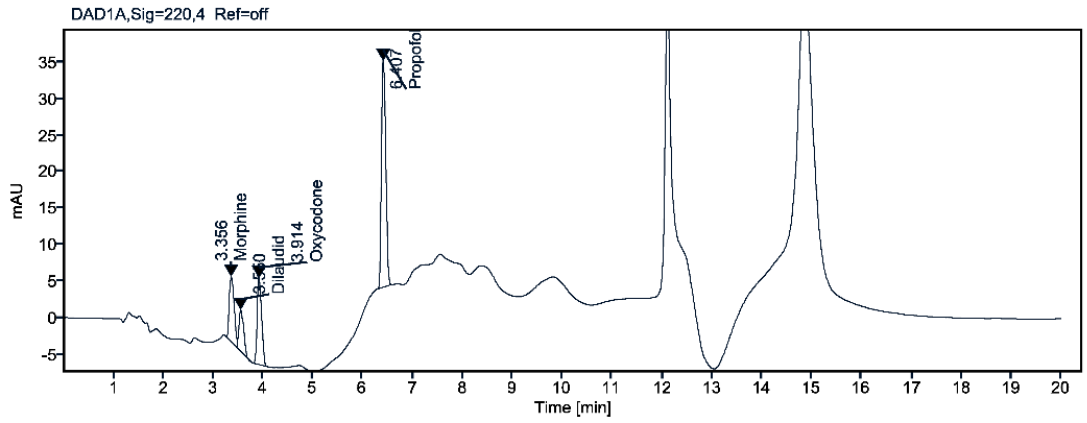
Signal: DAD1A,Sig=220,4 Ref=off

Name	RT [min]	RF	Area	Sample Multipliers	Sample Dilution Factors	Amount [mg/L]	Concentration [mg/L]
Morphine	3.03	-0.599	0.396	1;1;1;1;1	1;1;1;1;1	-0.661	-0.661
Dilaudid	3.56	13.087	76.046	1;1;1;1;1	1;1;1;1;1	5.811	5.811
Oxycodone	3.92	13.316	158.039	1;1;1;1;1	1;1;1;1;1	11.869	11.869
Propofol	6.42	14.957	261.991	1;1;1;1;1	1;1;1;1;1	17.517	17.517
					Sum	34.535	

Figure 25: HPLC Chromatogram - Sample after 07:59

Single Injection Report

Sample name:	Sample 7		
Data file:	Sample 717.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-01 21:54:35+02:00
Inj. volume:	10.000	**Location:**	7
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	Sample
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	
		Sample amount:	0.00
Manually modified:	Manual Integration		



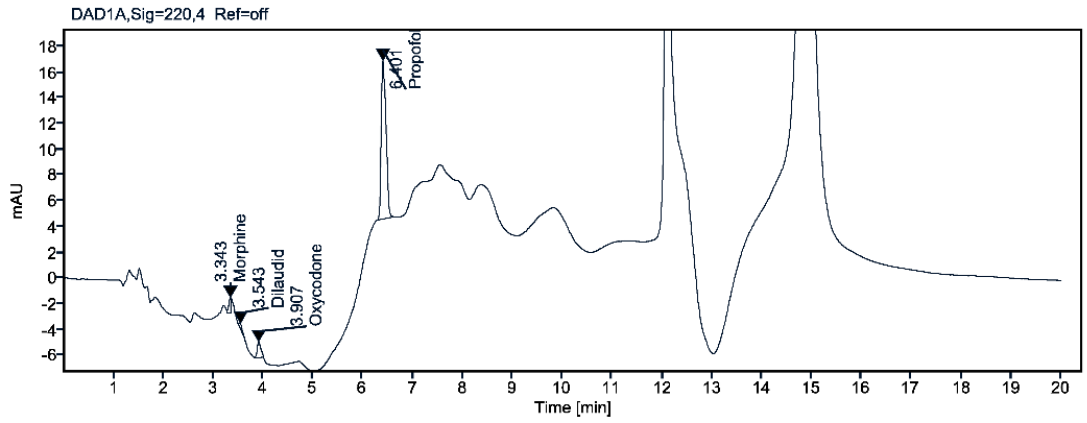
Signal: DAD1A,Sig=220,4 Ref=off

Name	RT [min]	RF	Area	Sample Multipliers	Sample Dilution Factors	Amount [mg/L]	Concentration [mg/L]
Morphine	3.36	20.515	61.657	1;1;1;1;1	1;1;1;1;1	3.005	3.005
Dilaudid	3.55	14.458	36.620	1;1;1;1;1	1;1;1;1;1	2.533	2.533
Oxycodone	3.91	13.767	74.921	1;1;1;1;1	1;1;1;1;1	5.442	5.442
Propofol	6.41	15.095	186.013	1;1;1;1;1	1;1;1;1;1	12.323	12.323
					Sum	23.303	

Figure 26: HPLC Chromatogram - Sample after 24:10

Single Injection Report

Sample name:	Sample 9		
Data file:	Sample 920.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-01 22:57:59+02:00
Inj. volume:	10.000	**Location:**	9
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	Sample
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	
		Sample amount:	0.00
Manually modified:	Manual Integration		



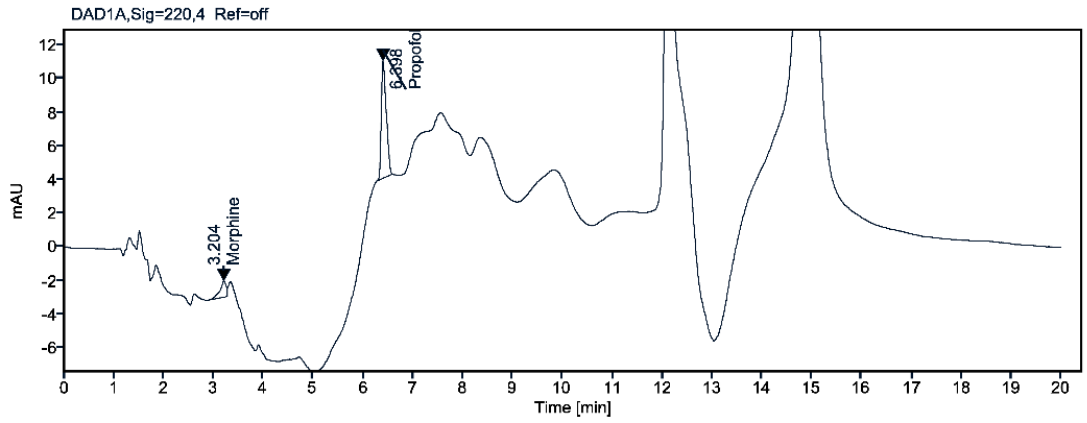
Signal: DAD1A,Sig=220,4 Ref=off

Name	RT [min]	RF	Area	Sample Multipliers	Sample Dilution Factors	Amount [mg/L]	Concentration [mg/L]
Morphine	3.34	-6.402	3.171	1;1;1;1;1	1;1;1;1;1	-0.495	-0.495
Dilaudid	3.54	-5.368	1.901	1;1;1;1;1	1;1;1;1;1	-0.354	-0.354
Oxycodone	3.91	46.220	6.303	1;1;1;1;1	1;1;1;1;1	0.136	0.136
Propofol	6.40	15.739	81.503	1;1;1;1;1	1;1;1;1;1	5.179	5.179
					Sum	4.466	

Figure 27: HPLC Chromatogram - Sample after 48:40

Single Injection Report

Sample name:	Sample 11		
Data file:	Sample 1122.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-01 23:40:10+02:00
Inj. volume:	10.000	**Location:**	11
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	Sample
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	
		Sample amount:	0.00
Manually modified:	Manual Integration		



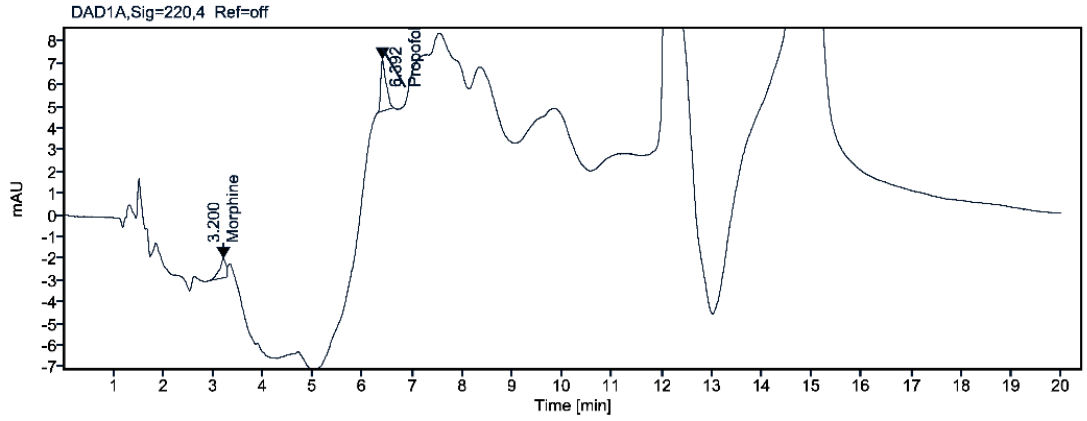
Signal: DAD1A,Sig=220,4 Ref=off

Name	RT [min]	RF	Area	Sample Multipliers	Sample Dilution Factors	Amount [mg/L]	Concentration [mg/L]
Morphine	3.20	-45.118	8.352	1;1;1;1;1	1;1;1;1;1	-0.185	-0.185
Propofol	6.40	16.633	47.697	1;1;1;1;1	1;1;1;1;1	2.868	2.868
					Sum	2.683	

Figure 28: HPLC Chromatogram - Sample after 121:02

Single Injection Report

Sample name:	Sample 13		
Data file:	Sample 1325.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-02 00:43:28+02:00
Inj. volume:	10.000	**Location:**	13
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	Sample
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	
		Sample amount:	0.00
Manually modified:	Manual Integration		



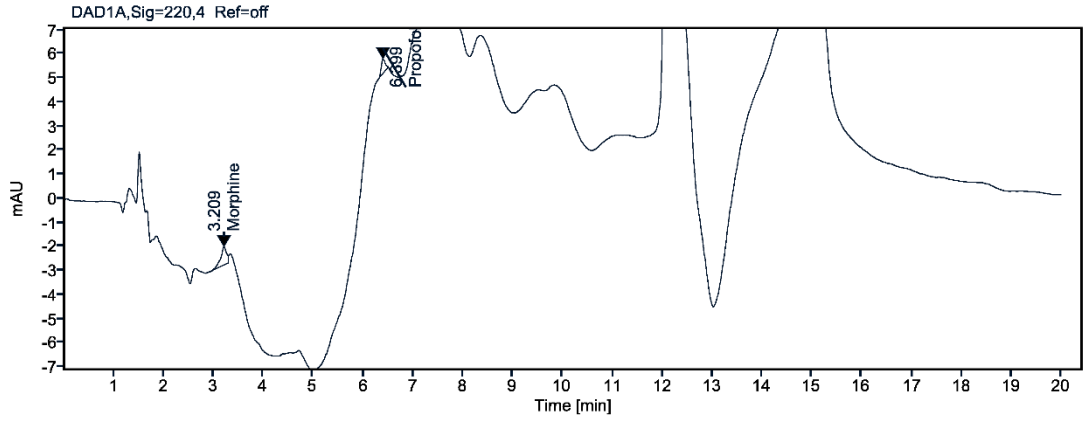
Signal: DAD1A,Sig=220,4 Ref=off

Name	RT [min]	RF	Area	Sample Multipliers	Sample Dilution Factors	Amount [mg/L]	Concentration [mg/L]
Morphine	3.20	-39.693	8.055	1;1;1;1;1	1;1;1;1;1	-0.203	-0.203
Propofol	6.39	21.742	17.568	1;1;1;1;1	1;1;1;1;1	0.808	0.808
					Sum	0.605	

Figure 29: HPLC Chromatogram - Sample after 168:16

Single Injection Report

Sample name:	Sample 15		
Data file:	Sample 1527.dx	**Operator:**	admin
Instrument:	1100 CTC	**Injection date:**	2022-04-02 01:25:38+02:00
Inj. volume:	10.000	**Location:**	15
Acq. method:	220401 HRL Multidrug SDS.amx	**Type:**	Sample
Processing method:	*HRL Multidrug.pmx	**Calib Level:**	
		Sample amount:	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=220,4 Ref=off

Name	RT [min]	RF	Area	Sample Multipliers	Sample Dilution Factors	Amount [mg/L]	Concentration [mg/L]
Morphine	3.21	-18.306	5.984	1;1;1;1;1	1;1;1;1;1	-0.327	-0.327
Propofol	6.40	-17.356	3.119	1;1;1;1;1	1;1;1;1;1	-0.180	-0.180
					Sum	-0.507	

10 Appendix B – LC-MS/MS Chromatograms

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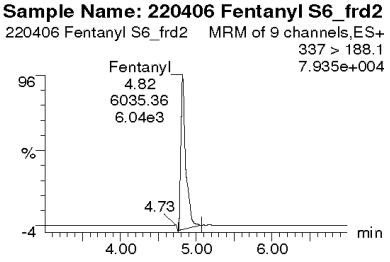
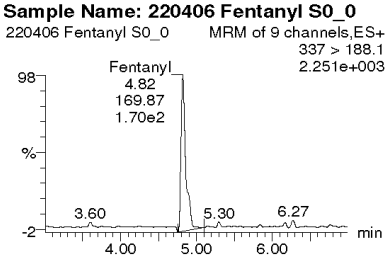
Figure 30: LC-MS/MS Chromatograms (Calibration Standards and Samples)

Method: C:\MassLynx\Default.pro\Methdb\Opiates 20180423.mdb 07 Apr 2022 06:54:07
Calibration: 22 Apr 2022 13:06:15

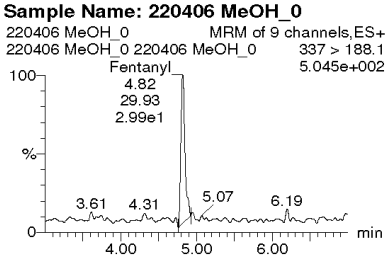
Sample Name: 220406 Fentanyl S6_frd2



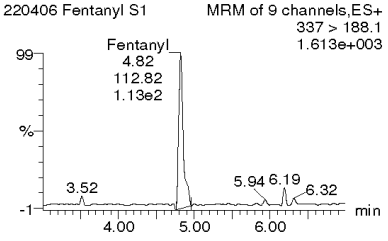
Sample Name: 220406 Fentanyl S0_0



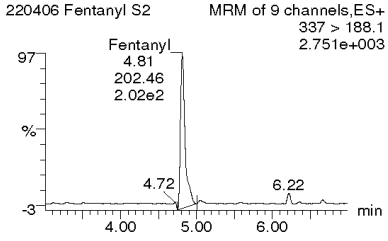
Sample Name: 220406 MeOH_0



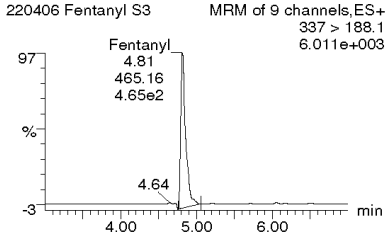
Sample Name: 220406 Fentanyl S1



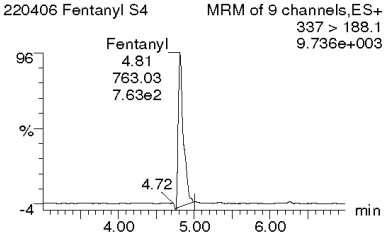
Sample Name: 220406 Fentanyl S2



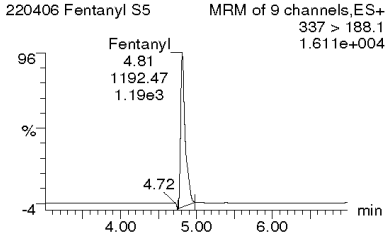
Sample Name: 220406 Fentanyl S3



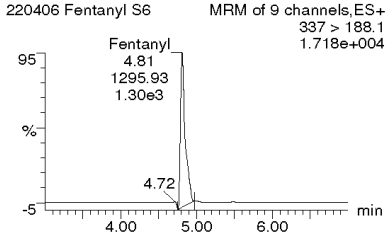
Sample Name: 220406 Fentanyl S4



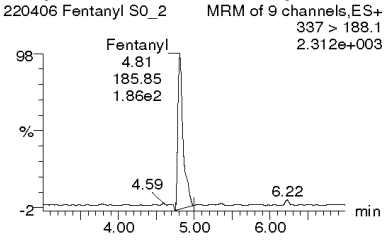
Sample Name: 220406 Fentanyl S5



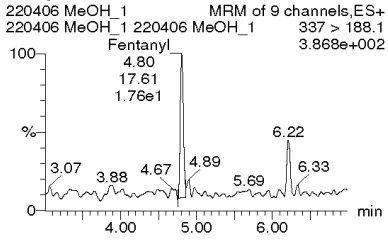
Sample Name: 220406 Fentanyl S6



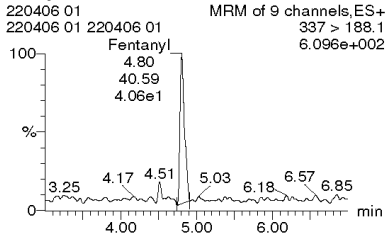
Sample Name: 220406 Fentanyl S0_2



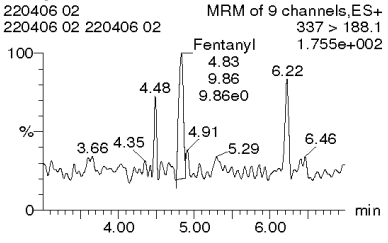
Sample Name: 220406 MeOH_1



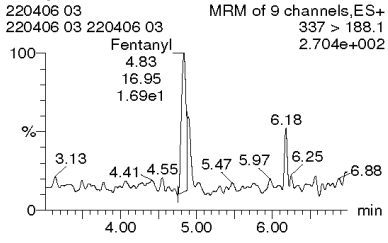
Sample Name: 220406 01



Sample Name: 220406 02



Sample Name: 220406 03



Sample Name: 220406 04

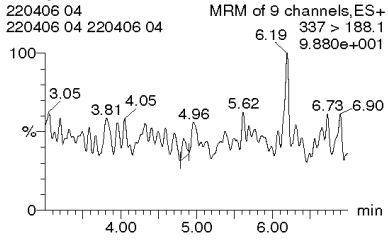
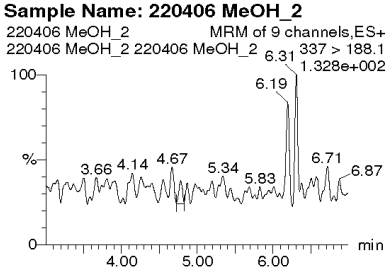
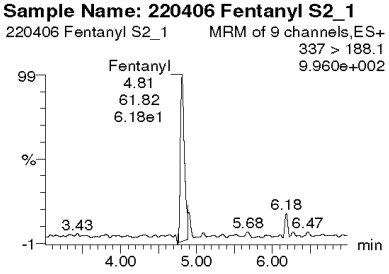


Figure 31: LC-MS/MS Chromatograms (Calibration Standards and Samples)

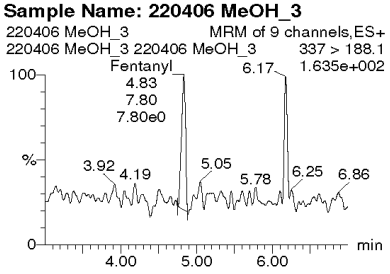
Sample Name: 220406 MeOH_2



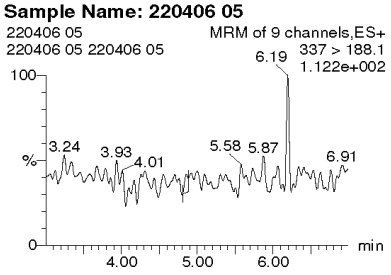
Sample Name: 220406 Fentanyl S2_1



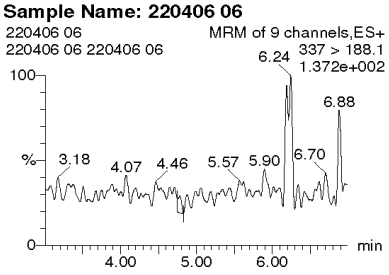
Sample Name: 220406 MeOH_3



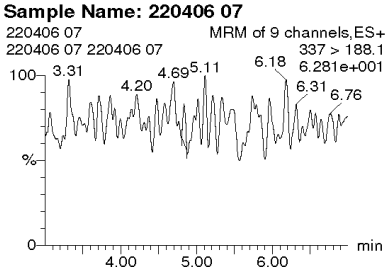
Sample Name: 220406 05



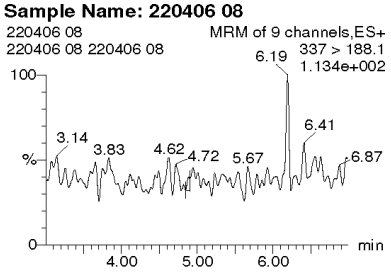
Sample Name: 220406 06



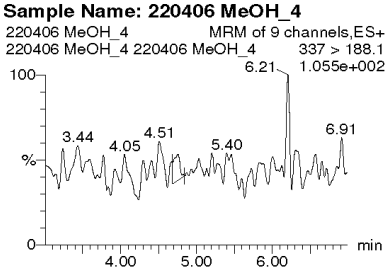
Sample Name: 220406 07



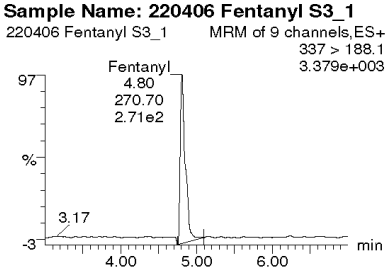
Sample Name: 220406 08



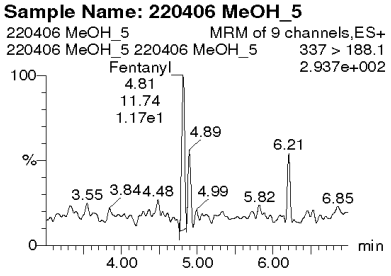
Sample Name: 220406 MeOH_4



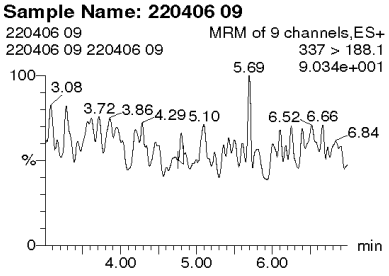
Sample Name: 220406 Fentanyl S3_1



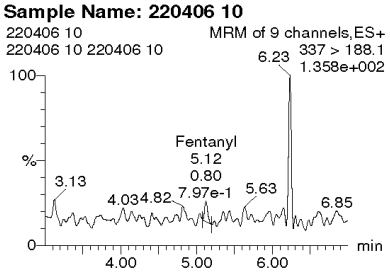
Sample Name: 220406 MeOH_5



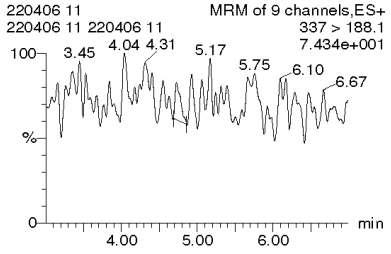
Sample Name: 220406 09



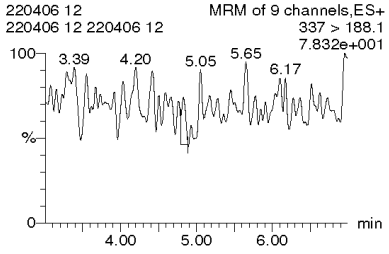
Sample Name: 220406 10



Sample Name: 220406 11



Sample Name: 220406 12



Sample Name: 220406 MeOH_6

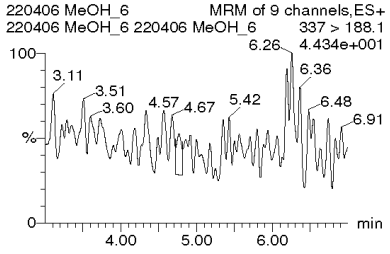
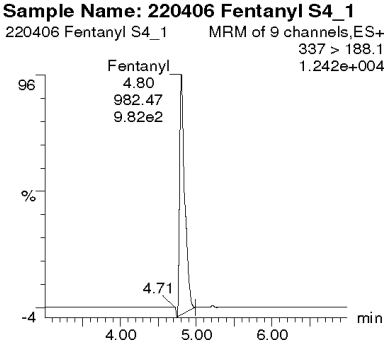
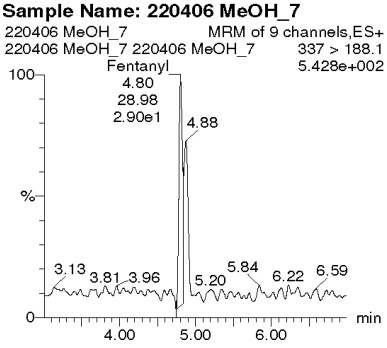


Figure 32: LC-MS/MS Chromatograms (Calibration Standards and Samples)

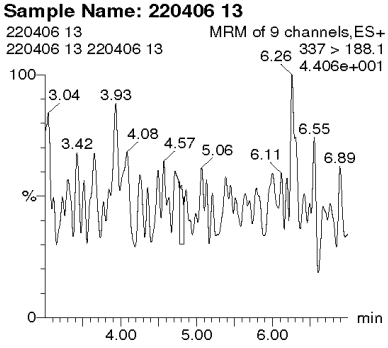
Sample Name: 220406 Fentanyl S4_1



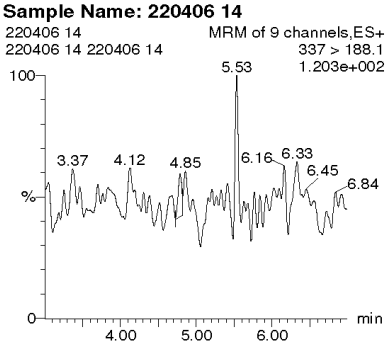
Sample Name: 220406 MeOH_7



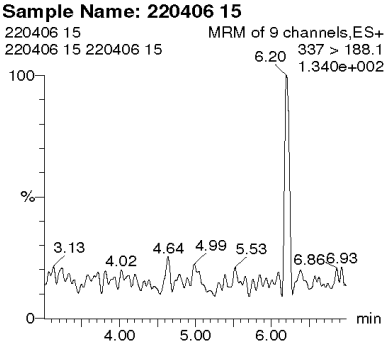
Sample Name: 220406 13



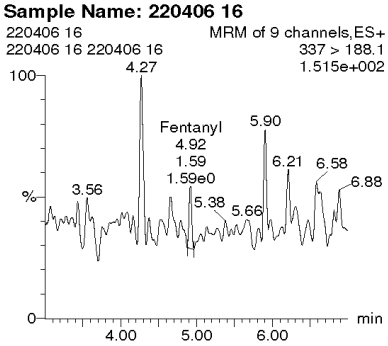
Sample Name: 220406 14



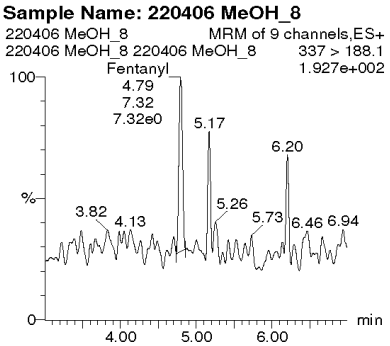
Sample Name: 220406 15



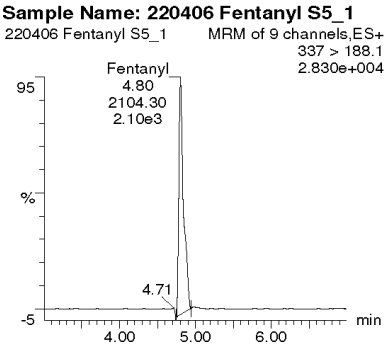
Sample Name: 220406 16



Sample Name: 220406 MeOH_8



Sample Name: 220406 Fentanyl S5_1



Sample Name: 220406 MeOH_9