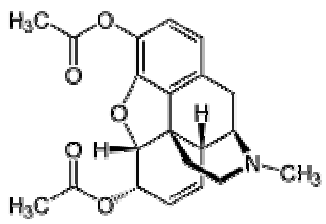
Appendix 1

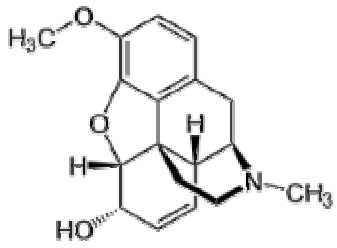
Table A1: Physical and chemical properties of heroin

Aspect	Description
Common name	Heroin (Diamorphine or Diacetylmorphine)
Chemical name	(5α,6α)-7,8-didehydro-4,5-epoxy-17-methylmorphinan-3,6-diol diacetate
Structural formula	
Molecular formula	$C_{21}H_{23}NO_5$
Molecular weight	369.41
Drug type	Narcotic analgesic
Melting point (^oC)	Base:173
	HCl salt: 229 – 233 or 243 – 244
Solubility	Base: soluble 1 in 1700 of water, 1 in 31 of ethanol, 1 in 1.5 of chloroform, and 1 in 100 of ether
	HCl salt: soluble 1 in 2 of water, 1 in 11 of ethanol, and 1 in 1.6 of chloroform; insoluble in ether
Dissociation coefficient	pK_a 7.6 (23 ^oC)
Infrared spectrum, cm^{-1}	HCl salt in nujol: principal peaks at 1245, 1764, 1178, 1215, 911, 1736
Mass spectrum, m/z	Principal ions at 327, 43, 369, 268, 310, 42, 215, 204
Bioavailability	<35% oral, 44 – 61% inhaled
Plasma half-life	3 min
Metabolism	Metabolized to morphine (refer to Table 2.4 for morphine)

(Bencharit, Morton, Xue, Potter & Redinbo, 2003; UNODC, 1998; Moffat, Osselton & Widdop, 2004)

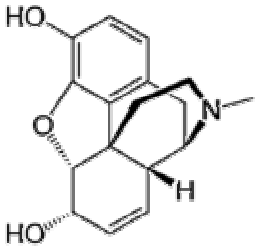
Appendix 2

Table A2: Physical and chemical properties of codeine

Aspect	Description
Common name	Codeine
Chemical name	(5α,6α)-7,8-didehydro-4,5-epoxy-3-methoxy-17-methylmorphinan-6-ol
Structural formula	
Molecular formula	$C_{18}H_{21}NO_3$
Molecular weight	299.4
Drug type	Narcotic analgesic
Melting point (^oC)	Base: 154 – 156 HCl salt: 280
Solubility	Base: soluble 1 in 120 of water, 1 in 15 of boiling water, 1 in 2 of ethanol, 1 in 0.5 of chloroform, 1 in 13 of benzene, and 1 in 18 of ether; freely soluble in amyl alcohol, methanol, and dilute acids; almost insoluble in petroleum ether or solutions of alkali hydroxides HCl salt: soluble 1 in 20 of water, 1 in 180 of ethanol and 1 in 800 of chloroform.
Dissociation coefficient	pK_a 8.2 (20 ^oC)
Infrared spectrum, cm^{-1}	In KBr disk: principal peaks at 1052, 1268, 1500, 1111, 793, 934
Mass spectrum, m/z	Principal ions at 299, 42, 162, 124, 229, 59, 300, 69
Bioavailability	90%
Half-life	2.3 – 3 hours
Metabolism	Not available (N.A)

(Canfield, Barrick & Giessen, 1987; Moffat *et al.*, 2004)

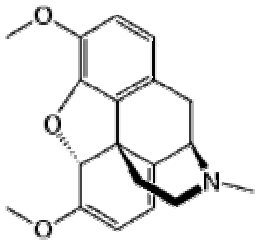
Table A3: Physical and chemical properties of morphine

Aspect	Description
Common name	Morphine
Chemical name	(5α,6α)-7,8-didehydro-4,5-epoxy-17-methylmorphinan-3,6-diol
Structural formula	
Molecular formula	$C_{17}H_{19}NO_3$
Molecular weight	285.3
Drug type	Narcotic analgesic
Melting point (^oC)	Base: 254 – 256
Solubility	Base: soluble 1 in 5000 of water, 1 in 210 of ethanol, 1 in 1220 of chloroform, and 1 in 125 of glycerol, practically insoluble in ether. HCl salt: soluble 1 in 17.5 of water and 1 in 100 of ethanol, slowly soluble in glycerol, practically insoluble in chloroform and ether
Dissociation coefficient	pK_a 8.0, 9.9 (20 ^oC)
Infrared spectrum, cm^{-1}	In nujol: principal peaks at 805, 1243, 1118, 945, 1086, 833
Mass spectrum, m/z	Principal ions at 285, 162, 42, 215, 286, 124, 44, 284
Bioavailability	20 – 30%
Plasma half-life	2 – 3 hours
Metabolism	Metabolized to form morphine-3- and 6-glucuronides.

(Mackay & Hodgkin, 1955; Moffat *et al.*, 2004)

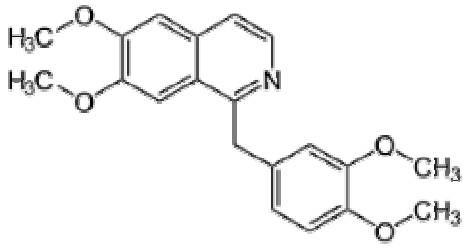
Appendix 4

Table A4: Physical and chemical properties of thebaine

Aspect	Description
Common name	Thebaine
Chemical name	(5α)-6,7,8,14-tetradehydro-4,5a-epoxy-3,6-dimethoxy-17-methylmorphinan
Structural formula	
Molecular formula	$C_{19}H_{21}NO_3$
Molecular weight	311.4
Drug type	Alkaloid
Melting point (^oC)	Base: 193
Solubility	Base: soluble 1 in 1460 of water, 1 in about 15 of hot ethanol, 1 in 13 of chloroform, 1 in 200 of ether and 1 in 25 of benzene
Dissociation coefficient	pK_a 6.1 (15 ^oC); 8.2 (20^oC)
Infrared spectrum, cm^{-1}	In KBr disk: principal peaks at 1234, 1605, 1144, 1270, 1030, 910
Mass spectrum, m/z	Principal ions at 311, 255, 42, 44, 296, 310, 312, 174
Bioavailability	N.A
Half-life	N.A
Metabolism	N.A

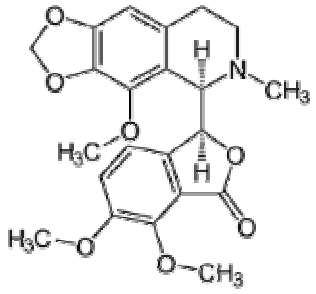
(Mahler, Stevens, Trudell & Nolan, 1996; Moffat *et al.*, 2004)

Table A5: Physical and chemical properties of papaverine

Aspect	Description
Common name	Papaverine
Chemical name	1-(3,4-dimethoxybenzyl)-6,7-dimethoxyisoquinoline
Structural formula	
Molecular formula	$C_{20}H_{21}NO_4$
Molecular weight	339.4
Drug type	Antispasmodic
Melting point (^oC)	Base:147 (from alcohol and ether)
	HCl: 220 – 225 (from water)
Solubility	Base: Almost insoluble in water, soluble in hot benzene, glacial acetic acid and acetone, slightly soluble in chloroform, carbon tetrachloride and petroleum ether
	HCl salt: soluble 1 in about 40 of water, 1 in 120 of ethanol, and 1 in 10 of chloroform, practically insoluble in ether
Dissociation coefficient	pK_a 6.4 (25^oC)
Infrared spectrum, cm^{-1}	HCl salt in KBr disk: principal peaks at 1279, 1508, 1263, 1026, 1292, 1238
Mass spectrum, m/z	Principal ions at 339, 324, 338, 325, 340, 308, 154, 292
Bioavailability	30%
Biological half-life	1-2 hours
Metabolism	Metabolized by demethylation and glucuronic acid and sulfate conjugation of the resulting phenolic groups

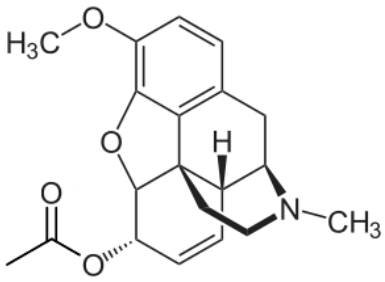
(Reynolds, Palmer & Gorinsky, 1974; Moffat *et al.*, 2004)

Table A6: Physical and chemical properties of noscapine

Aspect	Description
Common name	Noscapine (narcotine)
Chemical name	(3S)- 6,7-dimethoxy-3-[(5R)-5,6,7,8-tetrahydro- 4-methoxy-6-methyl- 1,3-dioxolo (4,5-g)isoquinolin-5-yl]- 1(3H)-isobenzofuranone
Structural formula	
Molecular formula	$C_{22}H_{23}NO_7$
Molecular weight	413.4
Drug type	Cough suppressant
Melting point (^oC)	Base: 176 HCl salt: 200
Solubility	Base: Practically insoluble in water, slightly soluble in ethanol and ether, soluble in acetone and chloroform HCl salt: soluble 1 in 4 of water and 1 in 8 of ethanol, freely soluble in chloroform, practically insoluble in ether
Dissociation coefficient	pK_a 6.2 (20^oC)
Infrared spectrum, cm^{-1}	In KBr disk: principal peaks at 1745, 1276, 1038, 1010, 1498, 1080
Mass spectrum, m/z	Principal ions at 220, 221, 205, 147, 42, 193, 77, 118
Bioavailability	30%
Plasma Half-life	1.5 – 4 hours
Metabolism	As free noscapine and metabolized to conjugated noscapine

(Moffat *et al.*, 2004)

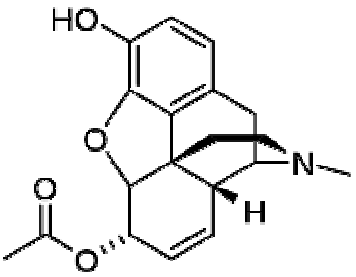
Table A7: Physical and chemical properties of acetylcodeine

Aspect	Description
Common name	Acetylcodeine
Chemical name	3-methoxy-6-acetyl-(5α,6α)-7,8-didehydro-4,5-epoxy-17-methylmorphinan
Structural formula	
Molecular formula	$C_{20}H_{23}NO_4$
Molecular weight	341.4
Drug type	N.A
Melting point (^oC)	Base: 133-142 or 134-135, HCl: 345
Solubility	N.A
Dissociation coefficient	N.A
Infrared spectrum, cm^{-1}	In KBr disk: principal peaks at 1233, 1731, 1272, 1042, 1055, 1501
Mass spectrum, m/z	Principal ions at 341, 282, 229, 42, 43, 59, 342, 204
Bioavailability	N.A
Half-life	N.A
Metabolism	N.A

(UNODC, 1998; Moffat *et al.*, 2004)

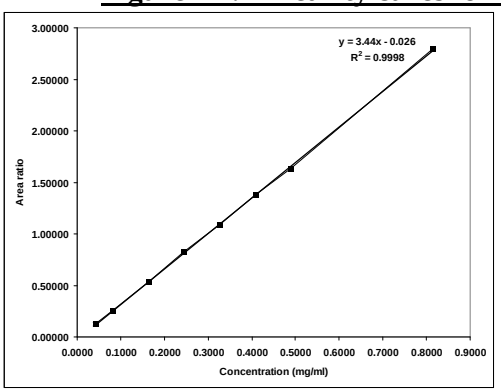
Appendix 8

Table A8: Physical and chemical properties of 6-monoacetylmorphine

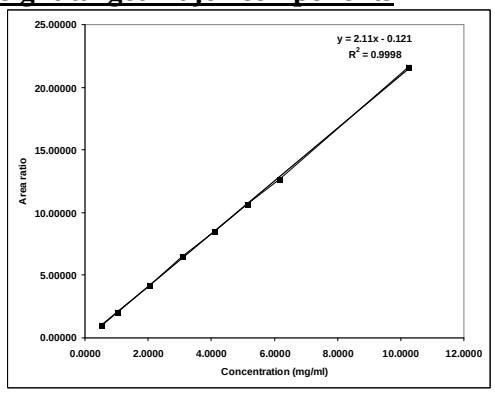
Aspect	Description
Common name	6-Monoacetylmorphine (6-MAM)
Chemical name	3-hydroxy-6-acetyl-(5α,6α)-7,8-didehydro-4,5-epoxy-17-methylmorphinan
Structural formula	
Molecular formula	$C_{19}H_{21}NO_4$
Molecular weight	327.4
Drug type	N.A
Melting point (^oC)	3-MAM base: 57 – 59, 6-MAM base: 190 – 200, 6-MAM HCl: 265 – 313
Solubility	HCl salt: soluble in water
Dissociation coefficient at 25^oC	N.A
Infrared spectrum, cm^{-1}	In KBr disk: principal peaks at 1238, 1730, 1213, 1050, 1030, 1131
Mass spectrum, m/z	Principal ions at 327, 268, 42, 43, 215, 44, 328, 269
Bioavailability	N.A
Half-life	N.A
Metabolism	Metabolized to morphine

(UNODC, 1998; Moffat *et al.*, 2004)

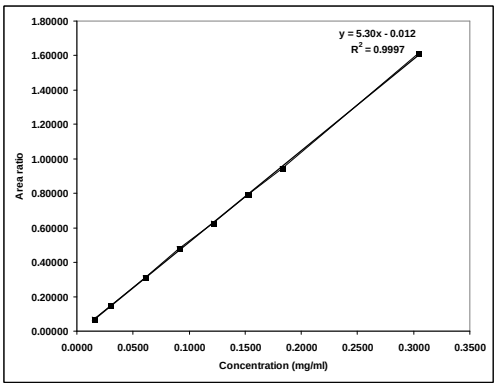
Figure A1: Linearity cures for eight target major components



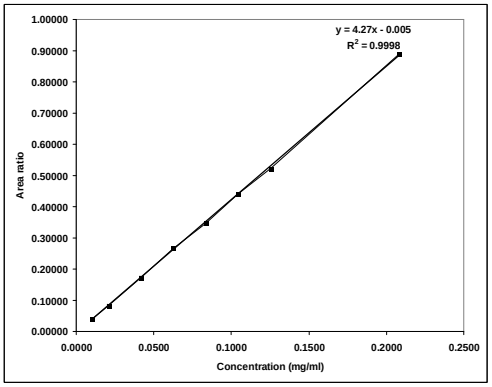
Paracetamol



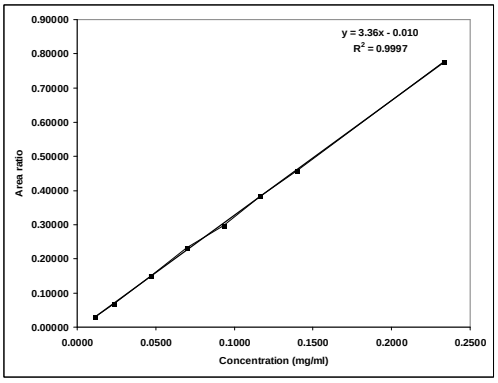
Caffeine



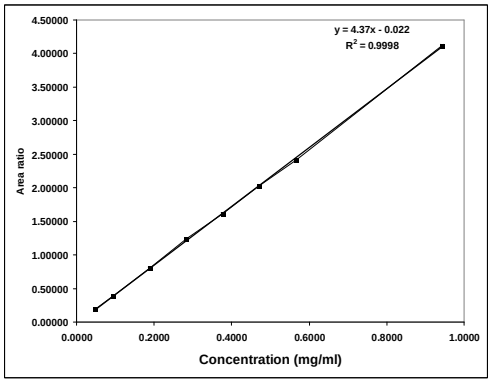
Dextromethorphan



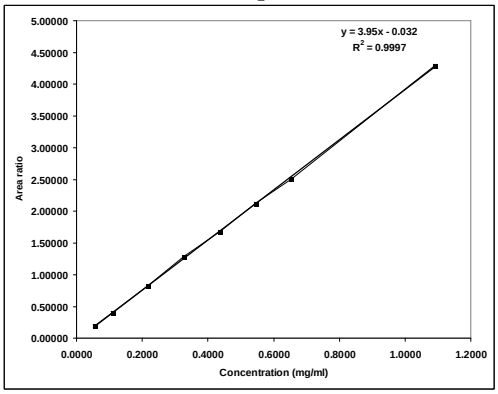
Codeine



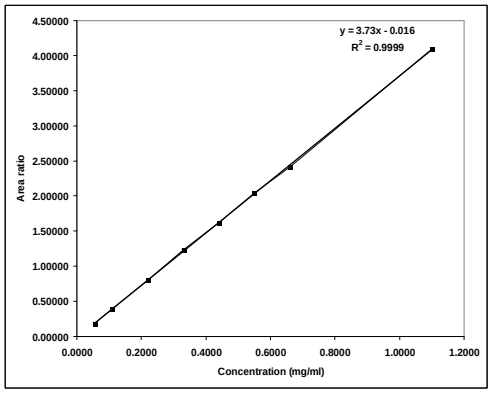
Morphine



Acetylcodeine



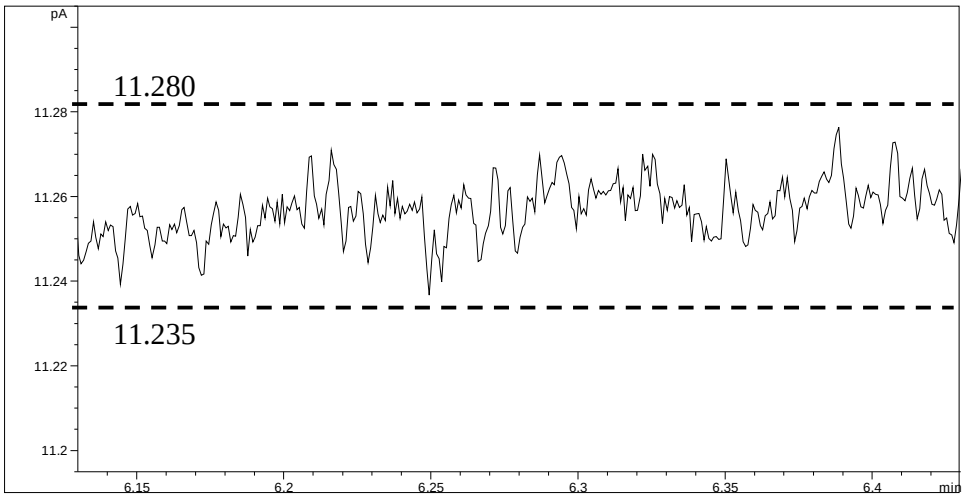
6-monoacetylmorphine



Heroin/diamorphine

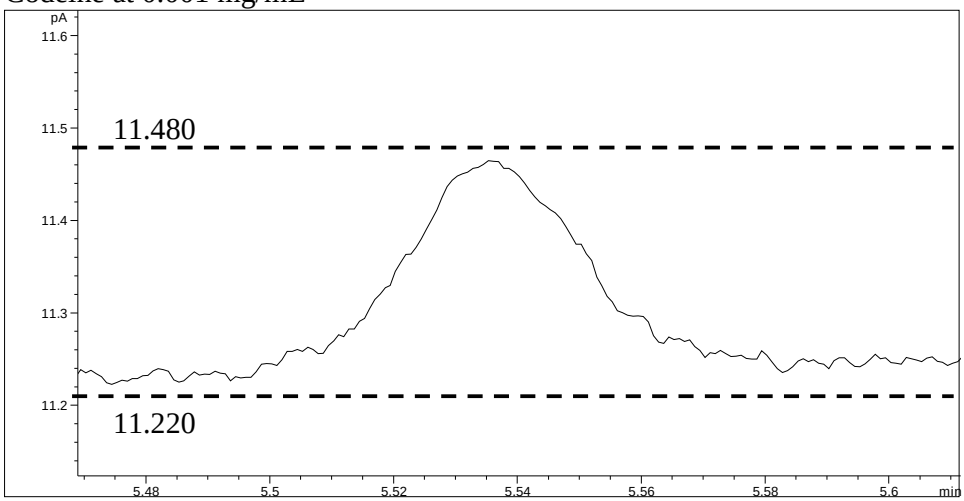
Figure A2: Example of three times signal-to-noise calculation

Blank



Blank signal-to-noise = 11.280 – 11.235
= 0.045

Codeine at 0.001 mg/mL



Codeine signal-to-noise = 11.480 – 11.220
= 0.260

LOD for codeine = $\frac{\text{Concentration of analyte}}{\text{Analyte signal}} \times \frac{S}{N}$
Blank signal

= $\frac{(0.001 \times 3)}{(0.260 / 0.045)}$

= 0.00052 mg/mL

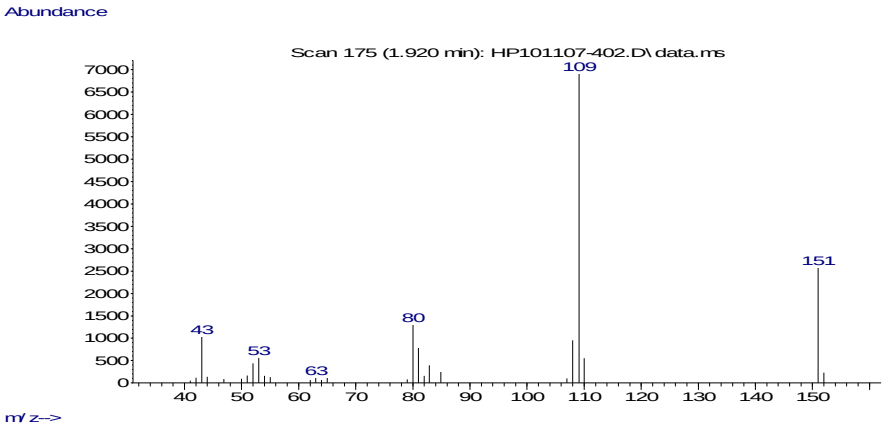
Appendix 11

Table A9: Normalized figures for alkaloids and cutting agents

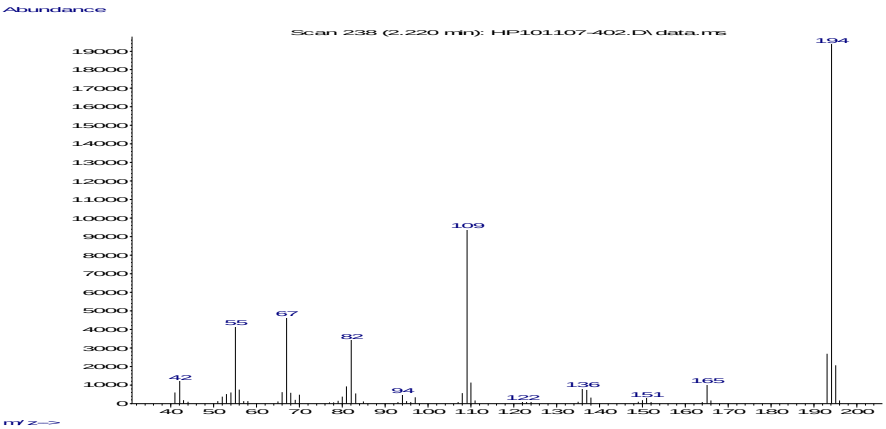
Sample	Opium-based alkaloids						Cutting agents							
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
A1OR	0.0666	0.9586	0.0622	0.0620	0.0694	0.0047	14.4041	0.0629	16.1441	7.0941	15.9004	0.1402	0.5412	0.4009
A1U1	0.0665	0.9449	0.0621	0.0621	0.0704	ND	14.2110	0.0621	16.0982	7.3065	16.0982	0.0822	0.1264	0.0442
A1U2	0.0669	0.9412	0.0625	0.0623	0.0711	0.0034	14.0604	0.0623	16.0551	7.0566	16.0551	0.0936	0.1469	0.0533
A1U3	0.0675	0.9240	0.0629	0.0627	0.0731	0.0046	13.6879	0.0636	15.9695	6.8723	15.7243	0.0865	0.1442	0.0577
A1U4	0.0675	0.9071	0.0628	0.0626	0.0744	0.0048	13.4378	0.0635	15.9913	6.8010	15.7445	0.0931	0.1800	0.0869
A1C1	0.0665	0.9743	0.0623	0.0623	0.0683	N.D.	14.6446	0.0623	16.0582	7.4177	16.0582	0.0833	0.1273	0.0440
A1C2	0.0674	0.9493	0.0629	0.0627	0.0710	0.0033	14.0915	0.0627	15.9503	7.0470	15.9503	0.0889	0.1390	0.0501
A1C3	0.0679	0.9119	0.0632	0.0630	0.0745	0.0047	13.4203	0.0640	15.8881	6.7785	15.6317	0.0870	0.1448	0.0578
A1C4	0.0690	0.8569	0.0639	0.0636	0.0805	0.0048	12.4149	0.0646	15.7317	6.4605	15.4752	0.0938	0.1808	0.0870
Mean	**0.0673**	**0.9298**	**0.0628**	**0.0626**	**0.0725**	**0.0043**	**13.8192**	**0.0631**	**15.9874**	**6.9816**	**15.8486**	**0.0943**	**0.1923**	**0.0980**
SD	**0.0008**	**0.0349**	**0.0006**	**0.0005**	**0.0037**	**0.0007**	**0.6711**	**0.0009**	**0.1242**	**0.2906**	**0.2164**	**0.0178**	**0.1323**	**0.1148**
C1OR	0.0911	0.3930	0.0740	0.0712	0.2318	0.0531	4.3141	0.0845	14.2408	2.5750	11.8442	0.5878	0.7012	0.1133
C1U1	0.0921	0.4049	0.0751	0.0725	0.2276	0.0500	4.3948	0.0859	13.9892	2.6252	11.6400	0.1384	0.1508	0.0124
C1U2	0.0905	0.3974	0.0737	0.0711	0.2279	0.0493	4.3899	0.0829	14.2318	2.6252	11.6400	0.1546	0.1707	0.0161
C1U3	0.0907	0.3902	0.0736	0.0708	0.2330	0.0516	4.3011	0.0829	14.2908	2.5840	12.0566	0.1798	0.2021	0.0223
C1U4	0.0914	0.3838	0.0738	0.0710	0.2382	0.0513	4.1997	0.0825	14.2443	2.5445	12.1276	0.1735	0.1947	0.0213
C1C1	0.0943	0.4357	0.0775	0.0755	0.2166	0.0394	4.6182	0.0880	13.4062	2.7868	11.3720	0.1447	0.1576	0.0129
C1C2	0.0918	0.3914	0.0744	0.0719	0.2346	0.0479	4.2635	0.0847	14.0911	2.5941	11.8105	0.1554	0.1715	0.0161
C1C3	0.0920	0.3838	0.0742	0.0715	0.2397	0.0502	4.1735	0.0829	14.1542	2.5393	12.0565	0.1863	0.2087	0.0224
C1C4	0.0920	0.3848	0.0743	0.0716	0.2392	0.0499	4.1801	0.0835	14.1348	2.5439	11.9724	0.1695	0.1898	0.0203
Mean	**0.0918**	**0.3961**	**0.0745**	**0.0719**	**0.2321**	**0.0492**	**4.3150**	**0.0842**	**14.0870**	**2.6020**	**11.8355**	**0.2100**	**0.2386**	**0.0286**
SD	**0.0011**	**0.0164**	**0.0012**	**0.0015**	**0.0073**	**0.0040**	**0.1407**	**0.0018**	**0.2717**	**0.0766**	**0.2484**	**0.1426**	**0.1746**	**0.0320**

1 = AC/HR, 2 = AC/MM, 3 = AC/(MM+HR), 4 = AC/(MP+MM+HR), 5 = MM/HR, 6 = (CD+MP)/(MM+HR), 7 = HR/MM, 8 = (CD+AC)/(MP+MM+HR), 9 = (CD+MP+MM+HR)/AC, 10 = HR/(CD+MP+AC+MM), 11 = (MP+MM+HR)/(CD+AC), 12 = PC/CF, 13 = (PC+DM)/CF, 14: DM/CF.
N.D. = Not detectable. This is not included in the mean value and SD.

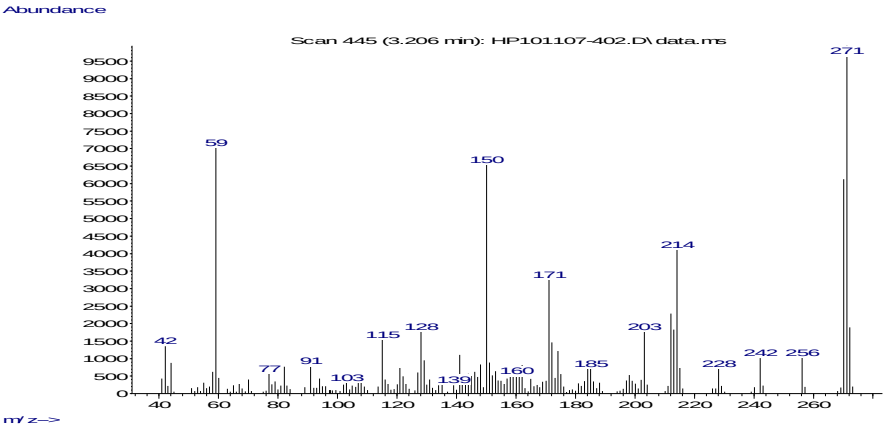
Figure A3: Mass spectra for 8 target major components



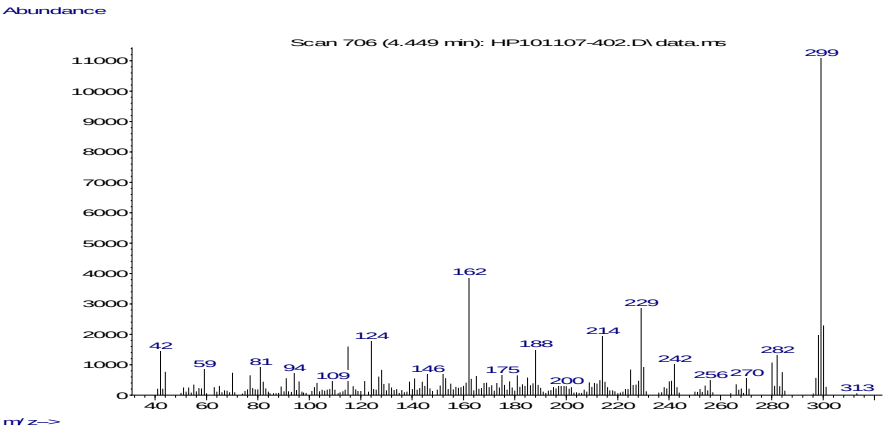
Paracetamol



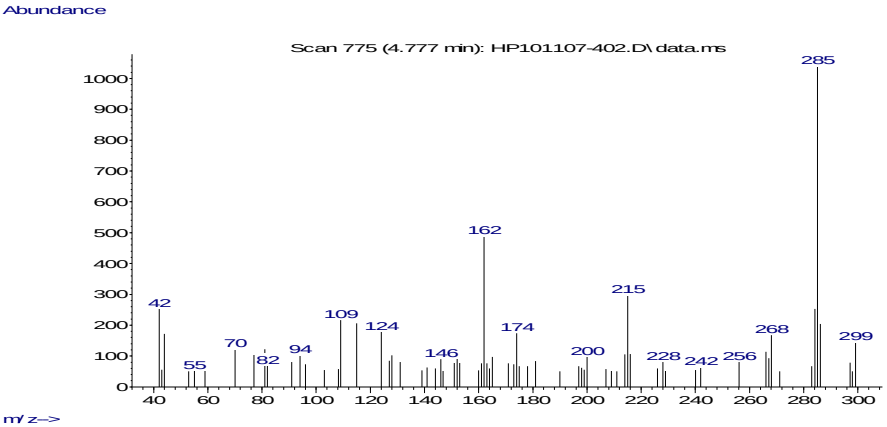
Caffeine



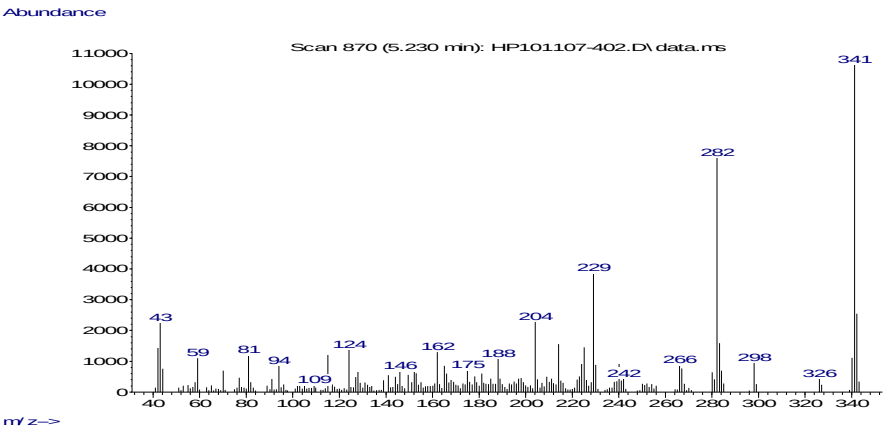
Dextromethorphan



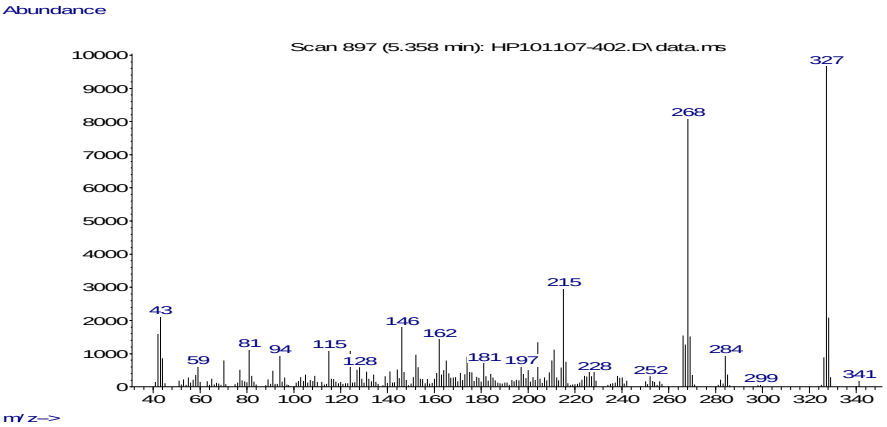
Codeine



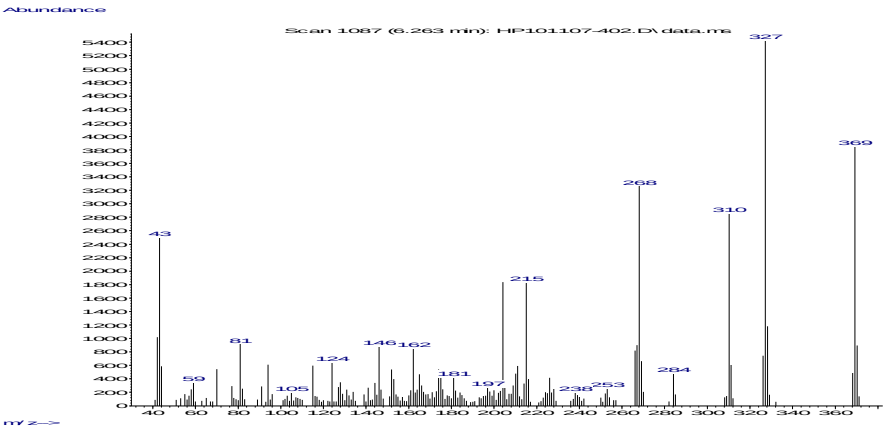
Morphine



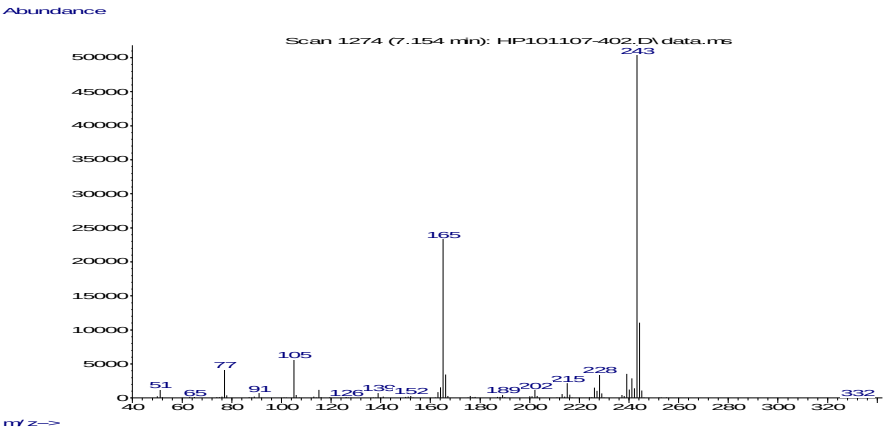
Acetylcodeine



6-Monoacetylmorphine

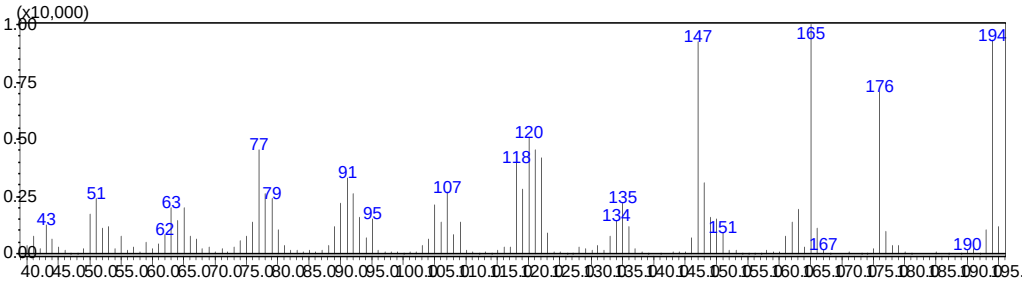


Heroin/diamorphine

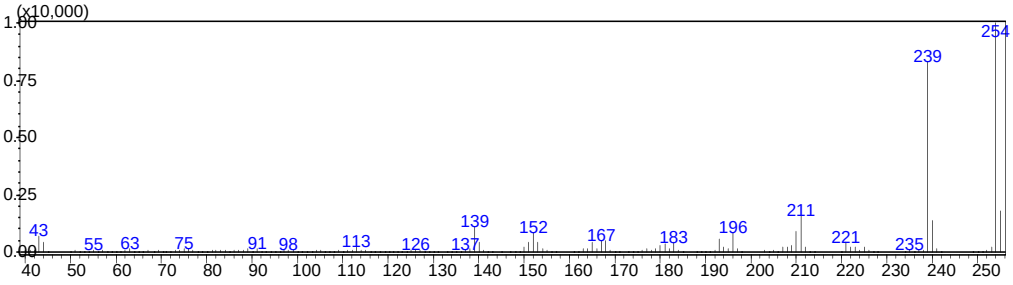


2,2,2 Triphenyl acetophenone

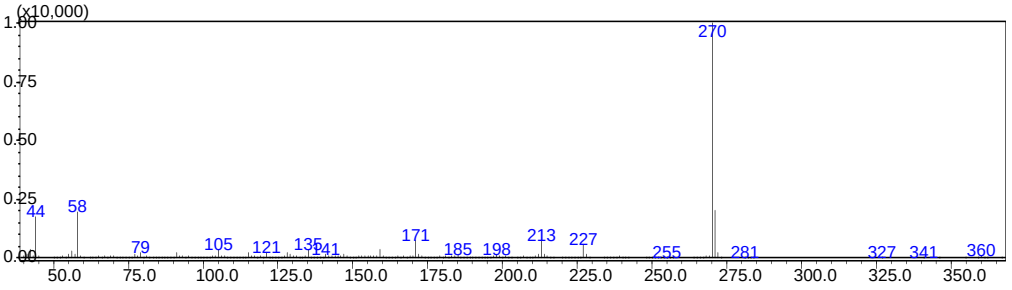
Figure A4: Mass spectra for 12 target manufacturing impurities



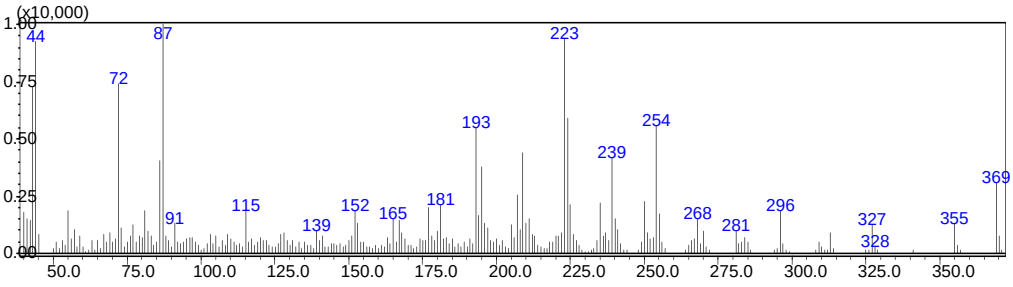
Meconine



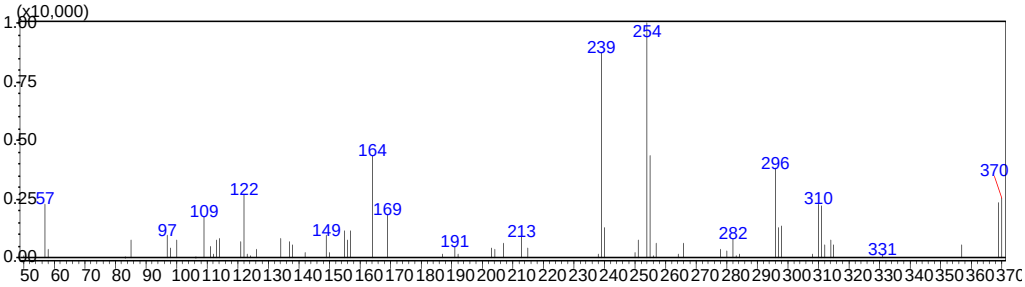
4-O-Acetylthebaol



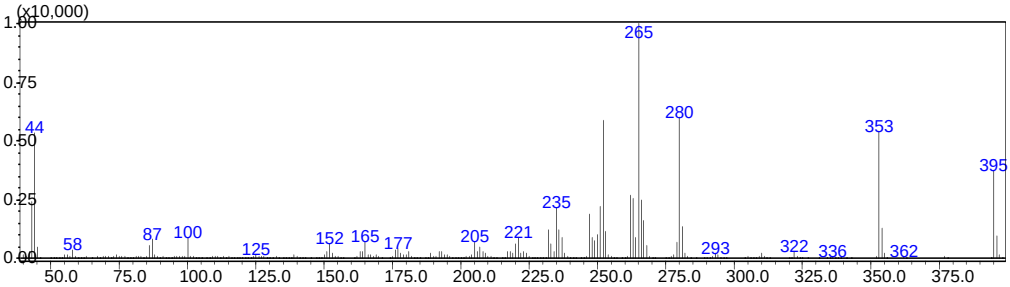
Unknown-270



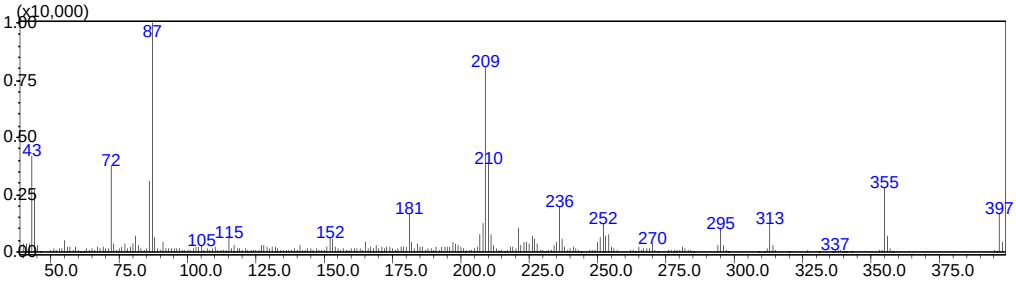
6-O,N-Diacetylnorcodeine



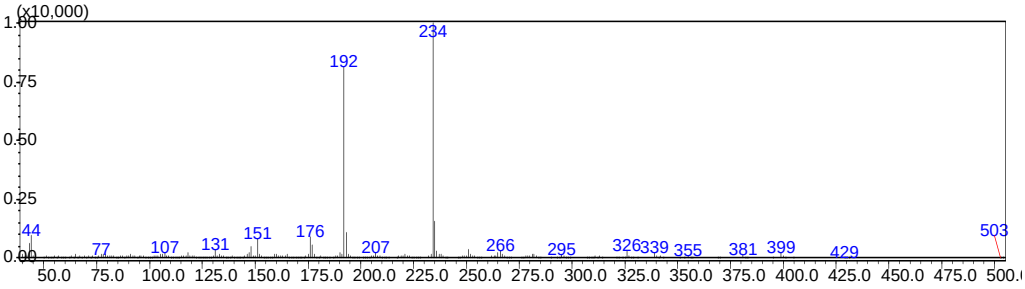
Unknown-254



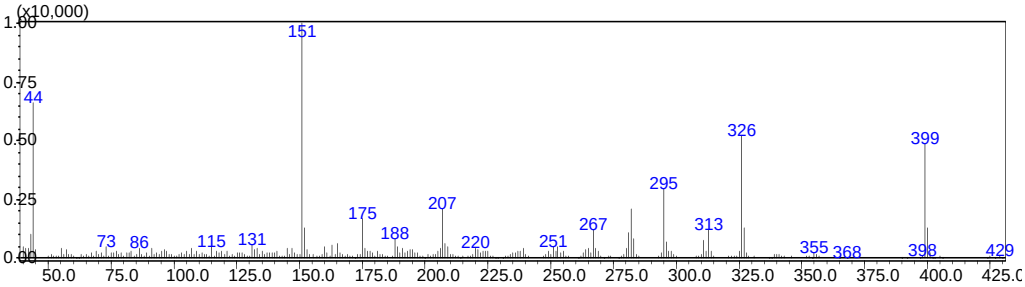
4-Acetoxy-3,6-dimethoxy-5-[2-(N-methyl-acetamido)]ethylphenanthrene



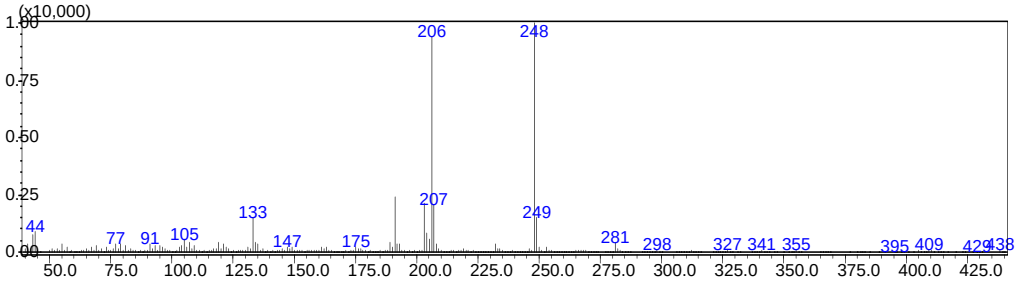
3-O,6-O,N-Triacetylnormorphine



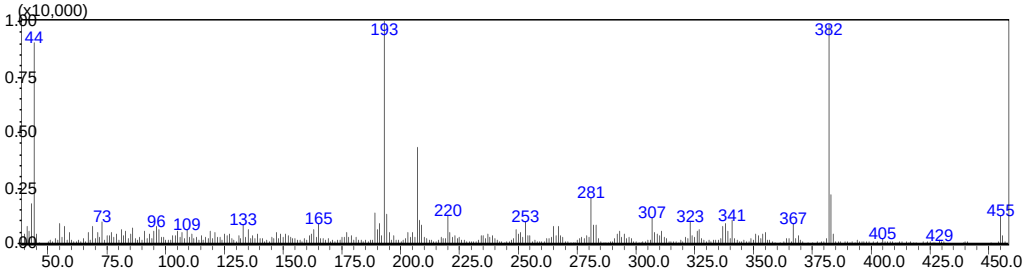
N-Acetylnorlaudanosine



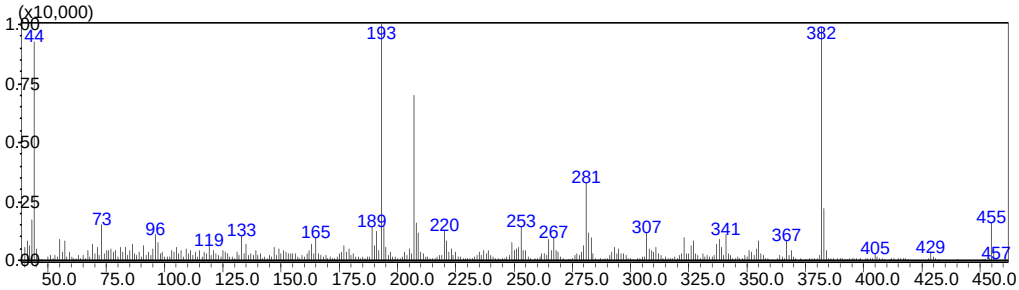
Unknown-151



N-Acetylnornarcotine



(E)-N-Acetylanhydronornarceine



(Z)-N-Acetylanhydronornarceine

Table A10: Summary of the percentage recovery (%) for the first extracts of three validation samples at four chosen acid strengths

Peak	A	B	C	Mean
		0.5 N		
1	79.2	83.1	76.7	79.7
2	95.9	96.1	94.3	95.4
3	N.D.	55.1	57.3	56.2
4	90.8	91.4	80.5	87.6
5	71.0	47.3	54.5	57.6
6	95.0	95.2	96.9	95.7
7	92.2	79.6	83.8	85.2
8	92.4	91.1	93.3	92.3
9	91.0	94.3	91.6	92.3
10	86.7	93.9	91.9	90.8
11	95.8	93.7	95.7	95.1
12	96.3	94.0	96.3	95.6
Mean	**89.7**	**84.6**	**84.4**	**85.3**
		1 N		
1	87.6	85.4	77.6	83.5
2	97.9	96.4	95.2	96.5
3	N.D.	50.3	53.6	52.0
4	91.9	93.3	82.3	89.1
5	65.0	50.9	50.6	55.5
6	95.5	95.6	96.5	95.9
7	92.4	81.2	80.3	84.6
8	91.1	91.4	91.9	91.5
9	87.8	95.8	89.3	90.9
10	88.7	97.2	92.2	92.7
11	94.9	94.3	94.8	94.7
12	95.0	94.1	95.2	94.8
Mean	**89.8**	**85.5**	**83.3**	**85.1**
		1.5 N		
1	88.8	88.2	81.4	86.1
2	95.5	96.7	96.0	96.1
3	N.D.	51.9	56.4	54.2
4	92.2	92.3	86.0	90.2
5	63.9	50.4	15.0	43.1
6	95.2	95.4	96.6	95.7
7	92.5	81.2	81.1	84.9
8	91.3	91.2	91.7	91.4
9	88.2	97.2	87.6	91.0
10	88.2	97.2	90.0	91.8
11	95.7	94.4	95.8	95.3
12	94.8	93.8	95.3	94.6
Mean	**89.7**	**85.8**	**81.1**	**84.5**

2 N

1	79.5	89.2	80.2	82.9
2	96.4	95.7	96.3	96.1
3	N.D.	55.2	55.7	55.4
4	93.2	93.6	86.8	91.2
5	65.7	57.9	49.7	57.8
6	95.2	96.2	96.3	95.9
7	92.3	83.2	81.4	85.7
8	90.6	92.7	91.8	91.7
9	81.6	98.1	91.5	90.4
10	91.9	95.6	90.6	92.7
11	95.0	94.0	95.5	94.8
12	93.9	94.4	94.7	94.3
Mean	**88.7**	**87.2**	**84.2**	**85.7**

N.D. = Not detected

Note: Due to the rounding-off, the grand mean value varies slightly when summing from the corresponding mean values.