Table S1 - Opioids

Drugs	Matrices	Sample amount	Sample pre-treatment	Microextraction technique	Optimized experimental conditions	Instrumental system	LOD (μg/L)	Absolute recovery (%)	Precision (%)	Ref
MTD	Urine	20 mL	Not needed	DI-SPME	• Sorbent: Cu nanocomposites • Extraction: 20 min (pH 9) • LD: ACN (0.4 mL, 5 min)	HPLC-UV	0.2	n.a.	≤ 8.96	[44]
MTD	Urine Whole blood	0.75 mL	• Dilution • pH adjustment • Protein precipitation • Centrifugation	LV-ESSM-LLME	• Extraction: 10 min (pH 4, 12 V, 1000 rpm) • SLM: NPOE • AP: HCl 10 mmol/L (0.025 mL)	HPLC-UV	0.7-2.0	23-28	≤ 7.5	[45]
	Plasma	1.5 mL		LV-EME	• Extraction: 20 min (pH 4, 15 V, 700 rpm) • SLM: NPOE • AP: HCl 10 mmol/L (0.025mL)		1.0-2.5	57-69	≤ 7.0	
MTD	Urine Plasma	10 mL	• pH adjustment • Dilution • Protein precipitation • Centrifugation	DES-AAELLME	• Extraction: 100 μL of TNO:CC (1:2 molar ratio) at pH 10 + 100 μL THF • Pushing and pulling from a syringe × 10 • Centrifugation • Supernatant injected (1 μL)	GC-FID	0.7	97.4	≤ 5.4	[46]
MTD	Plasma	0.2 mL	-	μSPE	• Sorbent: MIP • Extraction: 10 min by shaking (pH 7.4, 3 % NaCl) • LD: MeOH (0.2 mL, 6 min)	LC-MS/MS	1	80	≤ 8.0	[47]
MTD	Urine	10 mL	• pH adjustment • Lipidic precipitation • Centrifugation	MSPE	• Sorbent: MNGO • Extraction: 15 min (1100 rpm, pH 10) • LD: ACN (0.4 mL, 5 min)	HPLC-UV	25	97	≤ 7.98	[48]
MTD	Urine	2 mL	• Centrifugation • Dilution	DLLME-SFO	• Sample: NaCl (1.3% w/v) and borate buffer (pH 8.9) • DS: MeOH (580 μL) • ES: 1-undecanol (58 μL) • Rapid injection • Centrifugation • SFOs collected and injected.	HPLC-UV	1.67	97	≤ 5.12	[49]
	Serum	1 mL	• Protein denaturation and precipitation • Centrifugation • Dilution				3.34	95		

MTD	EBC	1 mL	Dilution	DLLME and ULLME	DLLME • Sample: pH 10 • DS: MeOH (1 mL) • ES: $CHCl_3$ (200 µL) • Rapid injection • Centrifugation • Evaporation on supernatant • Redissolution and injection ULLME • Sample: pH 10 • ES: $CHCl_3$ (200 µL) • Sonication • Centrifugation • Evaporation of supernatant • Redissolution and injection	HPLC-UV	0.5 (LLOQ)	n.a.	≤ 4.86	[50]
MTD	Urine	0.1 mL	-	MEPS	• Sorbent: C8 • Activation: 100 µL MeOH × 3 • Conditioning: 100 µL H_2O × 3 • Samples aspirated and discarded × 5 • Washing: 100 µL H_2O x 2 + 100 µL of 5 % MeOH × 1 • Elution: 50 µL of 0.1% COOH in MeOH	MS/MS	1.5	91.7-106.7	≤ 11.1	[40]
MTD	Plasma	4 mL	• Protein precipitation • Centrifugation • Dilution	SBME	• Extraction: pH 11.5 with 5% NaCl, 20 ºC, 700 rpm, 45 min • ES: 1-undecanol (25 µL)	GC-FID	7	15	≤ 7.3	[51]
	Urine	10 mL	Not needed				5.5	15.8		
MTD	Urine	3 mL	Not needed	TF-SPME	• Coating: C18- polyacrylonitrile • Precondition: 30 min in MeOH/H_2O (1:1) • Extraction: 10 min, 1200 rpm	DART-MS/MS	> 0.5	n.a.	≤ 4	[52]

MTD	Plasma	50 µL	Centrifugation	MEPS	• Sorbent: C18 • Activation: 100 µL ACN × 3 • Conditioning: 100 µL H_2O × 3 • Samples aspirated and discarded × 15 • Washing: 100 µL H_2O × 1 + 100 µL 5 % ACN × 1 • Elution: 250 µL ACN × 2 • Evaporation of supernatant • Redissolution and injection	HPLC-CD	1.2	90.1-95.5	≤ 5.8	[53]
	Dried blood spot	5- 50 µL	• Solid-liquid extraction • Evaporation to dryness • Redissolution						
MTD	Urine	Urine and plasma: 500 µL	Urine and plasma: • Centrifugation • Filtration • Dilution	DLLME	• Sample at pH 10 • DS: MeOH (2.5 mL) • ES: $CHCl_3$ (200 µL) • Centrifugation • Sediment dried and redissolved	HPLC-UV	4.9	98.6-100.3	≤ 6.4	[42]
	Plasma						7.3			
	Saliva	Saliva and sweat: 100 µL	Saliva and sweat: Dilution				25.12			
	Sweat						24.85			
MTD	Urine Plasma	5 mL	• Salt addition • pH adjustment	HS-SPME	• Coating: PPy-α- COOH • Extraction: 25 min, 600 rpm, pH 11, 20% NaCl, 45 ºC • TD: 280ºC, 2 min	GC-FID	0.035	n.a.	≤ 10.9	[54]

MTD	Urine	1.75 mL	• Dilution	HF-LPME-BE	• Extraction: 27 min (pH 9.8, 1000 rpm) • BE: 9.5 min • SLM: dibutyl ether (80 µL) • AP: phosphate buffer (0.01 M), 7 µL, pH 2.7	HPLC-UV	0.2	77	≤ 5.9	[55]
	Plasma	1.16 mL								
MTD	Urine	50 µL	Samples used without pre-treatment	MEPS	• Sorbent: C8 • Activation: 50 µL MeOH × 1 • Conditioning: 50 µL H_2O × 1 • Samples aspirated and discarded × 5 • Elution: 30 µL MeOH × 1, 40 ºC, 2 min	GC-MS	0.4	60	≤ 15	[56]
EDDP **MTD**	Saliva	0.1 mL	Dilution	DI-SPME	• Coating: PDMS • Extraction: 30 min • TD: 5 min, 250ºC	GC-MS	4-8	97.9 -103.6	≤ 4.3	[57]
EDDP **MTD**	Hair	50 mg	• Hydrolysis • Dilution • Salt addition • pH adjustment	DI-SPME	• Coating: PDMS • Extraction: 30 min, pH 9.2, 10% NaCl • TD: 5 min, 250ºC	GC-MS	0.15-2.48 ng/mg	103.6-107.2	≤ 13.3	[58]
EDDP **MTD**	Plasma	0.1 mL	• Dilution • pH adjustment	DI-SPME	• Coating: PDMS • Extraction: 30 min, pH 9 • TD: 10 min, 250ºC	GC-MS	5-9	n.a.	< 5.2	[59]
EDDP **EMDP** **MTD**	Hair	10 mg	Digestion	HS-SPME	• Coating: PDMS/DVB • Extraction: 20 min, 110ºC, 150 rpm • TD: 5 min, 260ºC	GC-MS	0.03-0.05 ng/g	10.5-17.4	≤ 7.2	[60]
MTD **PTD**	Urine	3 mL	• pH adjustment • Dilution • Salt addition	SPME	• Coating: PDMS • Extraction: 30 min, 15% NaCl, pH 11 • TD: 240ºC, 1 min	GC-NPD	< 1	n.a.	≤ 8.7	[61]
TMD	Rabbit brain tissue	2 g	• Solid-liquid extraction • Centrifugation • Evaporation • Dilution	DI-SPME	• Washing:1 mL acetone:ACN (3:1, v/v) • Eluting step:0.2 mL HCl (1 mol/L):MeOH (1:1, v/v)	HPLC-UV	1	76.2-91.2	≤ 8.2	[43]
TMD	Urine	7 mL	• pH adjustment • Salt addition • Dilution	DI-SPME	• Support: MWCNTf-ZnO • Solvent: 1-octanol (1.5 min) • Extraction: 30 min (800 rpm), 30% NaCl, pH 11 • LD: MeOH (50 µL), 15 min	GC-FID	0.03	n.a.	≤ 5.43	[62]

TMD	Urine Blood	Not available	• Dilution • pH adjustment	DLLME	• Sample at pH 12 • DS: EtOH (1.0 mL) • ES: CCl_4 (30 μL) • Centrifugation (5000 rpm, 3 min)	GC-MS	0.08	n.a.	≤ 3.6	[63]
TMD	Urine	9 mL	• pH adjustment • Salt addition	SA-DSDME	• Sample pH at 10.7, 5% NaCl with Triton X-100 (36 μL, 50 mmol L^{-1}). • ES: *n*-octanol (14 μL) • Extraction: 25 min at 55ºC (750 rpm)	GC-FID	5.1	63.8	≤ 10	[64]
	Plasma	4 mL	• Protein precipitation • Centrifugation • Dilution • pH adjustment • Salt addition				6.5	60.8		
TMD	Urine	5 mL	• pH adjustment • Salt addition • Centrifugation	BS-DLLME	• Sample at pH 12, 7.5% NaCl; • DS: acetone (0.6 mL) • ES: ethyl acetate (30 μL) and $CHCl_3$ (70 μL) • Centrifugation • Sediment collected and dried • Redissolution	HPLC-FD	0.2	n.a.	≤ 4.1	[65]
TMD	Urine	1 mL	• pH adjustment • Dilution • Filtration	PFSPE	• Sorbent: PMMA/PS • Conditioning: EtOH (100 μL) and H_2O (100 μL) • Extraction: Sample pushed through the syringe • Elution: MeOH (200 μL)	CD-IMS	1.6	n.a.	≤ 9.5	[66]
	Plasma	1.5 mL	• Protein precipitation • Centrifugation • Filtration • pH adjustment • Dilution				9.4	n.a.		
TMD	Urine	12 mL	Urine samples used without pre-treatment	SBME	• Extraction: pH 12.0, 1000 rpm, 25 min • ES: *n*-nonanol (4 μL)	GC-MS	0.02	86-109	≤ 5.9	[67]
	Plasma	2 mL	Dilution							

TMD	Urine Plasma	5 mL	• Protein precipitation • Dilution • pH adjustment	HF-LPME	• Extraction: 40 min (pH 11, 4 mol/L NaCl, 1000 rpm) • SLM: *n*-C12 • AP: ACN (25 μL)	GC-MS	0.08	n.a.	≤ 7.9	[68]
TMD	Urine	2 mL	pH adjustment	LPME	• Sample at 0.01 M NaOH, pH 11.5 • Extraction: *n*-C8 (100 μL), 25 min, 1250 rpm, 50ºC • BE: 3.5 μL phosphate buffer (0.01 mol/L, pH 2.5), 25 min, 1250 rpm, 50ºC	HPLC-FD	0.12	64	≤ 6.29	[69]
	Plasma	0.4 mL	• pH adjustment • Dilution							
TMD	Plasma	0.5 mL	• pH adjustment • Dilution	SPME	• Coating: PDMS/DVB • Extraction: 30 min, 100 ºC, 2000 rpm • TD: 2 min, 250ºC	GC-MS	0.2	n.a.	≤ 7.8	[70]
MOR	Urine	2 mL	• pH adjustment • Dilution	EME	• Extraction: 24 min (pH 6, 90 V, 1000 rpm) • SLM: NPOE, with 10% TEHP and 10% DEHP • AP: HCl 0.1 mol/L (20 μL, pH 1.0)	DPV(SPCE)	1.5	71-76	≤ 9.4	[71]
MOR	Hair	50 mg	• Washing • Digestion • Solid-liquid extraction • Filtration • Dilution	MSPE	• Sorbent: SMMNP • Extraction: 20 min (1100 rpm, pH 9) • LD: MeOH (0.3 mL, 10 min)	HPLC-UV	0.1	n.a.	≤ 2.59	[72]
COD **MOR**	Urine	2 mL	• Filtration • Sonication • Dilution	BAμE	• Coating: AC • Extraction: 2.5 h, 1000 rpm (pH 7) • LD: MeOH/ACN (1:1, 1.5 mL), 30 min • Evaporation to dryness and redissolution	HPLC-DAD	0.06-0.90	38.4-41.3	≤ 8.0	[41]
6-MAM **COD** **MOR**	Hair	10 mg	• Digestion • Evaporation • Derivatization	HS-SPME	• Coating: PDMS • Extraction: 25 min, 125 ºC • TD: 10 min, 260ºC	GC-MS	2-5 μg/g	n.a.	≤ 14.8	[73]

COD MOR OXY	Urine	4.8 mL	• Dilution • pH adjustment	EME	• Extraction: 10 min (pH 5, 90 V) 700 rpm • SLM: NPOE containing 15% (v/v) DEHP • AP: HCl 100 mmol/L (10 µL)	HPLC-UV	10.0-50.0	n.a.	≤ 12.6	[74]
BPN MTD N-BPN NLX	Plasma	0.1 mL	Not necessary	MEPS	• Sorbent: C8 • Activation: 100 µL ACN x 3 • Conditioning: 100 µL H_2O x 3 • Samples aspirated and discarded x 15 • Washing: 100 µL H_2O x 2 + 100 µL of 5% ACN x 1 • Elution: 250 µL ACN x 2 • Evaporation to dryness and reconstitution	HPLC-CD	0.04-0.9	86-96	≤ 4.3	[75]
FTY	Urine	0.8 mL	Not necessary	DLLME	• Sample at pH 10; • DS: 2-propanol (0.1 mL) • ES: chlorobenzene (30 + 20 µL) and $CHCl_3$ (70 µL) • Sonication (11 min, 45ºC) • Centrifugation • Sediment collected and redissolved	GC-MS	1.0	88.9-102.	≤ 14.3	[76]
FTY	Urine	5 mL	Dilution	Online-CME	• Sorbent: MIX • Extraction: sampling flow rate of 7 mL/min, 25 min • LD: MeOH (5 mL, 3 min)	HPLC-UV	3	n.a.	≤ 12	[77]
	Plasma	0.5 or 0.25 mL								
FTY	Breath	18 mL	• Gas-liquid extraction • Evaporation • Reconstitution	DI-SPME	• Sorbent: PDMS/DVB • Extraction: 60 min, 85ºC • TD: 265ºC, 5 min	GC-MS	10	n.a.	≤ 12.1	[78]
FTY	Urine	1.8 mL	• pH adjustment • Dilution	SDME	• Sample at 0.01 mol/L NaOH, pH at 10.7 • Extraction: *n*-C8 (100 µL), 30 min, 1000 rpm, 30 ºC	HPLC-UV	0.1	49	≤ 8.8	[79]

	Plasma	0.75 mL			• BE: 5 µL percloric acid (0.001 mol/L), 20 min, 700 rpm, 30 ºC				
FTY	Plasma	1 mL	• Protein precipitation • Centrifugation • pH adjustment • Salt addition	HS-SPME	• Coating: PDMS • Extraction: 30 min, pH 11, 25% NaCl and 25 % K_2CO_3, 80ºC • TD: 270ºC, 5 min	GC-MS	0.03	n.a.	≤ 4.9	[80]
FTY	Plasma	1 mL	• Dilution • pH adjustment • Salt adittion	DI-SPME	• Coating: PDMS/DVB • Extraction: 30 min, 6% NaCl • Washing: H_2O 30s, 20% MeOH 30 s • TD: 270ºC, 5 min	GC-MS	0.8 (LOQ)	n.a.	≤ 7.0	[81]
AFT **FTY** **SFT**	Urine	2.5 mL	Both: • Filtration DLLME: • Dilution	DLLME HF-LPME	DLLME • Sample at pH 10; • DS: MeOH (2 mL) • ES: $CHCl_3$ (162 µL) • Shaking (10 s) • Centrifugation (3500 rpm, 5 min) • Sediment collected and redissolved HF-LPME • Extraction: 20 min (45ºC, 0.5 mol/L NaOH, 1200 rpm) • SLM: isoamyl benzoate • AP: H_2SO_4 solution (0.05 mol/L, 10 µL)	HPLC-DAD	DLLME: 0.4-1.9 HF-LPME: 1.1-2.3	n.a.	≤ 15.9	[82]
	Plasma	1.25 mL	Both: • Filtration • Dilution DLLME: • Protein precipitation • Centrifugation • pH adjustment							
COD	Urine	Not available	• Filtration • Dilution	TFME	• Conditioning: 5 min using 20 mmol/L Tris-HCl, 140 mmo/L NaCl, 5 mmol/L KCl, and 1 mmol/L $MgCl_2$ at pH 7.4 solution and allowed to dry • Extraction: 30 min (400 rpm, 25ºC) • LD: 200 µL (ACN/ H_2O, 90/10, v/v) under vortex (10 min) • Evaporation to dryness and redissolution	EI-IMS	3.4	90.1	≤ 8.1	[83]

HER **OXYC**	Urine	0.25 mL	Filtration	Online-CME	• Sorbent: C18 or C18-Phe • Extraction: sampling flow rate of 0.02 mL/min, 12.5 min • LD: MeOH (0.25 mL, 2.5 min)	MS	0.6-10.9	n.a.	≤ 5.9	[84]
MOR	Urine	Not available	pH adjustment	DI-SPME	• Coating: Peptide functionalized CNTs • Extraction: 5 min sonication, pH 7 (40ºC) • LD: H_2O/MeOH (80/20, v/v, 200 µL), 2 min	HPLC-UV	0.1	n.a.	n.a.	[85]
COD **MOR** **MTD**	Urine	2 mL	• Centrifugation • Filtration • Dilution • pH adjustment	DLLME	• Sample at pH 9.8; • DS: acetone (0.5 mL) • ES: $CHCl_3$ (300 µL) • Shaking (30 s) • Centrifugation (10 min, 4000 rpm) • Sediment collected and redissolved	HPLC-DAD	9-25	87.5-107.9	≤ 6.1	[86]
MOR	Urine	1 mL	Not available	DI-SPME	• Coating: CNTs • Extraction: 2 min electric field (1 V); pH 5 (45ºC) • LD: H_2O/MeOH (80/20, v/v, 200 µL) using an electric field (1 V)	HPLC-UV	0.15	77	n.a.	[87]
COD **MOR**	Urine	10 mL	• Centrifugation • Filtration • Dilution. • pH adjustment • Salt adittion	DLLME-SFO	• Sample: NaCl (1.3% w/v) and K_2CO_3 (10% w/v, pH 10.2) • DS: MeOH (150 µL) • ES: 1-undecanol (40 µL) • Centrifugation (5000 rpm, 5 min) • Ice bath and extraction (5 min) • SFOs solidified, collected and injected • Rapid injection	HPLC-UV	5.0-17.0	n.a.	≤ 4.6	[88]
	Hair	20 mg	• Washing • Digestion • Filtration • Evaporation • Dilution • pH adjustment				5.0-8.5 µg/g			

MTD	Sweat	Cotton pad (0.5 × 0.5 cm) 4-6 rubbing on the forehead	• Acidic extraction • pH adjustment	HS-SPME	• Coating: PDMS • Extraction: 10 min (90ºC) + 3 min (90ºC) for derivatization • TD: 3 min, 250ºC	GC-MS	0.08 ng/pad	102.8	≤ 9.9	[89]
AFT **BPN** **EDDP** **FTY** **MOR** **MTD** **NBP** **NFT** **6-MAM** **SFT**	Blood	0.5 mL	• Protein precipitation • Centrifugation • Dilution • Salt addition • pH adjustment	DLLME	• DS: 0.25 mL of MeOH • ES: 100 µL $CHCl_3$ • Sonication (1 min) • Centrifugation (4000 rpm,5 min) • Infranatant collected, evaporated and redissolved • Rapid injection	UPLC-MS/MS	0.05-2	3-117	≤ 15	[90]
6-MAM **BPN** **COD** **DAM** **EDDP** **MOR** **MTD** **NBP**	Oral fluid	0.12 mL	• Dilution • pH adjustment • Protein precipitation • Sonication • Centrifugation	MEPS	• Sorbent: C18 • Conditioning: 250 µL MeOH × 2 + 250 µL H_2O/MeOH (80:20, v/v) × 2 • Samples aspirated and discarded × 5 • Washing: 100 µL 50 mM NH_3 in H_2O/MeOH (90:10, v/v) × 3 • Elution: 100 µL 5 mM COOH in MeOH × 5	LC-MS/MS	0.2-2	67-102	≤ 20	[91]
MTD **PTD**	Blood	1 mL	• Dilution pH adjustment	DLLME HF-LPME	DLLME • ES and DS: 100 µL toluene • Sonication (3 min) and manual shaking • Centrifugation (10000 rpm,3 min) • Supernatant collected HF-LPME • SLM: toluene • AP: toluene (10 µL)	GC-MS	0.5-2.5	DLLME: 83.3-99.1 HF-LPME 79.4-92.7	DLLME: ≤ 5.2 HF-LPME ≤ 3.7	[92]

	Urine				• Extraction: 10 min (500 rpm, pH 13.0, 30ºC) • For blood samples, 10 mg of NaCl was added to break emulsion					
6-MAM BPN COD DMP EDDP EMOR HER MTD NPD PTD	Urine	4 mL	• Centrifugation • Filtration • pH adjustment	DLLME	• DS: 1400 μL isopropanol • ES: 600 μL DCM • Extraction: pH ≥ 11.5 • Rapid injection • Centrifugation (10000 rpm,5 min) • Infranatant collected, evaporated and redissolved	CE-TOF-MS	0.25-10	0-107	n.a.	[93]
COC MOR	Horse urine	10 mL	pH adjustment	SDME	• Solvent: 5 μL of $CHCl_3$/MeOH (90:10, v:v) • Extraction: 20 min (25ºC, pH 11, 500 rpm) • Evaporation and redissolution	OT-CEC	5.12-8.27	103.1-108.3	≤ 2.1	[94]
ACOD COD HER	Urine	2 mL	• Filtration • pH adjustment • Dilution	MSPE	• Sorbent: Fe_3O_4/SiO_2/poly(MAA-*co*-EDMA) • Extraction: vortex (5 s, pH 9.2) • Washing: 0.5 mL H_2O × 5 • LD: 0.04 mL of acetone containing 0.5% COOH (v/v) with 10 s vortex.	CE-DAD	15-53	85.4-109.7	≤ 12.4	[95]
MTD	Hair	10 mg	• Washing • Drying • Digestion • Salt addition	HS-SPME	• Coating: PDMS • Extraction: 10 min (90 ºC) • Derivatization (3 min, 90ºC, with 5 μL of acetic anhydride) • TD: 4 min, 260ºC	GC-MS	0.05 ng/mg	9.5	≤ 9.9	[96]
COD MTD OXYC MFN, BZC, LDC, PRC,	Urine	0.5 mL	• Dilution • pH adjustment • Salt addition	DI-SPME	• Coating: PDMS/DVB • Extraction: 30 min (pH 12, 40 ºC) • Derivatization • TD: 260ºC, 2 min	GC-MS	20-200	90-114	≤ 10.9	[97]

MPV, TTC, BPC, DBC, PTC										
MTD	Hair	20 mg	• Washing • Drying • Digestion • pH adjustment • Salt addition	HS-SPME	• Coating: PDMS • Extraction: 5 min (90ºC, pH 10.3) • TD: 25 ºC, 3 min	GC-MS	0.35 ng/mg	n.a.	≤ 7.4	[98]
MOR NLX MTD 6-MAM	Oral fluid	0.5 mL	• Dilution • Salt addition • Protein precipitation	US-DLLME	• DS: 1.4 mL MeOH • ES: 200 µL $CHCl_3$ • Extraction: 2.5% NaCl, pH 8.0 • Ultrassound for 5 min • Centrifugation (3500 rpm, 5 min) • Infranatant collected, evaporated and redissolved	UPLC-MS/MS	0.1-25	80.9-129	≤ 14.5	[99]
MOR COD 6-MAM	Hair	10 mg	• Washing • Digestion • PLE extraction • Evaporation • Redissolution • Centrifugation • Dilution • pH adjustment • Salt addition	PLE-DLLME	• DS: 500 µL of 2-propanol • ES: 200 µL of $CHCl_3$ • Extraction: 24% NaCl, pH 11.0, 10% iso-propanol • Sonication for 10 min • Centrifugation (9000 rpm, 5 min, 3ºC) • Infranatant collected, evaporated and redissolved	HPLC-HRMS/MS	0.2-0.5 pg/mg	33-49	≤ 21	[100]
COD MOR	Urine and plasma	7 mL	• Dilution • pH adjustment	EME	• Extraction: 30 min (pH 6, 25 V) 500 rpm • SLM: Agarose gel 1 % (m/v) pH 3.0, 15 m thickness • AP: same as SLM	HPLC-UV	1.5	68-74	≤ 10.3	[101]
TMD MTD	Urine, plasma and saliva	2 mL	• Dilution • pH adjustment • Filtration • Centrifugation	MSPE	• Sorbent: Zn-Al layered double hydroxide intercalated with tyrosine • Extraction: ultrasound (5 min, pH 8) • LD: 0.1 mL of acetone, 15 min under sonication	GC-MS	0.15-2.5	n.a.	≤ 10.7	[102]
MTD	Saliva	1 mL	• Dilution • pH adjustment • Filtration	US-DLLME	• ES: 1 mL $CHCl_3$ • Extraction: pH 8.0 • Ultrasound for 5 min • Centrifugation (3500 rpm, 5 min) • Infranatant collected, evaporated and redissolved	GC-MS	50.0	94.2-107.5	≤ 7.9	[103]
MOR 6-MAM	Urine	1 mL	pH adjustment	MSPE	• Sorbent: Graphene oxide – Fe_3O_4 • Extraction: vortex (15 min, pH 6)	UHPLC-MS/MS	0.02-0.03	82.7-89.4	≤ 10.6	[104]

COD					• LD: 3 mL of MeOH with 10 % ammonia, 10 min vortex					
TMD	Urine	1.5 mL	• Dilution • pH adjustment	EME	• Extraction: 20 min (pH 4, 180 V) 1000 rpm • SLM: Porous Aromatic Framework-48 with the nitro functional groups with NPOE • AP: 100 mmol/L HCl (20 µL)	IMS	1.5	94-98	≤ 4.7	[105]

Table S2 - Cocaine

Drugs	Matrices	Sample amount	Sample pre-treatment	Microextraction technique	Optimized experimental conditions	Instrumental system	LOD (μg/L)	Absolute recovery (%)	Precision (%)	Ref
BE **BN** **CCE** **COC** **ECG** **m-HOBE** **NC** **NCE**	Urine	1 mL	• Dilution • pH adjustment • Centrifugation	MDSPE	• Sorbent: DVB+VP@SMPS@Fe_3O_4 • Extraction: sonication (1 min) + stirring (300 rpm, 20 min) • LD: 10 min (1 mL, MeOH/ACN, 4:1, v/v)	LC-MS	0.09-1.10	75.1-105.7	≤ 6.6	[114]
COC **ECGME**	Saliva	0.5 mL	• pH adjustment	LOV-μSPE	• Sorbent: Mixed-mode cationic/reversed-phase • Washing: H_2O (0.5 mL) + IPA (0.5 mL) • Drying: air (1.5 mL × 2) • Elution: 0.1 mL of (3% v/v) NH_3 in IPA	IMS	0.14-0.3	n.a.	≤ 28	[115]
AEME **BE** **CCE** **COC**	Hair	50 mg	• Washing • Digestion • Evaporation to dryness • Derivatization • pH adjustment	HF-LPME	• Extraction: 10 min (pH 2400 rpm, pH 9-10) • SLM: DHE • AP: 0.05 mol/L HCl (50-70 μL) • Evaporation • Derivatization	GC-MS	0.05-0.1 ng/mg	n.a.	≤ 14.4	[116]
CCE **COC** **NC**	Breast milk	0.5 mL	• pH adjustment • Salt adittion	HF-LPME	• Extraction: 30 min (2400 rpm, pH 9.0, 25% NaCl) • SLM: 1-octanol • AP: 0.4 mol/L HCl • Evaporation • Derivatization	GC-MS	5-7	32.0-67.4	≤ 15.9	[112]
BE **COC** **ECGME**	Urine	0.2 mL	• Centrifugation • Dilution • pH adjustment	MEPS	• Sorbent: 80 % C8 + 20 % SCX • Conditioning: 250 μL MeOH × 1 + 250 μL 0.1% COOH × 1 • Samples aspirated and discarded × 6 • Washing: 50 μL 0.1% COOH × 4 + drying • Elution: 100 μL of 1% NH_4OH in MeOH × 4 • Evaporation to dryness and derivatization	GC-MS	25 (LLOQ)	14.5-83.3	≤ 14.38	[111]
BE **CCE** **COC** **ECGME**	Plasma	0.1-1.0 mL	• pH adjustment • Dilution	μSPE	• Sorbent: MMIP • Extraction: 4 min (20ºC, 100 rpm, 0.2 mL *n*-C6) • Elution: 2 mL DCM/IPA/NH_4OH (75:20:5, v:v:v), ultrasound irradiation (5 min) • Evaporation to dryness • Re-dissolved with 0.04 mL of 2mM $C_2H_7NO_2$ in MeOH	LC-MS/MS	0.000013-0.00036	91-102	≤ 10	[113]

BE **CCE** **COC** **ECGME**	Plasma	0.1-1.0 mL	• pH adjustment Dilution	µSPE	• Sorbent: MIP • Extraction: 10 min (50ºC, 150 rpm) • Elution: 10 mL DCM/IPA/ NH_4OH (76:20:4, v:v:v), ultrasound irradiation (8 min) • Evaporation to dryness • Re-dissolved with 0.1 mL of 2mM $C_2H_7NO_2$ in MeOH	LC-MS/MS	0.061-0.87	94-103	≤ 12	[117]
BE **CCE** **COC** **ECGME**	Urine	5 mL	• pH adjustment Dilution	µSPE	• Sorbent: MIP • Extraction: 15 min (30ºC, 200 rpm) • Elution: 5 mL DCM/IPA/NH_4O (72:20:8, v:v:v), ultrasound irradiation (8 min) • Evaporation to dryness • Redissolved with 0.05 mL of 2mM $C_2H_7NO_2$ in MeOH	LC-MS/MS	0.049-0.5	89-100	≤ 10	[118]
CCE **LVM** **NC** **TCOC**	Hair	20 mg	• Washing • Digestion pH adjustment	DI-SPME	• Sorbent: PDMS • Extraction: 1 h, 80 ºC • TD: 2 min	GC-MS	0.1 ng/mg	n.a.	≤ 20	[119]
COC **LIDO**	Urine	3.5 mL	• pH adjustment Dilution	HF-LPME	• Extraction: 30 min (700 rpm, pH 11.0, 20 % NaCl) • SLM: *n*-C12 • AP: ACN (25 µL)	GC-MS	0.01-0.05	25-35	≤ 9.3	[120]
AEME **BE** **CCE** **COC**	Meconium	0.3 g	• Digestion • Agitation • Centrifugation pH adjustment	DPX	• Sorbent: SCX • Conditioning: 1 mL ACN • Samples sucked and held for 1 min • Washing: 1 mL H_2O • Elution: DCM/IPA/NH_4OH (78:20 :2, v/v/v), × 3, 1 mL • Evaporation to dryness and derivatization	GC-MS	2.5-15.0 ng/mg (LLOD)	50.7-98.9	≤ 12.05	[121]
COC	Urine	3 mL	Not needed	TF-SPME	• Coating: C18- polyacrylonitrile • Precondition: 30 min in MeOH/H_2O (1:1) • Extraction: 10 min, 1200 rpm	DART-MS/MS	> 0.5	n.a.	≤ 4	[52]
CCE **COC**	Plasma	0.4 mL	• Centrifugation pH adjustment	DI-SPME	• Coating: PDMS • Extraction: pH 9.0, 25 min, 5 % NaCl • TD: 5 min, 250 ºC	GC-MS	11-19	n.a.	≤ 19.2	[122]
CCE **COC**	Hair	50 mg	• Washing • Enzymatic hydrolysis • Dilution pH adjustment	DI-SPME	• Coating: PDMS • Extraction: pH 8.5, 20 % NaCl, 25 min • TD: 5 min, 250 ºC	GC-MS	0.02-0.08 ng /mg	n.a.	< 14.2	[123]
CCE **COC**	Sweat	Not applicable	• Digestion • pH adjustment Centrifugation	DI-SPME	• Coating: PDMS • Extraction: pH 8.5, stirring, 20 min • TD: 20 min, 250 ºC	GC-MS	5 ng/mL (12.5 ng/patch)	n.a.	< 8.6	[124]

BE **CE** **COC**	Hair	50 mg	• Washing • Digestion • Evaporation • Derivatization • pH adjustment • Dilution	DI-SPME	• Coating: PDMS • Extraction: pH 9-10, stirring, 20 min • TD: 20 min, 250 ºC	GC-MS	0.1-0.5 ng/mg	88.1-108.1	< 14.2	[125]
AEME **CCE** **COC** **ECGME**	Saliva	2 mL	• pH adjustment • Dilution	HF-LPME	• Extraction: 10 min (2000 rpm, pH 10.5) • SLM: $CHCl_3$ • AP: $CHCl_3$ (10 µL)	GC-MS	6-28	n.a.	< 11.0	[126]
AEME **CCE** **COC** **ECGME**	Urine	8 mL	• pH adjustment • Dilution	HF-LPME	• Extraction: 3 min (1600 rpm, pH 10.5) • SLM: $CHCl_3$ • AP: $CHCl_3$ (10 µL)	GC-MS	11-48	n.a.	< 9.5	[127]
COC	Urine	0.25 mL	Filtration	Online-CME	• Sorbent: C18 or C18-Phe • Extraction: sampling flow rate of 0.02 mL/min, loading time of 12.5 min • LD: MeOH (0.25 mL, 2.5 min)	MS	3.9	n.a.	< 9.1	[84]
BE **CCE** **COC**	Oral fluid	0.06 mL	• Dilution • Centrifugation • pH adjustment	MEPS	• Sorbent: C8/SCX • Conditioning: 100 µL MeOH + 100 µL H_2O • Samples aspirated and discarded × 6 • Washing: 50 µL of H_2O/MeOH 90:10 (v:v) • Drying (0.5 min) • Elution: 90 µL of DCM/IPA/NH_4OH (78:20:2, v:v:v) • Evaporation and redissolution • Cleaning: 100 µL of eluent, 100 µL of MeOH, 100 µL of H_2O × 4, 100 µL of a 0.1% COOH × 4 + 100 µL of MeOH × 4	UPLC-MS/MS	0.25-0.5	n.a.	< 6.9	[128]
BE **COC**	Oral fluid	90 µL	• Centrifugation • pH adjustment • Dilution	µSPE	• Sorbent: C18 • Washing: 100 µL H_2O • Elution: 100 µL with MeOH containing 10 mM of COOH	LC-MS/MS	0.3-0.5	79-84	≤ 8	[129]
BE **COC**	Urine Plasma	Urine: 90 µL Plasma: 180 µL	• Urine samples were diluted • Sonication • Centrifugation • pH adjustment • Dilution	µSPE	• Sorbent: C18 • Washing: 100 µL H_2O • Elution: 100 µL with MeOH containing 10 mM of COOH	LC-MS/MS	0.02-0.5	73-101	≤ 8	[130]
COC	Oral fluid	0.5 mL	• Dilution • Salt addition • Protein precipitation	US-DLLME	• DS: 1.4 mL of MeOH • ES: 200 µL $CHCl_3$ • Extraction: 2.5% NaCl, pH 8.0	UPLC-MS/MS	0.25	101.0-102.6	≤ 12.9	[99]

					• Ultrasound for 5 min • Centrifugation (3500 rpm, 5 min) • Infranatant collected, evaporated and redisolved •					
COC	Oral fluid	0.2 mL	• Dilution • pH adjustment	DPX	• Sorbent: monolithic polymer • Conditioning: 200 µL 1% acetic acid in MeOH and 200 µL H_2O • Samples aspirated and dispensed × 10 • Washing: 200 µL 10% IPA in H_2O and dried twice with 200 µL air • Elution: 100 µL 1% acetic acid in MeOH × 5	UHPLC-MS/MS	0.1	85	≤ 8.2	[131]
EME **BE** **NC** **COC**	Hair	10 mg	• Washing • Digestion • PLE extraction • Evaporation • Redissolution • Centrifugation • Dilution • pH adjustment • Salt addition	PLE-DLLME	• DS: 500 µL of IPA • ES: 200 µL of $CHCl_3$ • Extraction: 24% NaCl, pH 11.0, 10% IPA • Ultrasound for 10 min • Centrifugation (9000 rpm, 5 min, 3ºC) • Infranatant collected, evaporated and redisolved	LC-HRMS/MS	0.5-5 pg/mg	15-47	≤ 19	[100]
COC **BE**	Urine	1 mL	pH adjustment	MSPE	• Sorbent: Graphene oxide – Fe_3O_4 • Extraction: vortex (15 min, pH 6) • LD: 3 mL of MeOH with 10 % ammonia, 10 min vortex	UHPLC-MS/MS	0.02-0.2	80.4-86.4	≤ 13.7	[104]
COC	Saliva	0.5 mL	• pH adjustment • Dilution with ACN	HP-LPME	• Extraction: 35 min (300 V, pH 6.7) • SLM: cellulose cone tip • OP: 1-octanol (750 µL) • AP: 0.4 mol/L acetic acid • LD: 250 µL of a mixture of ACN/MeOH/acetic acid (45:45:10, v/v/v) in a vortex mixer for 30 s	UHPLC-MS/MS	0.3	80-104	< 16	[132]
BE **CCE** **COC** **EME** **NC**	Plasma	0.05 mL	• Dilution • pH adjustment	DI-SPME	• Coating: C18 • Extraction: pH 8, 500 rpm, 30 min, 22 ºC • LD: MeOH with 0.01 % COOH, 30 min, 500 rpm, 22 ºC	UPLC-MS/MS	0.5	13.2-70.2	< 10.8	[133]

Table S3 - ATS

Drugs	Matrices	Sample amount	Sample pre-treatment	Microextraction technique	Optimized experimental conditions	Instrumental system	LOD (µg/L)	Absolute Recovery (%)	Precision (%)	Ref
AMP **4-MAMP**	Urine	1 mL	• Filtration • Dilution • pH adjustment • Derivatization	EE-SDME	• Solvent: DCM (2 µL) • Extraction: 4 min (-4 V, pH 7)	GC-FID	0.14-0.27	82.7-96.2	≤ 12.8	[136]
				HS-SPME	• Coating: PDMS-DVB • Extraction: pH 7, 40 min (600 rpm, 60 ºC) • TD: 5 min, 250 ºC		0.05-0.09	90.7-112.5	≤ 8.5	
MET	Urine	5 mL	• pH adjustment • Centrifugation	dSPE	• Sorbent: ZIFs (40 mg) • Extraction: 5 min (2000 rpm) • Centrifugation • Desorption: 400 µL MeOH (sonication for 10 min) • Centrifugation	HPLC-UV	10	99.83	≤ 5.1	[137]
AMP **MET**	Plasma	6 mL	• Centrifugation • pH adjustment • Protein precipitation • Dilution	AA-EME	• Solvent: $CHCl_3$ and Ph-EtOH (250 µL) • 8 air-agitation cycles (pH 12) • Centrifugation (5000 rpm, 2 min)	HPLC-UV	2.0-5.0	63-66	≤ 8.4	[140]
AMP **MET** **MDA** **MDMA** **MDEA** **PTM**	Urine	5 mL	• Filtration • Dilution • pH adjustment	HS-SPME	• Coating: MWCNTs-COOH • Extraction: pH 10, 20 min, 10 % NaCl (m/v) (900 rpm, 80 ºC) • TD: 5 min, 250 ºC	GC-MS	0.2-1.3	88-107	≤ 9.8	[141]
MET	Urine	4 mL	• Derivatization • Dilution	SHS-HLLME	• Solvent: DPA (100 µL) • Addition of 100 µL of a 6 mol L^{-1} HCl solution • Extraction: shaking for 10 s and water bath for 2 min (40 ºC) • Addition of 100 µL of a 10 mol L^{-1} NaOH solution • Centrifugation (2 min)	GC-MS	1.5	97.4-101.2	≤ 7.8	[142]
4-MAMP **AMP** **FMC** **MDA** **MDEA** **MDMA** **MET**	Urine	2 mL	• Dilution • pH adjustment • Salt addition • Derivatization	DLLME	• DS: 350 µL of a 1:2.5 (v:v) $CHCl_3$/MeOH (Rapid injection) • Centrifugation (4400 rpm, 4 min) • Infranatant injected	GC-MS	2-50	92-115	≤ 14.8	[143]

	Blood		• Protein precipitation • Centrifugation • Dilution • pH adjustment • Salt addition • Derivatization						
AMP	Urine	0.2 mL	• pH adjustment • Dilution • Salt addition	µSPE	• Sorbent: MIP • Conditioning: H_2O (100 µL) • Extraction: 10 min (2500 rpm) • Washing: H_2O (200 µL) • Elution: 200 µL (MeOH, 6 min)	LC-MS/MS	1	80	≤ 8.5	[144]
AMP **MDA** **MDMA** **MET**	Whole Blood	0.2 mL	• pH adjustment • Dilution • Salt addition	DLLME	• DS: 1.3 mL MeOH • Vortex (2 min) • Centrifugation (4000 rpm, 5 min) • Supernatant collected • ES: 0.2 mL DCM • pH adjustment • NaCl addition • Sonication for 2 min • Centrifugation (3500 rpm, 5 min) • Infranatant injected	GC-MS	10	77.0-92.4	≤ 12.8	[145]
MPH	Urine	2.5 mL	• Dilution • Centrifugation • pH adjustment • Salt addition	SBME	• Extraction: 25 min (650 rpm, pH 11.6, 25ºC, 30 % NaCl (w/v)) • SLM: 1-octanol • AP: pH 4.0, 30 µL	HPLC-UV	15	n.a.	≤ 3.9	[138]
MDMA **MET**	Urine	2 mL	• Salt addition • pH adjustment	HS-SPME	• Coating: MWCNTs/ILs • Extraction: pH 11, 20 min, 20 % NaCl (w/v) (500 rpm, 80 ºC) • TD: 4 min, 250 ºC	GC-FID	0.097-0.39	n.a.	≤ 7.0	[139]
AMP **MBDB** **MDA** **MDEA** **MDMA** **MET**	Sweat	Cotton pad (0.5 × 0.5 cm) 4-6 times rubbing on the forehead	• Acidic extraction • pH adjustment	HS-SPME	• Coating: PDMS • Extraction: 10 min (90ºC) + 3 min (90ºC) for derivatization • TD: 3 min, 250 ºC	GC-MS	0.07-0.27 ng/pad	95.1-100.9	≤ 9.9	[89]
AMP **MET**	Urine	1 mL	• pH adjustment • Dilution • Salt addition	HF-LPME	• SLM: DHE • AP: 30 µL HCl 0.01 M	GC-MS	10-20	50.9-76.0	≤ 19.2	[146]

					• Extraction: 60 min (1200 rpm, pH > 12, 10 % NaCl (w/v), 20-24ºC) • Derivatization • Evaporation • Redissolution					
MET	Urine	10 mL	Filtration	DLLME	• DS: 0.50 mL MeOH • ES: ILs (50 µL) • Centrifugation (7000 rpm, 16 min) • Infranatant injected	HPLC-UV	1.7	80.5-81.6	≤ 6.4	[147]
MET	Urine	4 mL	• pH adjustment • Dilution • Filtration	HF-EME	• Extraction: 20 min (1000 rpm, pH 7, 60 V) • SLM: 1-octanol containing GO • AP: 20 µL 1-octanol	GC-FID	2.4	n.a.	≤ 7.2	[148]
	Hair	2 g	• Washing • Drying • Alkaline digestion • pH adjustment • Dilution • Filtration							
AMP **EPE** **MET**	Oral fluid	0.125 mL	• pH adjustment • Dilution Derivatization	In tube-SPME	• Coating: 35 % BP, 65 % PDMSE funcionalized with MWCNTs • Extraction: 20 µL (1 min) • Washing (20 µL) • LD: ACN:H_2O 70:30 (v/v)	HPLC-DAD	0.5-0.8	n.a.	≤ 5.0	[149]
FEN **DIE** **SIB**	Urine	5 mL	• Filtration • pH adjustment	DLLME	• DS: 1 mL of MeOH • ES: 300 µL $CHCl_3$ • Manual agitation (15 s) • Centrifugation (3000 rpm,5 min) • Infranatant injected	GC-MS	0.05-0.1	82.1-104.2	≤ 15.3	[150]
AMP **MET**	Urine	5 mL	Not necessary	CCSHLLE-DLLME-SFO	• Pour NaCl into a syringe barrel • Mix sample with 1 mL of ACN • Pass the mixture into the syringe barrel at a flow of 0.6 mL/min • Salting out occurs • Supernatant collected and transferred to a test tube • ES: 34 µL 1-undecanol	HPLC–UV	0.5-2	78-84	≤ 5	[151]

					• DS: K_2CO_3 solution (2% w/v, 5.00 mL) • Rapid injection • Centrifugation (4200 g, 4 min) • Ice bath (5 min) • SFO collected and injected					
MET	Urine	1 mL	• pH adjustment • Dilution • Salt addition	HF-SLPME	• SLM: 1-octanol • AP: MOF/GO dissolved in 1-octanol • Extraction: 30 min (900 rpm, pH 11.0, 30 % NaCl w/v) • LD: 40 µL MeOH (vortex for 3 min)	TC-ESI-MS	0.5	98.9-103.8	≤ 9.52	[152]
AMP **MET** **MPTM** **OMMA** **PEA**	Urine	Information not available	Not necessary	SDME	• Solvent: DCM (2 µL) • DP: 0.1 M NaOH • SLM: 1-octanol • AP: 20-mM AmFo buffer (pH 2.5) • Extraction: 10 min (-4 V, pH 7)	CE-MS	2-5 nM	n.a.	≤ 13	[153]
AMP **MDA** **MDMA** **MET**	Blood	0.5 mL	• Protein precipitation • Centrifugation • Dilution • Salt addition • pH adjustment	DLLME	• DS: 0.25 mL of MeOH • ES: 100 µL $CHCl_3$ • Rapid injection • Sonication (1 min) • Centrifugation (4000 rpm,5 min) • Infranatant collected, evaporated and redissolved	UPLC-MS/MS	0.5-2	3-124	≤ 15	[90]
AMP **MET**	Urine	5 mL	• Filtration • Dilution	EE-DI-SPME	• Coating: OMC/Nafion • Extraction: 20 min (750 rpm, -0.9 V) • TD: 4 min, 260 ºC	GC-FTD	1.2-4.8	66.2-79.5	≤ 8.5	[154]
	Serum	3 mL	Dilution							
AMP **MET**	Urine	5 mL	• Dilution • pH adjustment	EM-DI-SPME	• Coating: NCF • SLM: 85% NPOE and 15% TEHP • AP: H_2O, pH 7 • Extraction: 15 min (700 rpm, pH 4), 150 V • TD: 2 min, 280 ºC	GC-FID	1.0-2.0	9.0-18.8	≤12.5	[155]
	Whole blood	1 mL								

AMP **MDEA** **MDMA** **MET**	Oral fluid	0.12 mL	• Dilution • pH adjustment • Protein precipitation • Sonication • Centrifugation	MEPS	• Sorbent: C18 • Conditioning: 250 µL MeOH (× 2) + 250 µL H_2O/ MeOH (80:20, v/v, × 2) • Samples aspirated and discarded × 5 • Washing: 100 µL 50 mM NH_3 in H_2O/MeOH (90:10, v/v; × 3) • Elution: 100 µL 5 mM COOH in MeOH (× 5)	LC-MS/MS	0.3-1	18-90	≤ 18	[91]
AM **MACT** **MDA** **MDMA** **MET**	Urine Blood	1 mL	• Dilution • pH adjustment	HF-LPME	• SLM: toluene • AP: toluene (10 µL) • Extraction: 10 min (500 rpm, pH 13.0, 30 ºC)	GC-MS	1-5	79.3-94.9	≤ 4.5	[92]
				DLLME	• ES and DS: 100 µL toluene • Sonication (3 min) and manual shaking • Centrifugation (10000 rpm,3 min) • Supernatant collected • For blood samples, 10 mg of NaCl was added to break emulsion		1-4	79.9-100.3	≤ 5.7	
MET	Urine	3 mL	pH adjustment	DLLME	• DS: 200 µL ACN • ES: 70 µL ILs • Extraction: NaCl 20 % (w/v) pH 8.0, vortex 1 min + 6 min (50 ºC) + ice bath 11 min • Centrifugation (8000 rpm,4 min) • Infranatand collected and redissolved in MeOH	HPLC-UV	10	88.7	≤ 4.7	[156]
MET	Urine	1 mL	• Dilution • Shaking • Centrifugation • Protein precipitation • pH adjustment	MDSPE	• Coating: magnetic MWCNTs • Extraction: 10 min (3000 rpm, 10 % NaCl, pH 13) • LD: 10 min sonication, 100 µL ethyl acetate	GC-MS	0.044	79.5-86.6	≤ 7.4	[157]
	Blood	1 mL	• Protein precipitation • Shaking • Centrifugation							
EPE **MET**	Urine	5 mL	• Filtration • Dilution • pH adjustment • Salt addition	HS-SPME	• Coating: MWCNTs/ILs/Nafion	GC-FID	0.33-0.6	91.5-109.0	≤ 6.1	[158]

					• Extraction: 40 min (1000 rpm, 10-30 % NaCl, 2-10 mol/L NaOH, 60-85 ºC) • TD: 275 ºC					
AMP MET	Urine	0.1 mL	Not necessary	MEPS	• Sorbent: C8 • Activation: 100 µL MeOH (× 3) • Conditioning: 100 µL H_2O (× 3) • Samples aspirated and discarded x 5 • Washing: 100 µL H_2O (× 2) and 100 µL of 5 % MeOH (× 1) • Elution: 50 µL 0.1% COOH in MeOH and injection in MS system.	MS	1.5-6.0	91.7-106.7	≤ 17.1	[40]
AMP DIE FEN	Plasma	2 mL	• Protein precipitation • Vortex and centrifugation • pH adjustment • Derivatization	DI-SPME	• Coating: PDMS • Extraction: 35 min (1200 rpm, 10-30 % NaCl pH 10.2, 20ºC) • TD: 15 min, 260ºC	GC-MS	1.0-2.0	46.4-84.5	≤ 15.0	[159]
AMP MET	Hair	20 mg	• Washing • Drying • Digestion • Salt addition	HF-SPME	• Coating: PDMS/DVB • Extraction: 10 min (90ºC) TD: 5 min, 250ºC	GC-MS	0.3-2.0 ng/mg	n.a.	≤ 13.1	[160]
AMP MET	Urine	2 mL	• Centrifugation • Filtration • Dilution • pH adjustment • Salt addition	DLLME-SFO	• DS: 300 µL ACN • ES: 30 µL 1-undecanol • Extraction: K_2CO_3 2 % (w/v) pH 10.2 • Rapid injection • Centrifugation (5000 rpm,4 min) • Ice bath (5 min) • SFO collected and injected	HPLC-UV	2-8	58.5-62.4	≤ 7.8	[161]
MET	Urine	5 mL	• Dilution • pH adjustment	EE-DI-SPME	• Coating: CAR/PDMS • Extraction: 20 min (1000 rpm, pH 7, 12 V) • TD: 3 min, 250ºC	GC-MS	0.25	89.9	≤ 6.12	[162]
AMP MDA MDEA MDMA MET	Urine	1 mL	• Filtration • Derivatization • Dilution • Salt addition	DI-SPME	• Coating: PDMS/DVB • Extraction: 40 min (600 rpm, 60ºC, pH 7) • TD: 3 min, 250ºC	GC-MS	0.01-0.09	n.a.	≤ 10.2	[163]

AMP **EPE** **MBDB** **MDA** **MDEA** **MDMA** **MET** **PEPE**	Urine	4 mL	• Centrifugation • Filtration • pH adjustment • Dilution	DLLME	• DS: 1400 µL IPA • ES: 600 µL DCM • Extraction: pH ≥ 11.5 • Rapid injection • Centrifugation (10000 rpm,5 min) • Infranatant collected, evaporated and redissolved	CE-TOF-MS	0.25-0.50	61-75	n.a.	[93]
MDMA	Urine	4 mL	• Dilution • Salt addition • pH adjustment	DLLME	• DS: 1505 µL ACN • ES: 606 µL CH_2Br_2 • Extraction: 30%-NH_3 pH ≥ 11.5 • Rapid injection • Centrifugation (9500 rpm,5 min) • Infranatant collected, evaporated and redissolved	CE-UV	1.0-3.47	91.1	≤ 6.7	[164]
AMP **MDMA** **MET**	Urine	12 mL	• Salt addition • pH adjustment	INAT	• Coating: MIP • Washing: 2 mL H_2O • Extraction: 30 min (4 % NaCl (w/v), pH 8) • TD: 3 min, 280ºC	GC-FID	12-42	72-92	≤ 8.7	[165]
MDA **MDEA** **MDMA** **MDPA**	Urine	4 mL	• pH adjustment • Dilution	USAEME	• ES: 14 µL toluene • Extraction: pH 10, sonication (30 s), 25±3ºC • Centrifugation (3500 rpm, 5 min) • Supernatant collected and injected	GC-FID	0.2-0.4	38.0-71.7	≤ 13.1	[166]
AMP **FEN** **MDA** **MDMA** **MET**	Hair	50 mg	• Washing • Drying • Digestion • Salt addition	HF-LPME	• SLM: DHE • AP: 15 µL of HCl 0.1 mol/L • Extraction: 45 min (1000 rpm, 10 % NaCl) • Evaporation • Derivatization • Evaporation • Redissolution	GC-MS	0.01-0.04 ng/mg	36.0-89.6	≤ 11.4	[167]
MDA **MDEA** **MDMA** **MDPA**	Urine	1 mL	• Dilution • pH adjustment	DLLME	• DS: 1000 µL acetone • ES: 30 µL CS_2 • Extraction: pH 10 • Rapid injection • Centrifugation (3000 rpm,3 min) • Infranatant collected	GC-FID	0.3-0.8	27.1-55.1	≤ 11.5	[168]

MET MDMA	Urine	10 mL	• Centrifugation • pH adjustment • Salt addition	SPE-DLLME	SPE • Sorbent: MIP • Conditioning: 2 mL ACN + 5 mL H_2O • Sample: 3% (w/v) NaCl with pH 8 • Washing: 1 mL H_2O • Elution: 1 mL MeOH • Derivatization DLLME • ES: 30 µL $C_5H_9ClO_2$ • Rapid injection into 5 mL aqueous solution • Centrifugation (5000 rpm, 6 min) • Infranatant collected	GC-MS	2-18	78-89	≤ 7.7	[169]
AMP 4-MAMP	Urine	1 mL	• pH adjustment • Salt addition • Dilution	DLLME-SFO	• DS: 56.5 µL SDS • ES: 31 µL 1-undecanol • Extraction: pH 6.4, 0.3% (w/v) NaCl, 0.08 M surfactant • Rapid injection and vortex (30 s) • Centrifugation (4500 rpm,5 min) • Ice bath (5 min) • SFO collected and injected	HPLC-UV	2-3	24-28	≤ 5.6	[170]
4-MAMP MDA MDMA DOI)	Whole blood and post mortem blood	80 µL	Not necessary	EME	• SLM: ENB • AP: 10 µl 10 mM acetic acid • Extraction: 5 min (15 V • Dilution	UPLC-MS/MS	0.125-2.609	10-30	≤ 26	[171]
EPE	Horse urine	10 mL	pH adjusment	SDME	• Solvent: 5 µL $CHCl_3$/MeOH (90:10) • Extraction: 20 min (25 ºC, pH 11, 500 rpm) • Evaporation and redissolution	OT-CEC	7.71-8.27	n.a.	≤ 2	[94]
AMP, 4-MAMP, MDA MDMA	Urine	2 mL	• Filtration • pH adjustment • Dilution	MDSPE	• Sorbent: Fe3O4/SiO2/poly(MAA-co-EDMA • Extraction: vortex (5 s, pH 9.2) • Washing: 0.5 mL H2O (× 5)	CE-UV	43-105	85.4-109.7	≤ 10.3	[95]

					• LD: 0.04 mL of acetone containing 0.5% COOH (v/v) with 10 s vortex.					
AMP, 4-MAMP, MDA, MDMA, MBDB	Urine	3 mL	pH adjustment	EME	• SLM: NPOE containing 15% TEHP • AP: 15 µl 100 mM HCl • Extraction: 7 min (1000 rpm, 250 V, 10 mM HCl)	HPLC-DAD	5-10	54-70	≤ 10.2	[172]
AMP 4-MAMP	Urine	10 mL	No sample pre-treatment needed	EE-SPME	• Coating: MWCNTs/Nafion • Extraction: 10 min (750 rpm, 0.6 V) • TD: 4 min, 260ºC	GC-FID	0.12-0.26	1.3-4.0	≤ 8.0	[173]
AMP 4-MAMP MDA MDMA	Urine	3 mL	• pH adjustment • Salt addition	HF-LPME	• SLM: o-xylene • AP: o-xylene • Extraction: 20 min (1000 rpm, pH 12.5, 30 % NaCl, 30ºC)	GC-FID	8-82	n.a.	≤14.1	[174]
AMP 4-MAMP MDA MDMA MDE MBDB MDPA	Hair	10 mg	• Washing • Drying • Digestion • Salt addition	HS-SPME	• Coating: PDMS • Extraction: 10 min (90ºC) • Derivatization • TD: 4 min, 260ºC	GC-MS	0.06-0.12 ng/mg	3.1-16.6	≤ 9.9	[96]
MDMA	Hair	2 g	• Washing • Drying • Digestion • Filtration • pH adjustment	SDME	• Solvent: 350 µL1-octanol • Extraction: 3 min (0.1 mL Titron X-100, pH 11, 1000 rpm) • LD: 10 µL H_2O pH 12 (20 min, 600 rpm)	HPLC-DAD	0.1	n.a.	≤ 5.4	[175]
AMP 4-MAMP	Urine	2 mL	• Salt addition • pH adjustment • dilution • Filtration	HS-SPME	• Coating: ILs • Extraction: 20 min (35 % NaCl, NaOH 4 M, 1200 rpm, 50ºC) • Derivatization • TD: 220ºC	GC-MS	0.1-0.5	n.a.	≤ 11.3	[176]
AMP 4-MAMP MDA MDMA	Whole blood	1 mL	• Dilution • Filtration • pH adjustment • Salt addition	HS-SPME	• Coating: PA • Derivatization • Extraction: 15 min (10 % NaCl, K_2CO_3 5 M, 250 rpm, 80ºC) • Derivatization • TD: 6 min, 275ºC	GC-MS	10	n.a.	≤ 30.6	[177]
AMP	Urine	0.5 mL	Dilution	DPSC	• Sorbent: C18/monolithic silica	HPLC-DAD	100	~ 100	≤ 10.4	[178]

4-MAMP **MDMA** **MDA**					• Conditioning: 0.5 mL ACN + 0.5 mL H_2O • Centrifugation (3000 rpm, 5 min) • Extraction: sample + 0.4 mL buffer (pH 12) • Centrifugation (3000 rpm, 5 min) • Washing: 0.5 mL ACN and an alkaline buffer (pH 12; 10:90, v/v) • Elution: 0.2 mL ACN–phosphate buffer (pH 3.0, containing 20 mM sodium octanesulfate) (25:75, v/v)				
AMP **MDA**	Urine	4 mL	• Filtration • pH adjustment • Salt addition	HS-HF-LPME	• AP: *n*-nonanol containing derivatizing reagent • Extraction: 30 min (750 rpm, KOH 4 M, 36 % NaCl, 95 ºC)	GC-MS	0.25-1.00 (LOQ)	5.2-19.6	≤ 4	[179]
4-MAMP **MDMA**	Serum	0.2 mL	• Dilution • pH adjustment	HS-SPME	• Coating: PPy-DS • Extraction: 10 min (60 ºC) + 60 min (4 M NaCl, 600 rpm, pH 12, 55 ºC) • TD: 70 s, 240 ºC	IMS	5-8	n.a.	≤ 7.2	[180]
4-MAMP **MDMA**	Urine	1 mL	Dilution	HS-SPME	• Coating: PDMS • Derivatization • Extraction: 20 min (4 M NaCl, 600 rpm, pH 12, 90ºC) • TD: 1 min, 225ºC	GC-MS	50-100	n.a.	≤ 14.4	[180]
AMP **MET**	Urine	2.5 mL	• Filtration • pH adjustment • Salt addition • Dilution	HS-SDME	• Solvent: H_3PO_4 0.05 M • Extraction: 15 min (80ºC) + 20 min (4 M NaOH, 10 % NaCl, 1200 rpm)	HPLC-UV	0.3	n.a.	≤ 12.5	[181]
AMP **MET**	Urine	3 mL	• Dilution • pH adjustment • Filtration	SDME	• Extraction: 20 min (0.4 mL *n*-C6, 25 ºC, 0.5 M NaOH, 1200 rpm) • Back-extraction: 5 µL of 0.02 M H_3PO_4 (20 min, 1200 rpm)	HPLC-UV	0.5	n.a.	≤ 5.4	[182]
AMP **MET**	Hair	0.08 mg	• Washing • Drying • Digestion • pH adjustment	HS-SPME	• Coating: PDMS • Derivatization • Extraction: 20 min (1 M NaOH, 70ºC) • TD: 3 min, 250ºC	GC-MS	0.25-0.625 ng/mg	2.8-17.5	≤ 26.4	[183]

EPE **4-MAMP**	Urine	5 mL	• Dilution • pH adjustment • Salt addition	HS-SPME	• Coating: DM-β-CD/OH-TSO • Extraction: 35 min (pH 10-14, 50-80ºC, 40 % NaCl, 1000 rpm) • TD: 250ºC	GC-FID	0.33-0.60	n.a.	≤ 5.0	[184]
AMP **4-MAMP** **MDA** **MDMA** **MDEA**	Urine	2 mL	• pH adjustment • Salt addition	HS-SPME	• Coating: PDMS • Extraction: 30 min (pH 10-14, 95 ºC, 36 % NaCl, 600 rpm) • Derivatization • TD: 7 min, 260ºC	GC-MS	0.016-0.193	16.9-19.6	≤ 6.5	[185]
AMP **MET**	Serum	3 mL	• pH adjustment • Dilution	HS-SPME	• Coating: PDMS/DVB • Extraction: 30 min (pH 10, 1000 rpm) • Derivatization • LD: 80 % ACN, 15 min	LC-MS/MS	0.04-0.3	3-8	≤ 18	[186]
AMP **PHD** **PMT** **PDM** **DEP** **FCF** **NPEPE** **EPE** **PTM** **MET** **4-EAMP** **FFA** **MDA** **MDMA** **MDEA** **MBDB, meperidine** **BZP** **DAMP** **MTA** **OMMA** **MEPE**	Urine	0.5 mL	• Dilution • pH adjustment • Salt addition	DI-SPME	• Coating: PDMS/DVB • Extraction: 30 min (pH 12, 40ºC) • TD: 260ºC, 2 min	GC-MS	50-1000	n.a.	≤ 10.9	[97]
EPE	Urine	1 mL	• Dilution • pH adjustment	DI-SPME	• Coating: DVB/CAR/PDMS • Extraction: 30 min (pH 10, 80ºC) • TD: 260ºC	IMS	50	101	≤ 5	[187]
AMP **MET**	Urine	0.5 mL	Dilution	DI-SPME	• Coating: Carbowax • Extraction: 15 min	HPLC-FLD	100-1000	n.a.	≤ 21	[188]

MDMA					• Derivatization • LD: 0.2 mL ACN, 5 min				
AMP **MET** **MDA** **MDMA** **MDE** **MBDB**	Hair	20 mg	• Washing • Drying • Digestion • pH adjustment • Salt addition	HS-SPME	• Coating: PDMS • Extraction: 5 min (90ºC, pH 10.3) • TD: 250ºC, 3 min	GC-MS	0.35-1.61 ng/mg	n.a.	≤ 19.2	[98]
AMP **MET** **MDA** **MDMA** **MDEA**	Urine	1 mL	• pH adjustment • Salt addition	HS-SPME	• Coating: PDMS • Extraction: 30-45 min (60-90ºC) • TD: 220ºC, 1 min	GC-FID	30-40	5.1-47	n.a.	[189]
AMP **MET**	Saliva	1 mL	• Centrifugation • Dilution • pH adjustment	HS-SPME	• Coating: PDMS • Derivatization • Extraction: 20 min (70ºC) • TD: 250ºC, 15 min	GC-MS	0.5-5.0	68.2-104.4	≤ 7.7	[190]
AMP **MET** **MDA** **MDMA** **MDEA**	Urine	4 mL	pH adjusment	DI-SPME	• Coating: PDMS • Extraction: 12 min (25ºC, pH 10) • LD: 0.25 mM ammonium acetate in MeOH	FAIMS-MS	0.2-7.5	n.a.	n.a.	[191]
AMP **MET** **MDA** **MDMA** **MDEA** **MBDB**	Hair	10 mg	• Washing • Drying • Digestion • pH adjustment	HS-SPME	• Coating: PDMS • Derivatization • Extraction: 5 + 10 min (50ºC, 650 rpm) • Derivatization • TD: 240ºC, 2 min	GC-MS	0.01-0.17 ng/mg	0.3-7.5	≤ 17.0	[192]
MET **AMP** **MDA** **MDMA**	Urine	1 mL	• Derivatization • pH adjustment • Dilution	SBSE	• Coating: PDMS • Extraction: 60 min (500 rpm, pH 3) • LD: 1 mL ACN (30 min) • Evaporation and redissolution	LC-MS/MS	0.17-1.08	56.5-84.3	≤ 8.7	[193]
AMP **MET** **MDA** **MDMA**	Urine	3 mL	• pH adjustment • Dilution • Salt addition	SBSE	• Coating: titania-OH-TSO • Extraction: 20 min (700 rpm, pH 11, 20 % NaCl) • LD: 60 µL 80/20 (v/v) MeOH/phosphate buffer, pH 1.5 (20 min)	HPLV-UV	2.3-9.1	101.7-117.3	≤ 8.9	[194]
AMP **MET** **MDA** **MDMA**	Urine	2 mL	• Filtration • pH adjustment	SDME	• Solvent: $CHCl_3$(2 µL) • DP: 0.1 M NaOH • AP: (pH 10.5) • Extraction: 8 min	GC-PDHID	25-555	n.a.	≤ 23.5	[195]

MDEA										
MET **MDMA**	Urine	1 mL	• Derivatization • Dilution	HS-SPME	• Coating: PDMS • Derivatization • Extraction: 20 min (90ºC) • TD: 225ºC, 1 min	GC-MS	0.05-0.1	n.a.	≤ 14.4	[196]
AMP **MET** **MDA** **MDMA** **MDEA**	Oral fluid	90 µL	• Centrifugation • pH adjustment • Dilution	µSPE	• Sorbent: C18 • Extraction: 15 min (30ºC, 200 rpm) • Washing: 100 µL H_2O • Elution: 100 µL MeOH containing 10 mM COOH	LC-MS/MS	0.05-0.2	63-79	≤ 8	[129]
AMP **MET** **MDA** **MDMA** **MDEA**	Urine Plasma	Urine: 90 µL Plasma: 180 µL	• Urine samples were diluted • Sonication • Centrifugation • pH adjustment • Dilution	µSPE	• Sorbent: C18 • Washing: 100 µL H_2O • Elution: 100 µL with MeOH containing 10 mM of COOH	LC-MS/MS	0.6-2.0	55-103	≤ 10	[130]
AMP **MET** **PMA** **MDMA**	Urine	1 mL	• pH adjustment • Salt addition	DI-SPME	• Coating: PDMS/DVB • Extraction: 60 min, 42 % NaCl (m/v), pH 12.6 (2000 rpm) • LD: 65 µL MeOH + 10 µL HCl:MeOH (1:9) (2000 rpm) • Evaporation and derivatization • Evaporation and redissolution	GC-MS	5-10	2-80	≤ 13	[197]

MET	Oral fluid	0.2 mL	• Dilution • pH adjustment	DPX	• Sorbent: monolithic polymer • Conditioning: 200 µL 1% acetic acid in MeOH and 200 µL H_2O • Samples aspirated and dispensed x 10 • Washing: 200 µL 10% IPA in H_2O and dried twice with 200 µL air • Elution: 100 µL 1% acetic acid in MeOH × 5	UHPLC-MS/MS	0.5	71	≤ 4.2	[131]
AMP **MET** **MDMA**	Hair	10 mg	• Washing • Digestion • PLE extraction • Evaporation • Redissolution • Centrifugation • Dilution • pH adjustment • Salt addition	PLE-DLLME	• DS: 500 µL of IPA • ES: 200 µL of $CHCl_3$ • Extraction: 24% NaCl, pH 11.0, 10% IPA • Ultrasound for 10 min • Centrifugation (9000 rpm, 5 min, 3ºC) • Infranatant collected, evaporated and redissolved	HPLC-HRMS/MS	0.2-1 pg/mg	43-56	≤ 22	[100]
AMP **MAMP**	Urine	1 mL	pH adjustment	MSPE	• Sorbent: Graphene oxide – Fe_3O_4 • Extraction: vortex (15 min, pH 6) • LD: 3 mL of MeOH with 10 % ammonia, 10 min vortex	UHPLC-MS/MS	0.02-0.03	83.6-105.5	≤ 13.1	[104]
MPH	Urine	6 mL	• pH adjustment • Centrifugation	DSPE	• Sorbent: Silica-functionalized nano-graphene oxide composite • Extraction: 4000 rpm (15 min, pH 9) • LD: 0.4 mL of MeOH by sonication (20 min)	HPLC-UV	30.0	95.3	≤ 6.7	[198]

AMP **MAMP** **FEN** **MDMA** **MDA** **MDEA**	Whole blood	0.5 mL	• Dilution • pH adjustment	HP-LPME	• SLM: dihexyl ether • AP: 50 μL of 0.1 mol/L HCl (pH 3) • Extraction: 30 min (1500 rpm, pH 12, 45ºC) • Evaporated, derivatized and redissolved	GC-MS	1-3	69-110	≤ 10.0	[199]
MAMP	Urine	6 mL	• pH adjustment • Centrifugation	DSPE	• Sorbent: carbon-based conductive polypyrrole nanocomposite • Extraction: 6000 rpm (10 min, pH 9) • LD: 0.3 mL of MeOH by sonication (10 min)	HPLC-UV	9	99.8	≤ 6.0	[200]
MPH	Urine	1.5 mL	• Dilution • pH adjustment	EME	• Extraction: 20 min (pH 4, 180 V) 1000 rpm • SLM: Porous Aromatic Framework-48 with the nitro functional groups with NPOE • AP: 100 mmol/L HCl (20 μL)	IMS	3.6	94-99	≤ 5.2	[105]

Table S4 - Cannabinoids

Drugs	Matrices	Sample amount	Sample pre-treatment	Microextraction technique	Optimized experimental conditions	Instrumental system	LOD (μg/L)	Absolute recovery (%)	Precision (%)	Ref
THC **11-OH-THC** **THC-COOH**	Plasma	0.25 mL	• Protein precipitation • Dilution • Centrifugation • Evaporation • pH adjustment	MEPS	• Sorbent: 80% C8 and 20% SCX • Conditioning: 250 μL MeOH × 4 + 250 μL 0.1% formic acid × 4 • Sample loading cycles: 26 • Washing: 100 μL 3% acetic acid + 100 μL of 5 % MeOH • Elution: 100 μL of 0.1% 10% NH_4OH in MeOH (× 6 • Evaporation to dryness • Derivatization	GC-MS	0.1	53-78	≤ 14.25	[205]
THC-COOH	Urine	1 mL	• Alkaline hydrolysis • pH adjustment	HF-LPME	• Extraction: 30 min (pH < 3, 10 mg NaCl, 1200 rpm) • SLM: di-*n*-hexyl ether • AP: NaOH 0.1 mM (30 μL) • Evaporation to dyness • Derivatization	GC-MS	1.5	57.9-77.2	≤ 12.9	[206]
THC **CBN** **CBD**	Saliva	0.3 mL	• Dilution • pH adjustment	DI-SPME	• Coating: PDMS • Extraction: 30 min • TD: 270ºC, 2 min	GC-MS	0.5-2.0	n.a.	≤ 13.8	[207]
THC **CBN** **CBD**	Breast milk	0.05 mL	• Dilution • pH adjustment	HS-SPME	• Sorbent: PDMS • Extraction: 70ºC, 40 min, 25% NaCl • TD: 250ºC	GC-MS	10.0	n.a.	≤ 13.3	[203]
THC **11-OH-THC** **THC-COOH** **CBN** **CBD** **THCAA** **CBG** **THCV** **THC-gluc** **THC-COOH-gluc**	Urine	0.2 mL	• Centrifugation • Dilution • Protein precipitation • pH adjustment	DPX	• Sorbent: WAX • Samples aspirated × 4 • Upper layer diluted and centrifuged	LC-MS/MS	0.5-5.0	42.4-81.5	≤ 14.3	[201]
THC **11-OH-THC** **THC-COOH** **CBN** **CBD** **CBG** **THCV** **THCV-COOH**	Whole blood	0.2 mL	• Protein precipitation • Dilution • Centrifugation • pH adjustment	DPX	• Sorbent: WAX • Samples aspirated 4 times • Upper layer diluted and centrifuged	LC-MS/MS	0.5-1.25	54.0-84.4	≤ 8.5	[208]

THC-gluc **THC-COOH-gluc**										
THC **11-OH-THC** **THC-COOH** **CBN** **CBD**	Urine	0.09 mL	• Dilution • pH adjustment • Enzymatic and alkaline hydrolysis	DPX	• Sorbent: C18 (50 mg) • Conditioning: 100 µL H_2O/ACN (1:1, v/v) × 2 + 100 µL H_2O/MeOH (60:40, v/v) × 3 • Samples loads/release cycles × 5 (200 µL) • Washing: 100 µL H_2O × 3 • Elution: 10 µL MeOH × 5	LC-MS/MS	2.0-4.0	65-85	≤ 15	[209]
THC **11-OH-THC** **THC-COOH** **CBN** **CBD**	Saliva	0.125 mL	• Dilution • pH adjustment • Protein precipitation • Centrifugation	MEPS	• Sorbent: C18 • Conditioning: 250 µL MeOH (× 2) + 250 µL 1:1 H_2O/MeOH 50 mM COOH (× 2) • Sample loading cycles: 5 • Washing: 100 µL 10mM COOH • Elution: 25 µL of 50 mM NH_4OH in MeOH (× 10)	LC-MS/MS	0.008-0.12	50-105	≤ 14	[210]
THC **CBN** **CBD**	Hair	10 mg	• Washing • Alkaline digestion • Evaporation to dryness • Dilution	HF-LPME	• Extraction: 20 min (pH 14, 6.8% NaCl, 600 rpm) • SLM: butyl acetate • AP: 20 µL butyl acetate	GC-MS	0.5-15 pg/mg	4.4-8.9	≤ 13.7	[204]
THC **CBN** **CBD**	Hair	10 mg	• Washing • Alkaline digestion • Evaporation to dryness • Dilution	HS-SPME	• Sorbent: PDMS • Extraction: 90ºC, 40 min, 1000 rpm • TD: 250 ºC, 10 min	GC-MS	0.007-0.062	1.1-8.7	≤ 16.4	[211]
11-OH-THC	Urine	1 mL	• Alkaline hydrolysis • Dilution • pH adjustment	SBSE	• Sorbent: PDMS • Extraction: 120 min, 500 rpm, pH 3 • LD: ethyl acetate (1.5 mL), 30 min • Evaporation to dryness	LC-MS/MS	1.3	76.5	≤ 7.3	[212]
THC	Saliva	0.2 mL	• Centrifugation • Dilution • pH adjustment • Filtration	PMME	• Sorbent: p(MAA-co-EGDMA) • Conditioning: 0.3 mL MeOH + 0.3 mL phosphate buffer (20 mM, pH 7.0) at 0.15 mL/min • Extraction: 1 mL at 0.08 mL/min • Washing: 0.2 mL phosphate buffer (20 mM, pH 7.0) at 0.08 mL/min	GC-MS	0.68	89	≤ 12	[213]

					• Elution: 0.05 mL acetone was at 0.04 mL/min					
THC **11-OH-THC**	Blood	1 mL	• Protein precipitation • Dilution • Centrifugation	DPX	• Sorbent: SDVB • Conditioning: 800 µL H_2O/ACN (77:33, v/v) • Samples loads/release cycles × 1 • Washing: 800 µL H_2O/ACN (77:33, v/v) • Elution: 800 µL 50% ethyl acetate in ACN × 3 • Top layer evaporated to dryness • Derivatization	GC-MS	1-2	50-60	≤ 5.5	[214]
11-OH-THC	Urine	0.2 mL	• Alkaline hydrolysis • Dilution • pH adjustment	DPX	• Sorbent: SDVB • Conditioning: 400 µL H_2O/ACN (77:33, v/v) • Samples loads/release cycles × 1 • Washing: 400 µL H_2O/ACN (77:33, v/v) • Elution: 400 µL 50 % ethyl acetate in ACN × 3 • Top layer evaporated to dryness • Derivatization	GC-MS	3	n.a.	≤ 4	[214]
THC **CBN** **CBD**	Hair	100 mg	• Washing • Alkaline digestion • Dilution • Liquid-liquid extraction • Evaporation • Derivatization	HS-SPME	• Sorbent: PDMS • Extraction: 125ºC, 20 min, 250 rpm • TD: 270ºC, 10 min	GC-MS	0.01-0.02 ng/mg	14-66	≤ 13.4	[215]
THC **CBN** **CBD**	Hair	10 mg	• Washing • Alkaline digestion • Dilution • pH adjustment	HS-SPME	• Sorbent: PDMS • Extraction: 90ºC, 40 min • TD: 250ºC, 20 min	GC-MS	0.07 ng/mg	36-92	≤ 18	[216]
THC **11-OH-THC** **THC-COOH**	Plasma and urine	Urine: 1 mL Plasma: 0.1 mL	• Dilution • pH adjustment	µSPE	• Sorbent: MIP • Conditioning: 5 0.1 M/0.1 M phosphate/NaOH buffer solution (pH 6.0) for 10 min • Extraction: 150 rpm (12 min, 40ºC) • Rinsing: 5 mL of 0.1 M/0.1 M phosphate/NaOH buffer solution at pH 6.0 for rinsing	HPLC-MS/MS	Urine: 0.14-0.16 Plasma: 0.11-0.15	87-94	Urine: ≤ 6 Plasma: ≤ 11	[202]

					(ultrasound assistance, 37 kHz, 325 W, 8 min) • Elution: 2 mL of MeOH/aqueous acetic acid (90:10, v/v) through sonication (37 kHz, 325 W, 6 min)					
THC, CBN, 8THC, CBG, THCV, CBC, CBD	Bucal swap	n.a.	• Headspace derivatization	HS-SPME	• Sorbent: PDMS • Extraction: 150ºC, 5 min + 1 min • TD: 0.5 min	GC-MS(SIM)	0.2 µg/5 mg of buccal swab	n.a.	n.a.	[217]
Anandamide, 2-arachidonoyl glycerol	Plasma	0.4 mL	• Protein precipitation • Vacuum drying • Redissolution • pH adjustment	on-line in-tube SPME	• Sorbent: PIL • Extraction: sampling flow rate of 0.1 mL/min, 2 min • LD: 30:70 (v/v) mixture of 0.5% COOH in H_2O and ACN with 0.5% COOH (0.1 mL/min, 2 min)	UHPLC-MS/MS	0.05-0.1 (LLOQ)	n.a.	≤ 14	[218]
THC	Sweat	Cotton pad (0.5 × 0.5 cm) 4-6 rubbing on the forehead	• Alkaline extraction • Salt addition • pH adjustment	HS-SPME	• Coating: PDMS • Extraction: 10 min (90ºC) + 30 min (150ºC) + 10 min (90ºC, for derivatization) • TD: 3 min, 250ºC	GC-MS	0.09 ng/pad	100.7	≤ 9.3	[89]
THC **CBD** **CBN**	Oral fluid	1 mL	• Centrifugation	DI-SPME	• Coating: PDMS/DVB • Extraction: 15 min • TD: 270ºC (15 min	GC-MS	1-5	n.a.	≤ 8.3	[219]
THC-COOH **CBD** **OH-THC** **THC** **CBN**	Hair	10 mg	• Washing • Digestion • PLE extraction • Evaporation • Redissolution • Centrifugation • Dilution • pH adjustment • Salt addition	PLE-DLLME	• DS: 500 µL of 2-propanol • ES: 200 µL of chloroform • Extraction: 24% NaCl, pH 11.0, 10% iso-propanol • Sonication for 10 min • Centrifugation (9000 rpm, 5 min, 3ºC) • Infranatant collected, evaporated and redissolved	LC-HRMS/MS	0.1-5 pg/mg	73-87	≤ 25	[100]

Table S5 – Dissociative Drugs

Drugs	Matrices	Sample amount	Sample pre-treatment	Microextraction technique	Optimized experimental conditions	Instrumental system	LOD (μg/L)	Absolute recovery (%)	Precision (%)	Ref
PCP	Urine Whole blood	1 mL	• Protein precipitation • pH adjustment • Salt addition	HS-SPME	• Coating: PDMS • Extraction: 30 min, 50% K_2CO_3 (m/v) (900 rpm, 90ºC) • TD: 250 ºC	GC-SID	0.25-1.0	9.3-47.8	≤ 27	[222]
Dextromethorphan	Urine Plasma	Plasma: 0.8 mL Urine: 2 mL	• Dilution • pH adjustment	EME	• SLM: NPOE • AP: 20 μL 0.1 M HCl + 15 μL 0.1 M NaOH • Extraction: 20 min (110 V, 100 rpm)	DPV	1.5	64-79	≤ 4.7	[224]
Dextromethorphan	Urine Plasma	3 mL	• Filtration • pH adjustment	HF-LPME	• SLM: *n*-C12 • AP: MeOH • Extraction: 20 min (750 rpm)	IMS	0.3-0.6	83-96	≤ 8	[225]
Salvinorin A	Urine	20 mL	• Protein precipitation • pH adjustment • Salt addition	DI-SPME	• Coating: PA • Extraction: 30 min, (250 rpm, 30ºC) • TD: 280ºC, 2 min	GCxGC-TOF/MS	4	n.a.	≤ 6	[226]
Ketamine	Urine	3 mL	• pH adjustment • Dilution • Salt addition	SBSE	• Coating: titania-OH-TSO • Extraction: 20 min (700 rpm, pH 11, 20% NaCl) • LD: 60 μL 80/20 (v/v) MeOH/phosphate buffer,pH= 1.5 (20 min)	HPLC-UV	9.1	90.8	≤ 8.9	[194]
Ketamine	Urine	0.5 mL	• pH adjustment • Dilution • Salt addition • Filtration	DLLME	• DS: 350 μL ACN • ES: 40 μL IL • Hand-shaking (~ secs) • Centrifugation (4000 rpm, 5 min) • Supernatant collected • Back-extraction with 60 μL 0.1 M HCl • Hand-shaking (~ secs) • Centrifugation (4000 rpm, 5 min)	CE-UV	30	n.a.	≤ 12.8	[227]
PCP	Urine	2 mL	• Filtration • pH adjustment	SDME	• Solvent: chloroform (2 μL) • AP: (pH 10.5) • Extraction: 8 min, 0.1 M NaOH	GC-PDHID	70	n.a.	≤ 16.2	[195]
PCP **Ketamine**	hair	10 mg	• Digestions	HS-SPME	• Coating: not specified	GC-MS	n.a.	0.17-3.4	≤ 27	[228]

			• pH adjustment • Salt addition		• Extraction: 30 min, 8% Na_2SO_4 (m/v) (70ºC) + 15 min • TD: 250ºC				
Ketamine	Urine Blood	1 mL	• Dilution • pH adjustment	HF-LPME	• SLM: toluene • AP: toluene (10 µL) • Extraction: 10 min (500 rpm, pH 13.0, 30ºC)	GC-MS	2.5	81.3-98.6	≤ 4.5	[92]
				DLLME	• ES and DS: 100 µL toluene • Sonication (3 min) and manual shaking • Centrifugation (10000 rpm,3 min) • Supernatant collected • For blood samples, 10 mg of NaCl was added to break emulsion		1.5-2.5	87.3-103.4	≤ 3.5	
Ketamine norketamine (NK)	Urine Plasma	0.25 mL	• Centrifugation • Dilution • pH adjustment	MEPS	• Sorbent: 80% C8 and 20% SCX • Conditioning: 5 × 250 µL MeOH + 4 × 250 µL H_2O • Samples aspirated and discarded 8 or 26 times • Washing: 250 µL of acetic acid • Elution: 100 µL of 6% or 3 % NH_4 in MeOH • Evaporation and redissolution • Cleaning: 5 × 250 µL of MeOH + 4 × 100 µL of H_2O	GC-MS/MS	5	63-101	≤ 14	[229]
ketamine	Urine	3 mL	• pH adjustment • Salt addition	HF-LPME	• SLM: o-xylene • AP: o-xylene • Extraction: 20 min (1000 rpm, pH 12.5, 30% NaCl, 30ºC)	GC-FID	8	n.a.	≤ 8.9	[174]
Ketamine	Sweat	Cotton pad (0.5 × 0.5 cm) 4-6 times rubbing on the forehead	• Acidic extraction • pH adjustment	HS-SPME	• Coating: PDMS • Extraction: 10 min (90ºC) + 3 min (90ºC) for derivatization • TD: 3 min, 250 ºC	GC-MS	0.07 ng/pad	100.6	≤ 11.2	[89]
Ketamine	Urine	0.3 mL	Not necessary	DI-SPME	• Coating: C18/benzenesulfonic acid particle	MS	0.027	90.8-109.4	≤ 10.6	[230]

					• Extraction: 10 min, (1500 rpm,) • LD: 4 μL of 95:5 MeOH: H_2O (0.1% COOH,12mM ammonium acetate), 3 min					
Ketamine	Whole Blood	0.2 mL	• pH adjustment • Dilution • Salt addition	DLLME	• DS: 1.3 mL MeOH • Vortex (2 min) • Centrifugation (4000 rpm, 5 min) • Supernatant collected • ES: 0.2 mL DCM • Sonication for 2 min • Centrifugation (3500 rpm, 5 min) • Infranatant injected	GC-MS	10	86.3	≤ 11.1	[145]
Dextromethorphan and dextrorphan	plasma	0.5 mL	• Derivatization • Dilution • Salt addition • pH adjustment	HS-SPME	• Coating: sol-gel PDMS • Extraction: 30 min (70% of max rpm, pH 11.5-12, 20% NaCl, 60ºC) • TD: 290ºC (5 min)	GC-MS	0.010-0.015	n.a.	≤ 5	[231]
Ketamine	Blood	0.5 mL	• Protein precipitation • Centrifugation • Dilution • Salt addition • pH adjustment	DLLME	• DS: 0.25 mL of MeOH • ES: 100 μL CHL • Rapid injection • Sonication (1 min) • Centrifugation (4000 rpm,5 min) • Infranatant collected, evaporated and redissolved	UPLC-MS/MS	0.5	87-110	≤ 15	[90]
Ketamine Norketamine dehydronorketamine	Urine	2 mL	• Dilution • Salt addition • pH adjustment	HF-LPME	• SLM: eucalyptus essential oil • AP: HCl 1.0 mol/L • Extraction: 30 min (2400 rpm, pH > 10, 10% NaCl, 30 ºC) • Evaporation to dryness • Derivatization	GC-MS	0.1-0.25	64.6-101.0	≤ 16.9	[232]
Ketamine	Urine	14 mL	• pH adjustment • Dilution	HF-LPME	• SLM: *n*-C12 • AP: ACN (25 μL) • Extraction: 30 min (700 rpm, pH 11.0, 20% NaCl)	GC-MS	0.01	25-35	≤ 9.3	[120]

Ketamine	Hair	20 mg	• Washing • Drying • Digestion • pH adjustment • Salt addition	HS-SPME	• Coating: PDMS • Extraction: 5 min (90ºC, pH 10.3) • TD: 250 ºC, 3 min	GC-MS	0.59 ng/mg	n.a.	≤ 17.52	[98]
Ketamine	Urine	1 mL	• Derivatization • Dilution	HS-SPME	• Coating: PDMS • Derivatization • Extraction: 20 min (90ºC) • TD: 225ºC, 1 min	GC-MS	0.1	n.a.	≤ 14.8	[196]
Ketamine	Urine	1 mL	• Dilution • Shaking • Centrifugation • Protein precipitation • pH adjustment	MDSPE	• Coating: magnetic MWCNTs • Extraction: 10 min (3000 rpm, 10% NaCl, pH 13) • LD: 10 min sonication, 100 µL ethyl acetate	GC-MS	0.024	80.1-93.6	≤ 9.2	[157]
	Blood		• Protein precipitation • Shaking • Centrifugation							
PCP	Urine	4 mL	• Dilution • Salt addition • pH adjustment	DLLME	• DS: 1505 µL ACN • ES: 606 µL CH_2Br_2 • Extraction: 30%-NH_3 pH ≥ 11.5 • Rapid injection • Centrifugation (9500 rpm,5 min) • Infranatant collected, evaporated and redissolved	CE-UV	2.9-5.6	80.3	≤ 11.0	[164]
PCP **Ketamine**	Oral fluid	90 µL	• Centrifugation • pH adjustment • Dilution	µSPE	• Sorbent: C18 • Extraction: 15 min (30ºC, 200 rpm) • Washing: 100 µL H_2O • Elution: 100 µL with MeOH containing 10 mM of COOH	LC-MS/MS	0.1-0.5	79-85	≤ 8	[129]
PCP **Ketamine**	Urine Plasma	Urine: 90 µL Plasma: 180 µL	• Urine samples were diluted • Sonication • Centrifugation	µSPE	• Sorbent: C18 • Washing: 100 µL H_2O • Elution: 100 µL with MeOH containing 10 mM of COOH	LC-MS/MS	0.1-0.3	80-90	≤ 6	[130]

			• pH adjustment • Dilution						
Ketamine	Oral fluid	0.025 mL	• Dilution • Centrifugation • pH adjustment	MEPS	• Sorbent: C18 • Conditioning: 100 µL MeOH + 100 µL H_2O • Samples aspirated × 5 (50 µL) • Elution: 25×50 DCM:2-propanol:NH_4OH • Cleaning: 10×50 µL	DESI-HRMS	0.5 mg/L (LLOQ)	n.a.	≤ 9.6	[233]
Ketamine	Blood	0.5 mL	• Protein precipitation • Centrifugation • Dilution • Salt addition • pH adjustment	DLLME	• DS + ES: 350 µL of a mixture chloroform/MeOH 1:2.5, • Rapid injection • Sonication (2 min) • Centrifugation (4000 rpm,5 min) • Infranatant collected, evaporated and redissolved	UPLC-MS/MS	0.5	51-75	n.a.	[234]
Ketamine **PCP**	Hair	10 mg	• Washing • Digestion • PLE extraction • Evaporation • Redissolution • Centrifugation • Dilution • pH adjustment • Salt addition	PLE-DLLME	• DS: 500 µL of 2-propanol • ES: 200 µL of chloroform • Extraction: 24% NaCl, pH 11.0, 10% iso-propanol • Ultrasound for 10 min • Centrifugation (9000 rpm, 5 min, 3ºC) • Infranatant collected, evaporated and redissolved	HPLC-HRMS/MS	1-2 pg/mg	48-60	≤ 11	[100]
Ketamine **Norketamine**	Urine	0.5 mL	• Centrifugation • Acid hydrolysis • pH adjustment • Dilution	HT-BAµE	• Sorbent:NVP-DVB • Extraction: 30 min (1800 rpm) pH 11.0 • LD: sonication with 100 µL MeOH (15 min)	GC-MS	1.0	84.9-105.0	≤ 12.6	[223]
Ketamine	Urine	1.5 mL	• Dilution • pH adjustment	EME	• Extraction: 20 min (pH 4, 180 V) 1000 rpm • SLM: Porous Aromatic Framework-48 with the nitro functional groups with NPOE	IMS	2.7	92-97	≤ 4.3	[105]

• AP: 100 mmol/L HCl (20 μL)

Table S6 - NPS

Drugs	Matrices	Sample amount	Sample pre-treatment	Microextraction technique	Optimized experimental conditions	Instrumental system	LOD (μg/L)	Absolute Recovery (%)	Precision (%)	Ref
Synthetic cathinones MPD, BFD, 4-MEPE and PTL	Urine	1 mL	• pH adjustment • Salt addition	DI-SPME	• Coating: PDMS/DVB • Extraction: 60 min, 42 % NaCl (m/v), pH 12.6 (2000 rpm) • LD: 65 μL MeOH + 10 μL HCl:MeOH (1:9, v:v) (2000 rpm) • Evaporation and derivatization • Evaporation and redissolution	GC-MS	5-25	2-80	≤ 15	[197]
Synthetic cannabinoids UR-144, JWH-250, CP47497, CP47497-C8, JWH-200, JWH-081, AM 2201, JWH-019, JWH-122	Oral fluid	1 mL	• Centrifugation	DI-SPME	• Coating: PDMS/DVB • Extraction: 15 min • TD: 270ºC (15 min)	GC-MS	1-10	n.a.	≤ 12.8	[219]
Synthetic cathinones MTL, FPD, ECAT ECATEPE, EL, MEPE, BL, MPD, PD, MDPV, PV **Synthetic opioid** EDDP PBN	Oral fluid	0.06 mL	• Dilution • Centrifugation • pH adjustment	MEPS	• Sorbent: C8/SCX • Conditioning: 100 μL MeOH + 100 μL H_2O • Samples aspirated and discarded × 6 • Washing: 50 μL of H_2O/MeOH 90:10 (v:v) • Drying (0.5 min) • Elution: 90 μL of DCM/IPA/NH_4OH (78:20:2, v:v:v) • Evaporation and redissolution • Cleaning: 100 μL of eluent, 100 μL of MeOH, 100 μL of H_2O (× 4), 100 μL 0.1% COOH (× 4) and 100 μL MeOH (× 4)	UPLC-MS/MS	0.25	42-145	< 8.9	[128]
Synthetic cathinones MPD **Synthetic cannabinoid** UR-144, JWH-250, JWH-200, JWH-122, JWH- 019, AM-2201, JWH-081, HU-211, CP47497	Oral fluid	0.025 mL	• Dilution • Centrifugation • pH adjustment	MEPS	• Sorbent: C18 • Conditioning: 100 μL MeOH + 100 μL H_2O • Samples aspirated × 5 (50 μL) • Elution: 50 μL DCM/IPA/NH_4OH × 25 • Cleaning: 50 μL x 10	DESI-HRMS	0.25-0.5 mg/L (LLOQ)	n.a.	< 19.4	[233]
Synthetic cathinones	Oral fluid	0.5 mL	• Dilution • Salt addition	US-DLLME	• DS: 1.4 mL MeOH • ES: 200 μL $CHCl_3$	UPLC-MS/MS	0.1-2.5	74.6-125.3	≤ 14.8	[99]

ML, FPD, ECAT, ECATEPE, EL, MEPE, BL, MPD, PD, MDPV, PV **Synthetic opioid** EDDP, BPN			• Protein precipitation		• Extraction: 2.5 % NaCl (m/v), pH 8.0 • Ultrasound for 5 min • Centrifugation (3500 rpm, 5 min) • Infranatant collected, evaporated and redissolved				
Synthetic cathinones 4-FMC, CAT, NM2AI, 3-MMC, PD, MBDB, 4-MTA, ML, EL, BL, PL, α-PVP, 2-CB, MET, 4-MEC, MDPV, 4-MMC	Urine	2 mL	• Dilution • pH adjustment • NaCl addition • Derivatization	DLLME	• DS: 350 µL 1:2.5 $CHCl_3$/MeOH (v:v) through rapid injection • Centrifugation (4400 rpm, 4 min) • Infranatant injected	GC-MS	2-50	92-115	≤ 14.8	[143]
	Blood		• Protein precipitation • Centrifugation • Dilution • pH adjustment • NaCl addition • Derivatization						
Synthetic cannabinoids JWH-200, AB-005, JWH-018 5OH pentyl, AM-2201 4OH pentyl, JWH-018 4OH pentyl, UR-144 4OH pentyl, MAM-2201, JWH-250, JWH-073, XLR-11, JWH-018,	Plasma	0.1 mL	• Dilution • Protein precipitation • Centrifugation	µSPE	• Sorbent: C18 • Extraction: load and eject x 5 • Washing: 100 µL MeOH:H_2O (80:20, v:v) • Elution: 100 µL 10 mM COOH in MeOH × 3	LC-MS/MS	0.1-3.0	21-70	≤ 25	[238]

JWH-081, JWH- 122, UR-144 **Synthetic cathinones** MPD, 4-MEC, MDPV α-PVP, 2C-B, 2C-T-7										
Piperaine derivatives BZP, TFMPP, mCPP, MeOPP	Urine	0.1 mL	• Dilution	MEPS	• Sorbent: 80 % C8 and 20 % SCX • Conditioning: 100 µL MeOH + 100 µL H_2O • Samples aspirated × 8 • Washing: 250 µL 1% acetic acid and 100 µL 10 % MeOH in H_2O (v:v) • Elution: 50 µL 5 % NH_3 in MeOH (v:v) • Cleaning: 5 × 250 µL MeOH and 4 × 250 µL H_2O	HPLC-DAD	50-100	52.0-100.5	≤ 16.6	[239]
Piperaine derivatives BZP, TFMPP, mCPP, MeOPP	Urine	0.1 mL	• Dilution	MEPS	• Sorbent: C18 • Conditioning: 100 µL MeOH + 100 µL H_2O • Samples aspirated × 8 • Washing: 250 µL of 10 % MeOH in H_2O (v:v) • Elution: 50 µL of MeOH • Cleaning: 5 × 250 µL MeOH and 4 × 250 µL H_2O	HPLC-DAD	50-100	52.0-100.5	≤ 16.6	[240]
Mitragynine	Urine	1 mL	• Dilution	BAµE	• Sorbent: NVP • Extraction: 4 h (1300 rpm), pH 5.5 • Elution: 200 µL MeOH/ ACN (1:1, v:v) under sonication (10 min)	HPLC-DAD	0.1	103	≤ 15	[237]

Synthetic cannabinoids AM-2201, AM-2233, AM-694, CB-13, JWH-007, JWH-019, JWH-015, JWH-018, JWH-030, JWH-073, JWH-081, JWH-098, JWH-122, JWH-147, JWH-200, JWH-201, JWH-250, JWH-251, JWH-307, JWH-398, RCS4, JWH-018 4OH indole, JWH- 018 5OH pentyl, JWH-018-COOH, JWH-073 4OH butyl, JWH-073 5OH indole, JWH-073 COOH, JWH-250 5OH pentyl **Synthetic cathinones** 4-FAMP, 4-MEC, BL, BPD, CAT, EL, EPN, HML, HMO, MBDB, MDAI, MDPV, MPD, MD, ML, 4- MTA, NM-2-AI, PD, PL **Piperaine derivatives** BZP, mCPP	Blood	0.5 mL	• Protein precipitation • Centrifugation • Dilution • Salt addition • pH adjustment	DLLME	• DS + ES: 350 µL of $CHCl_3$/MeOH 1:2.5 (v:v), • Rapid injection • Sonication (2 min) • Centrifugation (4000 rpm,5 min) • Infranatant collected, evaporated and redissolved	UHPLC-MS/MS	0.2	4-110	n.a.	[234]
MDPV	Oral fluid	0.5 mL	Not necessary	LLME	• ES: 100 µL $CHCl_3$ • Centrifugation 3500 rpm (3 min)	IMS	4.4	n.a.	≤ 3.2	[241]
Synthetic cannabinoids AM-1220, JWH-200, AB-005, JWH-018-COOH JWH-018 5OH pentyl, WIN-55,	Oral fluid	0.09 mL	• Dilution • Centrifugation • Protein precipitation • Salt addition • pH adjustment	MEPS	• Sorbent: C18 • Conditioning: 250 µL H_2O/MeOH (75:25, v:v) × 3 • Samples aspirated × 5 • Washing: 200 µL H_2O/MeOH (90:10, v:v) × 3	UHPLC-MS/MS	0.005-0.850	31-96	≤ 20	[242]

XLR-11 4OH pentyl, MAM-2201 COOH, JWH-073, UR-144 4OH pentyl, JWH-250, MAM-2201, XLR-11, JWH-018, JWH-081, JWH-122, UR-144 **Synthetic cathinones** ML,DMCAT, MPD, ECAT BPD, BL, MD, 4-MEC, MET, MDPV, α-PVP, 2-CB **Piperazine derivatives** PPP, MeOPP					• Elution: 100 µL MeOH containing 10 mM COOH × 5 • Dilution with 100 µL of water					
Synthetic cathinones ML, BL, CAT, EL, MDPV, PL, PD, NPR, FPD, 3,4-DMMC	Urine	1 mL	• pH adjustment	µSPE	• Sorbent: MIP • Extraction: 200 rpm, 4 min • Washing: 2 mL 0.1 M phosphate buffer, pH 5.0 (orbital/horizontal shaking of 100 rpm for 10 min) • Elution: ultrasound (37 kHz) treatment with 2 mL of 75:20:5 *n*-C7/IPA/ NH_4OH (v:v:v) for 4 min • Evaporation to dryness and redissolution	HPLC-MS/MS	0.14-1.51	89-100	≤ 10	[243]
Synthetic cathinones 2-FAMP, 3-FAMP, 2-FMAMP, 4-FMAMP, 3-FEAMP, 3-MMAMP, 6-APB, ETCAT, 4-CECAT, 4-CMCAT, 4-MeMABP, α-PVP, α-PHP, MPHP, MXD, ML, BL, MDPPP, MDPBP, 2C-E	Oral fluid	0.2 mL	• Dilution • pH adjustment	DPX	• Sorbent: MP • Conditioning: 200 µL 1 % acetic acid in MeOH and 200 µL H_2O • Samples aspirated and dispensed × 10 • Washing: 200 µL 10% IPA in H_2O (v:v) and dried twice with 200 µL air • Elution: 100 µL 1 % acetic acid in MeOH (v:v) × 5	UHPLC-MS/MS	0.1	64-115	≤ 8.4	[131]
DCP	Oral fluid	0.09 mL	• Centrifugation • pH adjustment	MEPS	• Sorbent: C8 • Conditioning: 3 × 100 µL IPA and 2 × 100 µL H_2O • Extraction: 100 µL sample (adjusted to pH 7 × 4	IMS	30	Not available	≤ 14	[244]

					• Washing: 100 µL H_2O Elution: 50 µL IPA × 10 • Dilution with 100 µL H_2O					
Synthetic cathinones MDAI, ML, 4-FAMP, mCPP, PD, MET, MDPV, EPN, 2C-E, bromo-dragonfly, and AH-7921	Plasma Whole blood	Plasma: 0.125 mL Blood: 0.1 mL	• Dilution • pH adjustment	PALME	• SLM: 5 µL DCA with 1 % TOA (w/w) • AP: 50 µL 20 mM COOH • Extraction: alkaline solution (900 rpm, 120 min)	UHPLC–MS	0.1-147 (LLOQ)	11-117	≤ 20	[245]
Synthetic cathinones 2-FMC, ML, BPD, 2C-H, 2-MMC, BL, MPD, DECAT, 4-MEC, MET, 2-CB, α-PVP, MDPV, NBPN, 2C-T-4, 2C-T-7 **Synthetic cannabinoid** BPN, JWH-200, EDDP, XLR-11 OH pentyl, JWH-018-COOH, WIN- 55, JWH-018 5OH pentyl, JWH-018 4OH pentyl, MAM-2201 COOH, UR-144 4OH pentyl, JWH-081 5OH pentyl, AM-1220, 25I-NBOMe, AB-005, JWH-250, MT-45, JWH-073, XLR-11, MAM-2201, JWH-018, JWH-081, UR144, JWH-122	Hair	10 mg	• Washing • Digestion • PLE extraction • Evaporation • Redissolution • Centrifugation • Dilution • pH adjustment • Salt addition	PLE-DLLME	• DS: 500 µL of IPA • ES: 200 µL of $CHCl_3$ • Extraction: 24 % NaCl, pH 11.0, 10% IPA • Ultrassound for 10 min • Centrifugation (9000 rpm, 5 min, 3ºC) • Infranatant collected, evaporated and redissolved	HPLC-HRMS/MS	0.1-5 pg/mg	23-87	≤ 25	[100]
Synthetic cannabinoid CP47497, JWH-030, JWH-251, JWH-203, JWH-302, JWH-201, RCS4, JWH-250, JWH-015, JWH-075,	Urine and blood	2 mL	• Hydrolysis • pH adjustment • Salt addition • Protein precipitation	US-DLLME	• ES: 150 µL of $CHCl_3$, rapid injection • Sonication (5 min) • Centrifugation (4400 rpm, 5 min) • Infranatant collected, evaporated, derivatized and redissolved	GC-MS	1-5	47.8-100.0	≤ 15.8	[246]

AM-694, JWH-018, JWH-307, JWH-019, AM-2201, JWH-122, JWH-210, JWH-147, JWH-081, JWH-098, JWH-200, UR-144, XLR-11, AB-PINACA, AB-CHMINACA, AB-FUBINACA, AKB-48, JWH-007, JWH-250-5OH, JWH-018-4OH, JWH-018-5OH, JWH-018-COOH, JWH-073-4OH, JWH-073-5OH, JWH-073-COOH,