

IDX	Reference	Matrix	Compounds	Synonym	CAS	Method	Chromatographic column	Mobile phase	Sample preparation	Findings
1	Jeppesen et al. 2015	Urine	methyl ecgonidine ecgonidine	Anhydroecgonine methyl ester (AEME) Anhydroecgonine (AE)	43021-26-7 484-93-5	LC-MS/MS	XDB C18 1.8 mm (50 mm 4.6 mm i.d.)	(A) 25 mM formic acid; and (B) acetonitrile	NA	AE detected more frequently than AEME AEME still relevant Both compounds are biomarkers of crack-cocaine use
2	Cardona et al. 2006	Urine Blood Muscle	Anhydroecgonine methyl ester (AEME) cocaine (COC) benzoylecgonine (BE) norbenzoylecgonine (BNE) norcocaine (NCOC) ecgonine (ECG) ecgonine methyl ester (EME) m-hydroxybenzoylecgonine (HBZE) cocaethylene (CE) norcocaethylene (NCE) ecgonine ethyl ester (EEE)		43021-26-7	GC-MS	-	-	SPE, 10-ml BondElut	Ok recoveries for all analytes
3	Lewis et al. 2004	Postmortem fluids	Anhydroecgonine methyl ester (AEME) Anhydroecgonine (AE)		43021-26-7 484-93-5	GC-MS			Bond Elute-Certify I, 3ml, 130mg	AEME recovery 75% AE recovery 2.5%
4	Reley et al. 2001	Urine	Anhydroecgonine methyl ester (AEME) Anhydroecgonine (AE)		43021-26-7 484-93-5	GC-MS	-	-	NA	Both AEME and AE need to be measure for accurate determination of crack use
5	Fiorentin et al. 2018	Oral fluid Urine Blood	Anhydroecgonine (AE)		484-93-5	LC-MS/MS Method of Fiorentin et al. 2017 (see below)	Kinetex HILIC (30 °C)		Centrifugation Filtration 0.22µm Method of Fiorentin et al. 2017 (see below)	Concentration range AE in urine 56.60–5,746.24 ng/mL
6	Fiorentin et al. 2017	Oral fluid Urine Blood	Anhydroecgonine methyl ester (AEME) Anhydroecgonine (AE)			LC-MS/MS	Kinetex HILIC (30 °C) 150 mm x 4.6 mm, particle size of 2.6 µm	0.8 mL/min acetonitrile: ammonium acetate 13 mM pH 6.0: methanol (55:35:10) 10µL injection	1.5mL of urine 100µL of ACN Centrifugation Retrieve supernatant Filtration	AEME lower detectio frequency than AE
7	Paul et al. 2005	Urine Blood	cocaethylene nor-cocaine nor-cocaethylene methyl ecgonine ethyl ecgonine benzoylecgonine nor-benzoylecgonine m-hydroxybenzoylecgonine p-hydroxybenzoylecgonine and ecgonine methyl ecgonidine ecgonidine anhydroecgonine ethyl ester (AEEE) nor-anhydroecgonine	Anhydroecgonine methyl ester (AEME) anhydroecgonine (AE)		GC-MS			C8 + benzene sulfonic acid (200 mg, United Chemical Technologies ZCDAU020)	Anhydroecgonine methyl ester (AEME) anhydroecgonine (AE) were the 2 compounds with highest concentrations in the samples anhydroecgonine ethyl ester (AEEE) found in users consuming both crack and alcohol
8	Huestis et al 2007	Urine	cocaine (COC)			GC-MS			3mL urine buffered to pH 5.5	EME highest concentrations after COC and BE

		benzoylecgonine (BE) ecgonine methylester (EME) m-hydroxybenzoylecgonine (mOHBE) p-hydroxybenzoylecgonine (pOHBE) norbenzoylecgonine (NBE) ecgonine (EC)				SPE (Clean-Thru® Clean-Thru ZCDAU020L)	Paper provides information about excretion and peak concentration in urine after smoking of cocaine
9	Langman et al 2009	Urine	cocaine (COC) benzoylecgonine (BE) m-hydroxybenzoylecgonine (m-HOBE) norcocaine (NC) Cocaethylene (CE) Anhydroecgonine methyl ester (AEME) anhydroecgonine ethyl ester (AEEE)	LC-MS/MS	XDB-C8 (50 × 2.1 mm, 1.8 μm) flow 0.270 mL/min	20 mM ammonium formate (pH 2.7) methanol/acetonitrile (50:50)	1mL urine 3mL acetate buffer (pH 2.8) Clean Screen® Mixed Mode solid-phase extraction
10	Snozek et al 2012	Urine	Same as Langman et al 2009			Same as Langman et al 2009	
11	Hackett et al 2014	Blood	Anhydroecgonine methyl ester (AEME) anhydroecgonine (AE)	LC-MS/MS	Unison-C18column: 50 mm x 2 mm, 5 μm at 40°C	A: DI water containing 0.1% formic acid B: acetonitrile containing 0.1% formic acid	Clean Screen DAU SPE Cartridges, 200mg, 6ml (mixed mode) Authors performed a sequential extraction, using twice the same column but in the second stage the loaded sample was recovered and acidified to pH 2 No information on whether there's an improved recovery/lower matrix effects for AE with the sequential extraction
12	Giroud et al 2004		Anhydroecgonine methyl ester (AEME) and other cocaine metabolites	LC-MS/MS	Atlantis HILIC silica column (150 x 2.1 mm, 3μm)	acetonitrile/2mM ammonium acetate	Liquid-liquid extraction (LLE) AEME Rt: 13.8min
13	Xia et al 2000	Meconium	Anhydroecgonine methyl ester (AEME) and other cocaine metabolites	LC-MS/MS	Zorbax Eclipse XDB-C8 (2.1 x 150 mm, 5 μm)	A (20 mM ammonium acetate, pH 2.7) B (1:1 methanol/acetonitrile)	Bont Elut Certify SPE AEME Rt: ~ 3min
14	Carvalho et al 2008	Urine Study on stability of AEME, BE and COC in urine	Anhydroecgonine methyl ester (AEME) Cocaine (COC) Benzoylecgonine (BE)	GC-MS			Urine acidified with phosphate buffer (pH 5.5-6.0) No info over which SPE was used

Wastewater

IDX	Reference	Matrix	Compounds	Synonym	CAS	Method	Chromatographic column	Mobile phase	Sample volume	Sample preparation	Findings
1	Bisceglia et al. 2010	Wastewater	Anhydroecgonine methyl ester (AEME)			LC-MS/MS	Flow 0.2mL		200 mL	Strata XC, 500mg, 12mL	Good retention of AEME and AE
			Anhydroecgonine (AE)				Restek Viva PFPP (2.1x10 mm, 5 µm), Alternative column: Restek Ultra IBD (reverse-phase mode) @ 55 °C	Water +0.1%FA and ACN + 0.1%FA		Sample at pH 2	AEME: 5.89min
			and other illicit drugs					10 mmol/L ammonium acetate/acetonitrile			AE: 3.32min
2	Bisceglia et al. 2012	Wastewater	Same as Bisceglia 2010			LC-MS/MS					Hydrolysis of samples to transform all cocaine biomarkers to ecgonine, AE and norecgonine
3	Castiglioni et al. 2011	Wastewater	cocaine (COC)			LC-MS/MS	X-Bridge HILIC 100 2.1 mm, 3.5 mm (Waters)	A: Ammonium formate 5mM + FA to reach pH 4	20mL	Oasis MCX cartridge (60 mg) at pH 2.0	Good recovery of AE and AEME with MCX (> 60% for both)
			benzoylecgonine (BZE) norbenzoylecgonine (NBE) norcocaine (NCO) cocaethylene (COE) ecgonine methyl ester (EME) ecgonine (ECG) Anhydroecgonine methyl ester (AEME) Anhydroecgonine (AE)				Alternative options (personal communication with S. Castiglioni) Waters Atlantis T3 Waters XSELECT CSH C18	B: Acetonitrile 10µL injection		Also tested 150mg to improve recovery of ECG	AE: 6.75min AEME: 6.56 min
4	Gonzalez-Marino et al. 2019	Wastewater	cocaine (COC)			LC-MS/MS	Mixed-Mode WCX-1 column (50 × 3.0 mm I.D., 3 µm). Weak cation-exchange	(A) 10 mM of ammonium acetate in ultrapure water:ACN 90:10 at pH 3.5 (B) 10 mM of ammonium acetate in ultrapure water:ACN 10:90 at an aqueous-equivalent pH of 3.5	100mL	Oasis MCX-150 mg	No mass labelled IS was used for AE and AEME
			benzoylecgonine (BZE) cocaethylene (COE)				Flow 0.2mL injection 10µL			Sample at pH 2	Method allows also the analysis of levamisole, major cutting agent of COC Very good recoveries for all analytes
			levamisole (LEV) Anhydroecgonine methyl ester (AEME) Anhydroecgonine (AE)				Authors tested also Trinity P1 but had bad peak shapes in matrix for AE.				AE and AEME detected only in samples from Brazil, not in Spain
5	Baker et al. 2011	Wastewater	Anhydroecgonine methyl ester (AEME)			LC-MS/MS	AQUITY UPLC BEH C18 (1.7 µm; 1 mm × 150 mm)	A (pH 2.9): 79.7% H2O 20% MeOH 0.3% Acetic acid	100mL	Oasis MCX 60 mg	AEME Rt: 3.6
			Anhydroecgonine (AE)					B (pH 3.30): 99.7% MeOH, 0.3% Acetic acid		Sample at pH 2	AE Rt: 3.0
			large number of additional illicit drugs								Quite early elution of target crack biomarkers
6	Sodré et al 2017	Wastewater	Cocaine (COC) anhydroecgonine methyl ester (AEME) benzoylecgonine (BE) nor-benzoylecgonine (Nor-BE) ecgonine methyl ester (EME)			LC-MS/MS	Zorbax RRHD SB-C18 column (50 × 4.6 mm and 5 µm)	MilliQ + 0.01% FA MeOH Flow 0.3mL injection volume 2µL	50mL	Sample at pH 2 Strata X 500mg	ecgonine (ECG) and ecgonine methyl ester (EME) NOT recovered
7	Martins et al 2017	Wastewater	Cocaine (COC) benzoylecgonine (BE) Anhydroecgonine (AE)			LC-MS/MS	Phenomenex C18 Luna column of 150 × 4.6 mm and 5 µm	ultrapure water pH 3 (acidified with formic acid) and acetonitrile 75:25 (v/v) isocratic mode 0.5ml/min 20µL injection volume	100mL	SPE: Chromabond® C18 ec 6 ml/500 mg	Approximately 80% recovery for AE

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