Supporting information for

The Challenge Presented by Progestins in Ecotoxicological Research: A Critical Review

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Table S1: Biological activity of progestins to various human steroid receptors.

Progestins	Activity									
	PR	**ER**	**AR**	**GR**	**MR**	**Anti -ER**	**Anti -AR**	**Anti -GR**	**Anti -MR**	**Anti-GOR**
Progesterone	$+^{1,2}$	$-^{3,4}$	$-^{3,4}$	$+^{1}/-_{2,4}$	$-^{4,5}$	$+^{1,3}$	$+^{1,4}$	$-^{4}$	$+^{4,5}$	$+^{1}$
Medroxyprogesterone-acetate	$+^{4,6}$	$-^{4,7}$	$+^{1,4,6}$	$+^{4,6}$	$-^{4}$	$+^{1}$	$+^{8}/-^{4,6}$	$+^{6}/-^{4}$	$+^{4,8}/-_{1,2}$	$+^{1}$
Cyproterone acetate	$+^{1,6}$	$-^{1}$	$+^{6,8}/-_{1,2}$	$+^{1,6,9}$	$-^{5,8}$	$+^{1}$	$+^{1,6}$	$+^{6,8}$	$-^{1,5}$	$+^{1}$
Nomegestrol acetate	$+^{1,10}$	$-^{7,10}$	$-^{1,10}$	$-^{1}$	$-^{8}$	$+^{1}$	$+^{1,10}$		$-^{1}$	$+^{1}$
Nestorone	$+^{8,11}$	$-^{11}$	$-^{11}$	$+^{11}/-^{8}$	$-^{8}$	$+^{11}$	$-^{11}$	$-^{11}$		
Trimegestone	$+^{2,12}$	$-^{1,12}$	$-^{1,12}$	$-^{2,12}$	$-^{12}$	$+^{1}$	$+^{1,12}/-_{2}$	$-^{12}$	$+^{1,12}$	$+^{1}$
Norethisterone	$+^{4,6}$	$+^{4,6}$	$+^{4,6}$	$-^{1,4}$	$-^{4,8}$	$+^{1}$	$+^{6,8}/-_{1,4}$	$+^{8}/-^{4}$	$+^{4,8}/-_{1,2}$	$+^{1}$
Norethisterone acetate	$+^{13,14}$	$+^{14}$	$+^{13,14}$	$-^{13,14}$	$-^{5}$		$-^{13,14}$		$-^{5,14}$	
Dienogest	$+^{1,4}$	$+^{1,15}/-_{3,4}$	$+^{3,15}/-_{1,4}$	$-^{3,4}$	$-^{4,8}$	$+^{1,3}$	$+^{3,4}$	$-^{4}$	$-^{3,4}$	$+^{1}$
Levonorgestrel	$+^{1,2}$	$+^{7,8}/-_{1,3}$	$+^{1,3,9}$	$-^{1,3}$	$-^{5}$	$+^{1,3}$	$-^{1,3}$		$+^{8,13}/-_{3,5}$	$+^{1}$
Etonogestrel	$+^{1,15}$	$+^{7}/-^{1,3}$	$+^{1,3}$	$-^{1,3}$	$-^{5}$	$+^{1,3}$	$-^{1,3}$		$-^{3,5}$	$+^{1}$
Desogestrel	$+^{9,15}$	$-^{15}$	$+^{9,15}$	$-^{9}$			$-^{9,15}$		$-^{9}$	
Norgestimate	$+^{1,2}$	$-^{1,3}$	$+^{1,3,9}$	$-^{1,2}$		$+^{1,3}$	$-^{1,3}$		$-^{1,3}$	$+^{1}$
Gestodene	$+^{1,9}$	$+^{7}/-^{1,3}$	$+^{1,3,9,13}$	$+^{1}/-^{3,9}$	$-^{5}$	$+^{1,3}$	$-^{3,9}$		$+^{3,5,9,13}$	$+^{1}$
Drospirenone	$+^{16,17}$	$-^{16,17}$	$-^{16,17}$	$-^{16,17}$	$-^{17}$	$+^{1}$	$+^{16,17}$	$-^{16,17}$	$+^{16,17}$	$+^{1,16}$

Abbreviations: (anti)PR – (anti)progestogenic; (anti)AR – (anti)androgenic; (anti)ER – (anti)estrogenic; (anti)GR – (anti)glucocorticoid; (anti)MR – (anti)mineralcorticoid; (anti)GOR – (anti)gonadotropic activity

(+) – effective, (-) – not effective, (+ / -) – literature not consistent

Table S2: Reported concentrations of progestins in sewage influent, effluent and surface water.

Progestins	Sample preparation and separation	Detection	Levels (ng/L)			Country	Reference
			Influent	Effluent	Surface		
Progesterone	SPE with silica clean-up, LC	ESI-MS/MS	10 & 3.1 (2)	0.37 & 0.31 (2)	0.06 to 0.09 (4)	Japan	[18]
	SPE -C18, LC	ESI-MS/MS	NA	NM	0.88 (3)	Spain	[19]
	SPE (Oasis HLB, Superclean C18), Silica gel cartridge cleanup, RRLC	ESI-MS/MS	5.4 & 6.1 (2)	ND (2)	0.5 & 2.5 (2)	China	[20]
	SPC-C18, GC	MS	NA	NA	9.4 (21)	USA	[21]
	C18 online SPE; LC/LC	MS/MS	Trace (1)	ND (1)	3 & ND (2)	Canada	[22]
	Strata C18; LC	MS/MS	NA	NA	1.6 (71)	France	[23]
	SPE- Strata X, HLB; LC	MS	NA	8.0-16.9 (7)	NA	France	[24]
	SPE- Strata C18; LC	MS/MS	NA	NA	1.7 & 3.5 (2)	France	[25]
	CLLE; GC	MS	NA	NA	110 (70)	USA	[26]
	SPE (Oasis HLB) UPLC	MS/MS	66±36 (7)	2.3 (7)	NA	China	[27]
	SPC- C18 (Lichrolut RP-18), LC	DAD-MS0	ND (4)	ND (4)	ND (4)	Spain	[28]
	SPE- C18 (Lichrolut RP-18), LC	DAD-MS	<0.2-1.9 (4)	<0.2-1.5 (4)	NA	Spain	[29]
Norethisterone	Oasis MCX, LC	ESI-MS/MS	NA	188 (1)	<MDL	Malaysia	[30]
	C18 online SPE; LC/LC	MS/MS	205 & 70 (2)	53 (1)	ND (1)	Canada	[22]
	Strata C18; LC	MS/MS	NA	NA	2.0 (71)	France	[23]
	SPE- Strata X, HLB; LC	MS	NA	5.2-41.0 (7)	NA	France	[24]
	SPE- Strata C18; LC	MS/MS	NA	NA	2.7 & 2.8 (2)	France	[25]
	CLLE; GC	MS	NA	NA	48 (70)	USA	[26]
	SPE -C18, LC	ESI-MS/MS	NA	NM	ND (3)	Spain	[19]
	SPE (Oasis HLB, Superclean C18), Silica gel cartridge cleanup, RRLC	ESI-MS/MS	ND (2)	ND (2)	ND (2)	China	[20]
	SPE (Oasis HLB) UPLC	MS/MS	6.5±3.3 (7)	ND (7)	NA	China	[27]
	SPC- C18 (Lichrolut RP-18), LC	DAD-MS	ND (4)	ND (4)	ND (4)	Spain	[28]
	SPE- C18 (Lichrolut RP-18), LC	DAD-MS	<0.2-8.9 (4)	<0.2-17.4 (4)	NA	Spain	[29]
	SPE- ENVI-18, UPLC	ESI-MS/MS	NA	NA	ND (10)	China	[31]
Levonorgestrel	Oasis MCX, LC	ESI-MS/MS	NA	<MDL	38 (1)	Malaysia	[30]
	SPE (Oasis HLB, Superclean C18), Silica gel cartridge cleanup, RRLC	ESI-MS/MS	28.6 & 59 (2)	6.7 & 9.2 (2)	3.7 & 22.2 (2)	China	[20]
	SPE (IAC)-LC	UV-242	74.3 (1)	8.1 (1)	7.5 (1)	China	[32]
	C18 online SPE; LC/LC	MS/MS	150 & 170 (2)	30 (1)	ND (1)	Canada	[22]
	Strata C18; LC	MS/MS			3.6 (71)	France	[23]

	SPE- Strata X, HLB; LC	MS	NA	0.9-17.9 (7)	NA	France	[24]
	SPE- Strata C18; LC	MS/MS	NA	NA	5.3 & 7.0	France	[25]
	SPE- Oasis HLB, LC	MS/MS		1 (3)		Sweden	[33]
	SPE -C18, LC	ESI-MS/MS			ND	Spain	[19]
	LiChrolut EN/Bondesil C-18, GC	ESI-MS	NA	1(2)	NA	Germany	[34]
	SPC- C18 (Lichrolut RP-18), LC	DAD-MS	ND (4)	ND (4)	ND (4)	Spain	[28]
	SPE- C18 (Lichrolut RP-18), LC	DAD-MS	<0.2-16.1 (4)	<0.2-4.0 (4)	NA	Spain	[29]
	SPE- C18 cartridges (GracePureTM SPE C18-Low), HPLC	UV detection	5.6 (1)	1.1 (1)	NA	China	[35]
	SPE- ENVI-18, UPLC	ESI-MS/MS	NA	NA	ND (10)	China	[31]
Medroxyprogesterone	C18 online SPE; LC/LC	MS/MS	5 & ND (2)	ND (1)	ND (1)	Canada	[25]
	C18 SPE; GC	MS/MS	NA	14.9**	NA		[36]
	SPE- Strata C18; LC	MS/MS	NA	NA	ND (2)		[25]
	SPE- ENVI-18, UPLC	ESI-MS/MS	NA	NA	ND (10)		[31]
Medroxyprogesterone acetate	SPE with silica clean-up, LC	ESI-MS/MS	0.21 & 2.42 (2)	0.03 & 0.42 (2)	ND	Japan	[18]

Bracketed Numbers= Number of samples
SW= Surface Water
Inf= STP influent
Eff =STP effluent
RR=rapid resolution
*=Recovery in distilled water
**=maximum concentration
IAC= Immunoaffinity chromatography
ND=Not detected
NA=Not available
MLD=Method detection limit
DAD= Diode array detection

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