One Health Prescribing – New Analytical Methods to Inform Formulary Changes of Chiral Pharmaceuticals for Environmentally Friendlier Medicines.

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Hydro Nation Scholars Programme

One-Health Breakthrough Partnership

Vision: "**Non-toxic environment**".

Scottish Water – Trusted to serve Scotland

CREW – Centre of Expertise for Waters

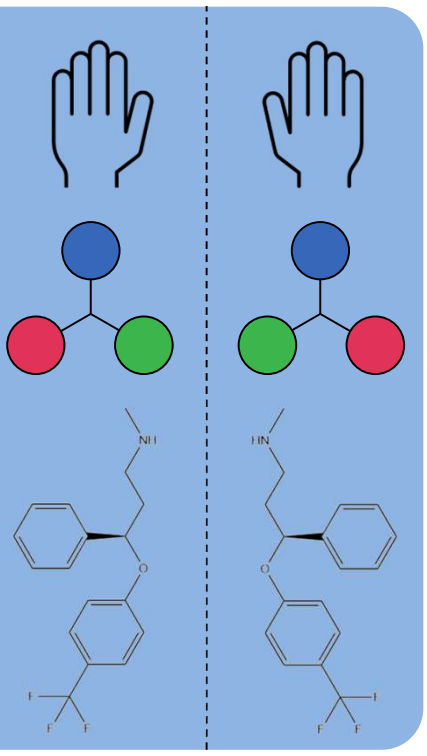
NHS Highland

SEPA – Scottish Environment Protection Agency – Buidheann Dìon Àrainneachd na h-Alba

eri – environmental research institute

Chirality

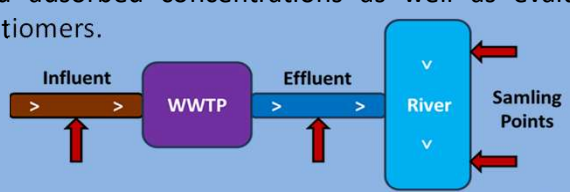
- Derived from the Greek word for hands meaning non-superimposable mirror images.
- Chiral compounds can exist in two or more mirror image forms (Enantiomers).
- Approximately half of all pharmaceuticals currently prescribed are chiral.
- Enantiomers share physicochemical properties but have different interactions with biological systems meaning they often have different therapeutic efficacies, effects, and toxicities.
- An equal proportion of enantiomers is termed racemic (50:50).
- A majority of chiral pharmaceuticals are prescribed as racemic.
- formulary changes, from racemic to pure enantiomer, have happened in response to human toxicity, I'll explore whether these changes can also be used to reduce ecotoxicity.



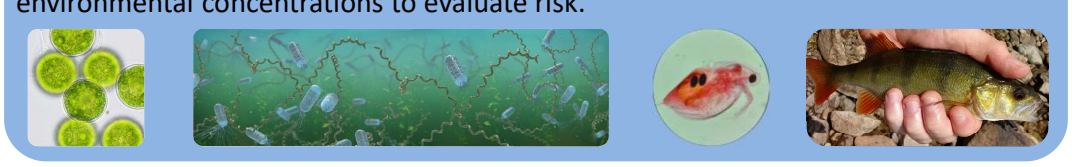
Target Pharmaceuticals	Human Therapeutic Enantiomeric Differences	Pharmaceutical Classification	Enantiopure Formulations	Treatment Period	Parent Excretion	Annual Prescribed Mass (Kg per year)
Amlodipine	(S) 1000 X	Calcium Channel Blocker	Levamlodipine (½ dose)	Long-term	10%	852
Atenolol	(S) Active	Beta-Blocker		Short- & Long-term	50%	2752
Baclofen	(R) Active	Muscle Relaxant		Long-term	70%	4216
Bisoprolol	(R) Preferentially metabolised	Beta-Blocker		Long-term	50%	349
Citalopram	(S) 30-40 X	SSRI Antidepressant	Escitalopram (½ dose)	Long-term	18%	940
Donepezil	(S) 2.2 X	Acetylcholinesterase Inhibitor		Long-term	17%	51
Fluoxetine		SSRI Antidepressant		Long-term	2.5%	1882
Hydroxychloroquine	(R) Preferentially metabolised	Immuno-Suppressant		Long-term	50%	1625
Ibuprofen	(S) Active	NSAID Painkiller	Dexibuprofen (¾ dose)	Short-term	<1%	267090
Methylphenidate	(D) 10 X	ADHD Stimulant	Dexmethylphenidate (½ dose)	Long-term	<1%	161
Mirtazapine	(S) Shorter half-life	Tetracyclic Antidepressant	Esmirtazapine (currently not used)	Long-term	4%	1186
Propranolol	(S) 100 X	Beta-Blocker		Short- & Long-term	0.5% (17% conjugated)	3319
Sulpiride	(-) Higher efficacy, Lower toxicity	Antipsychotic	Levosulpiride (½ dose - India)	Long-term	95%	270
Venlafaxine	(R) SNRI (S) SSRI	SNRI Antidepressant		Long-term	5%	3410

Project Plan

Develop and validate a novel UPLC-MS/MS method for the detection of chiral pharmaceuticals in waste- and surface waters.
The developed method will be applied to a one-year monitoring period using randomised sampling days and targeting low effluent-dilution high risk WWTPs.
Composite 24-hour pseudo-flow proportional sampling will be used to determine both aqueous and adsorbed concentrations as well as evaluating the relative proportion of enantiomers.

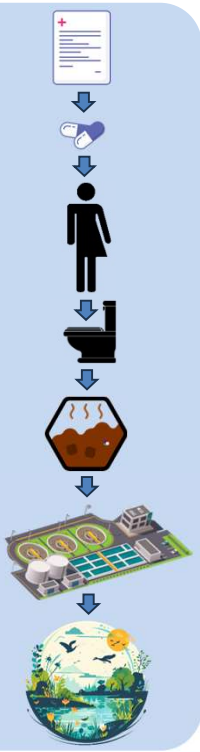


Detected analytes tested against aquatic organisms across 3 different trophic levels.
Enantiomers treated as individual contaminants with results compared to environmental concentrations to evaluate risk.



Outcomes

- **Novel Analytical Methodology** – Applicable for effective ecological risk assessments of chiral pharmaceuticals.
- **Degradation and Transformations** – Elucidate changes to pharmaceuticals from source to environment.
- **Presence and Fate** – Which pharmaceuticals are present in influent, effluent, and receiving waters; at what concentration, and what is the relative proportions of enantiomers.
- **Ecotoxicity** – Assess and compare the ecotoxicity of enantiomeric and racemic formulations.
- **Formulary change recommendations** – Switching from racemic to enantiopure formulations to reduce mass load and overall ecotoxicity.



Worked Impact Example

Citalopram 2022 prescribing = 940,464 kg
Escitalopram 2022 prescribing = 48,847 kg
2022 Total = 989,312 kg

Changing citalopram to escitalopram 2022
Total prescribing mass = 519080 kg (**45% reduction**)
If escitalopram less ecotoxic than R-Citalopram:
Additional reduction in overall ecotoxicity.

Scottish Funding Council
Comhairle Maoineachaidh na h-Alba

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