Using Community Prescribed Drug Data to Predict Emerging Pollutants

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Investing in Opportunities
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INTERREG IVB

Introduction

- ~3000 pharmaceutical products are permitted for use in Europe.
- Not all are completely absorbed or metabolised.
- Product and/or metabolites partially excreted and therefore reach the water cycle.
- Not all are removed by waste water treatment.

Pharmaceuticals in the Environment

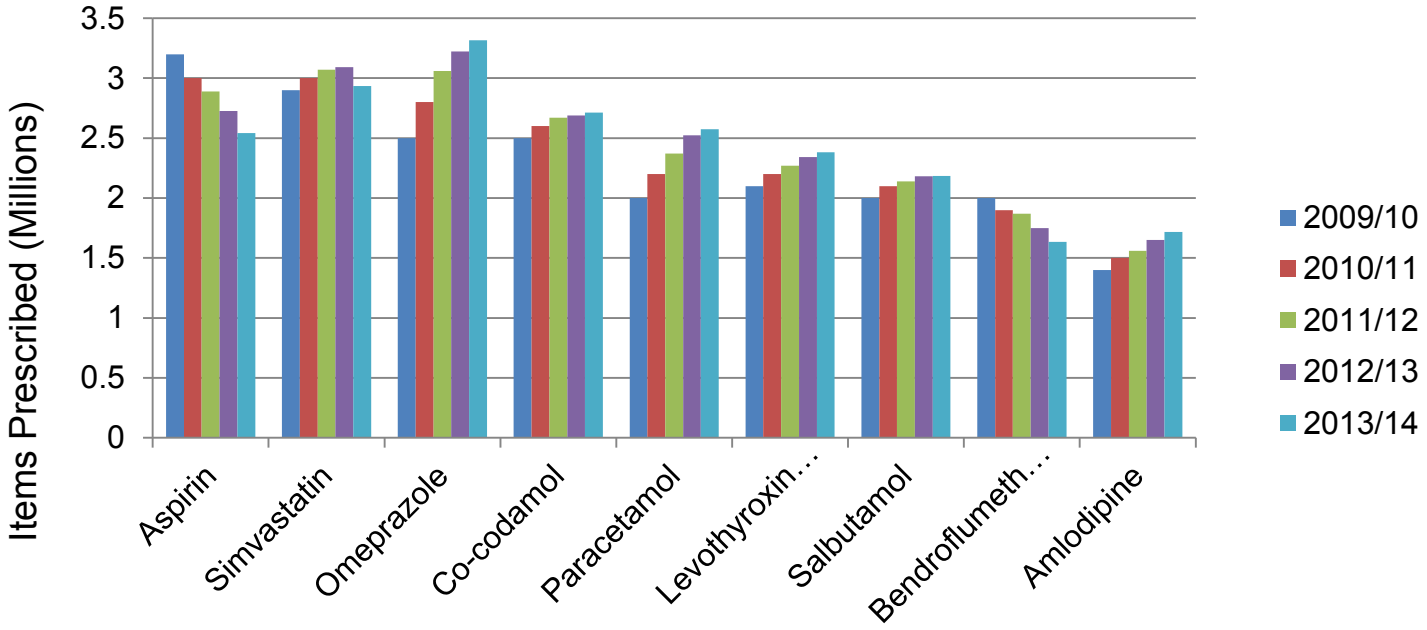
- Many studies worldwide have been carried out to measure pharmaceuticals in the environment.
- But with limited resources:
  - which pharmaceuticals should be targeted?
  - which are of most concern, both now….

  ……and in the future?

Aims

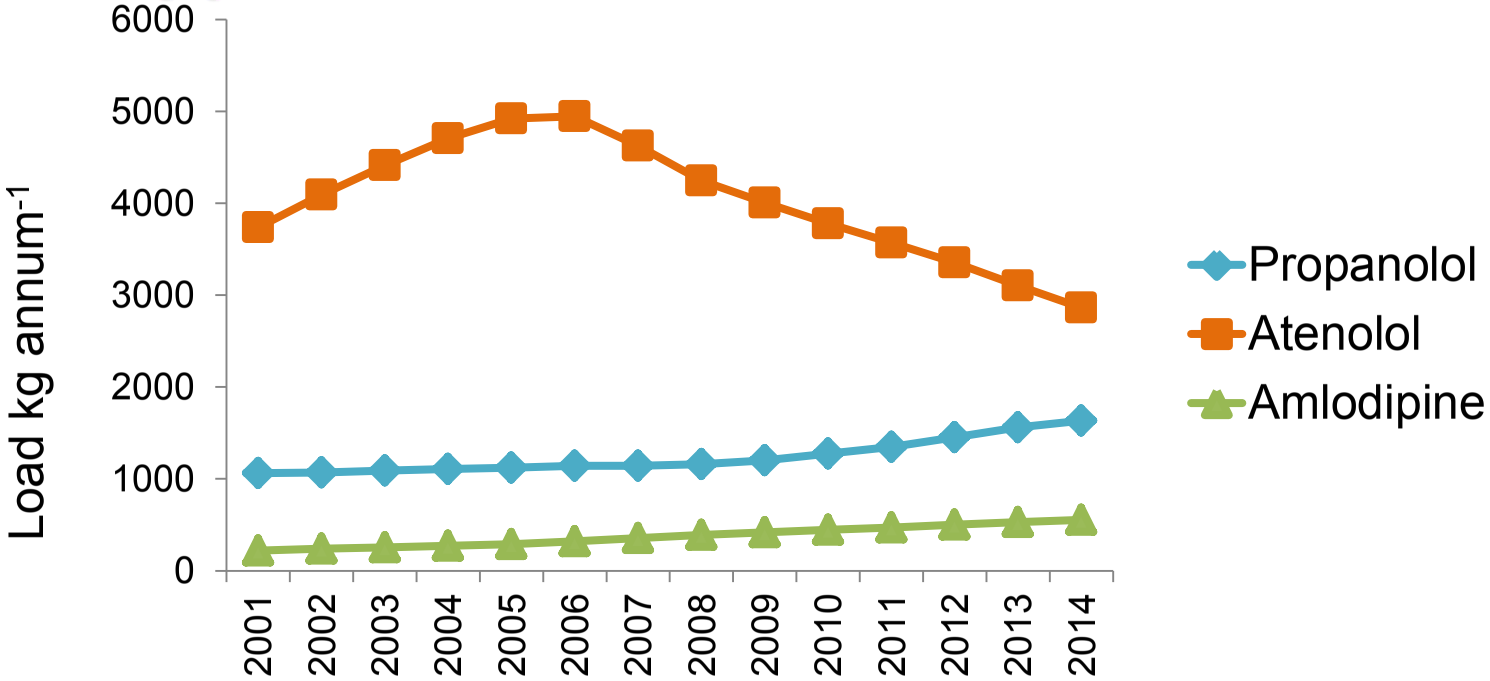
- Review community prescription data in Scotland 2009-2014.
- Identify trends in prescription patterns, e.g. increase in use of statins.
- Consider metabolites and breakdown products.
- Link usage data with known or predicted ecotoxicity.
- Produce “short-list” of drugs for environmental monitoring.

Top Prescribed Drugs Scotland 2009-2014

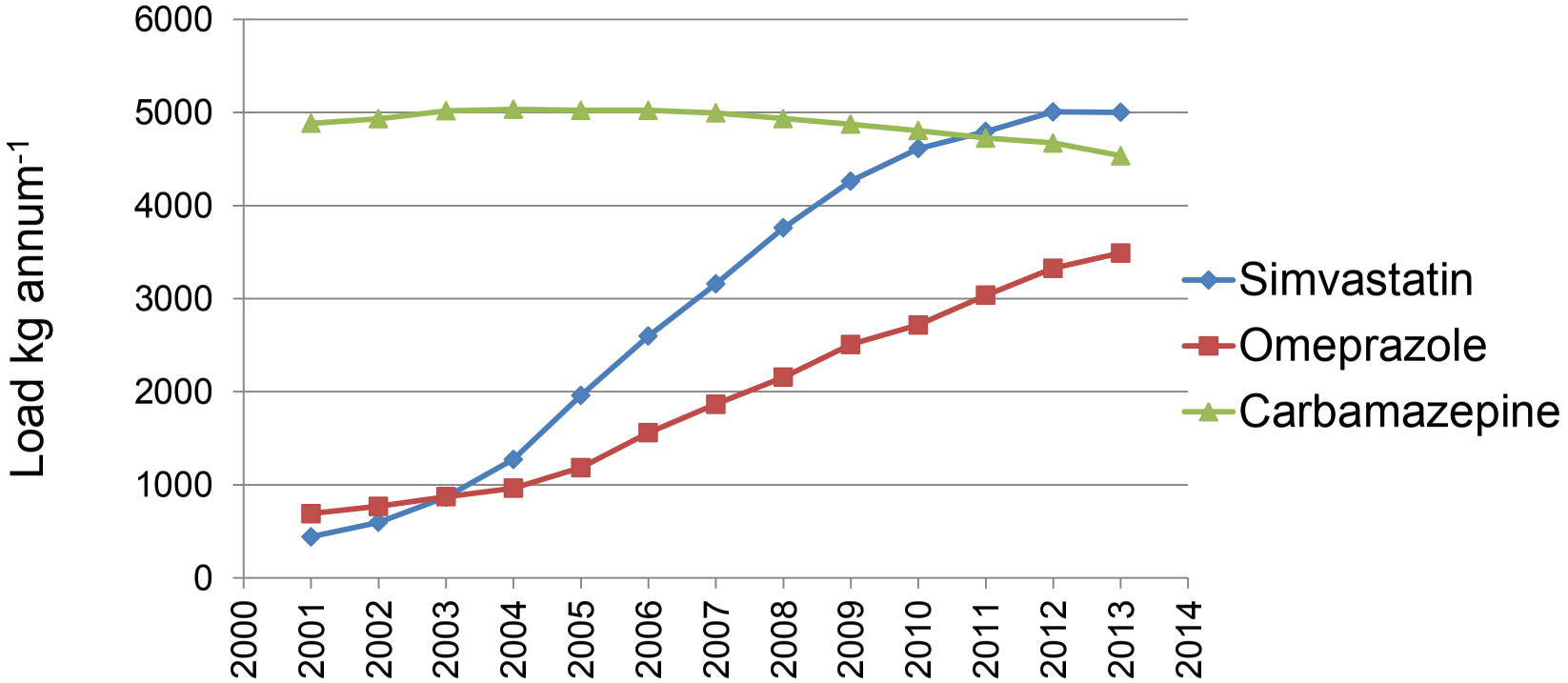


Information Services Scotland, (2014). Prescribing & Medicines: Prescription Cost Analysis.

Drug Load - antihypertensives



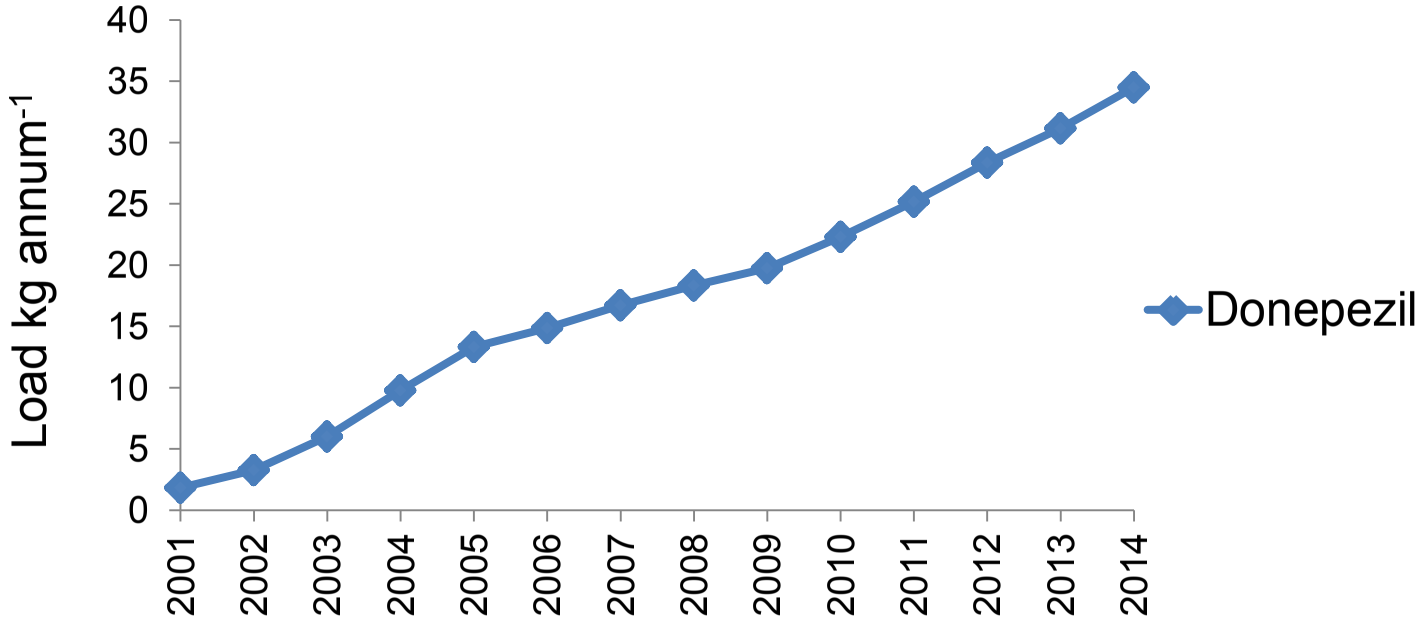
Drug Load


Load kg annum-1
6000
5000
4000
3000
2000
1000
0
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
Simvastatin
Omeprazole
Carbamazepine

Donepezil

- Acetylcholinesterase inhibitor used in treatment of dementia.
- Number of people in UK with dementia predicted to increase to 1 M by 2021.
- Donepezil load (2001-2014) increased x18, although still relatively low.

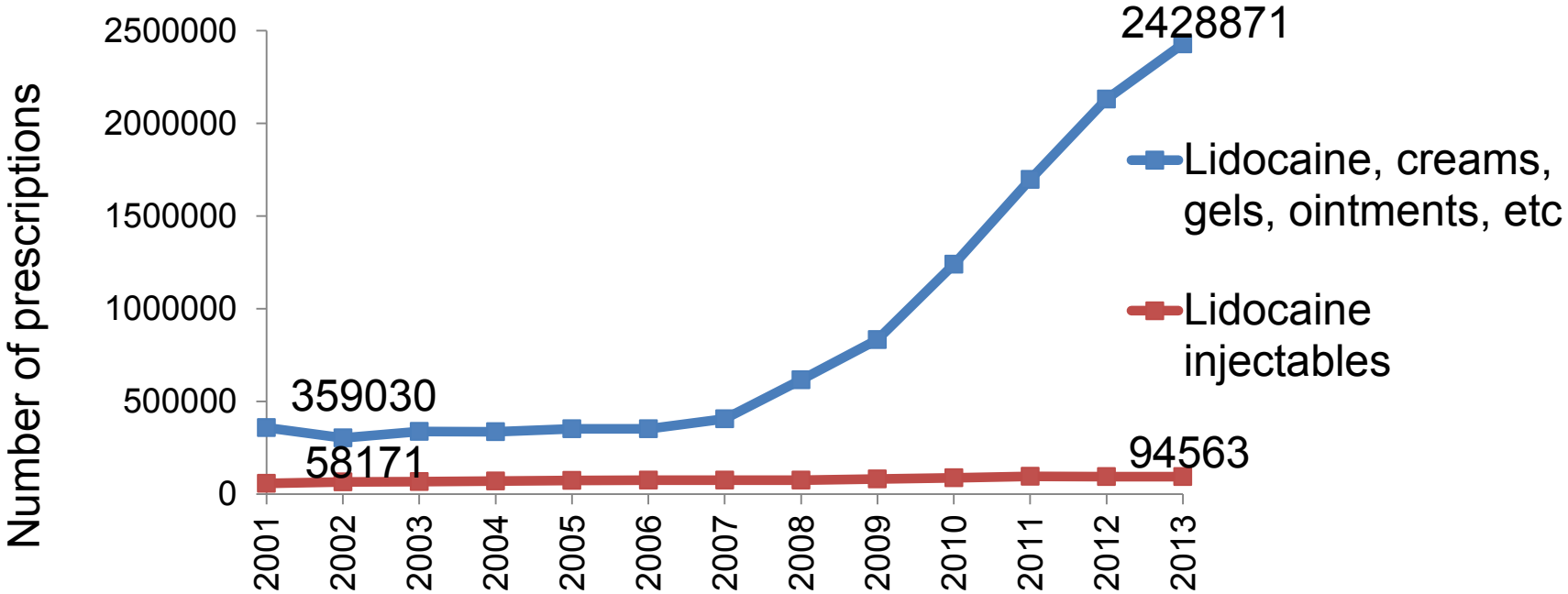
Drug Load - Donepezil



Identified Trends

- Rapid increase in load of simvastatin and omeprazole.
- Omeprazole now available without prescription.
- Carbamazepine load fairly constant.
- Slight decrease in atenolol load with corresponding increase in propanolol.
- Increase in donepezil load predicted to continue.

Lidocaine


Number of prescriptions
2500000
2000000
1500000
1000000
500000
0
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
359030
58171
2428871
94563
Lidocaine, creams, gels, ointments, etc
Lidocaine injectables

Lidocaine

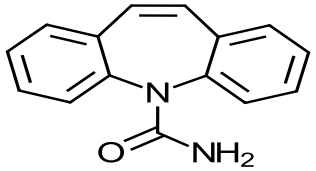
- Injectable – 95% of the dose is metabolised.
  10 mg dose – 0.5 mg lidocaine excreted.
- Gels, creams & ointments – only 5% of the dose is absorbed.
  1 ml application of 5% gel equivalent to 50 mg – 47.5 mg could be washed off.
- Could the increase in use of gels result in higher loads reaching waste water?

Environmental Toxicity

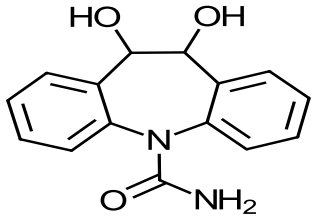
- Direct comparison of data difficult.
- Large variation depending on models used, e.g. PEC/PNEC, ECOSAR
- Metabolites and breakdown products rarely studied.

Carbamazepine

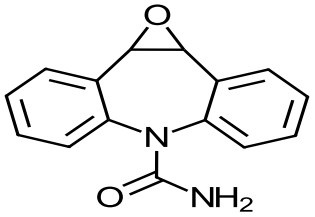
- Known to be persistent in environment.
- Excreted mainly as metabolites:



16% CBZ



71% DiOHCBZ



2.1% CBZEP

CBZ – carbamazepine
DiOHCBZ - 10,11-dihydro-10,11-dihydroxy carbamazepine
CBZEP - 10,11-dihydro-10,11- epoxy carbamazepine

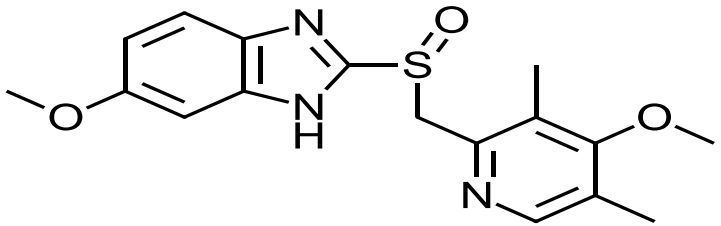
Carbamazepine ECOSAR

				Carbamazepine mg/L	DiOH CBZ mg/L	CBZEP mg/L
Substituted ureas	Fish		ChV	**0.901**	**66.408**	**8.744**
Substituted ureas	Daphnid		ChV	**1.171**	**100.0**	**12.289**
Substituted ureas	Green Algae		ChV	**0.130**	**0.929**	**0.366**

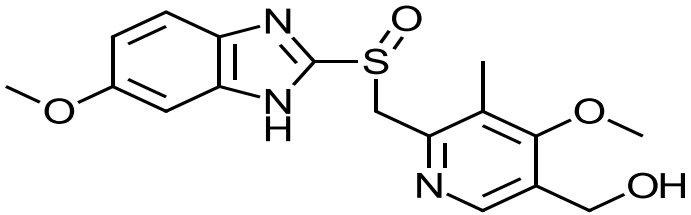
- Indicates metabolites less toxic than parent drug.

Omeprazole

- Pro-drug
- Excreted mainly as metabolite:



Omeprazole



5-hydroxyomeprazole

- Both known to be unstable in acid conditions

Omeprazole ECOSAR

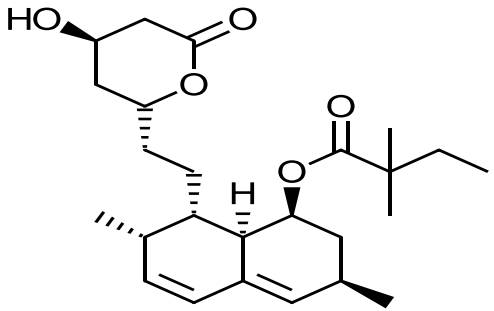
				Omeprazole mg/L	5-hydroxyomep mg/L
Imidazoles	Fish		ChV	**0.1**	**0.018**
Imidazoles	Daphnid		ChV	**0.092**	**0.021**
Imidazoles	Green Algae		ChV	**0.384 !**	**0.125 !**

- Metabolite more toxic than parent drug.

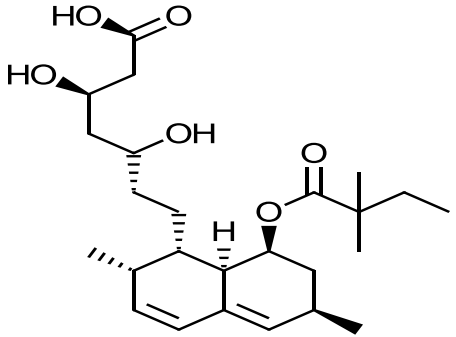
! = exclamation designates: The toxicity value was estimated through application of acute-to-chronic ratios per methods outlined in the ECOSAR Methodology Document provided in the ECOSAR Help Menu.

Simvastatin

- Pro-drug with complex metabolism.
- Major active metabolite is beta-hydroxy-acid of simvastatin.
- Simvastatin may be unstable in sewage conditions.



Simvastatin



Simvastatin acid

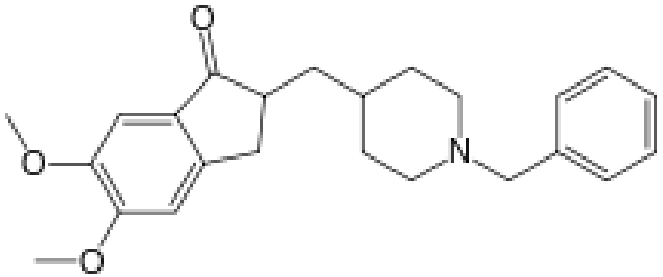
Simvastatin

				Simvastatin mg/L	Simvastatin Acid mg/L
Esters	Fish		ChV	**0.029**	**0.188**
Esters	Daphnid		ChV	**0.308**	**1.855**
Esters	Green Algae		ChV	**0.209**	**1.455**

- Metabolite less toxic than parent drug.

Donepezil

- Excreted mainly in un-metabolised form (57% in urine).
- Environmental load predicted to increase in line with increase in prescribed load.
- More toxicity data required.



Short-list

- Atenolol
- Simvastatin
- Omeprazole
- Donepezil
- Lidocaine
- Carbamazepine

Future Work

- Two WWTPs identified in Central Scotland:
  - One trickling filter, one activated sludge.
  - Serve similar populations.
- Sample influent and effluent at both WWTPs.
- Determine elimination of each drug at WWTPs.
- Determine the degradation products and metabolites for selected drugs.

Acknowledgments

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