MEDUWA-Vecht(e) Project 2017-2020

MEDizin Unerwünscht im WAsser / MEDicines Unwanted in WAter / MEDicijnen Uit het WAter

HCWH Workshop, November 12 2019, Brussels, Belgium

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inter-sectoral cross-border MEDUWA-Vecht(e) coalition

Alloksys

TDI tournois dynamic innovations bv

Dr. Eike G. Fischer
Aix Scientifics®
Contract Research Organisation

GEOPLEX

Noldus
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SAXION
Hogescholen

WEIL
Wasseraufbereitung
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InProSens
Innovative Process Sensors

THE
INTEGRATED
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SOCIETY

wetsus

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budget € 8.5 million

co-funders:

EUROPEAN UNION
European Regional Development Fund

provincie Gelderland

Niedersächsische Staatskanzlei

provincie Overijssel

Ministerie van Economische Zaken en Klimaat

PROVINCIE FLEVOLAND

Ministerium für Wirtschaft, Innovation, Digitalisierung und Energie des Landes Nordrhein-Westfalen

provinsje fryslân
provincie fryslân

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environmental cycle of pharmaceuticals & antimicrobial resistance

Many types of pharmaceuticals & multi-resistant organisms from various sources

pharma industry

hospitals

households

nursing homes

boats & trains

pets

animal husbandry including stables and slaughter houses

(ornamental) fish breeding

gardening (fruits)

Spreading via diverse routes

Industrial STP → **sewage** (incl. leakage & overflow) → **municipal sewage treatment plants** → **sludge** → manure storage and/or **direct deposition**

All environmental compartments contaminated

sediment ⟷ **surface water** ⇄ ground water ⇄ **soil** ← air

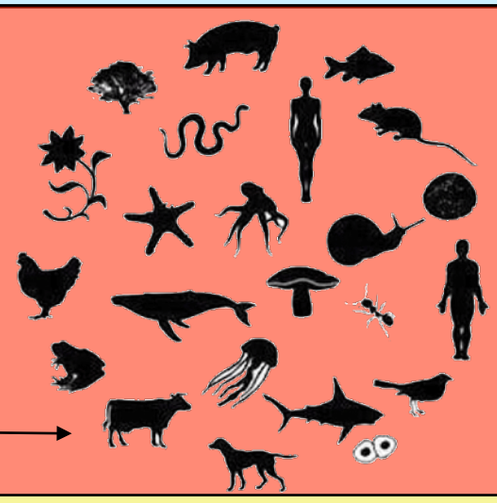
run off & irrigation

Exogenous exposure

tap water →

food chain →

direct environmental contact →



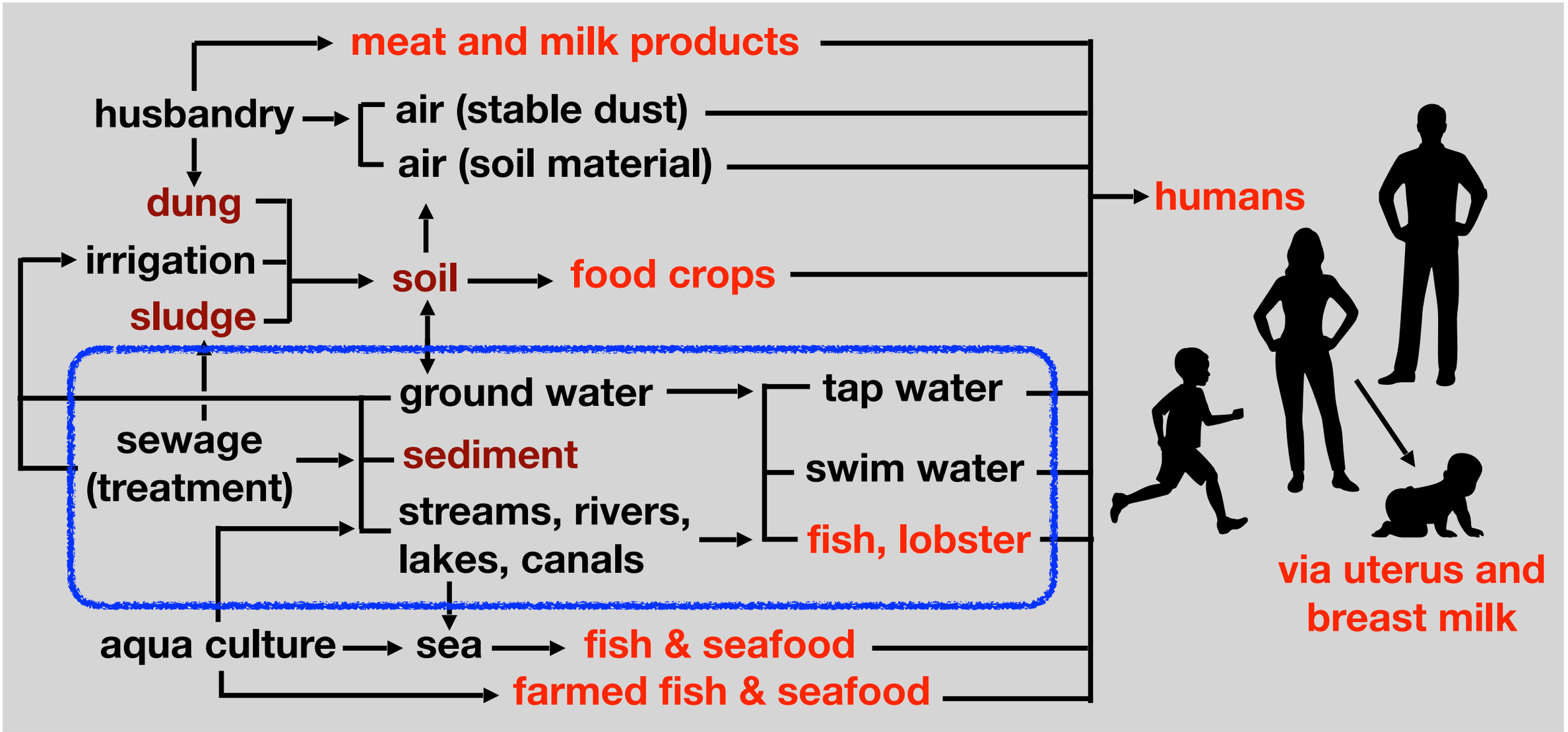
Endogenous exposure

congenital effects

Effects on society and ecology

Development of resistance + Increase is disease & untreatable infections → Increase in costs health care & mitigation

human exposure to medicines and antimicrobial resistance via food, water and air



Legend:

dark red = accumulation

light red = bioaccumulation and/or biomagnification

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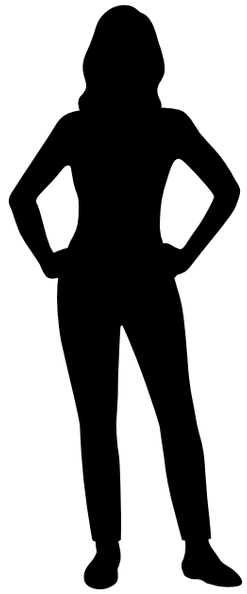
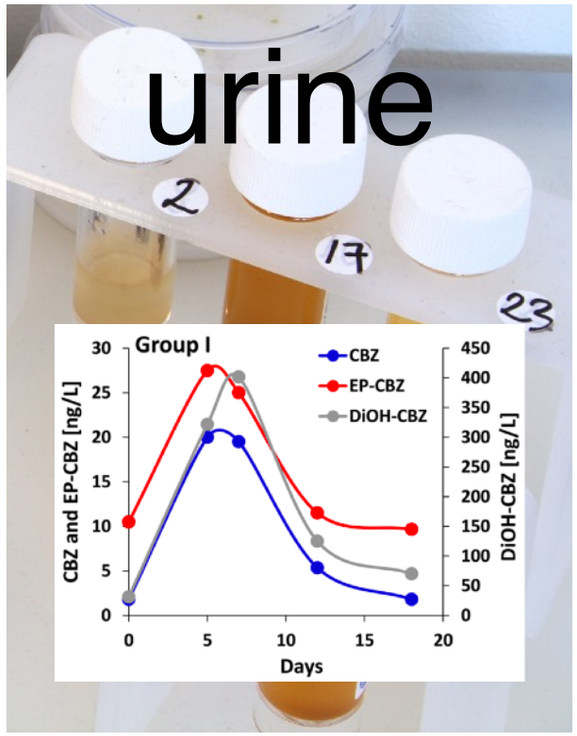
carbamazepine in urine of healthy people

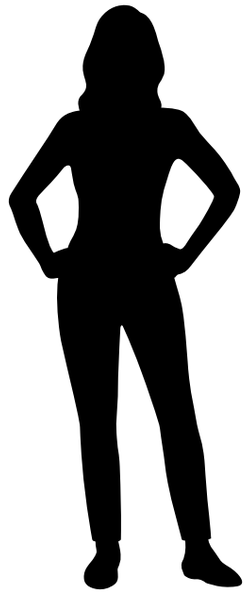


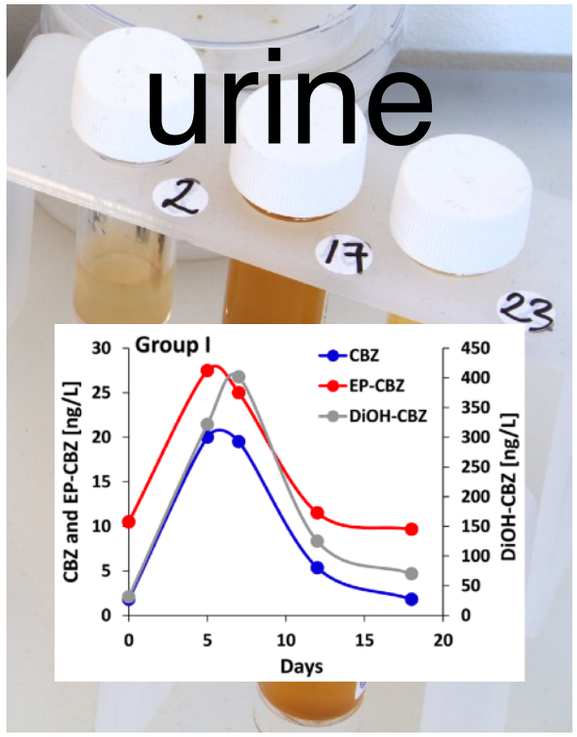


CBZ 5 µg/L

Paltiel O. et al. 2016

carbamazepine in urine of healthy people





CBZ 5 µg/L

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Paltiel O. et al. 2016

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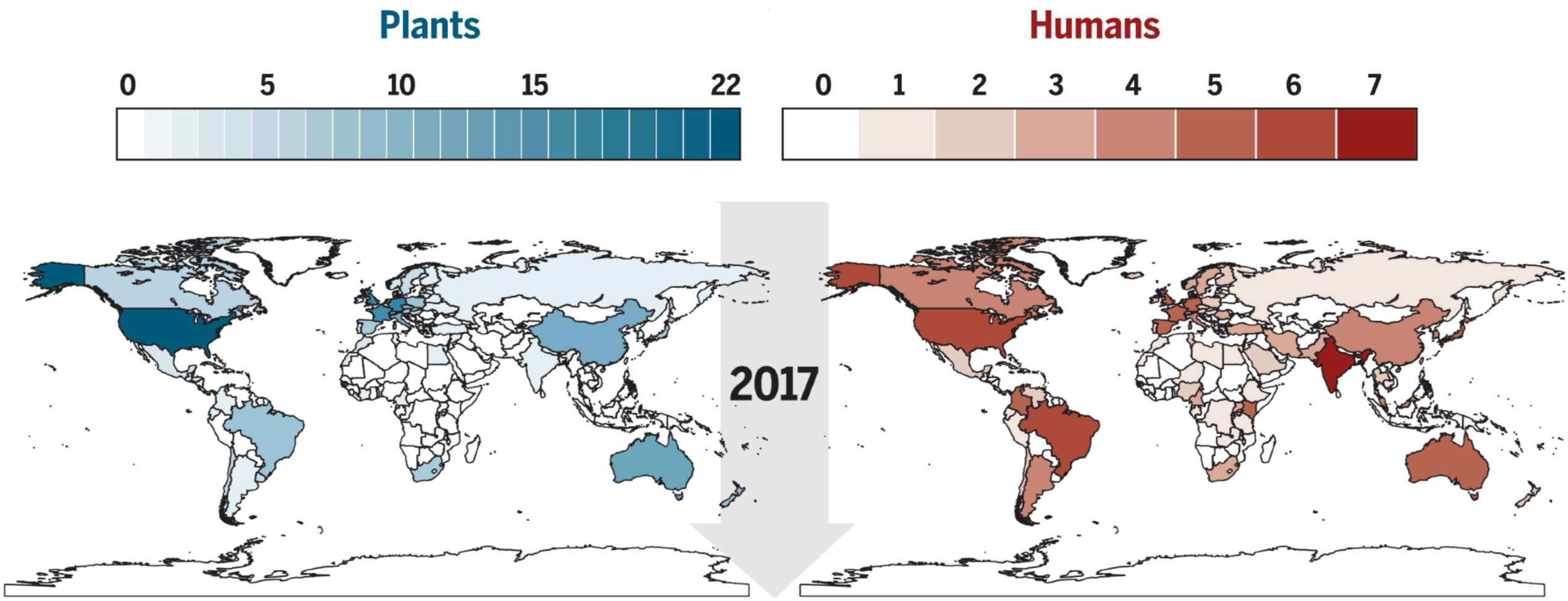
increase in azole resistant fungi in plants and humans



(Sources in) Fisher M. C. et al. 2018

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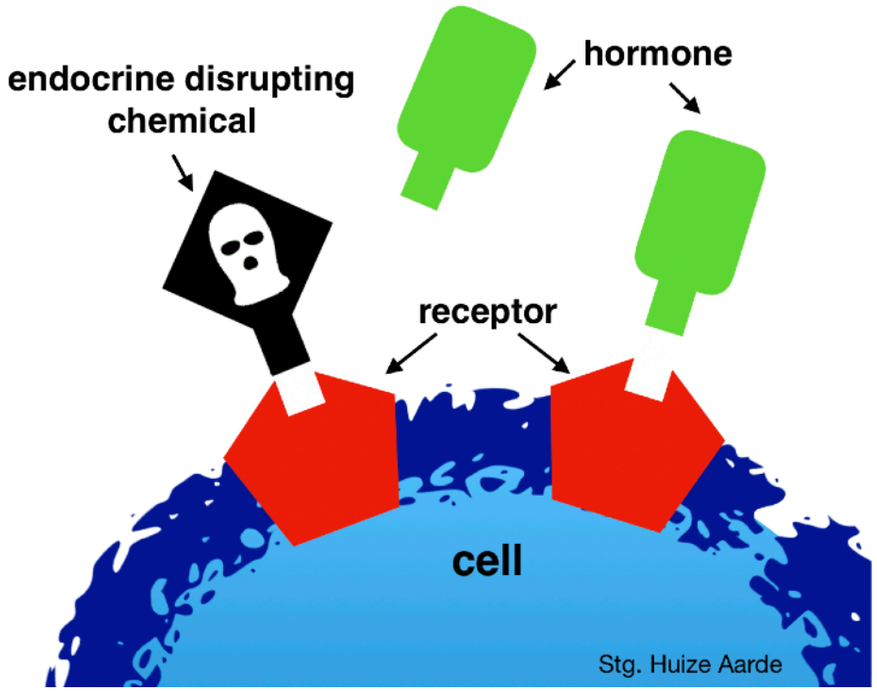
environmental medicines: endocrine disruptors?

non-hormonal medicines with ED-effect

medicine group	sub group	examples	number studies
analgesics	NSAID	ibuprofen acetaminophen	11
antidepressants	SSRI	fluoxetin sertralin	10
anti-fungal agents	azoles	ketoconazole clotrimazole	7
cholesterol reducers	fibrates	bezafibrate clofibrate	5
antihypertensives	beta-blockers	salbutamol propanolol	4
anti-cancer agents	anti-estrogenics	tamoxifen	2
antihypertensives	diuretics	furosemide	2
antibacterial agents	antibiotics	amoxicillin erythromycin	1
antiepileptics	Na-blocker	carbamazepin	1
antiacids	H2-blocker	cimetidine	1

(based on 30 publications till February 2014, Stg. Huize Aarde)



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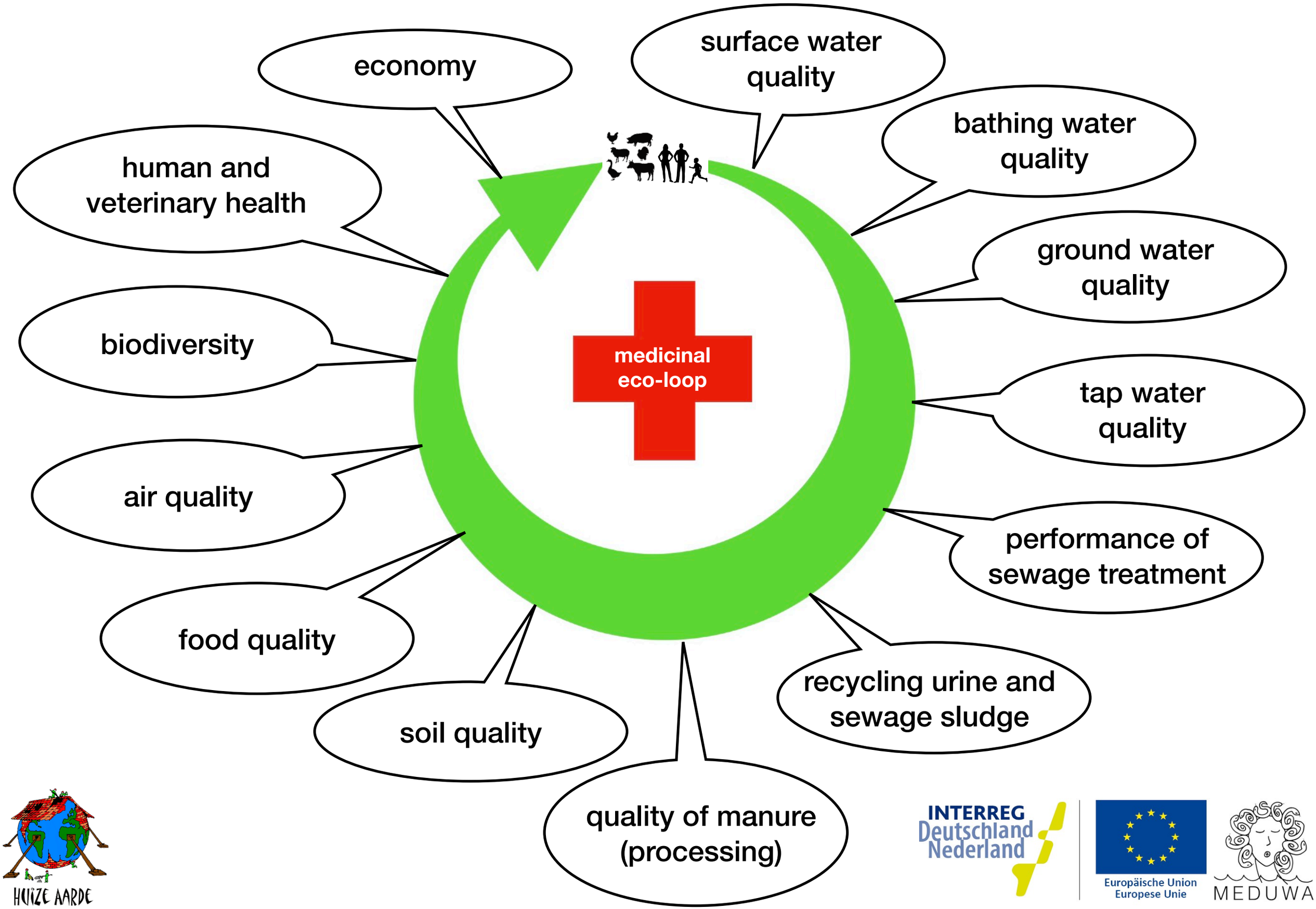
societal consequences of medicinal environmental cycle



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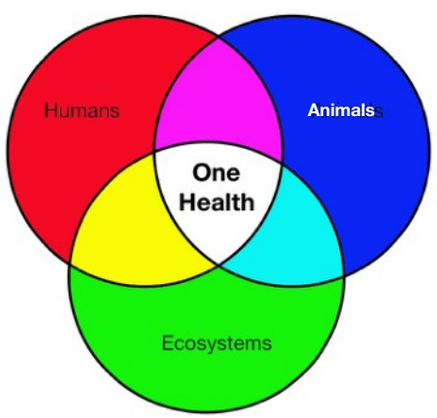
sustainability of measures

by human health sector

- advanced drinking water treatment
- advanced central sewage treatment
- advanced decentralized sewage treatment
- separating waste streams at source
- greening of molecules
- non-chemical diagnosis and treatment
- health promotion



by veterinary health sector

- fermentation or combustion of manure; oxidation of urine
- collection of excess medicines
- biological degradation in manure
- intelligent fertilization
- authorisation on the basis of an environmental impact assessment
- non-chemical diagnosis & treatment
- vaccination
- promotion of animal health
- reduced meat consumption; reduction of food waste

Human measures: Jones OAH 2007; Wenzel H et al. 2008
Veterinary measures: Jibichibi B et al. 2007; Eikelenboom D et al. 2012

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organogram of the MEDUWA-Vecht(e) Project

Work Package 1 Watershed Assessment Tools - IUSF University Osnabrück

- **WP 1.1 Watershed Information System,** IUSF, Geoplex, Wetsus
- **WP1.2 Gray Water Footprint, University Twente,** Geoplex
- **WP 1.3 Regional Risk Assessment,** Radboud University, AVIV
- **WP 1.4 Regional Approach,** Watershap Zuiderzeeland, IUSF, Univ. Twente, Radboud Univ., AVIV

Work Package 2 Monitoring and Filtration - Saxion

- **WP 2.1 Continuous Monitoring,** Saxion, InProSens, Novaris
- **WP 2.2 Wireless Monitoring,** Novaris, InProSens, Saxion, NX Filtration, WEIL Wasser, RUMC
- **WP 2.3 Nanofiltration,** NX Filtration, WEIL Wasser, Saxion

Work Package 3 PAW Oxidation - Univ. Münster IfMM

- **WP 3 Plasma Activated Water Oxidation,** University Münster IfH and IfMM, Vital Fluid, RUMC

Work Package 4 Phytotreatment - Univ. Münster IfH

- **WP 4.1 Phytoremediation,** University Münster IfH and IfMM, Europe Ayurveda Centrum
- **WP 4.2 Herbal Antibiotic Replacement,** University Münster IfH and IfMM, Europe Ayurveda Centrum
- **WP 4.3 Algal Antibiotic Replacement,** Microganic, University Münster IfH, Wetsus

Work Package 5 Farm Animal Monitoring - Noldus

- **WP 5 Farm Animal Monitoring,** Noldus, Demcon, Ubisense

Work Package 6 Biopharma-ceuticals, Tournois Dynamic Innovations BV

- **WP 6.1 Alkaline Phosphatase Production,** TDI, Alloksys
- **WP 6.2 Alkaline Phosphatase Targeting,** TDI, Alloksys, AMRIF, Aix Scientifics
- **WP 6.3 Alkaline Phosphatase Efficacy,** Alloksys, Aix Scientifics

Work Package 7 Management - Osnabrueck Univ.

- **WP 7 Project Management,** UOS, SHA, TIAS

Work Package 8 Communication - TIAS

- **WP 8 Project Communication** TIAS, SHA, UOS

MEDUWA Management Team

- SHA Stichting Huize Aarde
- Osnabrück University
- TIAS The Integrated Assessment Society

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intervention classes of MEDUWA

WP	product	prevention	mitigation	monitoring	simulation prediction	visualisation communication
1.1	Watershed info system				■	■
1.2	Gray water footprint				■	■
1.3	Risk assessment				■	■
2.1	Automatic in-situ monitoring			■		
2.2	Wireless water monitoring			■		
2.3	Nanofiltration		■			
3	PAW oxidation		■			
4.1	Phytoremediation		■			
4.2	Herbal antibiotic replacement	■	■			
4.3	Algal antibibiotic replacement	■	■			
5	Wireless cattle monitoring	■				
6	Biopharmaceuticals	■				

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MEDICINE CHAIN

development
testing
evaluation
production
education
marketing
diagnosis
prescription
use
emission

herbal antibiotic replacement V
algal antibiotic replacement V
biopharmaceuticals HV

focus of today

regional risk assessment HV
gray water footprint HV
watershed information system HV
wireless cattle monitoring V
wireless monitoring HV
automatic in-situ monitoring HV
nanofiltration HV
phytoremediation HV
PAW oxidation HV

12 innovations of MEDUWA

Human

Veterinary

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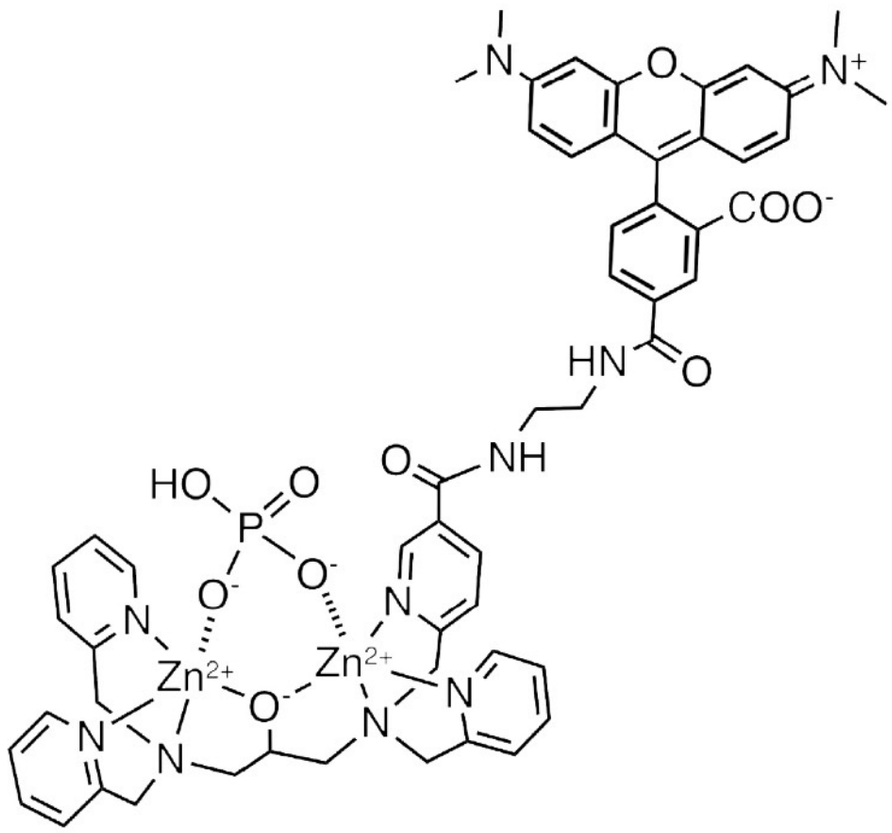
MEDUWA innovations

biopharmaceutical : alkaline phosphatase (AP)



- Production and application of AP as a natural anti-inflammatory medicine.
- **In humans:** eg. to prevent steroid use against inflammations in artritis, cystic fibrosis and during cardiac operations.
- **In animals:** to replace persistent chemicals against mastitis, colitis, weaning diarrhea.

Amrif

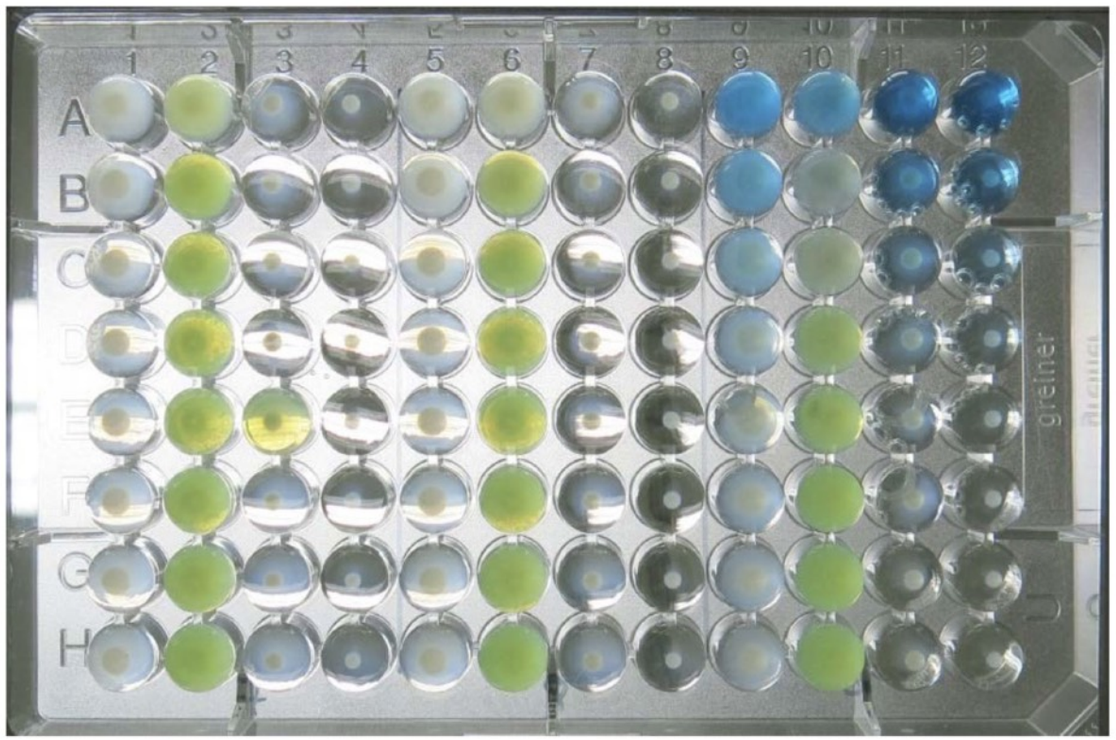
TDI tournois dynamic innovations bv

Alloksys

Dr. Eike G. Fischer Aix Scientifics® Contract Research Organisation

MEDUWA-innovations

plant and algae mixtures instead of antibiotics



To:

- replace antibiotics in animals and humans
- promote health and growth;
- prevent the contamination of soil, air and water with medicines;
- prevent the development of resistances;
- remediate contaminated water and soil (phytoremediation)

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MEDUWA-innovations

plant and algae mixtures instead of antibiotics

bacterial species

plant species

Bacillus subtilis	S. aureus	E. coli	Ps. aeruginosa
1:20 – 1:2560	1:20 – 1:2560	1:20 – 1:2560	1:20
n.e.	n.e.	n.e.	n.e.
n.e.	1:20 – 1:40	n.e.	n.e.
1:20 – 1:2560	1:20 – 1:2560	1:20 – 1:2560	n.e.
1:20 – 1:2560	1:20 – 1:2560	1:20 – 1:2560	1:20 – 1:40
1:20 – 1:2560	1:20 – 1:2560	1:20 – 1:2560	1:20 – 1:40
n.e.	n.e.	n.e.	n.e.
1:20	1:20	n.e.	n.e.
n.e.	n.e.	n.e.	n.e.
1:20 – 1:40	1:20	1:20	n.e.
n.e.	n.e.	n.e.	n.e.
n.e.	1:20	n.e.	n.e.
1:20 – 1:2560	1:20 – 1:1280	1:20 – 1:640	n.e.
n.e.	n.e.	n.e.	n.e.
1:20 – 1:2560	1:20 – 1:1280	1:20 – 1:1280	1:20
1:20 – 1:2560	1:20 – 1:1280	1:20 – 1:1280	1:20
1:20 – 1:160	1:20 – 1:160	n.e.	n.e.
n.e.	n.e.	n.e.	n.e.
1:20 – 1:2560	1:20 – 1:2560	1:20 – 1:1280	1:20
1:20 – 1:2560	1:20 – 1:1280	1:20 – 1:640	n.e.
1:20 – 1:2560	1:20 – 1:2560	1:20 – 1:2560	1:20
1:20 – 1:2560	1:20 – 1:2560	1:20 – 1:2560	1:20
n.e.	n.e.	n.e.	n.e.
1:20 – 1:2560	1:20 – 1:640	1:20 – 1:320	n.e.
1:20 – 1:2560	1:20 – 1:1280	1:20 – 1:640	n.e.
1:20	1:20	n.e.	n.e.
1:20 – 1:40	1:20 – 1:40	1:20	n.e.
1:20 – 1:2560	1:20 – 1:1280	1:20 – 1:640	1:20
1:20 – 1:40	1:20 – 1:80	n.e.	1:20
1:20 – 1:80	1:20 – 1:80	n.e.	1:20 – 1:40
n.e.	n.e.	n.e.	n.e.
1:20 – 1:256	1:20 – 1:256	1:20 – 1:2650	1:20 – 1:40

Intermediate results:

- 15 species and mixtures tested
- Effects differ between bacteria
- Some herbs kill bacteria (green)
- Some only inhibit growth (yellow)

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green medicines: utopia or option

examples of biodegradable medicines (according to OECD tests)

isosorbide dinitrate	> 90%
mesalazine	> 90%
penicillin V	> 90%
piracetam	> 90%
cytarabine	> 90%
acetylsalicylic acid	81%
valproic acid	78%
glufosfamide	72%

Kümmerer K. in Kümmerer K. and M. Hempel (Eds.), 2010, Green and Sustainable Pharmacy, Springer.

Prof. Klaus Kümmerer

- Stability does not exclude biodegradability.
- Biodegradability can be included intentionally.
- Biodegradability can improve therapeutic effect and reduce side effects.

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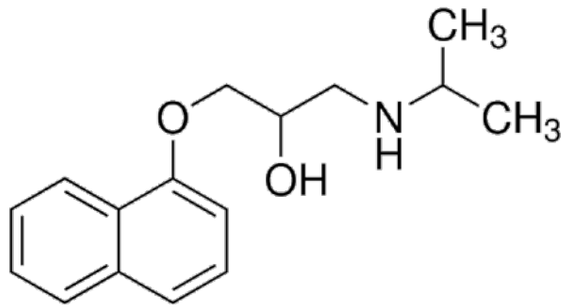
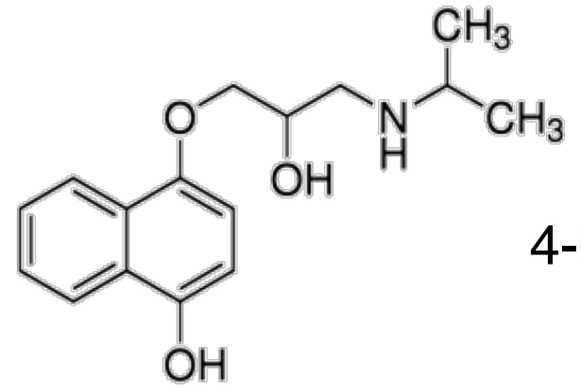
benign-by-design-medicines

not biodegradable **biodegradable**

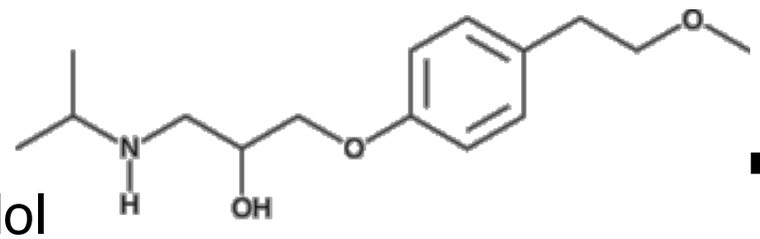
propranolol

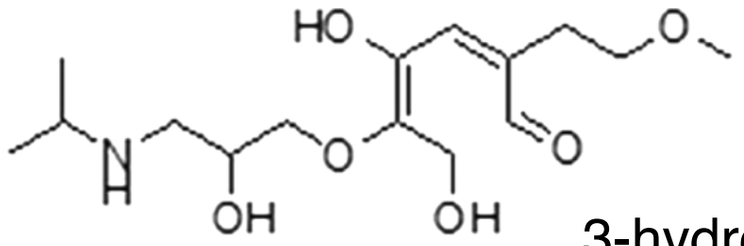




4-hydroxy-propranolol

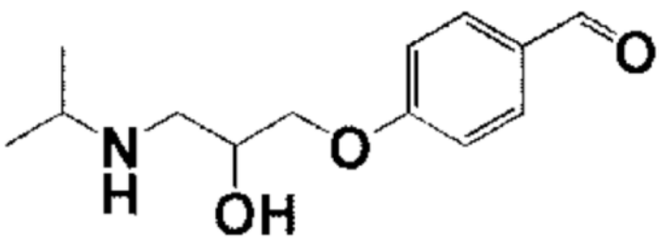
metoprolol

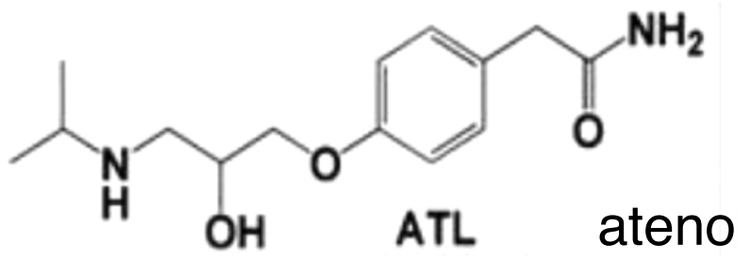




3-hydroxy-metoprolol

atenolol





atenolol TP 238

metoprolol: Rastogi T et al. 2014 Chemosphere
propranolol: Rastogi T et al. 2015 Env Sc Techn
atenolol: Rastogi T et al. 2015 RCS Advances

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green medicines: phytotherapeutics

International Journal of Neuropsychopharmacology, Page 1 of 11. © CINP 2014
doi:10.1017/S1461145714000017

Lavender oil preparation Silexan is effective in generalized anxiety disorder – a randomized double-blind comparison to placebo and paroxetine

Siegfried Kasper[1], Markus Gastpar[2], Walter E Müller[3], Hans-Peter Volz[4], Hans-Jürgen Möller[5], Sandra Schläfke[6] and Angelika Dienel[6]

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priorities for action

- Stimulate cross-sectoral pilot projects that work on the whole life cycle of medicines.
- Develop & test source oriented solutions, including prevention.
- Incentives for start-ups and universities for research in biodegradable medicines.

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thank you for you attention

More information: MEDUWA.eu

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