Benign by Design

Session 6: Sustainability from the beginning – the pharmaceutical example

Prof. Dr. Klaus Kümmerer
Klaus.Kuemmerer@uni.leuphana.de

LEUPHANA
Institute of Sustainable
and Environmental Chemistry

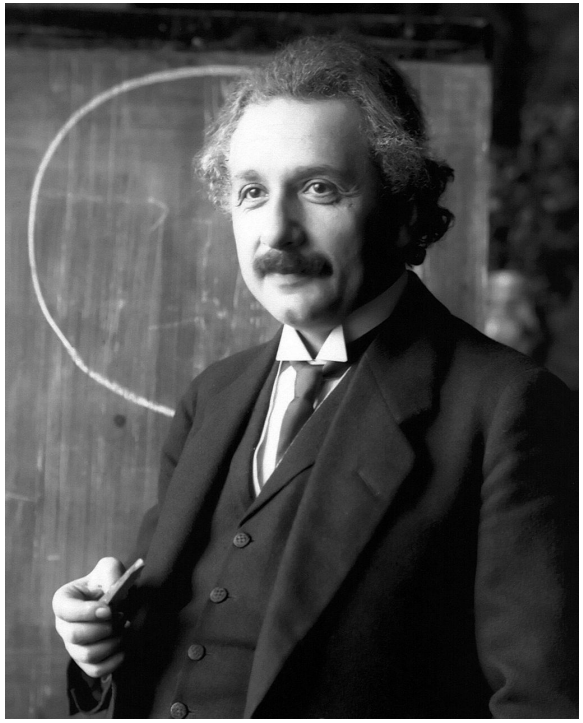
„Emerging“ Contaminants

- Myriads of parent compounds
- Multiplied by even more transformation products (in even lower concentration)
- Multiplied by nummerous environmental matrices, locations and points in time
- Multiplied by nummerous tests with even more endpoints and parameters

Risk assessment impossible !

A smart person solves a problem.

A wise person avoids it.



Attributed to Albert Einstein

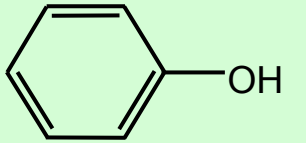
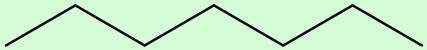
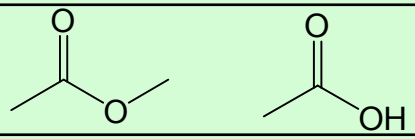
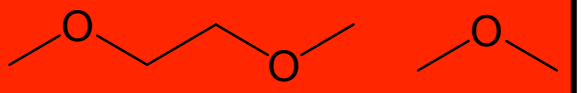
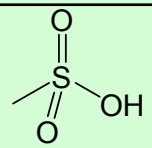
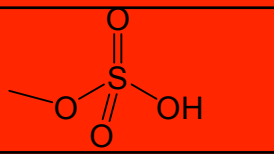
Persistence !

Biodegradability of Pharmaceuticals in the Aquatic Environment (in %)

API	OECD 301 D	OECD 301 F	OECD 302 B
Valproic acid	72	78	
Mesalazin	> 90	> 90	
Acetylsalicylic acid		81	
Penicillin V			> 90
Piracetam		> 90	> 90
Hydroxamic acid	50	90	

📖 Kümmerer and co-workers, unbublished

Impact on Biodegradability in the Aquatic Environment
Rules of Thumb

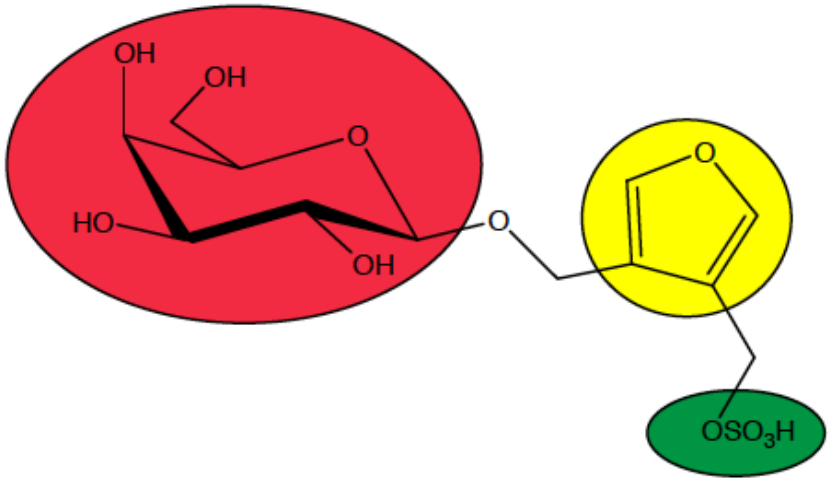
favorable	less favorable
	
	
	
	
	
	

Rieger R et al. (2002)
J. Biotechnol. 94, 101

Boethling R et al. (2007)
Chem. Rev.107, 2207

Kümmerer K (2007)
Green Chem. 9, 899

De Novo Synthesis
(1) Targeted Structure Variation



Goal: Improved Efficacy and biodegradability in the environment

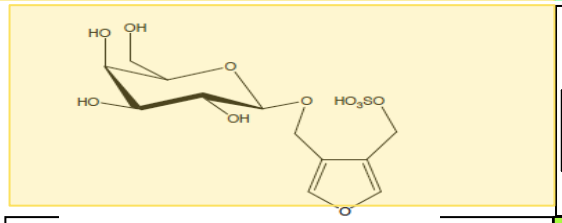
- **Improved by variation of the sugar?**
- **Improved by variation of substituents at the furan ring?**
- **Improved by variation of the aromatic ring?**

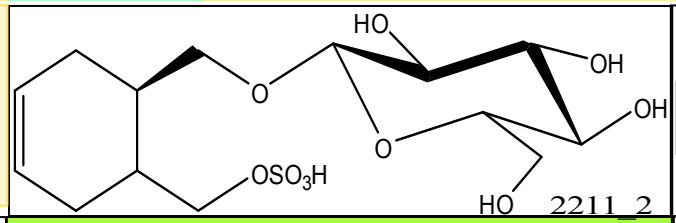
📖 Kümmerer K, Frei E, Marano G, in preperation

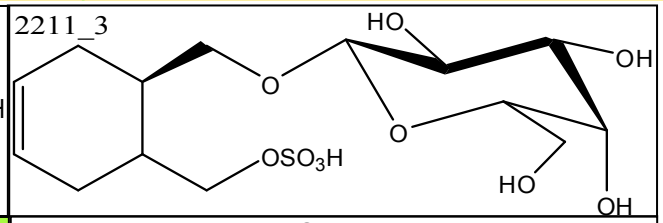
Improved Active Pharmaceutical Ingredient

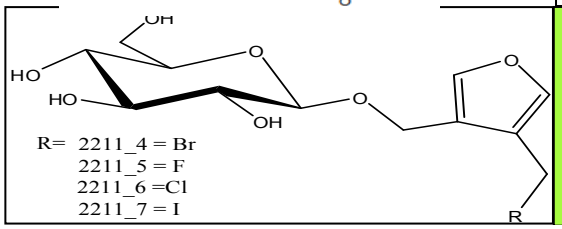
gefördert durch DBU Deutsche Bundesstiftung Umwelt www.dbu.de

Structure ID	Log Kow	Effect threshold (rel. units)	Biodegradation[%]
GSF	-2,1	1	19
2211_2 (Glu ,Cyclohex)	-1,8	> 1	37
2211_3 (Gal, Cyclohex)	-1,8	> 1	37
2211_4 (Glu-Br)	-0,5	> 1	14
2211_5 (Glu-F)	-0,9	> 1	14
2211_6 (Glu-Cl)	-0,7	> 1	14
2211_7 (Glu-I)	-0,5	> 1	14
2211_8	-2,0	<0,01	54
2211_9 (Desoxyglu)	-1,5	> 1	31



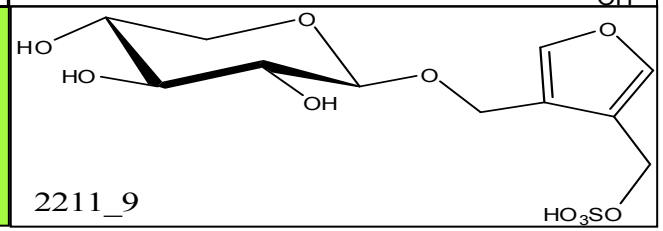






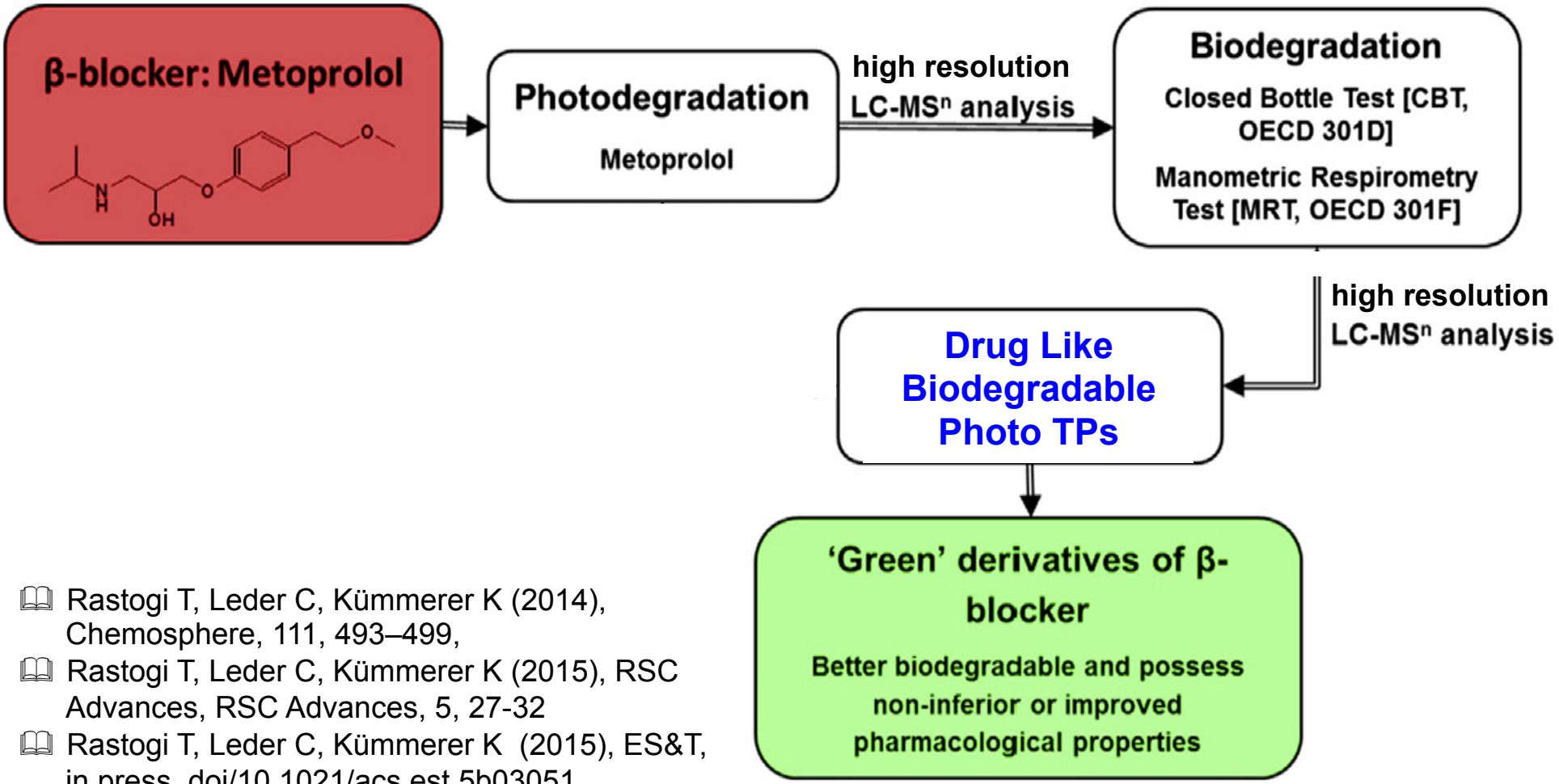
📖 **Frei et al., patent pending**

2211_8



📖 Kümmerer K, Frei E, Marano G, in preperation

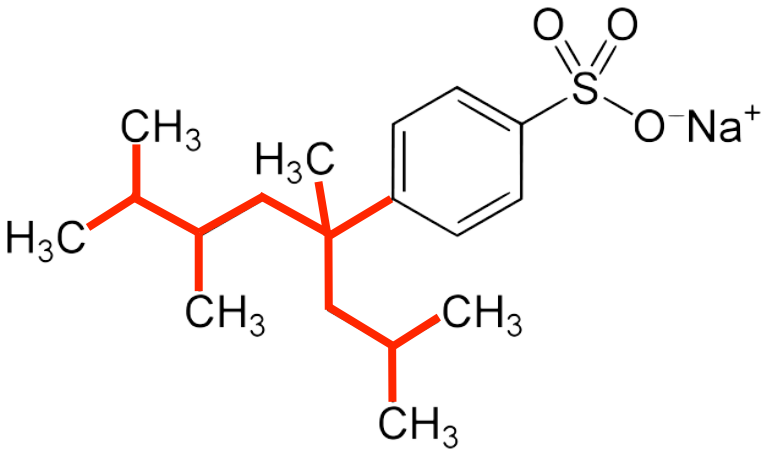
Re-Design



- Rastogi T, Leder C, Kümmerer K (2014), Chemosphere, 111, 493–499,
- Rastogi T, Leder C, Kümmerer K (2015), RSC Advances, RSC Advances, 5, 27-32
- Rastogi T, Leder C, Kümmerer K (2015), ES&T, in press, doi/10.1021/acs.est.5b03051

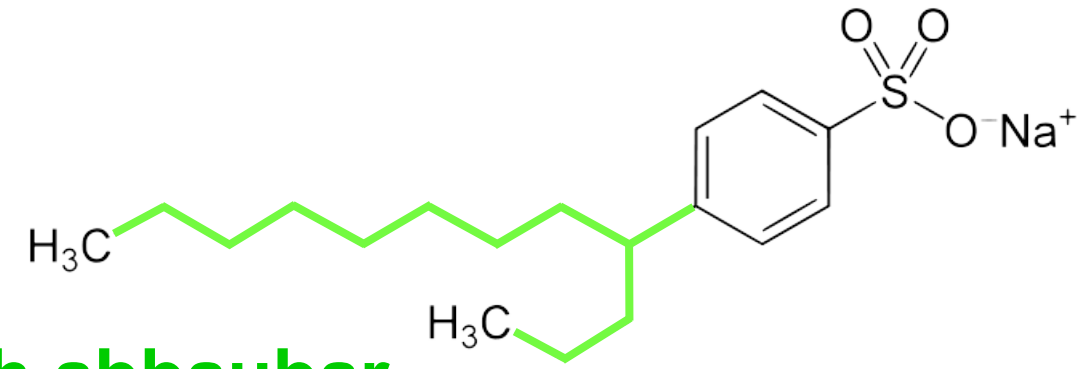
Biologische Abbaubarkeit
Tensid LAS

TPS:
nicht biol. abbaubar

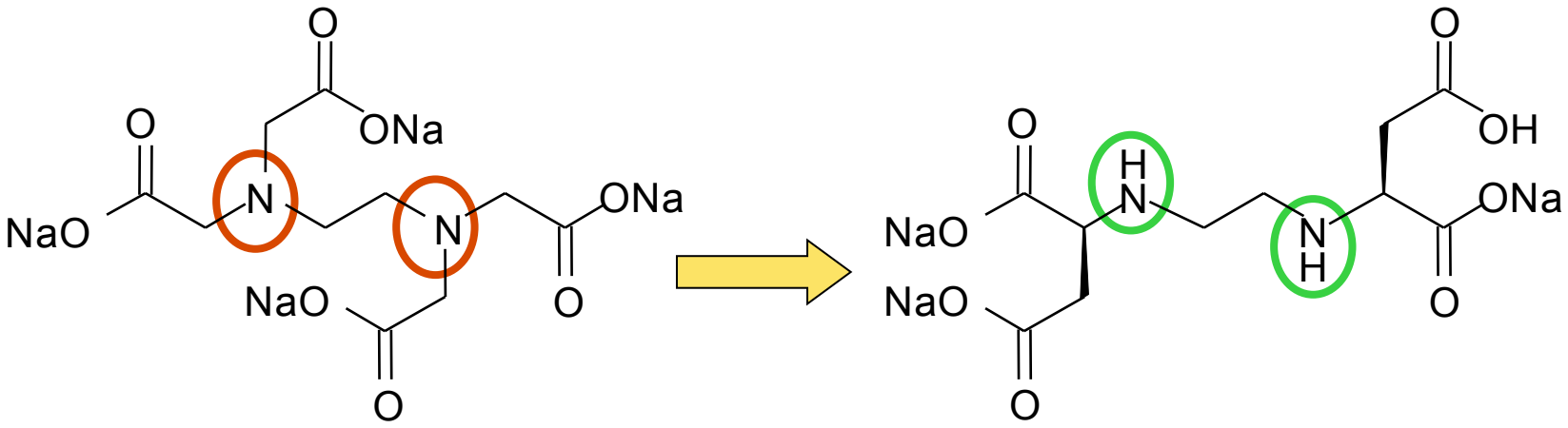


Tensidverordnung 1962

LAS:
leicht biologisch abbaubar



Gezielte Verbesserung
Komplexbildner EDTA vs. S,S-EDDS



EDTA

Tri-Natrium-[S,S]-EDDS

Dixon N. 2004 (http://www.euconferences.com/chemicalsmanagement04 /day2presentations.htm)

Carrots

- New business case
- Prolonged patent life-time
- Fast track authorization
- Precautionary principle (subset of arguments)
- Important contribution to CSR
- Increased reputation

📖 US- Department of Agriculture

... and Sticks

- EMA: Revision of EMEA guideline (EU Parliament)?
- EEA Report 1/2010: „Pharmaceuticals in the Environment“
- Legislation (e.g. EU Water Framework Directive)
- U.S. Senate Hearing
- The greener consumer

http://www.eea.europa.eu/publications/pharmaceuticals-in-the-environment-result-of-an-eea-workshop

Benign by Design

Also for

- Chemicals
- Materials
- Complex products
- Substance flows
- Material flows