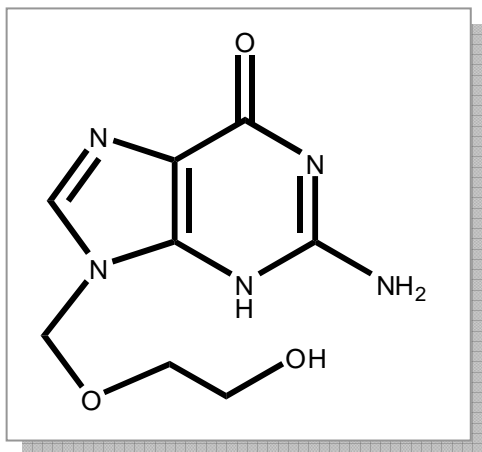


Occurrence and fate of pharmaceuticals in the urban water cycle - acyclovir as a case study

Carsten Prasse, Thomas A. Ternes

Federal Institute of Hydrology (BfG) Koblenz, Germany





Antiviral drug used for the treatment of Herpes infections (guanine derivative)

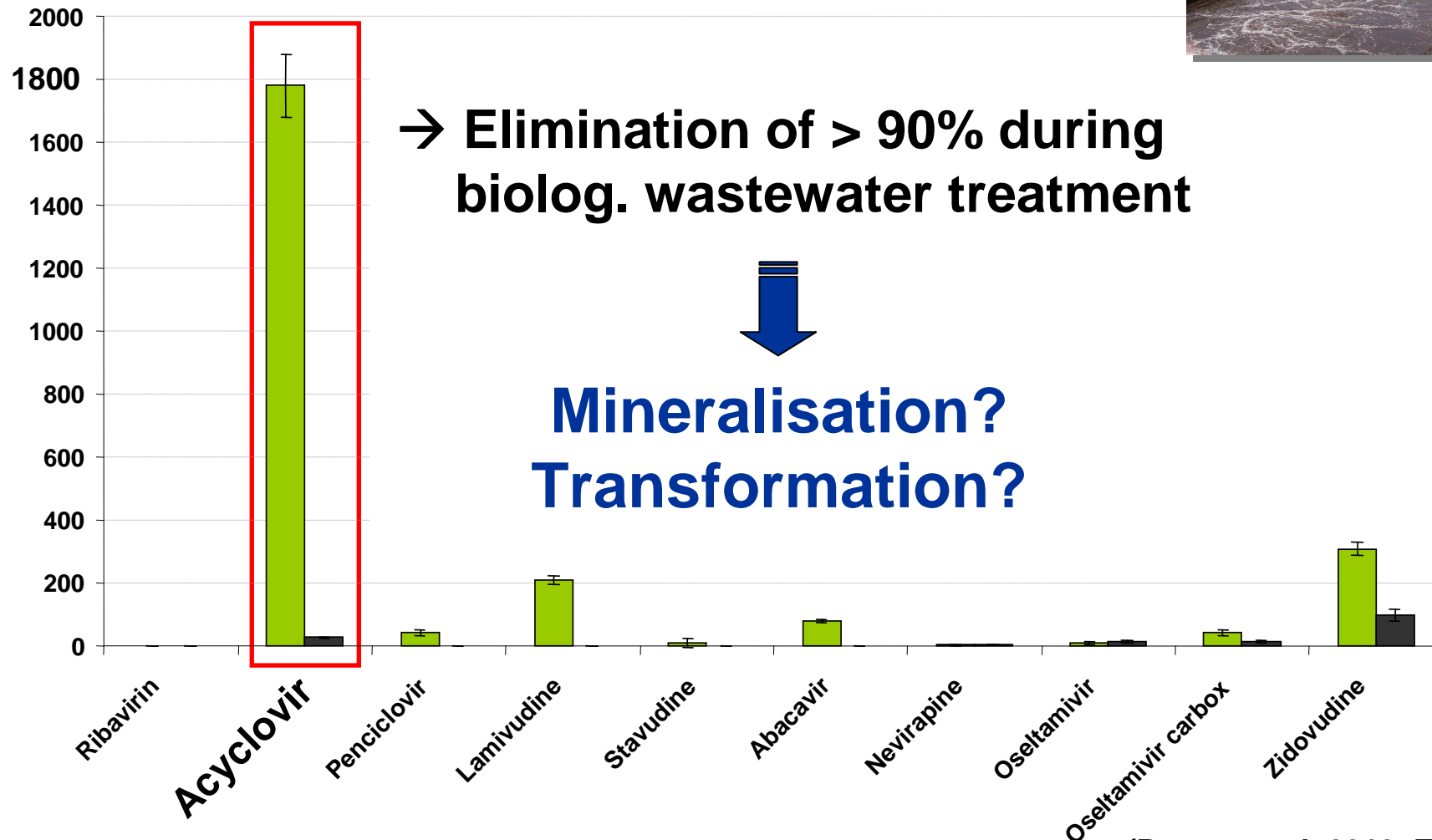
- Prescribed amount in Germany (2009): **10,0 t**
(source: Arzneiverordnungsreport 2010)
- Number of preparations available in Germany: **158** (23 are available without prescription (over-the-counter drugs); Crèmes < 2 g)
(source: www.db.oddb.org)



Wastewater treatment plant (WWTP) Koblenz, 330.000 PE



Conc. [ng L⁻¹]

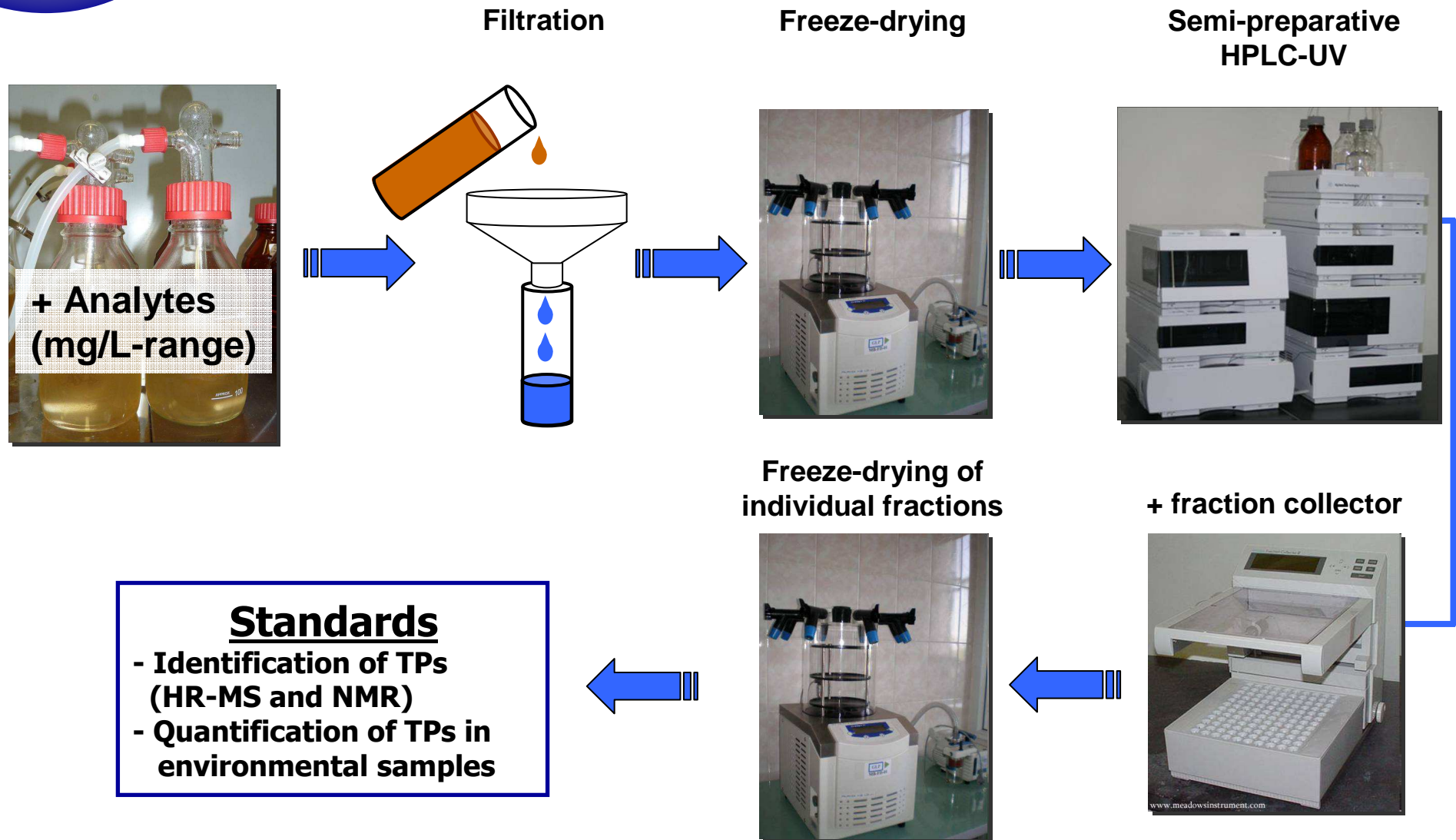


→ Elimination of > 90% during
biolog. wastewater treatment

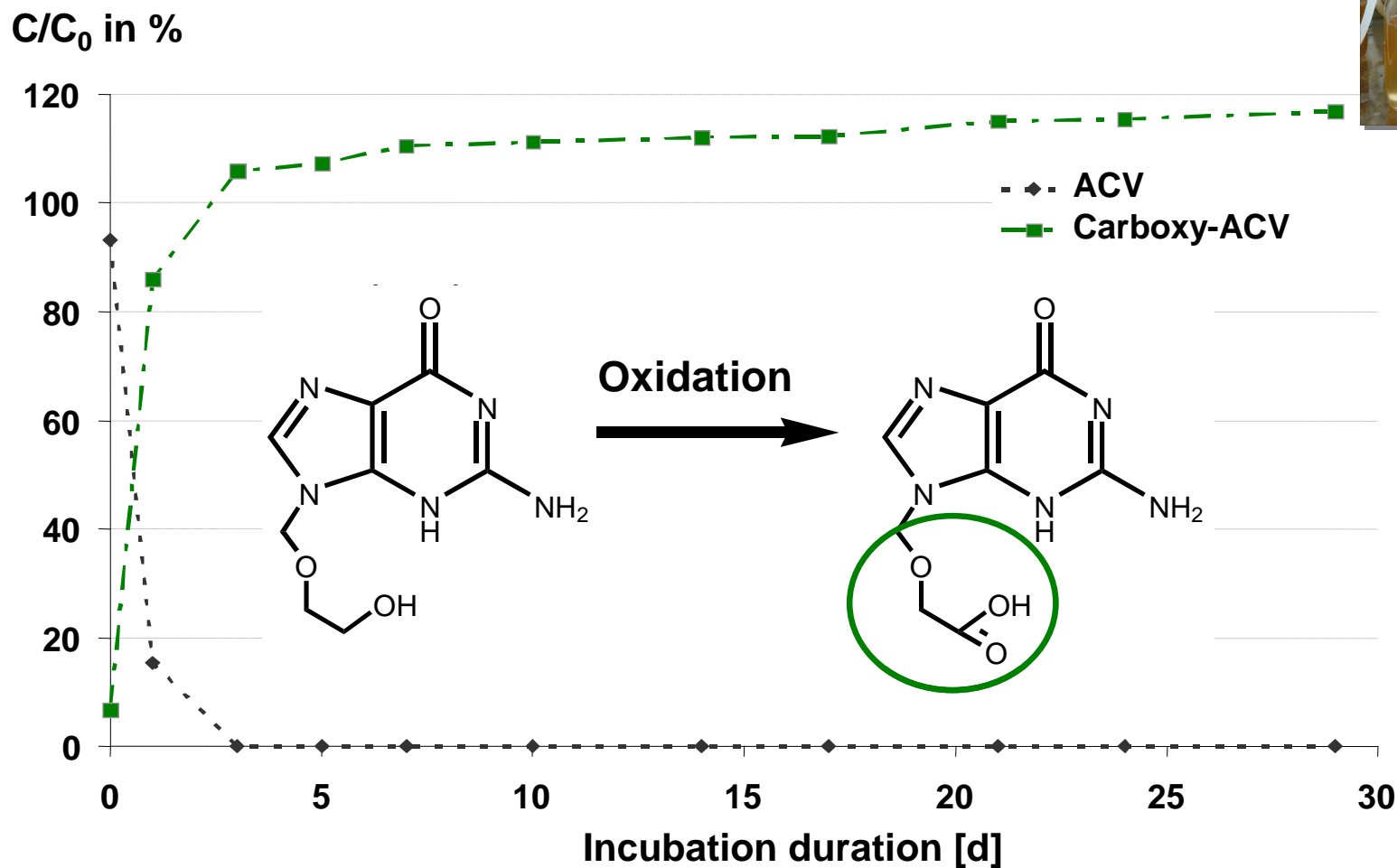


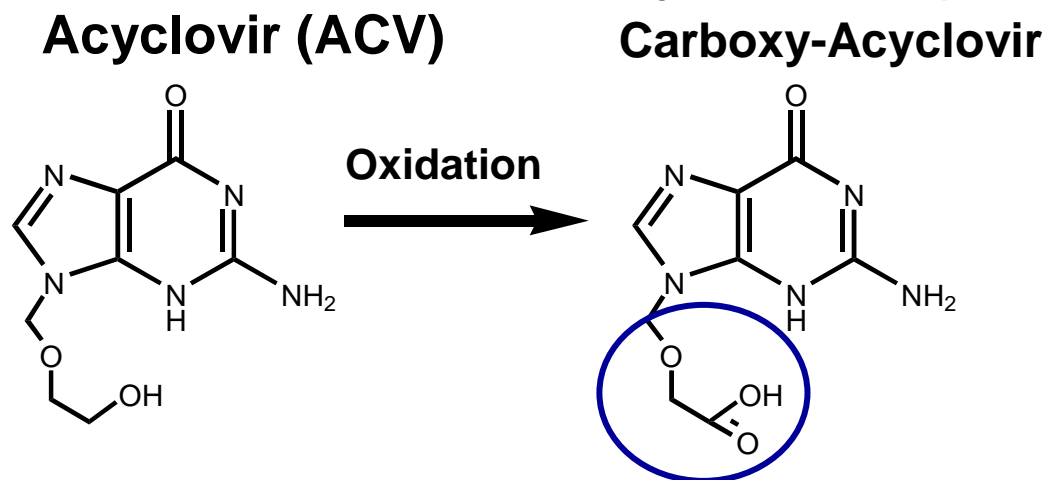
Mineralisation?
Transformation?

(Prasse et al. 2010, ES&T)



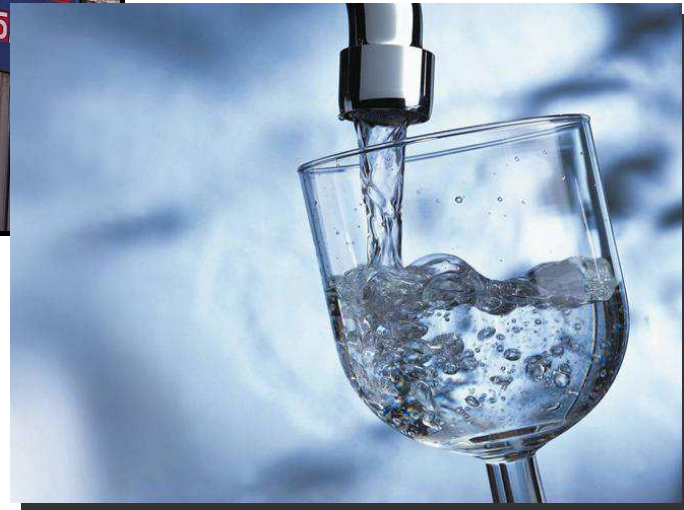
Transformation of acyclovir in sewage sludge





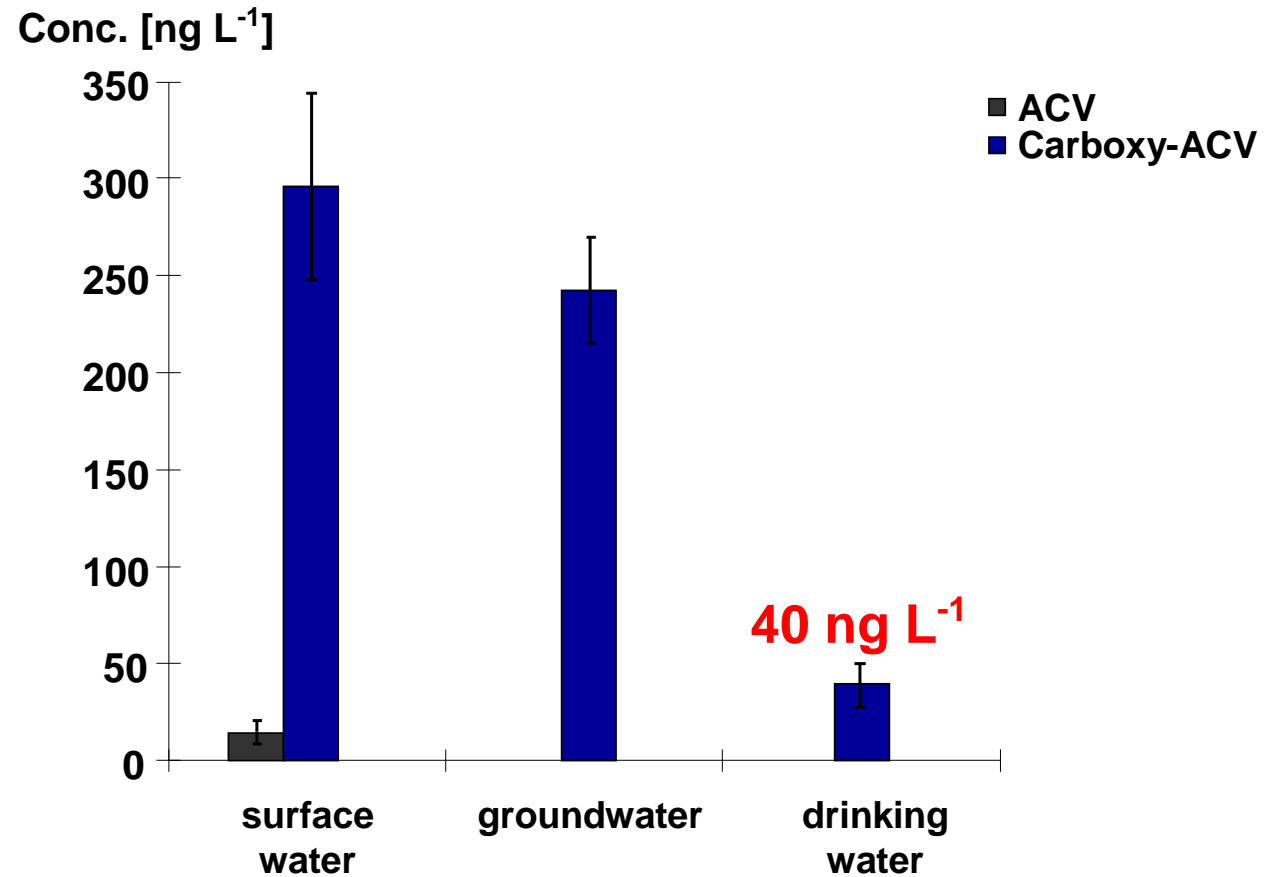
ng/L	ACV	Carboxy-ACV	Sum
Influent	2000	430	2430
Effluent	140	2400	2540
Elimination	93 %	- 453%	NO!

Occurrence of carboxy-acyclovir in the environment

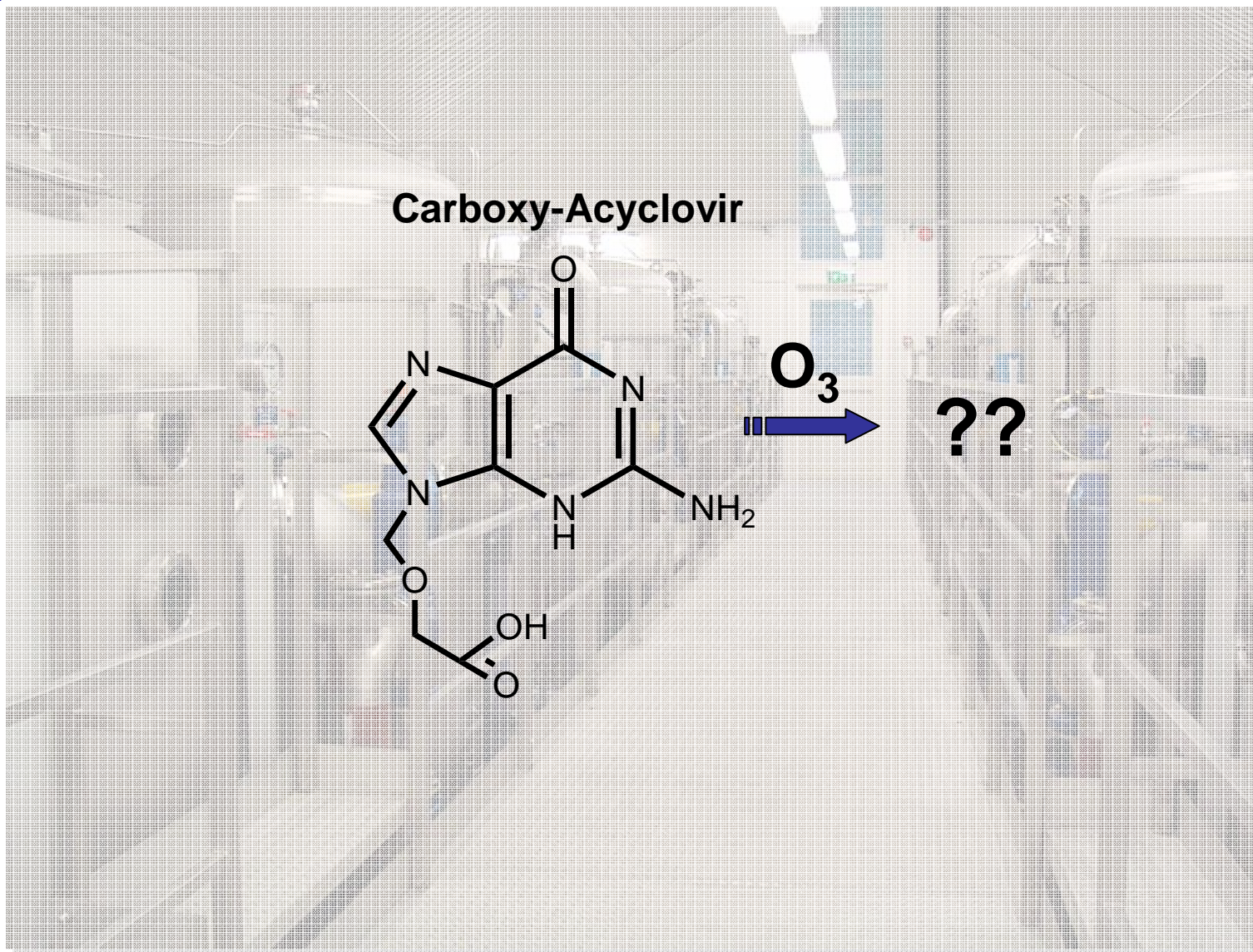


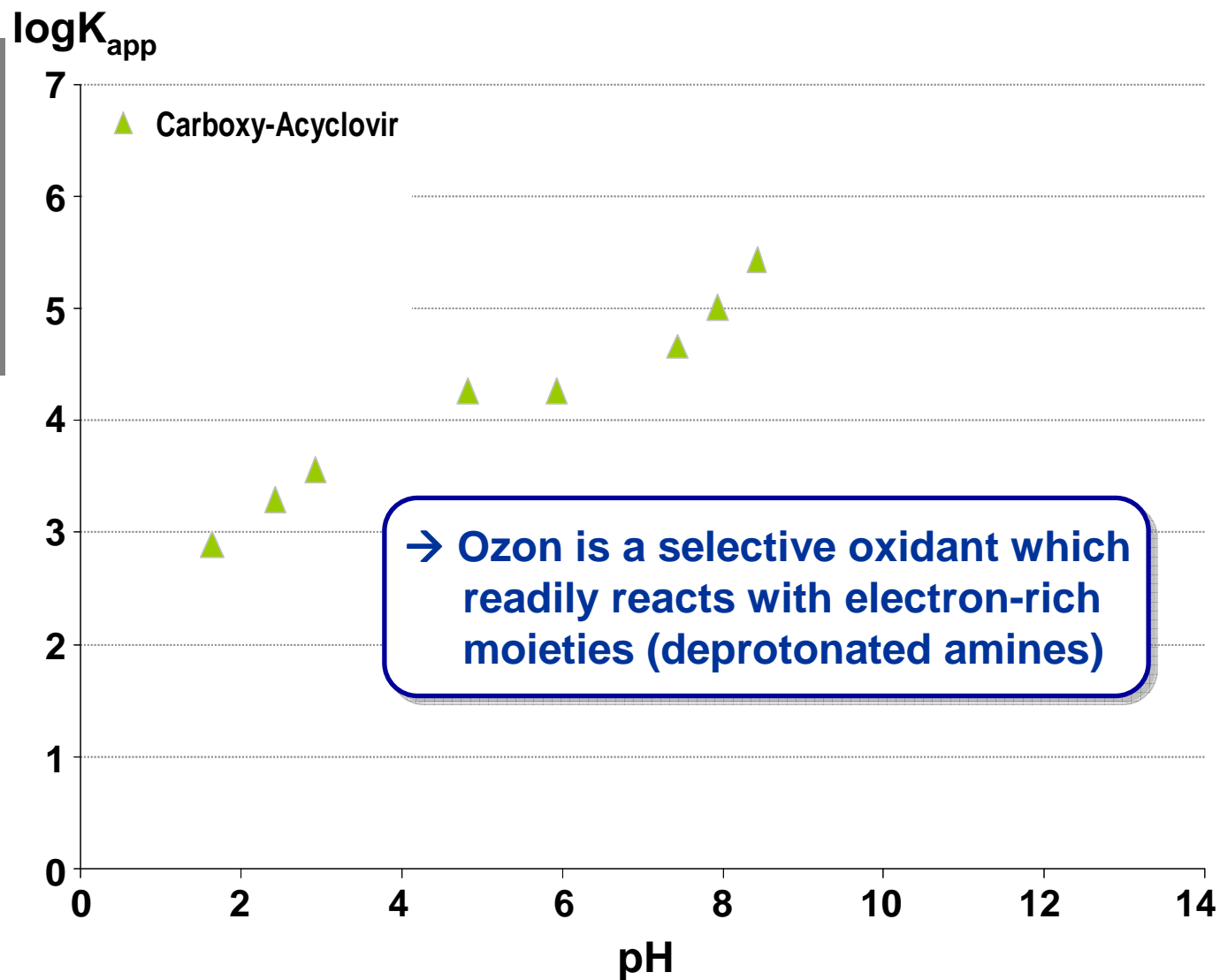
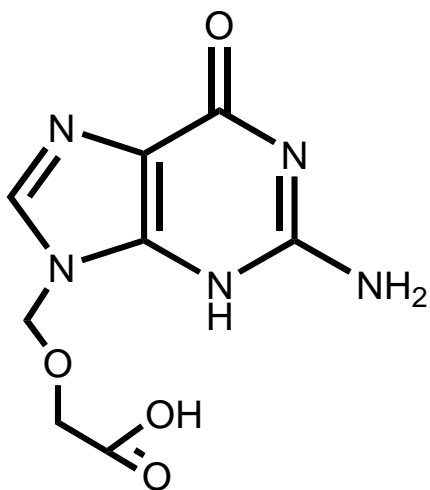


Surface water → groundwater → drinking water

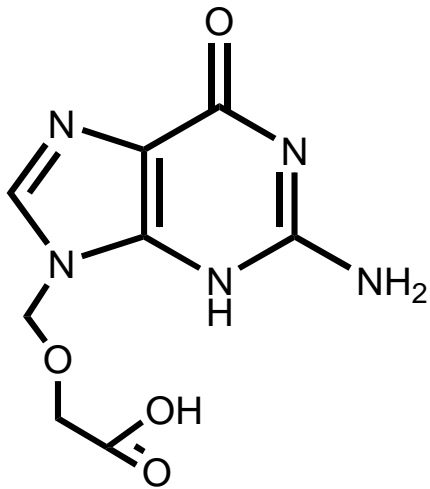


(Prasse et al. 2011, ES&T)

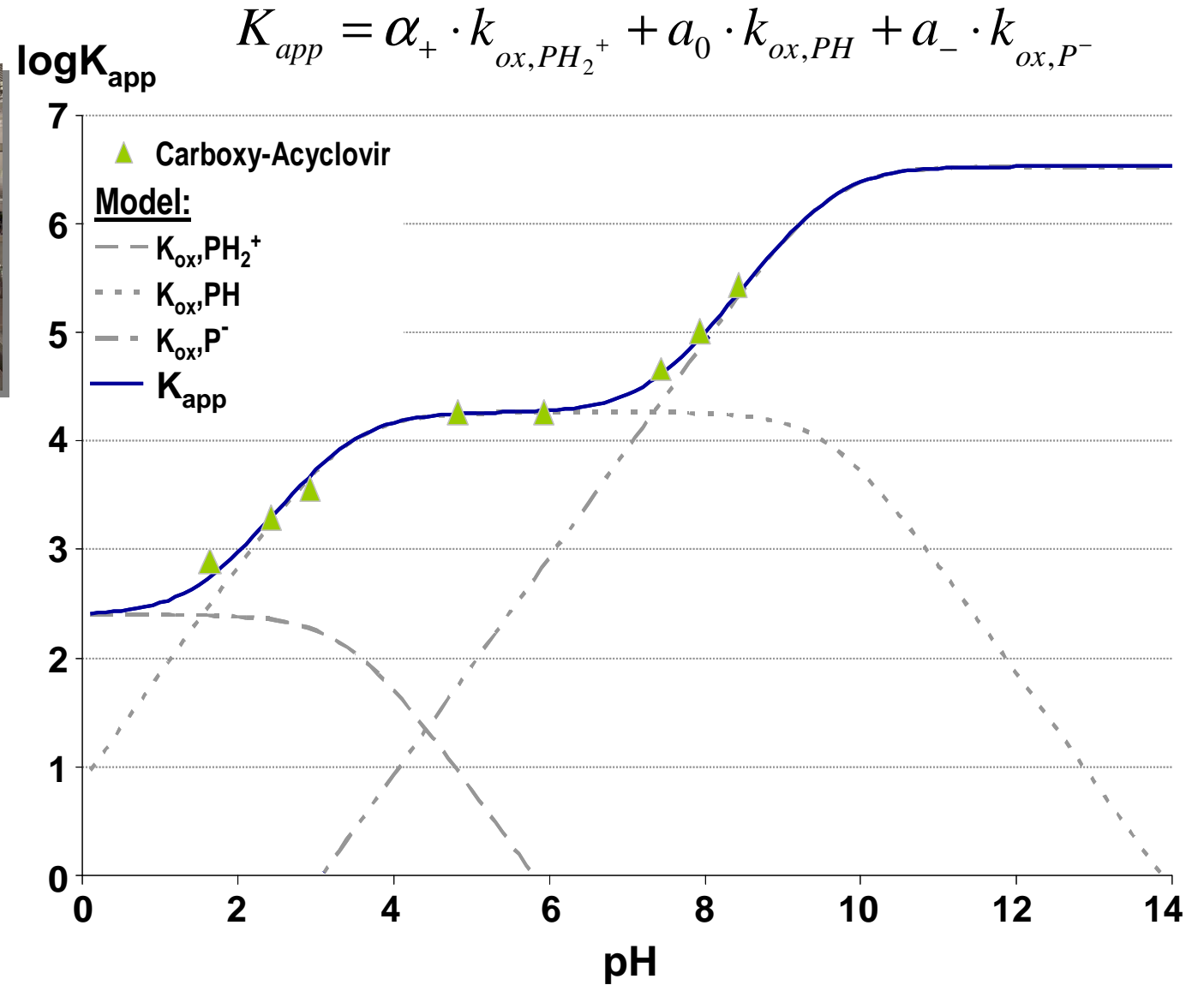




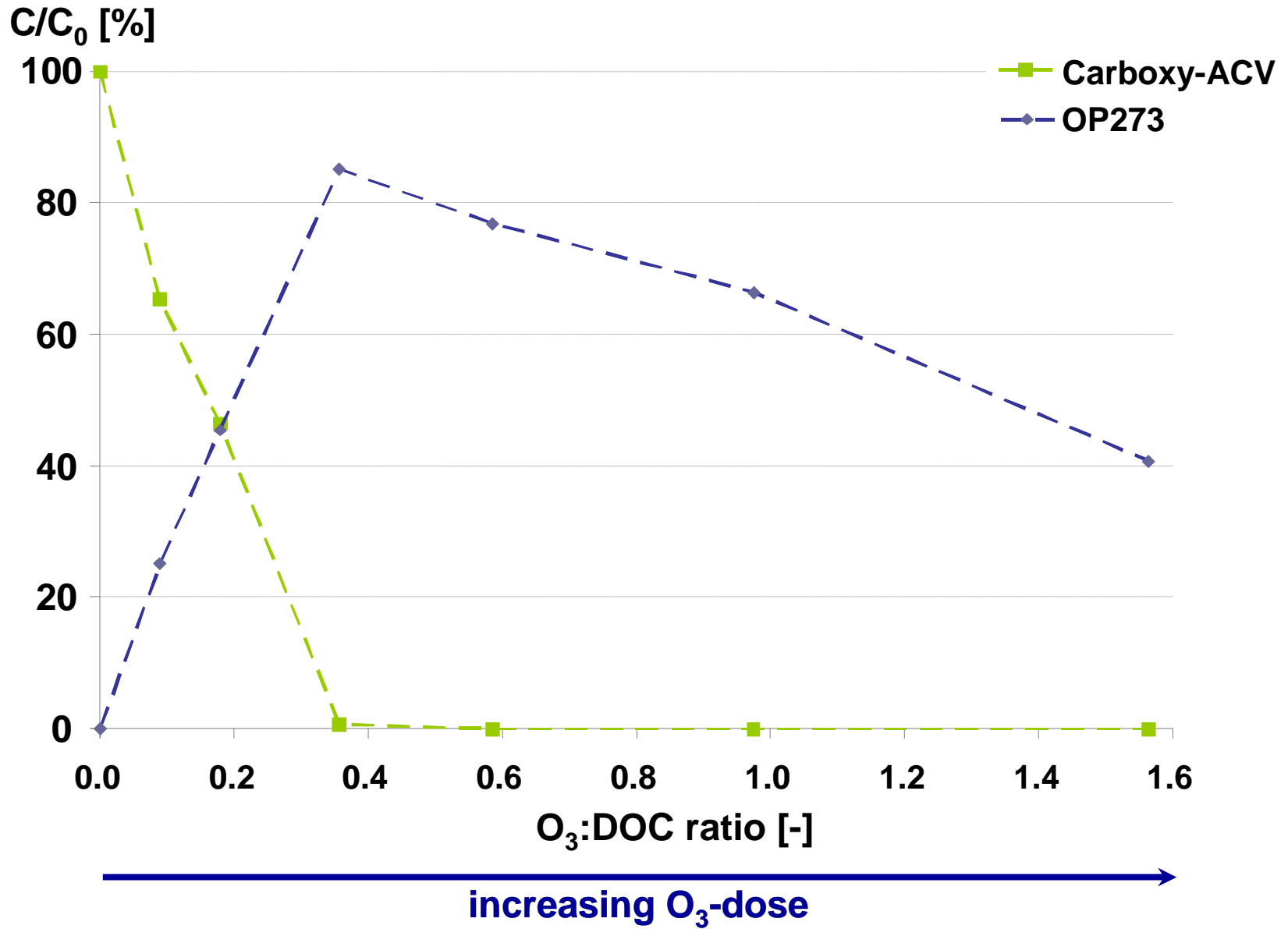
(Prasse et al. 2012, ES&T)



$pK_{a1} = 3,4$
 $pK_{a2} = 9,6$

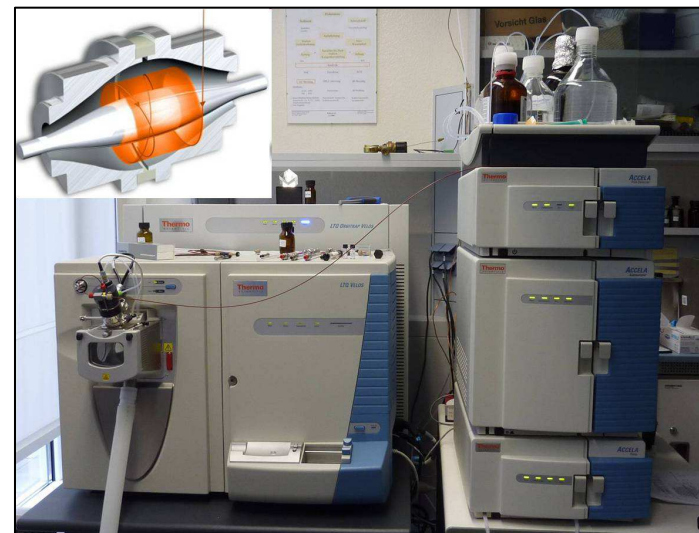


(Prasse et al. 2012, ES&T)



High-resolution mass spectrometry (LTQ Orbitrap Velos)

- A) Exact mass: **274.07739** (-1,3 ppm)
- **Sum formula** (neutral): **C₈H₁₂O₆N₅** (Carboxy-Acyclovir: C₈H₁₀O₄N₅)
- B) Fragmentation pattern MSⁿ:
- **primary amine group** (cleavage of NH₃)
 - **aldehyde moiety** (cleavage of CO)
 - **side chain unmodified** (cleavage of C₂H₄O₃)



Nuclear magnetic resonance spectroscopy (NMR; Bruker Advance 700)

A) ^1H - and ^{13}C -NMR

- only limited information (high number of hetero atoms)
- Indication of a quaternary carbon atom



Nuclear magnetic resonance spectroscopy (NMR; Bruker Advance 700)

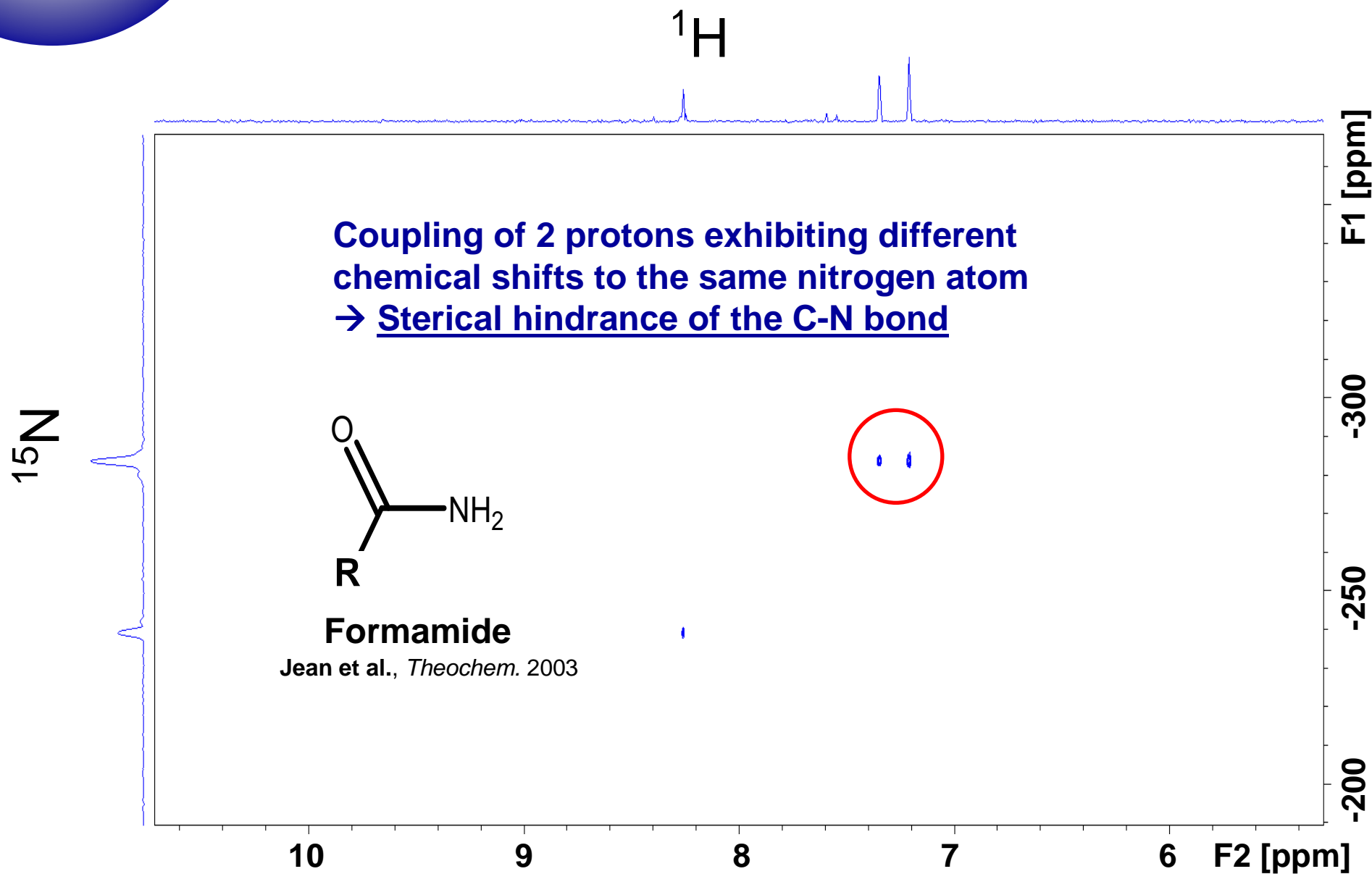
A) ^1H - and ^{13}C -NMR

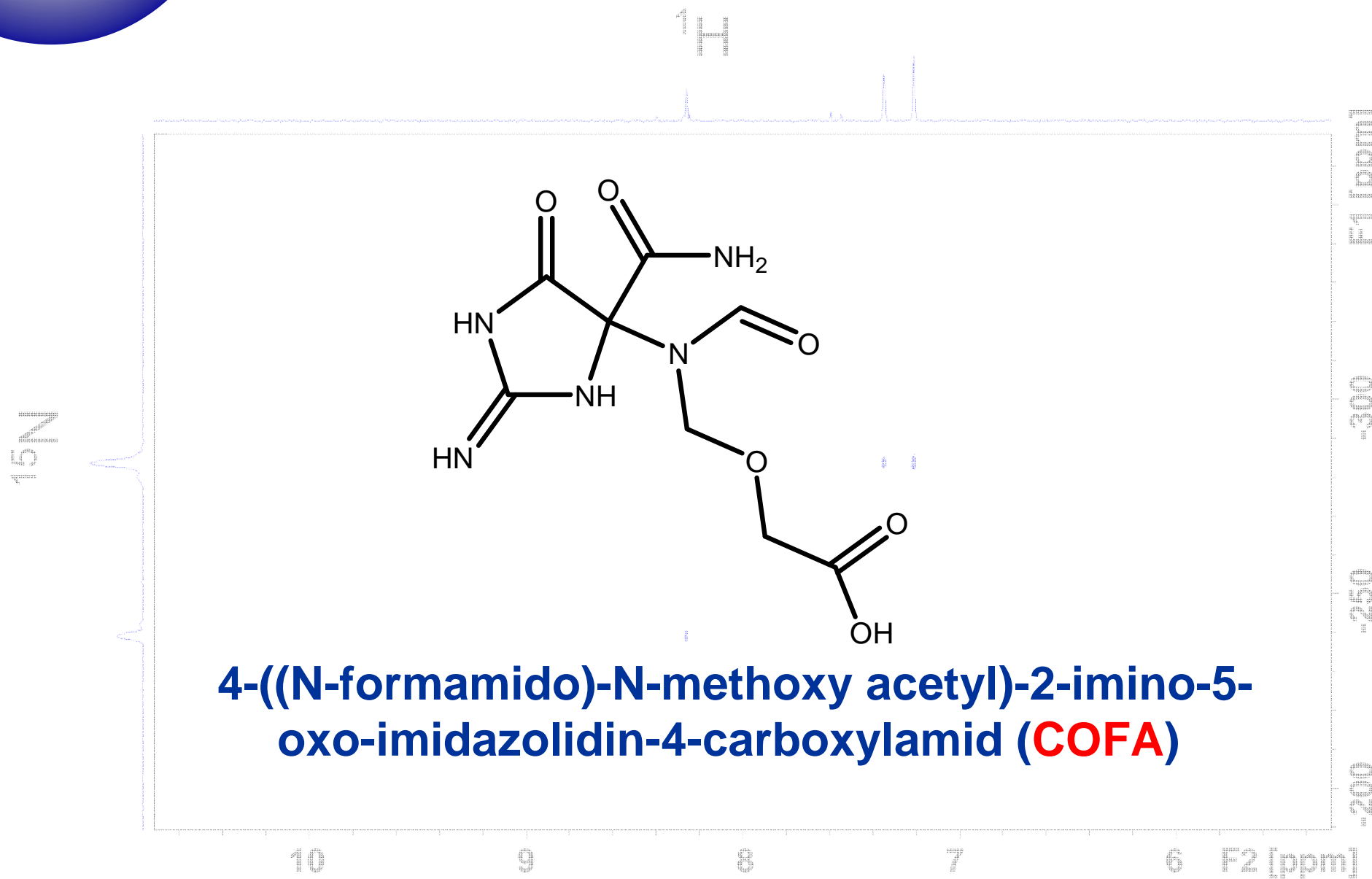
- only limited information (high number of hetero atoms)
- Indication of a quaternary carbon atom

B) 2D-NMR:

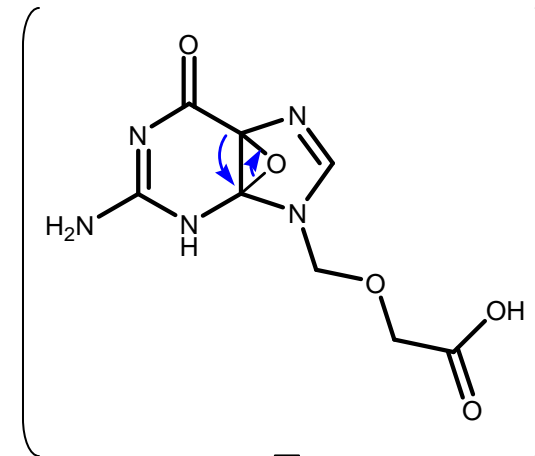
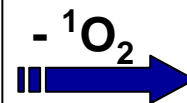
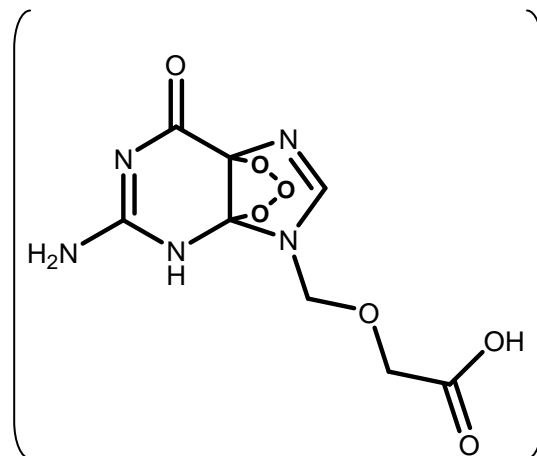
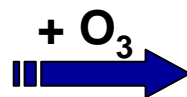
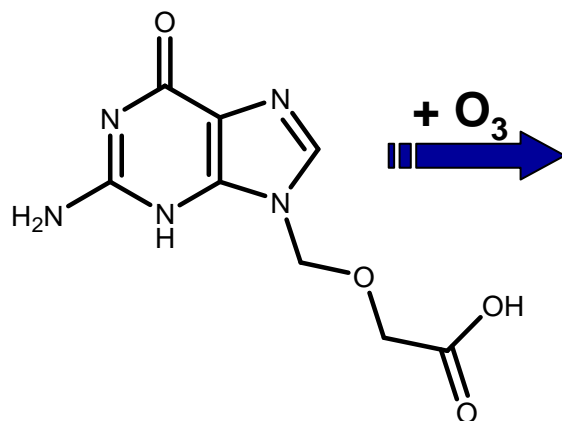
- $^1\text{H}, ^1\text{H}$ -COSY
- $^1\text{H}, ^1\text{H}$ -NOESY
- $^1\text{H}, ^{13}\text{C}$ -HSQC
- $^1\text{H}, ^{13}\text{C}$ -HMBC
- $^1\text{H}, ^{15}\text{N}$ -HSQC







Carboxy-Acyclovir

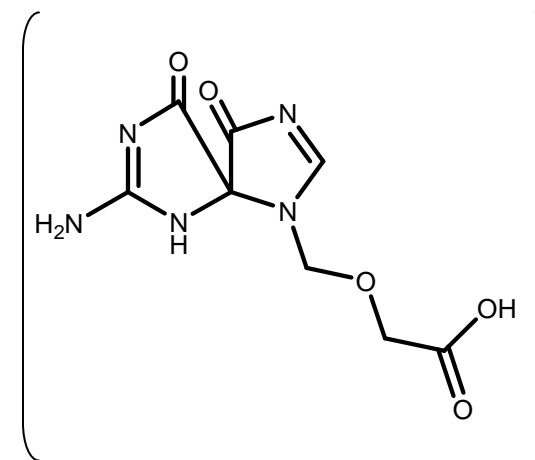
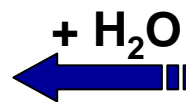
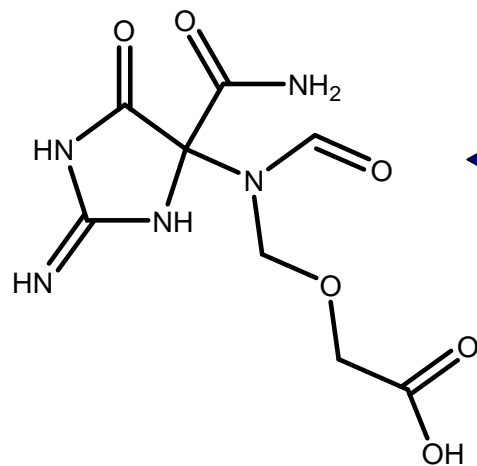


1,2-acyl shift

Ye et al., *Chem. Res. Toxicol.* 2006



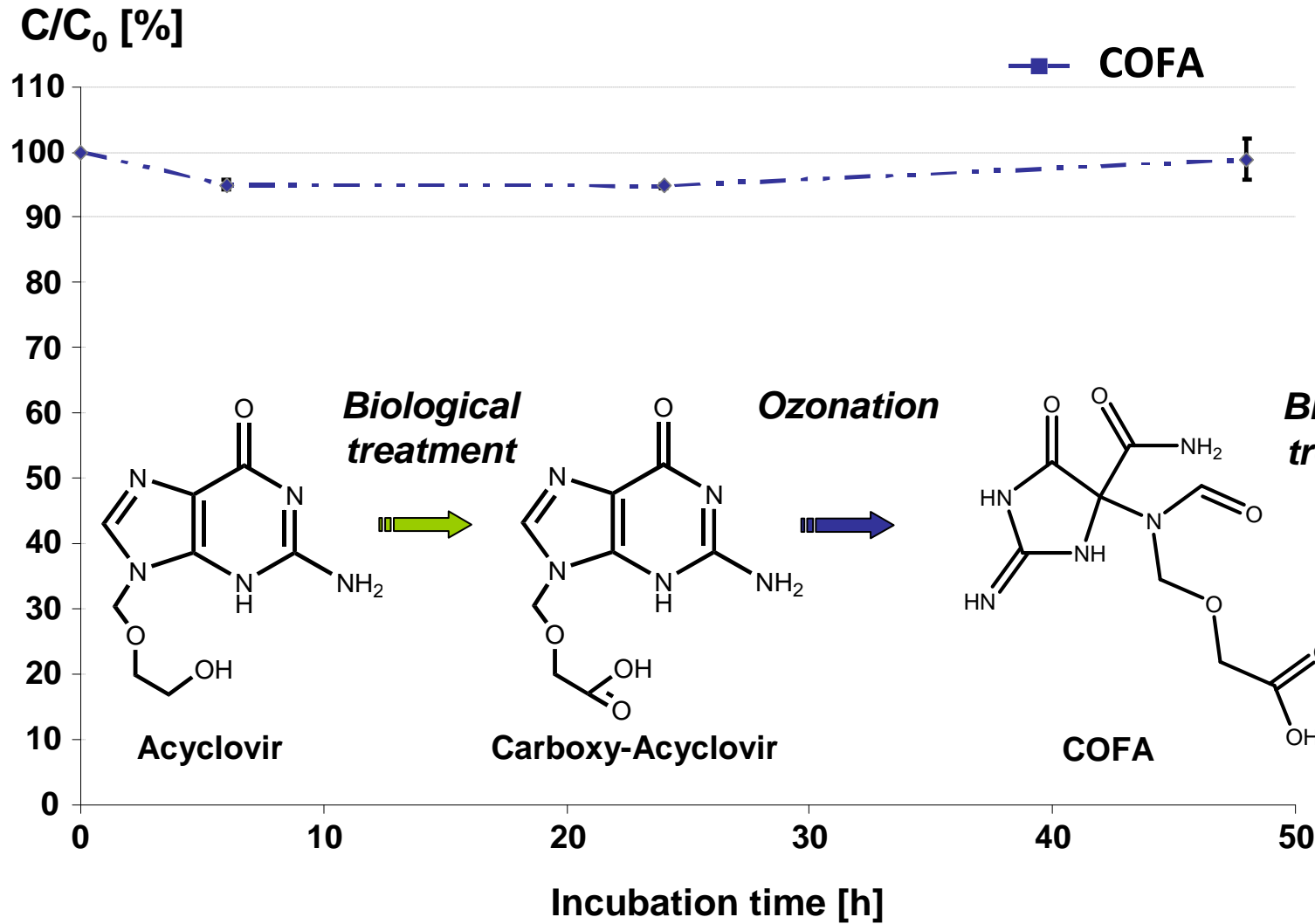
COFA



Enami et al., *J. Phys. Chem. B*, 2008

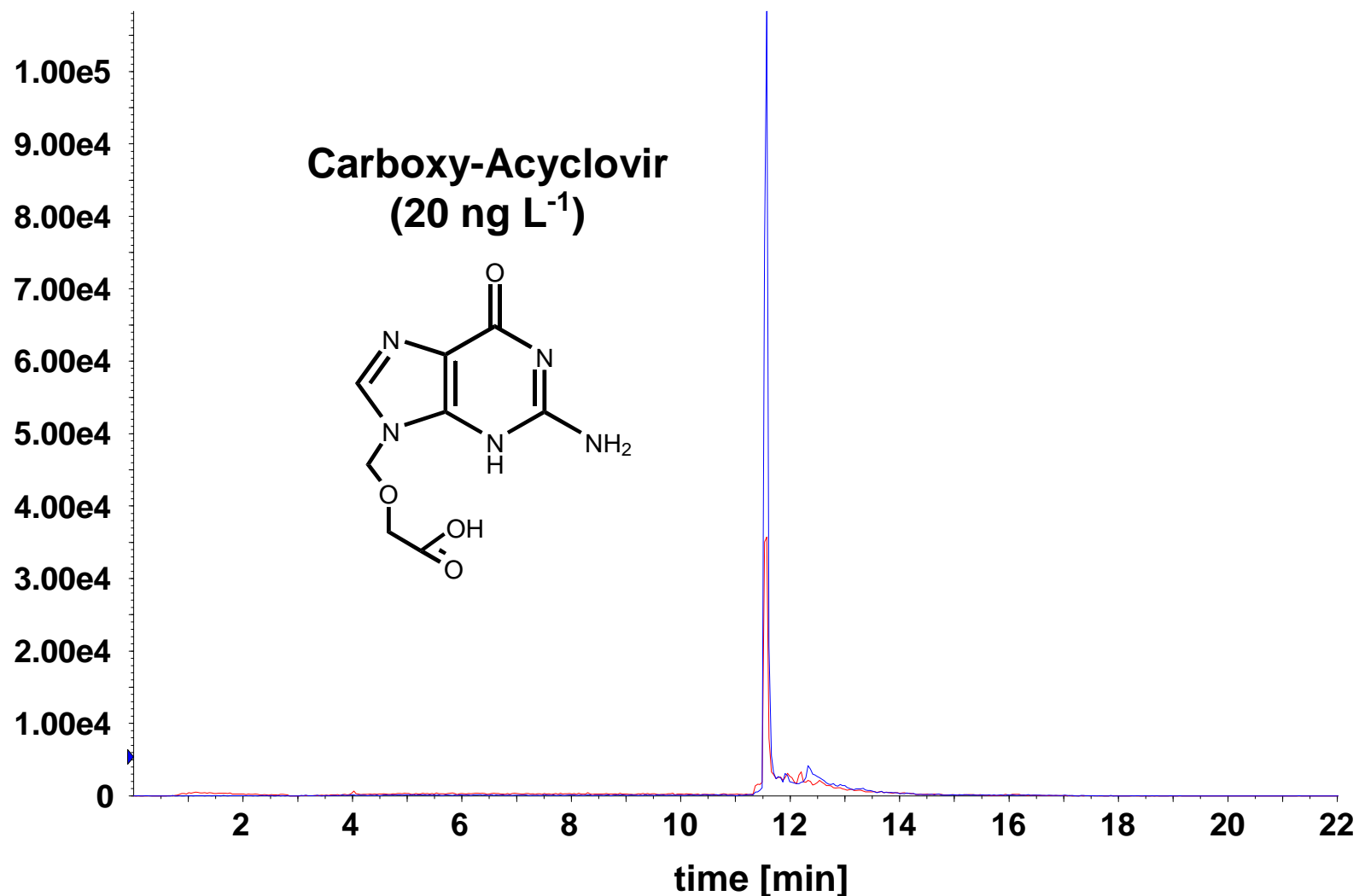
Munoz et al., *J. Chem. Soc., Perkin Trans.*, 2001

Degradation of COFA in sewage sludge



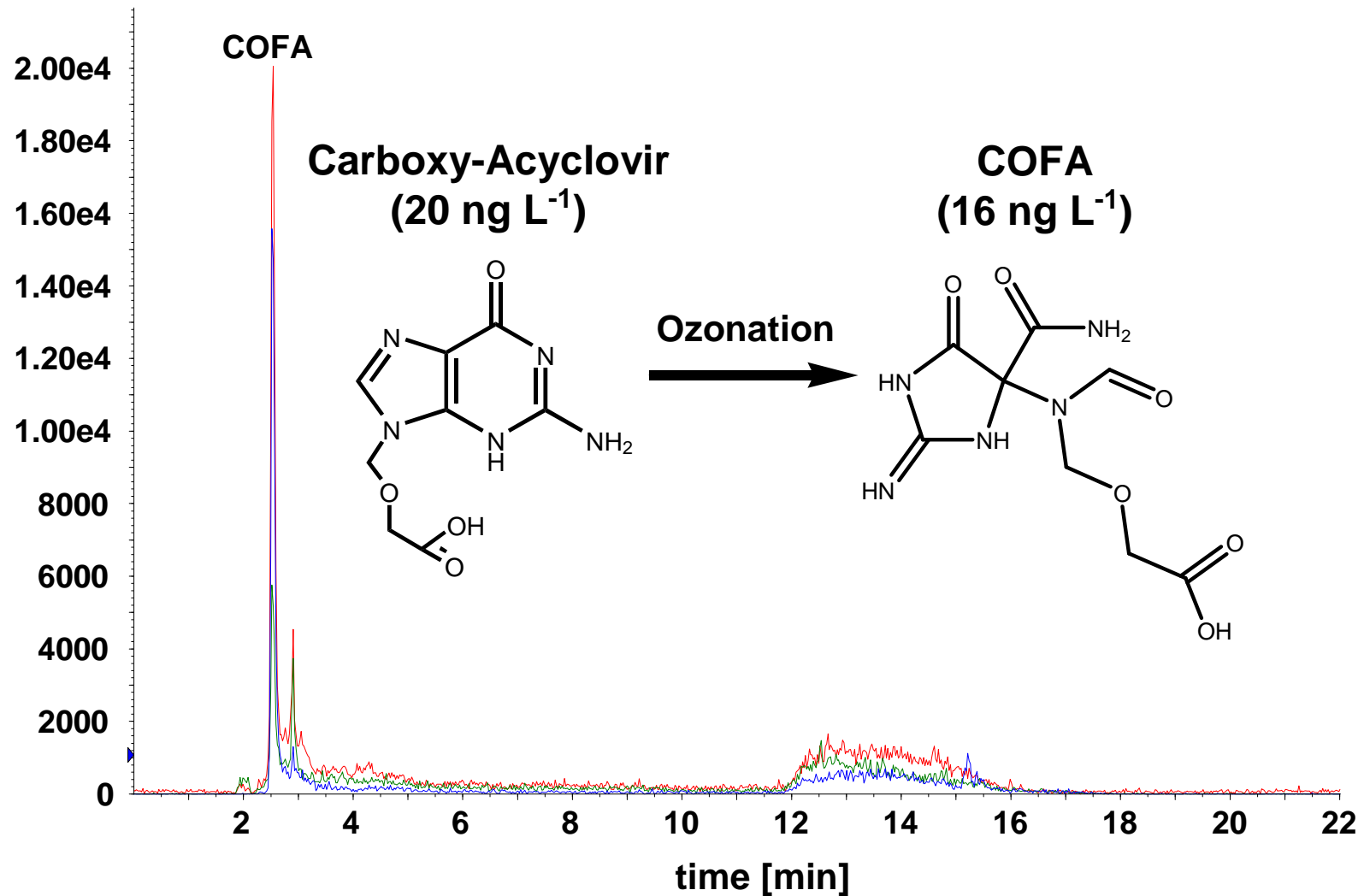
Raw drinking water

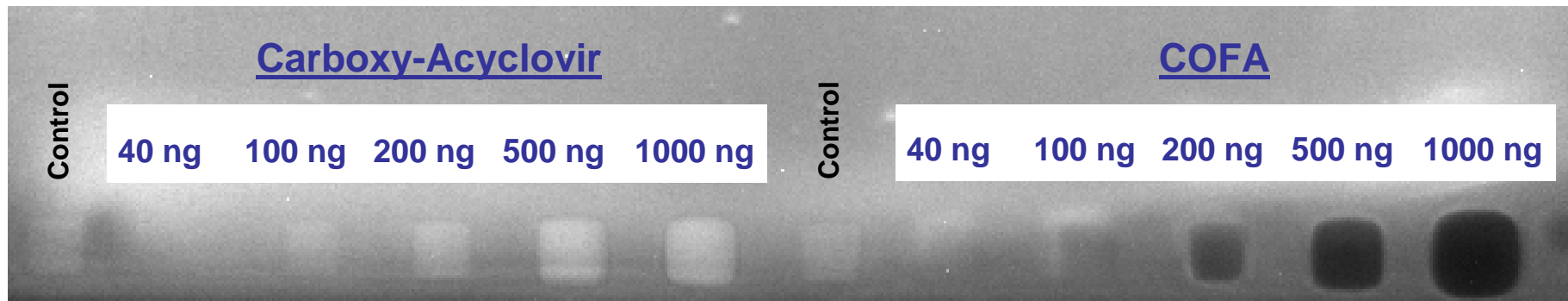
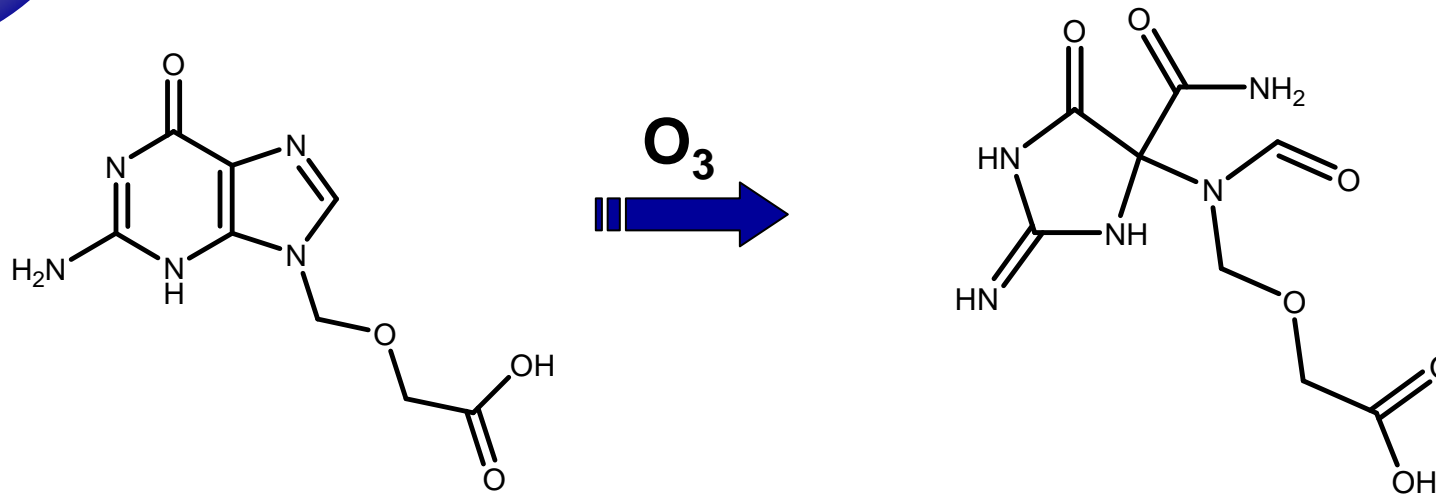
Intensity [cps]



Finished drinking water after ozonation and activated carbon filtration

Intensity [cps]





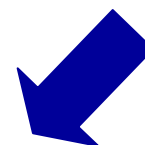
no (bacterial) toxicity

(bacterial) toxicity!

- **Acyclovir and its biological and oxidative TPs could be followed through the complete urban water cycle**
- **Acyclovir is efficiently eliminated in biological wastewater treatment**
 - **Elimination ≠ Mineralisation → Transformation**
- **Carboxy-acyclovir is highly persistent under aerobic conditions**
 - **Occurrence in drinking water**
- **Carboxy-acyclovir is efficiently eliminated from wastewater and drinking water during ozonation**
 - **Elimination ≠ Mineralisation → Transformation**
- **Ozonation can result in the formation of (bacterial)toxic oxidation products**
- **COFA was detected in a drinking water even after ozonation and subsequent activated carbon filtration**

Pharmaceuticals in the environment

Transformation products



Basis for:
i) Comprehensive risk characterization of pharmaceuticals in the urban water cycle and
ii) Evaluation of advanced treatment technologies regarding the formation of toxic transformation products



(Eco)toxicity

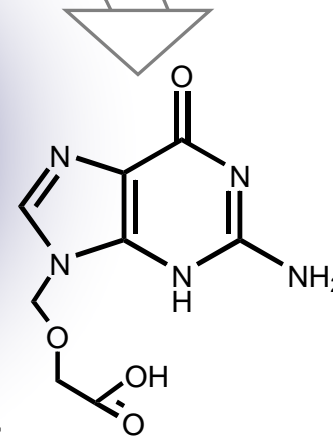
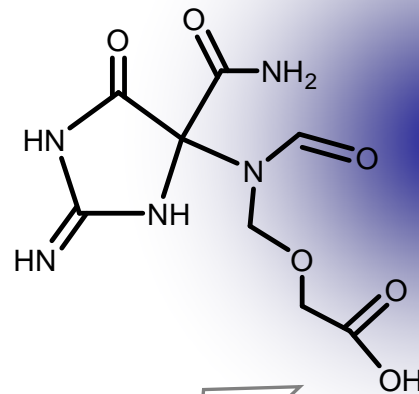
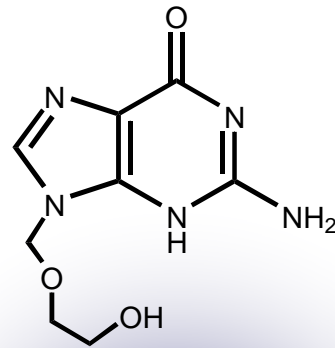


**Acknowledgment of Financial Support:
German Federal State Rhineland-Palatinate
EU-Project Neptune**



Thank you for your attention!

QUESTIONS??



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prasse@bafg.de