Innovative Strategies for Reducing the Environmental Impact of Pharmaceutical Substances

Roadshow «RI-CERR-care il futuro: Innovazione, Ricerca e Trasferimento Tecnologico in Emilia Romagna», Tappa #4, 24 giugno 2026

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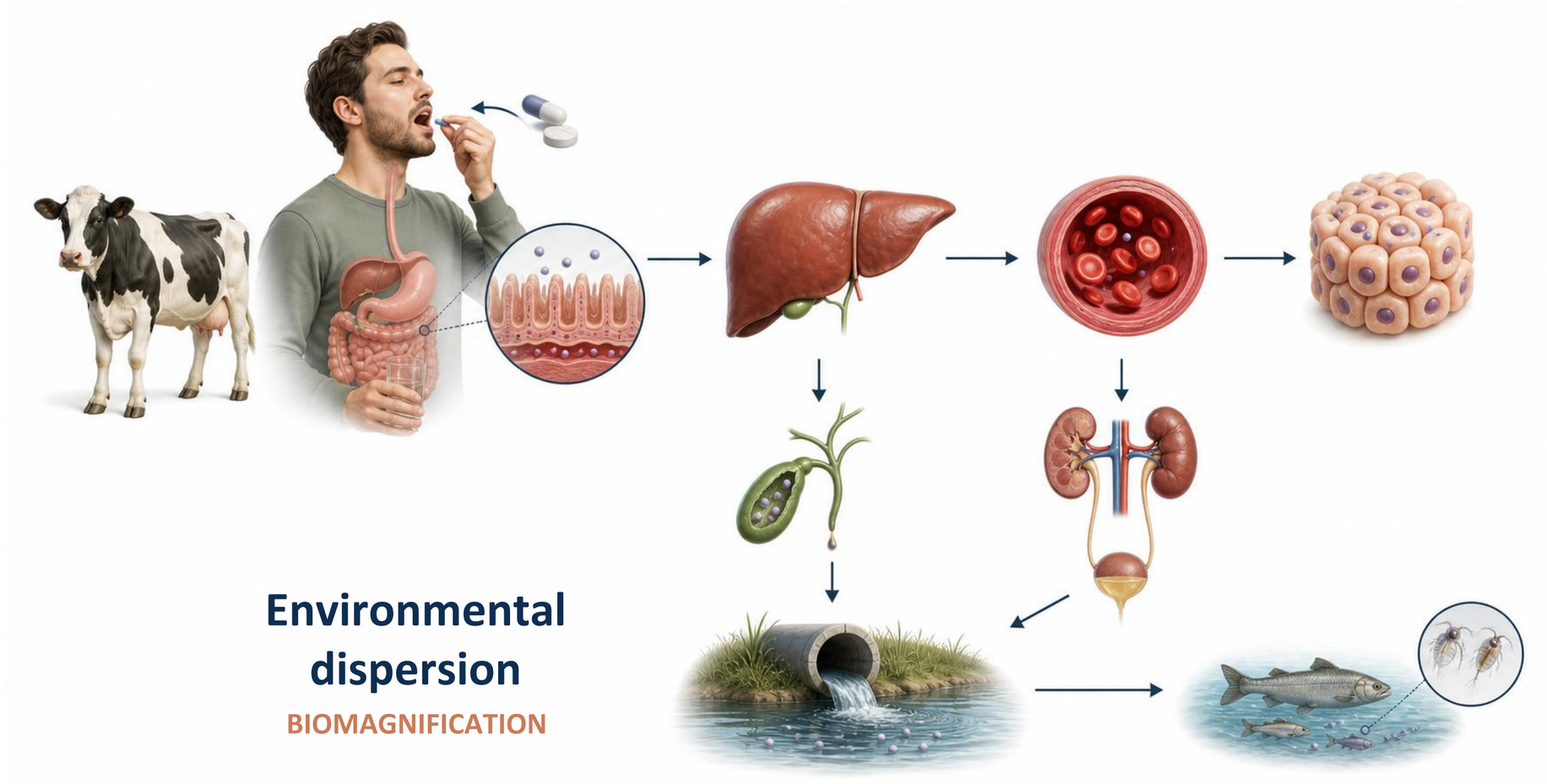
Pharmaceuticals: Healing and Polluting

The widespread use of drugs represents an indisputable benefit for society but is accompanied by significant ecotoxicological risks.

"Sustainable development is development that meets the needs of the present without compromising the ability of future generations to meet their own needs."

World Commission on Environment and Development, Our Common Future, Oxford University, 1987

Ashfield, Nahum, et al. Annual Review of Environment and Resources, vol. 50, no. 1, Oct. 2025, pp. 273–301.



Rzymski, P., et al. Limnological Rev 17, 97–107 (2017)

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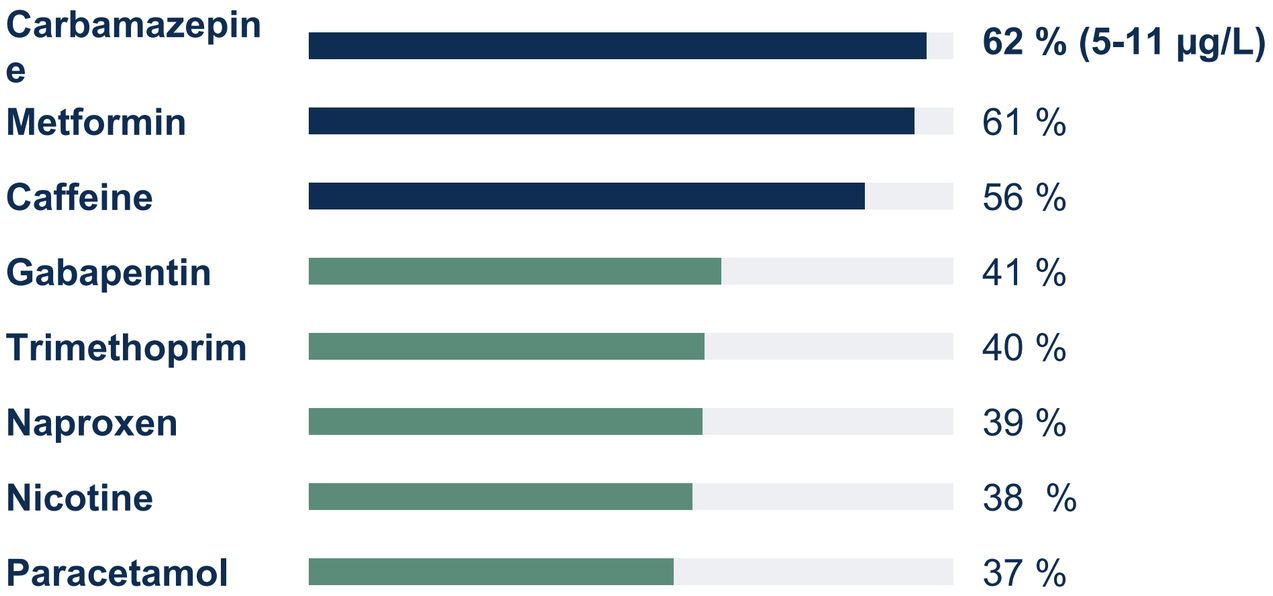
The most common drugs in the world's rivers

The highest concentrations of APIs were detected in sub-Saharan Africa, South Asia and South America.

DETECTION FREQUENCY



THE STUDY IN NUMBERS

1.052 sampling sites

140 countries across 6 continents

61 active pharmaceutical ingredients monitored

Hormones, steroids, antibiotics, NSAIDs, antiepileptic drugs, antidepressants — stable molecules, poorly metabolized, with low removal rates in wastewater treatment plants.

Wilkinson et al., Pharmaceutical pollution of the world's rivers, PNAS 119(8) e2113947119 (2022)

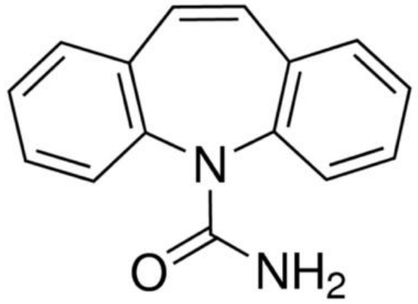
Poorly soluble drugs persist in the environment

Lipophilic drugs are less likely to remain dissolved in water and have affinity for sediments and biological tissues, increasing their persistence in the environment and contributing to biomagnification

Class I high solubility high permeability	**Class II** LOW solubility high permeability *Carbamazepine, Ibuprofen, Naproxen,*
Class III high solubility low permeability	**Class IV** LOW solubility low permeability *Furosemide, Hydrochlorothiazide*

CARBAMAZEPINE: the most frequently detected drug

Carbamazepine persists in wastewater, where it can show a dissipation half-life of 74–82 days.



BCS = Biopharmaceutical Classification System (Amidon et al., 1995)

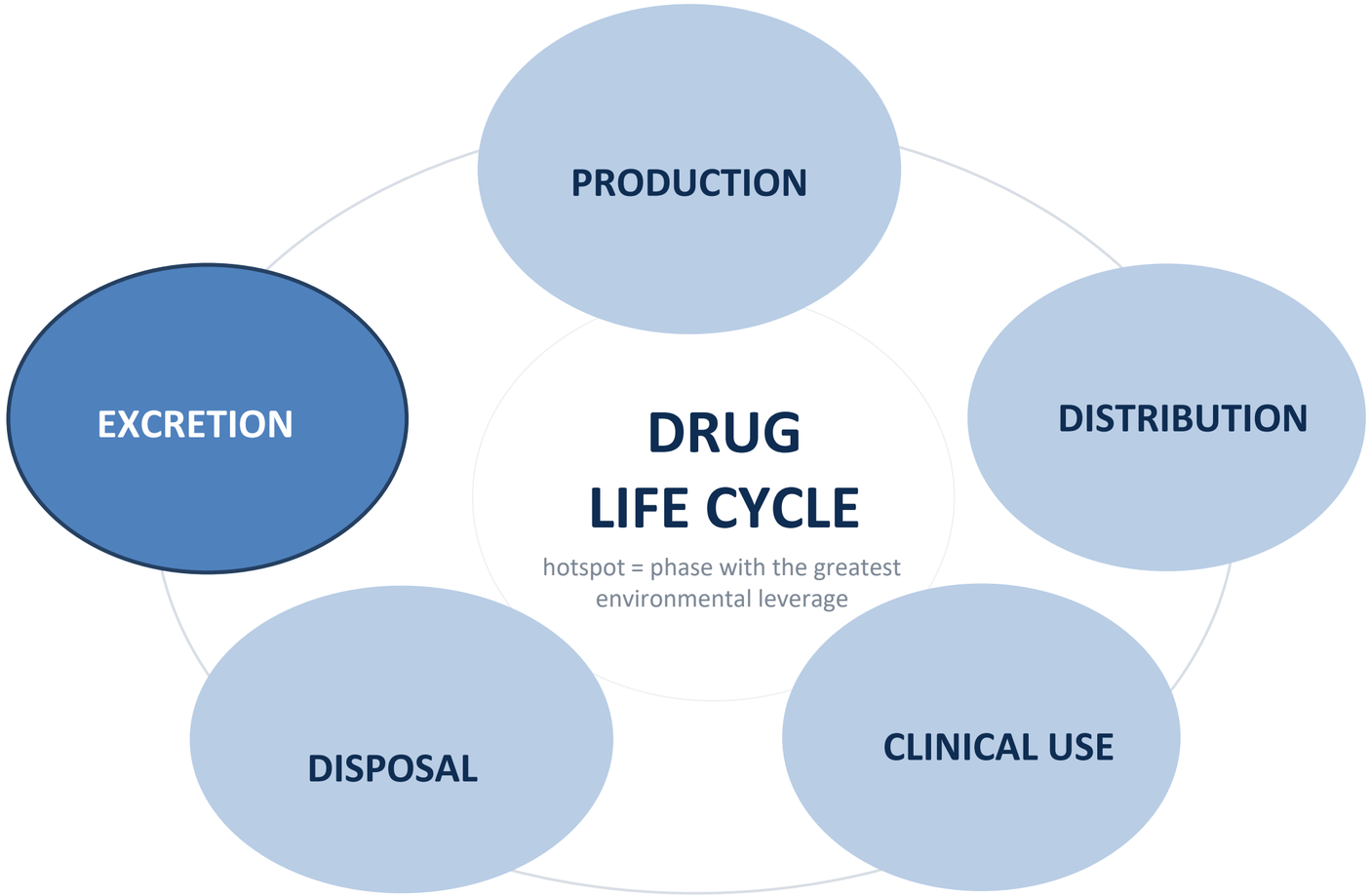
Drug life cycle: hotspots and drug-delivery strategies

The most critical hotspot is excretion: formulation can act on excretion to reduce impact before it becomes an emission

DRUG-DELIVERY STRATEGIES

1. Increase bioavailability
lower dose, lower active excretion

2. Degrade the unabsorbed fraction
In situ before excretion in the drug life cycle



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Environmental risk assessment: PEC/PNEC

The risk quotient (RQ) measures the toxicity of a drug for aquatic ecosystems

THE RISK QUOTIENT (RQ)

$$RQ = \frac{MEC}{PNEC}$$

MEC — maximum measured environmental concentration
PNEC — predicted no-effect concentration, the lowest value among LC_{50}, EC_{50} or NOEC.
PEC — predicted environmental concentration of a substance

RISK CLASSES

Low	RQ < 0.1
Medium	RQ < 1
High	RQ ≥ 1

DECISION THRESHOLD for marketing authorization — PEC/PNEC

PEC/PNEC < 1 → environmental risk unlikely

PEC/PNEC ≥ 1 → the substance is considered toxic

the applicant must provide additional data and risk management and mitigation measures before authorization.

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Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Review

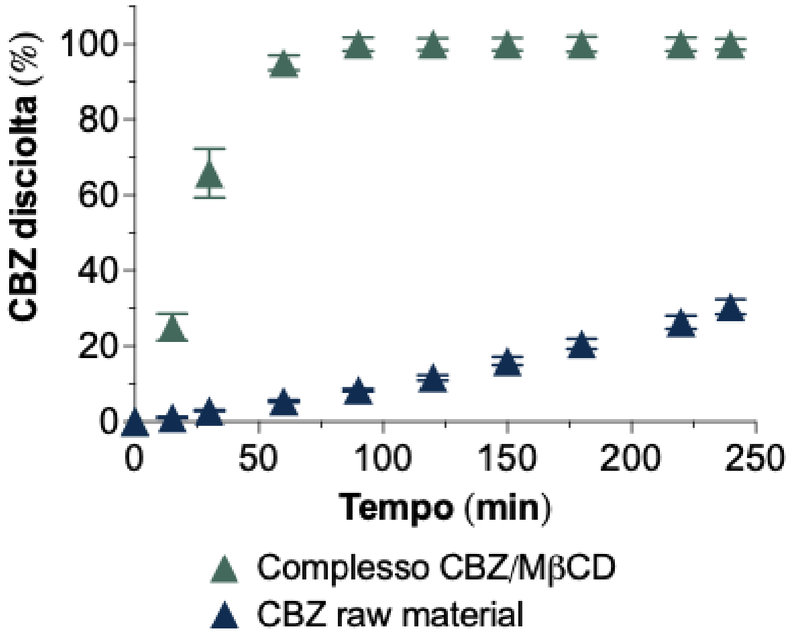
Drugs as contaminants of emerging concern: preventive approaches beyond detection, regulatory aspects and remediation

Umberto Cancelli, Eride Quarta, Davide D'Angelo, Gianluca Bazzoli, Annalisa Bianchera, Ruggero Bettini *

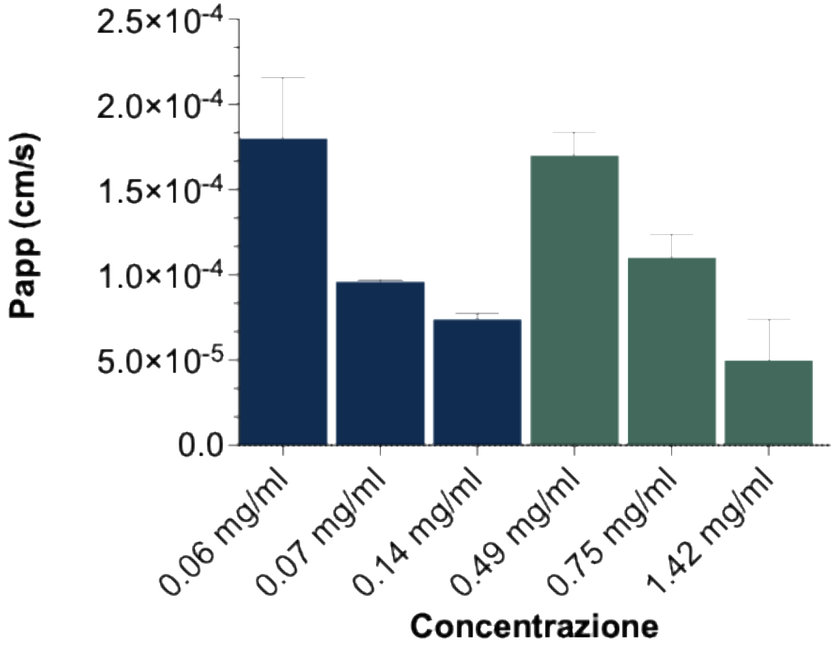
Department of Food and Drug Sciences, University of Parma, Parco Area delle Scienze 27/A, 43124 Parma, Italy

Biodegradable excipients to improve the bioavailability of poorly soluble drugs

Preparation of an amorphous spray-dried powder of the CBZ and M-β-CD complex in a 1:2 molar ratio



Cs raw material	**0.149 mg/ml**
Cs complex	**3.0 mg/ml**



Complexation of CBZ with M-β-CD increases solubility 20-fold and permeability across Caco-2 cells 8-fold compared with the raw material

Quarta et al. unpublished

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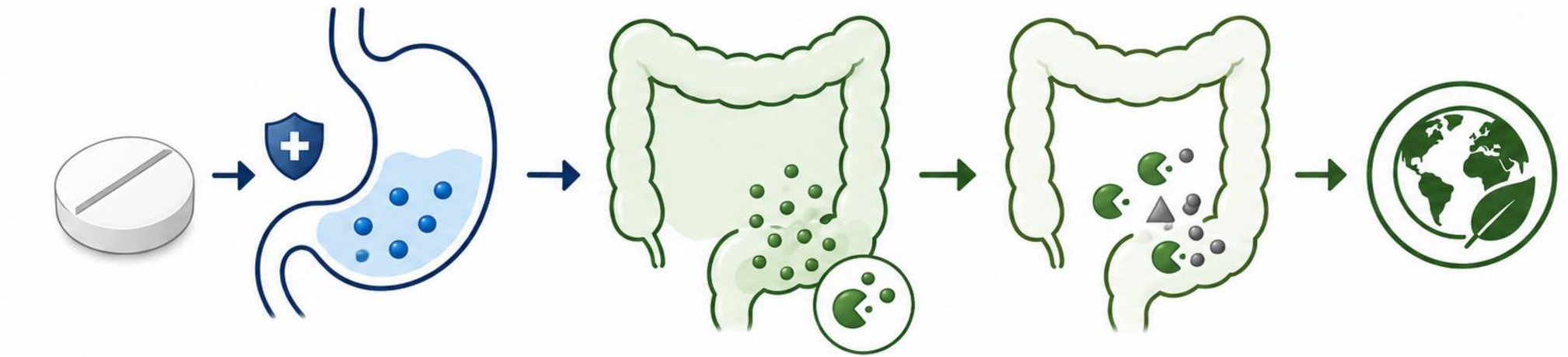
Development of a sequential controlled-release oral system

Gastro-resistant tablets with sequential release of the drug and enzyme in the gastrointestinal tract to reduce environmental impact



Gastric tract
API is released and absorbed

Intestinal tract
ENZYMES are released in the distal colon and inactivate unabsorbed active API

Environmental impact
Less API is excreted into the environment

API
Carbamazepine (CBZ)

ENZYME + MEDIATOR
Laccase and vanillin

GASTRO-RESISTANT SYSTEM
Eudragit S100 blended with lipids

D'Angelo et al. Unpublished

Enzymatic degradation of CBZ before excretion

Batch #	Eudragit S100 % (w/w)	Lipid A % (w/w)	Lipid B % (w/w)
Lipid A 20	80	20	-
Lipid A 35	65	35	-
Lipid A 50	50	50	-
Lipid B 20	80	-	20
Lipid B 35	65	-	35
Lipid A 50	50	-	50

Batch#	P_y (MPa)	$2P_y$ (MPa)	$3P_y$ (MPa)
Lipid A 20	175.93 ± 4.12	351.86	527.79
Lipid A 35	156.20 ± 0.46	312.40	468.60
Lipid A 50	135.73 ± 0.90	271.46	407.19
Lipid B 20	224.80 ± 25.20	449.60	674.40
Lipid B 35	149.00 ± 8.83	298.00	447.00
Lipid B 50	110.90 ± 4.11	221.8	332.70

Powder mixture and relevant tablet composition (% w/w).

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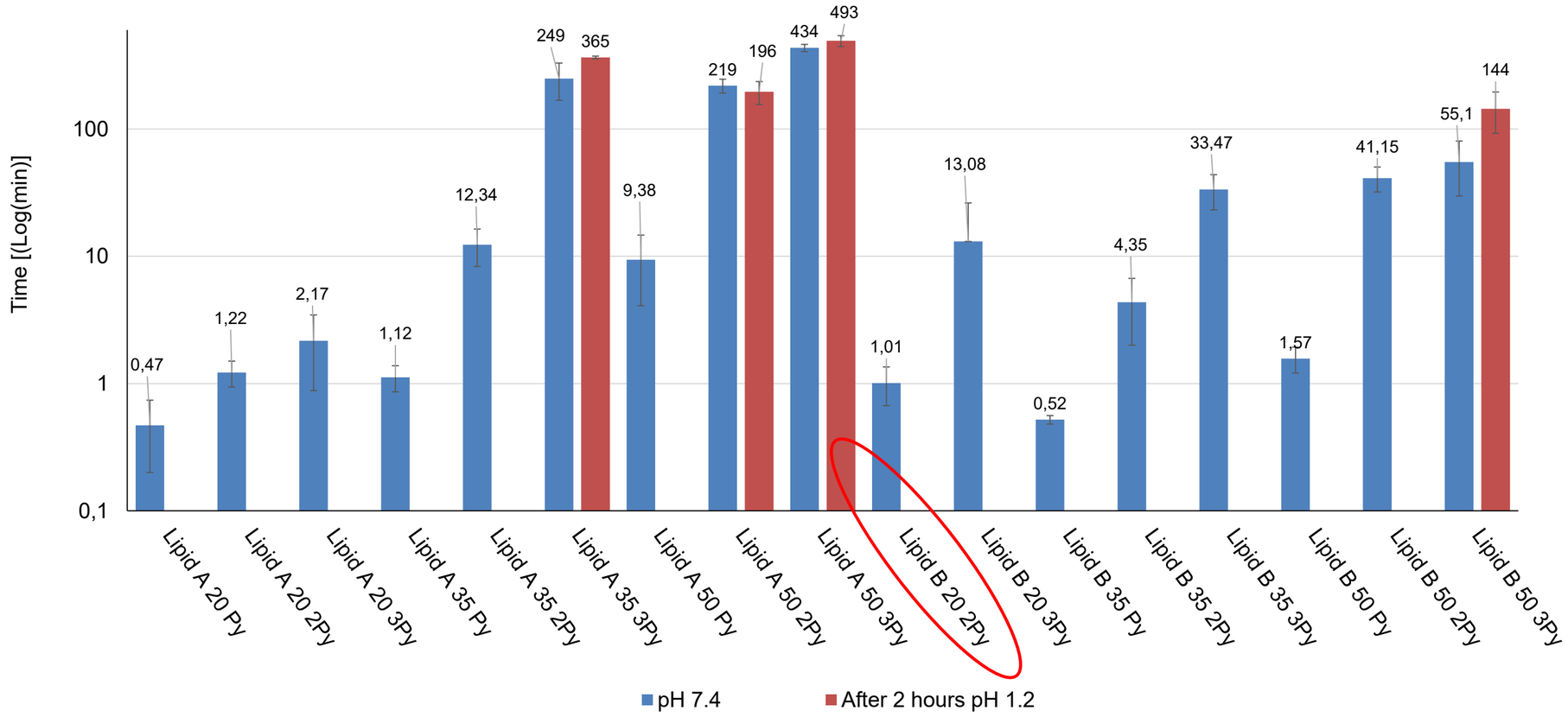
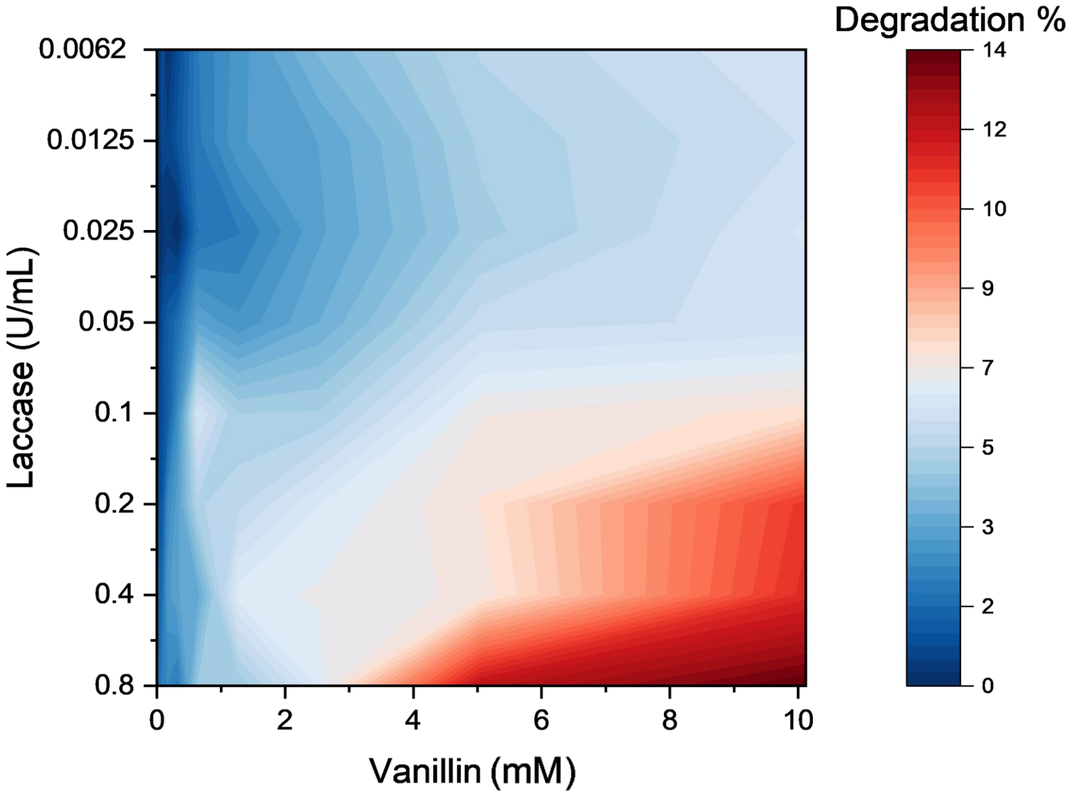
Enzymatic degradation of CBZ before excretion

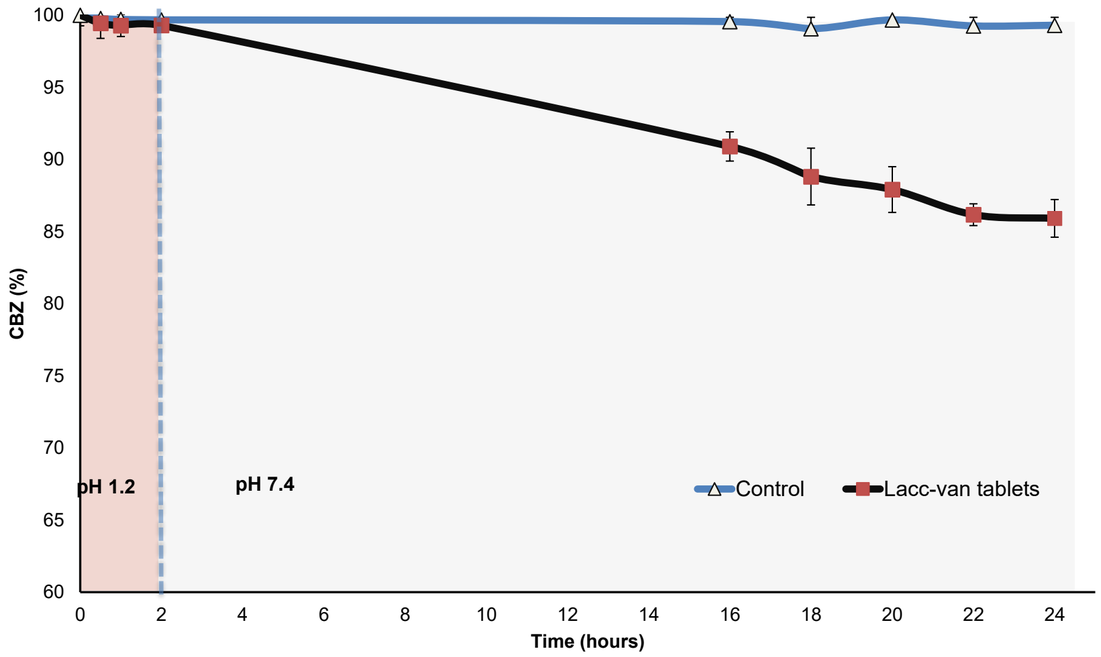
Optimization of the drug delivery system



Enzymatic degradation of CBZ before excretion

The gastro-resistant laccase–vanillin enzyme tablet degrades 15% of CBZ in 24 hours in gastrointestinal fluid





Laccase/ mediator vanillin ratio to degrade CBZ at a concentration of 15µg/mL.

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Environmental risk estimate: Risk Quotient (RQ)

Estimated effect of the improvement on the share of CBZ excreted into the environment — Risk Quotient (MEC/PNEC)

TEGRETOL®
Carbamazepine raw material

400 mg administered dose

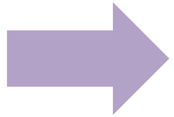
30% (≈120 mg) amount excreted into the environment

Environmental concentration MEC = 0.345–1 µg/L

RISK QUOTIENT (RQ)
14 - 40

HIGH RISK

≈20-fold
reduction in environmental risk



SPRAY-DRIED POWDER
CBZ/M-β-CD complex

20 mg estimated dose

About 3 mg reaches the environment

Environmental concentration MEC = 0.02–0.05 µg/L

RISK QUOTIENT (RQ)
0.6 – 1.7

REDUCED RISK

*Theoretical estimate based on in vitro tests. A real dose would require bioavailability, pharmacokinetic, metabolism and clinical efficacy data.

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µCT analysis of tablet structural changes upon aqueous coating

Aqueous coatings represent a more sustainable alternative to organic solvent-based coatings

	MCC	CPFX	SSG	MS
Batch 1	74	25	0	1
Batch 2	49	50	0	1
Batch 3	24	75	0	1
Batch 4	72	25	2	1
Batch 5	47	50	2	1
Batch 6	22	75	2	1
Batch 7	69	25	5	1
Batch 8	44	50	5	1
Batch 9	19	75	5	1

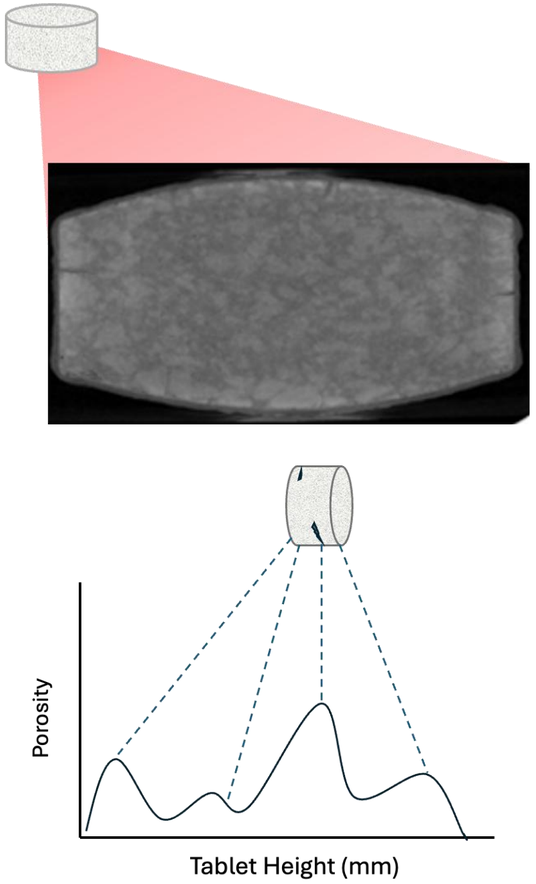
Powder mixture and relevant tablet composition (% w/w). MCC =Microcrystalline cellulose; CPFX =Ciprofloxacin; SSG =Sodium starch glycolate; MS=Magnesium stearate.

Coating

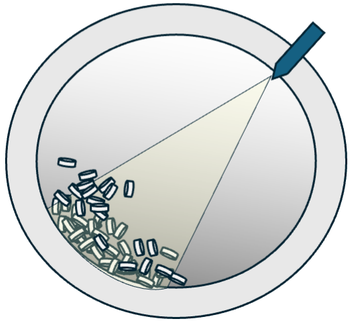
-HPMC + PEG

-Eudragit® FS30D (water based dispersion)

Porosity study (XµCT)



Pan Coating Process



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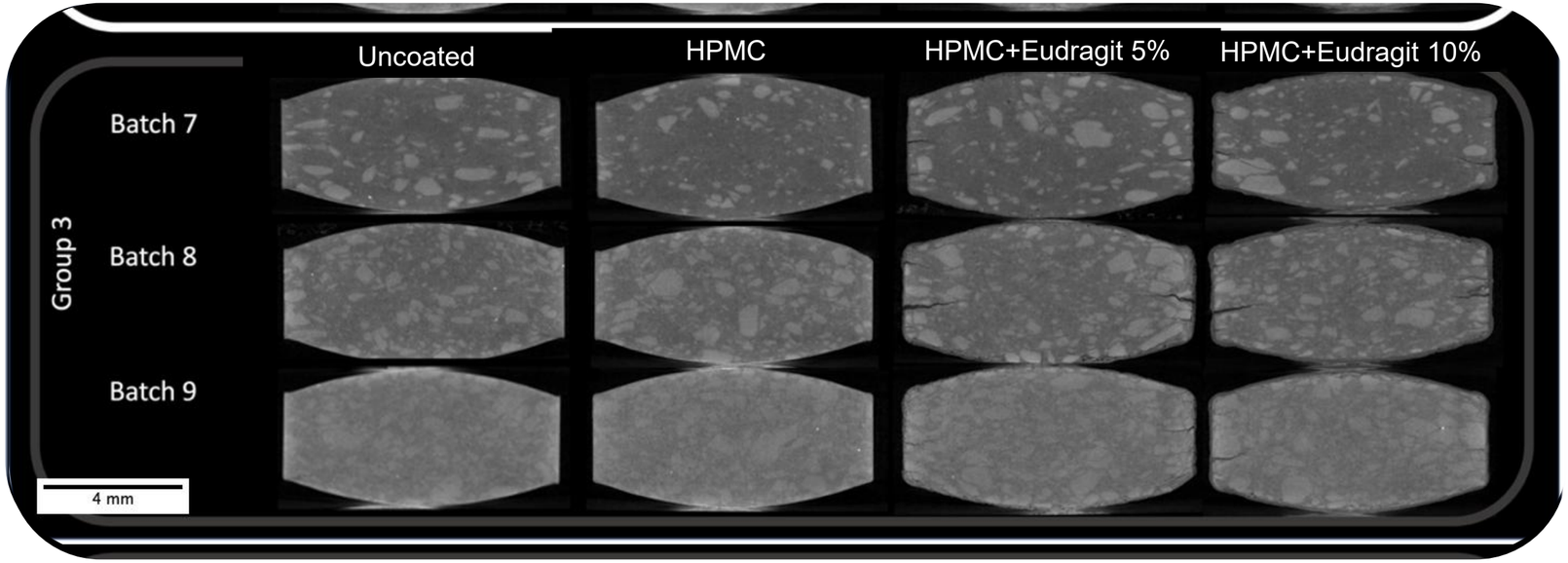
Unveiling tablet structural changes: A micro computed tomography analysis of aqueous coating effects

Davide D'Angelo, Eride Quarta, Gianluca Bazzoli, Annalisa Bianchera, Ruggero Bettini *

Department of Food and Drug Sciences, University of Parma, Parco Area delle Scienze 27/A, Parma 43124, Italy

Aqueous coating induces structural changes and increased porosity in tablets



Aqueous coating

↓

Water penetration during the coating

↓

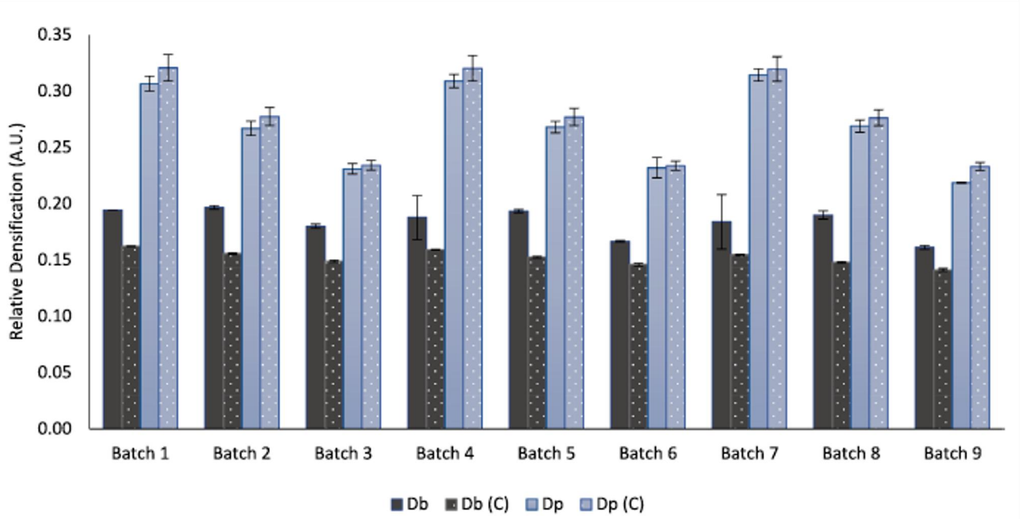
Tablet relaxation
Swelling + Cracking

↓

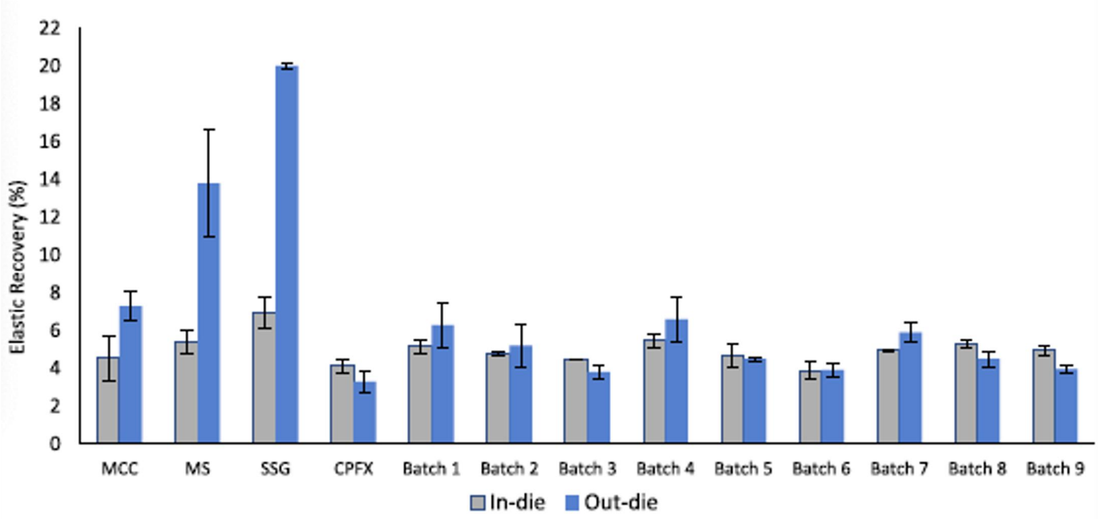
Porosity increase

↓

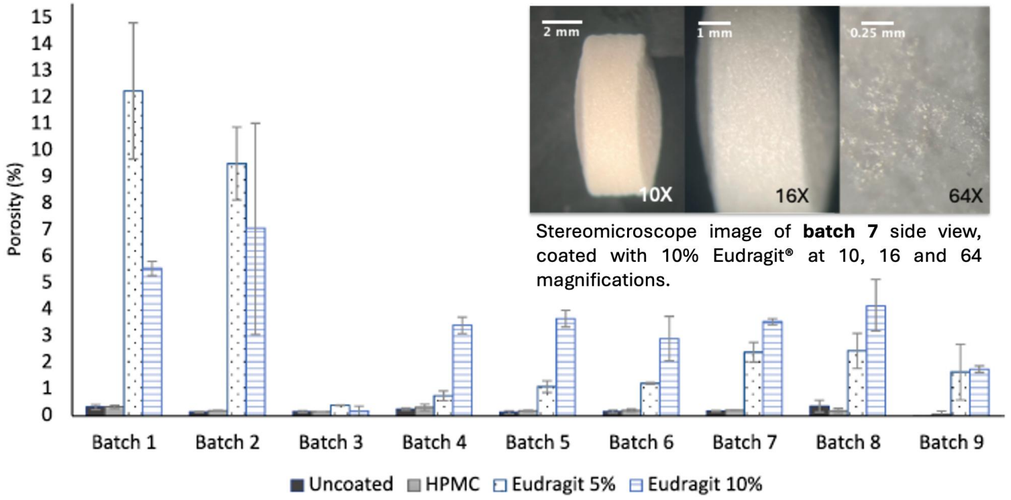
Risk of coating failure and possible impairment of enzyme release



Experimental and calculated (C) brittle (Db) and plastic (Dp) relative density values from Heckel plot analysis of the mixtures. The bars represent the standard deviation (n =3).

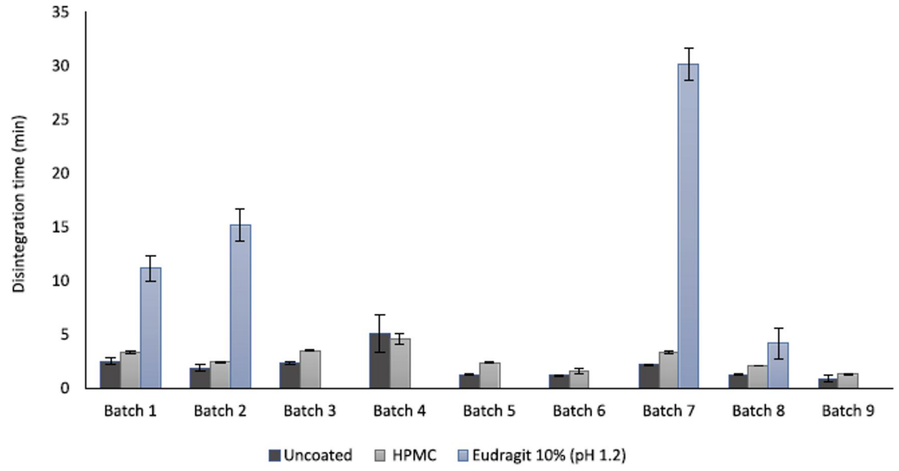


Percentage of in-die and out-die elastic recovery (Er) of single components of the mixtures and blends. MCC: microcrystalline cellulose; MS: magnesium stearate; CPFX: ciprofloxacin with 1 % (w/w) of MS. Data are expressed as mean and standard deviation from n =3 experiments.



Stereomicroscope image of **batch 7** side view, coated with 10% Eudragit® at 10, 16 and 64 magnifications.

Porosity percentage of uncoated tablets (black bars), after HPMC coating (grey bars) and after further coating with 5 % (dotted bars) and 10 % (w/w) (bars with lines) with Eudragit® FS30D. The bars represent the standard deviation (n =3).



Disintegration time of tablets, before coating (Uncoated, black bars) and after HPMC coating (grey bars) in distilled water and after 10 % (w/w) Eudragit® FS30D coating at pH 1.2 (blue bars). Data are expressed as mean and standard deviation from n =6 experiments.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