PHARMACEUTICALS ENVIRONMENTAL PROBLEM AND ITS POTENTIAL SOLUTION

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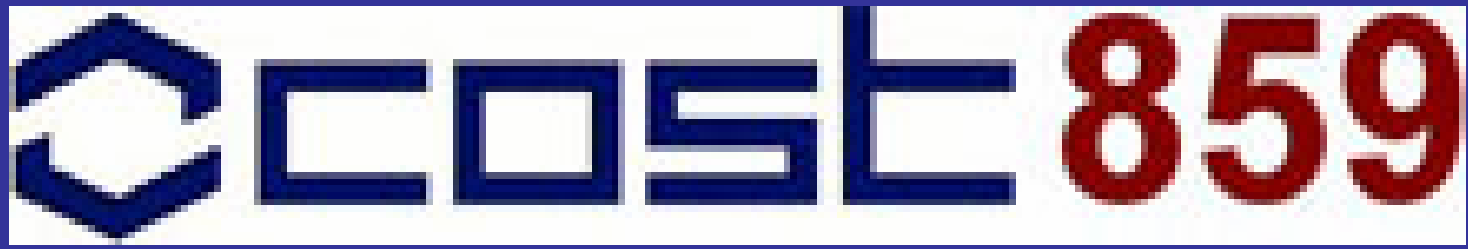

- **Phytotechnologies to promote sustainable land use and improve food safety**

- From green to clean: a promising and sustainable approach towards environmental remediation and human health for the 21st century

- JEAN-PAUL SCHWITZGUÉBEL, JURATE KUMPIENE, ELENA COMINO, TOMAS VANEK

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„New“ contaminants (pharmaceuticals, fragrances, etc.)

- Pharmaceuticals, hosekeeping chemicals, personal care products, wear, food and additives, building and road material, cars and industry, these are only some examples of chemical compound sources in urban water cycle. Solvents, fragrances, flavour, washing powders and pharmaceuticals, they are so called new contaminants.
- Nowadays knowledge of these compounds and their behaviour in the environment is limited.

Pharmaceuticals and personal care products (PPCPs)

- **products of the chemical industry used for increasing of human and animal life quality**
- **the biological activity is often present (primary biological activity in pharmaceuticals or secondary activity – mainly endocrine disrupting effect)**

Main groups of PPCPs

Therapeutic drugs
Veterinary drugs
Fragrances
Cosmetics
Sun-screen products
Diagnostic agents
Nutraceuticals (e.g., vitamins)

Sources of PPCPs

Human activity
Residues from pharmaceutical manufacturing Residues from hospitals
Illicit drugs
Veterinary drug use (antibiotics and steroids)
Agrobusiness

Endocrine disruptors

- chemicals affecting endocrine hormone level
- hormone mimetics
- altering hormone levels by influence on hormonal hierarchy

Health risk in wildlife

- Fish reproduction problems
- Resistence of microorganisms
- Influence on plankton and phytoplankton
- Input into food chain of animals
- Reproduction problems in wildling animals
- Health problems at livestock

Health risk at human

- Increased testicular cancer
- Decreased sperm count
- Increase in reproductive
- abnormalities
- Fewer male babies born
- Breast cancer
- Early puberty

Pharmaceuticals

-hormones (17-alpha-ethynylestradiol, component of anti-baby pills)

- other common used drugs

analgetics (ibuprofen, naproxen, diclofenac…)
psycholeptics (diazepam, fluoxetin…)
antiepileptic drugs (carbamazepine)
hypolipidemic drugs (clofibrate)
cardiovascular drugs (beta-blockers, ACE inhibitors)
antibiotics (amoxycillin, azithromycin…..)

Musk compounds

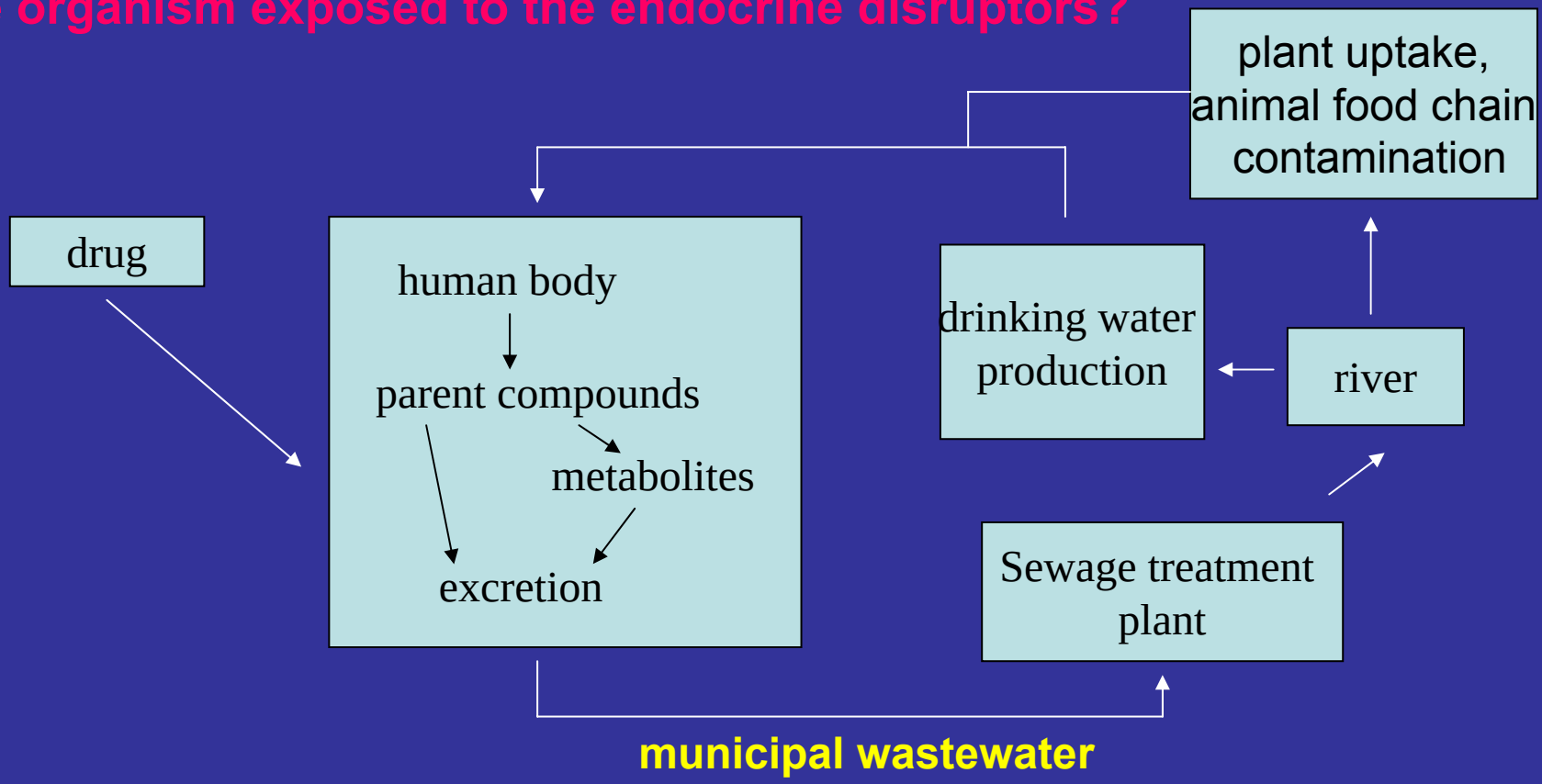
Fragrances for consumer chemistry (washing powders, household cleaning products, body parfumes, shower gels etc.)

Exposure routes

- direct exposition

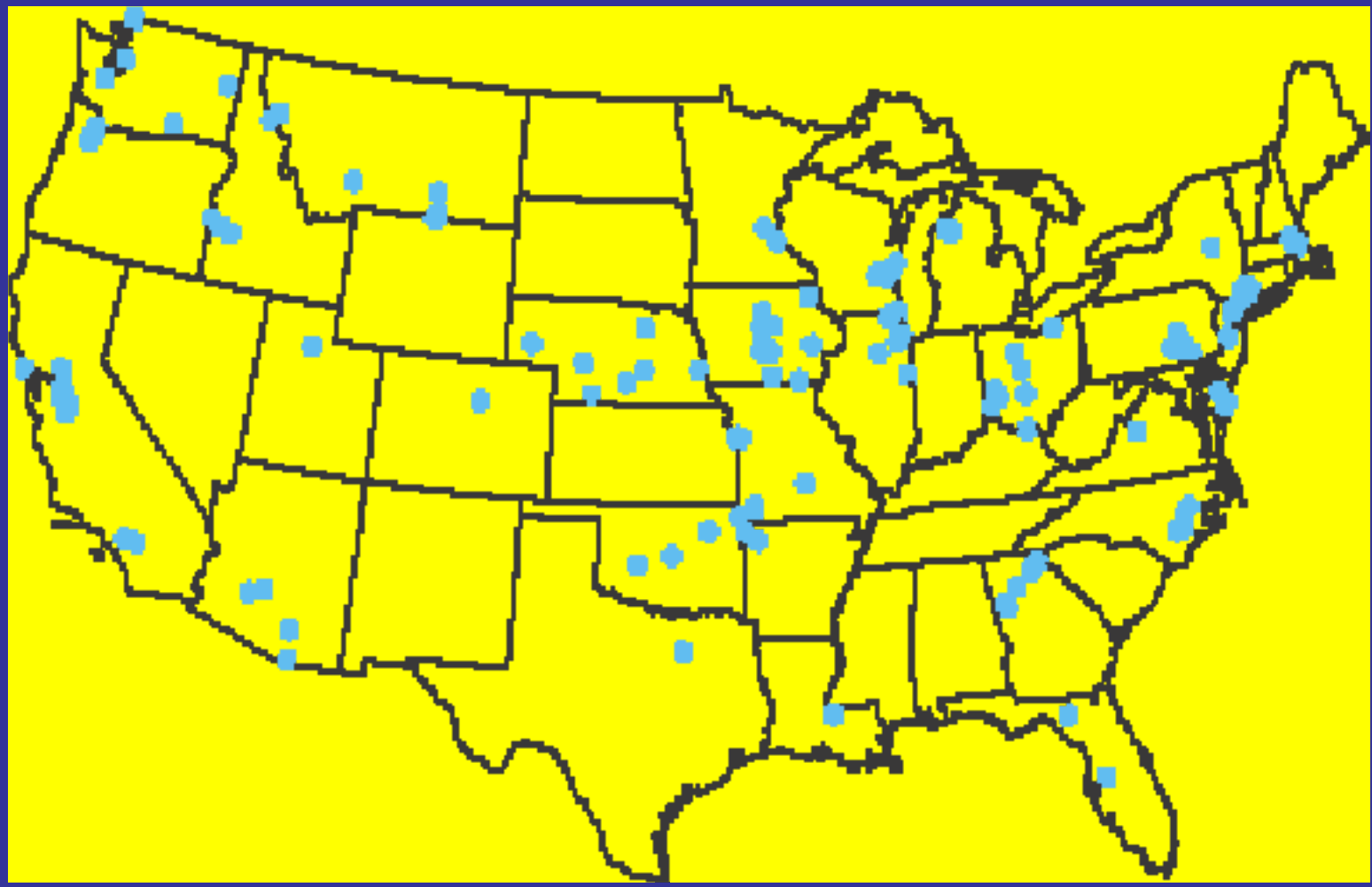
-use of contaminated water (long-time, low level exposition with unpredictable effect)

How are organism exposed to the endocrine disruptors?



Occurence of the selected pharmaceuticals in the aquatic environment

Pharmaceuticals in rivers 2005



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Diclofenac

– NSAID, analgetic drug

		Amount in ng/l	Year
Rhein	Germany	30	1995 – 1996
Main	Germany	250	1995 – 1996
Landgraben	Germany	680	1995 – 1996
Hamburg	Germany	26 – 387	2002
Greifensee	Swiss	0 - 10	1999
Var. water sources	Spain	26 – 72	2006
Berlin day water	Germany	5 – 960	1996
Berlin underground water	Germany	0-380	1996

*Literature data

Ibuprofen

– NSAID, analgetic drug Amount in ng/l Year

Rhein	Germany	70	1999
Main	Germany	70	1999
Saale	Germany	87	1999
Greifensee	Swiss	5 – 15	1999
Riera	Spain	230 – 1650	2000
Tibera (Roma)	Italy	0 - 200	2002
Tyne	Great Britain	144- 2370	2004
Berlin Underground water	Germany	0-200	2000

*Literature data

Sewage treatment plant efficiency

Sewage treatment plant efficiency

Primary treatment

- musk compounds (30 – 50 %), 17-beta-estradiol (20 %)

Aerobic treatment (activated sludges)

reduction of most compounds by 35 – 75 %

musk compounds (70 – 90 %)

anti-inflammatories (40 – 65 %)

17-beta-estradiol (ca. 65 %)

Ibuprofen

Localization	STP influx [ng/l]	STP efflux [ng/l]	Year
Frankfurt/Main	3700	370	1996
Lyon	3769	1960	2003
Lund	156	150	2003
Neapol	112	100	2001
Great Britain	3910	547	2004
Spain	540	270	2006

Literature data

Diclofenac

Localization	STP influx [ng/l]	STP efflux [ng/l]	Year
Uster (Swiss)	655	575	1998
Athens (Greece)	12 – 560	10 – 365	1999
Lyon (France)	3200	320	2003
Neapol (Italy)	5220	580	2001
Great Britain	3910	547	2004
Lund (Sweden)	727	160	2003

Literature data

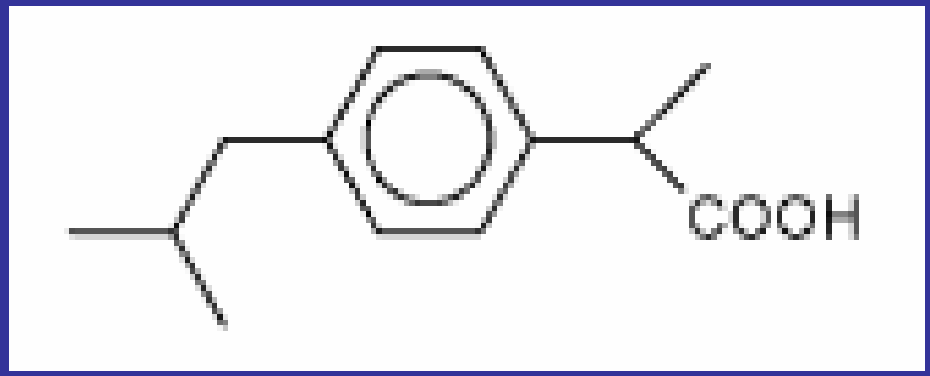
Pharmaceuticals - packages used 2007 in Czech Republic			
	ACTIVE COMPOUND		PACKAGES (MIL)
1.	paracetamol		15,38
2.	elektrolytes		10,94
3.	ibuprofen		10,49
4.	Acetylsalicylic acid		5,47
5.	Paracetamol in mixtures		4,69
6.	Acetylsalicylic acid in mixtures		4,08
7.	ambroxol		3,66
8.	xylometazolin		3,58
9.	atorvastatin		3,54
10.	metoprolol		3,54

Paracetamol – 10 000 kg….

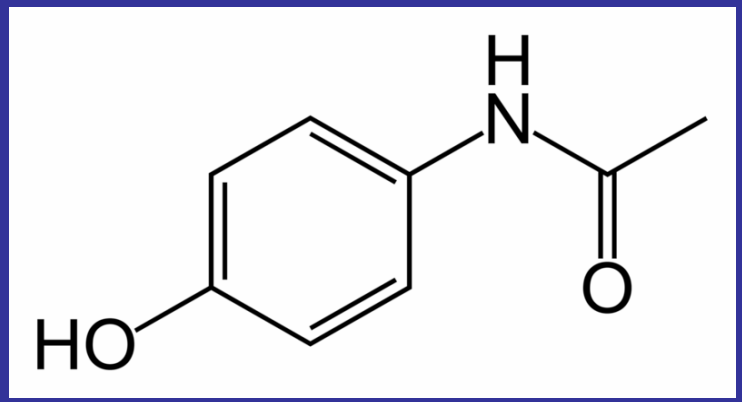
PHYTOREMEDIATION

Experiments about phytoextraction of pharmaceuticals

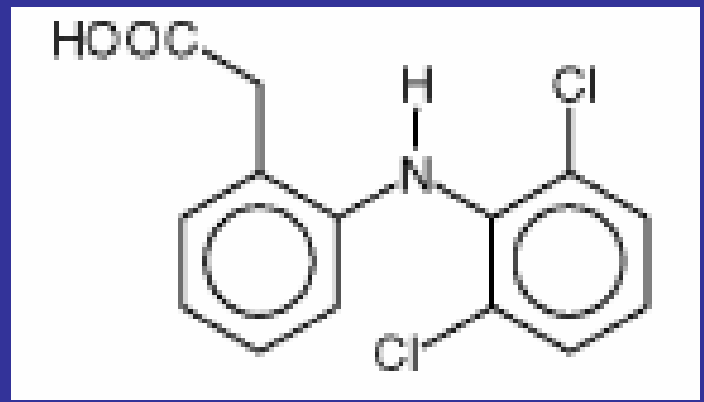
Selected pharmaceuticals



Ibuprofen



Paracetamol



Diclofenac

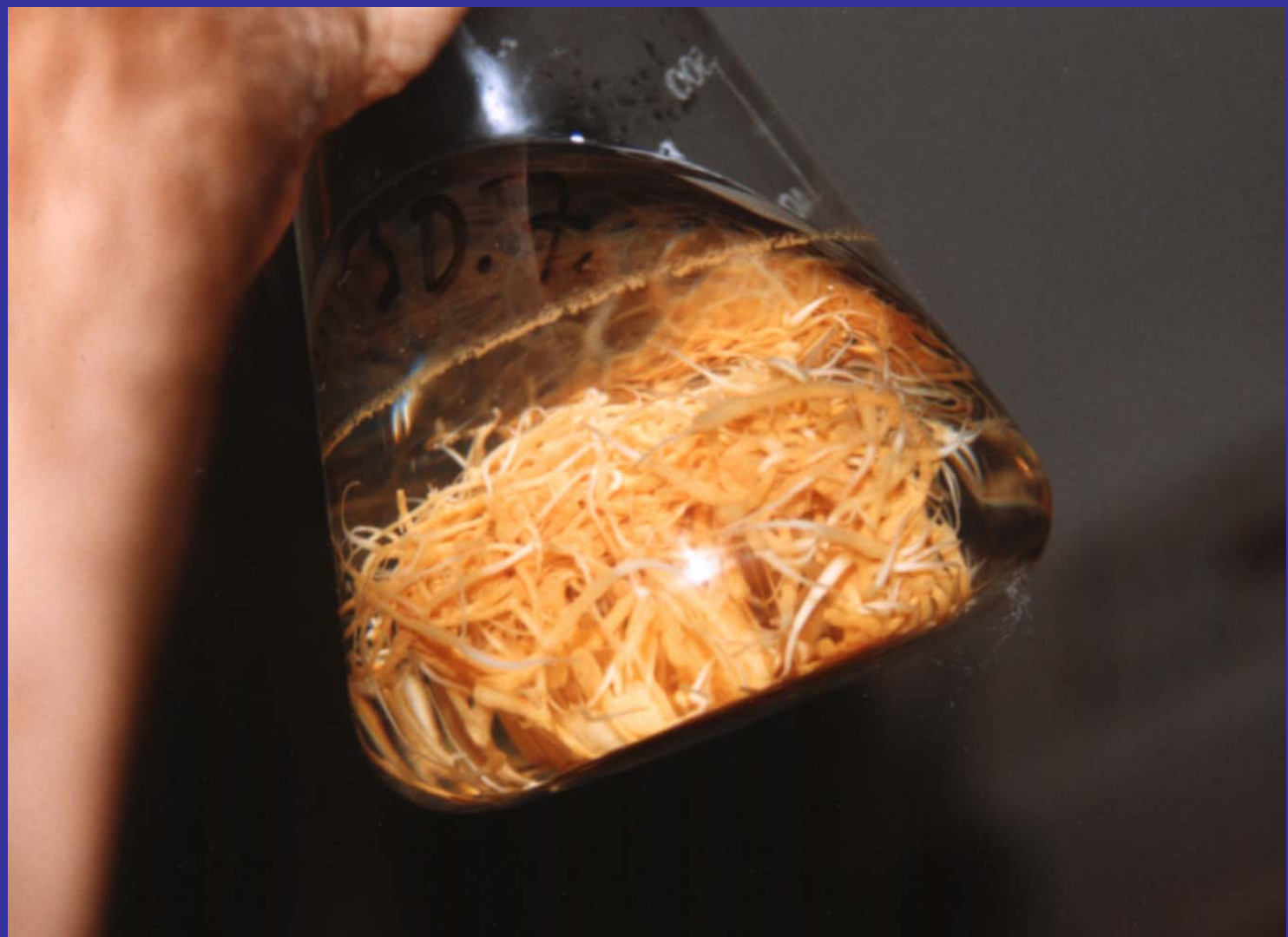
Drug properties

Drug	Chemical name of active compound	log $K_{o/w}$	solubility [g/l]	M_w
Diclofenac	2-(2,6-dichloranilino)phenylacetic acid Na salt	0.7	2.43	318,1
Ibuprofen	iso-butyl-propanoic-phenolic acid	3.97	0.021	206.28
Acetaminophen	N-acetyl-para-aminophenol	0.46	14	151.16

Plants used

- Plants *in vitro*
- Terrestrial plants
- Water plants

Armoracia rusticana hairy root culture



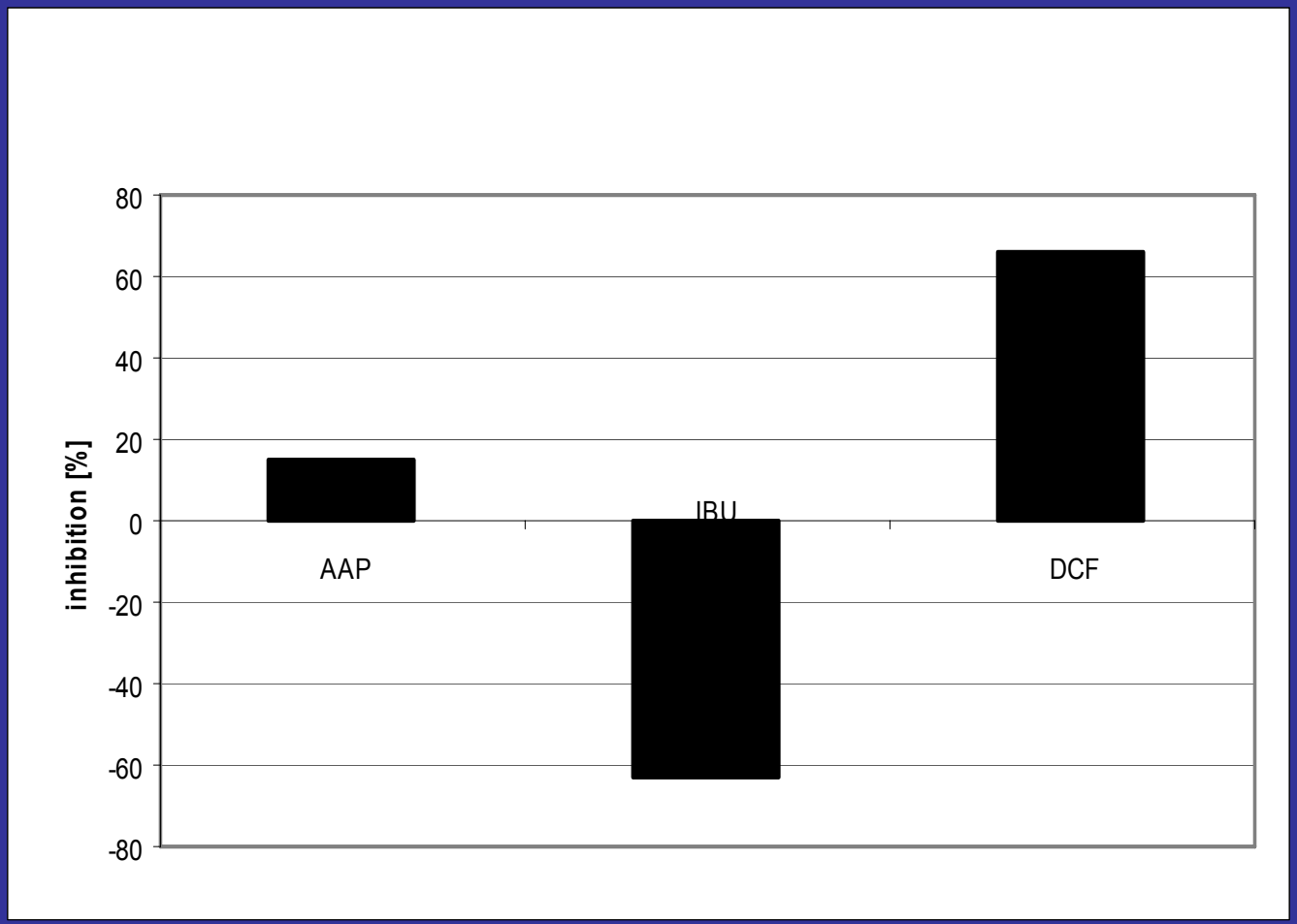
Phragmites australis

Common read

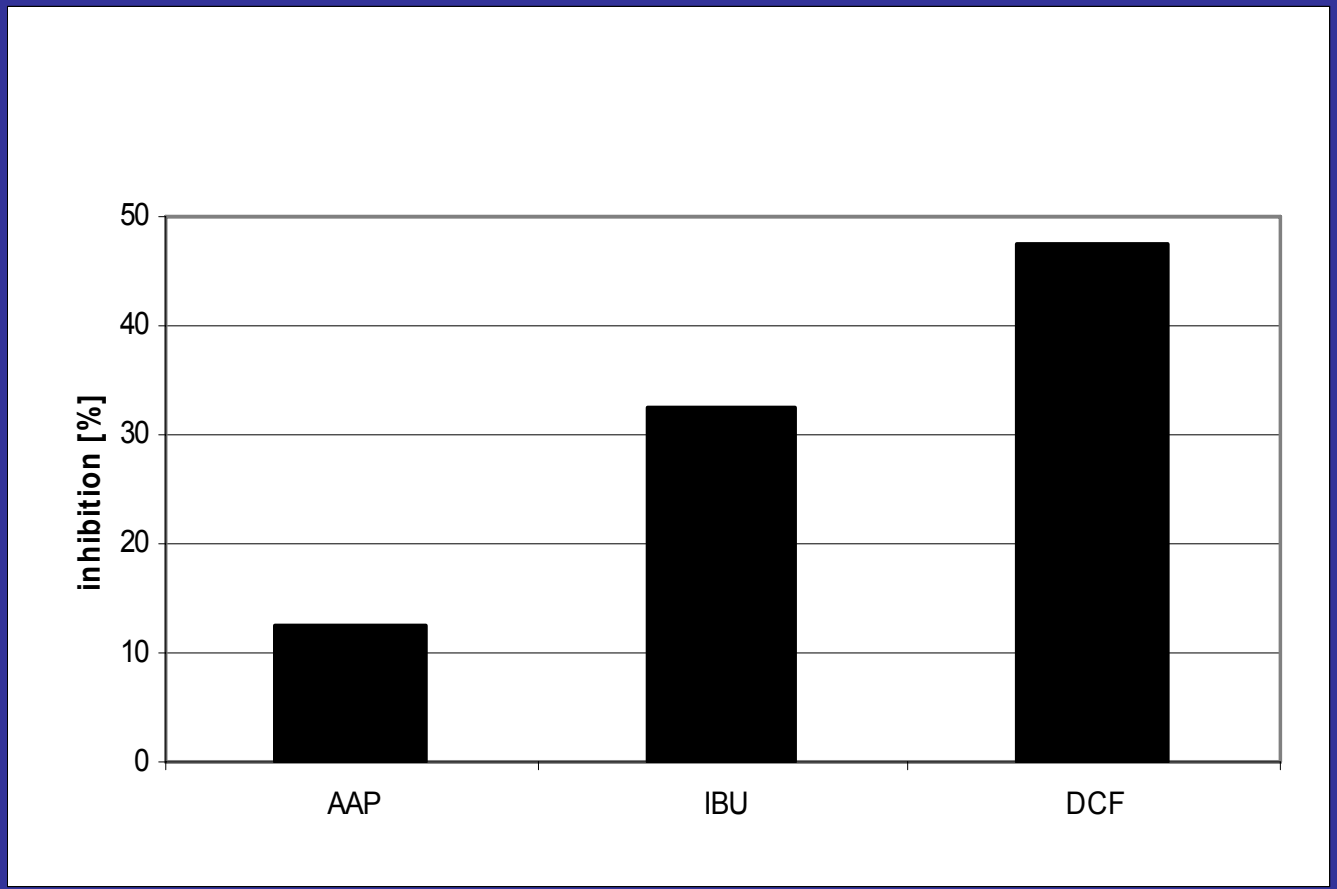
Juncus glaucus (inflexus)

Blue rush, Hard rush

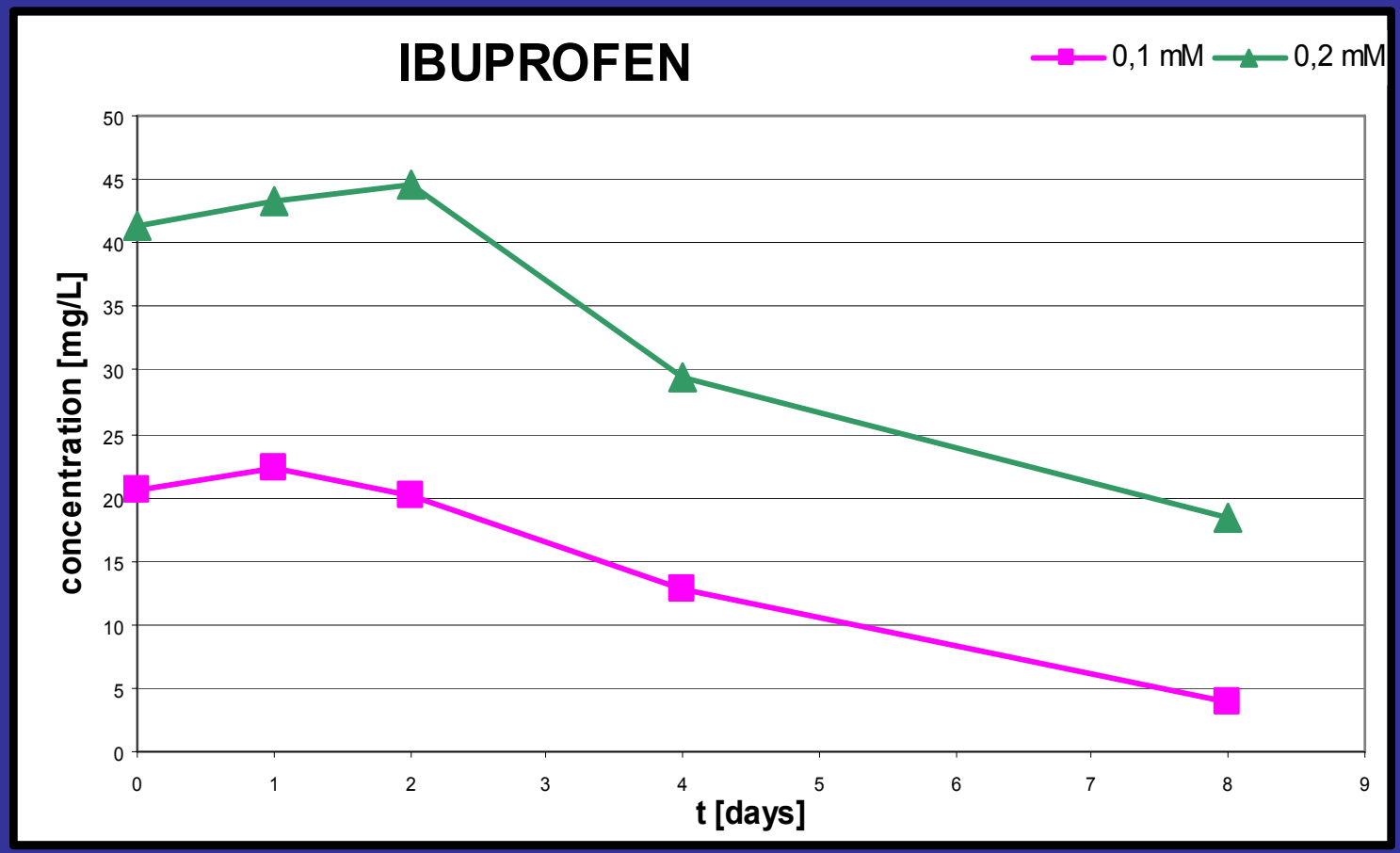
Decreasing of viability of *Armoracia rusticana* in 0.2 mM solution of pharmaceuticals



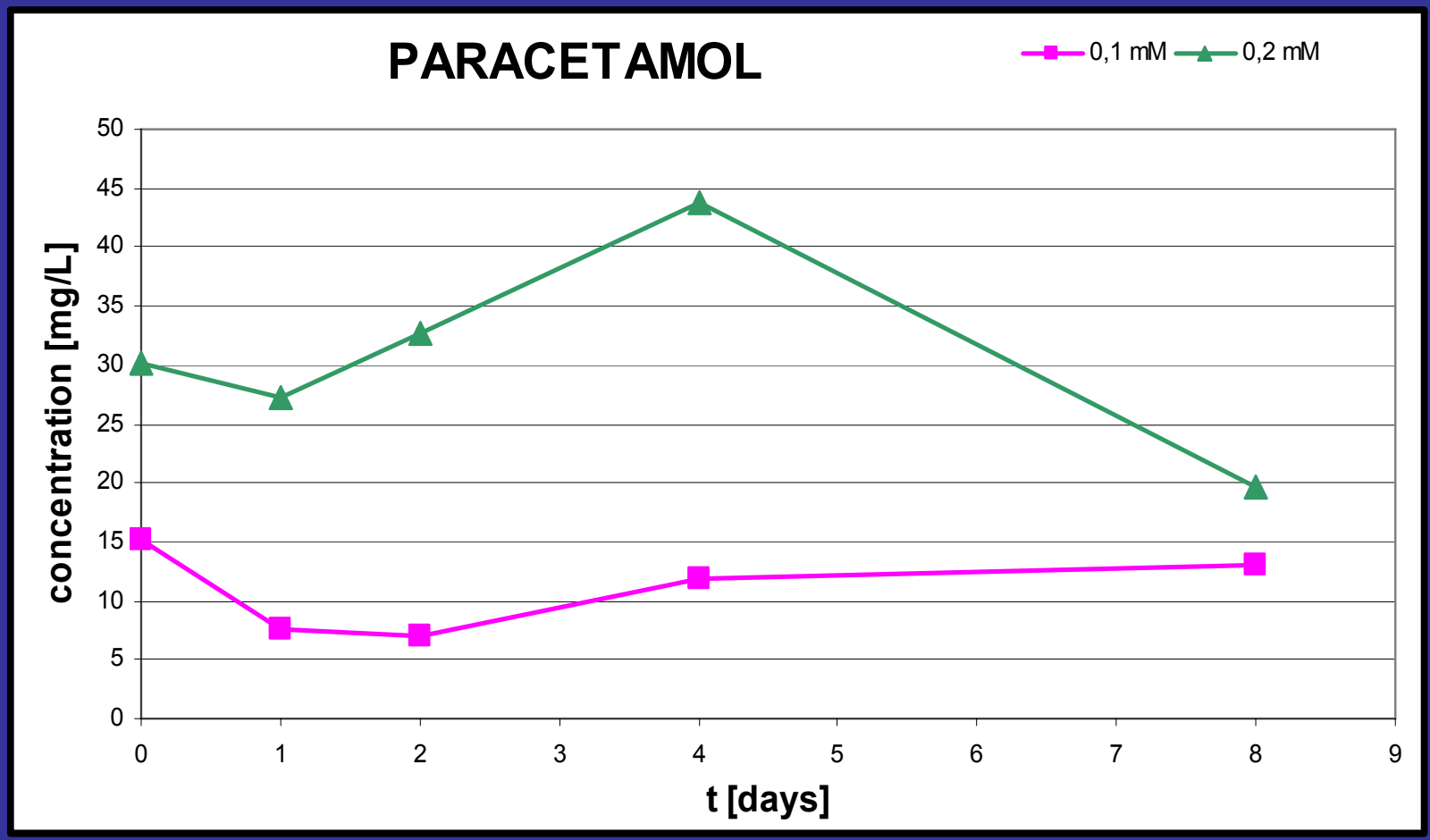
Decreasing of viability of Linum usitatissium in 0.2 mM solution of pharmaceuticals



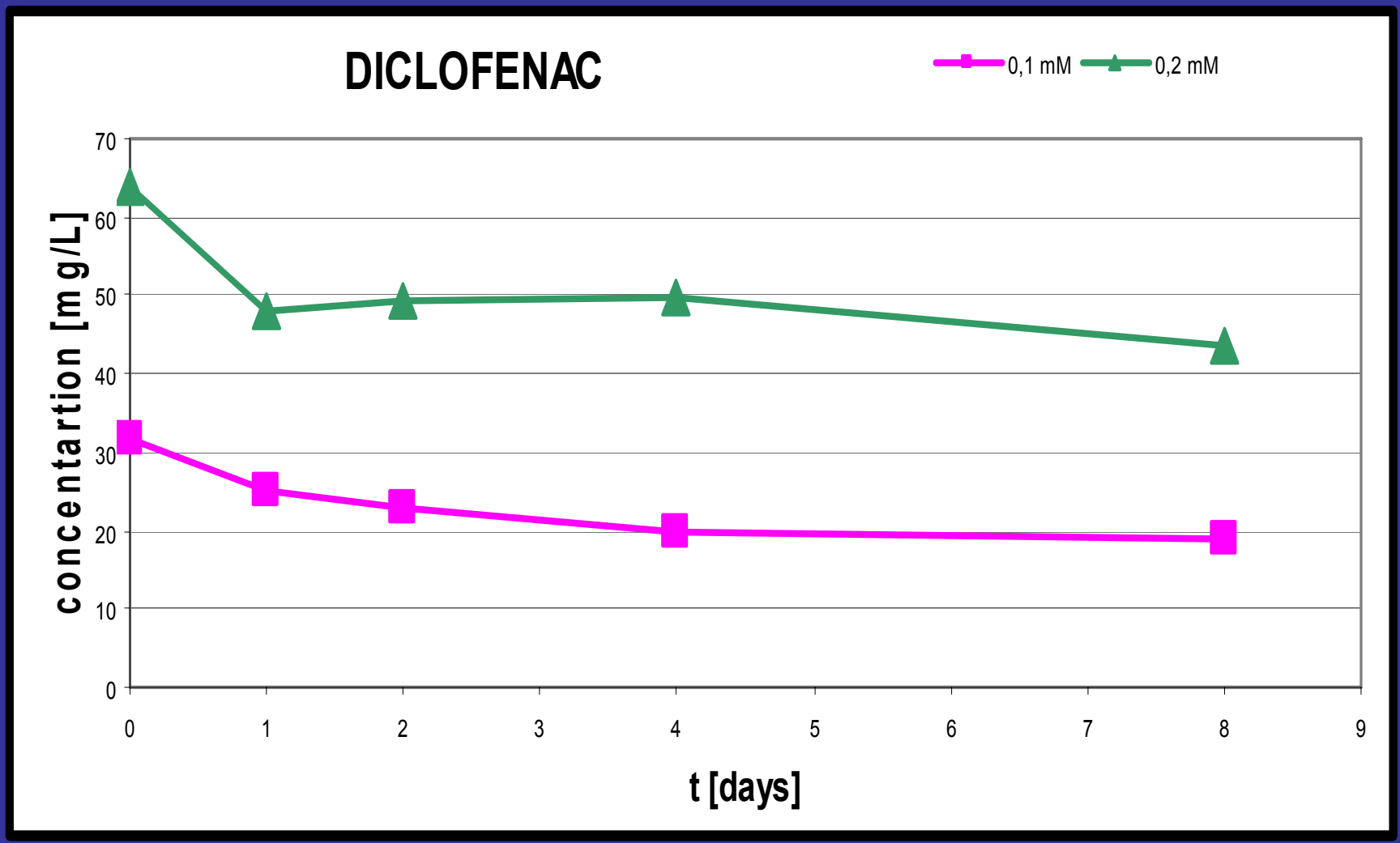
Accumulation of ibuprofen using Armoracia rusticana root cultures



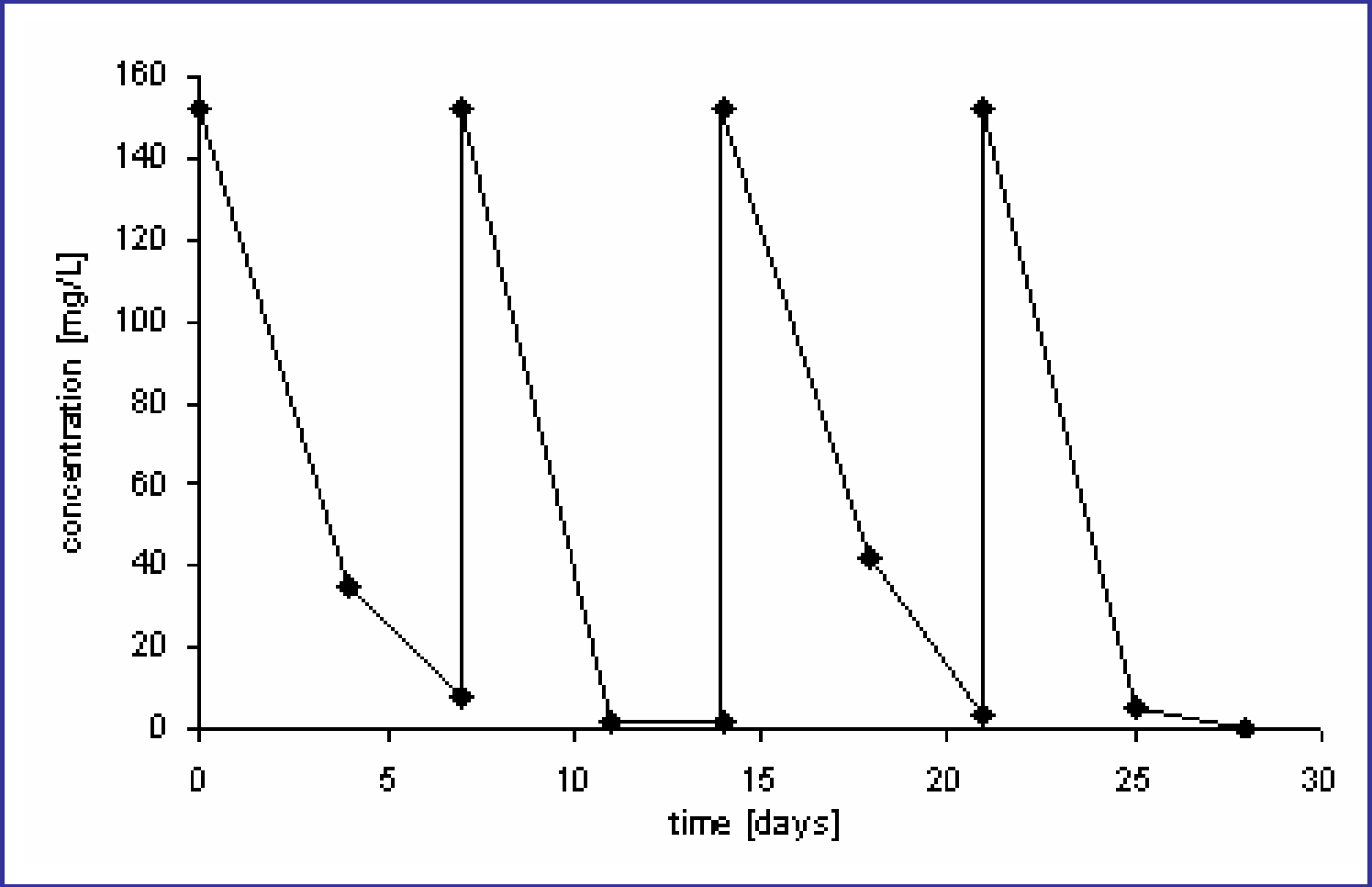
Accumulation of paracetamol using Armoracia rusticana root cultures



Accumulation of diclofenac using Armoracia rusticana root cultures



Consecutive accumulation of paracetamol in *in vitro* conditions using *Armoracia rusticana* hairy root culture

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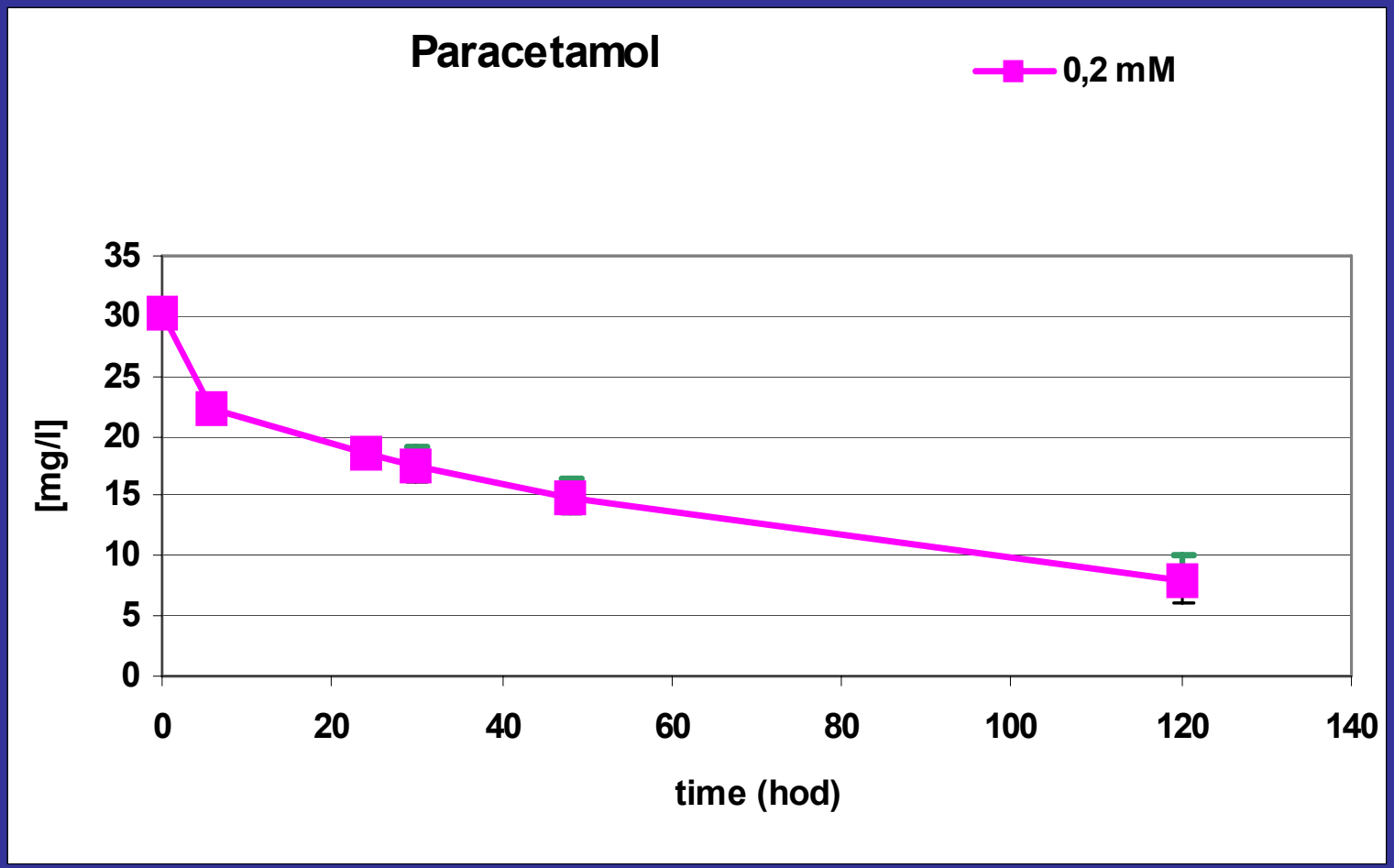
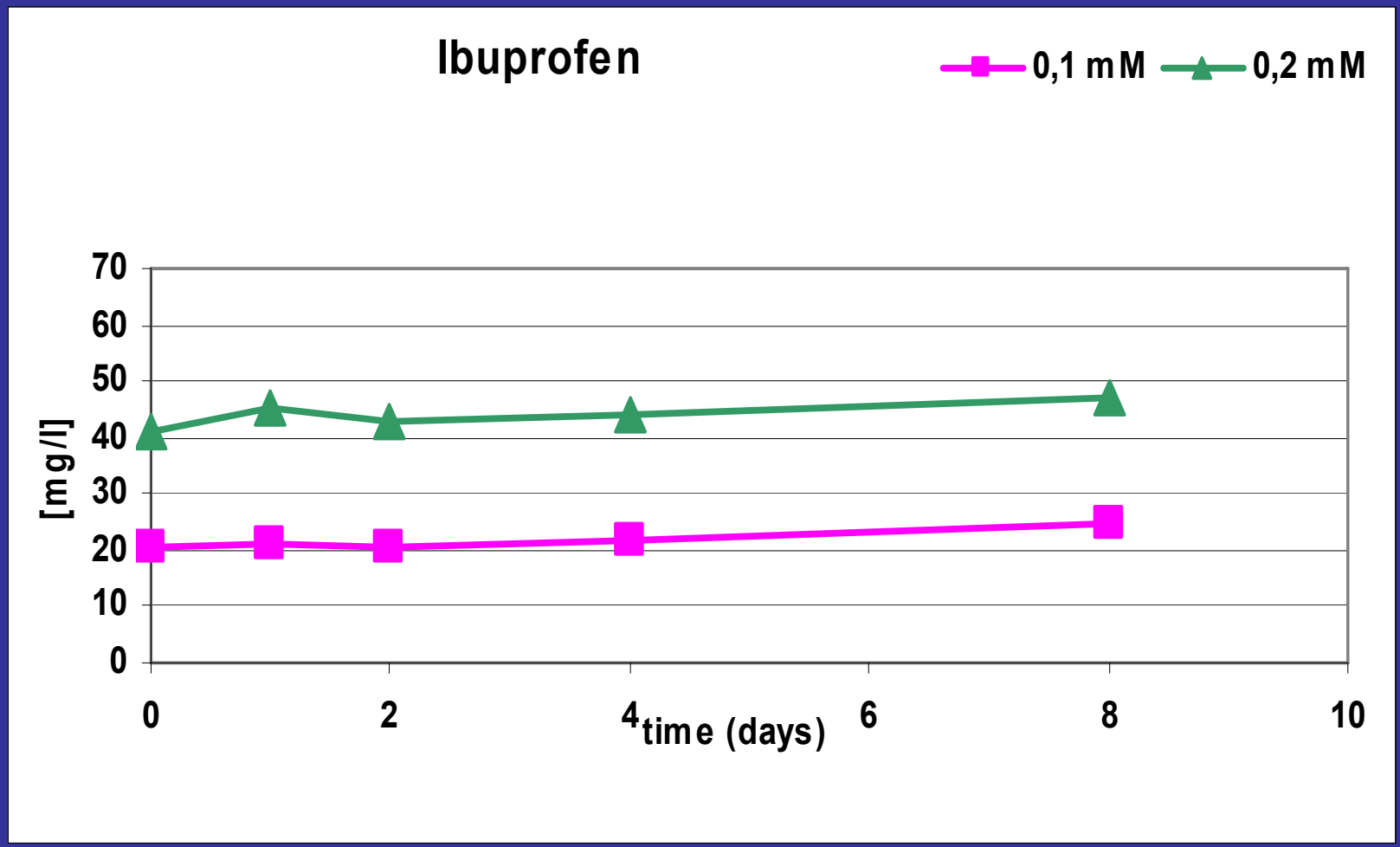
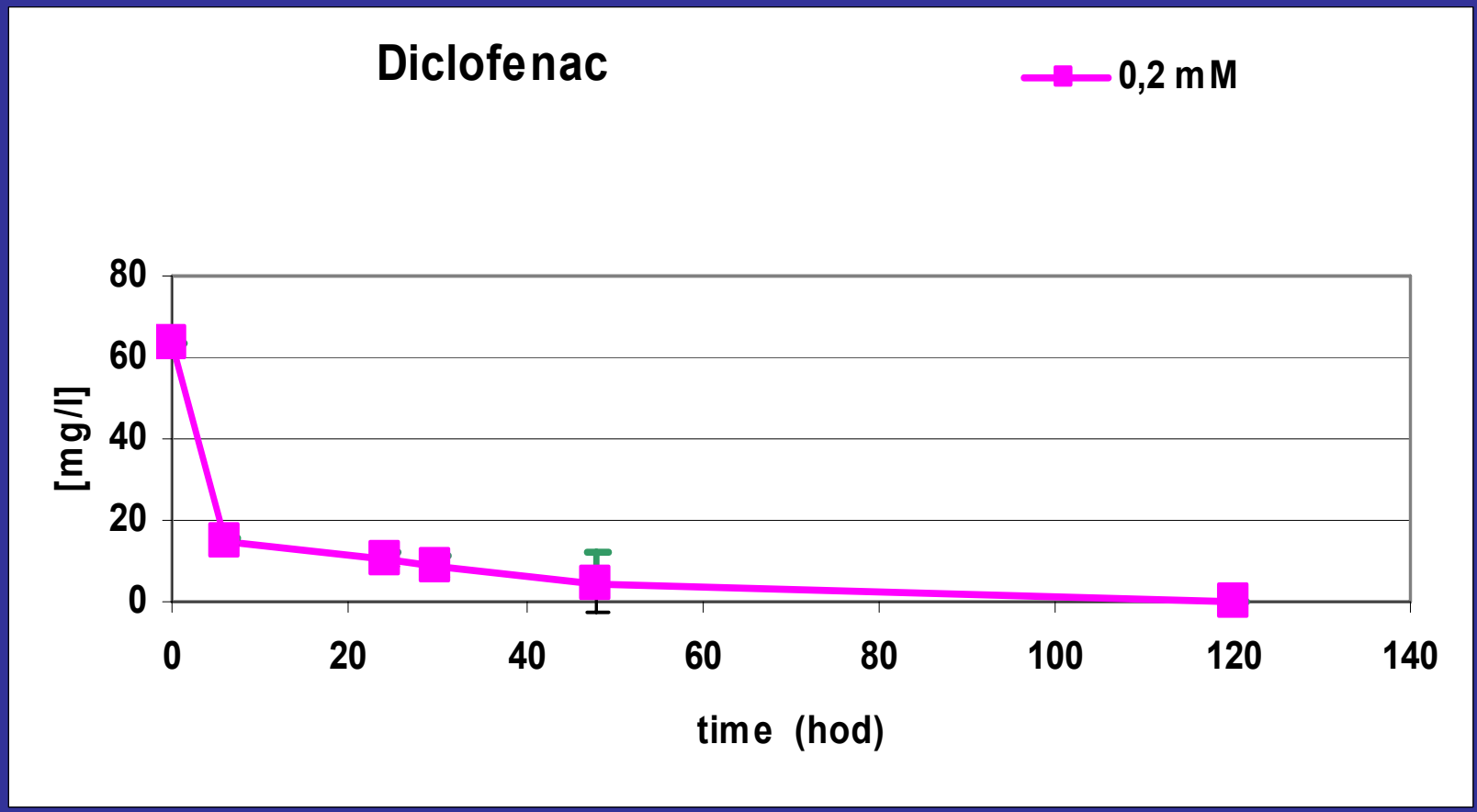
Accumulation of paracetamol using flax suspension cultures



Accumulation of ibuprofen using flax suspension cultures



Accumulation of diclofenac using flax suspension cultures



Accumulation of paracetamol after 8 days of hydroponic experiments

Plant species	Molar concentration	Initial concentration [mg/L]	Final concentration [mg/L]	Approx. Mass Removed [%]
Lupinus luteolus	0.1 mM	15.12	n/d	100
	0.2 mM	30.23	n/d	100
Hordeum vulgare	0.1 mM	15.12	2.59 ± 1.46	83
	0.2 mM	30.23	17.45 ± 1.83	42
Phragmites australis	0.1 mM	15.12	12.64 ± 1.80	16
	0.2 mM	30.23	31.89 ± 4.70	-5

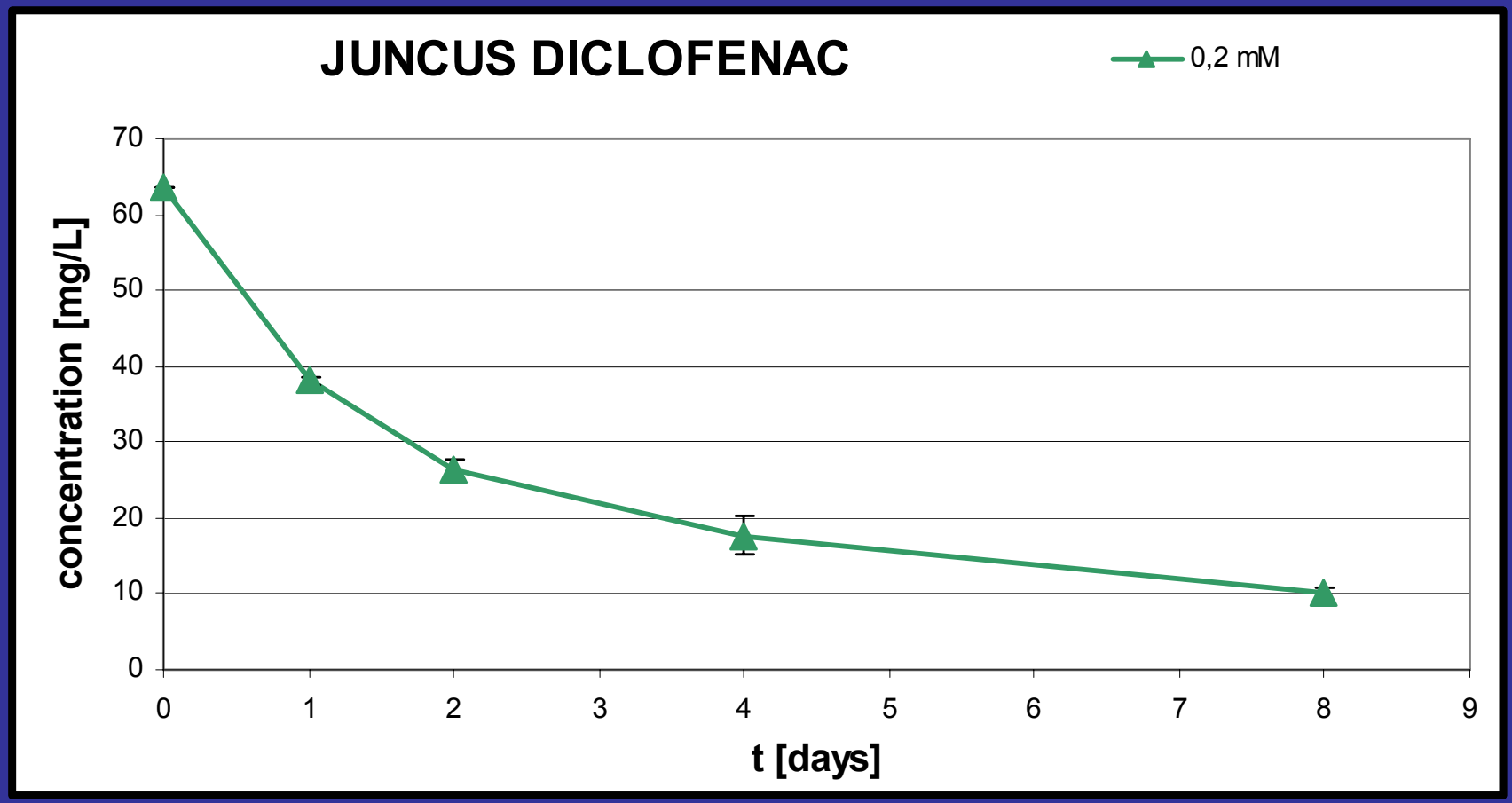
Accumulation of ibuprofen after 8 days of hydroponic experiments

Plant species	Molar Concentration	Initial concentration [mg/L]	Final concentration [mg/L]	Approx. Mass Removed [%]
Lupinus luteolus	0.1 mM	20.63	18.42 ± 1.08	11
	0.2 mM	41.27	39.79 ± 1.95	4
Hordeum vulgare	0.1 mM	20.63	8.67 ± 4.65	58
	0.2 mM	41.27	34.29 ± 1.89	17
Phragmites australis	0.1 mM	20.63	8.28 ± 2.02	60
	0.2 mM	41.27	20.92 ± 2.75	49

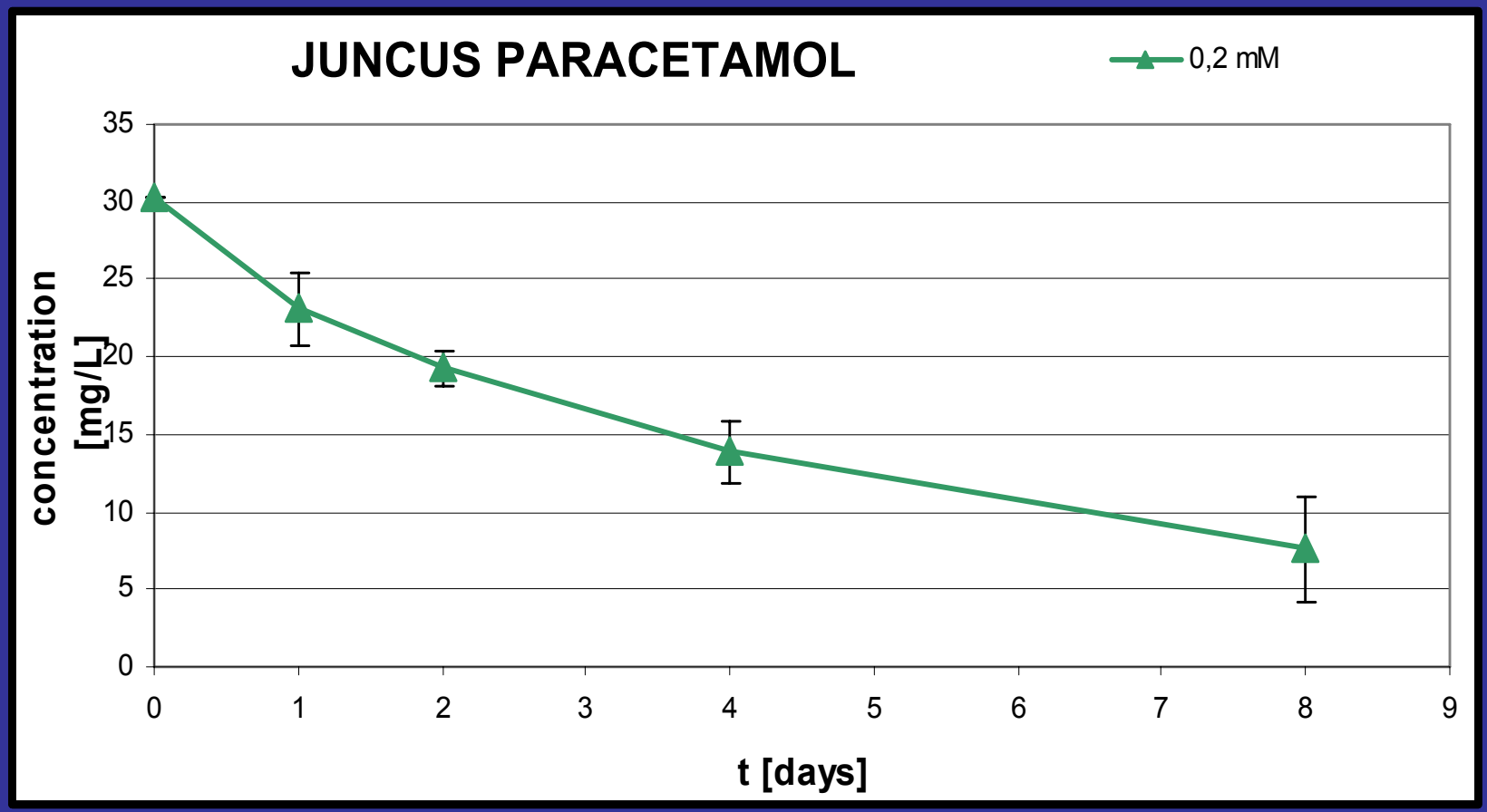
Accumulation of diclofenac after 8 days of hydroponic experiments

Plant species	Molar Concentration	Initial concentration [mg/L]	Final concentration [mg/L]	Approx. Mass Removed [%]
Lupinus luteolus	0.1 mM	31.83	29.62 ± 0.24	7
	0.2 mM	63.67	61.46 ± 0.92	3
Hordeum vulgare	0.1 mM	31.83	18.06 ± 4.50	43
	0.2 mM	63.67	47.85 ± 5.43	25
Phragmites australis	0.1 mM	31.83	26.01 ± 0.39	18
	0.2 mM	63.67	42.73 ± 1.61	33

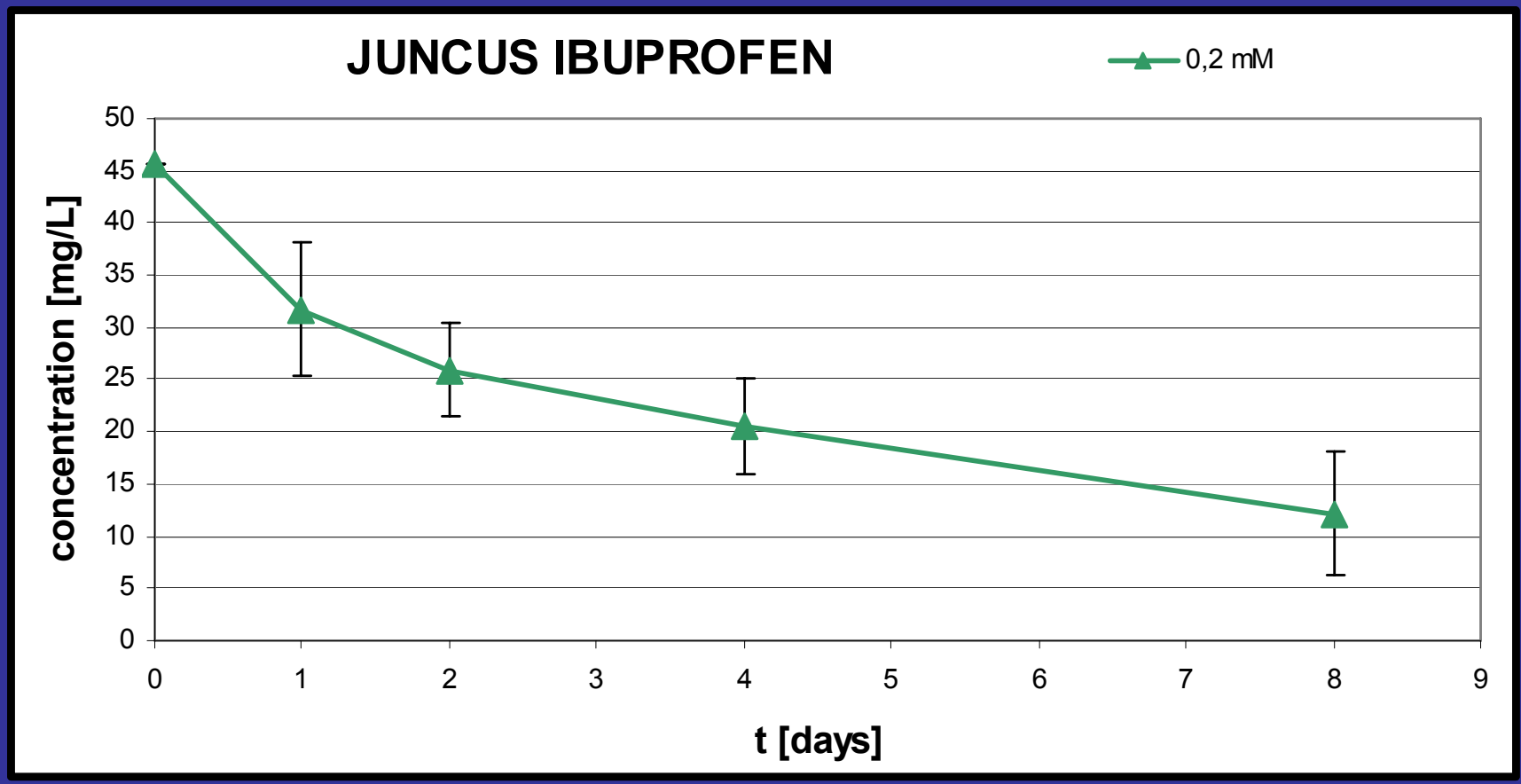
Accumulation of diclofenac using Juncus hydroponic cultures



Accumulation of paracetamol using Juncus hydroponic cultures



Accumulation of ibuprofen using Juncus hydroponic cultures

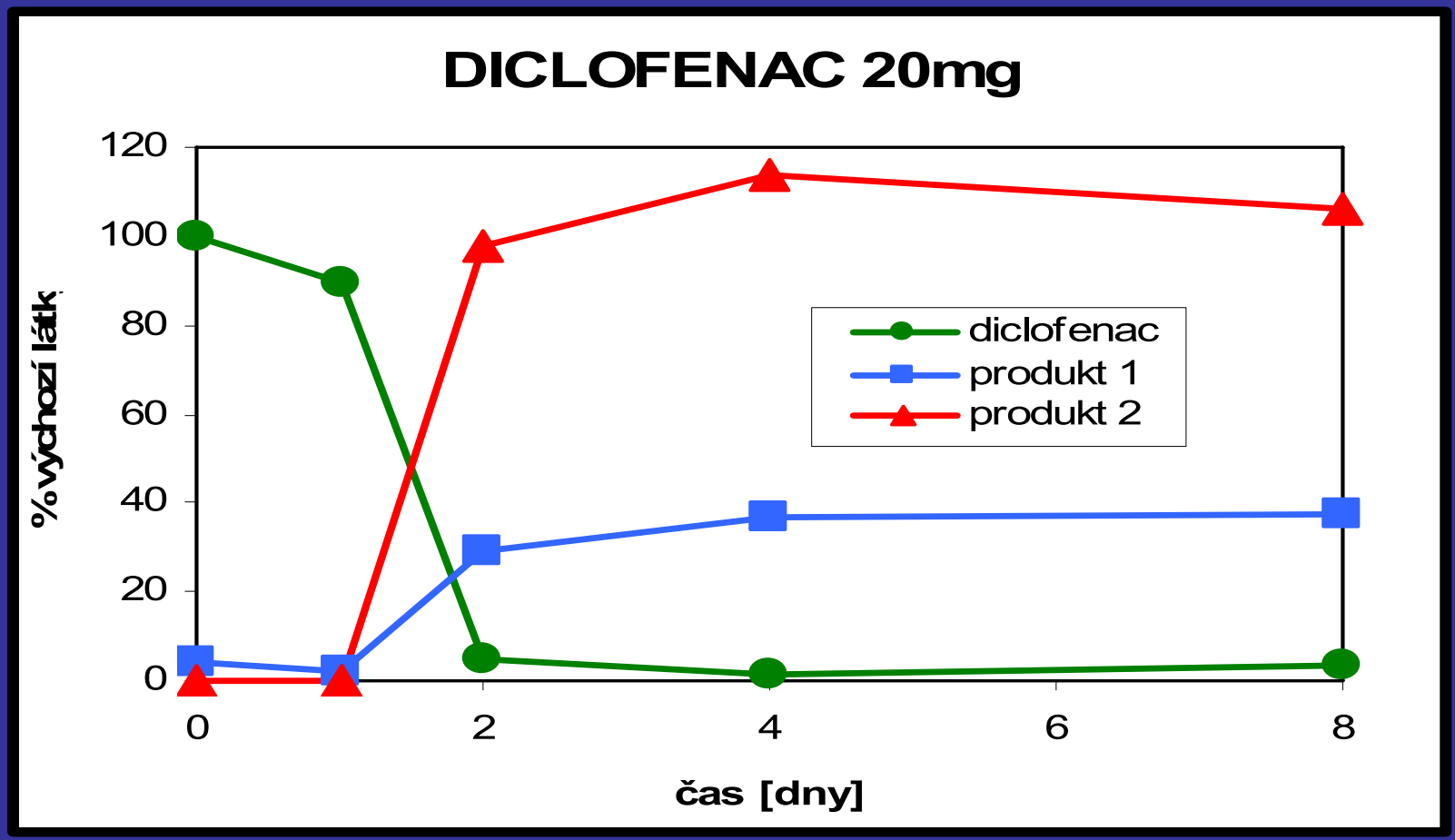


MECHANISM

- Degradation products
- Enzymes
- Genes
- GM plants

C^{14} labelled paracetamol

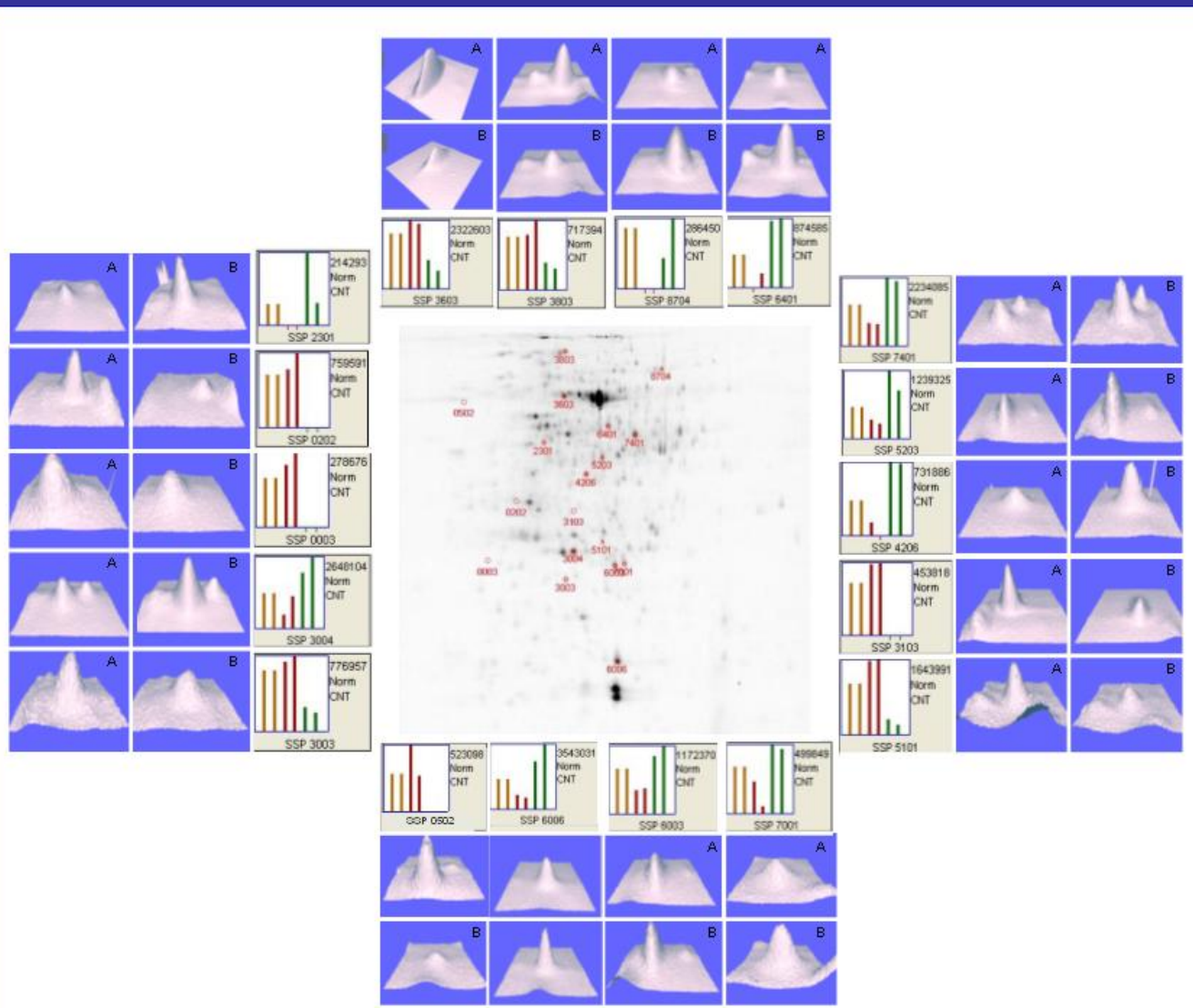
Accumulation of diclofenac using Armoracia rusticana root cultures



Metabolites identified

- Paracetamol – glycosides, glutathione conjugates
- Ibuprofen – glycosides
- Diclofenac – 2 ??????

DIGE


A
B
2322603 Norm CNT
SSP 3603
717394 Norm CNT
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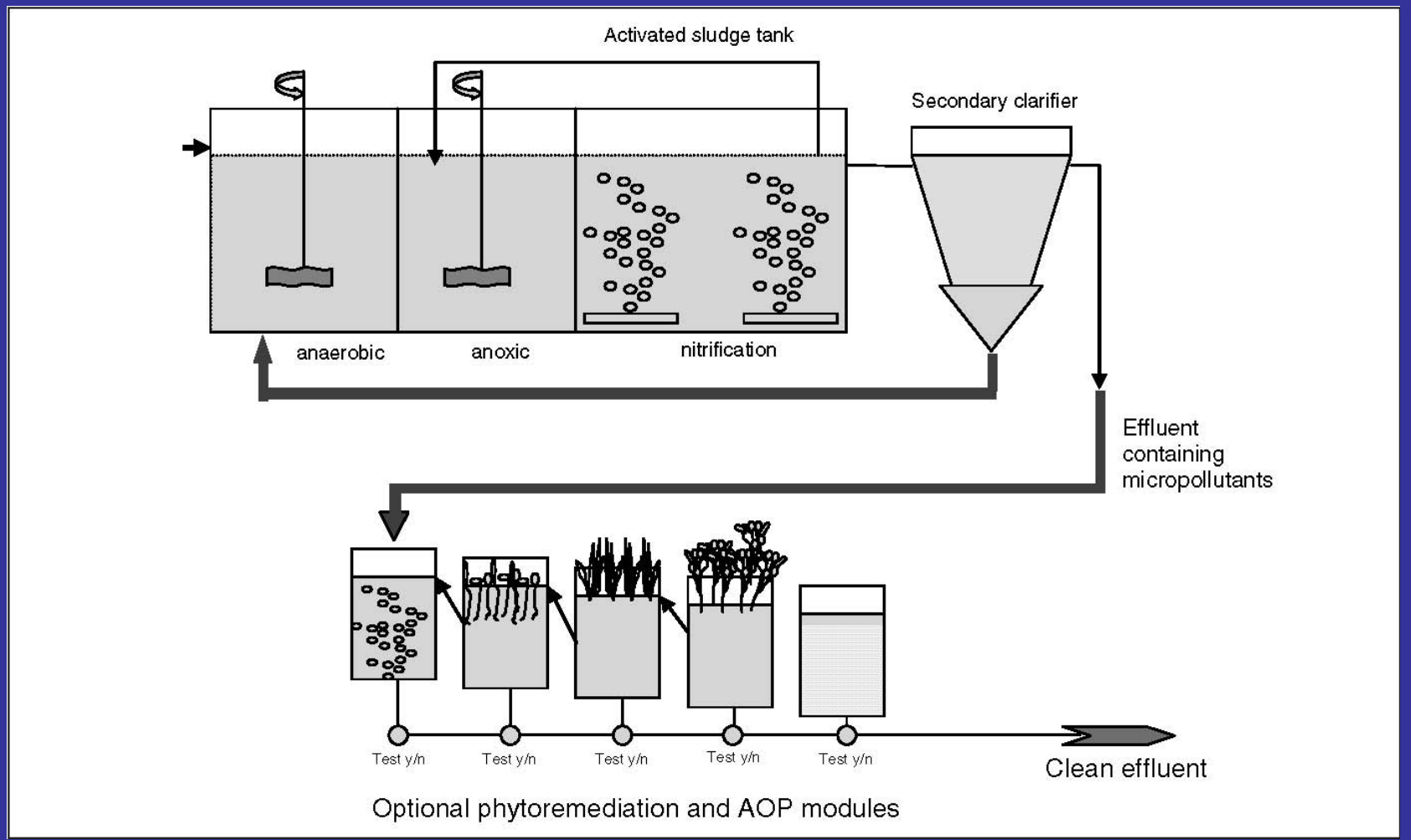
499649 Norm CNT
SSP 7001

Conclusions

- Phytoextraction of drugs from water media is possible and can be of technological importance in the future
- Plants are able to extract pharmaceuticals by root system and can be contaminated in the nature
- Additional experiments with lower concentrations of drugs are needed
- Study of metabolismus is necessary
- Use of water plants as substitution of root filtration is possible

Combined technology



Gravel transport

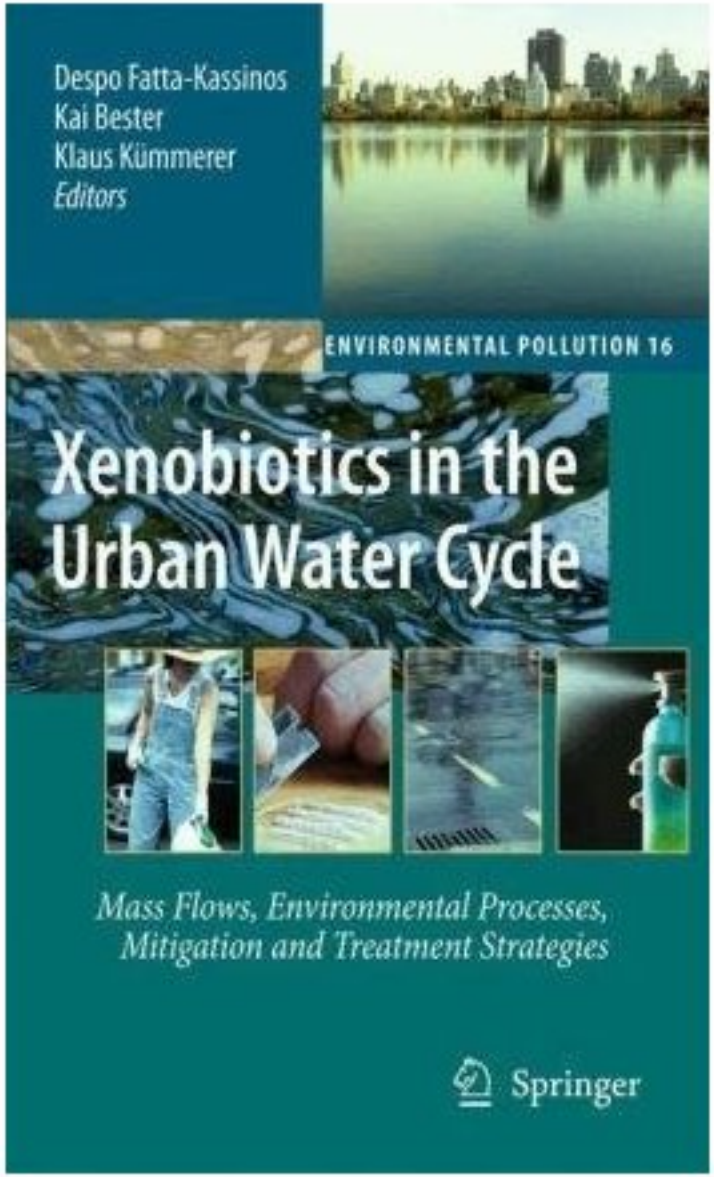
CONSTRUCTED WETLAND

Next step - GM plants?

- **PHYTOREMEDIATION OF PHARMACEUTICALS – PRELIMINARY STUDY**
- Jan Kotyza, Petr Soudek, Zdeněk Kafka,
- Tomáš Vaněk

- **International Journal of Phytoremediation**
- accepted

Xenobi
Process
(Editor)



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Thank you…