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Capacitive biosensor based on synthetic receptors for multiplex monitoring of amphetamine-type stimulants in the water system

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Amphetamine-type stimulants (ATS)

The threat of synthetic drugs is one of the most significant current drug problems worldwide. Amphetamine-Type Stimulants (ATS) are globally the second most widely used drugs after cannabis. ATS production contributes to environment pollution, so there is a demand to develop robust and sensitive sensors that can detect ATS and in environmental water samples.

ORAL   SNORTING   SMOKING (INHALATION)   INJECTION

Targets:

N-formylamphetamine (N-FA)

Benzyl methyl ketone (BMK)

Amphetamine (AMP)

4-methyl-5-phenylpyrimidine (4M5PP)

* The image is taken from www.localrehabs.com
** The image is taken from www.quora.com

Molecularly imprinted polymers (MIPs)

MIPs are polymers that have been processed using the **molecular imprinting technique,** which leaves cavities in the polymer matrix with **affinity to a "template"** molecule.

MIPs towards *N*-FA

(a) template, N-FA; (b) cross-linker, ethylene glycol dimethacrylate (EGDMA); (c) monomer: 2-hydroxyethyl methacrylate (HEM), (d) functional monomer, itaconic acid (IA).

SEM pictures of synthesized molecularly imprinted polymers (MIPs) for N-FA prepared via (a) bulk polymerization; (b) precipitation polymerization

Capacitive drop depending on the NFA concentration

MIPs towards BMK

Computational design

Binding energy template: monomer (ratio 1:1; kJ/mol)			
1-vinylimidazole	-17,92	allylamine	3,65
2-vinylpyridine	n.a.	urogranic acid ethyl ester	-10,86
acrylamido-2-methyl-1-propanesulfonic acid	n.a.	itaconic acid	-18,19
2-hydroxyethylmethacrylate	-9,16	methacrylic acid	-14,73
4-vinylpyridine	3,06	styrene	-26.23
acrolein	-0,49	uragranic acid	1,21
acrylamide	2,74	N,N-diethylamino ethyl methacrylate	9,95
acrylic acid	1,27	N-phenylacrylamide	10,43
acrylonitrile	2,98		

Analytical performance

Affinity tests

$y = 0,0017x + 1,9684$
$R^2 = 0,9983$

LOD was determined to be 1 µM.

SEM and optical microscopy

BMK concentration [µM] in the samples – set I (BMK_SS means BMK standard with no MIPs added). Samples BMK18_1 and BMK18_2 mean MIPs with pure water added, samples BMK18_3 and BMK18_4 mean MIPs with the standard added.

DLS measurement of the MIP towards BMK

MIPs towards 4M5PP

4-Methyl-5-phenyl pyrimidine   Pyrimidine   **Template**

Pyrmidine is chosen as a template compound to:
1. increase cross reactivity
2. decrease selectivity

Computational design

Tested Monomer	Binding Energy (kJ/mol)
Acrylic acid	-0.86
MAA	-0.16
P- Vinyl benzoic acid	-0.14
2-acrylamido-2-methyl-1-propanesulfonic acid	-0.15
2-Vinyl pyridine	-0.13
2-(trifluoromethyl)acrylic acid	1.79
Itaconic acid	1.62
4- Vinylpyridine	0.058

Capacitive sensor for (multi)detection of ATS

Principle of a capacitive biosensor

electrochemical double layer
analyte
receptor layer (MIP/NIP)
insulating layer
gold electrode

$$\frac{1}{C_{tot}} = \frac{1}{C_{iso}} + \frac{1}{C_{rec}} + \frac{1}{C_{analyte}} + \frac{1}{C_{EDL}}$$

6-channel transducer, improved with protection of the Pt/Pd tracks by an insulating coating

Scheme of the analysis

Spiking with mixture AMP/NFA/BMK

Manual sampling → Filtration → ANALYSES

Used biosensors

Evolution of portable sensor
1. Portable capacitive biosensor (generation 1: single measurement);
2. Portable capacitive biosensor (generation 2: connected to ASIC → multiplex measurements);
3. Pumps + valves + flow cell + ASIC generation → multiplex measurements)

Portable sensor

Analytical performance

ATS	LOD, µM	Linear range, µM
AMP	5	50-1000
NFA	5	10-1000
BMK	1	50-750

Baseline readout before (left) and after (right) sample injection.

"Blind" results	Actual samples
Single detection	
NFA	NFA
AMP	AMP
AMP	Acetophenone
Some kind of ATS (but not BMK/NFA/AMP)	APAAN
Blanc	Ethanol
AMP	DPIA
BMK	BMK
Multiplex detection	
Blanc	Sewage water
NFA+BMK	NFA+BMK in sewage water
NFA+AMP+BMK	NFA+AMP+BMK in sewage water

Conclusions

- Two "in-house" highly specific and sensitive MIPs towards ATS (N-FA and BMK) were synthesized.
- Commercial MIP towards AMP (Lipomed NV) is group-specific.
- Miniaturized capacitive sensor for multiplex detection of three ATS was developed and validated for analysis in sewage water.