



Introduction

MIPs allow for selective extraction of low levels of target compounds in the presence of a mixture of potentially interfering matrix components. Compared to biological receptors, MIP polymer recognition systems have the advantage of superior chemical and mechanical stability being compatible with most solvents, pressures and pH conditions.

The materials can be engineered for an almost unlimited variety of small molecules, such as drugs, natural products, pharmaceuticals, peptides and other types of molecules. The principles are outlined below.

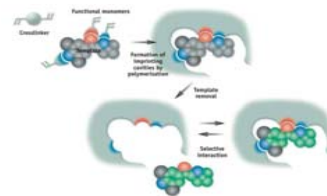


Figure 1. Molecular Imprinting Technology

Molecularly Imprinted Polymers are a class of highly crosslinked polymer-based molecular recognition elements engineered to bind a single target compound or a class of structurally related compounds with high selectivity. By engineering both the binding site and the polymer backbone a wide range of optimised separation phases can be produced. Selectivity is introduced during MIP synthesis in which a template molecule, designed to mimic the analyte, guides the formation of specific cavities or imprints that are sterically and chemically complementary to the desired target analyte(s).

Selective Extractions by MIPs

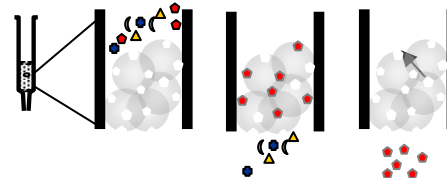


Figure 2.
The Figure shows a typical SPE procedure.

MIP based products for demanding separations

MIP[4]SPE-Beta-agonists MIP[4]SPE-NNAL

Minimised ion suppression A valuable screening tools

The class selective MIP[4]SPE-Beta-agonists has shown to be a valuable tool in screening and quantitative determination of beta agonists in muscle tissue from several kinds of animals. (1)

Cleaner extracts and minimize ion suppression compared to mixed phase SPE.

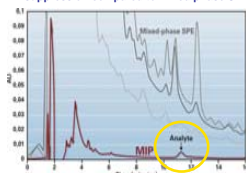


Figure 3.
The chromatograms show the extraction clean-up of a typical analyte from a 5 ml urine sample. Superior clean-up with the MIP sorbent is shown in red, whereas the other chromatograms show clean-up with a much higher level of chemical noise, using mixed-phase SPE sorbents (2).

Results in less than 1 hour instead of three days!

CDC (Centers for Disease Control and Prevention) has studied the presence of NNAL (tobacco specific nitrosamine) in urine using the MIP[4]SPE-NNAL and validated the method (3). Combining MIP extraction with LC-MS/MS detection gives a sensitive and simple analytical method, suitable for epidemiological investigations of health risks associated with the exposure to tobacco smoke.

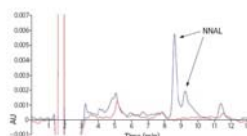


Figure 4.
Chromatograms obtained from 1 mL human urine spiked with 0.25 µg NNAL, (blue line) and 1 mL blank human urine (red line). NNAL displays a characteristic double peak around 9 min corresponding to its two rotamers.

MIP[4]SPE Chloramphenicol Very low detection limits! A fast and simple method

Using this MIP, Chloramphenicol can rapidly be extracted from biological samples. It allows extremely low detection limits, well below the minimum required performance limit (MRPL=0.3 ng/ml) for Chloramphenicol.

Detection limit well below MRPL

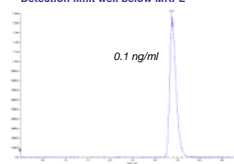


Figure 5.
MS detection of CAP (XIC of -MRM (3 pairs): 321.0/152.0 amu) from Milk sample spiked with 0.1 ng/ml)

List of References

1. The analysis of beta-agonists in bovine muscle using molecular imprinted polymers with ion trap LC/MS screening. P.K. Koosma et al. *Analystica Chimica Acta* 529 (2005) 75-81. National Institute of Public Health and the Environment, RIVM, Laboratory for Food and Residue Analyses, The Netherlands
2. Multi-residue liquid chromatography/tandem mass spectrometric analysis of beta-agonists in urine using molecular imprinted polymers. Van Hoof N et al. *Rapid Commun Mass Spectrom.* 2005;19(19):2801-8. Laboratory of Chemical Analysis, Ghent University, Department of Veterinary Public Health and Food Safety, Belgium.
3. Analysis of the tobacco-specific nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol in urine by extraction on a molecularly imprinted polymer column and liquid chromatography/atmospheric pressure ionization tandem mass spectrometry. Xia Y, et al. *Anal Chem.* 2005 Dec 1;77(23):7639-45.

MIP[4]Process - introducing selectivity into the process

Increase of Productivity



Figure 6.
The diagram shows a 25 times higher product capacity in unit mass/liter per hour using a MIP packed column compared with a conventional resin. (Figure based on calculations performed by the customer)

Unwanted contaminants or high value desirables can efficiently be extracted from large scale batches, resulting in more efficient production and cleaner products.

MIP Technologies develops and produces materials from the mg scale up to the ton scale and the polymer constituents can be engineered to meet regulatory requirements.

MIPs are known to withstand organic solvents, extreme pH and elevated temperatures without loss of selectivity. They are compatible with most process matrices such as pharmaceuticals, food and chemicals etc.

Separation and extraction materials for process scale applications can be developed to operate in various separation/extraction equipment (eg HPLC, SMB, LPLC or non-chromatographic batch type).

Conclusion

MIPs are very well suited for removal of contaminants from complex matrices also in the presence of a mixture of potentially interfering matrix components. Due to the stability of the MIP material highly selective separations are possible both for analytical applications and large scale extractions.

Features of MIPs

- ✓ Simple and rapid sample preparation
- ✓ Low detection and quantification limits
- ✓ Minimized ion suppression (below 10%)
- ✓ Lower risk of false positives
- ✓ High reproducibility and repeatability
- ✓ Very robust material and stable at high temperatures
- ✓ Usable in organic solvents
- ✓ Washable at extreme pH