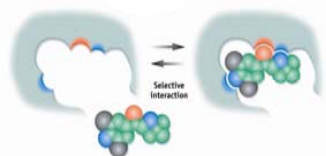




## Introduction

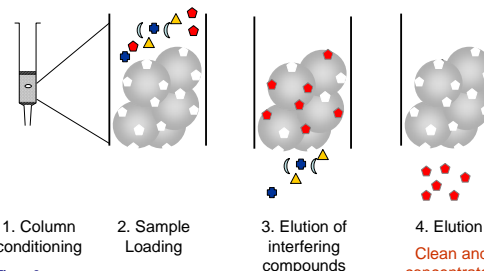
MIPs allow for selective extraction of low levels of target compounds in the presence of a mixture of potentially interfering matrix components. Compared to biological receptors, MIP polymer recognition systems have the advantages of superior chemical and mechanical stability and compatible with most solvents, pressures and pH conditions. The MIP materials can be engineered for an almost unlimited variety of small molecules, such as drugs, natural products, pharmaceuticals, peptides etc.

By engineering both the binding site and the polymer backbone a wide range of optimized extraction phases can be produced. The MIPs extract the targeted analytes with a high degree of selectivity if the template used to form them is designed to form strong interactions with the functional monomers. By taking into account the specific interaction mechanisms, the analytical SPE method can be optimised for each individual MIP material. The principle of the selective interaction mechanism is outlined in Figure 1 and the general SPE procedure is described in Figure 2.



**Figure 1. The Molecularly Imprinted Cavity**  
The MIP materials consist of highly cross-linked polymer phases that have pre-determined selectivity for a single analyte or a group of structurally related analytes. The MIP selective binding site has key recognition elements placed in sterically locked positions.

## Selective Extractions by MIPs



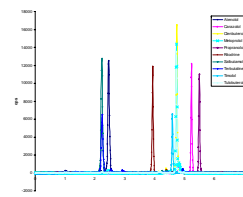
**Figure 2.**  
The Figure shows a typical MIP SPE procedure.

## MIP based solutions for demanding extractions

### SupelMIP™ Beta Receptor

**Simultaneous extraction of Beta agonists and Beta Blockers**

The class selective SupelMIP Beta Receptor is a valuable tool in the quantitative determination of Beta Blockers and Beta agonists in human urine and plasma or for screening in environmental water samples. In comparison to mixed phase SPE materials the SupelMIP-Beta receptor method has been shown to give lowered ion suppression.

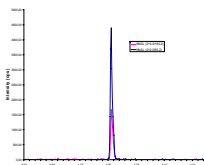


**Figure 3.**  
Chromatograms (LC/MS/MS) of eluates from SupelMIP Beta receptor for a urine sample spiked with 1 ng/mL of a mix of Beta Agonists and Beta Blockers (Atenolol, Carazolol, Metoprolol, Propranolol, Ritodrine, Salbutamol, Terbutaline, Timolol). Clenbuterol and Tulobuterol were spiked at 0.5 resp. 0.1 ng/mL.

### SupelMIP™ NNAL

**Results in less than 1 hour instead of three days!**

CDC (Centers for Disease Control and Prevention) has studied the presence of NNAL (toxic specific nitrosamine) in urine using the SupelMIP-NNAL and established a standard method<sup>(1)</sup>. 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.

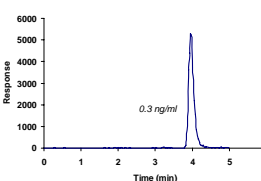


**Figure 4.**  
Chromatograms obtained from 1 mL human urine spiked with 1 ng NNAL (0.05 ng injected). Recovery above 90 %.

### SupelMIP™ Chloramphenicol

**A fast and simple method Applications in honey, milk and urine**

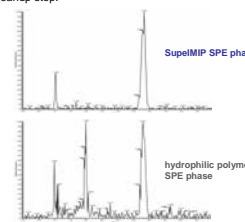
Using this MIP, Chloramphenicol can be rapidly extracted from biological samples. It allows low detection limits, well below the minimum required performance limit (MRPL=0.3ng/ml) for Chloramphenicol (CAP). Nestlé has evaluated the method and achieved a fast (< 2 hours) and reliable extraction of CAP from various kinds of milk.



**Figure 5.**  
MS detection of CAP (XIC of -MRM (3 pairs): 321.0/152.0 amu) from Honey sample spiked with 0.3ng/mL. Detection limit well below MRPL. Methods for extraction of CAP from milk, urine and honey are available.

**SupelMIP SPE phase v.s. hydrophilic polymer SPE phase**

The conventional hydrophilic polymer method needed an extensive sample pre-treatment involving a protein precipitation step, an SPE cleanup procedure, and three LLE steps<sup>(2)</sup>. The SupelMIP method only required a simple sample pre-treatment followed by a single SPE cleanup step.



**Figure 6.**  
Signal/noise ratio for the hydrophilic polymer SPE method is double that of the SupelMIP ion-chromatograms (320-323 m/z range). Blank milk samples processed using the SupelMIP were free of interfering responses in the elution area of chloramphenicol.<sup>(3)</sup>

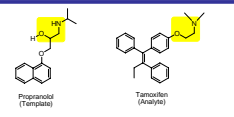
## Cross-reactivity of MIPs

MIPs may be thought of as artificial antibodies or receptors. The origin of the MIP selective binding is then key recognition elements placed in sterically locked positions. MIPs can be tailor-made with specific configurations of the recognition elements; the exact complementarity of site definition will result in different extents of cross-reactivity that can be utilized.

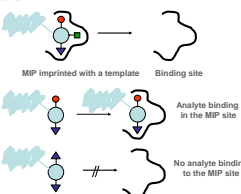
MIPs may sometimes recognize molecules that differ significantly from the template molecule used for imprinting, as exemplified in the literature: Martin et al<sup>(4)</sup> imprinted the beta antagonist propranolol and found that the MIP also bound tamoxifen, a compound used in the treatment of breast cancer (Figure 7). A further example can be found in reference 5.

This notion of 'sub-site based selectivity' is analogous to the concept of 'pharmacophores' in medicinal chemistry, where different molecules may have the same receptor function provided they exhibit the required pharmacophore features (see Figure 8). A growing library of MIP materials has now been developed and will be utilized for selective screening of extraction materials.

Using this concept selective separation of compound classes and larger molecules such as peptide and proteins is possible, for analytical, preparative and process scale applications.



**Figure 7.** Template and bound molecule in the work of Martin et al.<sup>1</sup>



**Figure 8.** The pharmacophore concept applied to MIP materials. The recognition elements placed in sterically locked positions enhance the selectivity of the binding site.

## List of References

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## Conclusion

The origin of MIP selective binding is key recognition elements placed in sterically locked positions.

MIPs are well suited for removal of contaminants from complex matrices and even in the presence of a mixture of potentially interfering matrix components. Examples of Beta agonists, Beta blockers, Nicotin metabolites and Chloramphenicol extractions are shown. The SupelMIP gives clean extracts and significantly reduces the total sample handling time. Due to the stability of the MIP material highly selective extractions are possible both for analytical applications and large scale extractions.

## Features of MIPs

- Simple and rapid sample preparation
- Low detection and quantification limits
- High reproducibility and repeatability
- Minimized ion suppression
- Lower risk of false positives
- Robust material

More information at  
[www.miptechnologies.com](http://www.miptechnologies.com) or  
[www.sigmaaldrich.com/supelmip](http://www.sigmaaldrich.com/supelmip)