

Summary

Molecularly imprinted polymers (MIP) are perceived to have several shortcomings such as heterogeneous binding site, template occlusion, and difficulties in template recovery and in upscaling for commercial exploitation. This thesis describes the development of novel methods to overcome these drawbacks, combining surface imprinting on nanoparticles with Reversible Addition Fragmentation chain Transfer polymerization (RAFT) to prepare well-defined MIP composites.

The first part of this thesis describes the use of R-immobilized RAFT technique from silica core to generate tunable core-shell structured cross-linked MIP nanoparticles for chiral discrimination. Before creating the cross-linked polymers, the grafting of linear polymers from RAFT modified silica nanoparticles was optimized. Imprinted copolymers of methacrylic acid (MAA) and ethyleneglycol dimethacrylate (EGDMA) were grafted from the supports in presence of L-phenylalanine anilide (L-PA) as chiral template. The relatively low ABDV/CPDB ratio reduced the amount of free polymer derived from the initiator and yet maintained a moderate polymerization rate. Silica nanoparticles with two different sizes, ca 20 nm and ca 200 nm, were used as a support material to investigate the effect of core size in binding properties of MIP particles. The resulting beads were subsequently characterised by FTIR, TEM, SEM, DLS, TGA and elemental analysis. In binding tests using reversed phase HPLC, the imprinted nanoparticles exhibited a much-higher binding affinity for the template molecule than the non-imprinted particles. In addition, the imprinted nanoparticles were able to discriminate the template L-PA and its optical antipode D-PA. Furthermore, core-shell particles with smaller core size displayed a higher binding affinity than those with larger cores.

In the second part of this thesis, the previously established, optimized synthesis route for core-shell nanoparticles imprinted with L-PA was applied in a solid-phase synthesis approach to prepare molecularly imprinted core-shell nanoparticles (MIPNPs) in template free form towards L-phenylalanine (L-Phe) immobilized on magnetic placeholder templates. The latter was achieved by grafting poly (MAA-co-EDMA) on RAFT-modified silica nanoparticles. To the best of my knowledge, this thesis presents the first artificial receptor that has successfully been produced using magnetic placeholder templates. All the materials were characterized using elemental microanalysis, FT-IR, TGA, SEM, TEM and DLS. In order to evaluate the

binding properties, the particles were subsequently tested for their affinity towards the template L-PA and D-PA in acetonitrile. The results demonstrated that the MIPNPs prepared via this method had highly accessible binding sites and good discrimination towards the template L-PA and D-PA.

The third part of this thesis illustrates engineering of epitope imprinted core-shell nanoparticles towards beta-amyloid template. The “epitope imprinting” consists of using only a short and exposed peptide sequences as a surrogate template for the whole protein. Beta-amyloid contains a pool of peptidic fragments in varying length, which are important biomarkers involved in the pathology of Alzheimer’s disease. With the aim of developing polymeric complements to one of these biomarkers, the peptide A β ₃₇₋₄₂ was used as template to generate an artificial receptor. The MIPs were prepared in organic media by using diarylurea as comonomer, ethyl ammonium methacrylate as a functional monomer and divinylbenzene as a crosslinker. The adsorption capacity of the resulting MIPs was examined by reversed phase HPLC.

The last part of this thesis had the aim to develop an artificial receptor for the human immunoglobulin G (IgG). The decapeptide fragment (T10) from the C-terminus of its heavy chain was used as template. Epitope imprinted nanoparticles were prepared by grafting of poly-(methacrylic acid-co-methacrylamide-co-ethylbisacrylamide) and/or poly-(bisphosphonic acid-co-methacrylamide-co-ethylbisacrylamide) in presence of the T10 template from a RAFT modified colloidal silica core. The resultant MIPs were characterised by FT-IR, TEM, TGA and elemental analysis. The polymers were examined by equilibrium rebinding for their affinity towards the template T10 in aqueous media by reversed phase HPLC. For polymers prepared in organic media, the resulting imprinted and nonimprinted particles revealed a similar adsorption capacity towards T10 template. When the synthesis was performed in aqueous media, the imprinted particles displayed a higher adsorption capacity than the nonimprinted particles. Compared to polymer grafted using the bisphosphonic acid monomer, polymer obtained via methacrylic acid as functional monomer showed better imprinting performance. Our results provide a new potential for peptide and protein imprinting in aqueous media using SI-RAFT technique and it might also be transferred to epitopes of other proteins. We believe that such synthetic MIP nanoparticles are highly promising alternatives to biological receptors with great potential in many analytical applications and other areas.