World Academy of Science, Engineering and Technology
International Journal of Pharmacological and Pharmaceutical Sciences
Vol:3, No:6, 2009

Development of Molecular Imprinted Polymers (MIPs) for the Selective Removal of Carbamazepine from Aqueous Solution

Bianca Schweiger, Lucile Bahnweg, Barbara Palm, and Ute Steinfeld

***Abstract*—**The occurrence and removal of trace organic contaminants in the aquatic environment has become a focus of environmental concern. For the selective removal of carbamazepine from loaded waters molecularly imprinted polymers (MIPs) were synthesized with carbamazepine as template. Parameters varied were the type of monomer, crosslinker, and porogen, the ratio of starting materials, and the synthesis temperature. Best results were obtained with a template to crosslinker ratio of 1:20, toluene as porogen, and methacrylic acid (MAA) as monomer. MIPs were then capable to recover carbamazepine by 93% from a 10^{-5} M landfill leachate solution containing also caffeine and salicylic acid. By comparison, carbamazepine recoveries of 75% were achieved using a non-imprinted polymer (NIP) synthesized under the same conditions, but without template. In landfill leachate containing solutions carbamazepine was adsorbed by 93-96% compared with an uptake of 73% by activated carbon. The best solvent for desorption was acetonitrile, with which the amount of solvent necessary and dilution with water was tested. Selected MIPs were tested for their reusability and showed good results for at least five cycles. Adsorption isotherms were prepared with carbamazepine solutions in the concentration range of 0.01 M to $5*10^{-6}$ M. The heterogeneity index showed a more homogenous binding site distribution.

***Keywords*—**Carbamazepine, landfill leachate, removal, reuse

I. Introduction

MANY pharmaceutical compounds and metabolites are often not eliminated by common waste water treatment plants and are detectable in the aquatic environment, in rivers, lakes, ground- and drinking water [1], [2] due to their high persistence and low biodegradability. Possible removal strategies for such and other organic compounds include ozonation of drinking water [3] and of sewage [4], advanced oxidation processes such as O_3/H_2O_2, O_3/UV, H_2O_2/UV, Fe/H_2O_2, and TiO_2/hν [5]-[9], and electric discharge processes [10]-[12]. Sorption processes such as activated carbon and oxidative processes were shown to be effective, but their efficiency on trace concentrations depends on the competition with other occurring organic constituents [13], [14]. Treatment with UV/H_2O_2 and TiO_2 requires large exposure time compared to ozonation and may be hindered by the presence of natural organic matter, which may deactivate catalysts by adsorption and adsorbs UV-light [8]. Toxic or mutagenic and carcinogenic degradation products may occur [9]. A more effective removal strategy might be the selective extraction of hard to degrade trace constituents.

Molecular imprinted polymers (MIPs) are crosslinked polymers, which are synthesized in the presence of template molecules. Crosslinking monomers enclose the prepolymerisation complex formed by functional monomers and template molecules. After polymerization the template is removed leaving cavities, which own the geometrical and binding properties of the template. Template or analogous molecules can rebind selectively in these cavities. Due to their high selectivity, mechanical strength, resistance against acids, bases, organic solvents, and high pressures and temperatures, MIPs were developed for extensive applications such as solid phase extraction (SPE), chromatography, enzymatic catalysis, and sensor technology [15].

In this study MIPs were developed for the effective removal of carbamazepine (CA) from aqueous solutions and landfill leachate. The antiepileptic drug carbamazepine is metabolized in the body by 70%-98%, but the unchanged carbamazepine is not removed by waste water treatment plants [1], [16]. Maximum concentrations of 11 nM [1] and 27 nM [16] were found for sewage treatment effluents in Germany. It has been detected at concentrations of 5 nM in rivers, streams, and groundwater [1], [17] and with maximum concentrations of 22 nM in landfill leachate [18]. In drinking water it was found with a concentration below 1 nM [17].

The predicted environmental concentration (PEC) to predicted no-effect concentration (PNEC) ratio is an indicator, if a substance may cause adverse effects on the ecosystem. PEC/PNEC ratios for carbamazepine were greater than one for effluents of sewage treatment plants in five European countries, so carbamazepine may have ecotoxicological effects on the aquatic ecosystem, if effluents are discharged without dilution [18].

To obtain a stable imprinted polymer with high selectivity, parameters varied were the type of monomer, crosslinker, and porogen, the ratio of starting materials, and the synthesis temperature. The synthesized MIPs and their corresponding

B. Schweiger, L. Bahnweg, and B. Palm are with the KIST Europe Forschungsgesellschaft mbH, Campus E 7.1, D-66123 Saarbruecken, Germany.

U. Steinfeld is with the KIST Europe Forschungsgesellschaft mbH, Campus E 7.1, D-66123 Saarbruecken, Germany (phone: +49-681-9382-220; fax: +49-681-9382-249; e-mail: steinfeld@kist-europe.de).

non-imprinted polymers (NIPs) were tested for their ability to remove carbamazepine from aqueous solutions. The results were compared with the sorption abilities of activated carbon. To obtain a more complex solution, landfill leachate solutions were also tested. The reusability of promising MIPs was investigated. It is intended, that for the removal of carbamazepine from the polymer only a small amount of solvent is necessary compared to the amount of loaded water, from which the compound is to be removed. The removed carbamazepine in concentrated solution may then be degraded by one of the methods mentioned above.

II. Materials and Methods

A. Chemicals

All fine chemicals, methacrylic acid (MAA), 4-vinylpyridine (4VP), ethylenglycoldimethacrylate (EGDMA), toluene, azobisisobutyronitrile (AIBN), carbamazepine, caffeine, salicylic acid, ethanol, acetonitrile, aceton, methanol (HPLC reagent), and acetic acid (100%) (HPLC reagent) were purchased from the companies Aldrich, Merck or Fluka and ultra pure water (Milli-Q water, Millipore, Billerica, MA, USA) was used. The unsaturated compounds MAA, 4-VP, and EGDMA were distilled under reduced pressure to liberate them from the stabilizer (hydroquinone monomethyl ether).

B. Synthesis

The template molecule carbamazepine was mixed in a 50 mL glass tube with functional monomers and cross-linkers in the selected solvent (porogen). The associated NIPs were synthesized analogously, but without carbamazepine. The initial quantities of the reactants are summarized in Table I. The mixture was put in a vortex shaker and outgassed with nitrogen for five min. After adding AIBN, the mixture was shaken again until complete dissolution. After the solution was purged with nitrogen for another five min, the tube was immediately sealed and heated in an oil bath for 24 h at 60 °C. The obtained polymer blocks were ground in a mortar to a fine powder. The template was removed from the imprinted polymers in a Soxhlet extraction apparatus with ethanol for 24 h at 120 °C. After washing with ethyl acetate, ethanol, and distilled water, the polymer was dried for 12 h at 60 °C. NIPs were prepared in the same way.

C. HPLC-Analysis

The chemical analysis was performed by HPLC using an Agilent 1100 Series HPLC system with a diode array detector. A Reprosil Pur 120 C18-AQ column with 3 µm particle size was used for the analysis of carbamazepine, caffeine, and salicylic acid. The mobile phase consisted of methanol and water/acetic acid (400:5). The mixing of solvents was 15:85 at 0 min, 65:35 at 15 min, and 15:85 at 32 min with a flow rate of 0.2 mL min^{-1} and a temperature of 25 °C. The injection volume was 50 µL. Carbamazepine and salicylic acid were detected at 242 nm, caffeine at 275 nm.

D. Landfill leachate

Landfill leachate was taken at the landfill site of the Entsorgungsverband Saar in Ormesheim, Germany, after biological treatment and downstream ultra filtration.

TABLE I
SYNTHESIS PARAMETERS

MIP	Template	Monomers		Crosslinker	Porogen		Initiator	Ratio	T (°C)
	CA (mmol)	MAA	4VP	EGDMA	type	volume (ml)	AIBN (mg)	T-M-C	
CA1	1	1		1	ethanol	12	100	1:8:20	60
CA2	1	1		1	acetonitrile	12	100	1:8:20	60
CA3	1	1		1	toluene	12	100	1:8:20	60
CA4	1		1	1	ethanol	12	100	1:8:20	60
CA5	1		1	1	acetonitrile	12	100	1:8:20	60
CA6	1		1	1	toluene	12	100	1:8:20	60
CA7	1			1	ethanol	12	100	1:0:20	60
CA8	1			1	toluene	12	100	1:0:20	60
CA9	1	2		1	ethanol	12	100	1:15:20	60
CA10	1	1		1.5	ethanol	12	100	1:8:30	60
CA11	1	0.63		1.5	ethanol	12	100	1:5:30	60
CA12	1	1		2	ethanol	12	100	1:8:40	60
CA3*	1	1		1	toluene	12	100	1:8:20	70
CA3**	1	1		1	toluene	12	100	1:8:20	50

E. Batch rebinding experiments

100 mg amount of polymer particles were shaken for 15 min and centrifuged for 10 min at 4000 rpm in 50 mL vials with 10 mL of a 0.01 mM aqueous solution of carbamazepine, salicylic acid, and caffeine. A sample was pipetted from the supernatant and centrifuged for another 10 min at 16000 rpm in a microcentrifuge. A final sample was taken from the supernatant to determine the concentration by HPLC. The washing step with distilled water for the removal of by-products and the desorption step for removal of carbamazepine with a solvent were performed in the same way. The difference of concentration before and after sorption is used to calculate the sorbed amount of carbamazepine or sorption in percent.

F. Desorption tests

100 mg MIP were suspended in 10 mL of 0.01 mM aqueous solution of carbamazepine, salicylic acid, and caffeine, washed with distilled water, and desorbed with 5 mL of acetone, acetonitrile, or ethanol. Tests with acetonitrile diluted with water in different ratios were also performed

G. Reusability tests

100 mg MIP were repeatedly suspended in 10 mL of 0.01 mM aqueous solution of carbamazepine, salicylic acid, and caffeine, washed with distilled water, and desorbed with 2 mL of an acetonitrile-water solution (1:1). Each time the samples were shaken for 15 min. The amount of carbamazepine in the supernatant was determined by HPLC.

H. Adsorption isotherms

100 mg of MIP CA3, CA9, and CA10 were suspended in aqueous solutions with carbamazepine concentrations in the range of 0.01 M to $5*10^{-6}$ M and shaken for 15 min. The amount of carbamazepine in the supernatant was determined by HPLC.

Freundlich-Model (Eq. (1)) was used to describe the adsorption isotherms.

Freundlich: $$q = A \cdot x^n \quad (1)$$

Where: q: adsorption capacity (µmol/g polymer), A and n: adsorption coefficients.

III. Results and Discussion

A. Ratios and selectivity

Ethanol, acetonitrile, and toluene were used as porogens with CA1 – 3 (MAA as monomer) and CA4 – 6 (4VP as monomer) with a ratio of template : monomer : crosslinker of 1:8:20 (Fig. 1). The uptake of carbamazepine was 88% with ethanol and 96% with acetonitrile and toluene for MAA as monomer and 96% for all three solvents with 4VP as monomer. The selectivity of MIPs with MAA as monomer is higher, because there is no sorption of salicylic acid compared to MIPs synthesized with 4VP as monomer. The aromatic system of 4VP may interact stronger with the aromatic analogue molecules than MAA. The corresponding NIPs showed the same results (Fig. 2). This might be due to the presence of weak interactions in the specific binding cavities and predominant non-specific binding between carbamazepine and polymer. The ratio between template, monomer, and crosslinker was varied with CA9 – CA12. The more cross-linker is used for a constant amount of monomer, the higher is the sorption of carbamazepine until a T:C ratio of 1:30 (CA10). For a constant amount of crosslinker the limit of increasing sorption is reached for a ratio of 1:15:20.

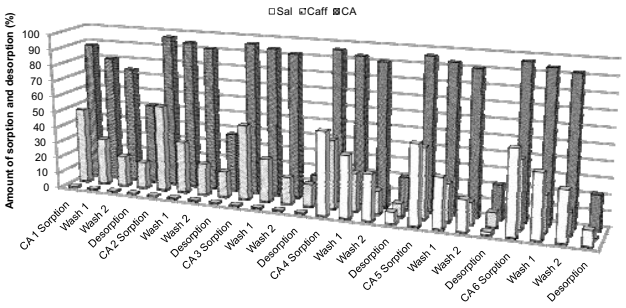

Fig. 1 Adsorption of carbamazepine (CA), caffeine (Caff), and salicylic acid (Sal) from a 10^{-5} M aqueous solution on MIP CA1 – CA6.

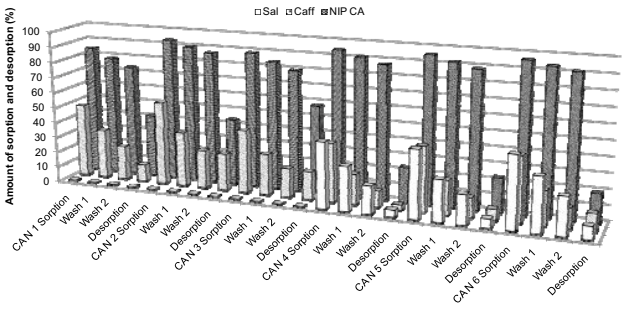

Fig. 2 Adsorption of carbamazepine (CA), caffeine (Caff), and salicylic acid (Sal) from a 10^{-5} M aqueous solution on NIP CA 1 – CA 6.

B. Landfill leachate

To simulate real conditions, carbamazepine, caffeine, and salicylic acid were dissolved in landfill leachate (all 10^{-5} M). Sorption of CA1, CA3, CA6, and CA10 was tested (Fig. 3). The uptake of carbamazepine from landfill leachate solutions was between 68% (CA1) and 96% (CA6). This is a decrease of 20% for CA1, 10% for CA10, and no obvious decrease for CA3 and CA6 compared with sorption results for distilled water. The selectivity is higher in landfill leachate solutions than in distilled water. Sorption of caffeine decreased by 16% for CA1, 27% for CA3, 10% for CA6, and 10% for CA10 compared with solutions made with distilled water. Salicylic acid was not sorbed or in only small amounts by MIPs synthesized with MAA. CA6, which was prepared with 4VP, showed a decreased sorption for salicylic acid by 27% and at the same time a still high sorption of carbamazepine of 96%.

Comparison of CA1 and CA10 shows the influence of different ratios. The sorption is better for CA10 with a T:C ratio of 1:30. Comparison of CA3 with CA1 shows the influence of the porogen. With toluene (CA3) as porogen sorption of carbamazepine and the selectivity is higher.

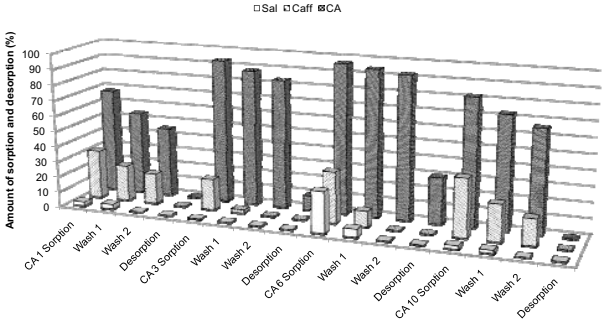

Fig. 3 Adsorption of carbamazepine (CA), caffeine (Caff), and salicylic acid (Sal) from a 10^{-5} M landfill leachate solution on MIP CA1, CA3, CA6, and CA10.

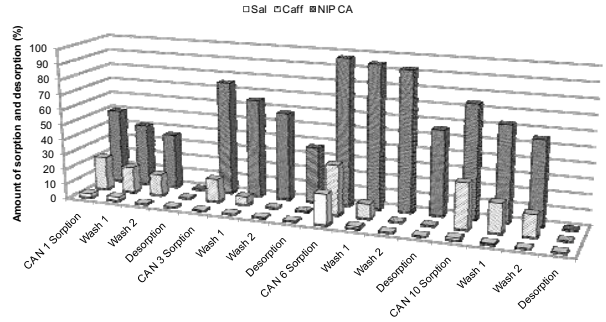

Fig. 4 Adsorption of carbamazepine (CA), caffeine (Caff), and salicylic acid (Sal) from a 10^{-5} M landfill leachate solution on NIP CAN1, CAN3, CAN6, and CAN10.

Besides CAN6, the corresponding NIPs show a decrease in sorption between 8 and 18% for carbamazepine and between 5 and 9% for caffeine (Fig. 4). CA1, CA3, and CA10 were prepared with MAA as monomer, whereas CA6 was prepared with 4VP. With MAA as monomer, a difference in the uptake of carbamazepine between MIPs and NIPs was observed, which could be an indicator for an imprinting effect. The developed MIP are able to adsorb carbamazepine selectively and with a high uptake even in a complex solution such as landfill leachate.

C. *Pre-polymerization complex*

To find out if a prepolymerisation complex between MAA and carbamazepine is necessary for the overall binding affinity, MIPs were synthesized without MAA and with ethanol and toluene as porogens (Fig. 5). With ethanol as porogen (CA7), sorption of carbamazepine decreases by three times compared to the sorption of MIP synthesized with MAA (CA1) (Fig. 1). With toluene as porogen (CA8), sorption stays comparable to the sorption of MIP synthesized with MAA (CA3) (Fig. 1). This could be due to structural arrangements of the polymer in the aromatic solvent, which provides favorable binding sites for carbamazepine. With ethanol as porogen the carboxylic groups of MAA are necessary for a high binding affinity.

The influence of different temperatures during synthesis, 50 °C, 60 °C, and 70 °C, on the MIP properties was tested, because it could have an influence on the formation of the pre-polymerization complex. A modification of the binding cavities should result in a modification of the selectivity. With a higher temperature polymerization is possibly faster, so that binding cavities are less specific and the selectivity is lower. Different temperatures showed no influence on the uptake of carbamazepine (about 95%) for the three temperatures. There was no uptake of salicylic acid. The sorption of caffeine decreased with increasing temperature from 64% (50 °C) to 34% (70 °C). The corresponding NIPs showed a lower selectivity for caffeine with an uptake of 88% at 50 °C and 53% at 70 °C.

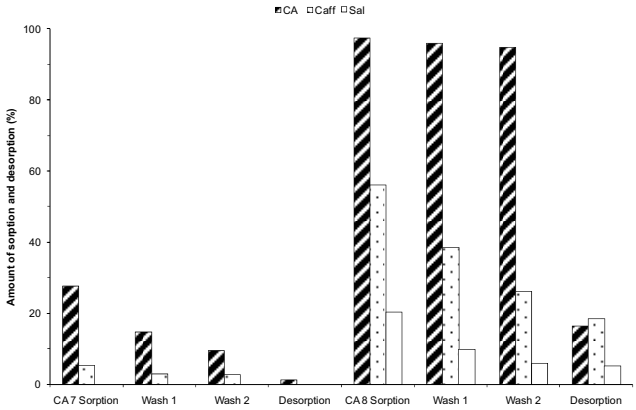

Fig. 5 Adsorption of carbamazepine (CA), caffeine (Caff), and salicylic acid (Sal) from a 10^{-5} M aqueous solution on MIP CA7 and CA8.

D. *Comparison with activated carbon*

Sorption and selectivity of MIPs was compared with the sorption and selectivity of activated carbon with solutions of carbamazepine, caffeine, and salicylic acid in distilled water and in landfill leachate (Fig. 6). Activated carbon showed a high uptake (>96%) in distilled water for all three compounds, and thus a low selectivity, but a low desorption for caffeine and salicylic acid and a desorption for carbamazepine comparable with some MIPs (CA1, CA2, CA12). In landfill leachate, the uptake of carbamazepine by activated carbon is still high (between 73% and 83%) (Fig. 6), but not as good as with CA3 (93%) and CA6 (96%) (Fig. 3), and the selectivity is low. Washing steps with distilled water decrease the sorption of caffeine and salicylic acid in MIPs, but not with activated carbon. The corresponding NIPs showed a lower sorption between 8% (CA3) and 18% (CA1, CA10) for carbamazepine. The effect of imprinting is observable in the different results between MIPs and NIPs.

CA1, CA3, and CA10 were made with MAA as monomer. The NIP of CA6, which was made with 4VP, showed a decrease in sorption only for salicylic acid. The overall performance of MIPs in distilled water is better than that of activated carbon concerning selectivity, while the uptake of carbamazepine is equal. In landfill leachate the uptake and the selectivity of selected MIPs is higher than of activated carbon,

which might be due to the uptake of other compounds present in landfill leachate by activated carbon.

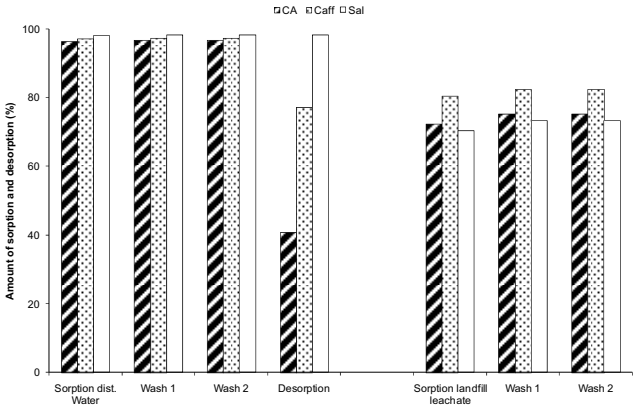

Fig. 6 Adsorption of carbamazepine (CA), caffeine (Caff), and salicylic acid (Sal) (all 10^{-5} M) from an aqueous and a landfill leachate solution on activated carbon.

E. Desorption

Desorption of the three compounds for removal and further treatment of carbamazepine and regeneration of the MIPs was tested with 5 mL of acetone, ethanol, and acetonitrile (CA10). With acetone, carbamazepine was removed after the second washing step to 85% (overall 87%), with ethanol to 73% (overall 77%), and with acetonitrile to 100%. Caffeine was removed after washing to 58% (overall 81%), with ethanol to 0% (overall 53%), and with acetonitrile to 69% (overall 88%). Salicylic acid was not sorbed by CA10. Because complete removal of carbamazepine was reached with acetonitrile and to minimize solvent consumption, desorption was also tested with a reduced amount of acetonitrile of 2 mL. Carbamazepine was removed after the second washing step to 99% and caffeine to 50%. Overall removal including washing steps was 99% for carbamazepine and 81% for caffeine. That means, removal efficiency with 2 mL is comparable to removal with 5 mL. Desorption efficiency was also tested with different acetonitrile to water ratios (1:0, 1:1, 0.75:1.25, 0.6:0.4, 0.3: 1.7) to reduce consumption of acetonitrile. With increasing water ratios removal of carbamazepine decreased from 100% (no water) to 10% (0.3:1.7). While with a ratio of 1:1, a removal of 90% is reached, all other tested ratios lay below 50%.

F. Reuse experiments

CA3, CA8, CA9, and CA10 were tested for their reusability in terms of stability and potential regeneration. Figure 7 shows results for five adsorption cycles. All four MIPs can be reused after desorption with 2 mL of an aqueous acetonitrile solution (1:1) and are stable without an obvious decrease in adsorption capacity for carbamazepine for at least five sorption-desorption-cycles. The amount of sorption was 97-94% for CA3, 98-95% for CA8, 92-87% for CA9, and 82-78% for CA10.

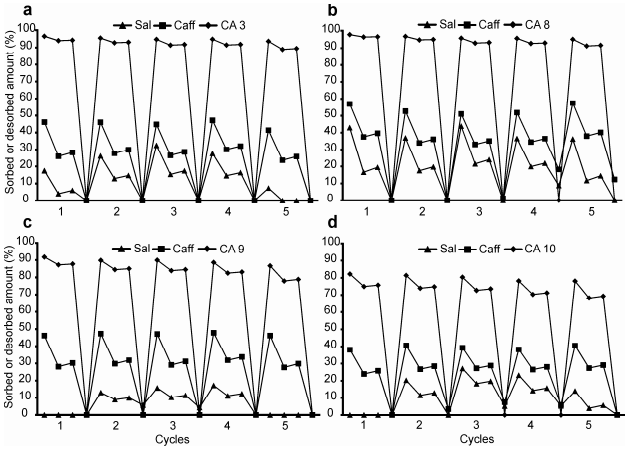

Fig. 7 Reuse cycles of MIPs (a) CA3, (b) CA8, (c) CA9, (d) CA10. Each cycle consists of a sorption step, two washing steps, and a desorption step.

G. Adsorption isotherms

The adsorption capacity can be described by adsorption isotherms. Figure 8 shows Freundlich adsorption isotherms of CA3, CA8, CA9, and CA10.

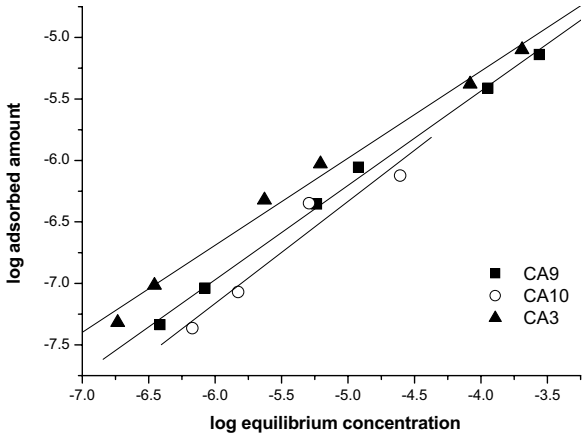

Fig. 8 Freundlich sorption isotherms of carbamazepine on MIP CA3, CA9, and CA10.

Adsorption coefficients are given in Table II. The adsorption coefficient A is a measure of affinity and average capacity, whereas n is the heterogeneity index.

TABLE II
FREUNDLICH PARAMETERS

MIP	A (μg g^{-1})(L $μg^{-1}$)	n	R^2
CA3	10.0	0.71	0.99
CA9	3.8	0.77	0.99
CA10	1.7	0.83	0.96

Values for n are near one, which shows a more homogenous binding site distribution than a heterogeneous one.

IV. Conclusions

Molecularly imprinted polymers for the selective extraction of carbamazepine from aqueous solutions were synthesized by bulk polymerization with MAA or 4VP as monomers and EGDMA as crosslinker. Selectivity and adsorption ability of the obtained MIP were very high for carbamazepine. Selectivity was higher when MAA was used as monomer. With toluene (CA3) as porogen, sorption of carbamazepine and the selectivity was higher. Synthesis temperature influenced the selectivity with regard to caffeine, which was less adsorbed by polymers synthesized at higher temperatures. The uptake of carbamazepine from landfill leachate solutions was between 68% (CA1) and 96% (CA6). The selectivity was higher in landfill leachate solutions than in distilled water. In comparison with activated carbon, MIPs showed a higher selectivity and in landfill leachate solutions a higher uptake of carbamazepine. In landfill leachate, carbamazepine competed with other constituents for uptake by activated carbon. The best desorption results were obtained with acetonitrile. 2 mL of acetonitrile diluted 1:1 with water were sufficient for good desorption results obtained with an adsorption solution volume of 10 mL. Selected MIPs were tested for reusability and showed no obvious decrease in adsorption capacity for carbamazepine.

The use of MIPs for the removal of specific compounds from loaded waters is advantageous compared with the use of activated carbon, which removes also other, often harmless, compounds [14]. Spent activated carbon is mostly regenerated by thermal regeneration, which has a high energy demand, because the temperature must be kept above 1100 K. Usually 5-15% of carbon are lost by wash-out and burn-off. For this treatment also a special treatment facility is needed which produces additional costs [20]. On the other hand, MIPs are regenerated with a solvent without loss of material or adsorption capacities. Concentrated desorption solutions containing mainly the target molecule can then be treated efficiently.

References

[1] T. A. Ternes, "Occurrence of drugs in German sewage treatment plants and rivers," *Water Res.*, vol. 32, pp. 3245-3260, Nov. 1998.

[2] T. A. Ternes, M. Bonerz, T. J. Schmidt, 2001. "Determination of neutral pharmaceuticals in wastewater and rivers by liquid chromatography–electrospray tandem mass spectrometry," *J. Chromatogr. A*, vol. 938, pp. 175-185, Dec. 2001.

[3] T. A. Ternes, J. Stüber, N. Herrmann, D. McDowell, A. Ried, M. Kampmann, B. Teiser, "Ozonation: A tool for removal of pharmaceutical contrast media and musk fragrances from wastewater?," *Water Res.*, vol. 37, pp. 1976-1982, Apr. 2003.

[4] H. Zhang, H. Yamada, S.-E. Kim, H.-S. Kim, H. Tsuno, "Removal of endocrine disrupting chemicals by ozonation in sewage treatment," *Water Sci. Technol.*, Vol. 54, pp. 123-132, 2006.

[5] C. Zwiener, F. H. Frimmel, "Oxidative treatment of pharmaceuticals in water," *Water Res.*, vol. 34, pp. 1881-1885, Apr. 2000.

[6] R. Andreozzi,V. Caprio, R. Marotta, A. Radovnikovic, "Ozonation and H_2O_2/UV treatment of clofibric acid in water: A kinetic investigation," *J. Hazard. Mater.*, vol. 103, pp. 233-246, Oct. 2003.

[7] D. Vogna, R. Marotta, R. Andreozzi, A. Napolitano, M. d'Ischia, "Kinetic and chemical assessment of the UV/H_2O_2 treatment of antiepileptic drug carbamazepine" *Chemosphere*, vol. 54, pp. 497-505, Jan. 2004.

[8] T. E. Doll, F. H. Frimmel, "Photocatalytic degradation of carbamazepine, clofibric acid and iomeprol with P25 and Hombikat UV100 in the presence of natural organic matter (NOM) and other organic water constituents," *Water Res.*, vol. 39, pp. 403-411, Jan.-Feb. 2005.

[9] S. Esplugas, D. M. Bila, L. G. T. Krause, M. Dezotti, "Ozonation and advanced oxidation technologies to remove endocrine disrupting chemicals (EDCs) and pharmaceuticals and personal care products (PPCPs) in water effluents," *J. Hazard. Mater.*, vol. 149, pp. 631-642, Nov. 2007.

[10] B. R. Locke, M. Sato, P. Sunka, M. R. Hoffmann, J.-S. Chang, "Electrohydraulic discharge and nonthermal plasma for water treatment," *Ind. Eng. Chem. Res.*, vol. 45, pp. 882-905, Feb. 2006.

[11] H. Krause, B. Schweiger, J. Schuhmacher, S. Scholl, U. Steinfeld, "Degradation of the endocrine disrupting chemicals (EDCs) carbamazepine, clofibric acid, and iopromide by corona discharge over water," Chemosphere, vol. 75, pp. 163-168, Apr. 2009.

[12] Y. Zhang, J. Zheng, X. Qu, H. Chen, "Design of a novel non-equilibrium plasma-based water treatment reactor," Chemosphere, vol. 70, pp. 1518–1524, Feb. 2008.

[13] T. A. Ternes, M. Meisenheimer, D. McDowell, F. Sacher, H.-J. Brauch, B. Haist-Gulde, G. Preuss, U. Wilme, N. Zulei-Seibert, "Removal of Pharmaceuticals during Drinking Water Treatment," *Environ. Sci. and Technol.*, vol. 36, pp. 3855-3863, Sept. 2002.

[14] M. Le Noir, A.-S. Lepeuple, B. Guieysse, B. Mattiasson, "Selective removal of 17*β*-estradiol at trace concentration using a molecularly imprinted polymer," *Water Res.*, vol. 41, pp. 2825-2831, June 2007.

[15] A. J. Hall, M. Emgenbroich, B. Sellergren, "Imprinted polymers," in *Top. Curr. Chem.*, vol. 249, pp. 317-349, Springer-Verlag Berlin Heidelberg, 2005.

[16] W. Schüssler, M. Sengl, "Arzneimittel in der Umwelt (Pharmaceuticals in the environment)," Materialien Nr. 114, Bayerisches Landesamt für Wasserwirtschaft, Germany, Aug. 2004.

[17] T. Heberer, "Occurrence, fate, and removal of pharmaceutical residues in the aquatic environment: a review of recent research data," Toxicol. Lett., vol. 131, pp. 5–17, May 2002.

[18] J. W. Metzger, „Drugs in municipal landfills and landfill leachate," In: Kümmerer, K. (Ed.). *Pharmaceuticals in the Environment: Sources, Fate, Effects and Risks*, Springer, Berlin, 2004, pp. 133-137.

[19] B. Ferrari, N. Paxéus, R. Lo Giudice, A. Pollio, J. Garrica, "Ecotoxicological impact of pharmaceuticals found in treated wastewaters: study of carbamazepine, clofibric acid, and diclofenac," *Ecotoxicol. Environ. Saf.*, vol. 55, pp. 359–370, July 2003.

[20] P. M. Álvarez, F. J. Beltrán, V. Gómez-Serrano, J. Jaramillo, E. M. Rodríguez, "Comparison between thermal and ozone regenerations of spent activated carbon exhausted with phenol," Water Res., vol. 38, pp. 2155-2165, Apr. 2004.