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Roza Bouchal,[a†] Ivana Miletto,[b†] Ut Dong Thach,[a] Bénédicte Prelot,[a] Gloria Berlier*[c] and Peter Hesemann*[a]

Mesoporous ionosilicas bearing ammonium groups appear as versatile adsorbent for anionic drugs. High amounts of the anionic drugs diclofenac and sulindac are irreversibly trapped within the materials whereas neutral species are hardly adsorbed. Our results open the route towards new ionic materials for wastewater treatment *via* ion exchange.

Introduction

A large volume of pharmaceuticals is used for the prevention, diagnosis and treatment of diseases in humans and animals. In industrialized countries, the average annual consumption of pharmaceuticals is estimated to be between 50 and 150 g per capita. Most pharmaceuticals are not completely degraded after application. As a result, pharmaceutical metabolites and some unchanged forms of these compounds are excreted and subsequently enter the ecosystem.[1] For this reason, efficient methods for the removal of drugs and their metabolites from wastewater and effluents are required. Non-steroidal anti-inflammatory drugs (NSAID) are among the most abused drugs in developed countries; among them, diclofenac (DCF) and sulindac (SUL, figure 1) are widely used to reduce inflammation and to relieve pain, working as an analgesic in conditions such as in arthritis or acute injury. The annual consumption of both drugs is of several hundreds of tons per year (diclofenac: approx. 900 tons[2]). Diclofenac and its metabolites are among the most frequently detected pharmaceutical residues in water bodies thus far.[3] After oral administration, these drugs are eliminated in rather short periods. For example, the elimination half life of diclofenac in the human body is of about 2 h. Approximately 65% of the dosage is excreted through urine in which six diclofenac metabolites have been identified, in particular partially oxidized species.[4] The efficient sequestration of drugs and their metabolites from wastewater is still a challenge.

Silica based materials are well established and widely used for separation processes and the sequestration of pollutants.[5] Mesoporous silica such as HMS[6] and SBA-15[7] were used for the adsorption of pharmaceuticals such as carbamazepine, diclofenac and ibuprofen.[8, 9]

The surface functionalization of nanostructured silica mesophases allows accessing a large variety of tailor made materials for the separation of both organic and inorganic pollutants. Functionalized silica-based materials containing trimethysilyl,[10] aminopropyl[11, 12] and mercaptopropyl groups[8] display enhanced adsorption capacities for pharmaceuticals. In the field of organic/inorganic hybrid materials, ion exchange involving silica based materials containing ionic groups appear as an interesting way for the sequestration of charged species, in particular of oxo-anions such as arsenate, chromate, perrhenate or pertechnetate.[13-18] Here, we investigated ionosilicas as efficient adsorbing materials for anionic drugs. Ionosilicas are defined as silica hybrid materials containing covalently bound ionic species and recently emerged as interesting functional materials for several applications in catalysis and separation.[15, 19, 20] Ionosilicas combine high porosity, regular architecture on the mesoscopic level with an unmatched chemical versatility, induced by the high variability and the high number of incorporated ionic species. In our recent work, we focused on the formation of structured ionosilicas via bottom-up approaches using ionic precursors.[21-23] This strategy allowed accessing a large variety of porous silica hybrid materials containing different types of ionic groups and displaying various textures. Here, we report that ionosilicas are efficient adsorbents for the sequestration of drugs from aqueous solutions. We used an ammonium type ionosilica (figure 2) for adsorption experiments of the anionic drugs diclofenac and sulindac.

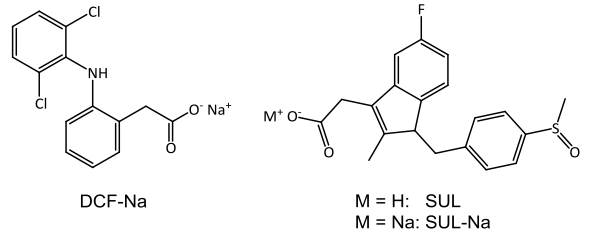

Figure 1. Structures of the drugs used in the present study

Materials and methods

Chemicals

Diclofenac sodium salt (98%) and Sulindac (99.5%) were purchased from abcr GmbH & Co. KG (Karlsruhe, Germany); the water used for loading and release test was deionized water from Millipore apparatus; all the other reagents and solvents were from Sigma Aldrich (Milan, Italy and Lyon, France) and were used as received unless otherwise specified. Sodium salt of sulindac (**SUL-Na**) was prepared by dissolving sulindac in its acidic form with sodium hydroxide at 1:1 molar ratio ($5.25\ 10^{-4}$ mol) in 40 ml of deionized water during 15h at room temperature. The ionosilica material **A** the silica material type MCM41 were synthesized following previously reported procedures[21, 24]

Methods

UV-Vis absorption spectra were acquired with a Cary5000 UV-Vis-NIR spectrophotometer (Varian Inc., California USA) in the transmission mode. The UV-Vis analyses were performed at a wavelength of 276 nm for diclofenac and of 330 nm for sulindac.

Photoemission steady-state spectra were acquired using a Fluorolog3 spectrofluorimeter (Horiba, Milan, Italy) equipped with a 450 W Xenon lamp and a Hamamatsu R928 photomultiplier. The spectral response was corrected for the

spectral sensitivity of the photomultiplier. In order to evaluate the content of drug in the low concentration loading experiments, calibration curves were prepared in a concentration range from $1 \cdot 10^{-6}$ M down to $1 \cdot 10^{-9}$ M.

Thermal gravimetric analyses (TGA) were carried out on a TAQ600 apparatus (TA instruments, Milan, Italy) by heating the samples, after equilibration, from 30 to 1000°C at a rate of 10°C/min in air.

FT-IR spectra were recorded on a Vertex70 spectrophotometer (Bruker, Milan, Italy) equipped with MCT detector and working at 2 cm^{-1} resolution over 64 scans. Samples of ionosilica and drug/ionosilica complexes were in form of self-supporting pellets suitable for transmission IR experiments and placed in a quartz cell equipped with KBr windows and designed for RT studies in vacuum and in controlled atmosphere. Before analysis the samples were outgassed at RT to remove physically adsorbed water. FT-IR spectra of diclofenac sodium salt, sulindac and sulindac sodium salt were collected in the ATR (Attenuated Total Reflection) mode by using a single reflection diamond ATR accessory (Platinum ATR accessory by Bruker).

Liquid NMR analyses (^{1}H and ^{13}C) were performed using a Bruker 300 NMR spectrometer. Deuterated methanol was used as solvent. Chemical shifts are expressed in parts per million (ppm) relative to tetramethylsilane.

Solid state ^{13}C CP MAS NMR experiments were recorded on a Varian VNMRS 300 MHz solid spectrometer using a two channel probe with 7.5 mm or 3.2 mm ZrO_2 rotors. The ^{29}Si solid state NMR spectra were recorded using One Pulse (OP) sequences with samples spinning at 6 kHz. For these experiments, π/6 pulse and 60 s recycling delay were used to obtain quantitative information on the silane–silanol condensation degree. The ^{13}C CP MAS spectra were obtained using 3 ms contact time, 5 s recycling delay and 5 kHz spinning rate. The number of scans was in the range 1000–3000 for ^{29}Si OP MAS spectra and of 2000–4000 for ^{13}C CP MAS spectra.

Gas-volumetric analysis (N_2 adsorption-desorption isotherms at liquid nitrogen temperature) was employed to measure specific surface area (SSA), pore volume and pore size with an ASAP 2020 physisorption analyzer (Micromeritics, Norcross, GA, USA). SSA was calculated by the Brunauer-Emmett-Teller method (BET); pore volume and average pore size were estimated using the Barrett-Joyner-Halenda method with the Kruk-Jaroniec-Sayari equation (BJH/KJS). All calculations were performed on the adsorption branch of the isotherm. Prior to analyses, the samples were outgassed overnight at 110°C.

Loading of anionic drugs on ionosilica material. Drug loading experiments were carried out in deionized water (**DCF-Na** and **SUL-Na**) or in ethanol (**SUL**). The drugs were dissolved in the proper solvent at 0.03M concentration and desired amount of material **A** was added to the solution in order to obtain a drug:ionosilica molar ratio of 1.1 : 1. The resulting suspensions were stirred at RT for 24 h, then the solid material was recovered by filtration and dried in vacuum at 60°C, resulting in the **A-DCF-Na/HC**, **A-SUL-Na/HC** and **A-SUL** samples. In the case of **DCF-Na**, loading experiments from low concentration solutions were carried out. For this purpose, material **A** was suspended in a $1.2 \cdot 10^{-5}$ M solution of **DCF-Na** at a drug:ionosilica molar ratio of 1:6000. The resulting suspension was then stirred for 24h at RT, then the loaded sample was recovered by filtration and drying under vacuum at 60°C. The samples prepared through this procedure are addressed to as **A-DCF-Na/LC**.

Release Tests. Diclofenac release studies were performed in vitro using deionized water (pH=6.5) and hydrocloric acid solution (pH=3) as releases medium. In one type of experiment, a dispersion of 3 ml containing 5 mg of loaded material (**DCF-Na/HC**) was incubated at room temperature without stirring. Several aliquots of the same dispersions were prepared for independent analysis and samples of the supernatant were withdrawn at prefixed time (15', 30', 1, 2, 3, 4, 6…..32h). In another type of experiment, a pellet of 26 mg of the loaded sample was prepared and kept in 13 ml of deionized water under statistic condition at room temperature. The supernatant was removed and replaced by the same quantity of deionized water after prefixed time. The release was monitored by UV-visible spectroscopy by analyzing the supernatant to determine the drug content.

Results and discussion

Materials synthesis

We used an ammonium type ionosilica for the separation experiments. The material **A** (figure 2a) was synthesized following published procedures by hydrolysis-polycondensation reactions from the corresponding *tris*-trimethoxysilylated ammonium iodide precursor **1** in the presence of anionic surfactant.[21, 24] This strategy allows obtaining nanostructured ammonium based ionosilica materials with regular pore architectures as shown in figure 2b. After elimination of the surfactant by repeated washing with ethanolic hydrochloric acid, we obtained an ionosilica containing ammonium chloride entites. The X-ray diffractogram (ESI figure S1-a) of the material **A** shows the (100), (110) and (200) reflections, indicating 2D hexagonal architecture. Nitrogen sorption experiment (ESI, figure S1-b) confirms that the material is highly porous (S_{BET} = 1038 m^2/g) and shows relatively high pore volume (0.55 cm^3/g). BJH analysis of the adsorption branch of the isotherm indicates narrow pore size distribution centered at 2 nm (ESI figure S2).

Adsorption experiments with diclofenac and sulindac

Here, the potential of porous ammonium hybrid ionosilica for the adsorption of the anionic drugs diclofenac and sulindac was evaluated. Diclofenac is usually supplied and used in pharmaceutical formulations as potassium or sodium salt, whereas sulindac is usually commercialized in its acidic form. We therefore used commercial diclofenac sodium salt (**DCF-Na**) and sulindac (**SUL**); The sodium salt of sulindac was prepared (**SUL-Na**) by overnight treatment of the acidic form of sulindac in sodium hydroxide solution (figure 1).

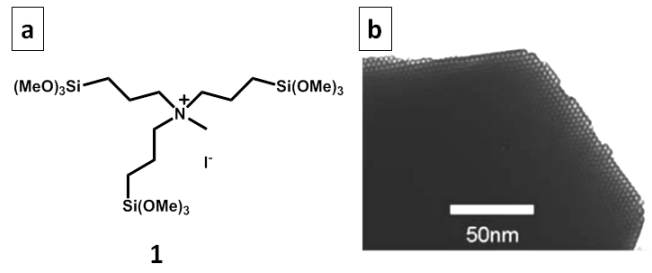

Figure 2. (a) Ammonium precursor **1** used for the preparation of ionosilica **A**; (b) HRTEM image of an ionosilica material displaying regular pore architecture, from reference [21]

The adsorption ability of the ionosilica material **A** was monitored towards **DCF-Na**, **SUL-Na** and **SUL**. All drugs were employed to test their adsorption from high concentration solutions (0.03M) at a molar drug-ionosilica ratio of 1.1 : 1, resulting in the **A-DCF-Na/HC**, **A-SUL-Na/HC** and **A-SUL** samples. In the case of diclofenac **DCF-Na**, experiments were also carried out using a diluted drug solution (3.82 $\mu g \cdot ml^{-1}$ / $1.2 \cdot 10^{-5}$ M) at a 1:6000 drug-ionosilica wt.-ratio in order to study the ability to adsorb traces of the drug, more realistic for real environmental waters (sample **A-DCF-Na/LC**). Furthermore, the loading was repeated on this sample in order to test the re-usability of the ionosilica as drug adsorbent. The corresponding ionosilica loaded samples were labeled as **HC** when prepared from high concentration solutions, and **LC** when prepared from low concentration ones.

For the drug adsorption experiments, the drugs were dissolved in a suitable solvent (deionized water in the case of **DCF-Na** and **SUL-Na** and ethanol in the case of **SUL**). Then, the ionosilica material was added to the solution. After 24 h stirring at room temperature, the suspensions were filtered and the solids were recovered and dried under vacuum at room temperature overnight. The adsorption of the drugs within the ionosilica material was qualitatively monitored *via* FT-IR and solid state NMR spectroscopies. The quantification of the loading within the ionosilica material was assessed *via* TGA measurements and UV-Vis absorption and emission spectroscopies of the supernatant**.**

FT IR spectroscopy was used to get a first information about the adsorbing process of the drugs. Figure 3 show the FTIR spectra of **DCF-Na**, measured in ATR mode, and of the ionosilica material **A** before and after loading with **DCF-Na**. The FT-IR spectrum of DCF-Na is discussed more in detail in the supporting information (ESI figure S3). The spectra were measured in transmission mode on self-supported pellets except **DCF-Na**, **Sul-Na** and **SUL** which was recorded in the ATR mode. Although the infrared spectrum of the **A-DCF-Na/HC** sample (figure 3, orange curve) is dominated, in the high frequencies range, by the signals of the ionosilica material (broad absorption due to OH groups involved in hydrogen bonding and CH stretching modes), the signals due to the drug are visible (absorption bands at 3073/3029 cm^{-1}). However, the characteristic absorption bands of the drug are more clearly visible in the low frequency range of the spectrum (absorption band at 1574 cm^{-1}).[25-27] Moreover, the broad absorption due to hydrogen-bonding interactions of ionosilica decreases on sample **A-DCF-Na/HC**, thus testifying the involvement of surface groups with the drug. On the contrary, in the case of the **A-DCF-Na/LC** sample (figure 3, pink curve), the drug content is too low to generate visible changes in the spectrum of the parent ionosilica material. It is clear that after interaction with the ionosilica material, diclofenac molecules remain in the carboxylate form, as indicated by the presence of signals at 1574 and 1369 cm^{-1}, which can be attributed to antisymmetric and symmetric stretching of the carboxylate group.[28] The slight shift of the lower frequency carboxylate peak observed in the drug/ionosilica complex with respect to the spectrum of the drug itself can be related to a modified interaction between the carboxylate ion and the cationic moiety of the ionosilica. To conclude the IR spectroscopic characterization of the solids, signals characteri- stic for diclofenac are clearly visible only in the high loaded sample **A-DCF-Na/HC**. The adsorbed diclofenac quantity is too low to be detected in the material **A-DCF-Na/LC** *via* FT-IR spectroscopy.

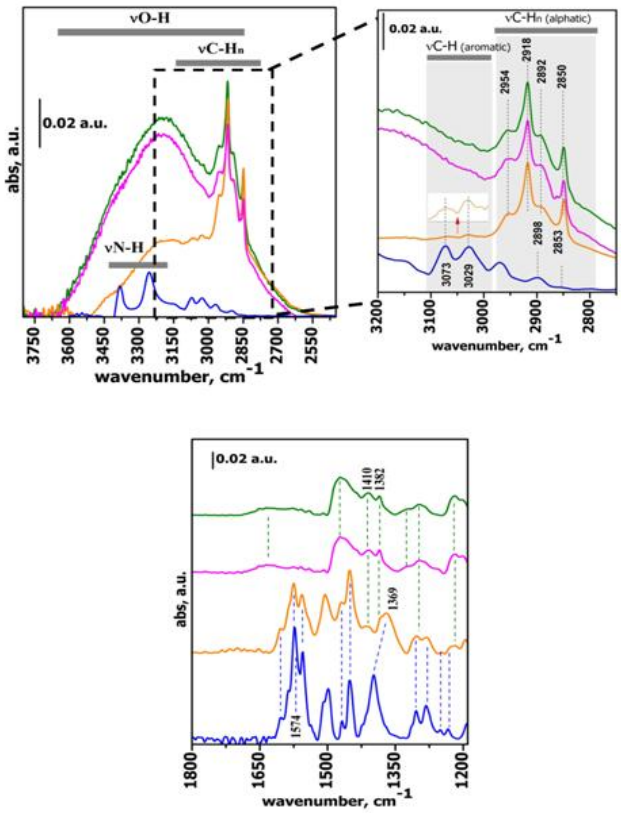

Figure 3. FT-IR spectra of DCF-Na (blue curve), ionosilica material (green curve) and drug/ionosilica complexes DCF-Na/HC (orange curve) and DCF-Na/LC (pink curve). Spectra in lower panel are vertically translated for the sake of clarity.

The adsorption of the sodium salt of sulindac **SUL-Na**, monitored via FT-IR spectroscopy, gave similar results (ESI figure S4). The FT-IR spectrum of the material **A-SUL-Na/HC** shows both the signals characteristic for the ionosilica material A and the drug in its salt form. In contrast, the spectrum of the material **A-SUL/HC**, obtained from the neutral form of sulindac, gives no indication for sulindac adsorption (ESI figure S4). This is a clear indication for a selective adsorption of anionic

compounds, whereas neutral compounds are not adsorbed by the ionosilica material.

The characterization of the pure ionosilica and the DCF loaded samples *via* **solid state NMR spectroscopy** confirms these results. Whereas the ^{29}Si OP-MAS NMR spectra of the loaded sample **A-DCF-Na/HC** (ESI figure S5) do not show noticeable differences compared to the spectrum of the parent material **A**,[21] significant changes can be observed in the ^{13}C CP-MAS NMR spectra of the parent ionosilica material **A** and the diclofenac loaded sample **A-DCF-Na/HC** (figure 4). The spectrum of the pure ionosilica **A** shows the three signals of the propyl linkers and the signal relative to the methyl group directly attached to the nitrogen atom. The spectrum of the DCF-loaded sample shows, additionally to the signals of the ionosilica material, a set of intense peaks characteristic for the DCF anions, in particular in the aromatic region (110-150 ppm). Furthermore, in nice agreement to the ^{13}C NMR spectrum of diclofenac in solution (ESI figure S6), the signals at 45 ppm and 179 ppm can be assigned to the methylene and the carboxylate group of the drug molecule, respectively. The high intensity of the signals characteristic of the diclofenac anions, in particular in the aromatic region, indicates a high loading of the ionosilica material and, accordingly, a high adsorption efficiency of the ionosilica towards diclofenac. However, it is not possible to quantify the amount of adsorbed diclofenac from the ^{13}C CP-MAS NMR spectrum. The ^{13}C CP-MAS NMR spectrum and ^{29}Si OP-MAS NMR spectra of the sulindac loaded sample **A-SUL-Na/HC,** given in the ESI (figures S7, S8, S9), give similar information.

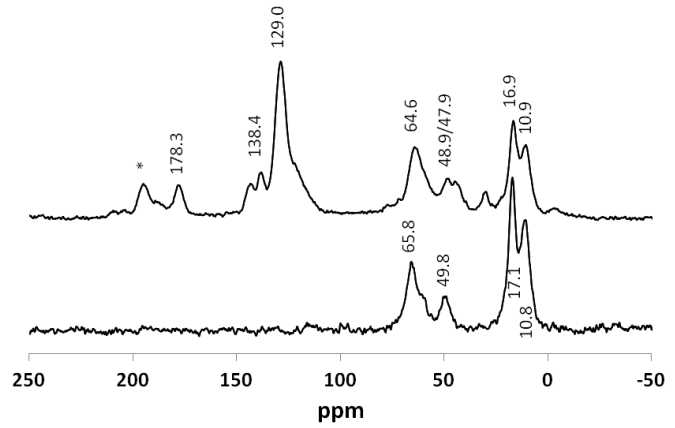

Figure 4. Solid state ^{13}C CP-MAS NMR spectra of the parent ionosilica material A (lower) and the diclofenac loaded material DCF-Na/HC (upper); spinning side band is marked by an asterisk.

After having ascertained qualitatively that the drugs were adsorbed onto the ionosilica material, we were interested to quantify the amount of adsorbed drug. The adsorption capacity and the encapsulation efficiency µ of the material were calculated by thermogravimetric analysis of the loaded ionosilica samples and by analysis of the supernatant after the loading *via* UV-Vis spectroscopy.

The **TGA thermograms** under air of the parent ionosilica material **A** and the loaded samples after adsorption with **A-DCF-Na/HC**, **A-SUL-Na/HC** and **A-SUL/HC** are given in figure 5. The thermogram of the pure ionosilica material **A** indicates that the material is stable up to ca. 180°C. The slight weight loss below 180°C can be ascribed to the desorption of physically adsorbed water. The chemical decomposition of the material starts at 200°C and ends at ca. 700°C. The product of this thermal decomposition is pure silica. For the pure material **A**, we observed a weight loss of 54.7%, which is slightly higher than the expected theoretical value (48.1%). This higher weight loss can be explained by incomplete condensation and the presence of silanol groups within the material after the hydrolysis polycondensation procedure, resulting in additional elimination of water during the calcination process. Regarding the thermograms of the samples loaded with the anionic drugs **A-DCF-Na/HC** and **A-SUL-Na/HC**, we observed a significantly higher mass loss of 73.7% and 72.5%, respectively. This increase is due to the adsorption of considerable amounts of the anionic drugs. In fact, the maximal mass loss we can expect for complete anion exchange reaction is of 74.2% and 76.6% for the materials **A-DCF-Na/HC** and **A-SUL-Na/HC**, respectively. Taking into account the elimination of the organo-ionic group together with the anionic drug during the calcinations, we can estimate the amount of adsorbed drug to be of 90% in the case of **DCF-Na** and of 68% in the case of **SUL-Na** (table 1, entries 1 and 2). The experimentally obtained values indicate once more that the ionosilica material adsorbs relatively high amounts of the anionic drugs **DCF-Na** and **SUL-Na**. In contrast, the thermogram of the sample **A-SUL/HC**, obtained from an adsorption of the neutral **SUL** compound, is similar to the original ionosilica material, thus indicating that sulindac in its neutral form is hardly adsorbed by the ionosilica material. This result is of considerable interest as it clearly indicates that the ionosilica material selectively adsorbs anionic species, whereas neutral compounds are not adsorbed. We can therefore conclude that the adsorption of drugs is driven by anion exchange.

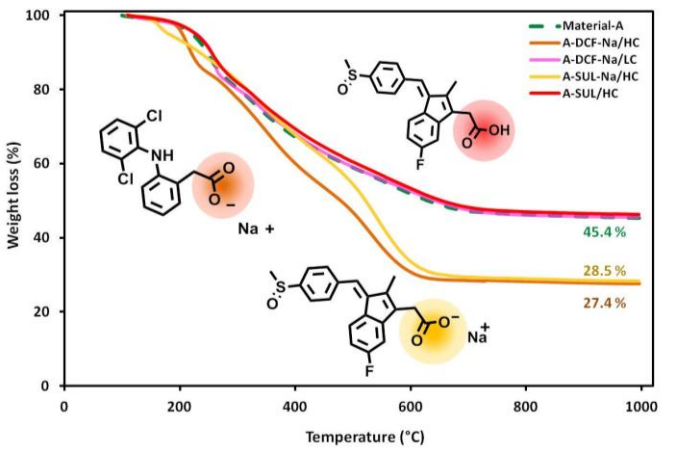

Figure 5. Thermogravimetric analysis: ionosilica material (green dashed curve), drug/ionosilica complexes DCF-Na/HC (orange curve), DCF-Na/LC1 (pink curve), SUL-Na/HC (yellow curve) and SUL/HC (red curve).

In the case of the material **A-DCF-Na/LC**, obtained by contacting the ionosilica material **A** with a solution containing a considerably lower DCF concentration (*vide supra*), the thermogram shows a similar shape and similar weight loss compared to the parent material **A**. This result can be explained

by the low quantity of the adsorbed diclofenac, which is too low to be detected *via* TGA.

Finally, the adsorption of the anionic drugs was addressed *via* **UV-Vis spectroscopic** analysis of the supernatant after the loading procedure. All these results are reported in table 1, together with the results of the thermogravimetric analyses.
In order to determine the saturation limit of the ionosilica, the material was firstly contacted with a high amount of the anionic drugs diclofenac and sulindac. As previously described, a 30 mL of a 0.03 M solution of **DCF-Na** and sulindac **SUL-Na** (corresponding to a quantity of 0.9 mmol of diclofenac /sulindac) was treated with 0.3 g of the ionosilica. This quantity of the material **A** contains approx. 0.86 mmol of immobilized ammonium entities. Hence, the used anionic drugs were used in slight excess related to the amount of cationic sites in the ionosilica material **A**. The characterization of the supernatant solutions after contacting with the material **A** showed that both diclofenac and sulindac, in their sodium salt form, are efficiently adsorbed by the ionosilica material. The upper saturation limit of material **A** for the adsorption of diclofenac and sulindac are 2.55 mmol/g and 1.59 mmol/g corresponding to 88% and 65% for **A-DCF-Na/HC** and **A-SUL-Na/HC**, respectively (table 1, entries 1/2). Furthermore, we found that the neutral form of sulindac is not adsorbed by the ionosilica material **A**, thus confirming the results obtained by TGA (table 1, entry 3). Once more, these results confirm that the separation process is driven by anion exchange. However, it has to be mentioned that the adsorption process, carried out in aqueous media, led to a complete collapse of the mesopore architecture of the material. As already described above, material **A** is a material displaying mesoporosity (average pore diameter: ca. 2 nm, specific surface area: > 1000 m^2/g). After adsorption of **DCF-Na**, the resulting material **A-DCF-Na/HC** displayed considerably lower specific surface area and, in particular, no mesoporosity (ESI figures S10). The collapse of the mesopore architecture can be explained by rearrangements *via* reversible siloxane (Si-O-Si) opening and closing reactions.
Furthermore, to get an idea about the adsorption of **DCF-Na** on pure silica and the contribution of the ionic entities of ionosilica material, we performed the adsorption of **DCF-Na** on MCM-41 mesoporous silica.[29] Similarly to the experiments involving the ionosilica material **A**, the adsorption capacity of MCM-41 was quantified using UV-Vis spectroscopic analysis of the supernatant after contacting (ESI table S1) and thermogravimetric analysis (ESI figure S11). These analyses indicated an adsorption capacity of 0.16 mmol/g (UV-Vis analysis) and 0.09 mmol/g (TGA), respectively, and show that pure silica absorbs diclofenac in a very low extent compared to the ionosilica material **A**. These results are in agreement with those of Bui *et al.* concerning the adsorption of diclofenac on SBA-15 mesoporous silica.[9] These authors observed an even lower adsorption capacity of < 0.01 mmol/g. It clearly appears that the presence of cationic sites in the ionosilica material framework is essential to obtain high adsorption capacities towards anionic drugs.

Finally, the uptake ability of the ionosilica material **A** was studied with highly diluted drug solutions. These studies are of particular importance as low concentrations of pollutants are more similar to real conditions in waste water bodies. For this purpose, the material was contacted twice with a $1.2 \cdot 10^{-5}$ M aqueous solution of **DCF-Na**, thus yielding the materials **DCF-Na/LC$_1$** (after the first contact) and **DCF-Na/LC$_2$** (after the second contact) Both procedures, involving the same material, led to an almost complete adsorption of the anionic drug onto the material (table 1, entries 4/5). These results indicate the high affinity of the anionic drugs towards the ionosilicas and indicate that the material can be used as efficient anion trap even for low concentrations of pollutants. The material is therefore highly interesting for applications under real environmental conditions. As in the experiences involving solutions containing high drug concentrations, the adsorption of traces of anionic drugs led to a material displaying low porosity and no mesoporous contribution. The decrease of specific surface area after the adsorption process is therefore independent of the quantity of adsorbed drug, but is related to rearrangement reactions of the material in aqueous solution. However, even after the collapse of the mesopore structure, the material is still able to adsorb drug, as shown by the second diclofenac adsorption in the case of the **DCF-Na/LC$_2$** sample.

Table 1. Encapsulation efficiency (μ) and the adsorption capacity (mmol/g) of the prepared samples measured by different techniques

entry	Samples	UV/Vis Supernatant analysis [a]		Thermogavimetric analysis [b]
		Q (mmol/g) [c]	μ (%) [d]	μ (%)
1	**A-DCF-Na/HC**	2.55	88	90
2	**A-SUL-Na/HC**	1.59	65	68
3	**A-SUL/HC**	0	0	0
4	**A-DCF-Na/LC$_1$**	n.d.	98	-
5	**A-DCF-Na/LC$_2$** [e]	n.d.	99	-

[a] analysis was carried out by UV-Vis absorption spectroscopy in the case of HC samples and by UV-Vis emission spectroscopy in the case of LC samples

[b] The encapsulation efficiency μ estimated by TGA was determined by the mass ratio as a percentage of anionic drug after loading and of chloride before loading compared to the mass molar ratio of the two compounds

[c] Q = (mole of loaded drug / weight of the material)

[d] % $\mu = (C_{init} - C_{final})/C_{init}$, where C_{init} is the initial diclofenac concentration, while C_{final} is the diclofenac concentration after 24 h exchange with the material.

[e] **DCF-Na/LC$_2$** was prepared by loading procedure using a low concentrated DCF-Na solution on **DCF-Na/LC$_1$** sample

Release tests

In a last set of experiences, the release of the drugs from the ionosilica material was addressed. In this way, the material was

characterized with regard to its adsorption/release performances and recyclability. The stability of the drug/ionosilica complex was verified by release test, which was carried out with the **A-DCF-Na/HC** sample using distilled water as solvent medium. The release was monitored over 32 h via UV-Vis absorption spectroscopies assessing that less than 3% of the loaded drug was released from the different complexes (ESI figure S12 and S13). Release tests carried out in acidic media (hydrochloric acid, pH=3) with the same sample **A-DCF-Na/HC** gave similar results, thus proving the high stability of the drug-ionosilica system. These results can be both explained by the high affinity of the anionic drug towards the ionosilica material, and the trapping of the anionic compound within the material, *i.e.* the irreversible capture of the drug *via* the collapse of the mesoporous architecture of the adsorbent material.

Conclusions

We demonstrated that nanostructured cationic ionosilicas bearing quaternary ammonium groups are efficient and re-usable adsorbents with high capacity and high selectivity for the adsorption of anionic drugs. In adsorption experiments with diclofenac, the materials show capacities up to 2.55 mmol/g, corresponding to ca. 750 mg of drug per gram of material. However, the capacity of the material depends on the nature of the studied adsorbent: the smaller and more hydrophilic sodium diclofenac **DCF-Na** is adsorbed in higher extent compared to the bigger and more hydrophobic sodium-sulindac **SUL-Na**. The ionosilica is a highly efficient adsorbent even for traces of anionic drugs, thus highlighting the high affinity of these compounds towards the material. In contrast, no adsorption was observed using the drugs in the acidic, neutral form. Finally, the high affinity of anionic species towards the ionosilica material was also monitored via drug release tests involving loaded samples. No significant release was observed after contacting the sample during 32h both with water or hydrochloric acid (pH=3). However, it has to be mentioned that these treatments led to a complete collapse of the pore structure of the material, and a completely non-porous material was recovered after these tests.

In conclusion, we report that ammonium based ionosilicas are high capacity adsorbing phases for anionic drugs. Our findings may open the route towards more efficient anion adsorbing materials which may find wide applications in wastewater treatment. Acknowledgements

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