

INORGANIC/ORGANIC CORE-SHELL MAGNETIC MATERIALS FOR REMOVAL OF ENDOCRINE DISRUPTING PHARMACEUTICALS FROM WATER

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Abstract

The presence of pharmaceutical substances in aqueous effluents represents one of the major concerns in environmental protection, as most of them present a profound endocrine disrupting character. The present study evaluates the use of organic/inorganic core-shell magnetic composites for the removal of two types of endocrine disrupting pharmaceutical substances. The results presented show a good affinity of the nickel ferrite/chitosan composite towards the adsorption of Na naproxen (89% at 48 h), while the best results for the adsorption of diltiazem HCl were obtained for the copper ferrite/chitosan composite (56% at 48 h); in the same time, the magnetic properties of the composites allow the easy removal of the adsorbents from the aqueous effluents.

Rezumat

Prezența substanțelor farmaceutice în efluenții apoși reprezintă una dintre preocupările majore în domeniul protecției mediului, deoarece majoritatea prezintă un efect puternic de perturbare endocrină. Prezentul studiu evaluează utilizarea compozitelor magnetice *core-shell* organice/anorganice pentru îndepărtarea a două tipuri de substanțe farmaceutice care afectează sistemul endocrin. Rezultatele obținute prezintă o bună afinitate a compozitului de ferită de nichel/chitosan pentru adsorbția naproxenului sodic (89% la 48 ore), în timp ce rezultate superioare pentru adsorbția clorhidratului de diltiazem au fost obținute pentru compozitul de ferită de cupru/chitosan (56% 48 h); în același timp, proprietățile magnetice ale compozitelor permit îndepărtarea ușoară a adsorbanților din efluenții apoși.

Keywords: composite; core-shell magnetic materials; adsorption; endocrine disrupting pharmaceuticals

Introduction

Good-quality potable water represents one of the key elements regarding our present world's sustainable development. Life without safe drinking water would be if not impossible, at least very difficult to imagine [1]. Even though tremendous improvements were accomplished in the last decades regarding environmental protection in general and water sources protection in particular, we all must be aware that practically every industrial process that contributes to our modern way of life leads to the release in the environment of huge quantities of pollutants.

Among the pollutants, endocrine disrupting chemicals are of particular interest due to their action that can lead to the development of a series of very serious conditions and even death [2]. Generally speaking,

endocrine disrupting chemicals (EDC) represent compounds that can alter the functioning of the endocrine system. From the large class of EDCs, the pharmaceuticals and personal care products (PPCP) represents one of the main concerns, due to their potential harmful effects on the wildlife and on human health, even at the low concentration at which they are usually found in water. Their presence can usually be correlated with the increase of population density and the insufficient wastewater treatments. Several studies present the widespread of such compounds in the water sources, all over the world, as well as their potential harmful effects [1-6].

The pharmaceutical EDCs selected for the present study are presented by literature data as having endocrine disrupting potential: naproxen (2-(6-methoxynaphthalen-2-yl)propanoic acid) and its salt

((S)-6-Methoxy- α -methyl-2-naphthaleneacetic acid sodium salt) represents a widely used non-steroidal anti-inflammatory drug, associated with hormonal side-effects [7], while diltiazem ([[(2S,3S)-5-[2-(dimethylamino)ethyl]-2-(4-methoxyphenyl)-4-oxo-2,3-dihydro-1,5-benzothiazepin-3-yl] acetate) represents a non-dihydropyridine calcium channel blocker, with endocrine disrupting potential [8].

For the removal of pharmaceutical EDCs, several expensive and difficult to implement strategies can be applied (such as the use of activated carbon, catalytic ozonation, etc.), but their success is limited [9].

We propose an alternative method for the removal of pharmaceutical EDCs from wastewater, by using magnetic inorganic/organic core-shell materials. They have the advantage of facile utilization and separation from the water matrices, as well as good removal efficiency. The synthesized materials were characterized in terms of structure (X-ray Diffraction, X-ray Fluorescence, Thermal analyses), morphology (Transmission electron microscopy), magnetic properties and removal efficiency (using High-performance liquid chromatography).

Materials and Methods

Adsorbent materials

The core-shell adsorbents used for the study were obtained by adding a chitosan shell over two different types of magnetic cores: copper and nickel ferrite. The ferrites were synthesized *via* a co-precipitation method [10] from $\text{CuSO}_4 \times 5 \text{ H}_2\text{O}$ and $\text{Fe}_2(\text{SO}_4)_3 \times 5 \text{ H}_2\text{O}$ (Merck KGaA, Germany) (in a molar ratio Cu:Fe = 1:2) dissolved in 200 mL distilled water. Under vigorous mechanical stirring, the pH was slowly raised to 11 by adding drop-wise NaOH solution (Chimreactiv, Romania) and continued stirring. The synthesis was conducted at a temperature of 70°C, for six hours. After cooling, the precipitate was washed ten times with bi-distilled water and dried at 90°C for 24 h. Subsequently, the obtained material was calcined in air at 600°C for four hours. For the synthesis of nickel ferrite, a similar method was followed using $\text{NiSO}_4 \times 7 \text{ H}_2\text{O}$ (Merck KGaA, Germany) as nickel source and a 700°C calcination temperature.

For the obtaining of the core-shell materials, the surface of magnetic materials was coated with a solution of chitosan (CS, Sigma Aldrich, USA, deacetylation degree 86%) [11]. Typically, 0.25 g of previously obtained magnetic materials (copper or nickel ferrite) were dispersed in a CTAB solution (4 grams of CTAB - Fisher Scientific, USA - dissolved in 800 mL of distilled water), thus obtaining Solution A. Then, 200 mL chitosan solution (0.04 grams CS powder dissolved in 200 mL of 1% (w/v) acetic acid solution) was slowly dropped into Solution A. The mixture was thoroughly stirred for 4 h at

room temperature. At the end of the synthesis process, the core-shell materials were magnetically separated from the solution, thoroughly washed several times with ethanol and distilled water and dried at 60°C for 24 hours. The final composites were kept in formaldehyde vapours to obtain the crosslinking of the chitosan [12].

Pharmaceutical substances

Naproxen sodium (CAS Number 26159-34-2), 98 - 102% and diltiazem hydrochloride (CAS Number 33286-22-5) represents commercial available substances (Sigma-Aldrich, USA).

Analytical methods

The thermal analyses were performed with a TGA Q5000 (TA) instrument, at a heating rate of 10°C per minute, in a temperature interval 24 - 900°C.

X-ray fluorescence (XRF) analyses were performed using a PW4025 MiniPal2 PANalytical EDXRF Spectrometer. The determinations were carried out in helium atmosphere, for 300 s, at a voltage of 20 kV and automatic current intensity; for the construction of the sample cups, a 3.6 μm Mylar film was used.

X-ray diffraction (XRD) data were obtained using a Rigaku SmartLab diffractometer using $\text{CuK}\alpha$ radiation ($\lambda = 1.54059 \text{ \AA}$) operating at 40 kV and 200 mA, in parallel beam configuration. Powder diffraction patterns were obtained in continuous mode, $2\theta = 15 - 90$ degrees. For the analysis of the obtained diffractograms, the PDXL Program was used.

The magnetization *versus* magnetic field strength investigations at room temperature were performed on a Lake Shore's fully integrated Vibrating Sample Magnetometer system 7404. The equipment was used to record magnetic data at room temperature, using nitrogen gas, in variable magnetic field [0 - 21,700] Oe, with the following parameters: resolution of magnetization: $0.1 \times 10^{-6} \text{ emu}$; step control of applied magnetic field: 70 mOe; moment stability: better than $\pm 0.05\%$ of full scale/day for fixed coil, constant field and temperature; resolution of magnetic field intensity: 3 ppm resolution; standard procedures for periodical calibration based on NIST standards (SRM 772a, SRM 762, SRM 2853) [13].

The transmission electron microscopy (TEM) images have been registered with HRTEM – High Resolution Transmission Electron Microscope type TECNAI F30 G2STWIN at 300 kV acceleration voltage. The resolution of the microscope was 1 $\text{\AA}$.

The HPLC analysis of the selected compounds was carried out using a Waters liquid chromatographic system (Waters, Milford, MA, USA), equipped with a 600 E Multisolvant Delivery System, Waters AF in line degasser, 2487 Dual Absorbance Detector and Waters 717 plus autosampler. Data acquisition and processing were performed using Empower Pro software (Waters, Milford, MA, USA).

The chromatographic separation was achieved on a Hypersil Gold, 5 μm 150 $\times$ 4 mm column (Thermo

Fisher Scientific, Waltham, MA, USA), maintained under constant temperature (30°C). The mobile phase consisted of an isocratic mixture of 0.1% trifluoroacetic acid:acetonitrile (50:50 v/v), delivered at 1.0 mL/min flow rate [14]. The injection volume was 10 µL. The eluent was monitored at 260 nm (naproxen) and 236 nm (diltiazem). All solutions were filtered through a 0.45 µm pore size nylon filter.

The linearity assessment for each compound was performed in the range 12.5 - 200 µg/mL, using five concentration levels. All analyses were performed in triplicate. Calibration curves and corresponding determination coefficients (R^2) were calculated by least squares linear regression analysis [15].

Adsorption experiments

For the adsorption experiments, the batch technique was applied. A typical experiment was conducted by weighing 0.02 g of test material (core-shell organic/inorganic composites) and mixing with 20 mL pharmaceutical substance solution (100 mg/L) into glass tubes. The tubes were introduced into a test tube rotating shaker (GFL 3025) for different amount of

time (1 - 48 h) in order to reach adsorption equilibrium [16]. In order to maintain the relevance for *real-life* experiments, the solution pH was kept to 7.00 ± 0.1 . Tubes content were filtered through 0.45 µm syringe filters and the remaining pharmaceuticals from aqueous solutions were analysed by HPLC. The amount of target substance retained on solid surface (at a time t was calculated by the following equation):

$$q_t = \frac{(C_0 - C_t) \times V}{m},$$

where C_0 and C_t are the initial pharmaceutical concentration and the concentration at the time t in the solution (mg/L), V is the volume of the solution (L), and m is the amount of the adsorbent (g).

Results and Discussion

Synthesis of the core-shell materials

The synthesis of the ferrites was confirmed by XRD analyses. Figure 1 presents the XRD diffractograms of both the ferrites and the final core-shell materials.

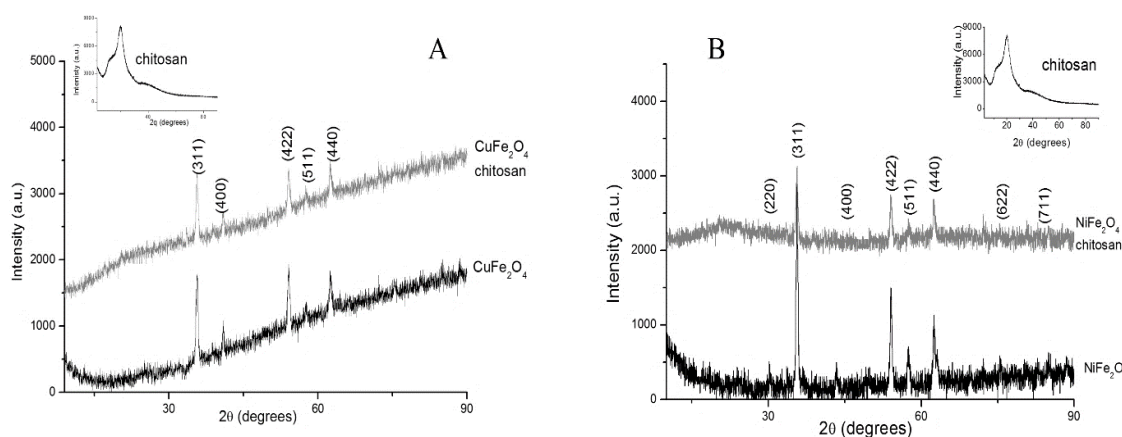


Figure 1.

XRD diffractograms of the obtained materials: a) copper ferrite and copper ferrite/chitosan composite; b) nickel ferrite and nickel ferrite composite. Inset in both images – the diffractogram of the chitosan precursor.

The phases presented in Figure 1 were identified by comparison with the ICDD database: cuprospinel (CuFe_2O_4 , PDF Card No. 01-077-0010) and, respectively, nickel iron oxide (NiFe_2O_4 , PDF Card No. 01-078-6781). The crystallite size (determined using the Scherrer equation) was 19.79 nm (for the copper ferrite), 22.85 nm (for the nickel ferrite), 21.29 nm (for the copper ferrite/chitosan composite), and, respectively, 24.07 nm (for the nickel ferrite/chitosan composite).

Upon the formation of the composites with chitosan, the XRD diffractograms do not suffer any major modification (as expected, given the amorphous nature of chitosan). However, it can be observed in both diffractograms a small hump around 25 degrees (2θ), due to the amorphous phase.

The XRF analyses confirm the presence of only the expected elements (Rh lines represent a characteristic of the X-ray tube).

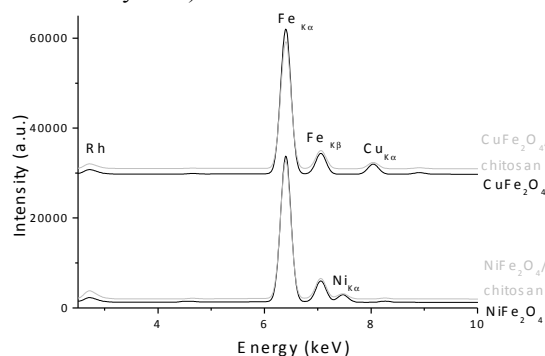


Figure 2.

XRF spectra of the obtained materials. Rh lines are characteristic to the X-ray tube.

Formaldehyde reacts with hydroxyl groups from the polymer chain to form acetals. The reaction between two polymeric chains crosslinks chitosan chains creating a very dense network around the magnetic materials [12].

The thermal analyses (Figure 3) confirm the deposition of the organic material (as shown by the DTG peak around 230°C, characteristic for the reticulated chitosan [17]).

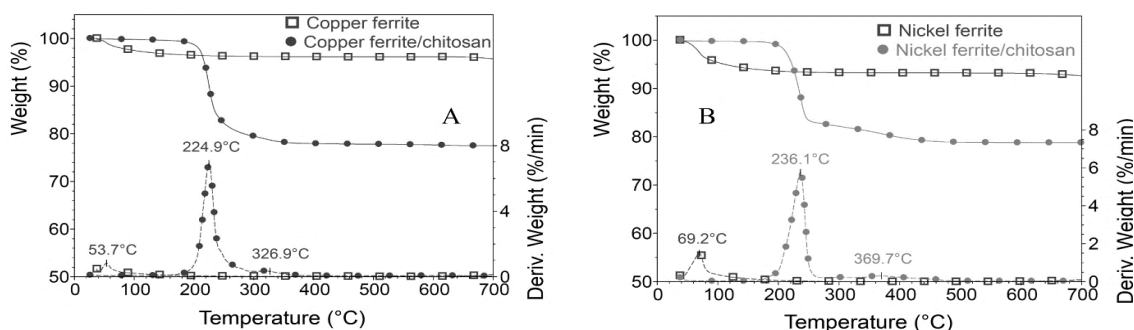


Figure 3.

TG and DTG curves of the obtained materials: a) copper ferrite, copper ferrite/chitosan composite; b) nickel ferrite, nickel ferrite/chitosan composite.

For both ferrites, the thermal analyses reveal a mass loss up to 150°C (3.2% for copper ferrite and 5.85% for nickel ferrite) due to the evaporation of water or OH groups adsorbed on the surface of the samples. The residues found for the ferrite samples were over 90% (95% for the copper ferrite, 93% for the nickel ferrite). The composites with chitosan show a much smaller loss in the first region (around 0.3%) most probably due to the formaldehyde treatment. The major loss appears, as already mentioned, around 230°C, specific for a low crystallinity reticulated

chitosan. The residues found for the chitosan composites were 77% (for the copper ferrite/chitosan) and, respectively, 78.7% for the nickel ferrite/chitosan, suggesting higher chitosan content for the copper ferrite/chitosan composite.

The TEM images (presented in Figure 4) reveal that the magnetic nanoparticles are spherical and have an average size of 13 - 17 nm. Thus, the immobilized polymer on nanoparticles did not lead to the aggregation between the particles.

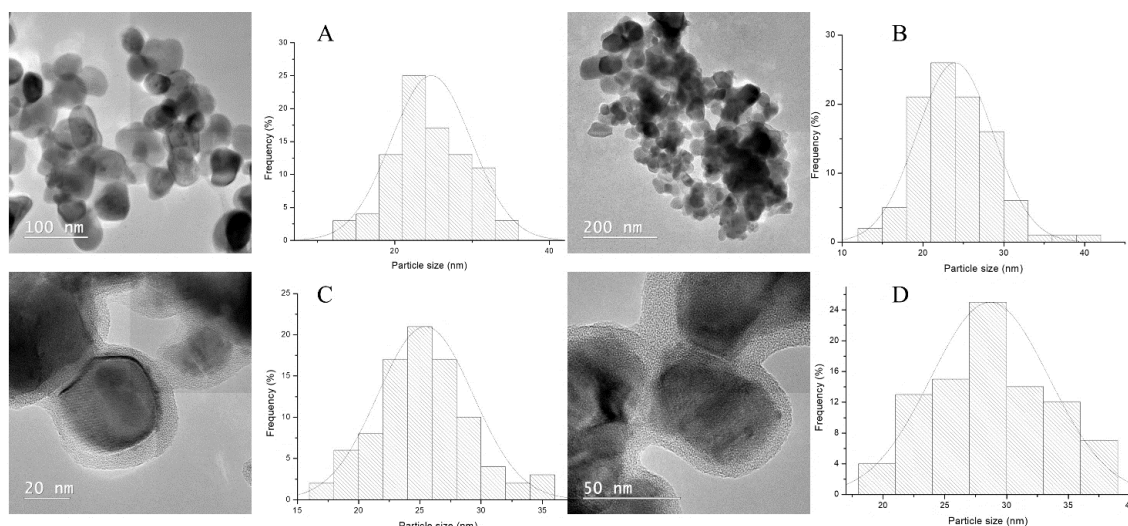


Figure 4.

TEM images and size distribution of the particles for the analysed samples

Magnetic properties of the obtained materials were evaluated for both the initial ferrites and the final organic/inorganic core-shell materials (Figure 5). All the samples exhibited ferromagnetic and paramagnetic behaviour, having saturation magnetization (M_s) values of 1.8 emu/g (copper ferrite), 6.6 emu/g

(nickel ferrite), 2.5 emu/g (copper ferrite/chitosan), and respectively, 6.8 emu/g (nickel ferrite/chitosan). The increase of the saturation magnetization is most probably due to the increase of the particle size (as determined by XRD) [13].

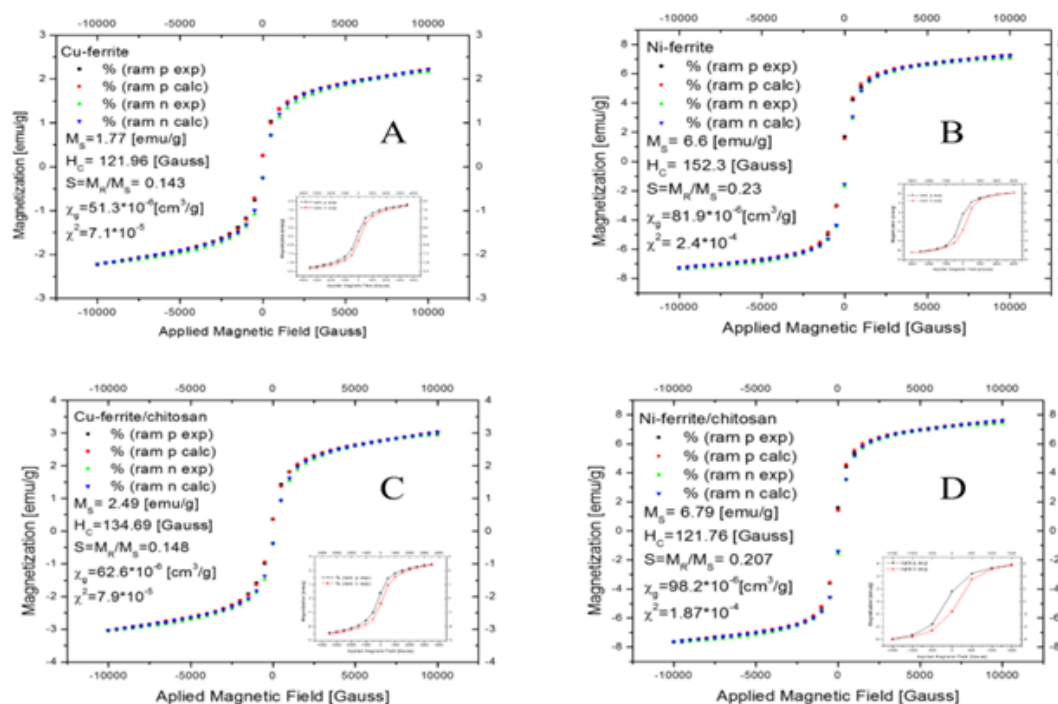


Figure 5.

Experimental and calculated magnetic data for magnetization loop, for the studied samples: a) copper ferrite; b) nickel ferrite; c) copper ferrite/chitosan; d) nickel ferrite/chitosan. “ram P” – part of hysteresis loop for descending magnetic field; “ram N” – part of hysteresis loop for ascending magnetic field.

Adsorption experiments

The chromatograms of the standard samples used for the calibration curves are presented in Figure 6, while

the calibration curves parameters are presented in Table I.

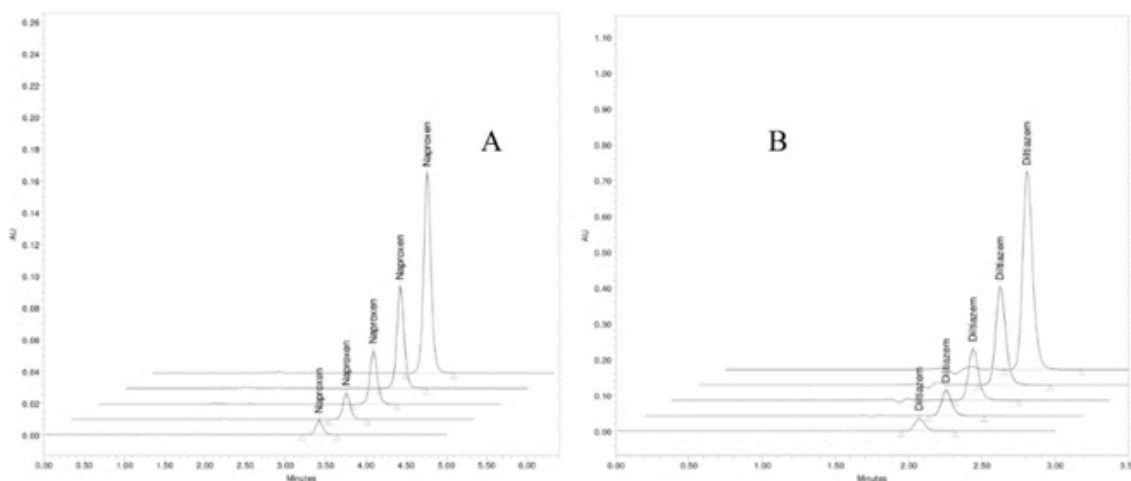


Figure 6.

Standard samples chromatograms: a) naproxen sodium; b) diltiazem hydrochloride.

Table I
Calibration curves parameters

Substance	Calibration domain (μg/mL)	Slope	Intercept	R ²
Na naproxen	12.5 - 200	9284.50	4024.51	0.99985
diltiazem HCl	12.5 - 200	13213.85	13348.16	0.99984

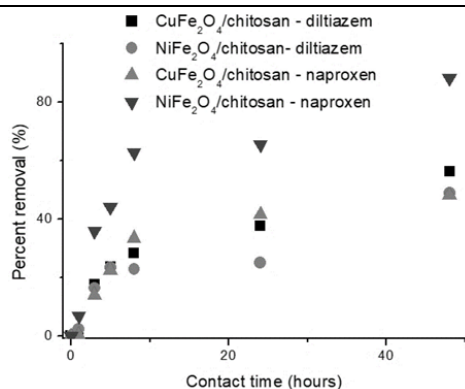


Figure 7.

Removal efficiency of the composites for the two pharmaceuticals

The pharmaceuticals removal as a function of time is presented in Figure 7.

The experiments regarding the removal of the pharmaceuticals showed the highest affinity towards the removal of Na naproxen of the nickel ferrite/chitosan composite at 48 hours contact time (approx. 89%). Nickel ferrite/chitosan and copper ferrite/chitosan composites show similar adsorption efficiency for diltiazem HCl and, respectively, Na naproxen (48.8% and, respectively, 48.1%), while the copper ferrite/chitosan composite achieved a 56.3% adsorption of diltiazem HCl at 48 hours contact time. The up-take capacity at 48 hours (q_{48} , mg of pharmaceutical substance/gram of adsorbent) of the synthesised materials is presented in Table II.

Table II

Adsorption capacity of the obtained materials

No	Composite	Pharmaceutical substance	q_{48} (mg/g)
1	NiFe ₂ O ₄ /chitosan	Na naproxen	52.78
2		diltiazem HCl	29.19
3	CuFe ₂ O ₄ /chitosan	Na naproxen	28.81
4		diltiazem HCl	33.65

The results obtained suggest a good adsorption capacity of the used materials: thus, Khazri *et al.* obtained a value of 37 mg/g for the adsorption of naproxen onto clay [18]; our results suggest a better up-take capacity of the nickel ferrite/chitosan composite and a similar capacity of the copper ferrite/chitosan composite. Lu *et al.* obtained a maximum adsorption capacity for nifedipine (another calcium channel antagonists) on spherical activated carbons of 19.5 mg/g [19].

Conclusions

Two types of adsorbents were obtained, characterised and evaluated for their potential regarding pharmaceutical EDCs removal. The nickel ferrite/chitosan composite shows the highest affinity towards the adsorption of Na naproxen (89% at 48 h), while the best results for the adsorption of diltiazem HCl were obtained for the copper ferrite/chitosan composite (56% at 48 h). The magnetic properties of the composites allow the easy removal of the adsorbents from the aqueous effluents.

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