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Cyclodextrin polymers for ibuprofen extraction in aqueous solution: recovery, separation, and characterization

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ABSTRACT

Novel cyclodextrin polymers prepared by using citric acid as cross-linked agent were employed for removal of ibuprofen from aqueous solution; five insoluble cyclodextrin polymers with different cyclodextrin types were used. Adsorption tests were carried out, with experimental apparatus consisting of a continuous up flow column. Results of adsorption experiments showed that these polymers exhibited high adsorption capacities toward ibuprofen. Studies concerning the effect of several operating variables (i.e. the effects of contact time, ibuprofen concentration, and mass of adsorbent, pH, and ionic strength) are presented and discussed. Moreover, the extraction of ibuprofen has been studied alone and in a mixture of two pharmaceuticals, and the extraction mechanism was investigated by using numerous methods of characterization.

Keywords: Ibuprofen; Cyclodextrin polymer; Pharmaceutical residue; Adsorption

1. Introduction

Pharmaceuticals are designed to have a specific mode of action in human and veterinary medicine, but they often have important side effects too. When introduced into the environment, they may affect the same pathways in animals having identical or similar target organs, tissues, cells, or biomolecules. Large quantities of pharmaceuticals like beta-blockers, anti-inflammatory drugs, contraceptives, antibiotics, lipid regulators, neuroactive compounds, and many others are sold and consumed worldwide for treatment or diagnosis of diseases and are thus, perceived in the environment. Pharmaceuticals may be introduced into environment via several routes: pharmaceutical industry, hospitals, medical facilities, households, farming.

Ibuprofen, a non-prescription drug that is among the most consumed pharmaceuticals all over the world, is a well-known non-steroidal anti-inflammatory drug. The presence of this molecule in the environment was reported in the literature essentially in

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surface water [1–3] municipal and hospital wastewater [4,5], industrial and agricultural waste stream [6].

Some ionophore antibiotics used as veterinary drugs were detected in sediments at higher concentrations than in water. Large amounts of gemfibrozil, ibuprofen, and diclofenac were also found to be bound to sewage sludge [7].

The presence of ibuprofen in the environment may induce bad effect on the health of several species; they may affect the reproduction and feminization of males [8,9], growth [10–12], and can also cause death [13].

To remove ibuprofen from the environment, several methods have been used such as membrane bioreactors and activated sludge [14], photocatalysis or photodegradation [15,16], coagulation–flocculation and flotation [17], nanofiltration and ultrafiltration [18], reverse osmosis [19] and adsorption on activated carbon [20]. However, these purification methods have many disadvantages such as high price (reverse osmosis) and low efficiency (coagulation–flocculation and flotation); moreover, they cause harm to the environment by generation of another form of pollution (photocatalysis or photodegradation) or they are not selective (activated carbon).

Adsorption, which is one of the most widely used separation methods, has gained a wide acceptance and popularity for removal of pollutants because it is an efficient and economically feasible process for purification.

Insoluble cyclodextrin polymer (P-CD) is one of the recently used adsorbent because it gives high extraction yield and more cycle number then other adsorbents, Ozmen et al. show in their study that cyclodextrin polymer gives more cycle number than activate carbon [21], it can be obtained using cyclodextrin (CD) as complex molecule and bi or polyfunctional substance as cross-linking agent. These cyclodextrin polymers have been successfully applied to the removal of diverse organic pollutants from water: dyes [22,23], aromatic amines [23], phenols [24], pesticides [25], and chlorophenols [26].

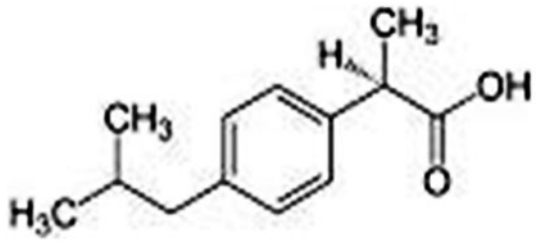

Fig. 1. Molecular structure of ibuprofen.

The main objective and the novelty of the present work is the use of a novel insoluble cyclodextrin polymer crosslinked with citric acid without using either organic solvent or elevation temperature in the preparation (which is harmful to the environment), in the ibuprofen extraction from aqueous solution. The extraction experiments unroll in a column; several effects are investigated, such as contact time, pH, the flow rate, and the ionic strength.

2. Experimental

2.1. Chemicals

Ibuprofen (Fig. 1) was purchased from Hubei Granules-biocause phaemaceutical CO, LTD (china) and was used without further purification, the progesterone was purchased from Sigma-Aldrich (USA) and was used without further purification, cyclodextrin polymers insoluble ((Poly-β-cyclodextrin (P-β-CD), Poly-α-cyclodextrin (P-α-CD), Poly-α-γ-cyclodextrin (P-α-γ-CD), and Poly-α-γ-β-cyclodextrin (P-α-γ-β-CD), were acquired from start-up In-Cyclo®, University of Rouen-France. All other reagents were of analytical grade.

2.2. Synthesis of cyclodextrins polymers

Cyclodextrins polymers (Fig. 2) were synthesized by direct melt copolycondensation, according to the method reported by Skiba [27]. Briefly, a mixture of known amount of cyclodextrins (β, α or γ), citric acid, and sodium phosphate dibasic was transferred into a reactor which was maintained at temperature ranging between 140 and 150°C for fixed time. The obtained solid form was dissolved in water and dialyzed using polyether sulfate membrane filter with molecular weight cut off of 10,000 Da. After the dialysis, the resulted solution was spray dried using BUCHI Mini Sprayer Dryer B-290, two fractions were obtained soluble and insoluble polymer. Then, the insoluble polymer which is used as adsorbent in this work was washed with methanol and dried at 60°C [28,29].

2.3. Adsorption experiment

Adsorption tests were carried out, with experimental apparatus consisting of a continuous up flow column with a volume of 125 cm^3 (ID 35 mm; height 120 mm) (Fig. 3).

Various amounts of water insoluble cyclodextrin polymer were charged and then 60 cm^3 of ibuprofen aqueous solution was supplied to the column and

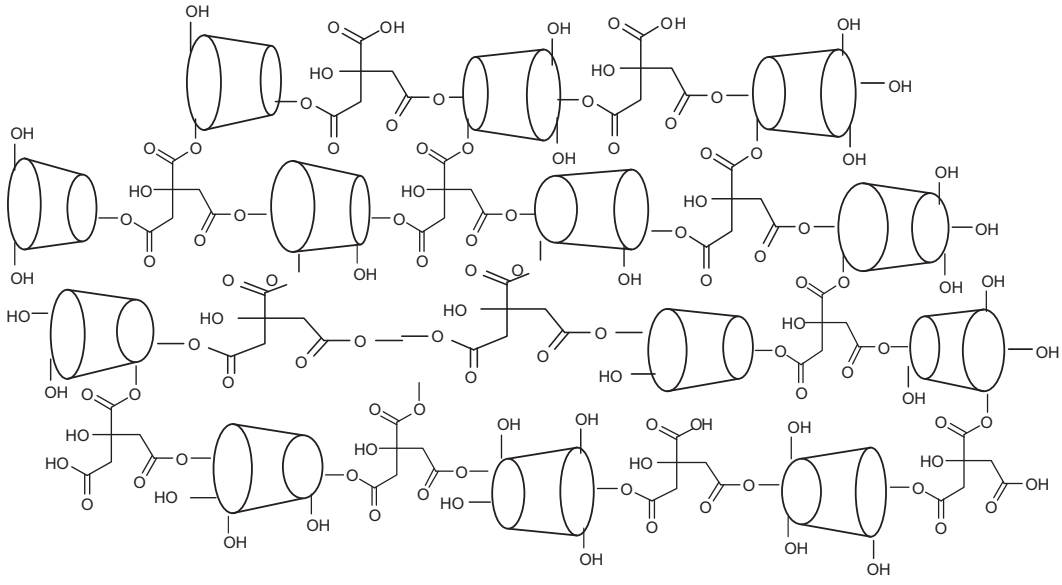

Fig. 2. Molecular structure of cyclodextrin polymers.

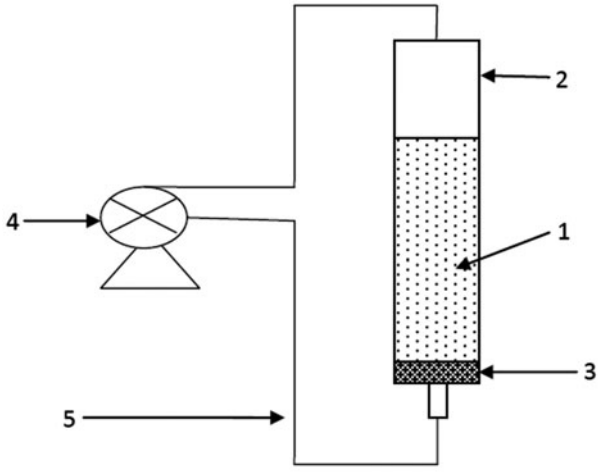

Fig. 3. Experimental setup for the ibuprofen extraction with cyclodextrin polymer in column procedure.

circulated at different liquid velocities. The flow rate, initial concentration, and adsorbent amount (AA) were varied according to experiment. The time courses of the ibuprofen uptake over 6 h were followed by determination of the ibuprofen concentration. Triplicate measurements were carried out for each study, and the mean values are presented, the error obtained was ±5%. All experiments were conducted at ambient temperature.

Stock solution of ibuprofen was prepared in deionized water. The experimental solutions with desired ibuprofen concentration were obtained by successive dilution of this stock solution with deionized water. Calibration curve of ibuprofen was prepared by measuring absorbance of samples with predetermined concentrations at 223 nm (corresponding to a maximum absorbency of ibuprofen) using a UV/VIS spectrophotometer (JASCO, V-R30, JAPAN).

2.4. Adsorption study

At different interval times, a volume of 800 µl of solution was taken; the amount of ibuprofen contents was determined by UV–vis spectrometry at 223 nm.

The amount of ibuprofen adsorbed by the insoluble cyclodextrin polymer, q_t (mg g^{-1}) and removal (%) were calculated by Eqs. (1) and (2), respectively.

$$q_t = \frac{V(C_0 - C_t)}{m} \tag{1}$$

$$\text{Removal } (\%) = \frac{C_0 - C_t}{C_0} \times 100 \tag{2}$$

where C_0 (mg L^{-1}) and C_t (mg L^{-1}) are the initial and at time t, concentrations of ibuprofen in liquid phase, respectively, V (L) is the volume of the aqueous solution, and m (g) is the cyclodextrin polymer mass.

2.5. Characterization

2.5.1. Fourier transforms infrared (FTIR) spectroscopy

Infrared spectra were recorded between 4,000 and 400 cm^{-1} with a resolution of 2 cm^{-1}, using Prestige-21 FTIR spectrophotometer IRAffinity-1 SHIMADZU spectrometer.

2.5.2. X-ray powder diffraction

To perform XRD analysis of polymers and ibuprofen, an xpert pro panalytical diffractometer was used over the 3–90° 2θ at a scan of 4° min^{-1} using a monochromatized X-ray beam from Cu K radiation (wavelength $\lambda = 0.154$ nm). The operation voltage and current were 40 kV and 20 mA, respectively, with speed 0.017° s^{-1}.

2.5.3. Differential scanning calorimetry

Differential scanning calorimetry (DSC) analysis of the different cyclodextrin polymers and ibuprofen were achieved with PERKIN ELMER apparatus. Accurately weighted amounts of samples were placed in aluminum pans and heated at a scanning rate of 10°C min^{-1} from 35 to 300°C, under a nitrogen purge gas flow rate of 25 mL min^{-1}.

3. Result and discussion

3.1. Effect of operating variable on ibuprofen extraction by cyclodextrin polymer

3.1.1. Effect of contact time and AA

The contact time in this manuscript may be defined by the necessary time to reach the equilibrium in ibuprofen adsorption on cyclodextrin polymer, when the adsorbent (cyclodextrin polymer) amount changes at same concentration of the solute (ibuprofen).

As it is shown in Fig. 4, at fixed concentration of ibuprofen ($C = 30$ mg L^{-1}), removal of ibuprofen by the β-cyclodextrin polymer presents a fast kinetic particularly at the first 60 min, this fact is due to its high swelling capacity in water (The swelling capacity (%), in the sample is defined as the mass loss before and after swelling in water), which makes adsorption sites easily accessible.

We also note that the removal efficiency increases with AA and moreover the adsorption kinetic is improved: when 25 mg of the adsorbent is used, the removal efficiency is about 67% and the equilibrium is reached at 180 min. But with increasing the quantity of β-cyclodextrin polymer to 300 mg, the efficiency attains 85% and the equilibrium time decreases until 30 min.

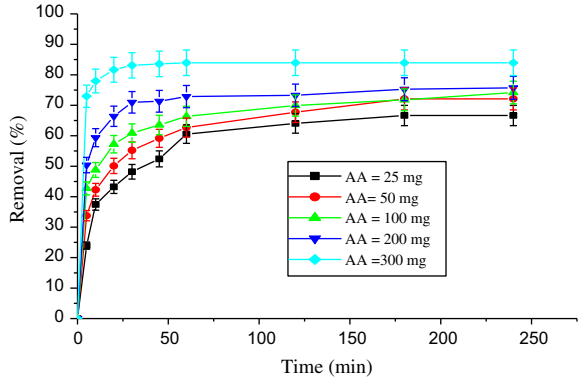

Fig. 4. Effect of contact time and AA on ibuprofen extraction by β-cyclodextrin polymer, conditions: flow rate 1.5 L h^{-1}, volume of solution 60 mL, initial concentration of ibuprofen 30 mg L^{-1}.

3.1.2. Effect of initial concentration of ibuprofen

The effect of the initial ibuprofen concentration on the removal efficiency was studied by varying the ibuprofen concentration in the range of 5–30 mg L^{-1} (ppm). As shown in Fig. 5, the removal capacity of the polymers decreases with the increase in the initial ibuprofen concentration. In the case of lower ibuprofen concentrations, the ratio of initial number of ibuprofen molecules to the available functional sites is low. At higher concentrations, the number of these sites becomes less and subsequently the removal of ibuprofen depends on the initial concentration.

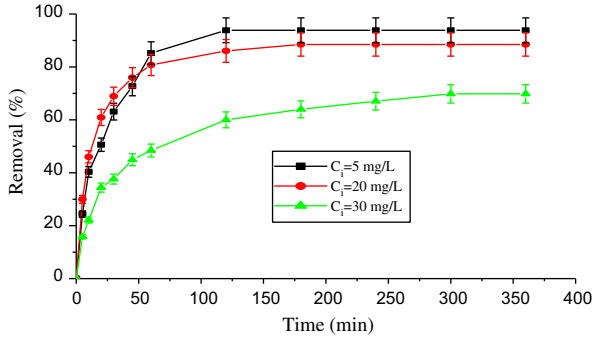

Fig. 5. Effect of initial concentration on ibuprofen extraction by β-cyclodextrin polymer, conditions: adsorbent amount 25 mg, flow rate 1.5 L h^{-1}, volume of solution 60 mL.

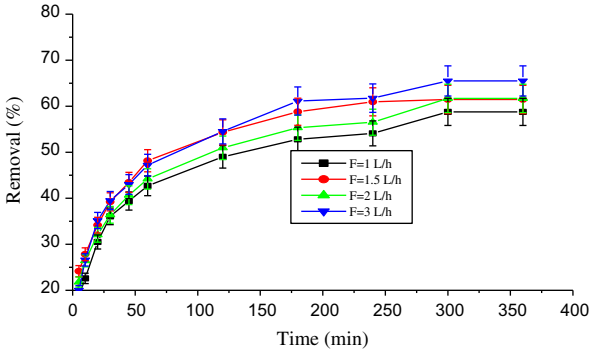

Fig. 6. Effect of flow rate (F) on extraction of ibuprofen by β-cyclodextrin polymer, conditions: adsorbent amount 25 mg, initial concentration of ibuprofen 30 mg L^{-1}, volume of solution 60 mL.

3.1.3. Effect of flow rate

The increase of the flow rate lets to improve kinetic and removal of ibuprofen (Fig. 6), by increasing the transfer of the solute from the bulk solution to the solid surface, which permits the decrease of the thickness of the diffusion boundary layer formed around the particles of the polymer.

3.1.4. Effect of ionic strength

The presence of electrolytes in solution can modify the strength of adsorbate–adsorbent electrostatic interactions. These interactions, either attractive or repulsive, can be increased or reduced by varying the solution ion strength [30].

The effect of electrolyte presence in the adsorption process was analyzed by adding NaCl (concentrations between 0 and 1 M) to ibuprofen aqueous solution. Fig. 7 shows that, with an increase in NaCl concentrations from 0.0 to 1.0 M, the adsorption percentage of ibuprofen by the β-cyclodextrin polymer augments. The expansion of the ionic strength causes diminution in the ibuprofen solubility, which favors the electrostatic interactions in the cyclodextrin polymer network and the formation of inclusion complex.

3.1.5. Effect of pH

In general, pH plays a crucial role on the adsorption efficiency. In our case, for pH higher than pKa of the ibuprofen 4.91 [31,32], the molecule will be deprotonated and it became negatively charged, so the adsorption of ibuprofen decreases due to its negative charge which is unfavorable for a formation of an inclusion complex with β-cyclodextrin due to electrostatic repulsion with negative charge of the acidic groups of cyclodextrin polymer formed in pH interval.

As it is shown in Fig. 8, the removal efficiency is enhanced at acidic pH where the ibuprofen and the β-cyclodextrin polymer are uncharged.

This trend is comparable to the results obtained by Cho et al. [33], who reported that the sorption of the ibuprofen onto carbon nanotubes decreased as the pH increased from 4 to 10. The sorption capacity was found to be pH-dependent, and more adsorption was observed at pHs below their pKa values.

3.1.6. Effect of the particle size

It was reported in the literature that the polymer with high particle size, pore volume, and swelling

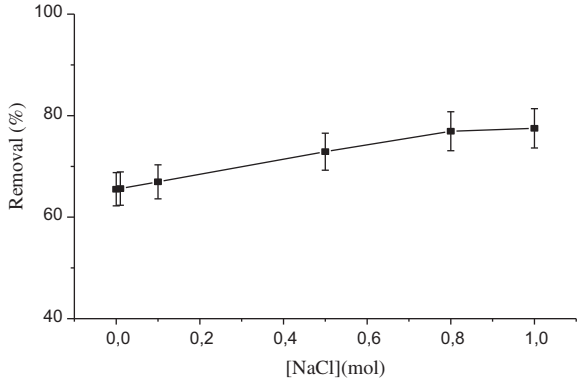

Fig. 7. Effect of ionic strength on ibuprofen extraction by β-cyclodextrin polymer, conditions: flow rate 3 L h^{-1}, adsorbent amount 25 mg, volume of solution 60 mL, initial concentration of ibuprofen 30 mg L^{-1}.

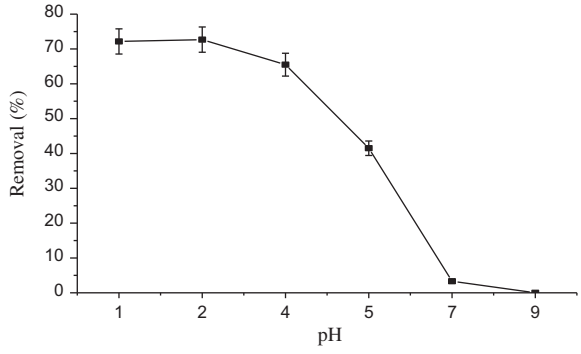

Fig. 8. Effect of pH on ibuprofen extraction by β-cyclodextrin polymer, conditions: adsorbent amount 25 mg, volume of solution 60 mL, initial concentration of ibuprofen 30 mg L^{-1}, flow rate 3 L h^{-1}.

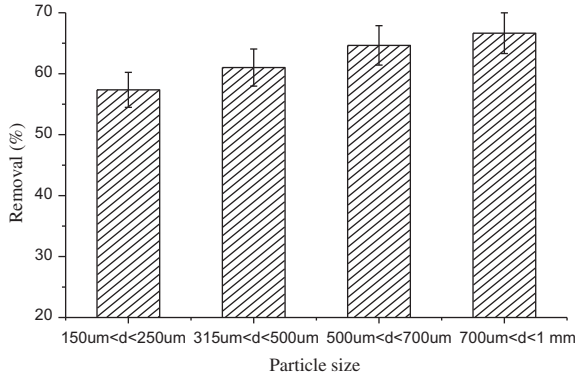

Fig. 9. Effect of particle size on ibuprofen extraction by β-cyclodextrin polymer, conditions: adsorbent amount 25 mg, initial concentration of ibuprofen 30 mg L^{-1}, volume of solution 60 mL, flow rate 3 L h^{-1}, pH = 2.

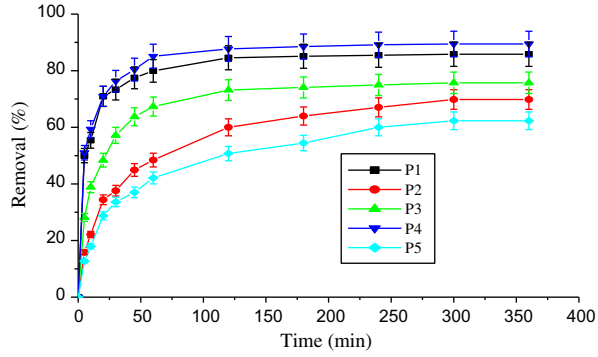

Fig. 10. Effect of cyclodextrin polymer type on ibuprofen extraction by β-cyclodextrin polymer, conditions: adsorbent amount 25 mg, initial concentration of ibuprofen 30 mg L^{-1}, volume of solution 60 mL, flow rate 3 L h^{-1}, pH = 2, P1 (P-α-CD), P2 (P-β-CD), P3 (P-γ-CD), P4 (P-α-γ-CD), P5 (P-α-γ-β-CD).

capacity is prone to have more rapid expansion, looser network structures, and it makes adsorption sites easily accessible [25]. Our results concerning the effect of the particle size on ibuprofen extraction by β-cyclodextrin polymer (Fig. 9) confirm that increasing of particle size allows the increase of ibuprofen removal. Similar results were found in a recent study of solid phase extraction of brilliant blue with β-cyclodextrin polymer [34].

3.1.7. Effect of cyclodextrin polymer type

To examine the effect of the nature of the cyclodextrin in the ibuprofen adsorption, in addition to Poly-β-cyclodextrin (P-β-CD), four other insoluble cyclodextrin polymers (Poly-α-cyclodextrin (P-α-CD), Poly-α-γ-cyclodextrin (P-α-γ-CD), and Poly-α-γ-β-cyclodextrin (P-α-γ-β-CD)) were tested. The results represented in Fig. 10 show that the α-cyclodextrin polymer gives higher extraction capacity than γ-cyclodextrin polymer; this is probably due to the best size match between ibuprofen and the cavity size of α-cyclodextrin, which is good to form a stable inclusion complex compared to the cavity of γ-cyclodextrin. The ibuprofen removal by poly-γ-CD is also higher than that obtained with poly-β-CD, this effect is probably due to the high swelling capacity of poly-γ-CD compared to the poly-β-CD one.

The extraction of ibuprofen is improved with poly-γ-α-CD compared to Poly-γ-CD and Poly-α-CD; addition of γ-cyclodextrin and α-cyclodextrin gives a synergic effect for ibuprofen removal. At last, the association of the three types of cyclodextrin (poly-α-β-γ-CD) gives an antagonistic effect where the ter-polymer gives the lowest extraction capacity compared to all other polymers.

3.1.8 Removal of ibuprofen in a mixture of two pharmaceuticals

Fig. 11 represents the ibuprofen extraction, alone and in a presence of another molecule which is progesterone (mixture of two molecules) by the different cyclodextrin polymers; as it is shown. The removal of ibuprofen with P-α-CD, P-α-γ-CD, P-α-γ-β-CD decreases in the presence of progesterone, this achievement may be due to the competition between the two molecules to occupy the actives sites of the polymers. On the other hand, the adsorption efficiency of ibuprofen increases, with the presence of progesterone in the case of P-β-CD, P-γ-CD that is due to the

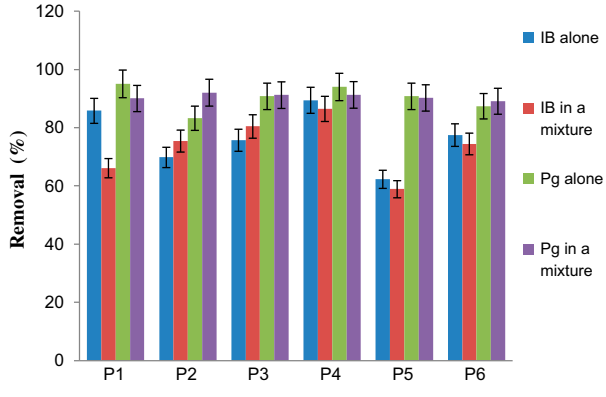

Fig. 11. Extraction of a mixture of two pharmaceuticals (ibuprofen and progesterone) by cyclodextrin polymers, conditions: adsorbent amount 25 mg, flow rate = 3 L h^{-1}, pH = 2, Pg: Progesterone; IB: Ibuprofen; 1: P-alpha-CD; 2: P-gamma-CD; 3: P-beta-CD; 4: P-alpha-gamma-CD; 5: P-alpha-gamma-beta-CD.

decrease of ibuprofen solubility, which is favorable to inclusion complex formation between ibuprofen and cyclodextrins.

3.1.9. Regeneration of cyclodextrin polymers

The complete cyclodextrin polymer regeneration was carried out by using a distilled water at a pH 9, in basic pH ibuprofen is deprotonated, the acidic group in the molecule becomes a carboxyl anion (−COO−) which is unfavorable for the formation of inclusion complexes between cyclodextrin and ibuprofen. The acidic groups in the polymer may be also deprotonated, which induce a repulsion effect between the polymer and the adsorbate in the polymer network; these two effects let the release of ibuprofen from the polymer, and favor the adsorbent regeneration.

The β-cyclodextrin polymer regenerated can be reused for several cycles with the same capacity (over 10 cycles), then we conclude that this polymer keeps his extraction proprieties, without any alteration, for a long time.

3.2. Physicochemical characterization

3.2.1. Differential scanning calorimetry

The thermal behavior of the ibuprofen–CD polymer complexes was studied using DSC in order to confirm the formation of these complexes. Fig. 12 shows the DSC thermograms of the different cyclodextrin polymers before and after adsorption of ibuprofen. The thermogram of pure ibuprofen exhibited an endothermic peak at $T = 81.73$°C, corresponding to its melting point, while the cyclodextrin polymers exhibited endothermic peaks corresponding to loss of the crystal water contained in different cyclodextrin polymers.

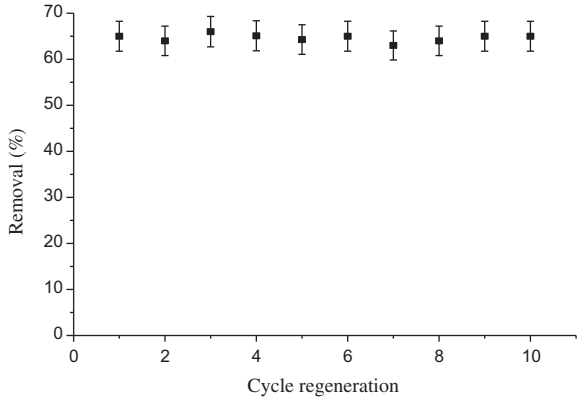

Fig. 12. The cycle number of β-cyclodextrin polymer use for ibuprofen adsorption.

The thermograms of cyclodextrin polymers after extraction of ibuprofen are different from those of before extraction, the decreasing in intensities and the change of endothermic peaks in cyclodextrin polymers and the absence of the endothermic peak corresponding to the melting point in the ibuprofen gives clear evidence that there is formation of inclusion complexes between the solutes and cyclodextrins containing in polymers [35,36]. A similar behavior was previously observed when the inclusion complex is formed between ibuprofen and cyclodextrins [37].

3.2.2. FTIR spectroscopy

In FTIR spectra (500–4,000 cm^{-1}) of ibuprofen and cyclodextrin polymers illustrated in Fig. 13, we observe that the C=O and C–H stretching vibration which occurs, respectively, at 1,719 cm^{-1} and 2,990 cm^{-1} in ibuprofen are absent in all cyclodextrin polymers after extraction, this effect confirms the interaction of ibuprofen with cyclodextrins which could result in the inclusion of the ibuprofen monomer into the hydrophobic cyclodextrin cavities [38]. These results agree well with those obtained with the thermal analysis (DSC).

3.2.3 X-Ray powder diffraction

The X-ray powder diffraction (XRPD) patterns of ibuprofen and cyclodextrin polymers after extraction of ibuprofen are shown in Fig. 14. The diffractogram of ibuprofen exhibited a series of intense and sharp peaks, indicative of its crystalline nature.

The XRPD pattern of the cyclodextrin polymers after extraction showed a completely diffused pattern with no diffraction peaks of ibuprofen. These differences indicate the formation of a real amorphous inclusion complex between ibuprofen and cyclodextrine polymers. Similar results were found in literature [38–40].

Several works reported in literature show that ibuprofen is able to form an inclusion complex with native cyclodextrin which is characterized with XRPD [41].

The absence of crystalline form of ibuprofen in cyclodextrin polymer after extraction may be also attributed to a mono-molecular dispersion of ibuprofen molecules into the polymeric cyclodextrin matrix

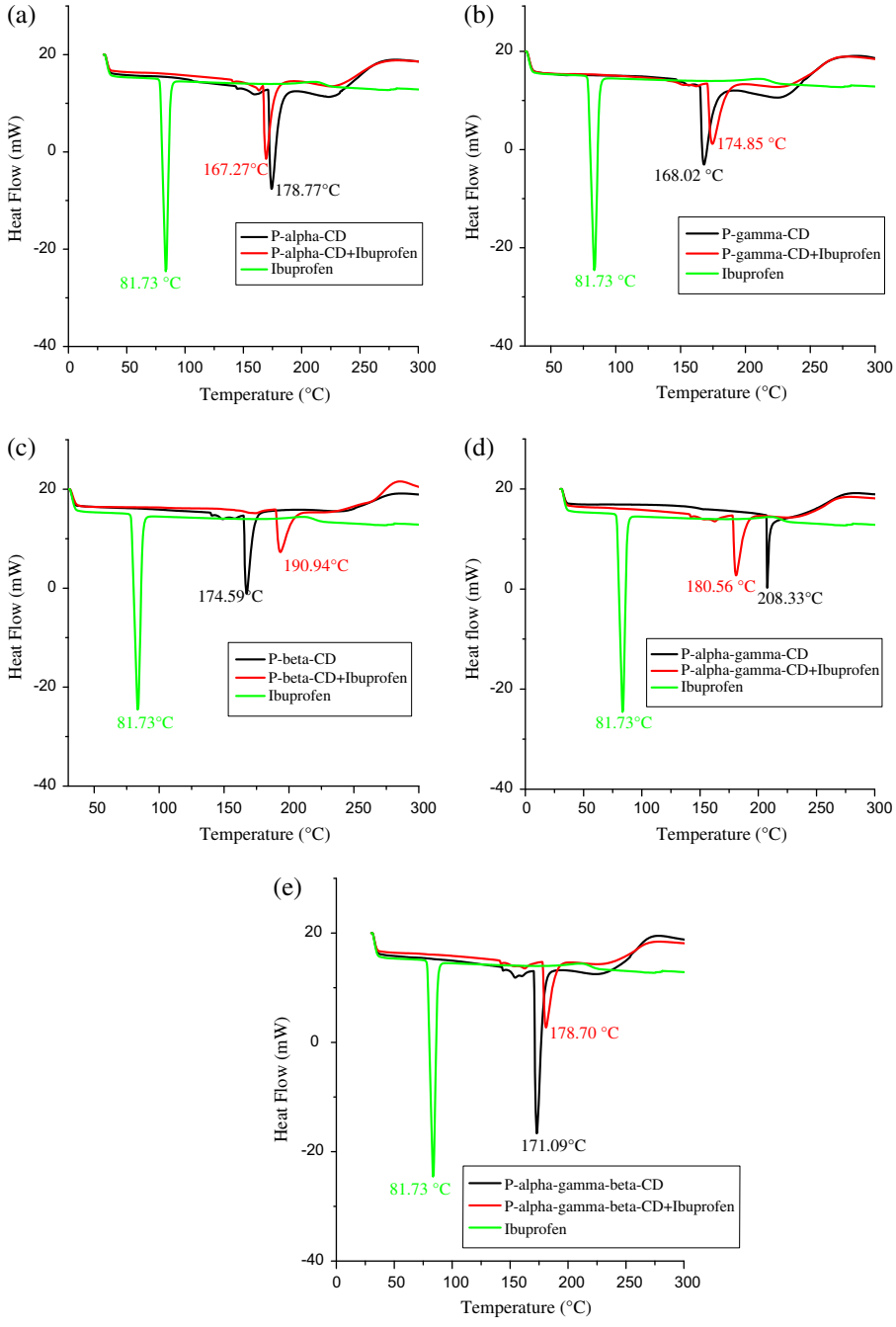

Fig. 13. Differential scanning calorimetry (DSC) of Ibuprofen and different cyclodextrin polymers after and before extraction of Ibuprofen, (a) P-alpha-CD after and before extraction of ibuprofen, (b) P-gamma-CD after and before extraction of ibuprofen, (c) P-beta-CD after and before extraction of ibuprofen, (d) P-alpha-gamma-CD after and before extraction of ibuprofen, and (e) P-alpha-gamma-beta-CD after and before extraction of ibuprofen.

for physical adsorption [42], but this dispersion or physical adsorption is neglected, where the extraction mechanism is governed by formation of an inclusion complex between ibuprofen and cyclodextrin, which is also confirmed with DSC, FTIR, and XRD analysis (Figs. 13–15).

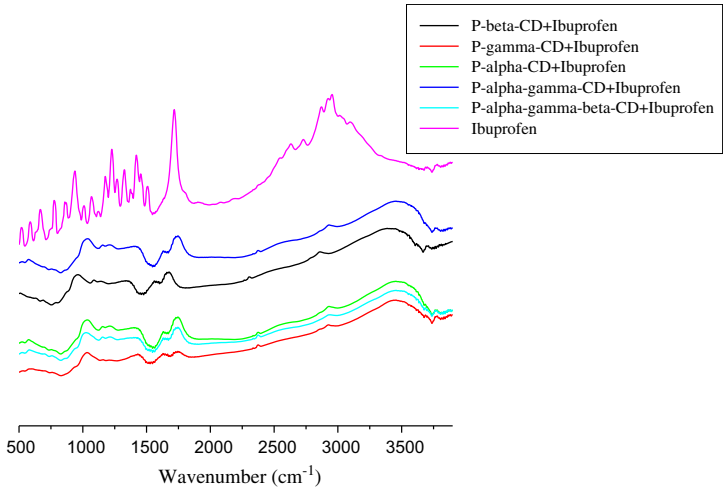

Fig. 14. FTIR spectra of ibuprofen and cyclodexrin polymers after ibuprofen extraction.

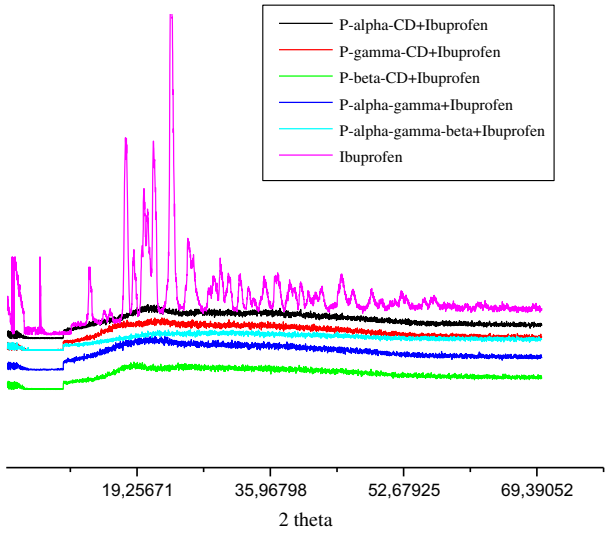

Fig. 15. X-ray diffractogram of ibuprofen and cyclodextrin polymers after ibuprofen extraction.

4. Conclusion

The adsorption of ibuprofen on five insoluble cyclodextrin polymers (P-α-γ-CD > P-α-CD > P-γ-CD > P-β-CD > P-α-γ-β-CD) was investigated. Results of experiment adsorption in recycling column showed that all cyclodextrin polymers exhibited high adsorption capacities toward ibuprofen alone and in a mixture of two pharmaceuticals, the order of the ibuprofen retention on the five polymers is: P-α-γ-CD > P-α-CD > P-γ-CD > P-β-CD > P-α-γ-β-CD.

The maximum adsorption capacity occurred in acidic pH (<pKa) where ibuprofen is in molecular form which is favorable to the electrostatic interaction and inclusion complex formation; the ionic strength contributes to increase the extraction capacities of the cyclodextrin polymers. The structural characterizations of the polymers after adsorption are in good agreement and confirm that ibuprofen forms inclusion complexes with the different cyclodextrin polymers tested. The cyclodextrin polymers may be successfully used for the treatment of the effluent and for the removal of trace pollutant from drinking water. High-quality regeneration of these polymers is a good asset for their use in comparison with conventional adsorbents. The kinetic and thermodynamic studies of the ibuprofen adsorption on the cyclodextrin polymers were investigated in the second part of this work.

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