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Novel Cyclodextrin-Chitosan Polymer for Adsorption of Pharmaceutical Residues

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Highlights:

- We designed poly(α,β,γ-cyclodextrin-chitosan) polymer for drug extraction from wastewater
- Interactions between drugs and polymer were physic-chemically characterized
- Kinetic model of drug extraction by this polymer was determined
- This polymer could be regenerated without alteration at least 23 times
- This polymer shows up to 85% efficiency in extracting ibuprofen and progesterone.

Abstract: A novel polymer containing α-cyclodextrin, β-cyclodextrin, γ -cyclodextrin and chitosan (cyclodextrin-chitosan) was synthesized, characterized and used for removing of two kinds of pharmaceuticals ibuprofen and progesterone. The present polymer is amorphous, porous with a high swelling capacity, cyclodextrin-chitosan polymer exhibits high extraction capacity toward progesterone and ibuprofen, effect of different operator variables was studied and discussed (i.e. the effects of contact time, solute concentration, pH, ionic strength and temperature), in this study adsorption kinetic was investigated, it follows a pseudo-second order model in case of ibuprofen and progesterone.

Keywords: cyclodextrin polymer; chitosan; pharmaceutical residue; adsorption; ibuprofen; progesterone

1. Introduction

Recently drugs have received more attention, as emerging pollutants [1,2] for their possible threats to aquatic environment and human health.

Progesterone and ibuprofen are very used as drugs, for this they are detected in surface water, municipal and hospital wastewater, industrial and agricultural waste stream, progesterone a natural hormone utilized as a contraceptive and for postmenopausal therapy, ibuprofen is considered to be a well-known non-steroidal anti-inflammatory, that is believed to be among the most consumed pharmaceuticals all over the world, the presence of these drugs in the environment may be harmful to fauna and flora and causes damages to human health, like other pharmaceuticals.

Several methods have been used for removal of these pharmaceuticals, such as photooxidation [3], nanofiltration and ultrafiltration [4,5], ozone oxidation [6], electrodialysis membrane [7], coagulation-flocculation and flotation [8], membranes [9].

However, the majority of these methods encounter problems from economic, technical, health and environmental because of its low efficiency, extended timeframe, excessive energy consumption and the substantial use of hazardous materials. quantity of hazardous materials used. However, adsorption is an attractive method related to high efficiency, ease of handling, and the availability of different adsorbents [10]. Various kinds of adsorbents for removing and recovering of progesterone and ibuprofen have been reported [11,12]. Amongst them, polymeric and biopolymeric materials are regarded to be particularly effective because of their high selectivity, a good chemical stability and above all they are regenerable.

Insoluble cyclodextrin polymers (P-CD) a biopolymer which can be aquired using cyclodextrin (CD) as complex molecule, now bi or polyfunctional substance is regarded as cross-linking agent such as epichlorohydrin [10,12], hexamethylene diisocyanate (HMDI) [13] and citric acid [14,15]. Cyclodextrin polymers are largely used in removing of pollutants from water such as dyes [16,17], phenol [12], aromatic amine [13] and pharmaceuticals [18,19].

Chitosan is an N-deacetylated derivative of chitin and it is known to be the most biopolymer existing in nature after cellulose, this natural polymer is very used in removing of contaminants from water such as metals [20], dyes [21] and benzoic acid [22]. Chitosan in powder is soluble in acidic medium and his separation from aqueous solution is difficult which limits his use as adsorbent. For this, it is considered to change the physical characteristics of chitosan.

Several chitosan-based materials have been synthesized, such as, chitosan polymer [23,24], hydrogel [25], film [21] and chitosan grafted cyclodextrin [22]. In our recent work, a novel polymer containing chitosan and three cyclodextrins (β-cyclodextrin, α-cyclodextrin, γ -cyclodextrin) was synthesized and used for removing of two pharmaceuticals (ibuprofen and progesterone) from aqueous solution, this association may enhance the ability of the present polymer to remove a wide type of organic molecules.

2. Experimental

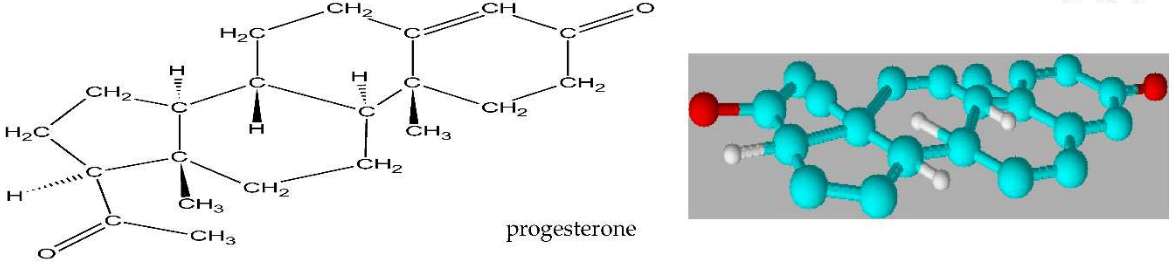
2.1. Materials

Progesterone and ibuprofen **(Figure 1)** were obtained respectively from UP John Company (USA) and Hubei Granules-biocause pharmaceutical CO, LTD (china), they were used without further purification.

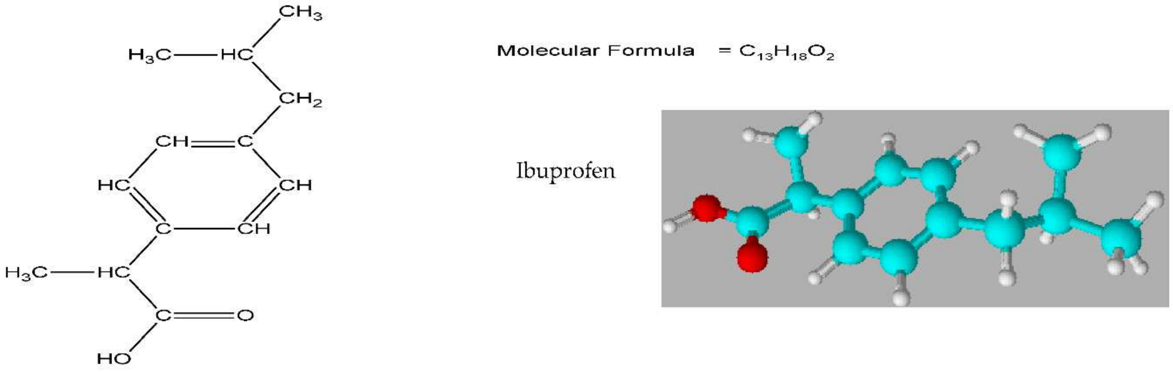
Insoluble Poly-alpha-gamma-beta-cyclodextrin-chitosan polymer with a molecular weight of 10,000 Da was procured from start-up In-Cyclo® , Rouen France.

Chitosan with molecular weight of 300 Da is obtained from SIGMA-ALDRICH, it was put to use without further purification. All other reagents were of analytical grade.

Molecular Formula = $C_{21}H_{30}O_2$



progesterone



Molecular Formula = $C_{13}H_{18}O_2$

Ibuprofen

Figure 1. Molecular structure of progesterone and ibuprofen drawn with ShemSketch 3 software program.

2.2. Apparatus

XRPD analysis of ibuprofen, progesterone and cyclodextrin-chitosan polymer before and after extraction was carried out with a diffractometer kind Oxpert pro panalytical. The condition of current and voltage were respectively 20 mA and 40kV, this analysis was occurred using a monochromatized X-ray beam from Cu Ka radiation with a wavelength λ= 0.154 nm, it was carried out over the 3–90° 2θ at a scan of 4° min^{-1} .

The scanning electron microscopy Jeol JSM-6031by with the LFD mode was used to explain the morphology of the material.

Differential scanning calorimetry analysis of ibuprofen, progesterone and the cyclodextrin-chitosan polymer after and before extraction was obtained with PERKIN ELMER. Appropriate amounts of samples were put in perforated aluminum pans and heated from 35 to 300 °C at a scanning rate of 10 °C/min, using a nitrogen purge gas flow with a rate of 25 ml/min.

JASCO spectrophotometer was used to obtain UV/VIS spectra with, and for progesterone and ibuprofen quantifications in aqueous solutions at respectively λ_{max}= 250 nm and 223 nm.

pH values measurements are carried out using a digital pH meter model Inolab.

2.3. Swelling capacity (SC)

To determine swelling capacity of this material, sufficient amount is immersed in water, which is removed at different times and wiped until have a constant weight [26].

The swelling capacity (%), is defined as the mass lost before and after swelling and it was determined as [27]:

$$\mathrm{SC}= \frac{\mathrm{We}-\mathrm{W0}}{\mathrm{W0}} \qquad (\%)$$

where, W_0 and W_e are the mass of sample at dry state respectively before and after swelling equilibrium (g).

2.4. Total Acidic groups (TA) of the cyclodextrin-chitosan polymer

The estimate of total acidic groups (TA), as well as ester and carboxylic groups was carried out by titration method. 0.1 g of polymer was introduced in a beaker which contains 20 ml of 0.1 M of NaOH solution, the mixture was then blend for 15 hours at 30°C. The cyclodextrin-chitosan polymer was dissolved and hydrolyzed.

The titration of the final solution is carried out using 0.1M HCl solution until obtain pH 7 [13].

The following equation is used to determine TA :

$$\mathrm{TA} = \frac{\mathrm{C}(\mathrm{V}_0 - \mathrm{V}_1)}{W}$$

C : the concentration of HCl solution (mmol L^{-1});
V_0 : volume of HCl solution consumed by blank solution (L);
V_1 : volume of HCl solution consumed by sample solution (L);
W i : weight of the cyclodextrin-chitosan polymer (g).

2.5. Synthesis of cyclodextrin-chitosan polymer

Insoluble alpha-beta-gamma-cyclodextrin tetrapolymers were synthesized by a direct melt polycondensation with grafted chitosan: Initially, 3g of citric acid and 0.3g of chitosan were introduced into a reactor maintained at a temperature of 140°C. Then, a mixture of 1g of alpha-cyclodextrin, 1.3 g of beta-cyclodextrin, 1.5 g of gamma-cyclodextrin, and 1g of sodium phosphate dibasic (Na2HPO4) as a catalyst was added. The solution was stirred under vacuum for 30 minutes.

The solid residue, obtained in accord with the invention, was washed successively with three volumes of 20 mL water [15–28].

2.6. Determination of the molar mass of cyclodextrin polymers

The molar mass (Mn) of cyclodextrin polymer is determined by size exclusion chromatography coupled with multi-angle laser light scattering (SEC/MALLS): This method allows the determination of mass distributions of polymers. Size Exclusion Chromatography (SEC) is used to separate macromolecules according to their size (their hydrodynamic volume in solution). For that, the polymer solutions are injected and then eluted onto columns filled with non-adsorbent porous material. At the outlet of the column, the fractions are separated according to their characteristics. Contrary to the techniques based on standard polymers and a simple detection of concentrations (usually with a differential refractometer), the addition of a second detection by diffusion of multiangle laser light, sensitive to molecular weights, gives access to instantaneous variations of the giration radius and to the average molar mass (Mw) of the eluted species at each time of elution.

2.7. Adsorption experiments

Adsorption tests are realized with experimental apparatus, with a continuous up flow column (ID 35 mm; height 120 mm), contains 125 cm^3 of pharmaceutical solution **(Figure 2)**.

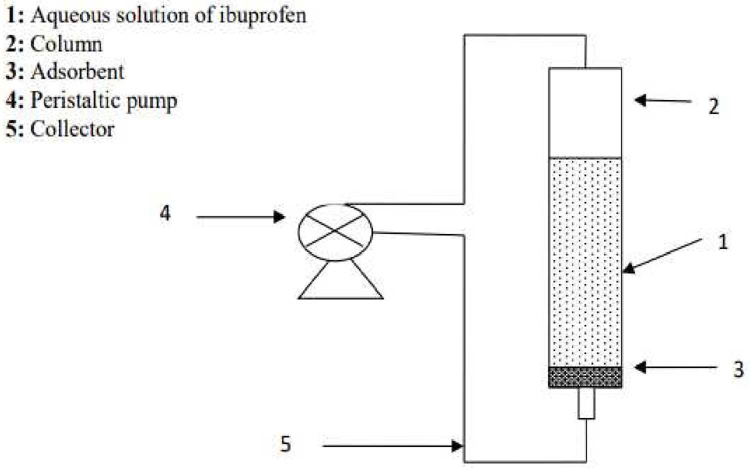


Figure 2. Experimental setup for the pharmaceuticals extractions with cyclodextrin-chitosan polymer in column system.

Various quantities of our material were introduced in 60 cm^3 solutions contain respectively ibuprofen, progesterone and a mixture of two pharmaceuticals (ibuprofen and progesterone), the solution was supplied to the column and circulated at different liquid velocities. Operating parameters (initial concentration, temperature, flow rate, adsorbent amount) were varied according to experiment.

The time-courses of the ibuprofen and progesterone uptake over respectively 6 hours and 2 hours, were followed by determination of the ibuprofen and progesterone concentration, triplicate measurements were carried out for each study, and the mean values are presented, the error found was ± 2.

Stocks solutions of ibuprofen (30 mg/L) and progesterone (20 mg/L), were prepared respectively in deionized water and a mixture of deionized water/ethanol (60ml / 40ml).

The solutions with desired concentrations were prepared by successive dilution of these stocks solutions.

2.8. Adsorption kinetics

At certain intervals, 800 μL of the solution was taken; the quantity of pharmaceuticals was checked using UV-Vis spectrometry at 223 nm and 250 nm respectively for ibuprofen and progesterone.

The adsorbed amount of pharmaceutical by insoluble cyclodextrin-chitosan polymer q_t (mg/g) and removal efficiently (%) were calculated respectively by equation (1) and (2).

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

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

C_0 (mg/L) initial concentration of pharmaceuticals;
C_t (mg/L) real-time concentrations of pharmaceuticals;
V (L) volume of solution;
m (g) is the mass of cyclodextrin-chitosan polymer.

3. Results and discussion

3.1. Characterization

3.1.1. X-ray analysis of cyclodextrin-chitosan polymers

To study the structure of cyclodextrin-chitosan polymer XRD is used, The X-ray diffractometry (XRD) presented in **Figure 3** shows one broad peak and absence of diffraction peaks, and these results report the amorphous structure of cyclodextrin-chitosan polymer.

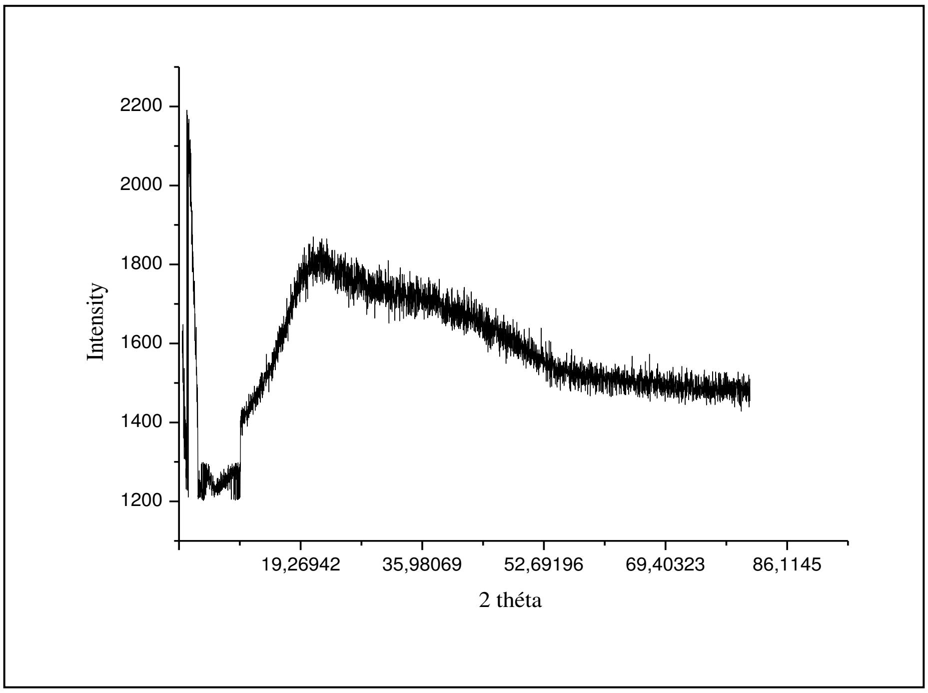


Figure 3. X-ray diffractogram of cyclodextrin-chitosan polymer.

3.1.2. Properties of cyclodextrin-chitosan polymer

The results of swelling capacity (SC), total acidic (TA), molar mass (Mn) and average molar mass (Mw) are reported in **Table 1**, we note a high swelling capacity of the polymer, and a considerable quantity of total acidic groups.

Table 1. Properties of cyclodextrin-chitosan polymer.

Property	SC (%)	TA (mmol/g)	Mn (g/mol)	Mw (g/mol)
P-α-β-◎-CD-chitosan	71.41	9.50	43 000	310 000

3.1.3. Scanning electron microscopy (SEM)

The SEM features (Figure 4) clearly reveal the nature surface of the dry polymer, his structure resembles to a sponge with thick, homogenous and smooth cavities, cyclodextrin-chitosan polymer has a porous structure with mesopores and some nanocavities, these properties let to high swelling capacity of the polymer **(Table 1)** consequently, its network can be rapidly expanded to permit a fast diffusion for adsorbates into polymer [26].

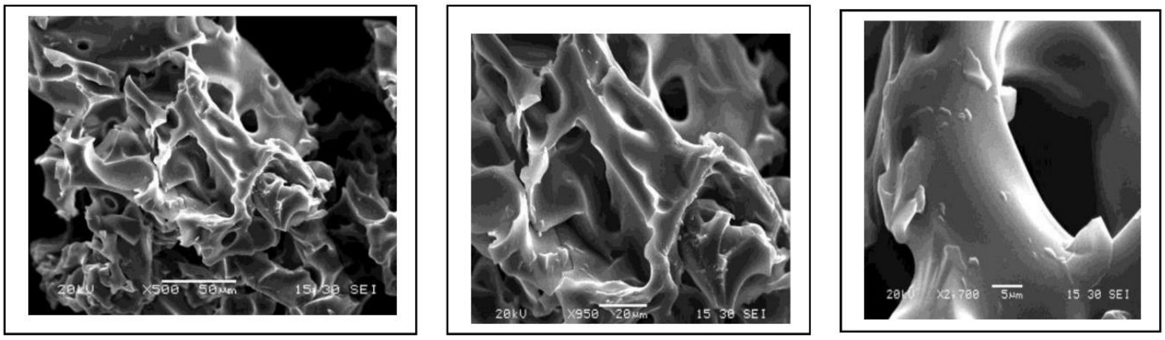


Figure 4. Features (SEM) of cyclodextrin-chitosan polymer with different magnifications.

3.2. Removal of pharmaceutical and effect of operators parameters

The effect of different operator parameters was tested for two pharmaceuticals, such as initial pH, ionic strength, temperature, contact time,

The effect of flow rate was tested only with progesterone. The initial concentration was chosen according to the solubility limit of pharmaceuticals in deionized water which is 10 mg/L and 30 mg/L respectively for progesterone and ibuprofen.

3.2.1. Effect of contact time

Figure 5 shows the removal capacity of ibuprofen and progesterone by cyclodextrin-chitosan polymer at initial concentration of 10 mg/L and 30mg/L respectively for progesterone and ibuprofen, the adsorption equilibrium is reached at 180 min in case of progesterone and at 300 min for ibuprofen.

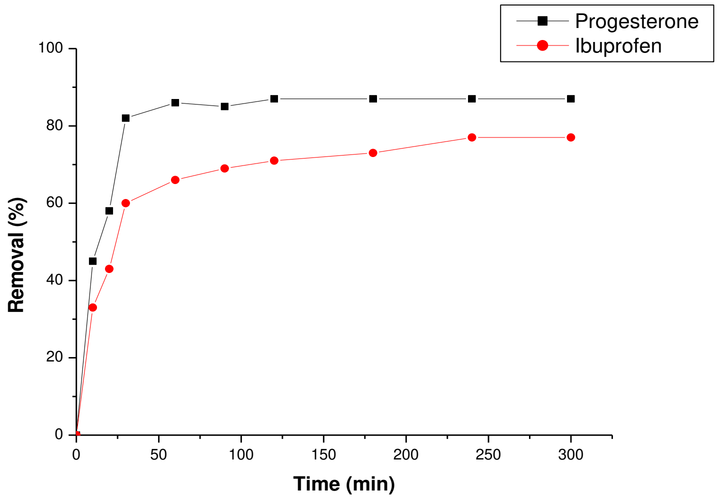


Figure 5. Effect of contact time on pharmaceuticals adsorption onto cyclodextrin-chitosan polymer conditions : flow rate =1.5 l/h, temperature 25 °C, initial concentration of progesterone and ibuprofen respectively 10 ppm and 30 ppm; pH= 2 in case of ibuprofen and pH=7 in case of progesterone.

3.2.2. Effect of flow rate

The **Figure 6** reveals effect of flow rate on progesterone extraction. The increase in flow rate contributes positively to progesterone removal, this fact may be attributed to the increase of transfer solute from bulk solution to solid surface and the decrease of boundary layer depth formed around the solid surface by increasing of cycle number.

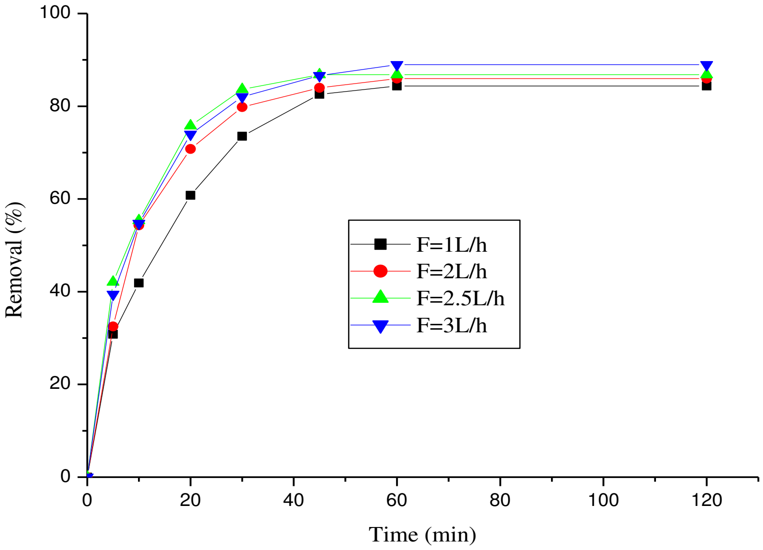


Figure 6. Effect of flow rate (F) on progesterone removal, conditions: amount of adsorbent 25 mg, temperature 25 °C, initial concentration of progesterone 10 ppm, pH= 7.

3.2.3. Effect of initial pH

The effect of initial pH on progesterone and ibuprofen adsorption on cyclodextrin-chitosan polymer is illustrated in **Figure 7**. The initial pH has a significant role in the uptake of progesterone and ibuprofen.

We note a little Increase of progesterone adsorption with increasing of pH, when the pH is less than 6.5 (the pK$_a$ value of chitosan) the surface of the polymer is charged positively because the amino group available inside the cyclodextrin-chitosan polymer corresponding to chitosan are protonated, for pH high 6.5 the polymer surface is uncharged

which is favorable to the progesterone adsorption because it is a neutral molecule and is undissociated under pH, these results confirm that chitosan available in cyclodextrin-chitosan polymer play a crucial role in progesterone adsorption by forming electrostatic binding between the two species.

The ibuprofen removal decreases with increasing of initial pH, for pH higher than pK$_a$ of the ibuprofen 4.91 [27–30], the molecule will be deprotonated and it becomes negatively charged and the adsorption decreases due to its negative charge, which is unfavorable for the formation of an inclusion complex with cyclodextrins, and because of electrostatic repulsion with negative charge of acidic groups in cyclodextrin polymer formed in basic pH.

The removal efficiency is recorded at acidic pH, which confirms that the main mechanism of ibuprofen removal is the inclusion complex formation, between ibuprofen and cyclodextrins. Chitosan seems do not have significant role in ibuprofen adsorption.

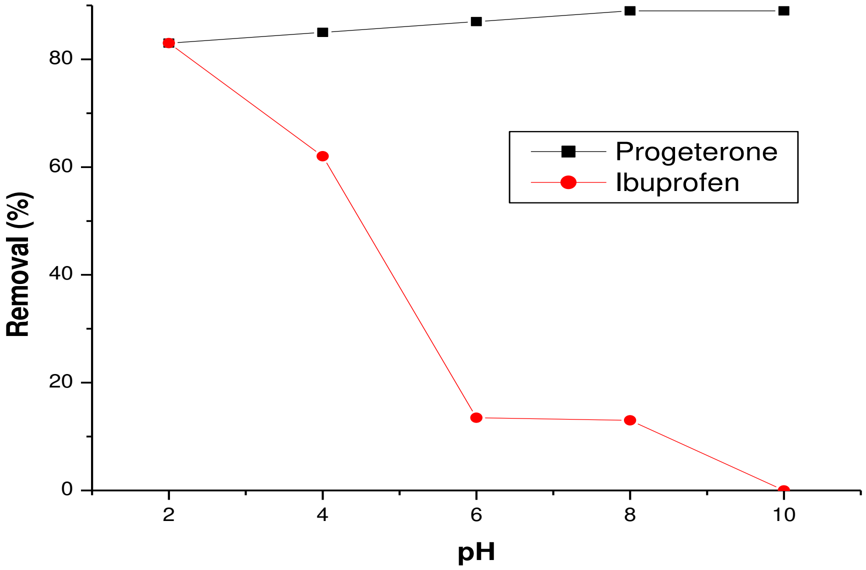


Figure 7. Effect of pH on pharmaceuticals adsorption, conditions: adsorbent amount = 25 mg, flow rate =3 l/h, temperature 25 °C, initial concentration of progesterone and ibuprofen respectively 10 ppm and 30 ppm.

3.2.4. Effect of ionic strength

The influence of ionic strength on adsorption of the two pharmaceuticals is shown in **Figure 8**.

In case of progesterone ionic strength seems do not have significant effect (a slight decrease), because it is a neutral molecule.

For ibuprofen the extraction increases with ionic strength, this effect may be attributed to the screen of the negative charge in ibuprofen molecule and the solubility decrease, which is favorable to the formation of electrostatic interactions and inclusion complexes between cyclodextrins and ibuprofen.

3.2.5. Effect of temperature

Removal of progesterone with cyclodextrin-chitosan polymer decreases as temperature increases (**Figure 9**), the removal amount is maximal at room temperature (20 °C), however, in case of ibuprofen his removal increases with temperature this effect is due to increasing rates of adsorbate intraparticle diffusion into the pores of adsorbent at higher temperature due to the pores expanding of the polymer or creation of new actives sites.

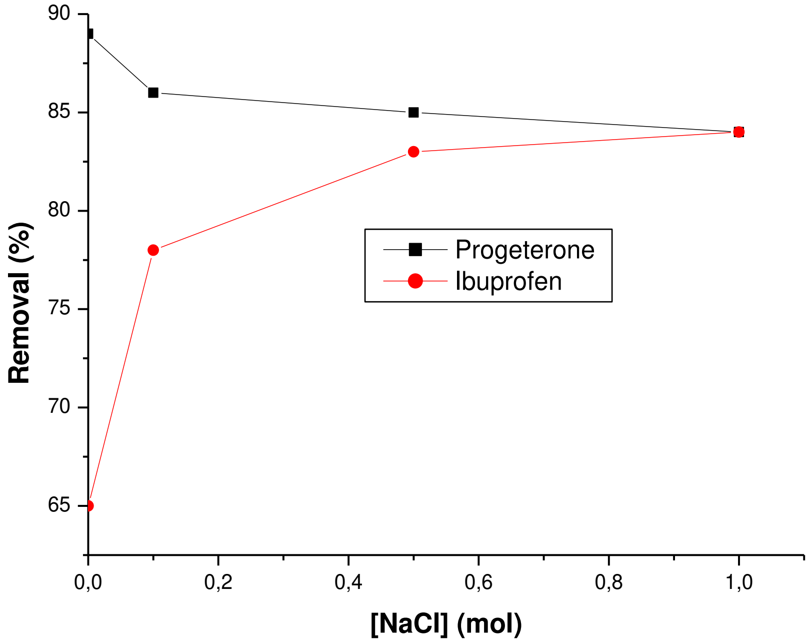


Figure 8. Effect of NaCl concentration on pharmaceuticals removal, conditions: amount of adsorbent = 25 mg, flow rate =3 l/h, temperature 25 °C initial concentration of progesterone and ibuprofen are respectively 10 ppm and 30 ppm, pH =2 in case of ibuprofen and pH= 7 in case of progesterone.

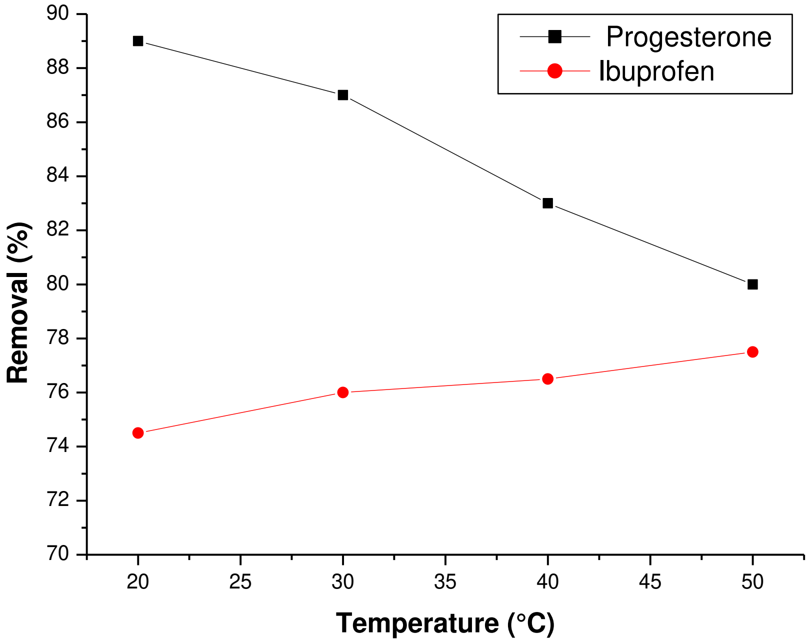


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Figure 9. Effect of temperature (T) on pharmaceuticals, conditions: adsorbent amount is 25 mg, flow rate =3 l/h, initial concentration of progesterone and ibuprofen respectively are 10 ppm and 30 ppm, pH =2 in case of ibuprofen and pH= 7 in case of progesterone.

3.3. Thermodynamic study

Thermodynamic parameters are determined such as, entropy (ΔS) and enthalpy (ΔH),. The temperature-dependence of the distribution coefficient, allows deduction of these parameters by plotting of ln(K_d) versus 1/ temperature.

$$K_d = \frac{q_e}{C_e} \tag{3}$$

With:
q_e: Adsorbent amount of the solute at equilibrium (mg/g).
C_e : Concentration of the solute at equilibrium (mg/L).
Hence,

$$K_d = \frac{C_0 - C_e}{C_e}\frac{V}{m} \tag{4}$$

C_0: initial concentration of the solute.
The free energy change can be obtained from the following formula:

$$\Delta G = \Delta H - T.\ \Delta S$$

The free energy change can be also expressed as follow:

$$\Delta G = \Delta G^0 + RT\ \ln K_d.$$

At equilibrium $\Delta G = 0$

$$\Delta G^0 = -RT\ \ln K_d$$

In the other hand

$$\Delta G^0 = \Delta H^0 - T.\ \Delta S^0 \tag{5}$$

$$\text{Then } \ln K_d = \frac{\Delta S^0}{R} - \frac{\Delta H^0}{RT} \tag{6}$$

This is Vant Hoff s' law.

Figure 10 illustrates ln K_d plotted versus the inverse of absolute temperature (T), the plots are a good linear regression, it lets us to deduct thermodynamic parameters with precision.

The slope A and the intercept B of the resulting straight line can be calculated from the relationship:

$$A = -\ \Delta H^0/R$$

$$B = \Delta S^0/R$$

These are used for determine enthalpy changes (ΔH^0) and the entropy changes (ΔS^0).

Then the free energy changes can be obtained from the equation (5).

The thermodynamic parameters calculated are summarized in **Table 2**, the positive value of enthalpy for progesterone indicates that adsorption process on cyclodextrin-chitosan polymer is endothermic; the negative value of the enthalpy in case of ibuprofen indicates the exothermic process.

The positives values of the entropy for the two pharmaceuticals show that the adsorbed molecules on the cyclodextrin-chitosan polymer surface are organized in a more random fashion compared to those in the aqueous phase [31].

Table 2. Thermodynamic parameters of ibuprofen and progesterone adsorption on cyclodextrin-chitosan polymer.

Molecule	C_0(mg/l)	T (K°)	ΔH° (J/mol)	ΔS° (J/°K.mol)
Progesterone	10	296	38.2319	18.5077
		305		
		315		
		325		
Ibuprofen	30	296	-2.7103	4.4770
		305		
		315		
		325		

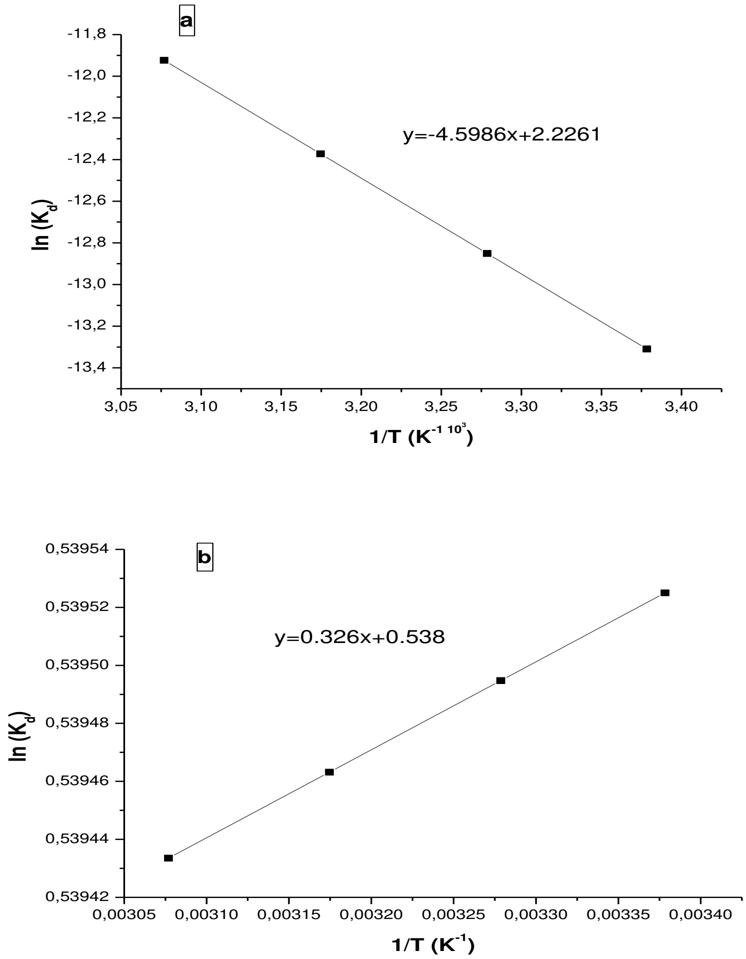

Figure 10. Vant'Hoff plots of lnK_d versus 1/ T for (a) progesterone, (b) ibuprofen.

3.4. Adsorption kinetic study

Adsorption kinetic gives information about adsorption quantity and velocityof the adsorption. Pseudo-second and pseudo-first order models, were utilized to study progesterone and ibuprofen adsorption on cyclodextrin-chitosan polymer.

In case of pseudo first order, Lagergren's rate equation is one of the most utilized to describe the rate of adsorption [32].

$$\frac{dq_t}{dt} = k_1\,(q_e - q_t) \tag{7}$$

k_1 (min^{-1}) is the pseudo first order adsorption rate coefficient.

For the boundary conditions at ($t=0$, $Q_t=0$) and ($t = t$, $q_t = q_t$), the integration of the equation (7) gives the equation (8).

$$\ln\,(q_e - q_t) = \ln q_e - k_1\, t \tag{8}$$

q_e : amount adsorbed per unit mass at equilibrium;

q_t : amount adsorbed per unit mass at any time t;

The second order kinetic is described by the following equation [29,32]:

$$\frac{dq_t}{dt} = k_2(\,q_e - q_t)^2 \tag{9}$$

k_2 is the second order rate coefficient.

The integration and application of the boundary conditions ($q_t=0$ at $t=0$ and $q_t=q_t$ at $t=t$) give a linear form (equation 10).

$$\frac{t}{q_t} = \frac{1}{k_2 q_e^2} + \frac{t}{Q_e} \tag{10}$$

The integral form of the model, represented by the equation (10) predicts that the ratio of the time/adsorbed amount (t/q_t) should be a linear function of time [32].

The validity of each model could be checked by the linear regression value (correlation coefficient, R^2) and a normalized standard deviation Δq (%) which can be obtained by the following equation [32]:

$$\Delta q\ (\%) = \sqrt{\frac{\sum[(q_{exp} - q_{cal})/q_{exp}]^2}{n-1}} \times 100 \tag{11}$$

q_{exp} : the experimental adsorbed amount per adsorbent mass at equilibrium;

q_{cal} : the calculated adsorbed amount per adsorbent mass at equilibrium;

n is the number of data points.

The regression coefficient (R^2) in case pseudo-first order model is 0.856 and 0.672 respectively for progesterone and ibuprofen, results represented in **Tables 3** and **4** show the low regression coefficient (R^2) and the high values of Δq (%) which denote the invalidity of the model.

The pseudo-second order model is substantially applicable for adsorption kinetics of cyclodextrin-chitosan polymer toward ibuprofen and progesterone, because of the low values of Δq and high regression coefficients R^2 (**Figure 11, Table 3 and 4**).

The higher goodness of fitting for the pseudo-second order model could be ascribed to the nature of cyclodextrin-chitosan polymer with multiple adsorption sites, which are responsible to different adsorption steps [33]. This model indicates the dependence of the adsorption process on both adsorbent and adsorbate proprieties.

Adsorption phenomena occur in general, in three consecutive stages:

- liquid film diffusion;
- Intraparticle diffusion or pores diffusion;
- Adsorption of the adsorbate molecule at the active sites on the internal surface of the sorbent.

The last stage is very speed. Therefore, the solute adsorption on adsorbent may be governed by film diffusion process and/or intraparticle diffusion [32].

An intraparticle diffusion model proposed by Weber-Morris [32] is expressed as follows:

$$q_t = k_i t^{1/2} + C \tag{12}$$

q_t (mg/g) : the adsorbed amount at time t (min);
k_i (mg g^{-1} $min^{-1/2}$) : the intraparticle diffusion rate constant;
C : the intercept.

If the plot of q_t versus $t^{1/2}$ is a straight line, the adsorption process follows the intraparticle diffusion model [32].

Using the equation (12), the graph of adsorbed amount (q_t) versus $t^{1/2}$ for intraparticle transport of ibuprofen and progesterone on cyclodextrin-chitosan polymer were drawn (**Figure 11**). We constate that the plots don't give a single straight line, they shown a multilinearity which indicated a multi-step process, the initial linear portion for about 45 min and 120 min for respectively progesterone and ibuprofen, are the gradual adsorption stage, this shows the application the intraparticle diffusion model.

The horizontal linear portion representes the system at equilibrium [34].

Because the plots don't represent a single straight line and they don't pass by the origin, we may say that intraparticle diffusion is not the stage governing the kinetics [32].

The liquid film diffusion model is represented by the following equation :

$$\ln(1-F) = -k_{fd}\, t \qquad (13)$$

F is the fractional attainment of equilibrium it equals q_t/q_e,and k_{fd} (min^{-1}) is the film diffusion rate coefficient.

If the plot of $-\ln(1-F)$ versus time t is straight line with zero intercept, we can say that the film diffusion through the liquid film controls the adsorption process [32].

The ibuprofen and progesteroneadsorption on cyclodextrin-chitosan polymer is also not governed by film diffusion, because the plots (plots not showed) have not zero intercept, for this the film diffusion is not the rate-determining step.

Kinetics of ibuprofen and progesterone adsorption is also studied by testing the Elovich model, for this model the solid surface of the adsorbent is energetically heterogenous, and the interaction between the adsorbates molecules don't affect the adsorption kenitic [32].

The Elovich Equation [32] has been used in the form:

$$\frac{dq_t}{dt} = \alpha \exp(-\beta\, q_t) \qquad (14)$$

α and β are the Elovich coefficient,.

The linear form of the equation (14) is given by [31]:

$$q_t = \beta \ln(\alpha\beta) + \beta \ln t \qquad (15)$$

The high values of regressions coefficients (R^2) and the low values of Δq (%) for the two pharmaceuticals indicate that Elivoch equation is applicable for adsoption kinetics modelling of progesterone and ibuprofen, this is shown respectively in **Table 3** and **4**.

Table 3. Results of R^2, k and Δq (%) for different equations used to model the kinetic extraction of progesterone by cyclodextrin-chitosan polymer. .

Equation	**(8)**	**(10)**	**(12)**	**(13)**	**(15)**
R^2	0.856	0.9998	0.856	0.963	0.932
k (g $mg^{-1}min^{-1}$)	-	0.0020	-	-	-
Δq (%)	95.08	0.52	41.26	-	9.53

Table 4. Results of R², k and Δq (%) for different equations used to model the kinetic extraction of ibuprofen by cyclodextrin-chitosan polymer.

Equation	(8)	(10)	(12)	(13)	(15)
R²	0.692	0.9997	0.7270	0.6920	0.8300
k (g mg^{-1}min^{-1})	-	0.0003	-	-	-
Δq (%)	85.87	5.94	-	-	8.91

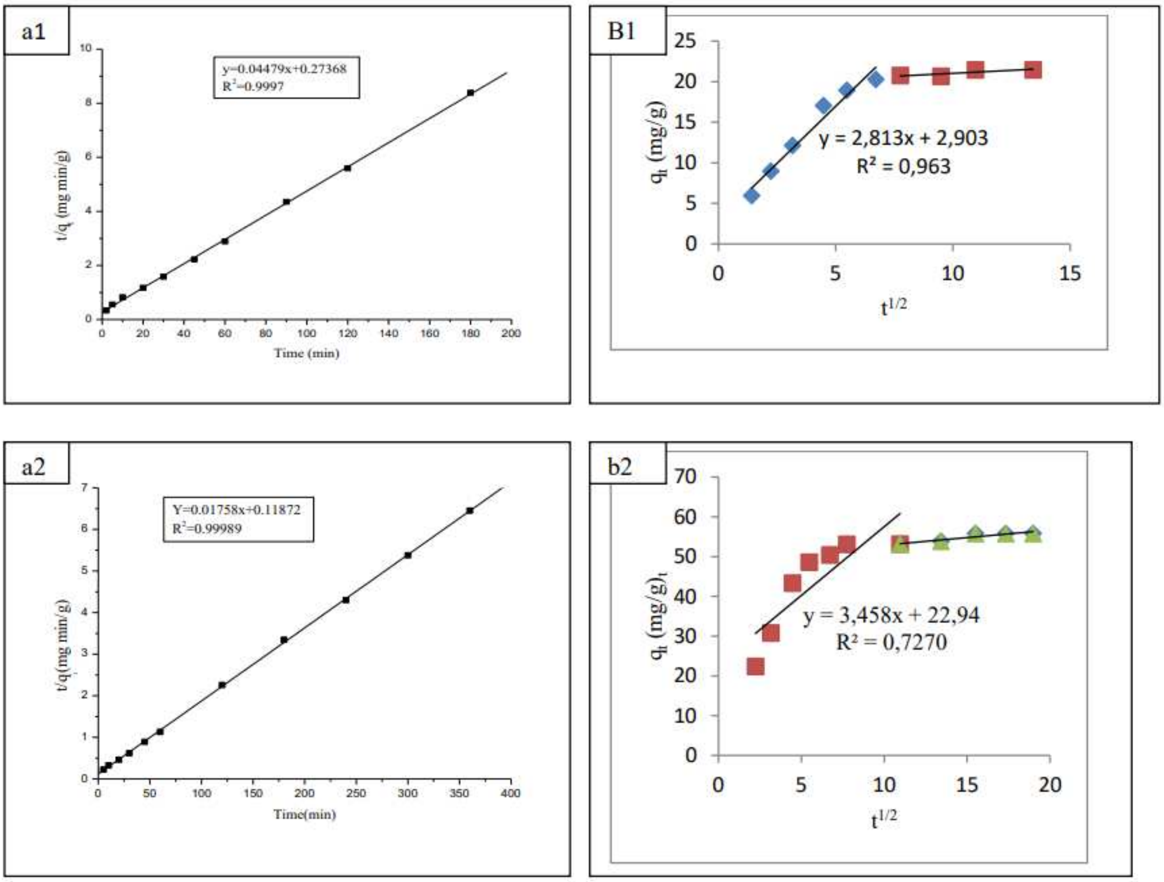

Figure 11. Curve-fitting plot of (a1) and (a2) pseudo-second order model for adsorption kinetics respectively of progesterone and ibuprofen, progesterone (b1) and ibuprofen (b2) Curve-fitting plot of intraparticle model.

3.5. Comparison between cyclodextrin polymer, cyclodextrin-chitosan polymer and chitosan for removal of pharmaceuticals

A comparison between cyclodextrin polymer, cyclodextrin-chitosan polymer and chitosan alone for extraction of pharmaceuticals was done and presented in **Figure 12**. It is clear that extraction of progesterone by cyclodextrin polymer and chitosan alone give the same results but it decreases when the cyclodextrins are polymerized with chitosan, this association gives an antagonistic effect.

For ibuprofen, his extraction with cyclodextrin polymer is better than in case of chitosan used alone and it is improved when the cyclodextrin and chitosan are polymerized together, the association of the two gives a synergic effect.

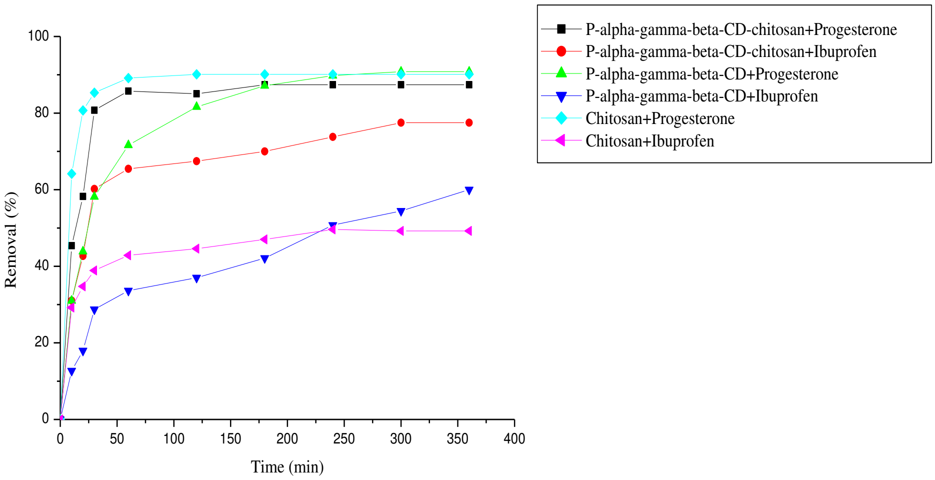

Figure 12. Comparison between cyclodextrins-chitosan and chitosan alone for extraction of ibuprofen and progesterone, amount of adsorbent = 25 mg, flow rate =3 l/h, temperature 25 °C initial concentration of progesterone and ibuprofen are respectively 10 ppm and 30 ppm, pH =2 in case of ibuprofen and pH= 7 in case of progesterone.

3.6. *Removal of a mixture of two pharmaceuticals (progesterone and ibuprofen)*

In a real effluent, we find never one molecule alone, but they exist in a mixture of several molecules, for this we have investigated the removal of mixture of progesterone and ibuprofen with cyclodextrins-chitosan polymer, when they are presented alone and/or in a mixture of two pharmaceuticals.

The results reported in a **Figure 13** reveal that the removal of the two pharmaceuticals is unchanged when they are alone or in a mixture, cyclodextrins-chitosan polymer is able to absorb the two molecules with the same yield.

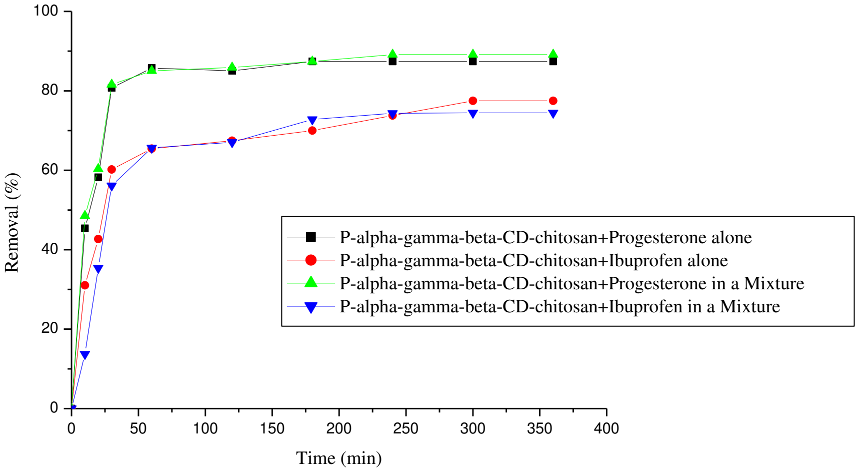

Figure 13. Removal of ibuprofen and progesterone alone and in a mixture of the two pharmaceuticals, amount of adsorbent = 25 mg, flow rate =3 l/h, temperature 25 °C initial concentration of progesterone and ibuprofen are respectively 10 ppm and 30 ppm, pH = 2 in case of ibuprofen and pH= 7 in case of progesterone.

3.7. Physico-chemical methods

3.7.1. X-ray powder diffractometry (XRPD)

Cyclodextrins-chitosan polymer is amorphous, while ibuprofen and progesterone exhibited a series of intense and sharp peaks which shows its crystalline nature (**Figure 14**).

The cyclodextrins-chitosan polymer, shows the same amorphous structure after extraction of progesterone and ibuprofen, the absence of diffraction peaks of progesterone and ibuprofen in diffractogram of cyclodextrin-chitosan after extraction, may be due to the formation of a less organized system indicating the formation of a real amorphous inclusion complex between pharmaceuticals and cyclodextrins, presented in the cyclodextrins-chitosan polymer, similar results were found in literature [35,36].

This effect can be also due to a mono-molecular dispersion of progesterone and ibuprofen molecules into the polymeric cyclodextrins-chitosan polymers matrix for physical adsorption [37].

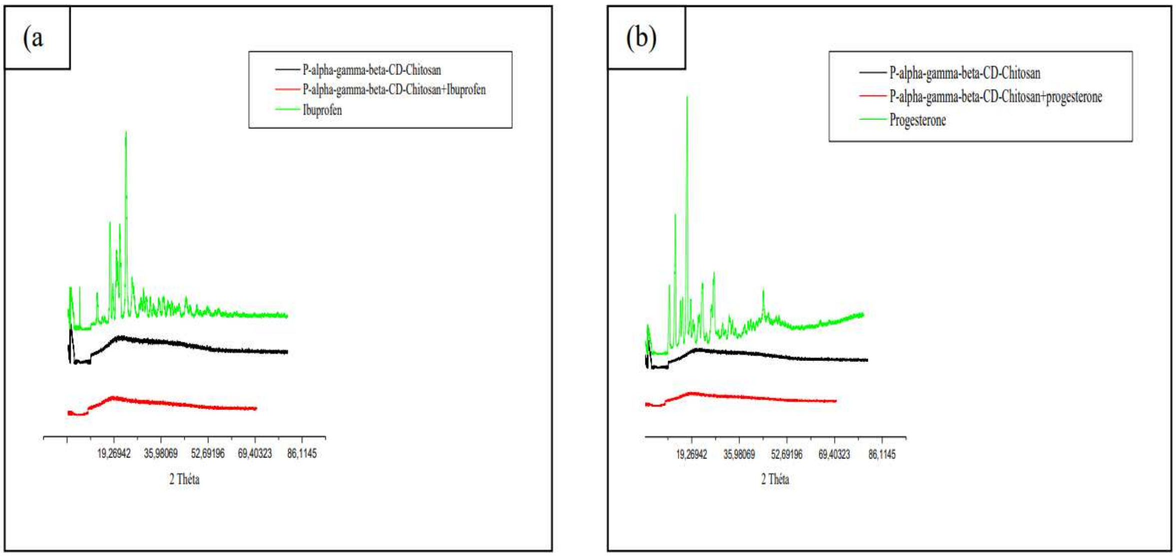

Figure 14. X-ray diffractogram of (a) ibuprofen, (b) progesterone and cyclodextrins-chitosan polymers before and after extraction.

3.7.2. Differential scanning calorimetry (DSC)

The results of differential scanning calorimetry analysis of ibuprofen, progesterone and cyclodextrin-chitosan polymer after and before extraction of pharmaceuticals are shown in **Figure 15**.

Ibuprofen and progesterone thermograms exhibited endothermic peaks respectively at 81.33 °C and 133°C, corresponding to the melting points, while the cyclodextrin-chitosan polymer exhibited a broad endothermic peak corresponding to loss of crystal water containing in the polymer.

The change of endothermic peak in cyclodextrin-chitosan polymer, and the absence of the endothermic peak, corresponding to the melting point of ibuprofen and progesterone in the cyclodextrin-chitosan polymer after extraction, may be due to the interaction of pharmaceuticals with polymer, essentially the formation of inclusion complexes between solute and cyclodextrins containing in polymer and the formation of electrostatic interactions in the network of the polymer.

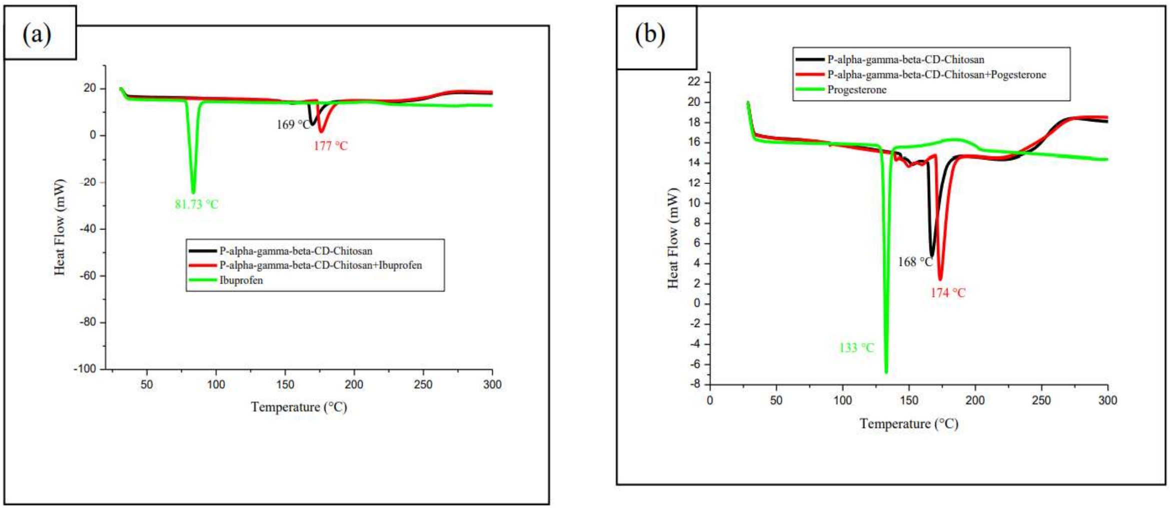

Figure 15. Differencial scanning calorimetry (DSC) of Ibuprofen, Progesterone cyclodextrin-chitosan polymer after and before extraction of ibuprofen and progesterone, (a) cyclodextrin-chitosan polymer after and before removal of ibuprofen, (b) cyclodextrin-chitosan polymer after and before removal of progesterone.

3.7.3. Regeneration of cyclodextrin-chitosan polymer

Cyclodextrin-chitosan polymer is regenerated after progesterone adsorption with a mixture of water/ethanol with respectively the following proportion (70/30), but in case of ibuprofen it was regenerated with distilled water at pH 9, the number of the regeneration cycles (adsorption and desorption) is presented in **Figure 16,** which is investigated with progesterone, after twenty three cycles the removal efficiently remains constant.

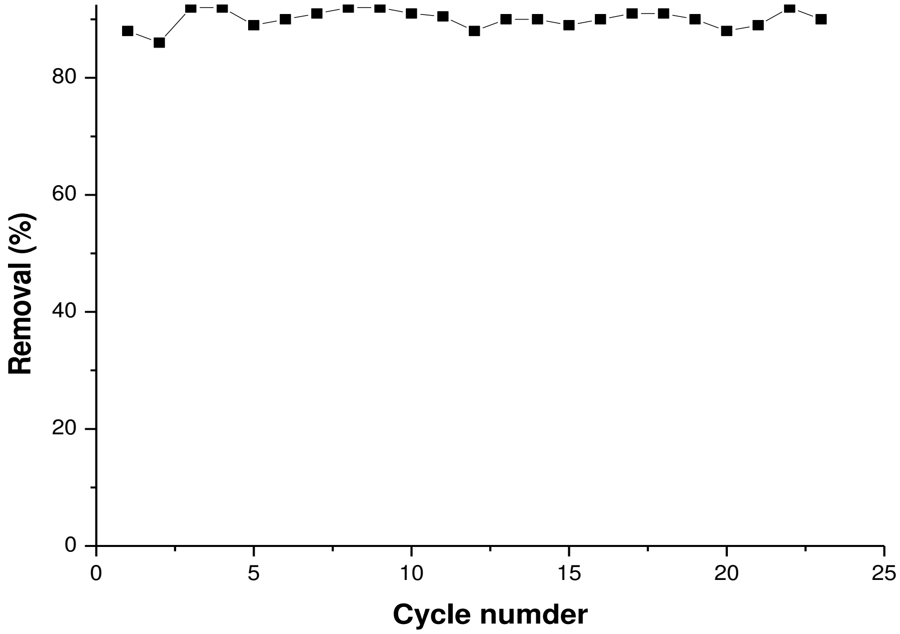

Figure 16. Cycle of adsorption – desorption of chitosan-cyclodextrin polymer.

4. Conclusions

Cyclodextrin-chitosan polymer exhibits high adsorption capacity toward ibuprofen and progesterone, essentially in case of ibuprofen. The combination of chitosan and different cyclodextrins in one polymer lets to the amelioration of the adsorption, comparing to chitosan and cyclodextrin polymer alone. Adsorption kinetic of ibuprofen and progesterone follows pseudo-second order.

Studies of different operator variables show that pH has a significant effect on ibuprofen and progesterone adsorption, ibuprofen removal decreases in alkaline medium, while progesterone extraction is unflavored in acid medium, temperature contributes positively to adsorption of ibuprofen but not for progesterone. Mechanism extraction of the two pharmaceuticals is investigated by using different characterization methods like DSC and DRX, they show that the two pharmaceuticals are extracted by inclusion complex formation between cyclodextrins and pharmaceuticals, and by formation of electrostatic binding in the network of the polymer.

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