Experimental Study of the Ibuprofene's Interaction with Some Natural Supports

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Abstract
The interaction of ibuprofene with two natural solid supports (orange peel and cotton fibre) was studied at three different temperatures (25, 35 and 45 ^{o}C) aiming to establish the best theoretical adsorption model and the corresponding thermodynamic parameters (enthalpy and entropy) of the process. For the investigated systems, the time necessary for attaining the adsorption equilibrium was estimated through a series of preliminary experiments, which indicated periods of time ranging from 195 to 380 minutes. Further, the experimental data resulted from the adsorption process was fitted to the Freundlich and Langmuir classical adsorption models, but also to the Sips and Jossens isotherm models, which were not tested yet in the case of the present studied systems. The obtained results showed that for both investigated systems it was the Sips model which described better the interaction of the model drug with the investigated solid supports.

Introduction
Different ingredients used in pharmaceutical formulation, or in dosage forms can constitute a source of microbial contamination, or can initiate or participate to some physical or chemical interactions with the active ingredients, and this could generate the degradation of the active pharmaceutical compounds, compromising in some extent their therapeutic effect. Orange peel and cotton are natural ingredients presenting a great deal of interest in the pharmaceutical field, and their interaction with drugs was not thoroughly investigated till present. [1-6]

The interaction between drugs and excipients can be studied considering the adsorption isotherms. Usually, the description of the adsorption isotherms onto different excipients was based on classical Langmuir and Freundlich models, which are models with two parameters. However, in different fields of interest (different organic polluants) it was found the two-parameter models showed some limits of application, and thus, models based on more parameters have been developped and used in several studies [7-12]. The interest for this kind of models is maintly due to their accuracy, as well as to their wide range of applicability.

Experimental
Ibuprofene (98%) was supplied by Aldrich Sigma. The cotton was purchased from a local drug store and the orange peel was prepared in our laboratory from Washington Navel oranges (*Citrus sinensis* "Washington Navel").

The UV-VIS spectroscopy study was carried-out with a CECIL CE 7200 spectrophotometer, using two analytical wavelenghts, e.g. 265 nm and 273 nm.

The experimental study involved in the first stage the preparation of a series of stock solutions containing Ibuprofene in 0,1 M NaOH aqueous solutions and the measurement of the optical density of the drug solutions at 265 nm and 273 nm. The obtained results were

used in order to obtain the corresponding calibration curves, according to Lambert-Beer law. In the first stage, we investigated the time necessary to reach the adsorption equilibrium. Further, based on these results, we investigated the extent of adsorption of the drug on the specified solid supports. The preliminary experiments were carried-out according to some previous works [7-12], using each time 10 mL of an initial ibuprofene solutions and 0,2 g (±0,0001) of solid supports. The mixtures were placed in a shaking bath which was set at different temperatures (ranging from 25, 35 and 40^{o}C (± 1^{o}C)) and were shaken for different periods of time (12-60 h). At the end, the mixtures were filtered, and the distribution of the drug between solution and support was assesed spectrophotometrically, using the Lambert Beer's plot previously obtained.

The adsorption isotherms of the ibuprofene on the two investigated supports were obtained according to a similar procedure, starting from drug solutions of different concentrations, namely 1x10^{-5} to 3,2x10^{-4} mol/L. Control experiments, in which no drug was added, were performed in parallel, and the filtrate was used as a reference solution. The experiments were performed in triplicate, the values used in the analysis of the adsorption processes representing the average values of the three experiments.

In order to calculate the amount of the adsorbed drug on the solid support, equation (1) was used:

$$[D]_{ad} = ([D]_i - [D]_s) \cdot V / 1000 \cdot m \qquad (1)$$

where $[D]_{ad}$ represents the equilibrium drug concentration on the solid supports (mmol/g), $[D]_i$ is the initial concentration, $[D]_s$ the equilibrium concentration of the drug solution (both in mmol/L), V is the volume of drug solution (L), and m represents the amount of the solid support (g).

Results and discussion

In this present work, the investigation of the interaction of Ibuprofene with two natural supports was carried-on as a function of drug concentration and temperature. The sorption isotherms (see Figure 1) were obtained at the three mentioned temperatures, at the optimised condition of shaking time, which were established through preliminary experiments (see Table 1).

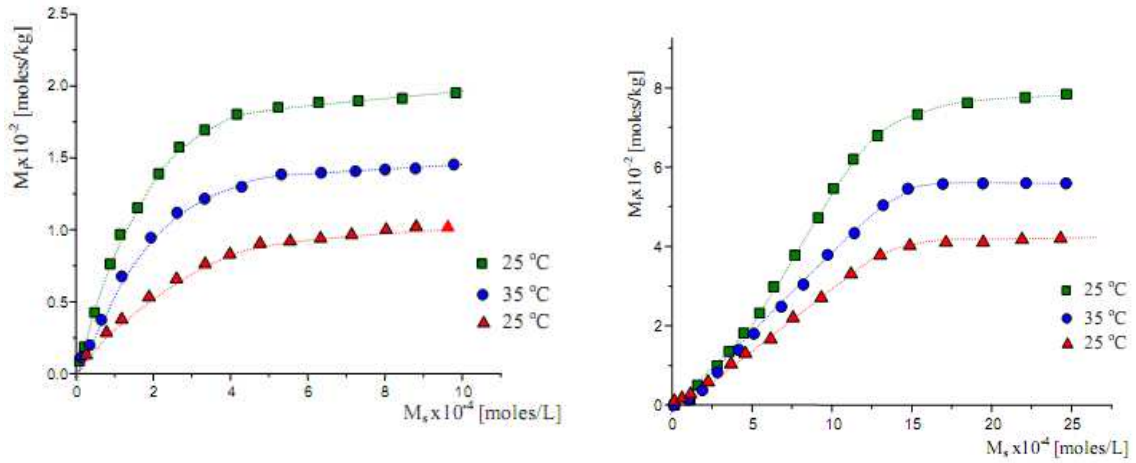
Table 1. Equilibrium time for the adsorption of Ibuprofen on orange peel and cotton at 25, 35 and 40^{o}C

Solid support	Time [min]	Time [min]	Time [min]
	T= 25 ^{o}C	T= 35 ^{o}C	T= 45 ^{o}C
Orange peel	380	325	270
Coton	335	265	195

As shown in Figure 1, the adsorption of ibuprofene on the two studied solid supports was quite fast in the initial stages, decreasing gradually with the progress of the adsorption process. One could also notice that greater temperatures induced a negative effect onto the adsorption process on both supports. This behavior could suggest that increasing temperature could generate a decrease of the number of accessible sites of the investigated supports. One should also consider that the decreasing sorption associated to the increase of temperature could be explained by the exothermicity of the sorption process, in a similar way with dye-fibre interactions.

The adsorption equilibrium data of Ibuprofen onto the orange peel and cotton were analyzed by non-linear curve fitting analysis, using Origin 6.1 software, in order to fit the experimental data to the considered isotherm models (see equations from Table 2). The principal statistical criteria was the squared multiple regression coefficient (R^2) (see Table 3).

The inspection of data depicted in Table 3 indicate that the isotherm model which provided the best representation of the experimental results was the three-parameter model of Sips. This result suggests that the adsorption process of Ibuprofene on both investigated supports occurs after a combined model: Frendlich and Langmuir, involving a diffused adsorption on low drug concentration, and a monomolecular adsorption with a saturation value - at higher concentrations. For this model, the corresponding thermodynamic parameters: saturation value (S_f), equilibrium constant (K_s) and the value of the parameter n, were calculated. The obtained results are illustrated in Table 4.



a **b**

Figure 1. Adsorption isotherms of ibuprofene on orange peels (a) and cotton (b) at 25°C, 35°C and 45°C.

Table 2. Equations of the theoretical adsorption models

Langmuir	*Freundlich*	*Sips*	*Jossens*
$C_f = \frac{S_f \cdot K_L \cdot C_S}{1+K_L \cdot C_S}$	$C_f = K_F C_S^{1/n}$	$C_f = \frac{S_f \cdot (K_S \cdot C_S)^{1/n}}{1+(K_S \cdot C_S)^{1/n}}$	$Ce = \frac{q_e}{H} exp\left(F \cdot q_e^p\right)$

Table 3. Statistical parameters for the adsorption process of Ibuprofene on orange peel and cotton at 25, 35 and 40°C

Orange peel								
T [°C]	Langmuir R^2	SE	Freundlich R^2	SE	Sips R^2	$SExE^{-2}$	Jossens R^2	SE
25 °C	0,96	0,21	0,873	0,685	0,998	1,75	0,969	0,246
35 °C	0,959	0,17	0,872	0,524	0,995	1,65	0,959	0,218
45 °C	0,965	0,11	0,904	0,297	0,996	0,55	0,976	0,119
Cotton								
T [°C]	Langmuir R^2	SE	Freundlich R^2	SE	Sips R^2	$SExE^{-2}$	Jossens R^2	SE
25 °C	0,973	0,32	0,882	0,656	0,997	1,85	0,971	0,26
35 °C	0,97	0,21	0,87	0,618	0,998	0,85	0,98	0,159
45 °C	0,955	0,12	0,842	0,704	0,998	0,25	0,986	0,157

Table 4. Values of Sips's equation parameters

Support	Temperature [°C]	S_f [mol/kg]	n	K_s [L/mol]
Orange peel	25	6,879±7,886 E^{-2}	0,445±2,235 E^{-2}	2610,4±54,6
	35	6,025±0,086 E^{-2}	0,448±2,035 E^{-2}	2565,78±53,1
	45	5,617±5,986 E^{-2}	0,444±0,835 E^{-2}	1916,67±29,2
Cotton	25	7,203±7,086 E^{-2}	0,283±1,235 E^{-2}	1705,67±13,5
	35	6,491±6,386 E^{-2}	0,283±1,435 E^{-2}	1673,71±12,6
	45	6,584±5,186 E^{-2}	0,298±1,235 E^{-2}	1606,88±16,3

Further, the thermodynamic parameters of the adsorption process were calculated in order to obtain more information about the effect of temperature onto the adsorption process (see Table 5). The Gibb's free energy (ΔG^0), was calculated according to equation (2) and the corresponding enthalpies (ΔH^0) and entropies (ΔS^0) were computed from van't Hoff equation (3), from the slope and intercept of the linear plot of lnK versus 1/T:

$$\Delta G^0 = -RT \ln K_S \quad (2)$$

$$ln\, K_S = \frac{\Delta S^0}{R} - \frac{\Delta H^0}{RT} \quad (3)$$

Table 5. Thermodynamic parametersfor the adsorption of Ibuprofene on orange peel and cotton

Support	Temperature [°C]	ΔG^o [kJ/mole]	ΔH^o [kJ/mole]	ΔS^o [J/mole.K]
Orange peel	25	-18,06	-9,643	83,27
	35	-18,98		
	45	-19,92		
Cotton	25	-18,64	-6,577	41,36
	35	-19,51		
	45	-20,26		

Conclusion

The adsorption isotherms of Ibuprofene ontwo natural supports were studied using two classical isotherm models: Freundlich and Langmuir, as well as two three –parameter isotherm models: Sips and Jossens.

According to the statistical analysis of the obtained results, the Sips model described better the adsorption process in the case of all studied drug-cellulosic supports systems.

The values of the corresponding thermodynamics parameters of the sorption process indicate that the process is spontaneous and exothermic.

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