USE OF SOME NATURAL SUPPORTS FOR THE ADSORPTION OF THEOPHYLLINE FROM AQUEOUS SOLUTIONS

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Abstract
In this work, the interaction of Theophylline with lemon peel and olive leaves (two natural solid supports) was studied at 25, 35 and 45 ^{o}C in order to identify the most appropriate theoretical adsorption model, as well as the corresponding thermodynamic parameters (free energy of Gibbs, enthalpy and entropy) of the adsorption process. In the first stage, the time necessary for attaining the equilibrium was established in a series of preliminary experiments, which indicated periods of time ranging from 182 to 356 minutes. The experimental data obtained from the adsorption process was fitted to the Freundlich and Langmuir classical adsorption models by linear regression analysis. The obtained results indicate that for both studied systems, the Langmuir model described better the interaction of Theophylline with the solid supports taken in work.

Introduction

Adsorption of pharmaceutical substances on different solid supports influences the bioavailability as well as other characteristics of the active substances. Despite this, the number of studies on the adsorption of pharmaceutical substances on different solid supports or excipients is quite limited in the speciality literature. The study of the adsorption process of drugs on some natural supports (peel of citrus fruits and other plant waste, different species of wood, cotton, jute, etc) is even more poorly represented in the literature of specialty, despite its rich potential application in the pharmaceutical field, and its implications on the health of the environment, especially with regard to the purification of residual waters [1-4].
Citrus (oranges, lemons, etc) are known for their antioxidant activity, which results from their rich composition in phytochemical components. The peel of these fruits is particularly rich in nutrients, presenting also an important antimicrobial activity. For this reason, one could use them both as drugs and dietary supplements. Since the number of antibiotic-resistant pathogens becomes increasingly large, in-depth research on such compounds becomes highly topical [5-11].
In the last years, olive leave extracts have been found to preserve the immune system, also acting against viral bacterial and fungal infections. It was also found that this vegetal material improves blood circulation, prevents and treats hypertension and arteriosclerosis. [12-17].
Theophylline is a methylxanthine type alkaloid, acting as a diuretic, stimulant, bronchodilator and as lipolytic agent. Theophylline acts at the level of intracellular calcium movements. It has a broncho-dilatatrice action, strengthening the respiratory muscles and with inotropic cardiac positive action. Theophylline is also a phosphodiesterase inhibitor [18].
The aim of this present work is to study the adsorption process of some aqueous solutions of Theophylline on two natural supports: the lemon peel and the olive leaves, at different temperatures, in order to obtain original experimental data whose analysis could provide

information of great interest onto the interaction of this active substance with the specified solid supports.

Experimental

Theophylline (1,3-Dimethyl-7H-purine-2,6-dione) was supplied by Aldrich Sigma as a reagent of high purity (99%). The solid supports used as adsorbents were the lemon peel originating from Eureka lemon variety (*Citrus lemon L.)*and olive leefs *(Olea europaea)*. Lemons were purchased from a local market (Timișoara, Romania) and the olive leefs were collected from Tunisia in march 2016. The vegetal materials were washed with tap water, then with de-ionized water, and dried in the shade at constant temperature for several days. Thereafter, they were dried in an incubator at 60^{o} ($\pm 5°C$) for 10 hours. The dried materials were grounded into powder (mesh size of about 120 ± 5 micron) with an electrical sieve shaker. The adsorbents thus prepared were analysed by microscopy (Olympus microscope, 400x magnifier) as well as by FTIR spectroscopy, by means of IR JASCO FT-IR 4200 spectrometer, in the wavelengh range of 4000 – 400 cm^{-1}.

The adsorption experimental study was carried out in a similar mode as it was described in previous work [4,19]. The measurement of the optical density of the drug solutions at 270 nm was performed on a Perkin-Elmer-Lambda-950 spectrophotometer. The calibration curve was obtained, according to Lambert-Beer law. The adsorption experiments were carried out in a Julabo ED 5M bath, at 25, 35 and $40^{o}C$ ($\pm 1^{o}C$)). The amount of the adsorbed drug on the solid support was calculed according to equation (1):

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

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

Results and discussion

In this work, the study of the interaction of Theophylline with two natural solid supports, e.g. lemon peel and olive leaves powder was carried-on at 25, 35 and $40^{o}C$ ($\pm 1^{o}C$).

The main criteria in the choice of the solid supports were their natural origin, as well as their great potential for pharmaceutical and/or environmental protection applications. The FT-IR spectra of the two adsorbents indicate the complex structure of these adsorbents. The spectra display broad, intense peaks around 3400 cm^{-1} (lemon peel) and 3423,03 cm^{-1} (olive leaves) which could result from the O-H stretching mode of hydroxyl groups, while the bands at 1700-1200 cm^{-1} can be attributed to the aromatic C-C bond. The peaks situated at 1104,05 and 1053,91 1080 cm^{-1} in the case of the lemon peel, or at 1158,04, 1099,23 et 1028,84 cm^{-1} (olive leaves) can be attributed to C-O symmetric or –C-O-C- ring asymmetric stretching vibration. The peaks from the 2000-2400 cm^{-1} region: 2105,89 and 2366,23 cm^{-1} for lemon peel; 2344,05 cm^{-1} in the case of olive leaves could indicate the carbon dioxide from normal air [20].

Generally, the results of adsorption processes can be reported as sorption isotherms, the most used in the case of drugs being the Freundlich and Langmuir classical models described by equations (2) and (3):

$$[D]_s = K_F \cdot [D]_{sol}^{x} \qquad (2) \qquad \frac{1}{[D]_s} = \frac{K_L}{S_f \cdot [D]_{sol}} + \frac{1}{S_f} \qquad (3)$$

where $[D]_s$ represents the drug concentration in the support at equilibrium, in mol/kg dry support, $[D]_{sol}$ represents the drug concentration in solution at equilibrium, in mol/L, K_F is the Freundlich

equilibrium constant and x is a sub-unitary power; S_f is the saturation value in mol/kg fibre and K is the equilibrium constant.

The sorption isotherms of Theophylline on the two natural supports (lemon peel and olive leaves) were obtained at the three mentioned temperatures, at the corresponding times established through the preliminary experiments, which are presented in Table 1.

Table 1. Equilibrium time for the adsorption of Theophylline on lemon peel and olive leaves at 25, 35 and 40°C

Solid support	Time [min]	Time [min]	Time [min]
	T= 25 °C	T= 35 °C	T= 45 °C
Lemon peel	356	310	254
Olive leaves	321	245	182

In order to find out the classical model which fitts better to the adsorption of Theophylline on lemon peel and olive leaves respectively, the experimental data resulted from this study were fitted by linear regression analysis to the general equations (4) and (5), corresponding to the Freundlich and Langmuir models:

$$\ln y = b_o + b \cdot \ln x \qquad (4)$$

$$y^{-1} = b_o + \frac{b}{x} \qquad (5)$$

where y represents the drug concentration in the support at equilibrium, x the drug concentration in solution at equilibrium, b_o the logarithm of the equilibrium constant (K_F), b a sub-unitary power; b_o is $1/S_f$ and b represents K_L/ S_f.

The linear regression analysis was performed by means of the STATISTICA package [21].The main statistical criteria were the squared multiple regression coefficient (r^2), the standard deviation (SE) and the Fischer test (F). The obtained results are shown in Tables 2 and 3.

Table 2. Statistical parameters for the adsorption process of Theophylline (THP) on lemon peel (LEP) and olive leaves (OLL) at 25, 35 and 40°C , according to equation (4)

System	Temp. [°C]	b_o	b	r^{2*}	SE*	F*
THP-LEP	25	3,036±0,0429	0,591±0,049	0.968	0.178	139.81
	35	3,021±0,0431	0,589±0,063	0,972	0,206	116,24
	45	3,014±0,424	0,595±0,053	0,969	0,114	198,47
THP-OLL	25	2,651±0,028	0,498±0,038	0,971	0,119	176,67
	35	2,751±0,345	0,506±0,041	0,965	0,311	103,12
	45	2,552±0,332	0,499±0,039	0,972	0,138	164,47

Table 3. Statistical parameters for the adsorption process of Theophylline (THP) on lemon peel (LEP) and olive leaves (OLL) at 25, 35 and 40°C , according to equation (5)

System	Temp. [°C]	b_o	b	r^{2*}	SE*	F*
THP-LEP	25	2,440±0,0703	$0{,}010.10^{-3}\pm0{,}021.10^{-6}$	0,999	0,182	16392,18
	35	2,312±0,0661	$0{,}011.10^{-3}\pm0{,}029.10^{-6}$	0,998	0,296	10820,12
	45	2,319±0,0597	$0{,}012.10^{-3}\pm0{,}048.10^{-6}$	0,997	0,232	13969,48
THP-OLL	25	1,621±0,0482	$0{,}011.10^{-3}\pm0{,}011.10^{-6}$	0,996	0,291	9875,45
	35	1,5312±0,0454	$0{,}009.10^{-3}\pm0{,}007.10^{-6}$	0,998	0,224	143959,42
	45	1,543±0,446	$0{,}011.10^{-3}\pm0{,}010.10^{-6}$	0,997	0,251	11784,62

The values of the thermodynamic parameters: the Gibb's free energy (ΔG^0), the enthalpy (ΔH^0) and the entropy (ΔS^0) are presented in Table 4.

Table 4. Caracteristic thermodynamic parameters for the adsorption process of Theophylline on lemon peel and olive leaves

Solid support	Temperature [K]	ΔG^o [kJ/mole]	ΔH^o [kJ/mole]	ΔS^o [J/mole.K]
Lemon peel	298,15	-20,43	-9,235	80,23
	308,15	-21,07		
	318,15	-21,7		
Olive leaves	298,15	-19,97	-8,172	67,36
	308,15	-20,61		
	318,15	-21,15		

Conclusion

The adsorption isotherms of Theophylline on lemon peel and olive leaves were studied using Freundlich and Langmuir isotherm models.

The statistical analysis of the experimental results indicates that the Langmuir model describes better the adsorption of Theophylline on lemon peel and olive leaves.

The corresponding thermodynamics parameters of the adsorption process were calculated and their values show the spontaneity and the exothermicity of the studied processes.

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