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Synthesis and characterization of polyacrylamide hydrogel for the controlled release of aspirin

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Abstract

Background: The hydrogel is hydrophilic polymer that has the ability to absorb, yet not dissolve in, water at physiological conditions (pH, temperature and ionic strength). This porosity of hydrogel allows drugs loading into the gel matrix, and then release, at a diffusion coefficient-dependent rate of the gel network. Therefore, this study was conducted to study adsorption-desorption systems of drug (aspirin) on selected surfaces (polyacrylamide hydrogel) at variable conditions of pH and temperature. Methods: The adsorption experiments were done by using the UV-Visible spectrometer. Hydrogels of polyacrylamide (PAAm) were prepared by free radical polymerization. Chemical structures of polymer hydrogels were analyzed by FTIR (Fourier transform infrared spectrometer). Results: When the adsorption phenomenon was examined as at three different temperatures (15, 25 and 37°C), it was found that the extent of adsorption of aspirin on hydrogel was increased with temperature lowering (exothermic). The quantities of drug that were adsorbed on the hydrogel surface at different pH, were in the following order: 7.2 < 4.0 < 1.2. Therefore, a hydrogel can be used for aspirin adsorption from solution and the Freundlich isotherm model can describe aspirin adsorption adequately

Key words: Aspirin, adsorption, hydrogel, desorption, polymer.

1. INTRODUCTION

The hydrogel is hydrophilic polymer that has the ability to absorb, yet not dissolvein, water at physiological conditions (pH, temperature and ionic strength), because of the presence of a three-dimensional network structure [1]. The cross-links of the network could be represented by covalent bonds, electrostatic, hydrophobic or dipole-dipole interactions while the hydrophilicity is attributed to the presence of hydrophilic groups, such as hydroxyl, carboxyl or amide groups along the polymer chain[2]. So the polymeric hydrogel has two main features: cannot dissolve due to the covalent crosslink and the water uptakes far in excess of those achievable with hydrophilic linear polymers can be obtained [3]. The porosity of hydrogel allows drugs loading into the gel matrix, and then release, at a diffusion coefficient-dependent rate of the gel network [4]. A depot formulation is made from which drugs elute slowly with the maintenance of a high local concentration of drug in the surrounding tissues over an extended period [5]. In general, there are three integral parts of the hydrogels preparation: monomer, initiator and cross linker. For controlling the heat of polymerization and final hydrogel properties, diluents can be used, such as water or other aqueous solutions [6]. Polyacrylamide (PAAm) is a neutral hydrogel that is suitable for drug delivery systems as it is biocompatible, chemically inert and nontoxic. The formation of PAAm gels depends on several factors, including the concentration of acrylamide, the acrylamide: N, N'-Methylene bis acryl amide (MBA) weight ratio, and the presence of additives or solvents other than water used for gel preparation. Therefore, it is important to understand the physical properties of the gels and the influence of additives, like a drug, on the gel properties [7]. Aspirin is an anti-inflammatory and antipyretic drug used in the treatment of mild to moderate pain. It acts as an inhibitor of cyclooxygenase that leads to inhibition of prostaglandins biosynthesis. Aspirin also used for prevention of arterial and venous thrombosis by inhibiting platelets aggregation [8].

Therefore, the objective of current study was to study adsorption-desorption systems of drug (aspirin) on selected surfaces (polyacrylamide hydrogel) at variable conditions of pH and temperature.

2. MATERIALS AND METHODS

2.1. Materials

Monomer, acrylamide (AAm), initiator (Potassium Persulfate, APS) and crosslinking agent (N,N'-Methylene bis acrylamide, MBA) were purchased from Merck reagent Co., sodium hydroxide and hydrochloric acid were purchased from BDH reagent Co., aspirin is a model drug was purchased from Sigma-Aldrich Chemical Co.

2.2. Preparation of hydrogels

Acryl amide aqueous solution (1g/mL) was heated to 45°C under nitrogen protection in a three-necked round bottom flask equipped with a reflux condenser and a stirring apparatus. Then 1.25 mL of 1% MBA was added to the aqueous solution, 1 mL of APS (5g/100 mL water) as an initiator, and finally, 1.25 mL of 1% TEMED aqueous solution. The reaction was stopped after 2 h and the prepared hydrogel was poured into a Petri dish and dried in the oven at 50°C for 24 h, then soaked in distilled water for one day to remove any possible residual monomers and dried in vacuum at 80 ◦C for 5 h. to form cross-linked polyacrylamide hydrogels.

2.3. Preparation of calibration curve

The wavelength of maximum absorbance (λ_{max}) was recorded for model drug aspirin dissolved in aqueous media and found 275nm (Figure 1). This wavelength was utilized for aspirin standard curve construction in the range of 10 to 250 ppm that falls in the region of applicability of Beer-Lambert's law (Figure 2).

2.4. Determination the adsorption isotherm

0.05 g of the prepared hydrogel was mixed with 10 mL solutions containing drug concentrations from 10 to 250 ppm. The mixtures shacked for 45 minutes and centrifuged 3000 rpm for 10 minutes. Then drug concentration in the suspensions was determined spectro-photometrically. The amount of drug adsorbed was calculated by using the following equation:

$$\frac{x}{m} = \frac{V(C_o - C_e)}{m}$$

Where x: adsorbed quantity (mg), m: adsorbent weight (g), C_o: initial concentration (mg/L), C_e: concentration at equilibrium (mg/L) and V: volume of solution (L).

2.5. Factors affecting adsorption

Two factors were studied and their effect on the adsorption process were determined; temperature and pH. Adsorption experiment were done at 15, 25 and 37°C to estimate the basic thermodynamic functions and also were carried out as a function of pH (1.2, 4.0, 7.1) using a fixed drug concentration.

2.6. Desorption Experiments

Different concentrations of each adsorbate were added to 0.05 g of surface and placed in the water bath at 37°C. After equilibration, the suspensions were centrifuged and the

supernatant was decanted. A 10-mL volume of DW was added, shaked for 60 min, centrifuged, clear supernatant was decanted again and the adsorbate quantity was determined.

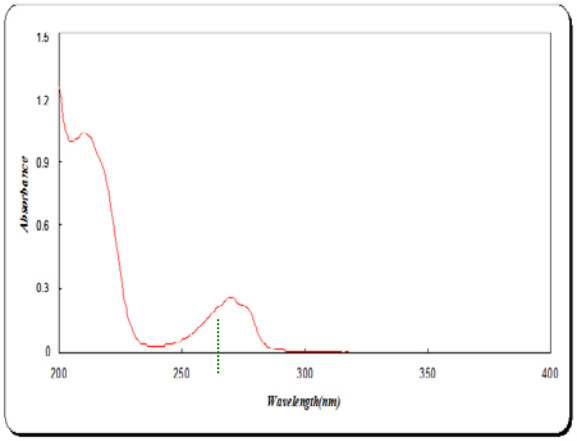

Figure 1: UV spectrum of Aspirin

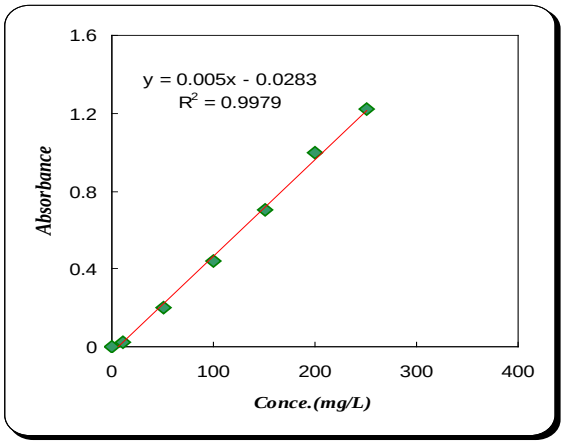

Figure 2: Aspirin calibration curve at λ max 275 nm

3. Results and Discussion

3.1. Fourier transform IR measurements

The disk was prepared by grinding the dried hydrogel with KBr and compressing the mixture then recording FTIR spectra. The spectra were recorded before and after the adsorption of the drug on hydrogel (Figure 3 and Table 1).

Table 1: FTIR of assignment groups of adsorbents

Wave number (cm^{-1})	Assignment groups
3494	N-H Stretching of amide
3178	Hydrogen-bonded
2947	C-H (-CH_2) Stretching
2792	N-H Stretching
1697	C=O carbonyl group of acrylamide
1589	N-H bending
1404	C-N Stretching
1319	C-O Stretching in Carbonyl group of the amide
1195	C-C Stretching
1118	C-H bending alkanes
972	C-H bending

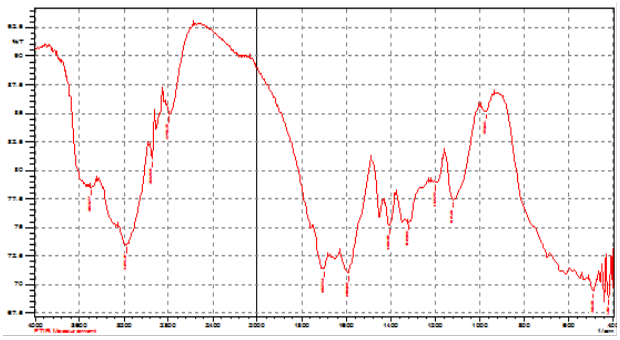

Figure 3: FTIR spectra of adsorbents

3.2. Adsorption Isotherm

Drug adsorption from aqueous solution on hydrogel was studied at different temperatures (15, 25 and 37°C) and the obtained adsorption isotherm is given in Figure 4. The adsorption efficiency and surface effectiveness was increased with increasing initial drug concentration [9] while adsorption capacity depends on many parameters; one of them is the specific surface area [10].

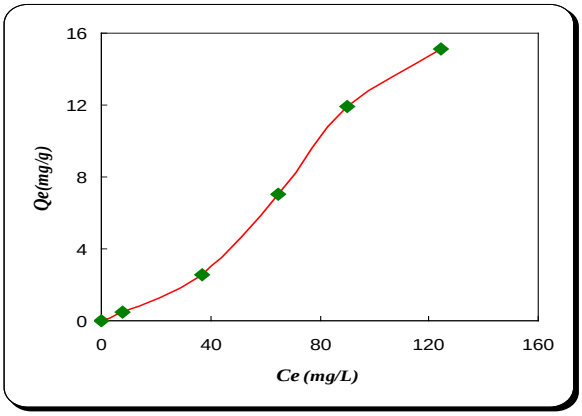

Figure 4: Adsorption isotherm of Aspirin onto hydrogel (at 15 °C)

According to Giles, the shape of drug isotherm can be classified as S-type which depends on Freundlich assumption about surface heterogeneity [11]. Presence of various planes usually results in heterogeneous adsorption behavior which is an expected feature due to different unsaturated adsorption sites with different energetic behavior [12]. Adsorption isotherm (Langmuir and Freundlich models) can be used to mathematically express the equilibrium of drug removal.

The relationship between adsorption heat variation and adsorbate concentration may be accounted for empirically by using the Freundlich equation which has the general formula [13].

$$Q_e \text{ or } \frac{x}{m} = kC_e^{1/n}$$

Where Q_e: amount adsorbed per unit mass of adsorbent, C_e: equilibrium concentration of solute, k: Freundlich constant, (if C_e = 1, k is equal to adsorption capacity); and n: an exponent related to the intrinsic heat of solute adsorption [14].

The results of current study (Figure 5) also showed that a linearized Freundlich model was obtained for the drug adsorption isotherm (a linear relationship between **logQ_e** and **logC_e**)

$$\log Q_e = \log k + \frac{1}{n}\log C_e$$

Correlation coefficient and Freundlich constant values showed that isotherm data fit the Freundlich model [15] (Table 2).

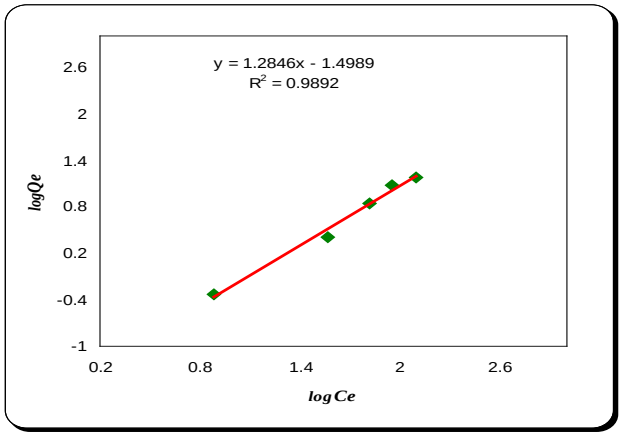

Figure 5: Aspirin Freundlich isotherm on hydrogel

Table 2: Freundlich constants for aspirin adsorption on hydrogel

N	K_f	r
0.8656	0.4457	0.9892

3.3. Temperature effect

The effect of temperature, in the range of 15, 25 and 37 °C, on drug adsorption is shown in (Fig. 6).

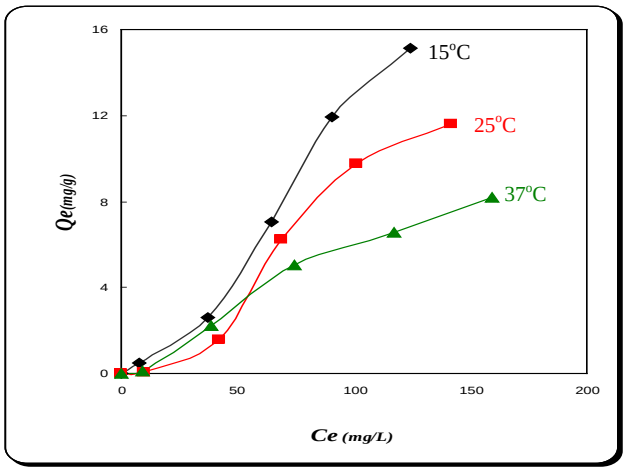

Figure 6: Adsorption isotherms of aspirin on hydrogel at different temperatures

Temperature elevation is accompanied by adsorption capacity increment of the hydrogel (the higher the temperature is better the adsorption).

Information about bond strength, randomity and spontaneity can be obtained by thermodynamic treatment of adsorption process. It is important to note that an essential prerequisite for adsorption studies at different temperatures is taking into consideration the changes in solution density and substance solubility with temperature [16].

The heat change that occurs when a solution is brought in contact with a solid is not as simple to be considered as the evolved heat of adsorption of a single gas by a solid. The former is usually very smaller and can be obtained by measuring the concentration required to produce a given amount of adsorption at different temperatures [17,18].

The heat of adsorption (ΔH) can be determined from the following equation:

$$\ln X_m = \frac{-\Delta H}{RT} + Constant$$

Where X_m is the maximum adsorption at a certain equilibrium concentration (C_e)

Thus, a plot of lnX_m against $1/T$ gives a straight line with a slope equal to $-\Delta H / R$

When equilibrium is established, the equilibrium constant (K) for the adsorption process at each temperature can be calculated as follows [19]:

$$K = \frac{Q_e \times m(g)}{C_e \times V(L)}$$

q_e: quantity adsorbed in *mg/ g*,

C_e: equilibrium concentration of the adsorbate in *mg/ L*,

m: weight of adsorbent (g) and *V*: volume of adsorbate solution (*L*).

ΔG (change in free energy) may be calculated from the equation:

$$\Delta G = -RT\ln K$$

ΔS (change in entropy) can be obtained from Gibbs equation:

Substituting ΔG from the equation, then:

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

$$\ln K = -\frac{\Delta H}{RT} + \frac{\Delta S}{R}$$

If *ln K* plotted versus *1/T*, we would obtain a straight line having a slope of $-\Delta H / R$ and an intercept $\Delta S / R$.

Table 3 and Figure 7 demonstrate these parameters while Table 4 shows the values of thermodynamic calculations of aspirin adsorption onto hydrogel [20].

Table 3: The relation between temperature and aspirin maximum adsorption quantity on hydrogel

T (k)	10^3 / **T**(k^{-1})	X_m (mg / g)	Ln (X_m)
		Ce = 124.4	
288	3.472	15.1	2.715
298	3.355	10.9	2.389
310	3.225	6.9	1,932

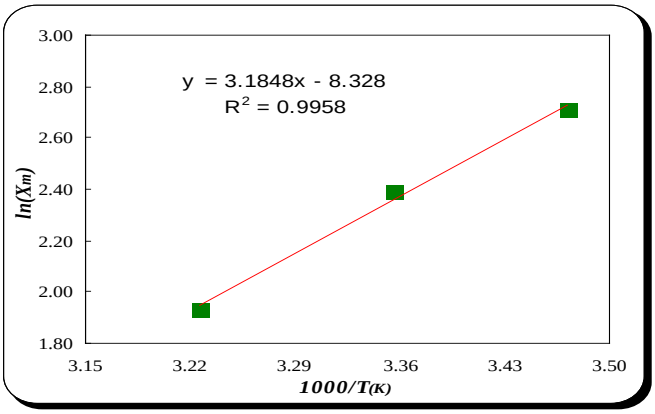

Figure 7: ln Xm against reciprocal absolute *T*

Table 4: Thermodynamic parameters for aspirin adsorption on hydrogel

T(°C)	**K**	**ΔS** ($J.mol^{-1}.k^{-1}$)	**ΔG** ($kJ.mol^{-1}$)	**ΔH** ($KJ.mol^{-1}$)
15	1.752	-84.598	-0.253	-26.478

The negative value of ΔH indicates exothermic adsorption process

that is possibly explained by the fact that the drug and surface are both solvated in water. Therefore for a drug to be adsorbed, it has to lose part of its hydration shell. This dehydration process of the drug and surface requires energy [21].
So, the adsorption processes exothermicity will be superseded by dehydration processes. The drug diffusion into the chemical structure of the adsorbent is manifested by, or concluded from, the negative ΔS and ΔG values.

3.4. pH effect

The effect of initial pH of the solution on the amount of drug adsorbed was studied at 1.2, 4.0 and 7.2 pH values. An increase in initial pH decreases the amount of drug adsorbed (Figure 8). Solution pH affects the surface charge of adsorbent, and therefore the adsorption process, through functional groups dissociation [22].

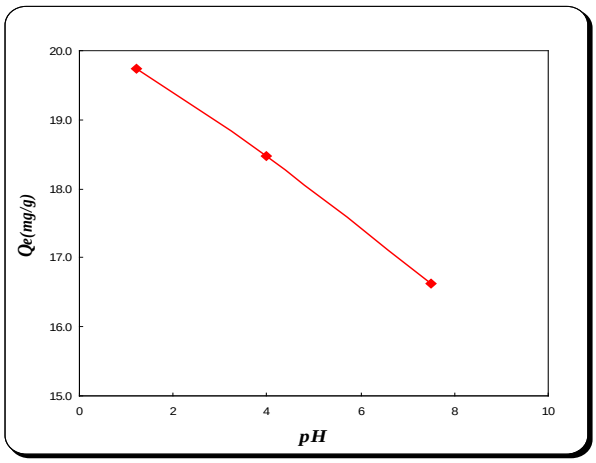

Figure 8: Relation of pH to aspirin uptake by hydrogel at 20°C

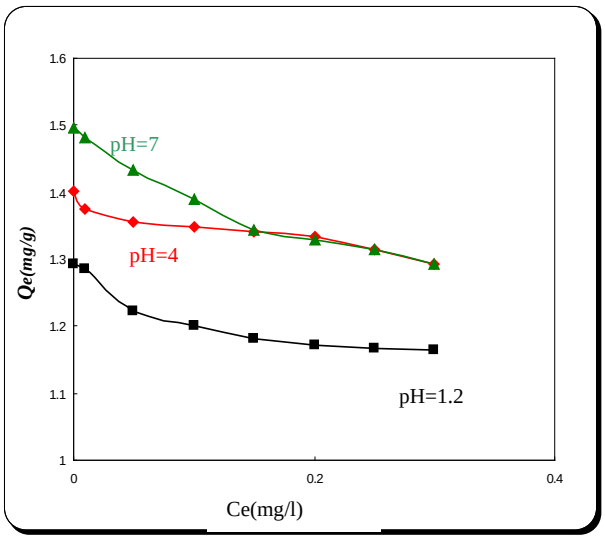

Figure 9: Releasing of aspirin from hydrogel as a function of amount adsorbed at 37°C

3.5. Release process

At low temperatures, adsorbed species may remain on surface almost indefinitely. As the temperature is raised, the thermal energy of the adsorbed species increased and a point will be reached at which one of the following changes may occur:

1- Gas products or other surface species may be yielded by molecular decomposition,
2- The reaction of adsorbate with the substrate to form a specific surface compound or diffuse into the bulk of the underlying solid or
3- Species desorption may occur from the surface and return to original state.

If there is no decomposition, the desorbing species will generally be the same as that originally adsorbed, but this is not necessarily always the case [23]. There are many factors that may affect the desorption process in solution such as the nature of adsorbate and adsorbent surface, pH, temperature and solvent nature [24]. Rapid and complete desorption may be achieved if a suitable solvent or a strongly competitive adsorbate has been used [25]. For solid surfaces, desorption is an important process in the determination of surface area [26].

4. Conclusions

Depending on experimental results of current study, we can conclude that a hydrogel can be used for aspirin adsorption from solution and the Freundlich isotherm model can describe aspirin adsorption adequately. Adsorption process of the drug on hydrogel was exothermic as confirmed by thermodynamic studies. ΔG value is negative for a system that indicates a spontaneous process. The drug removal percentage was depending on the pH and temperature of the solution.

Ethical Clearance: It was obtained from the Research Ethics Committees in the College of Pharmacy and College of Education/ University of AL-Qadisiyah, Iraq.
Financial Disclosure: There is no financial disclosure.
Conflict of Interest: None to declare.

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