Kinetic and Thermodynamic Studies for Mebeverine hydrochloride
Adsorption from Aqueous Solution using prepared chitosan polymer
in delivery drug system

Jubran G. JabbarAlmukhtar¹, Faiq F.Karam²
¹,²Chemistry department, College of Science, University of Al-Qadisiyah
jubran.gazwan@gmail.com

ABSTRACT

In different applications, pharmaceutical products are widely distributed and frequently released into the environment. The adsorption of Mebeverine hydrochloride (MB.HCl) on chitosan polymer was studied under certain conditions. The Adsorption Isotherms can be well defined using the Freundlich and Temkin equations. The pH of the solution significantly influences the adsorption potential of chitosan, the adsorption of chitosan increased from the initial pH of 1.1 and then decreased over the (2-10) pH range. Adsorption is sensitive to the change in ion strength, indicating that electrostatic attraction is an important mechanism for the sorption process. Adsorption of chitosan to MB.HCl is defined as endothermic adsorption by enthalpy change (ΔH). The value of the (ΔG) is negative at all the temperatures studied, which suggests the spontaneous trend to adsorb MB.HCl to chitosan. The value of (ΔG) decreased when the temperature rose from 5°C to 25°C, indicating higher adsorption of MB.HCl at an increased temperature. The positive value of (ΔS) represents chitosan 's attraction to drugs as well as that randomness on its solid-solution interface

KEYWORDS: Adsorption, Mebeverine hydrochloride, Kinetic, thermodynamic, chitosan drug carrier

1. Introduction

A simple and lowcost adsorbent chitosan prepared from shrimp shell waste was used in the research reported here to adsorb the Mebeverine hydrochloride (MB.HCl)[1].Chitosan (CS) is the most important derivative of chitin which is prepared by the alkaline deacetylation of chitin[2]. The structure of chitosan consists of β-1,4-linked 2-amino2-deoxy-β-D-glucose (deacetylated D-glucosamine) and N-acetyl - D-glucosamine units as shown in figure (1)[3]. According to the United States Food and Drug Administration (USFDA), it is a GRAS
(Generally Recognized as Safe) material and has therefore found a wide range of pharmaceutical and biomedical applications[4]. It is classified as a bioactive agent that has demonstrated a variety of biological properties such as antitumor, immunosuppressive, antifungal, antimicrobial, antioxidant, and wound healing activities. These characteristics, plus other outstanding properties such as non-toxicity, biodegradability, biocompatibility, and low cost, have contributed to its broad medicinal uses, including biomedicine with the potential of therapeutic usage, drug delivery systems. [5]. Mebeverine hydrochloride (MB.HCl) therapy belongs to the anti-spasmodic category of medications, since it stimulates the smooth muscles of the digestive system, causing it to relax, which is used to combat Irritable Intestinal Syndrome (IBS) disorder, which stimulates much of the world's population and chemical structure shown in figure (2)[6]. This study, which is aimed at preparing and using chitosan nanoparticles for MB.HCl will aid many patients from taking MB.HCl orally in reducing their daily drug doses, as most patients taking MB.HCl irregularly to treat colon cramps have been found not to have the necessary therapeutic effectiveness, therefore MB. HCl was loaded with chitosan nanoparticles as a drug carrier.

Figure (1): Chitosan structure

Figure (2): Chemical structure of Mebeverine hydrochloride

2. Materials and methods

Materials

Prepared Chitosan (CS) has been extracted from shrimp shells. Sodium Hydroxide (Fluka), Hydrochloric Acid (Fluka), Mebeverine hydrochloride (RA CHEM PHARMA LIMITED, India), Acetic acid (Fluka), Potassium chloride (Fluka), Sodium Chloride (Fluka), Carbonate Calcium (Fluka).

Methods

Chitosan was produced from the shrimp shells through three-stage (deproteinization, demineralization, and deacetylation)[7, 8], then chitosan solution was prepared by dissolve (0.5g) in (1% acetic acid) a (3 mL) of Chitosan solution was taken and added to the beaker,
followed by 1 mL of MB.HCl drug (10 mg / L) was added and the solution was kept under continuous stirring of 190 rpm for a period of (15min) adsorption between the functional drug group and the Chitosan polymer chain.

3. Result and discussion

The following results were achieved by measure the residual of unabsorbed drug by CS.

3-1. The effect of contact time on adsorption medicine

It is very important to know the time of equilibrium of the adsorption reaction necessary to reach the equilibrium state and completely Saturation of the surface with the adsorbent material. As the time of drug MB. HCl (1mL) (10 mg\L), the equilibrium time was studied on the surface of the chitosan polymer at different times within a range of (0-60) min after fixing all conditions affecting the adsorption reaction such as weight of chitosan (0.5g) volume of chitosan (3mL), The results appeared that the adsorption amplitude increases with increasing response time until it reaches its maximum value in (15 min) as shown in Figure(1). In the event of equilibrium, there is a strong electrostatic attraction between the negative charges on the surface of the chitosan polymer and the positive charges on the surface of the drug [9].

![Figure(3): The equilibrium time for MB.HCl on the chitosan polymer](image)

3-2. Effect of volume of Chitosan solution on the adsorption process:

The results show that an increase in the volume of chitosan surface adsorbent with constant weight (0.5 g) leads to an increase in the adsorption process, which means an increase in the number of active sites prepared for the adsorption drug MB.HCl (1mL) (10 mg\L) also increased the amount of adsorbent to mean electrostatic attraction between the active site and the drug molecules after the saturation stage as shown in figure (2). [7]
Figure (4). Effect of volume of Chitosan solution on the adsorption of mebeverine hydrochloride

3-3. Effect of temperature:

So that the form of exothermic or endothermic adsorption reaction is determined the effect of temperature on the adsorption of MB.HCl over the surface of the chitosan polymer at the varying temperatures (5.15, 25 °C) as shown in Figure (5). We observe a decrease in the adsorption of MB.HCl, with a rise in the temperature due to an increase in the movement of drug particles. [10][11].

Figure (5): Effect different temperature on the chitosan polymer adsorption process

3-4. Thermodynamic functions

Thermodynamic functions have been calculated based on the Vant-HoffArrhenius equation (1). At different temperatures, we can find enthalpy in constant concentration, then by drawing (lnXm) versus (1/T) we can extract enthalpy reaction from slope = (-ΔH/R), as shown in Table (1) and Figure (4), showing the values of enthalpy change, free energy, entropy change, and the equilibrium constant of the adsorption of MB.HCl on the chitosan polymer. The negative value of free energy (ΔG) indicates that the process adsorption occurs (spontaneous). The positive change in entropy (ΔS) indicates an increase in the randomness of adsorbent molecules on the adsorbent surface. Finally, the negative value of the enthalpy change (ΔH) indicates that the adsorption process is an (exothermic process) clarify at the table (2).[12]

\[
\ln \frac{X_{m2}}{X_{m1}} = \frac{\Delta H (T_2 - T_1)}{RT_1T_2} \quad (1)
\]
Table (1): Temperature effect of the adsorbent maximum amount of MB.HCl adsorption on the chitosan surface

| Drug  | T (°C) | T (K)  | $\frac{1000}{T}$ (K$^{-1}$) | $C_e = 8.97$ |
|-------|--------|--------|-----------------------------|----------|
|       |        |        | $X_m$                        | ln$X_m$ |
| Duspitalin | 5      | 278    | 3.597122                     | 8.25     | 2.110213 |
|        | 15     | 288    | 3.472222                     | 7.8      | 2.054124 |
|        | 25     | 298    | 3.355705                     | 7.15     | 1.967112 |

Figure (6): ln$X_m$ versus inverted absolute temperature for the adsorption of MB.HCl to the chitosan polymer

Table (2): Thermodynamic functions of adsorption of MB.HCl for chitosan polymer at 15°C

| Drug      | $\Delta H$ (kJ.mol$^{-1}$) | $\Delta G$ (kJ.mol$^{-1}$) | $\Delta S$ (J.mol$^{-1}$.K$^{-1}$) | Equilibrium Constant (K) |
|-----------|-----------------------------|-----------------------------|-----------------------------------|---------------------------|
| Duspitalin| -4913.82342                 | -6745.18955                 | 6.145523927                       | 3.985507246               |

3-5. Isothermal model of adsorption

Adsorption isotherm of type S4 appears Study Compliance with Freundlich and Temkin isotherms indicating the adsorption multilayer because the surface has heterogenic energy to the active site as shown in Figure (5) and Table (3) where the values of Langmuir Freundlich and Temkin isotherms are clarified.
Figure (7): Isotherms models (A) Lungmuir (B) Freundlich (C) Temkin
Table (3): Amounts of MB.HCl uptake of chitosan polymer at 15°C and application of the Langmuir, Freundlich and Timken equations

| Drug   | Langmuir equation | Freundlich eq. | Tempkin eq. |
|--------|-------------------|----------------|-------------|
|        | $K_L$ (L/mg)      | $q_m$ (mg/g)  | $R^2$       |
| MB.HCl | -0.10244          | -2.49004      | 0.1069      |
|        | $K_F$             | $n$            | $R^2$       |
| MB.HCl | 0.710559          | 0.889686      | 0.9396      |
|        | $K_T$ (L/g)       | $B$ (J/mol)   | $R^2$       |
| MB.HCl | 1.569577          | 2.4627        | 0.8934      |

3-6. Kinetic of Adsorption

Two equation models were considered for the description of speed adsorption drug on chitosan polymer: first pseudo and second pseudo-order. The table (4) displays kinetic, qe, and R2 values, the presence of adsorbent process following pseudo-second-order[13, 14]

Table (4): Adsorption kinetics parameters for the adsorption of MB.HCl on adsorbent chitosan

| Drugs | Pseudo -First Order | Pseud-SecondOrder |
|-------|---------------------|-------------------|
|       | k1 (min^-1)         | qe (mg.g^-1)     | R^2       |
|       |                     | $K_2$ (mg.g^1.min^-1) | qe (mg.g^-1) | h   | R^2 |
| MB. HCl | 0.000006         | 38.03855          | 0.8894    | 17.46564 | 1.973554 | 68.02721 | 1 |

3-7. Effect of pH

The acid function is one of the important factors in controlling the process of drug adsorption on the surface of the chitosan polymer. In this study, the acid function was studied in a variety of media (1.1-10). It was found that the amplitude of the drug adsorption decreased with an increase in acid function. In the case of the drug MB.HCl, the adsorption capacity in the acid media increases compared to the adsorption capacity in the base media due to an increase in positive charges due to ions (H+) on the surface of the chitosan polymer to increase the electrostatic attraction with negative charges of the drug MB.HCl and thus increase the adsorption capacity as shown in figure(6) [15].

Figure (8): Effect of pH values on the adsorption of MB.HCl to chitosan polymer at 15°C
3-8. Effect of Ionic Strength

The presence of salts in solutions plays a major role in the adsorption of drugs on the chitosan polymer, as it affects the adsorption capacity. As salts (NaCl, KCl, and CaCO3) were used at different weights. To interpret some theoretical evidence, if the electrostatic forces between the adsorbate and the adsorbent are attractive in this case, the adsorption decreases while, in contrast, the repulsion increase of the ionic strength increases the adsorption capacity, which also competes between the salt cation and drug on the active site of the chitosan, and is observed whenever the smaller salt ion decreases the adsorption of the capacity as shown in figure (7) [16].

![Figure (9): Effect of ionic strength on the adsorption of MB.HCl in the chitosan polymer at 15°C](image)

Conclusion

Optimal condition for adsorption Mebeverine hydrochloride on chitosan polymer was determined during this study to be used in the delivery drug system. The study showed 15°C, pH=1.2, 0.5 g, and 15min, 91.2% can be removed from the drug in aqueous solution. The study showed adsorption was an exothermic and spontaneous reaction, adsorption on pseudo-second-order was also shown.

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