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Metoprolol Tartrate Drug Loading and Release from Prepared Mesoporous Silica; Kinetic of Adsorption and Release

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Abstract

Mesoporous silica was developed to transport metoprolol tartrate (MPT). The data obtained from the kinetic experiments of adsorption of 15 ppm of MPT drug at 293 K was fitted in the pseudo-first-order, pseudo-second-order, and intraparticle diffusion models. The results show that the adsorption process obeys the pseudo-first-order equation and the rate-controlling step, not just the intraparticle diffusion step. The MPT drug load onto mesoporous silica was 15.13 mg/g. The release profile shows that the MPT drug was about 55% released after 40 min when released in water, while in phosphate-buffered saline (PBS) media, the release reached 90% after 60 min at body temperature (37°C). Three kinetic release versions, including first-order, Kopcha, and Korsmeyer-Peppas, were used to fit the in vitro drug release data. The results indicate that the Korsmeyer-Peppas model provided the best fit. The predicted n values show that the release process for water and PBS pH 7.4 media is not Fickian.

Keywords: Metoprolol tartrate, drug carrier, mesoporous silica, drug release, adsorption kinetics.

1. Introduction

A promising material for drug delivery systems is mesoporous silica (DDS). It is certified by the American Food and Drug Administration (FDA) as "Generally Recognized as Safe" (GRAS), so it can be used as a food additive and in cosmetic products [1]. The instance of these materials in pharmaceutical applications dated to 2001 by Vallet-Regi in the ibuprofen release [2].

Amorphous mesoporous silica has been studied for use in pharmaceutical applications because it is less toxic than the crystalline version [3–5]. For several drugs, mesoporous silica has been employed as a carrier in the adsorption and loading process, including atenolol [6], carbamazepine [7], celecoxib [8], ibuprofen [9], indomethacin [10], ketoprofen [11], methotrexate [12], naproxen [13], piroxicam [14], prednisolone [15], and rufinamide [16]. Recently, this work studied different mesoporous silica-drug systems. The behavior of magnetic mesoporous silica as an adsorbent and delivery system for ciprofloxacin [17], as well as the

kinetics of adsorption and release [18]. Metoprolol is a widely used blood pressure drug; however, because it is weakly soluble in water, it is usually administered in the soluble forms of MPT or succinates. Lopressor (MPT) is a selective β-blocker drug. It slows the heart, allowing it to exert less strain on the body's blood arteries. Slowing the heart puls will enable it to use less oxygen, which alleviates chest pain [19]. In this research, mesoporous silica (MPS) was created using a conventional surfactant as a template, and its suitability as a vehicle for the regulated release of a drug called metoprolol was investigated. A study was done on the adsorption and release rates as well.

2. Materials and Methods

2.1 Mesoporous silica sample

It was created in the manner described in a prior study [20]. By impregnating the synthetic carriers, the drug was loaded onto them. In a normal synthesis, MPT was dissolved in distilled water at an appropriate concentration (100 mg/L). Metoprolol drug solution is then added to the MPS adsorbent, left in the ambient temperature (25°C) and magnetic stirrer position for 24 hours to achieve equilibrium. The MPT supernatant was removed from the centrifuged MPS after it had been spinning at 3000 rpm for 15 minutes in order to determine the concentration of MPT by the UV-visible technique at λ_{max} 274 nm. The drug-loaded MPS composite was subsequently dried for 12 hours at 50°C.

2.2 *In vitro* MPT release study

The following steps were taken to conduct an in vitro investigation of metoprolol release from the MPS carrier: In a typical experiment, a drug-loaded MPS was maintained at 37 °C with continuous shaking (150 rpm) in 100 mL of distilled water or a buffer phosphate solution, pH 7.4. UV spectrometry at 274 nm (SHIMADZU (UV-1800)) was used to measure the drug concentration in the liquid phase after 1 mL of each sample was taken at preset intervals [21].

3. Results and Discussion

3.1 Metoprolol adsorption kinetics

The experimental findings from the adsorption process of 15 ppm of the drug MPT at 293 K were mentioned in **Eq. 1** for pseudo-first-order and **Eq. 2** for pseudo-second-order models [22-24]:

$$\ln (q_e - q_t) = \ln q_e - k_1 t \quad (1)$$

$$t/q_t = 1/k_2 q_e^2 + t/q_e \quad (2)$$

where q_t and q_e were the amounts of MPT adsorbed at time t and at equilibrium, respectively; t was the time of adsorption (min); k_1 (min^{-1}), k_2 ($g\ mg^{-1}min^{-1}$) were respectively the rate constants of pseudo-first-order adsorption and pseudo-second-order adsorption.

Figure 1 displays the plots of the adsorption kinetics. The slope and intercept values from the linear plots of the two equations were used to construct the correlation coefficients (R^2) and adsorption kinetic parameters, which are illustrated in **Table 1**.

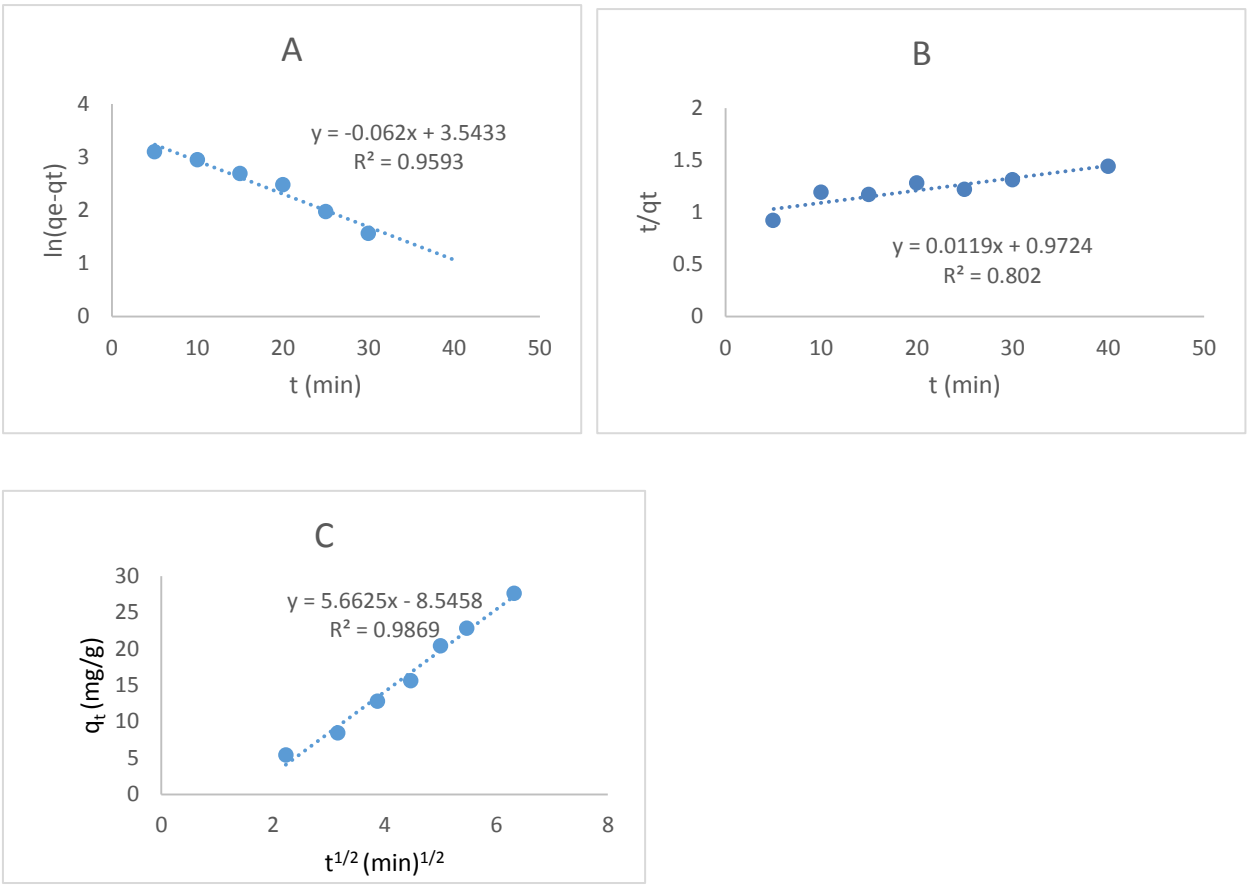


Figure 1. The linear plots of the A) Pseudo first order B) Pseudo second C) Intra particles diffusion kinetics models.

Table 1. The kinetics parameters of the adsorption of MPT drug onto MPS.

qt (mg/g) (exp.)	Pseudo-first-order			Pseudo-second-order			Intraparticle diffusion	
	q_e(cal) (mg/g)	k_1(min)$^{-1}$	R^2	q_e(cal) (mg/g)	k_2 (g/mg/min)	R^2	K_D (mg/g·min$^{1/2}$)	R^2
27.6	34.58	0.062	0.9593	84.033	1.45	0.802	5.6625	0.9869

Table 1 demonstrates that the correlation values R^2 of the pseudo-second order (0.8020) were insufficient. The pseudo-first-order correlation, on the other hand, is (0.9593). In addition adsorption is governed by a pseudo-first-order equation. Furthermore, the observed q_e value agreed well with the q_e obtained from the pseudo-first-order linear plots but not with the q_e acquired from the pseudo second-order linear plots.

3.2 The MPT Adsorption Mechanism

The findings of the kinetic experiments were suited to Weber's intra-particle diffusion model [25, 26] to investigate the adsorption mechanism and define the rate-controlling steps:

$$q_t = K_D\, t^{1/2} + C \quad (3)$$

where: C is the intercept; k_D is the intraparticle diffusion constant (mg/g·h$^{1/2}$). D was calculated from the slope of the linear plot q_t versus $t^{1/2}$. **Figure 1C** shows a linear plot of **Eq. 3** and the results obtained from the slope are presented in **Table 1**.

Intra-particle diffusion can be recognized as a rate-limiting step if the regression of q_t versus $t^{1/2}$ crosses the origin [27]. The results of this investigation show that the plot was linear but did not pass through the origin, implying that other factors, in addition to intra-particle diffusion, may have contributed to restricting the rate of MPT drug adsorption onto MPS.

3.3 Loading and release study

The following **Eq. 4** was used to calculate the quantity of MPT drug loaded in the MPS:

Loading (mg drug/g sample) = $(m_{orig} - m_{solu}) / m_{MPS}$ (4)

Where m_{orig} is the weight of MPT in the 5 mL of solution, m_{solu} is weight of MPT in the solution after impregnation, and m_{MPS} is the weight of the MPS sample. The calculated amount of MPT loaded in the samples is calculated to be 15.13 mg drug/g sample. This loading capacity is consistent with other adsorbent-drug capacities mentioned in earlier research [18, 28, 29]. **Figure 2** displays the MPT-loaded silica sample's release patterns up to 60 minutes in water and PBS solution at 37 °C.

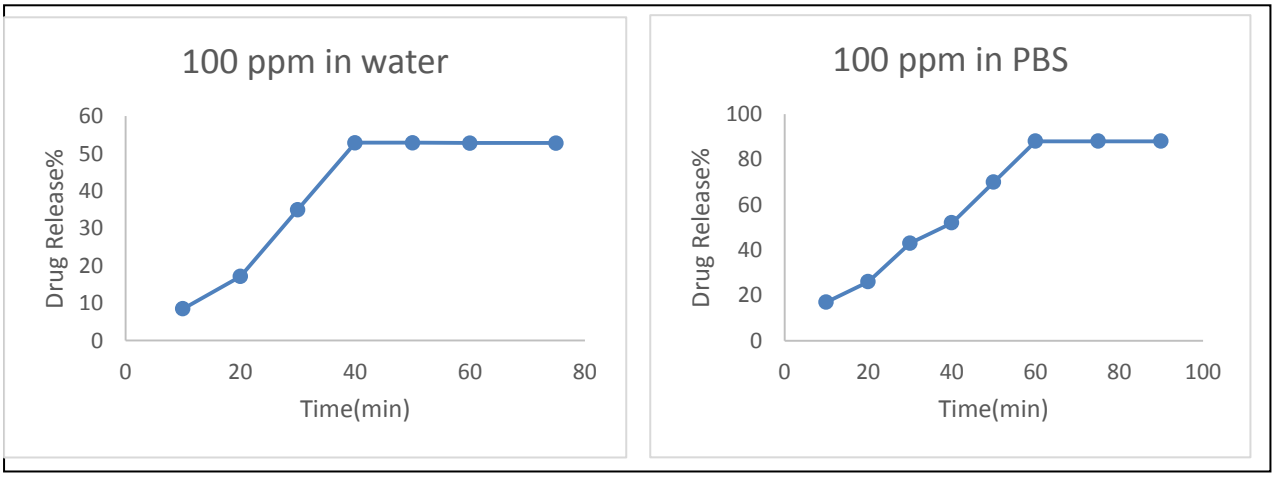


Figure 2. The releasing profile of MPT drug loaded MPS in water and PBS.

The results of **Figure 2** show that the MPT drug was about 55% released after 40 min when the release occurred in water, while in PBS media the release reached 90% after 60 min. In water media, the profile shows a slower release rate in comparison with PBS media, so the release in PBS media was higher, which shows that the drug adsorbs at the adsorbent's porous exterior surface and inside its mesoporous interior [30].

3.4 Kinetics release

Drug discharge kinetics is the primary feature of a drug delivery system that defines the drug release mechanism. The in vitro drug release data was fitted to the Korsmeyer-Peppas (**Eq. 5**), pseudo-first-order (**Eq. 6**), and Kopcha Kinetics (Eq. 7) models of MPT drug release from mesoporous silica carrier. The obtained kinetic curves in water and PBS are presented in **Figures 3** and **4**, and the kinetic functions determined from the intercept and slope of the three models in water and PBS media are listed in **Table 2**.

$M_t / M_\infty = k_{K\text{-}P}\, t^n$ (5)

$M_t / M_\infty = 1 - e^{-kt}$ (6)

$M_t = At^{1/2} + Bt$ (7)

Where $k_{K\text{-}P}$ is a kinetic constant associated with the host-guest pair, n is associated with the host shape and drug release mechanism, and M_t is the quantity of MPT loaded in MPS particles at

time t in minutes. The first-order rate constant k is utilized here. A represents the contribution of diffusion, while B represents the contribution of erosion [31].

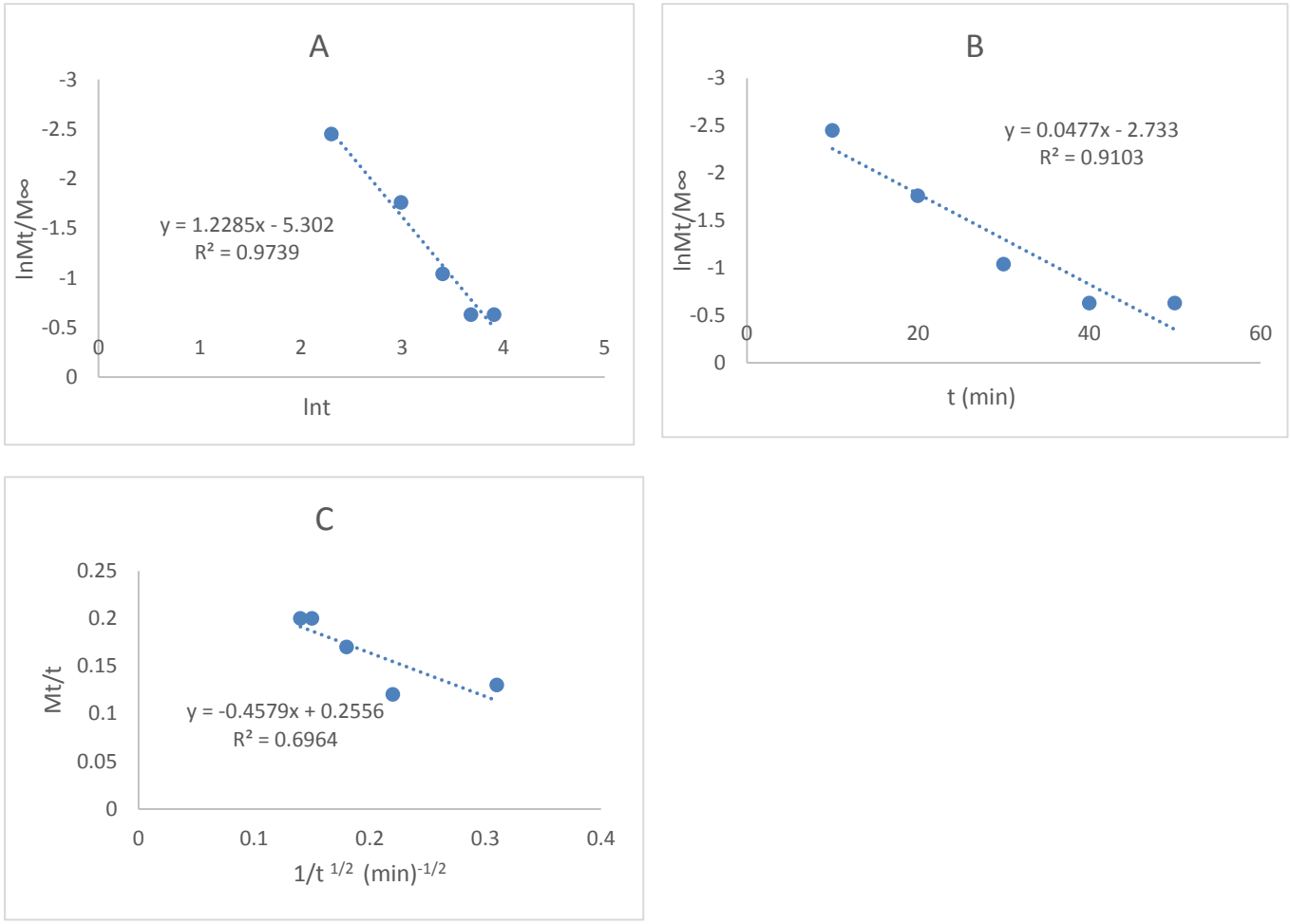
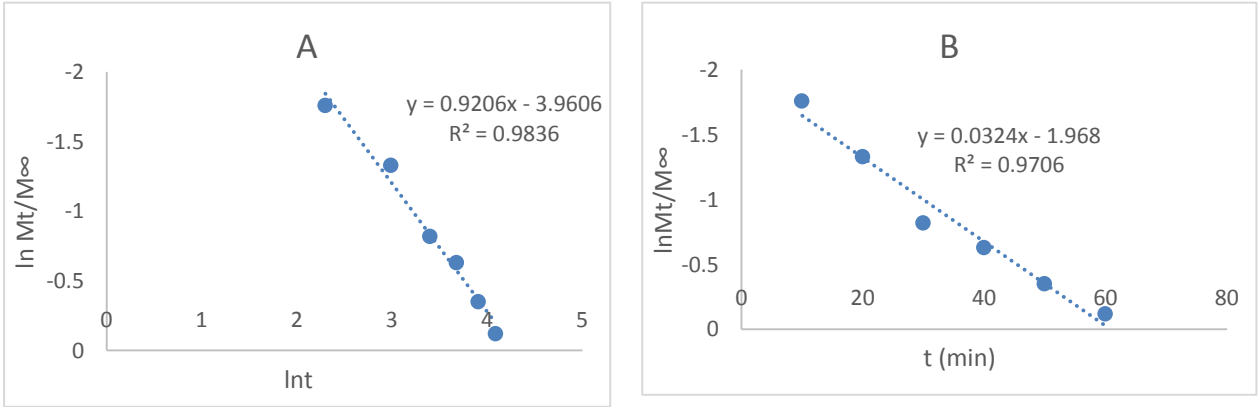


Figure 3. The linear plots of; A) Korsmeyer- Peppas; B) Pseudo first-order; and C) Kopcha models of kinetic release in water media.

Table 2. The kinetics parameters of the releasing of MPT drug from MPS.

Model	Korsmeyer-peppas model			Pseudo-first-order		Kopcha model		
Parameters	**n**	**k_{K-P}**	**R^2**	**k**	**R^2**	**A**	**B**	**R^2**
PBS	0.9206	0.01905	0.9836	0.03	0.9706	0.225	0.176	0.4945
water	1.2285	0.00489	0.9739	0.05	0.9103	-0.457	0.255	0.6964



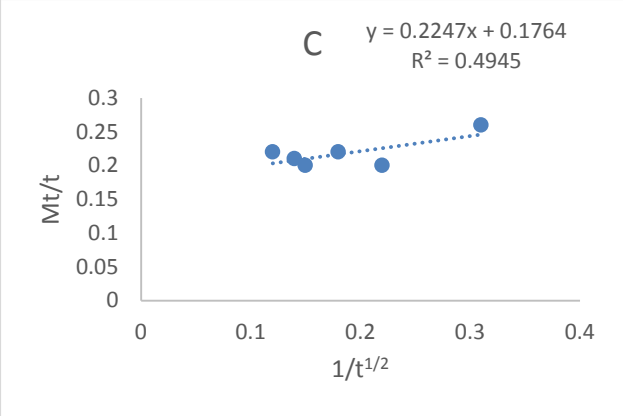


Figure 4. The linear plots of; A) Korsmeyer- Peppas; B) Pseudo first-order; and C) Kopcha models of kinetic release in PBS media.

Based on R_2 values, the Korsmeyer-Peppas model, which allows estimating n from the slope of a linear plot, made the best matches. The estimated n values indicate that the release process for water and PBS pH 7.4 media is non-Fickian. The Fickian diffusion was defined when n was 0.5, and the strange mechanism was defined when n was between 0.5 and 1 [32]. This shows that the release mechanism was as follows: initially, the release was triggered by free drug molecules leaching from the pore's entrance and then the interacting molecules [33,34].

4. Conclusion

Mesoporous silica was effectively created as a carrier for the loading and release of MPT. The loading rate was 15.13 mg/g of substance. The enhanced MPT release was investigated in pH 7.4 PBS medium and water. In water and PBS media, the MPT release duration was 40 and 60 minutes, respectively, with 84% in water and 75% in PBS releasing efficiency. The Korsmeyer-Peppas model provided the best match to the releasing kinetics data, and values of n suggest that non-Fickian diffusion governs the kinetics of MPT release from MPS in both water and PBS media. While the results of the intra-particle diffusion model show that the rate-controlling step was not just the intra-particle diffusion step, the pseudo-first-order kinetics model was the best fit with the experimental data from the adsorption kinetics, indicating that the adsorption process was first-order.

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Conflict of Interest

The authors declare that they have no conflicts of interest.

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Ethical Clearance

This work has been approved by the Scientific Committee at the University of Baghdad/ College of Science for Women.

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