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Preparation on Sustained-Release Drug of Na-MMT-Miglitol

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Abstract. In order to sucessfully prepare Na-MMT-Miglitol composite, the adsorption effect factors of the different concentrations, temperature, pH and time for miglitol were investigated respectively. By means of the adsorption capacity changes of Na-MMT, the maximum adsorption capacity of Na-MMT as the experimental conditions to prepare the sustained-release drug of Na-MMT-Miglitol, in addition, the Na-MMT-Miglitol was characterized by Fourier Transform infrared Absorption Spectrum (FTlR) and Scanning Electron Microscopy (SEM).The results show that the adsorption capacity of Na-MMT can reach maximum adsorption when the experimental conditions of the initial concentration of miglitol 5mmol / L, temperature 40℃, pH 2 and the adsorption time 1.5h were selected. the characterization results of FTIR and SEM can infer that miglitol and Na-MMT are reacted to prepare Na-MMT-Miglitol composite successfully.

Introduction

The main purpose of sustained-release drug is to reduce allergic reaction and toxic symptoms of patients during taking medicines. The slow release of drug can not only increase the adsorption efficiency of body, but also can effectively avoid the physical side effects, so there is a big market of development for sustained-release drug [1]. Sustained-release drug is usually in the composite form of drug carrier and drug. Drug carrier usually choose non-toxic, and good biocompatibility with tissue, blood and immunity of body, in addition to has also the necessary strength and good sustained release function. The MMT, LDHs, attapulgite, kaolinite and other layer silicate minerals not only has high medicinal value, its layered crystal structure also has a larger surface area and good adsorption, therefore it is the first choice of drug carrier materials [2].

Miglitol is an α-glucosidase inhibitor for non-insulin-dependent diabetes, which can reduce blood glucose levels after meals, it is a simpler structure than acarbose for effective treatment drug of diabetes [3, 4].The experimental conditions of adsorption is explored to prepare sustained-release drug of Na-MMT-Miglitol by miglitol as adsorbate and Na-MMT as drug carrier, and supply with a new applied way of miglitol in the treatment of diabetes.

Experimental

Experimental Materials and Apparatus

Na-MMT was got by Zhejiang Feng Hong Clay Chemical Ltd., Hu'zhou China, miglitol was supplied by Jinan Huifengda Chemical Ltd., Ji'nan China, KMnO4 and

NaOH were used to aid the content determination of miglitol, and these reagents all reached A.R. The constant temperature bath oscillator(SHZ-A) was used for adsorption process studies, The content of miglitol was determined by the double-beam UV-Vis spectrophotometer(TU-1900),The raw material was weighed by Electronic Analytical Balance(FA2004N).

Content Determination of Miglitol

The content of miglitol was determined by spectrophotometer by means of The method of alkaline permanganate potassium [5]. Specific experimental procedures were as follows: A certain amount of miglitol with high purity was weighed accurately to put into 100mL volumetric flask , added deionized water to dissolve and dilute it, the contentration of 0.115 mg/mL solution was obtained, and supplied for the initial standard solution. The standard solution by 1ml pipette was taked out 0.1mL, 0.3mL, 0.5mL, 0.7mL, 0.9mL and separately placed into five 10ml volumetric flasks.The each volumetric flask was added into 1ml NaOH solution(0.5mol/L) and 2.5mL $KMnO_4$ solution(0.01mol /L), shaked well and filled with pure water to the fixed scale, placed at room temperature for more than 25min, and then the solution absorbancy (Abs) was measured by spectrophotometer(TU-1900) at 610.00nm,the regression equation was got, it was Abs = 919.13C +0.0025 (R^2 = 0.9984). The R^2 value of correlation coefficient was 0.9984 and concluded that there was a good linear relationship between absorbancy and the concentration of miglitol, so the unknown concentration of miglitol solution could be determined by the regression equation.

Exchange Adsorption Capacity of Drug

A fixed mass of 0.5g Na-MMT was weighed accurately and added to a conical flask (250mL), then a certain concentration solution of miglitol was taked a certain volume into the conical flask, the conical flask was shaked to reach adsorption equilibrium, Temperature was kept constant at 30℃,and at last the content of miglitol in residual solution was analyzed by spectrophotometer. The equilibrium adsorption capacity was calculated with the following formula [6]:

$$q_e=(C_0-C_e)V/W. \tag{1}$$

where q_e(mmol/g) is the equilibrium adsorption capacity, C_o and C_e(mmol/L) are the initial and equilibrium concentration of drug in solution, V (L) is the volume of aqueous solution , and W(g) is the amount of Na-MMT.

Results and Discussion

Effect of Initial Concentration

The initial concentration of miglitol on the adsorption effect of Na-MMT is shown in Fig.1. It can be seen that the adsorption capacity gradually increases with raising of the initial concentration. The adsorption capacity is unchangeable when the initial concentration of miglitol reachs more than 5mmol / L, it is mainly due to ion exchange with miglitol and Na-MMT.A fixed amount of Na-MMT has the fixed exchangeable counter ion, so the adsorption capacity reachs maximum under the conditions of the initial concentration of miglitol,5mmol/L.

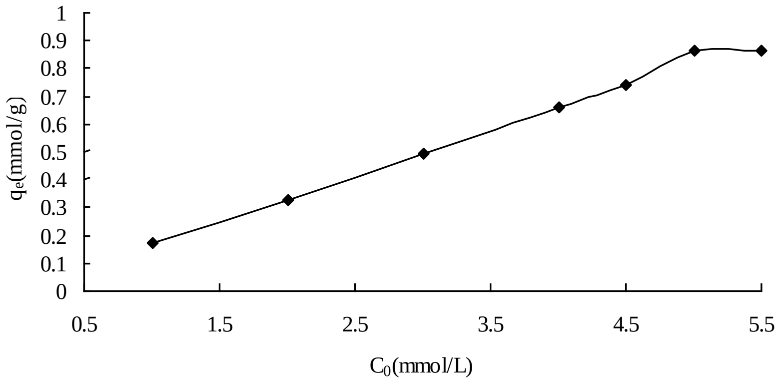


Fig.1. Initial concentration of miglitol on the adsorbed effect of miglitol onto Na-MMT

Effect of temperature

Fig.2 shows adsorption temperature on the effect of adsorption capacity, as seen from Fig.2, the adsorption capacity presents first increasing and then decreasing trend with enhancing temperature. The adsorption capacity reachs maximum at 40℃.Adsorption process is usually divided into ion exchange and non-ion exchange, the common ion exchange is endothermic, the non-ion exchange is exothermic , the adsorption capacity will be different with increasing temperature for different adsorption process.The results in Fig.2 will be concluded that the total adsorption behavior of miglitol onto Na-MMT is not a simple ion or non-ion echange. The adsorption capacity increases with temperature increasing when the temperature is less than or equal to 40℃,the adsorption process is mainly controlled by ion exchange. In addition, the adsorption capacity decreases when the temperature exceeds 40℃,it is controlled jointly by ionic and non ionic exchange.

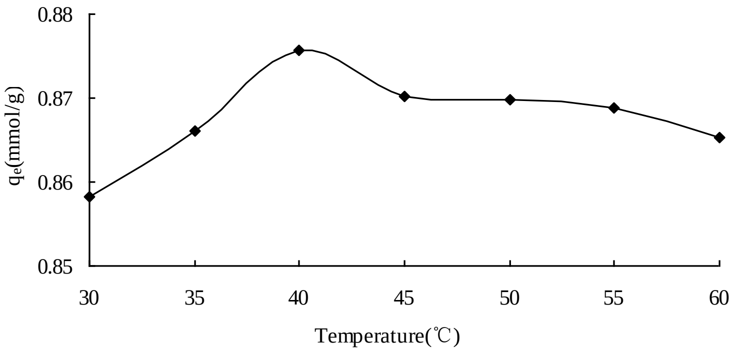


Fig.2. Temperature on the effect of adsorption capacity

Effect of pH

As the pH of solution will influence the ionization of the surface functional groups for Na-MMT, and further bring about the changes of adsorption capacity. The pH value in the solution was selected to range from 2 to 13 with the purpose of exploring the effect of pH on adsorbed efficiency of miglitol ions. The changes of pH value in solution are adjusted by adding a certain amount of hydrochloric acid or sodium hydroxide. The results are presented in Fig.3. As seen from Fig.3, the equilibrium adsorption capacity of the Na-MMT reaches maximum by selected the pH 2. The H^+ in acidic solution can be combined with miglitol ions and form complexes positive ions, and increase the adsorption capacity. However, the Na^+ in alkaline solution can inhibite the surface ions of Na-MMT to be exchanged, so the increase in pH may cause a decrease in the adsorption capacity.

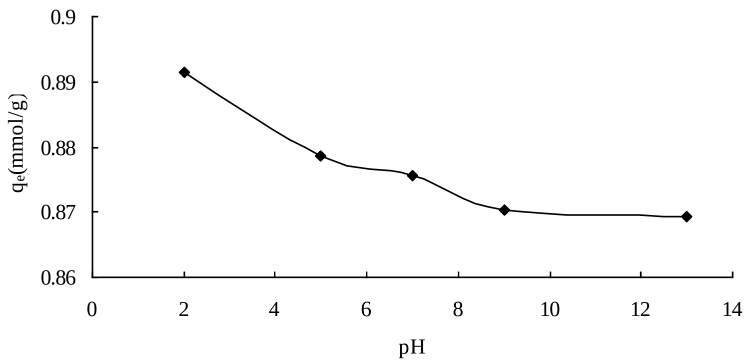


Fig.3. pH on the effect of adsorption capacity

Determination of Optimum Adsorption Time

The adsorption time on the effect of adsorption capacity was investigated after the initial concentration, 5mmol/L, temperature 40℃, pH2 were selected. Fig.4 shows that miglitol is adsorbed fastly within 1.5h, the maximum adsorption capacity of Na-MMT reachs at 1.5h. Due to the adsorption being a dynamic process, so the following adsorption curve change presents fluctuate slightly. However, the adsorption capacity of Na-MMT changes slowly and tends to adsorption equilibrium. Therefore, the suitable adsorption time, 1.5h is selected for the adsorption of miglitol onto Na-MMT.

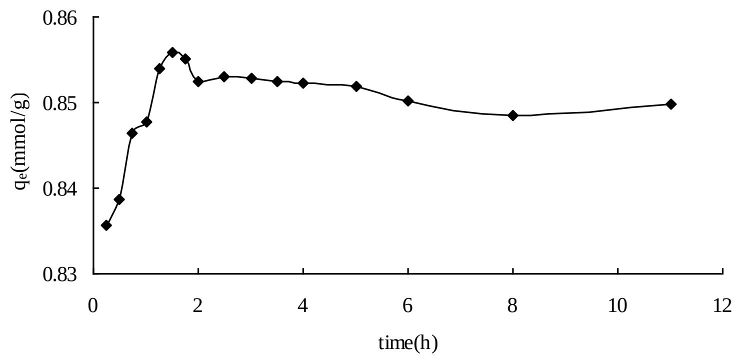
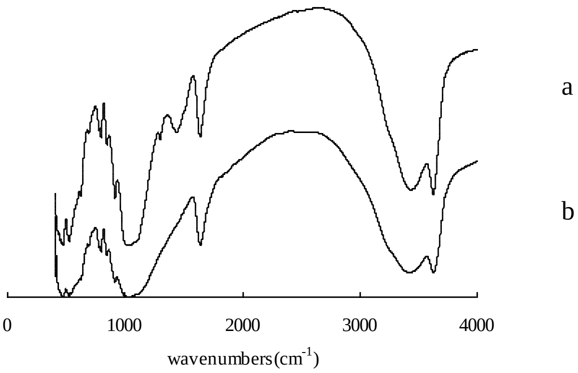


Fig.4. Adsorption time on the effect of adsorption capacity

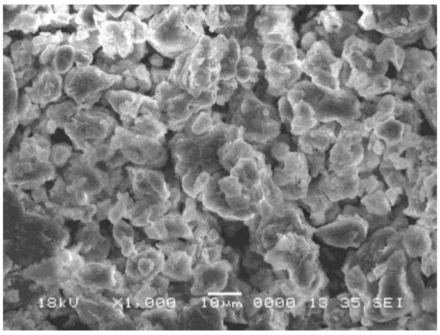
Composite Analysis of FTIR and SEM

According to the above optimum experimental conditions to prepare Na-MMT-Miglitol, its structure and morphology are characterized by FTIR and SEM, the results are shown in Fig.5 and Fig. 6, respectively. As seen from Fig.5 that the -OH stretching vibration peak at 3630cm-1 and the N-H stretching vibration peak at 1638cm-1 have higher intensity for FTIR spectra of Na-MMT-Miglitol than for FTIR spectra of Na-MMT, meanwhile, A new -CH2- stretching vibration peak at 1437 cm-1 emerges and the spectra of Na-MMT-Miglitol occurs spectral blue shift comparing spectra of Na-MMT-Miglitol. The results show that miglitol is combined successflly onto Na-MMT. In addition, the surface of Na-MMT in Fig.6 (a) shows smooth surface and clear flower shape, but Na-MMT-Miglitol composite in Fig.6 (b) presents rough surface and honeycomb, so it is concluded that the morphology of Na-MMT changes after miglitol is adsorbed onto Na-MMT.

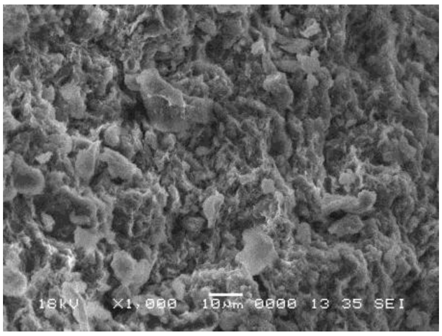


(a) Na-MMT-Miglitol; (b) Na-MMT

Fig.5. FTIR spectra of Na-MMT-Miglitol and Na-MMT



(a) Na-MMT



(b) Na-MMT-Miglitol

Fig.6. SEM of Na-MMT and Na-MMT-Miglitol

Conclusions

The initial concentration, temperature, pH and adsorption time in this study were discussed to the effect of adsorption capacity. The maximum adsorption capacity of Na-MMT is got by selecting initial concentration of miglitol, 5mmol/L, 40℃, pH2 and adsorption time 1.5h.The analysis result of FTIR and SEM shows that the miglitol is adsorbed onto Na-MMT and the Na-MMT morphology is changed ,and then get composite successfully.

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