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Preparation and Characterization of (MCM-41)-Carvedilol Composite Material

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With sharply increase in the amount of patients with elevated blood pressure population, seeking the effective treat medicine and the loading medicine carrier becomes a hot research spot. This paper used MCM-41 to take a carvedilol medicine carrier using hydrothermal method to synthesize MCM-41 and in it carvedilol was loaded. The amount of assembly capacity was 180 mg/g (drug/MCM-41). The prepared composites were characterized by chemical analysis, powder X-ray diffraction, Fourier transform infrared spectroscopy, scanning electron microscopy, transmission electron microscopy and N_2 adsorption-desorption and the release law in human body simulated fluid was made. Powder X-ray diffraction showed that during the process of incorporation the framework of the molecular sieve was not destructed and crystalline degrees of molecular sieve in the host-guest composite materials prepared were still very high. FT-IR spectra showed that the frameworks of host molecular sieves of the prepared host-guest composite materials were intact. Low-temperature nitrogen adsorption-desorption results at 77 K showed that the specific surface area and the pore volume of the host-guest composite material decreased compared to those of the host molecular sieve, indicating that the guest has partially occupied the channels of the molecular sieve. Transmission electron microscopic results showed that two-dimensional hexagonal mesoporous channels of molecular sieve in the composite materials were maintained. Scanning electron microscopic results showed that the composite materials were maintained as fibrous crystals. In simulated body fluid, it is discovered by studying release law of drug in the composite materials that drug release effective time was up to 32 h and release ratio was 99.4 %. In simulated gastric fluid, composite drug release time was up to 4 h and release rate was up to 23 %. In simulated intestinal fluid, the drug release time up to 9 h can be more effective and the release rate was 72.7 %. The above results showed that MCM-41 is a well-controlled drug delivery carrier.

Key Words: Carvedilol, MCM-41 mesoporous material, Sustained release.

INTRODUCTION

With the change in the improvement of living standards and the pace of life, known as Three High Disease of Diseases of Affluence (*i.e.*, hypertension, high blood sugar and high cholesterol) the number of patients also keeps growing and the patients tended to younger development. Many people are suffered from varying degrees of hypertension. The structure of carvedilol {1-(9*H*-carbazole-4-oxy)-3-[2-(2-methoxyphenoxy) ethylamino] -2-propanol)}, $C_{24}H_{26}N_2O_4$ is as follows (Fig. 1):

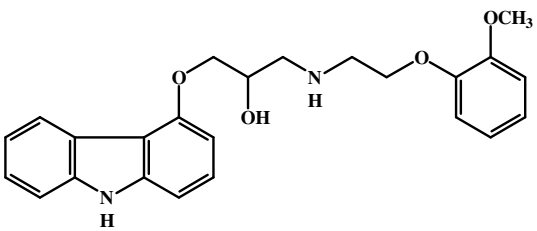

Fig. 1. Structure of carvedilol

It blocks the receptor for α, β and has vasodilator effect, which is used to treat mild and moderate hypertension or renal insufficiency, diabetes, high blood pressure patients. For patients with essential hypertension it is used for drug alone, can also be combined with other antihypertensive drugs, especially thiazide diuretics. It is also used for cardiac insufficiency, mild or moderate ventricular dysfunction, the merger application of digitalis drugs, diuretics and angiotensin converting enzyme inhibitors. It can also be used for cardiac insufficiency of angiotensin converting enzyme inhibitors intolerance with or without digitalis drugs, hydralazine or nitrate ester treatment. Taking carvedilol is easily absorbed, whose absolute bioavailability is approximately 25 to 35 % and has obvious first excessive effect and the elimination half-life is about 7-10 h. When taken with food, the absorption is slowed down, but is no significant impact for bioavailability and this can reduce the risk of causing orthostatic hypotension. At the same time, carvedilol is basic lipophilic compound and its binding rate with plasma protein is greater than 98 %. Its steady-state volume

of distribution is about 1.5 L and plasma clearance rate is 500-700 mL/min. Carvedilol is completely metabolized in the body and its metabolites is discharged *via* the bile then through the feces, only less than 2 % unchanged in the urine is discharged.

MCM-41 with one-dimensional pore channels of the hexagonal regular arrangement belongs to a member of the M41S series ordered mesoporous materials. The uniformity of pore size distribution of MCM-41 can be modulated between 1.5 and 10 nm[1,2]. The findings of this mesoporous materials not only make the microporous range of molecular sieve and zeolite expand to mesoporous range, but also build a bridge between the micopore materials (zeolite) and macroporous materials (such as amorphous aluminosilicate). Its unique structural features and its large specific surface area (1000 m^2/g), have opened up new horizons for the application of the molecular sieve, which have become a hot spot of research[3-6]. At the same time, MCM-41 is non-toxic, with thick walls and high hydrothermal stability. So MCM-41 has a potential application prospect in the medicine and other fields[7]. To our best of knowledge of loading of carvedilol drug model in MCM-41 has not been reported so far. In this study, carvedilol is loaded into the MCM-41 molecular sieve and the loaded molecular sieve composite materials were characterized and at the same time the sustained release effect is studied. The results show that the use of MCM-41 as the carvedilol carrier has significance of practice and cutting-edge.

EXPERIMENTAL

Cetyltrimethylammonium bromide (CTMAB), NaOH and hydrochloric acid were purchased from Beijing Chemical Plant, China. Tetraethyl orthosilicate (TEOS) was kindly supplied from Shanghai Chemical Co. Ltd., China. $NaAlO_2$ was obtained from Tianjin City Jinke Fine Chemical Engineering Research Institute, China. White carbon black (SiO_2) was bought from Beijing Red Star Chemical Plant, China. Carvedilol was obtained from Beijing Giant Energy Pharmaceutical Co. Ltd., China. Anhydrous alcohol, triethanolamine, NaCl, KCl and $CaCl_2$ were obtained from Beijing Chemical Plant, China. Triketohydrindene hydrate and $NaHCO_3$ came from National Medicine Group Chemical Reagent Co. Ltd., China. K_2HPO_4 was the product of Tianjin Kemiou Center for Chemical Reagents Development, China). $MgCl_2$ was the product of Liaoning Medicine Economic and Trade Company, China. Na_2SO_4 was kindly supplied from Tianjin East China Reagent Factory, China); All the reagents used in the experiment were of analytical purity and the water was deionized water.

Synthesis of MCM-41: CTMAB, NaOH, $NaAlO_2$, SiO_2 and deionized water was mixed in accordance with molar ratio of 1.0: 1.9: 0.1: 4.0: 200, stirred for 2 h. Then, heating of the mixture was carried on for 5 d in PTFE stainless steel autoclave under atmospheric pressure at 373 K. The product was washed with distilled water, filtered, dried at room temperature. The synthetic MCM-41 was calcined for 6 h at a temperature of 873 K to remove the surfactant CTMAB to derive product[8].

Loading and release method of drug

Quantitative methods of carvedilol: 2.5-20 mL of 2 μg/mL working solution was taken and transferred to a series of 25-mL volumetric flasks. Firstly, 0.5 mL of 1 % NaOH solution was added and then 2 mL of 0.3 % hydrated ninhydrin was added. The solution was uniformity mixed and stood for 5 min, then diluted with deionized water to the mark and mixed well. At 402 nm,with the corresponding reagent blank as reference the absorbance of each solution was determined[9]. The standard curve regression equation was: A = 0.1008 + 0.033 C, the correlation coefficient r = 0.9950, where A stands for absorbance and C represents carvedilol concentration (μg/mL).

Loading of carvedilol in MCM-41 and the maximum loading drug amount concentration determination: 0.3 g of MCM-41 was placed into a 100 -mL beaker and 40 mL of a concentration of 5 mg/mL carvedilol solution was added. The mixture was stirred for 48 h at room temperature, filtered, quickly washed, dried. The molecular sieve for loading drug was obtained. 1.0 mL of filtrate solution was accurately taken and appropriately diluted. Afterwards, residue amount of the drug in the filtrate solution was determined by the spectrophotometric method, using differential subtraction to calculate the content of carvedilol in the composite body.

Drug release in simulated body fluid

Preparation method of simulated body fluid: NaCl (7.996 g), $NaHCO_3$ (0.350 g), KCl (0.224 g), $K_2HPO_4 \cdot 2H_2O$ (0.228 g) of $MgCl_2 \cdot 6H_2O$ (0.305 g), 1 $mol \cdot L^{-1}$ HCl (40 mL) and $CaCl_2$ (0.278 g), Na_2SO_4 (0.071 g), $NH_2C(CH_2OH)_3$ (6.057 g) were dissolved in water and then it was diluted to the mark of 1-L volumetric flask with water.

Preparation method of simulated gastric juice: 6.217 g of concentrated hydrochloric acid was placed into a 1 L volumetric flask and then diluted with water to the mark to get the simulated gastric juice (pH = 1.3).

Preparation method of simulated intestinal fluid: A pH 7.4 buffer solution of Na_2HPO_4-KH_2PO_4 was used.

Sustained release method: 0.3 g of drug-assembled molecular sieve was weighed. 50 mL of simulated body fluids (gastric juice, intestinal juice) was accurately measured and taken. The above-stated molecular sieve and body simulated fluid were mixed and then stirred at a constant temperature of 37 ºC. The released liquid was taken from time to time every 1-2 h and the equal amount of artificial simulated body fluids (gastric juice, intestinal juice) after each imbibition was replenished and appropriately diluted. The concentration of carvedilol was determined by the spectrophotometry to draw release curve.

Constant temperature magnetic stirrer (Jiangsu Jintan City Ronghua Instrumentation Manufacture Co. Ltd., China) was used for the control of temperature and for experimental stirring. Powder X-ray diffraction analysis experiments were carried on a D5005 type X-ray diffraction analyzer. In the test CuK_α was selected as target material. The X-ray wavelength used for experiment was λ = 1.5418 Å and the operating voltage (tube voltage) was 30 kV and operating current (tube current) was 20 mA. Fourier transform infrared (FT-IR) spectroscopic experiments were completed on a BRUKER Vertex-70 Fourier transform infrared analyzer. In the test, powder sample was pressed to become slice using KBr for characterization of the skeleton structure vibration of the material. Low-temperature nitrogen adsorption-desorption tests were conducted in

a Micromeritics ASAP 2010M adsorption analyzer and the temperature of experiment was 77 K for determination of pore channel structure (pore size, pore volume, specific surface area, *etc*.) of molecular sieve material. Before the test was made, sample was firstly degassed and vacuumized at 573 K for 12 h. The specific surface area was calculated by using BET (Brunner-Emunett-Teller) method and the pore size distribution was calculated by means of BJH (Barrett-Joyner-Halenda). Transmission electron microscopy photograph was shot in a JEOL2010 transmission electron microscope. Scanning electron microscopy images were determined on a JEOL JSM-5600 L scanning electron microscope. Carvedilol component content determination in the prepared host-guest composite material and carvedilol release process experiments in simulated body fluids were completed by the spectrophotometry[9] in a 722 S type spectrophotometer (Shanghai Lengguang Technology Co. Ltd., China).

RESULTS AND DISCUSSION

Maximum loading drug amount: The carvedilol in the carvedilol/MCM-41 composite material sample was aimed for spectrophotometric determination. Guest carvedilol content in the composite material determined was 180 mg/g (drug/MCM-41molecular sieve). The result shows that carvedilol has gone into the MCM-41.

Powder X-ray diffraction: Curves A, B and C of Fig. 2, are XRD small-angle diffraction patterns for carvedilol, MCM-41 and carvedilol loaded MCM-41 molecular sieve composite, respectively. From curve B the obvious (100), (110) and (200) diffraction peaks can be observed, showing that their structural ordering is very high. Besides the main peak (100) appearing at $2\theta = 2.2^{\circ}$ in the XRD patterns of MCM-41, the three weak diffraction peaks between $3^{\circ} < 2\theta < 6^{\circ}$ are clearly visible. *i.e.* the sample appears three weaker diffraction peaks at (110), (200), (210) crystal face. These are typical MCM-41 mesoporous phase diffraction pattern, indicating that the sample inside ordered degree was higher and the molecular sieve belonged hexagonal dense stack crystal phase structure. From curve C it can be observed that compared the composite material with unloaded molecular sieve, (110) (200) diffraction peaks disappeared. This indicates that the composite material is still of long-range order and a hexagonal dense stack crystalline phase structure but its orderly degree declined.

Curves A, B and C of Fig. 3 are the wide angle XRD patterns of the original drug carvedilol, MCM-41 molecular sieve and carvedilol/MCM-41 composite body, respectively. Under the wide angle X-ray diffraction conditions, the diffraction pattern has no sharp peak shape, indicating that in unassembled MCM-41 crystal structure did not exist. There is a large diffraction peak at around 23º. MCM-41 is a non-crystal amorphous materials and behaves as long-range disorder. It can be seen that a phenomenon appeared that from the figure the diffraction peak of the composite at around 23º weakened, indicating that the crystal structure and the order degree of the composite material reduced.

Infrared spectra: Fig. 4 showed the IR spectra of the samples. Curves A, B and C are the infrared spectra of carvedilol, MCM-41 and composite material, respectively. It can be seen

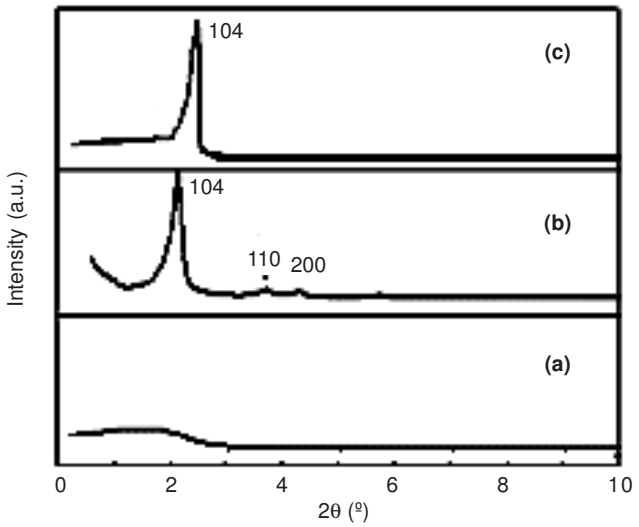

Fig. 2. XRD small angle patterns: a) carvedilol; b) MCM-41; c) composite material

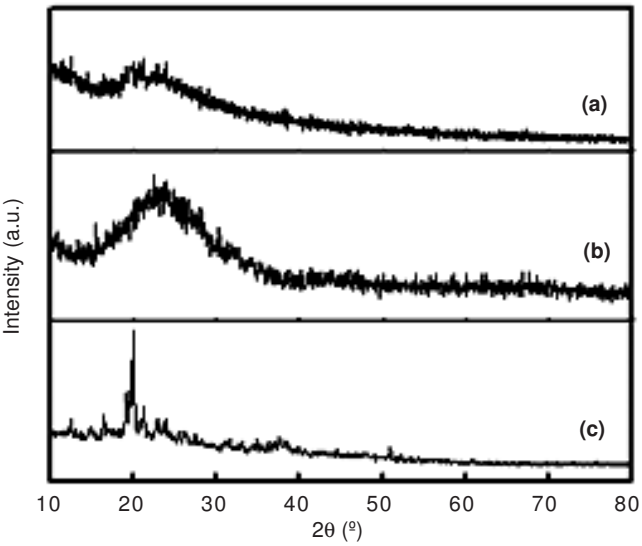

Fig. 3. XRD wide angle patterns: a) composite material; b) MCM-41; c) carvedilol

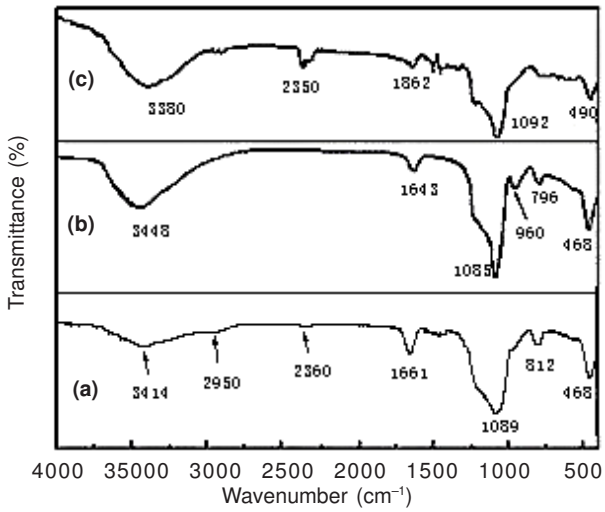

Fig. 4. IR spectra: a) carvedilol drug; b) MCM-41 molecular sieve; c) composite material

from the spectra that the carvedilol molecules have infrared absorption peaks at 3414, 2950, 2360, 1661, 1089, 812 cm^{-1}. It can be seen that carvedilol/MCM-41 composite body (curve C) not only kept the characteristic absorption peaks of MCM-41, but still appeared an absorption peak of the original drug at 2350 cm^{-1}. The absorption band at 3380 cm^{-1} is attributed to adsorbed asymmetric stretching vibration of water molecules and surface hydroxyl groups. The absorption peaks at 1862, 1092 and 490 cm^{-1} are corresponding to vibrations of -OH band, the asymmetric stretching vibration of Si-O-Si of MCM-41 and T-O bending vibration of MCM-41, respectively. The presence of these peaks explained that carvedilol had been successfully loaded into the MCM-41.

Scanning electron microscopy analysis: Figs. 5 and 6 are the SEM images of MCM-41 molecular sieve and the MCM-41 molecular sieve composite after loading carvedilol drug, respectively. From the images it can be observed that MCM-41 molecular sieve is spherical morphology and the average particle size is 170 nm. The MCM-41 after encapsulating carvedilol drug is also spherical morphology and the average particle diameter is 182 nm.

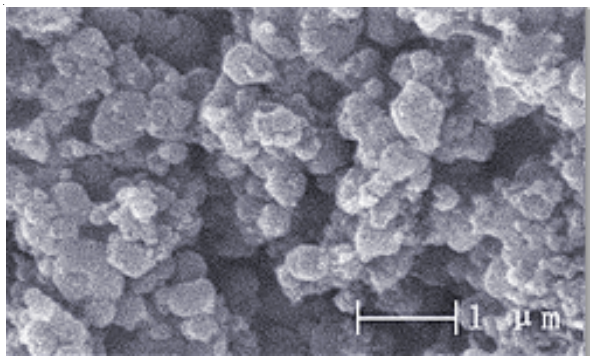

Fig. 5. SEM images of MCM-41

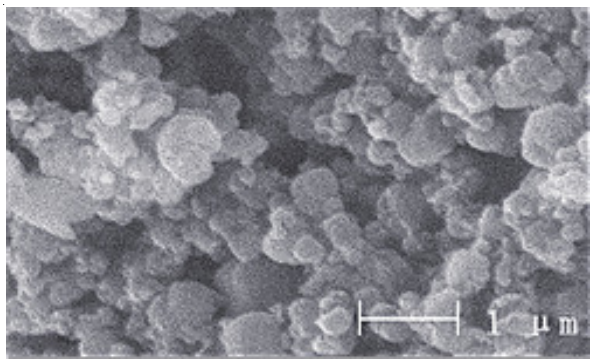

Fig. 6. SEM images of composite material

Transmission electron microscopy analysis: The parallel lines presented on TEM images are considered to be parallel arrangements of the tubular hexagonal pore. And sponge-like is considered to be the crystal phase arrangements lack of long-range order. Figs. 7 and 8 are TEM pattern of MCM-41 molecular sieve and the drug-loaded composite material, respectively. From the figure it can be seen that the MCM-41 molecular sieve has a highly ordered hexagonal straight pore structure. Molecular sieve after loading carvedilol drug became the spongy, being lack of long-range ordered arrangement. But its crystalline degree is good and the lattice line is clear and identifiable.

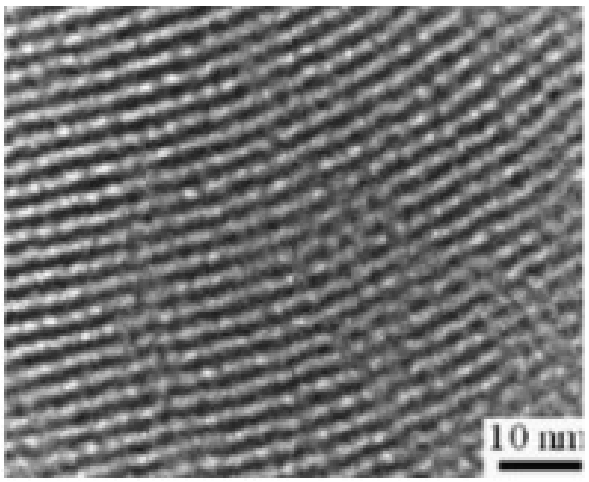

Fig. 7. TEM images of MCM-41 molecular sieve

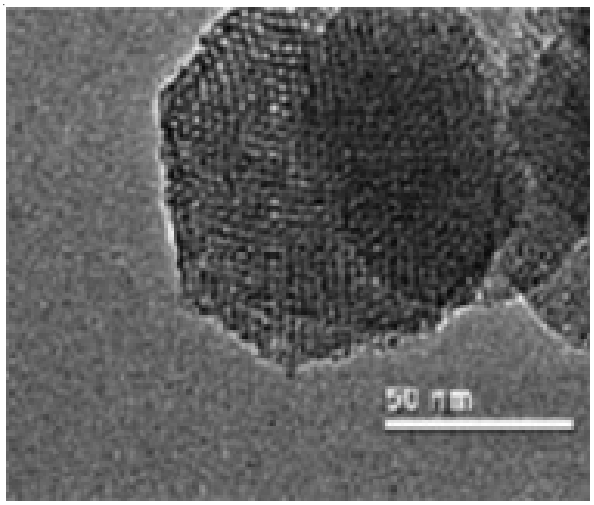

Fig. 8. TEM images of composite material

Low-temperature nitrogen adsorption-desorption isotherms and material pore parameters analysis: Figs. 9 and 10 show N_2 adsorption-desorption isotherms and pore size distribution curve of calcined MCM-41 and drug-loaded MCM-41 samples, respectively. It can be known from Fig. 9 that the two samples are of both IV type isotherms. The characteristics hysteresis loops of nitrogen adsorption-desorption isotherm of the prepared samples have one obvious adsorption and desorption branch. The steep adsorption branch and desorption branch can show that the prepared MCM-41 mesoporous molecular sieves and (MCM-41) host-guest composite materials have relatively narrower mesoporous size distribution, which has been proved by mesoporous pore size distribution curves of prepared MCM-41 mesoporous molecular sieve and (MCM-41)-carvedilol host-guest composite material. In the adsorption-desorption isotherms, molecule was adsorbed on the surface of molecular sieve in the form of a single molecule and the multi-molecular layer adsorption did not occur until the pressure was high enough. According to capillary enrichment theory, the relation between pressure of capillary enrichment occurred and pore channel diameter is as follows: only monolayer adsorption occurs when the partial pressure of the gas is less than one at the time of capillary enrichment occurred. The pores will be completely filled with medium

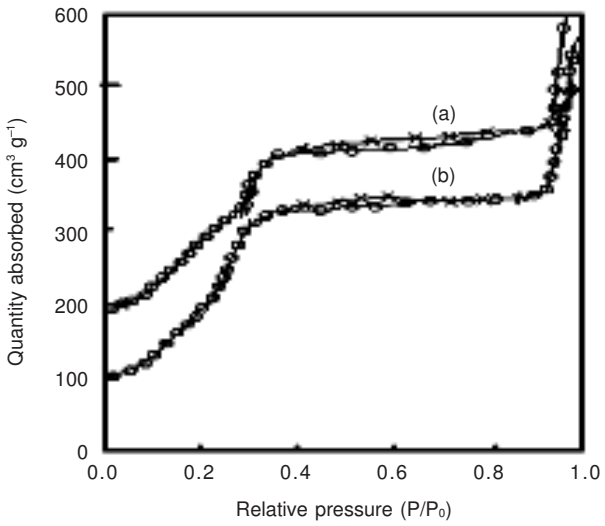

Fig. 9. Low temperature N_2 adsorption-desorption curves: a) MCM-41; b) (MCM-41)-carvedilol

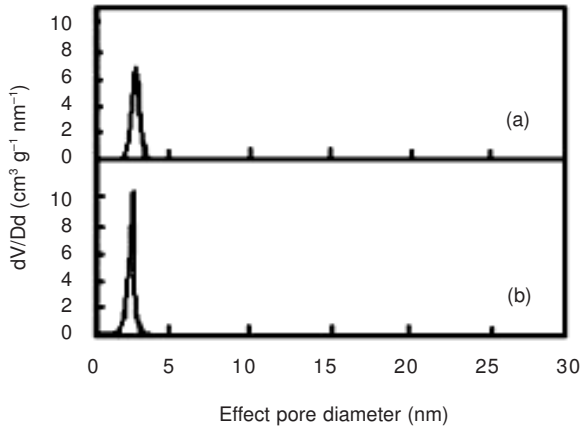

Fig. 10. Pore size distribution patterns of the samples: a) MCM-41; b) (MCM-41)- carvedilol

when the gas pressure is equal to or higher than the partial pressure at the time of capillary enrichment. In accordance with the theory of capillary enrichment, for a specific adsorbate, when the partial pressure is P and temperature is T, aperture r will be content with the range from 0 to r* and pores will be filled with adsorbate. According to Kelvin's capillary enrichment model, when the aperture r is ≤ 2, for adsorbate the physical adsorption of the surface occurs, with the size of r* dependant on P and T. The beginning of the hysteresis loop in the adsorption isotherm is the start of capillary enrichment phenomenon. In this study, for the synthesized samples of MCM-41 sample, when the relative partial pressure (value p) reached 0.73, the adsorption branch and desorption branch of the adsorption-desorption isotherms appeared to a sudden change. In the material having mesoporous channels, the relative pressure of capillary enrichment (capillary agglomeration) phenomenon occurred is an increasing function of the mesoporous pore diameter. Namely, the greater the mesoporous channel diameter of a material is, the higher the relative pressure of capillary agglomeration phenomenon occurred is, which can be proved by the aperture parameters of various materials. The decrease of amount of adsorbed N_2 can be attributed to the decrease of pore volume and smaller pore sizes led to capillary enrichment at a lower relative pressure (P/P_0). In addition, the hysteresis appeared in the higher relative pressure range is in accordance with the mesoporous characteristics of MCM-41 moleculer sieve material, which proved that after carvedilol was assemblied in MCM-41 pore channels, characteristics of the mesoporous structure still existed. It can also be seen from the nitrogen adsorption-desorption curves of prepared materials. For the prepared MCM-41 sample. When the relative partial pressure reached 0.85, the adsorption branch overlaped with desorption branch again, which is the phenomenon that desorption branch lagged the adsorption branch no longer. For the prepared (MCM-41)-carvedilol composite sample, the phenomenon that desorption branch lags the adsorption branch did not appear. When the relative pressure of sample reached 0.80, the phenomenon that desorption branch lags the adsorption branch did not appear again. This phenomenon is mainly when the mesoporous channels have been filled with gas under the higher relative pressure and after capillary enrichment phenomenon accomplished, the adsorption behaviour mainly occurred in the outer surface of the material and this process is reversible, leading the phenomenon that desorption branch lags the adsorption branch did not appear again. The related data of various parameters were based on the adsorption branch of the nitrogen adsorption-desorption isotherms. After assembly of the drug molecules, the specific surface area, average pore diameter and pore volume were decreased to 1005 $m^2 \cdot g^{-1}$, 2.69 nm and 1.47 $cm^3\ g^{-1}$ and the decline rate were 10.27, 2.18 and 8.13 %, respectively. It is shown that the drug molecules have been loaded in mesoporous molecular sieve channels and the channels structure of mesopores were maintained. The specific surface area, average pore size and pore volume of mesoporous molecular sieves presented a decrease trend (Table-1).

TABLE-1
PORE STRUCTURE PARAMETERS OF SAMPLES

Sample	d_{100} (nm)	a_0[a] (nm)	BET surface area (m^2/g)	Pore volume[b] (cm^3/g)	Pore size (W_d)[c] (nm)
MCM-41	4.20	4.85	1120	1.60	2.75
Composite material	5.16	5.98	1005	1.47	2.69

[a] $a_0 = \frac{2}{\sqrt{3}} d_{100}$; [b] BJH adsorption cumulative volume of pores

[c] Pore size calculated from the adsorption branch

In order to quantitatively calculate the carvedilol impediment effect on MCM-41 molecular sieve pore channels, this study calculated the normalized surface area of materials. Based on normalized surface area value of the material the existence state of guest material in the composite material can be estimated:

(1) When normalized surface area is << 1 in the composite: The guest material will form relatively larger particles. These particles enter the molecular sieve pore channels, blocking the pore channels to make the pore volume, the specific surface area and pore size of the molecular sieve material dramatically become small (Fig. 11).

Fig. 11. Host-guest composite material state type I

(2) When normalized surface area of the composite is approaches 1: Guest material will form a non-crystal layer, closely covering the inner surface of the molecular sieve (Fig. 12). Because these particles are attached to the inner surface of the molecular sieve pore channels and a new surface is formed and this new surface only covers the original surface, so the normalized surface area value of this kind of materials is close to 1.

Fig. 12. Host-guest composite material state type II

(3) When normalized surface area of composite material is > 1: Guest material will form very small nanocrystals dispersed on the inside and outside surface of the molecular sieve (Fig. 13). As particle size of these nanocrystals is very small, so the specific surface area of composite materials was greatly increased, so its normalized surface area value is much larger than 1.

Fig. 13. Host-guest composite material state type III

Normalized surface area formula is as follows[10]:

$$NSA = \frac{SA_1}{1-y} \times \frac{1}{SA_2}$$

Here, SA_1 and SA_2 are surface area of (MCM-41)-carvedilol composite and of MCM-41 molecular sieve matrix, respectively; y is the mass fraction of carvedilol in the composite sample.

In the present study, the normalized surface area value is 0.99, close to 1. This shows that after carvedilol particles were attached to the inner surface of the molecular sieve pore channels, a new surface was formed and it only covered the original surface. These results and the nitrogen adsorption-desorption isotherms results were consistent.

Drug sustained-release curve

Sustained release in simulated body fluid: Fig. 14 is a profile of drug release in simulated body fluid. From the figure it can be seen that release process of the prepared drug is divided into four stages. In the first stage, within 1 h for the sample release the drug release rate was very fast, mainly due to the reason that the drug adsorbed on the outer surface of carrier at drug release the early period, was rapidly dissolved into the body fluid. In the second stage, within the sample release of 2-14 h, the drug release rate was slow compared to the one of previous stage, but faster than that in a later stage, mainly because of the relatively rapid release of drug adsorbed near the carrier pore channel mouth neighborhood. In the third stage, within the sample release of 14-32 h, drug release was very slow, mainly because it resulted from that the drug adsorbed in the mesoporous channels of the carrier was slowly dissolved in body fluid. In the fourth stage, after the sample release of 32-h, mainly because the release of drug adsorbed on the carrier was already complete, that after the solution was taken out from the system and the body fluid was added led to lower of drug concentrations. At 1 h, the release rate was 18 %. The release rate was 79 % at 14 h. At 32 h, the release rate was 99.3 %. At 36 h, the release rate was 99.4 % and was basically not unchanged, indicating that release has been completed.

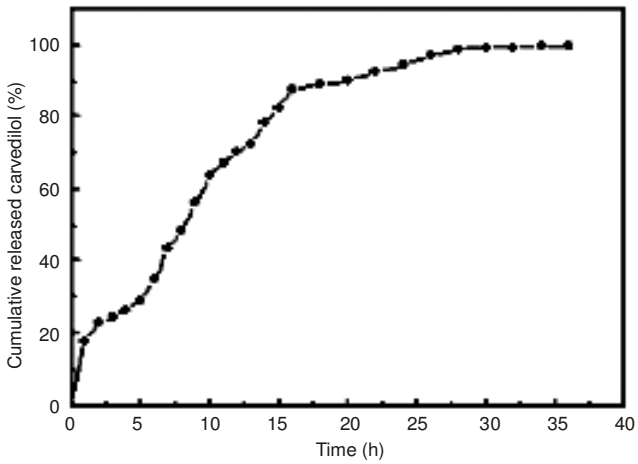

Fig. 14. Sustained release pattern of (MCM-41)- carvedilol drug in simulated body fluid

Sustained release in simulated gastric juice: Fig. 15 shows the curve of drug release in simulated gastric juice. It can be seen from the figure that the release process of drug prepared is divided into two phases. From 1 h to 4 h, the release is relatively fast. Because the drug of carvedilol, which was dispersed in the outer surface of MCM-41 by the physical and chemical adsorption process and the ones which distributed in the pores of MCM-41 have large contact area with gastric juice, dissolution as well as release is of high rate. The release rate was 23 % at 4 h and then steady after 4 h. The release process is related to the presence way of the drug carvedilol. The assembly process of carvedilol in MCM-41 is that a number of organic functional groups replaced surface silanols of mesoporous molecular sieve, so that carvedilol was grafted into MCM-41. Carvedilol and the mesoporous silica were connected by hydrogen bond. This interaction is not very stable, because under the effect of gastric juice the hydrogen bond breaks and then the carvedilol drug was released in the gastric juice. In addition, due to the high mobility of the gastric juice, it can enter the pore channels of mesoporous molecular

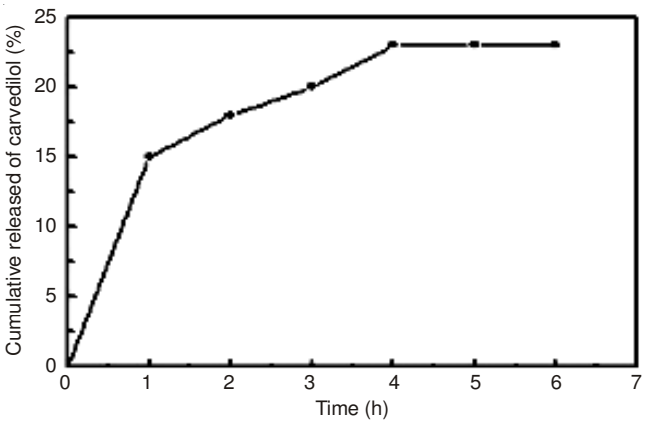

Fig. 15. Sustained release pattern of (MCM-41)-carvedilol drug in simulated gastric juice

sieve, making drugs in the pores be released. However, as the pore channel diameter of mesoporous materials is very small, which makes the resistance for the gastric juice go into the pore channels become great. The drug must be firstly slowly dissolved in the gastric juice and then diffused out of capillary-like channels. It made carvedilol drug release become sluggish, which extends the period of the release of carvedilol, slows drug release and increases duration of drug action, thereby enhancing the drug release.

Release in simulated intestinal fluid: Fig. 16 shows the drug release profile in simulated intestinal fluid. From the figure we can see that the prepared drug release process is divided into three stages. For 1-3 h, the release rate was relatively flat, mainly because the drug adsorbed on the outer surface of the carrier in drug release early period was dissolved into the intestinal fluid. The release was relatively fast within 3-9 h. Since the drug within the pores released out, the pH value of intestinal fluid was suitable for sustained release of drug. The slow release rate reached 72.7 % after 9 h and the release was complete.

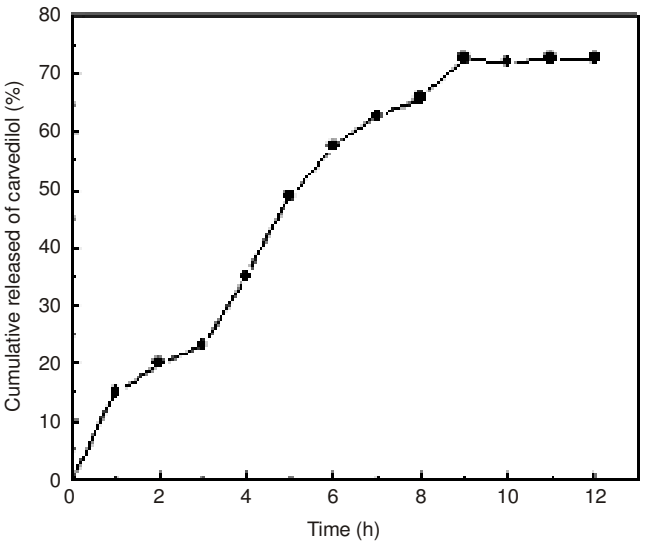

Fig. 16. Sustained release pattern of (MCM-41)-carvedilol drug in simulated intestinal fluid

Conclusion

In this study, the loading and slow release of carvedilol in the MCM-41 was carried on. Through a series of characterizations the following conclusions can be drawn:

(1) When carvedilol was encapsulated in mesoporous molecular sieve MCM-41, the maximum loading drug amount was 180 mg/g (drug/MCM-41 molecular sieve).

(2) Carvedilol drug release experiments in simulated body fluids showed that carvedilol drug release rate reached 60 % within 12 h, and at the release rate of 99.4 % was completed at 36 h. This showed that by using the mesoporous MCM-41 molecular sieve as the carrier of carvedilol drug the drug release could be effectively controlled and the efficacy of the drug carvedilol could be improved, which found a very good carrier for later carvedilol's carry. Using MCM-41 as drug delivery system the drug release can be controlled and the efficacy can be improved.

(3) Because MCM-41 molecular sieve has a unique pore structure and characteristics, it can be used for a variety of carrier of bioactive molecules. Use of the system as a carrier of drugs can prolong the cycle of drug action, improve the targeting of drugs. MCM-41 molecular sieve has a potential application foreground as a drug carrier.

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