Application and Preparation of Enteric Coating Materials

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Abstract. In this paper, polymethacrylate enteric coated materials based on the equal mass of methyl acrylic acid and ethyl acrylate as the main raw materials were synthesized through emulsion polymerization. Omeprazole Enteric-coated Capsules were prepared by the fluidized bed coating technology using above materials as enteric layer and in vitro enteric test was considered according to standard. The results showed that the material had good coverage in the surface of omeprazole isolated pellets, excellent acid resistance in artificial gastric acid environment, and reached the disintegration effect in the buffer solution of 20min. Moreover the drug release reached 88.2% and had excellent long-term storage.

1. Introduction

Omeprazole was widely used in treatment of gastric ulcer and duodenal ulcer because of its strong acid-suppression, high specificity and long duration, which was a representative drug of first generation proton pump inhibitors (PPIs). However, its property of easy decomposition for the structure that the human body is not easy to absorb in an acid environment, decided that their oral preparations are all enteric preparation. Poly methacrylate has been widely concerned as coating materials， which could be prepared for enteric coated materials for its COOH group in the molecular structure. This material can control disintegration of drug in a specific pH environment, while in the gastric acid environment not released, so as to guarantee the effectiveness of drug treatment [1~4]. At present, there has been many studies on enteric coated polyacrylic acid resin. Yao et al[5,6] prepared enteric coating materials, according to change -COOH content, using methycl acrylic acid and methyl methacrylate as raw materials, which can be dissolved in pH＞6 or pH＞7 medium. However, it was necessary to add mass plasticizer before use.

This paper aimed at preparing enteric coated pharmaceutical coating materials with good solution in pH＞5.5 medium, which took methacrylic acid and ethyl acrylate as raw materials. Then this material was used to coat on the omeprazole isolated pellets to form capsules by fluidize bed coating technology. And in vitro enteric test results meet the limits of "Chinese pharmacopoeia" for various index.

2. Experimental

2.1. Materials.

Methacrylic acid (MAA) (Sanyi Technology Co.，Jiangsu，China) were purified by distillation under reduced pressure before use. Ethyl acrylate (EA) and potassium persulfate (C. P. grades) were supplied by Tianjin Taixing Reagent Factory. Alkyl ether sulfates, disodium laureth sulfosuccinate and fatty alcohol-polyoxyethylene ether were donated by Honesty Fine Chemical Co., Ltd. (Shanghai, China). Omeprazole isolated pellets were obtained from Hebei pharmatrade Biotechnology Co., Ltd. Triethyl citrate (99.9% of purity, Sinopharm Chemical Reagent Co. China), talcum powder (10μm of size) and distilled water were used.

2.2. Synthesis of Enteric Polymethacrylate Coating Materials.

The pre-emulsion with solid content of 46% was obtained through pre-emulsified technology. The equal mass of methyl acrylic acid and ethyl acrylate were put into a reactor. Then the emulsifier and initiator and distilled water were added into reaction system. And the amount of emulsifier (the ratio of anionic emulsifier and nonionic emulsifier was 3:1) and initiator were 3% and 0.46%, respectively. Subsequently the pre-emulsion was obtained after 1 hour's pre-emulsification under high-speed mixing. Moreover, the seeded emulsion was obtained by adding 1/5 of the pre-emulsion and remaining deionized water into a reactor, and heated to 80 ℃ for 0.5 h. Then the remaining mixture was added dropwise for 4~5 hours, and the reaction mixture was maintained for 1h at 80 ℃. After cooled to room temperature and filtered, the enteric polymethacrylate water dispersion coating materials were obtained.

2.3. Preparation of Omeprazole Enteric-coated Capsules.

1%(w/w) triethyl citrate and 2.4%(w/w) talcum powder were added to distilled water and stirred until a homogenous dispersion was obtained. And the 15%(w/w) enteric coating liquid was obtained after adding polymethacrylate emulsion into the dispersion. Fluidized bed coating technology was adopted to prepare omeprazole coated pellets under the following conditions: fan frequency of 40Hz，inlet air temperature of 45℃， feed rate of 1~1.2rpm, atomization pressure of 0.1Mpa. Then omeprazole coated capsules were obtained with coated pellets weight gain of 33% after drying for 20 min in the fluidized bed and baking for 2h in the oven of 38℃.

2.4. Characterization.

The molecular structure of polymethacrylate was analyzed by Fourier Transform Infrared Spectrometer (FT-IR). Particle size and distribution were recorded on the LS900 laser particle size analyzer. The molecular weight of the polymer was measured via gel permeation chromatography and an eluent of tetrahydrofuran, at a flow rate of 1ml/min was selected. The release of omeprazole enteric coated capsules was tested according to standard of " Chinese pharmacopoeia ".

3. Results and Discussion

3.1. Basic Physicochemical Properties of Enteric Polymethacrylate Coating Materials.

The basic physicochemical properties and molecular structure of enteric polymethacrylate coating materials were tested and analyzed, which were shown in Figure.1 and Table 1.

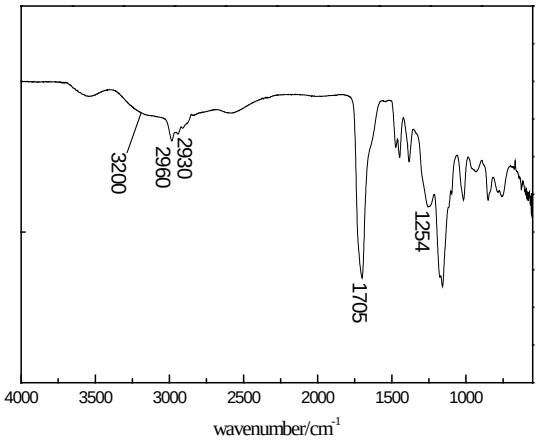
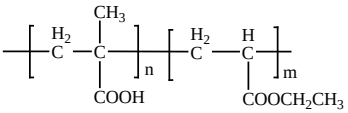


Figure.1. The FT-IR spectra of enteric polymethacrylate coating materials

The existence of carboxyl groups are the key for polymethacrylate enteric coated materials. Figure.1 depicted the FT-IR spectra of this material. There was no -C=C- stretching vibration at 1640cm-1, which indicated monomer react completely. The FT-IR showed some characteristic bands, C-O and C=O stretching vibrations were presented at 1254cm-1 and1705cm-1. And –OH stretching vibrations can also be found at 3200cm-1. These results indicated that there are COOH groups in the molecular chain and correspond to the acidity test of 2.3 in Table 1. Thus the enteric polymethacrylate coating material was prepared successfully. From Table 1 we knowed that this material has properties of low viscosity, small particle size, which benefit for the coating operation.

Table1. Basic physicochemical properties of enteric polymethacrylate coating materials

Name	Polymethacrylate	Norm
Shape	Milky white liquid	——
Structure		——
Molecular weight	230000	——
Particle size/nm	≤180	——
Viscosity /mPa.s	10	3~10
Acid value	320	300~330
Acidity	2.3	2.0~3.0
Amount of residue after Evaporation	29.7%	28.5%~31.5%
Residue on ignition	0.01%	0.1%<

3.2. Preparation of Enteric Coated Omeprazole Capsules.

The enteric coating material was coated on the surface of omeprazole isolation pellets by fluidized bed coating technology, and increasing weight about 33%. Then white omeprazole enteric coated pellets of

smooth appearance were obtained, which were stored in condition of (25±2) ℃, RH(60±5) %. The results showed that, the acid resistance and the release rate of three batch of omeprazole enteric coated capsules were (99.19±1.2)%、(97.00±1.6)%、(96.85±2.0)% and (86.97±1.4)%、(92.14±1.8)%、(93.44±2.2)%, respectively. And the acid resistance and the release rate were no less than 90% and 80%, coinciding with standard of " Chinese pharmacopoeia " and showing excellent acid resistance and release properties. Figure.2 showed the dissolution effect of enteric coated pellets in buffer dissolution. Pellets were intact and no apparent discoloration rupture with the acid resistance of （96.85±2.0）% when put in artificial gastric juice 2h. While in buffer solution 20 min, the drug release up to 88.2% and achieve the disintegration effect.

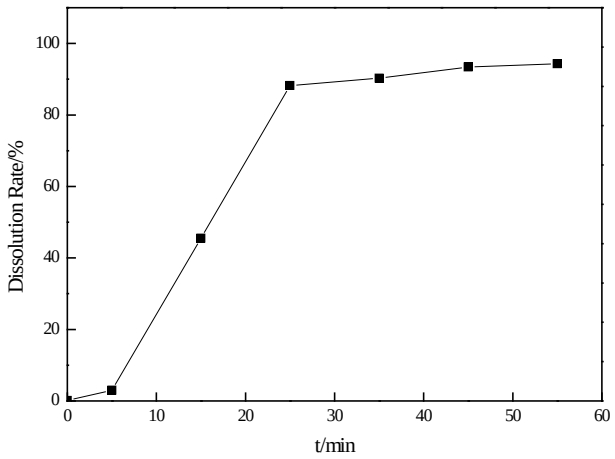


Figure.2. Dissolution curve of omeprazole enteric capsules

3.3. Stability of Long-term Storage of Enteric Coated Omeprazole Capsules.

The omeprazole enteric capsules were stored in（25±2）℃, RH（60±5）％environment. In order to observe the long-term storage stability of capsules, their acid resistance and release properties were tested every 3 month.

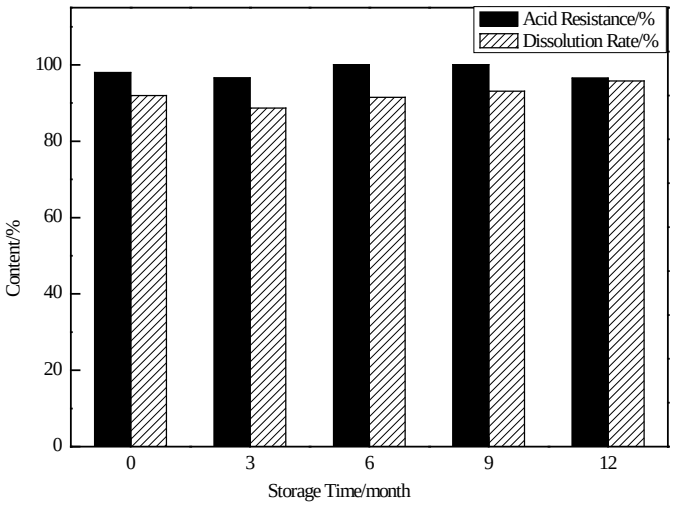


Figure.3. Stability of long-term storage of enteric coated omeprazole capsules

Figure. 3 showed that the acid resistance and release of omeprazole enteric capsules are in accordance with the limits prescribed in the standard, and have excellent long-term storage property.

4. Summary

In this paper, the enteric coating materials with low viscosity, small size were synthesized successfully through emulsion polymerization. Enteric coated omeprazole capsules were prepared by fluidized bed coating technology. The experimental results showed that taking this material as enteric layer has a good performance of excellent acid resistance, release rate, good disintegrating effect and long-term storage stability.

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