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Preparation and Characterization of Ethyl Menthane Carboxamide Microcapsules Using PLA

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ABSTRACT: Using polylactic acid (PLA) as wall and ethyl menthane carboxamide (EMC) as core substance, microencapsulated EMC (MEMC) agents were prepared based on solvent evaporation method. The structure and morphology of MEMC were analyzed by Fourier transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM), and laser particle size analyzer. The MEMC agents had a mean diameter of about 10–20 μm. Moreover, the thermal properties of the MEMC agents were measured by differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA). The melting point and thermal stability were improved due to the encapsulation of PLA resin. In addition, polyvinyl alcohol (PVA) and PLA concentration, stirring rate, and oil/water ratio were investigated for their effects on the particle size. As demonstrated by experimental results, the diameters of the microcapsules decreased with increasing stirring rate and oil/water ratio, and increased with increasing PLA concentration. © 2012 Wiley Periodicals, Inc. J. Appl. Polym. Sci. 129: 665–671, 2013

KEYWORDS: biodegradable; morphology; properties; characterization

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INTRODUCTION

Cooling chemicals, particularly ethyl menthane carboxamide (EMC), have now played an important role in the flavor and fragrance industry.[1] EMC is the common name for *N*-ethy-2-isopropyl-5-methylcyclohexane carboxamide. This class of molecules is further investigated for use in confectionary and oral care products. A wide array of products like toothpaste, mouthwashes, minty chewing gums, and candy mints, upon usage, leads to building up of a so-called "cooling sensation," a sensation strongly associated with freshness and cleanliness.[2] In addition, this compound has excellent effects of insecticide.

However, EMC is volatile and its utilization is limited due to decreasing efficiency in a given environment for its quick release properties.

The encapsulation of the EMC can solve these problems. Microencapsulation is a process of enveloping microscopic amounts of matter in a thin film of polymer.[3,4] The encapsulated substance can be liberated by fusion or dissolution of the impermeable shell or by diffusion across a porous shell.[5,6]

Biodegradable polymers such as polylactic acid (PLA) were used as microcapsule shell materials. Yu et al.[7] prepared ciprofloxacin polylactic microcapsules by phase separation process. Two types of PLA, poly(D, L)lactic acid and poly(L)lactic acid, were combined as membrane materials to prevent the aggregation which happened frequently in the phase separation process. The polymer compositions of the microcapsules can influence the release rate of ciprofloxacin. The optimal release rate of the drug can be obtained by modifying microcapsule compositions. Fu et al.[8] researched the properties of chitosan (CS)/PLA/ tripolyphotspate (TPP) nano-sized microcapsules prepared by emulsion-evaporation. The average diameter of the obtained nano-sized microcapsules was around 100-300 nm, and a homogeneous size distribution and good dispersion were observed. The entrapment efficiency of the nano-sized CS/PLA/TPP microcapsules for rapamycin increased with the increase in amount of PLA. Jonnalagadda[9] used PLA for controlled drug delivery applications. Its properties were limited by unfavorable physical properties such as hydrophobicity, high intrinsic crystallinity, low permeability, and high glass transition temperatures. The microcapsules were formed by a coacervation method using a methylene chloride/hexane solvent/nonsolvent system. High intrinsic crystallinity and dual endothermal character for PLA melting were obtained. Till now, the preparation of microcapsulated ethyl menthane carboxamide (MEMC) agents using PLA resin had not been researched.

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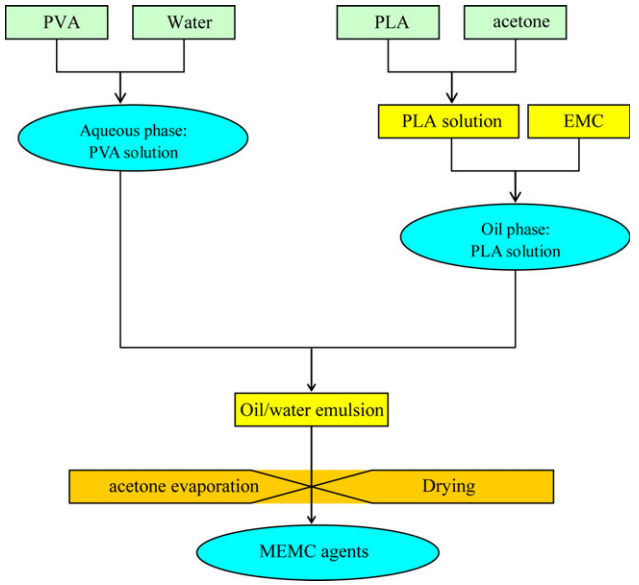


Scheme 1. Preparation process of MEMC agents. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

In the present work, a type of microcapsules containing EMC agents was prepared by the solvent evaporation method via oil-in-water (O/W) emulsion. The parameters of microcapsules preparation in the emulsion system such as the particle size, inner structure, and properties were investigated.

EXPERIMENTAL

Materials

EMC, industrial grade, was obtained from Hubei Xingyinhe Chemical Company (Hubei, China). D,L-PLA ($\overline{M_w}$:100,000), industrial grade, was obtained from Shenzhen Guanghuaweiye (Shenzhen, China). Polyvinyl alcohol (PVA) and acetone, analytical grade, were supplied by Shanghai Guoyao Agent Company (Shanghai, China).

Preparation of MEMC Agents

The process established in this study was illustrated in Scheme 1. About 1–5 g of PVA was dissolved in 95–99 g of water, and the solution was cured for 1–2 h at 20°C to let it swell. Then, the mixture was heated to 80–90°C and treated at this temperature for 2–3 h to let it dissolve completely. PVA solution was thus prepared.

Nearly 16–18 g of acetone was poured into a three-necked flask, and 2–4 g of PLA was added in, respectively. The system was cured for 2–3 h. 0.1 g of EMC was added into this PLA solution. Thus, PLA-acetone solution was obtained.

Nearly 50–90 g of PVA solution was poured into a four-necked flask, and 10 g of PLA-acetone mixture was added. The system was cured for 2–3 h. Then, the temperature was adjusted to 40–60°C, and stirred for 1–2 h to let acetone evaporated. The resulting emulsion was rinsed several times by distilled water, and then placed in a vacuum oven at 50–60°C for 12 h to dry. The dried cake was ground to obtain the MEMC agents.

Characterization

FTIR spectra of the surface functional groups of EMC and MEMC agents were recorded on a Nicolet Avatar 370 Fourier transform infrared spectrophotometer in the range 4000∼ 700 cm^{-1} at a resolution of 2 cm^{-1}. Samples were ground and mixed with KBr to form pellets. Sixty-four scans were necessary to obtain spectra with good signal-to-noise ratios.

Samples of EMC and MEMC agents were mounted on brass stubs using double sided cellotape and coated with Pt/Pd (ca. 2 nm) using an agar high resolution sputter coater. Ultrastructural observations were performed with an Hitachi S-4800 field emission scanning electron microscopy (FE-SEM) using an acceleration voltage of 15 kV and a working distance of 6 mm.

The heat of fusion and melting temperature of PLA resin, EMC, and MEMC agents was obtained with a DSC PT-10 from Linseis. Thermogravimetric analysis (TGA) was carried out at 20°C min^{-1} under nitrogen (flow rate 5 × 10^{-7} m^3 s^{-1}) using a Linseis PT-1000 microbalance. In each case, the mass of samples used was fixed at 10 mg and the samples were positioned in open vitreous silica pans. The precision of the temperature measurements was 1°C over the whole range of temperatures.

The particle size and distribution of MEMC agents were analyzed by a laser particle size analyzer (model Psl.rfd PIDS included, Beckman Coulter). The particle size analyzer was equipped with a measurement cell. A lens capable of detecting particles in the size range of 0.01–80 μm was attached to the optical measurement unit. For protection of the analyzer, aggravating liquids were avoided and only mild liquids, such as ethanol, were used for dispersing the MEMC agents.

RESULTS AND DISCUSSION

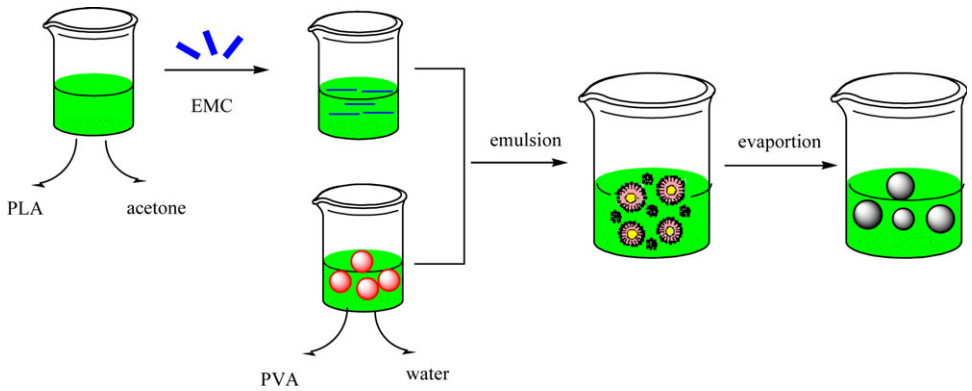
Mechanism of Shell Formation

The solvent evaporation method of microcapsule shell formation might conform to the following process as shown in Scheme 2. First, an aqueous solution containing emulsifier was prepared. The emulsifier, PVA, was used for O/W interface. Emulsification was carried out by agitation. Second, a polymer solution in organic solvent such as acetone was presented. PLA was the most widely used biodegradable synthetic polymers for sustained-release preparations. EMC was then dissolved in this polymer solution. Third, the PLA-EMC solution was added into above continuous PVA aqueous phase. Organic solvent, acetone, in dispersed phase was removed by solvent evaporation. Last, in the solvent evaporation process, hardening of emulsion occurred when volatile organic solvent in dispersed phase leached into continuous phase and evaporated from continuous phase at atmospheric pressure. A moderate increase in temperature can accelerate the evaporation of organic solvent.[10]

Characterization of MEMC Agents

Structure of MEMC Agents. FTIR spectra of the EMC and MEMC agents were shown in Figure 1(a,b).

It was observed from Figure 1(a), the EMC spectrum, that there were two obvious absorption peaks at 3350 and 1580 cm^{-1}. These corresponded to the stretching and bending vibrations of N—H presented in the structure.[11] C=O stretching vibrations



Scheme 2. Shell formation process of MEMC agents. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

were shown at 1680 cm^{-1}, and C—H stretching vibrations were observed between 2800 and 3000 cm^{-1}. Its chemical formula was shown in Scheme 3(a).

In the spectrum of the MEMC agents, Figure 1(b), the main absorption peaks appeared at 3000–3650, 2800–3000, and 1850 cm^{-1}. The characteristic absorptions at 3000–3650 cm^{-1} were resulted from the stretching vibrations of O—H groups. The obvious absorption peaks at 1850 cm^{-1} corresponded to the stretching vibrations of C=O groups, and the absorption peaks at 1110 and 1200 cm^{-1} were related to C—O. This illustrated the existence of —COO groups in the structure. These groups were in good accordance with the structure of PLA resin, and the chemical formula of which was shown in Scheme 3(b).[12]

In addition, the characteristic absorptions of the EMC, the peaks at 3350 cm^{-1} and others, strongly weakened, which to some extent can illustrate that PLA resin had successfully encapsulated the EMC agents.[13]

Morphology of MEMC Agents. The microscopic morphology of EMC and MEMC agents was supported by FE-SEM photomicrographs (Figure 2). As evidenced here, Figure 2(a), the EMC was columnar in shape and aggregated together. This was due to the strong interaction among the EMC agents. From Figure 2(b), it was revealed that the micropellets were spherical in shape and had a porous surface. They were separated obviously from each other. This may be caused by the less interaction among MEMC agents.[14]

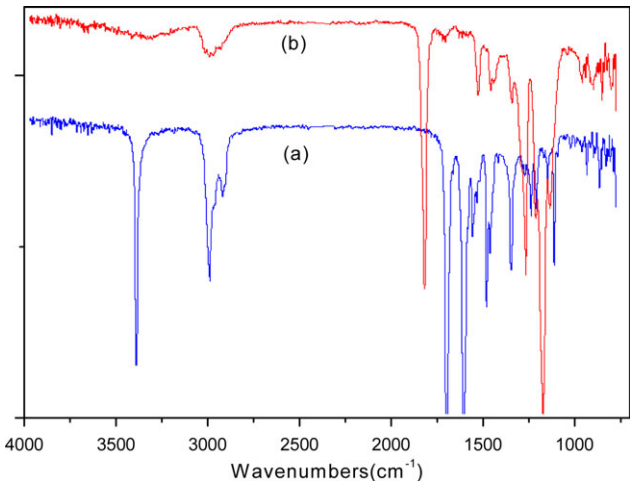
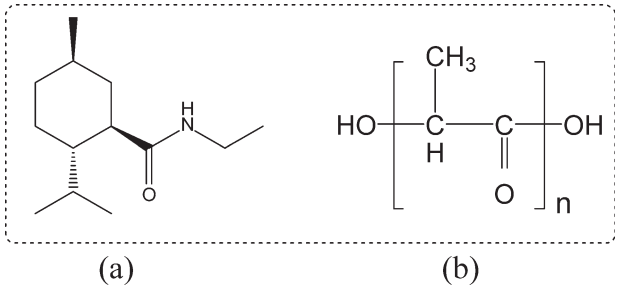


Figure 1. FTIR of (a) pure EMC; (b) MEMC agents. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Thermal Properties of MEMC Agents. The EMC could be either dispersed in crystalline amorphous form or dissolved in the polymeric matrix during the process of microencapsulation. Also, any abrupt or drastic change in the thermal behavior of either the EMC or the polymer may indicate a possible core-shell interaction. The DSC curves of the pure EMC and EMC-polymer micropellets were presented in Figure 3. A sharp endoderm observed at the temperature 66°C corresponded to the melting point of EMC, and the peak at 210°C was attributed to its decomposition point. In the case of MEMC agents, obvious endothermic peak was observed in the temperature ranges 120–150°C. This was related to the characteristic and well-recognizable melting point of PLA. The same thermal behavior of the EMC was also observed in the micropellets with thermal peak at 64°C but loss of its sharp appearance.[15]

TGA curves of the EMC and MEMC agents were presented in Figure 4. In Figure 4(a), the EMC first lost initial weight at 150°C and showed the highest degradation degree at 210°C. This phase change of EMC from liquid to gas state was in good accordance with the results shown in DSC. The second step starting at 210°C was ascribed to the rupture and degradation of the amine group in the EMC. Figure 4(b) was TGA study of the MEMC agents synthesized. The degradation also occurred in two steps. The first step started at 280°C and degraded intensively at



Scheme 3. Chemical formula of (a) pure EMC; (b) PLA.

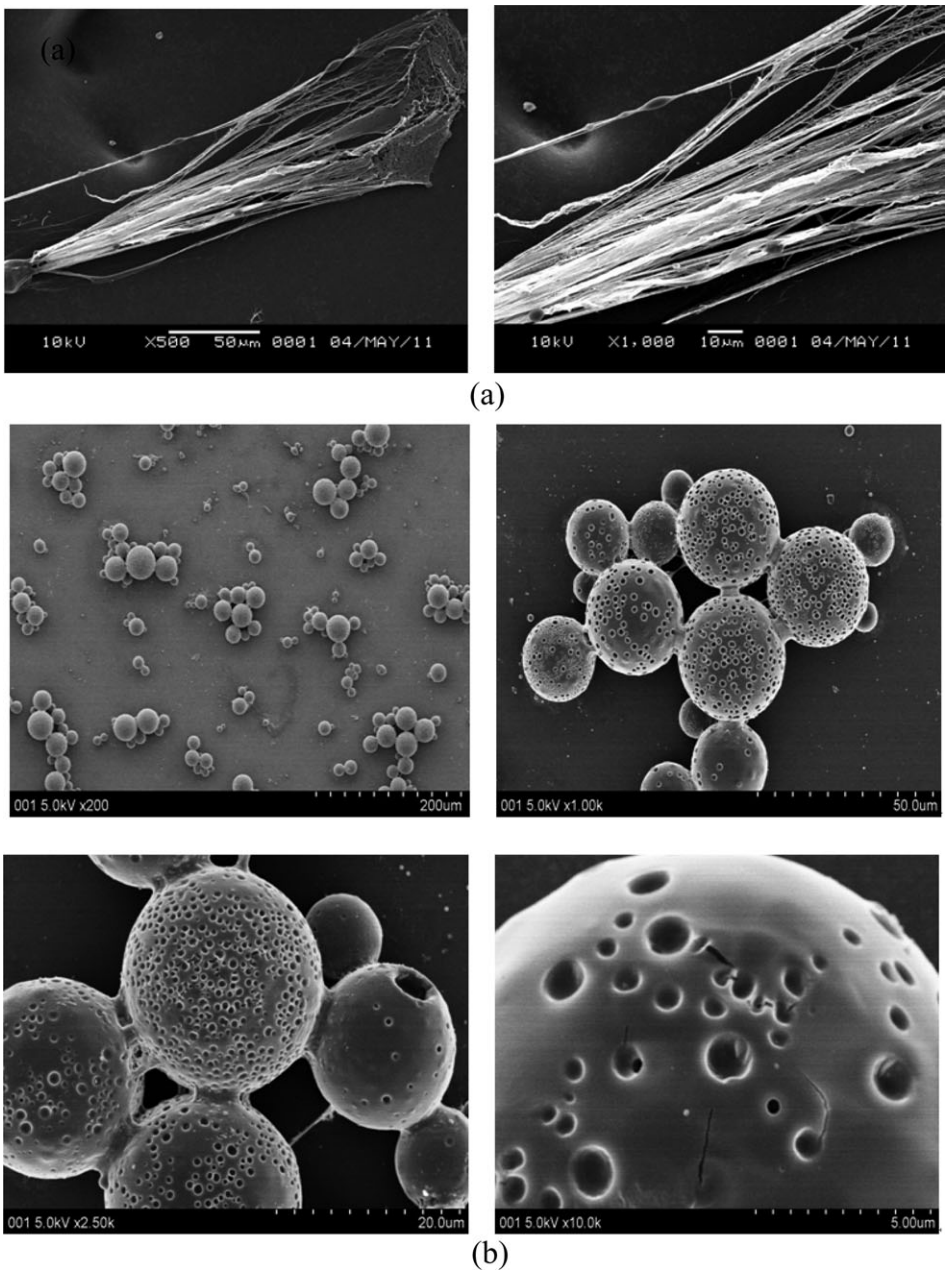


Figure 2. FE-SEM of (a) pure mint amide; (b) MEMC agents.

340°C. This can be ascribed to the rupture and degradation of the PLA resin covered over the EMC. The second step started at 340°C, and this may be ascribed to the hydrolysis of the residue. In addition, the degradation degree of the MEMC agents decreased after encapsulation of PLA resin on its surface, which was resulted from the improved thermal stability compared with that of the EMC. This was beneficial for the application of EMC in the matrices, such as plastics and rubber composites, which requires higher operating temperature.[16–18]

Analysis of Influencing Parameters on the Particle Size of MEMC

Effect of PLA Concentration on the Particle Size. The effect of PLA concentration was found to have a major influence on the final particle diameter (Figure 5). The average diameter of the MEMC particles increased from 10.3 to 21.5 μm as the PLA concentration was raised from 2 to 6%. Stover[19] fabricated PDVB microspheres by dispersion polymerization in acetonitrile or ethanol solution with polyvinylpyrrolidone as the stabilizer, and found that larger particles were formed when monomer concentration increased. Moreover, this was usually accompanied by a broadening of the particle size distribution. The PLA concentration acted the same as the monomer. It could affect the particle size by altering the solubility of the critical chain length in the continuous phase. This way, larger and more numerous nuclei could be obtained. Correspondingly the coagulation rate would increase, and larger particle could thereby be fabricated.[20]

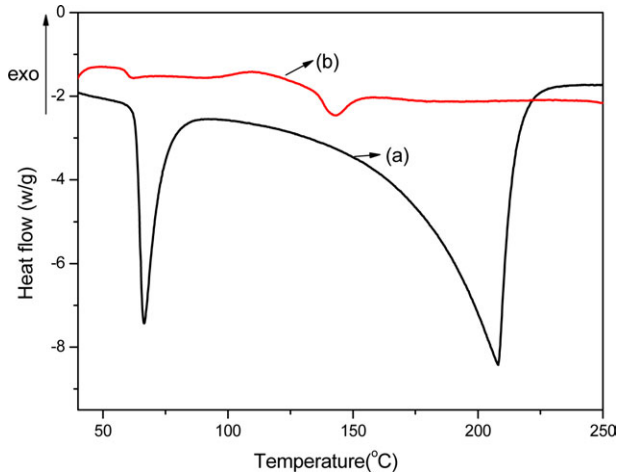


Figure 3. DSC of (a) pure EMC; (b) MEMC agents. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Effect of Stirring Rate on the Particle Size. The effect of shearing force on the particle size of MEMC agents was such an extent that a high shearing force yielded a narrow particle size distribution range and finer average particle size. This phenomenon was directly related to the stirring rate (Figure 6).[21] In the application of low agitation rate of stirring, the coalescence of the primary colloidal droplets continued unabatedly, leading to the formation of very large coacervated particles and, finally, to macroscopic phase separation. It was evident that as the agitation rate increased high enough, the capsule size gradually decreased. This may be resulted from the increasing turbulent kinetic energy associated with the drop breakage process. It can be postulated that drop breakage in turbulent fields may be caused by viscous shear forces resulting from the high impeller speed, the turbulent pressure fluctuations, and/or relative velocity fluctuation.

Effect of PVA Concentration on the Particle Size. PVA concentration had an important influence on the synthesis of MEMC agents, and correlated well with the particle size. The

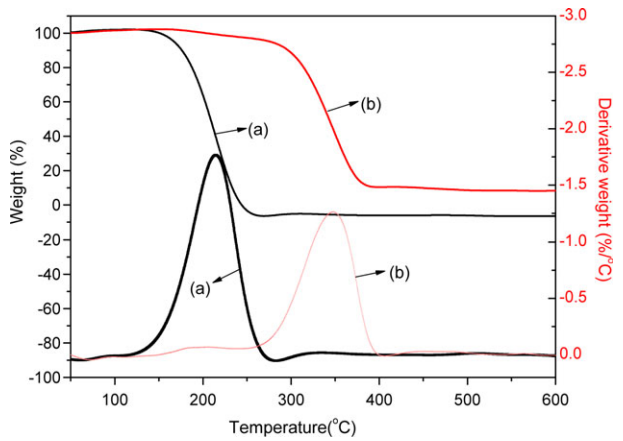


Figure 4. TGA curves of (a) pure EMC; (b) MEMC agents. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

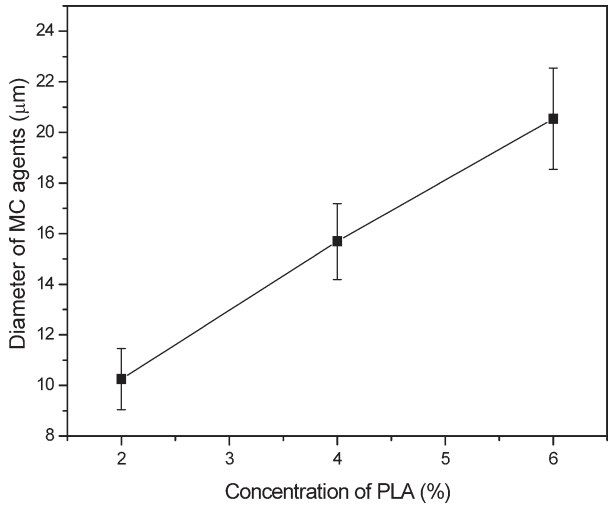


Figure 5. Relationship between concentration of PLA and particle size of MEMC agents.

interfacial tension of the oil/water system will depend on the temperature and concentration of PVA. The mechanism of the influence of concentration on the particle diameter distribution depended on the interfacial tension of the system during synthetic process.

The MEMC agents exhibited larger particle size when the concentration of PVA was lower than 3% (Figure 7). This may be due to the low interfacial tension between PVA and the EMC agent, which led to larger particle size. When the concentration increased to 5%, the particle size also increased. The initial breakdown of the dispersed phase into the smaller droplets was hindered, and this led to the formation of bigger microcapsules.[22] Park et al.[23] obtained the almost same results. When the emulsifier content was higher than 10%, the particle distribution of microcapsules becomes larger due to adhesion of the particles by increasing viscosity. Lankveld and Lyklema[24] also reached a conclusion that the observed relationship between the interfacial tension and PVA concentration was related to the

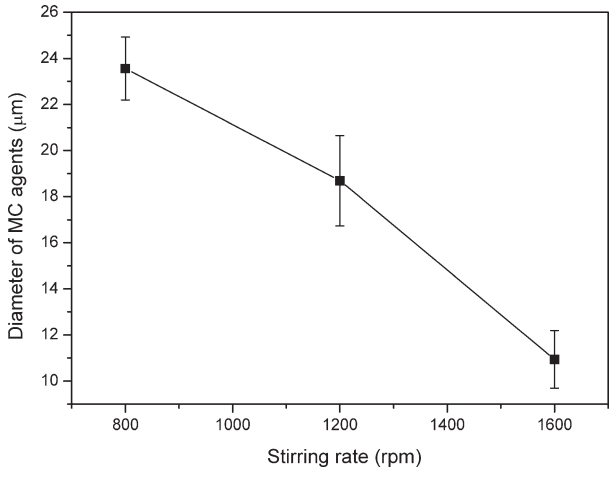


Figure 6. Relationship between stirring rate and particle size of MEMC agents.

number of adsorbed polymer segments per unit area of the solid–liquid interface, the interaction free energy per segment in the loops of the adsorbed polymer molecules, and the average loop length. The combined effect of the segmental adsorption as well as loop interaction tended to increase the interfacial tension, and thus can increase the diameter of the MEMC agents.

Effect of Oil/Water Ratio on the Particle Size. To investigate the effect of the volume of the organic and aqueous dispersed phases on the size distribution of the microcapsules, the oil/water ratio was varied from 1 : 3 to 1 : 7 (Figure 8). At higher volume of oil phase, the dispersed phase was highly viscous, adhered to the propeller shaft and vessel wall, and was agglomerated. When oil volume decreased, the dispersed phase became more and more fluid and was converted into particles of gradually decreasing sizes. This could be attributed to less collision between the micropellets while stirring because of the lower viscosity of the system.

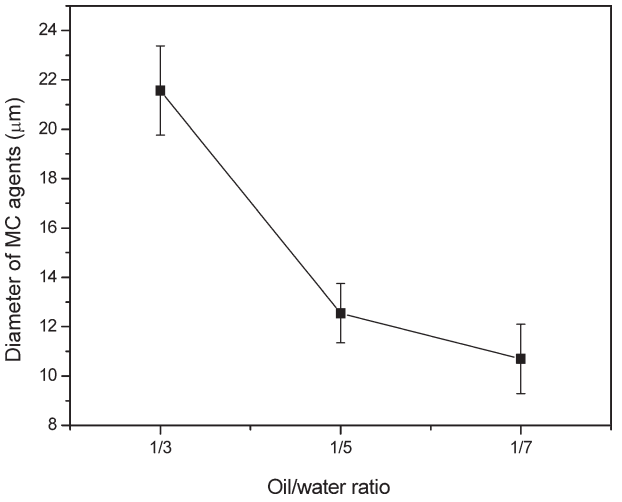


Figure 8. Relationship between oil/water ratio and particle size of MEMC agents.

CONCLUSIONS

In this work, PLA microcapsules containing EMC were prepared by solvent evaporation method. The expected advantages of this concept of encapsulated EMC agent lay in its slowing release rate and biodegradation.

The morphology and thermal properties of the MEMC agents were analyzed by FTIR, SEM, DSC, and TGA. The melting point and thermal stability of the EMC were obviously improved, which was caused by the encapsulation of PLA resin over the surface. It was also revealed that the particle size of the microcapsules were largely dependent on the PLA and PVA concentration, stirring rate, and the oil/water ratio.

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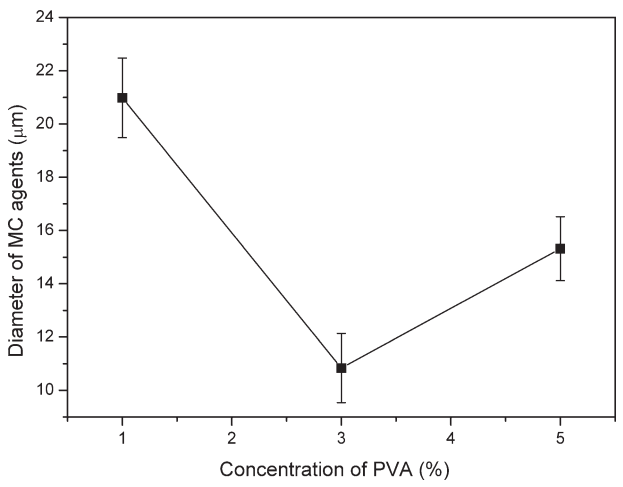

Figure 7. Relationship between concentration of PVA and particle size of MEMC agents.

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