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RESEARCH PAPER

Comparative Evaluation of Microcapsules Prepared by Fluidization Atomization and Melt Coating Process

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ABSTRACT

Microcapsules were prepared from potassium chloride as a highly water-soluble model drug, and coated with white beeswax by the fluidization and melt methods. Dissolution profiles, microscopic surface topography, and diffusion reflectance spectra of microcapsules were evaluated by comparative studies. The results show remarkable differences in the examined parameters of the microcapsules prepared by different techniques. The results demonstrate that melt coating is able to control the drug release and may serve as an advantageous solvent-free alternative of fluidization.

INTRODUCTION

Several pharmaceutical investigations were carried out to develope new types of sustained-release solid oral dosage forms and controlled-release drug delivery systems (1). Attempts have been made to develop long-acting preparations by coating the drug with poorly water-soluble, swollen or nonswollen polymers or other substances to achieve once-a-day dose treatment for better patient compliance (2), due to a constant and slow release (3,4). The most widely used oral controlled-release dosage form is the diffusion-controlled type (5,6).

Melt coating is solvent-free and hence one of the most economical and less hazardous coating methods. The low melting point makes wax or other waxy-type materials preferable for melt coating (1,7–10).

MATERIALS

Potassium chloride USP 23 grade was selected as a highly water-soluble model drug for core material of

microcapsules. The coating material was white beeswax, USP 23 grade (melting range of 61°–65°C). Dehydrated alcohol USP 23 grade was used as organic solvent of the white beeswax in the fluidization atomization method.

METHODS

Preparation of Microcapsules by Fluidization Atomization Process

Potassium chloride, 100 g, (particle size 400–600 μm) was coated with 5% dehydrated alcoholic solution of white beeswax in Aeromatic STREA-1 fluidization equipment (11). Bottom atomization was applied at 8 m^3/hr of air flow rate, at 0.6 m^3/hr atomizing air, and at 18 rpm of a Watson–Marlow-type peristaltic pump.

Preparation of Microcapsules by Melt Coating Method

The core material and the wax were filled into Erweka equipment (type: SG 3/W, Erweka GmbH, Germany). The temperature-regulated container was heated to 70°C. Constant stirring was applied (30 rpm) until the wax was completely molten. To prevent the sedimentation of the higher-density component, 5% glycerol monostearate was added to increase the viscosity.

In Vitro Dissolution Studies

For the determination of dissolution profiles of the microcapsules, the rotating paddle method of USP 23 at 100 rpm was used (PTW2 dissolution test apparatus, Pharmatest Apparatebau GmbH, Hainburg). The study was conducted in 500 ml of pH = 1.2 simulated gastric fluid, prepared with 0.1 N HNO_3 instead of HCl. The dissolution was continously monitored by a digital pH meter (Radelkis OP 211/1, Budapest), equipped with a chloride-selective electrode (Radelkis OP-Cl 7111P).

Recording Diffuse Reflectance Spectra

The diffusion reflectance was measured by a Hitachi U-2501 ultraviolet–visible–near infrared (UV/VIS/NIR) spectrophotometer (Hitachi, Japan) equipped with integrating sphere (d = 60 mm) and PbS detector. The reflectance of samples was detected in the 210- to 2000-nm wavelength range using a 5-mm layered cell.

Scanning Electronmicroscopy Study

The surface morphology of the specimens was studied by scanning electron microscope (Jeol JSM-25, Jeol, Japan) after gold vacuum coating.

RESULTS AND DISCUSSION

To characterize the dissolution process mathematically, the Rosin–Rammler–Sperling–Bennett–Weibull (RRSBW) distribution (12) was applied according to the following formula:

$$M_t = M_\infty [1 - \exp\{-(t - t_0/\tau_d)^\beta\}]$$

where M_t is the released amount of the drug (%) at time t (min); M_∞ is the total amount of drug released, the plateau of the dissolution curve; t_0 is the lag time (min) of the drug dissolution; β is the shape parameter of the curve; τ_d is the mean dissolution time (min), when 63.2% of M_∞ has been released.

Figures 1 and 2 show the observed data and predicted curves of drug release. The estimated parameters of the fitted mathematical model are demonstrated in Table 1.

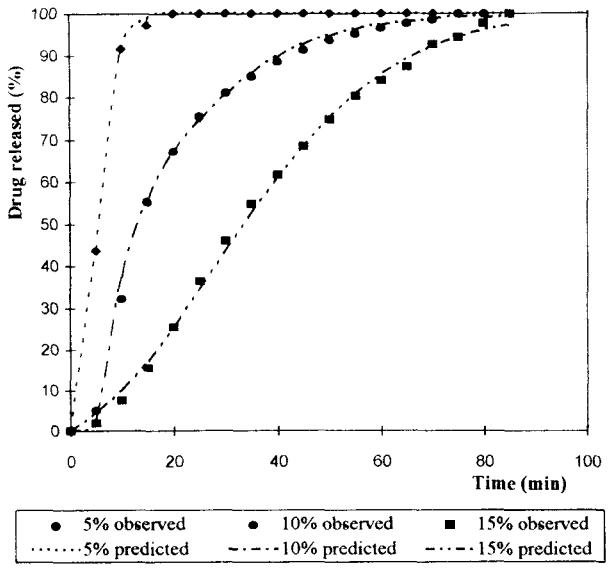


Figure 1. Observed and predicted (using the Weibull distribution) values of drug release curves of microcapsules prepared by melt coating (correlation: 5%: 0.99981, 10%: 0.99881, 15%: 0.999881).

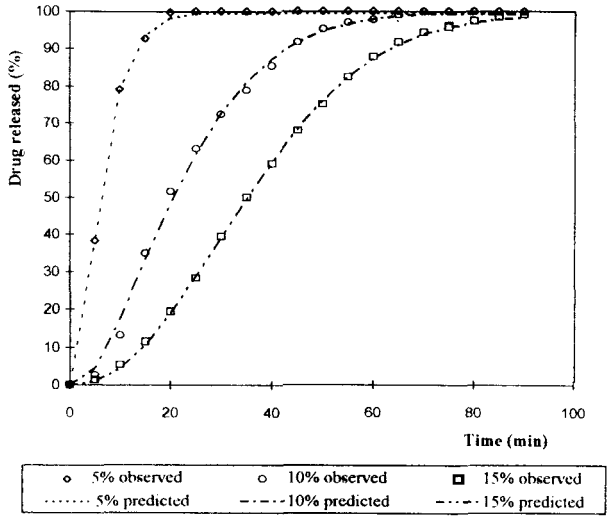


Figure 2. Observed and predicted (using the Weibull distribution) values of drug release curves of microcapsules prepared by fluidization atomization process (correlation: 5%: 0.99783, 10%: 0.993264, 15%: 0.998845).

Table 1

Characteristic Parameters of the RRSBW Distribution

Sample	τ_d	β
5% coating level		
Fluid	3.1	1.0939
Melt	5.1	1.1035
10% coating level		
Fluid	21.5	1.2124
Melt	23.7	1.5336
15% coating level		
Fluid	45.4	1.9265
Melt	40.6	2.0300

The dissolution was sustained at each coating level without delaying the release (lag time $\approx$ 0). The rate of dissolution can be controlled by the extent of coating, and this connection can be characterized by a linear regression between the mean dissolution time (τ_d) and coating level (Fig. 3). The slope parameter a (Table 2) demonstrates the higher efficiency of melt coating in controlling the drug release.

The change in shape parameter β follows the tendency of the coating level, too. At 5% coating level $\beta \approx 1$, which refers to first-order dissolution kinetics. At higher coating levels $\beta > 1$, which reports upon the parallel moving courses in addition to diffusion (disintegration, erosion) (12).

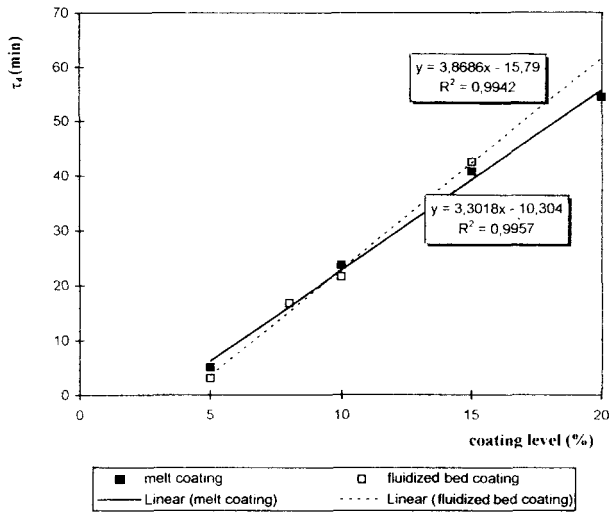


Figure 3. Dependence of mean dissolution time (τ_d) on coating level.

Table 2

Inserted Regression Functions Describing the Dependence of Mean Dissolution Time (τ_d) on Coating Level

Method of Preparation	Regression Function Type	Regression Function Parameters	R^2 Values
Fluidization–atomization	1. **Linear:** $y = ax + b$	a = **3.8686**; b = **-15.79**	**0.9942**
	2. Power: $y = ax^b$	a = 0.0864; b = 2.3627	0.9390
	3. Exponential: $y = ae^{bx}$	a = 1.4672; b = 0.2428	0.8352
	4. Logarithm: $y = a \ln(x) + b$	a = 35; b = -55.158	0.9664
Melt method	1. **Linear:** $y = ax + b$	a = **3.03**; b = **-10.304**	**0.9957**
	2. Power: $y = ax^b$	a = 5.7233; b = 1.7349	0.9736
	3. Exponential: $y = ae^{bx}$	a = 3.3472; b = 0.7659	0.8752
	4. Logarithm: $y = a \ln(x) + b$	a = 35.189; b = 3.0104	0.9809

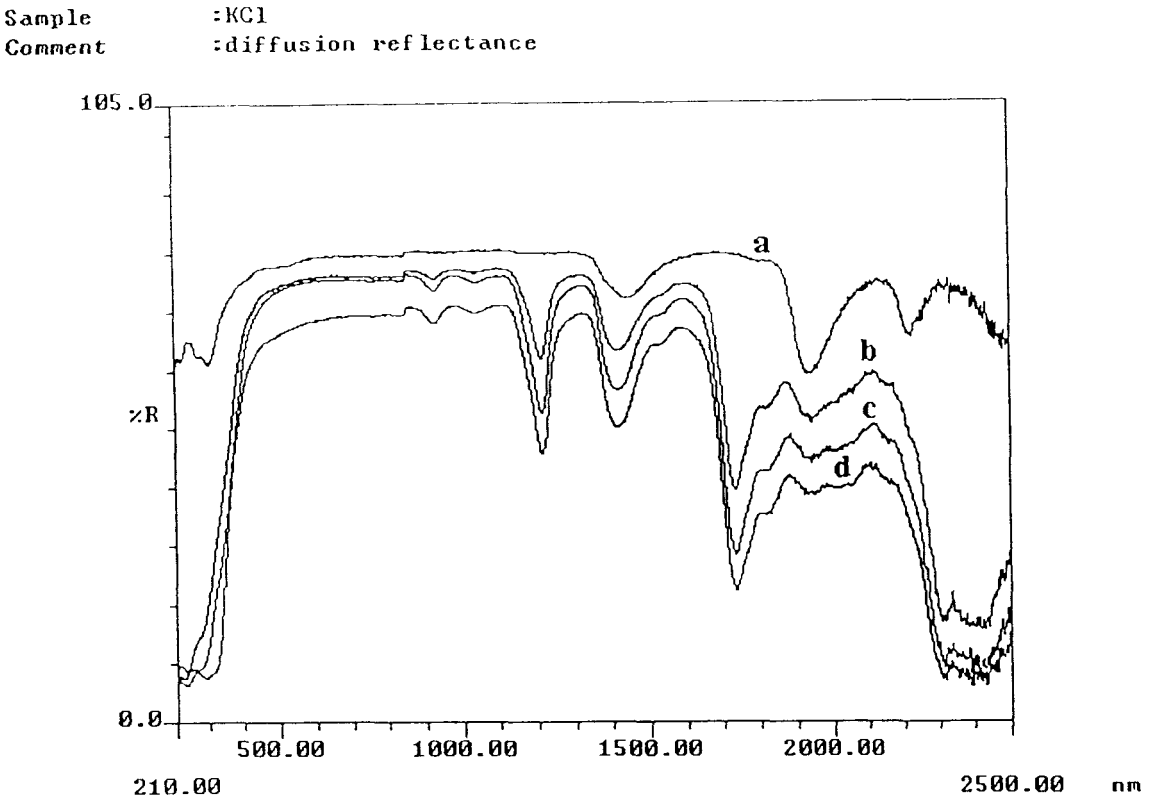


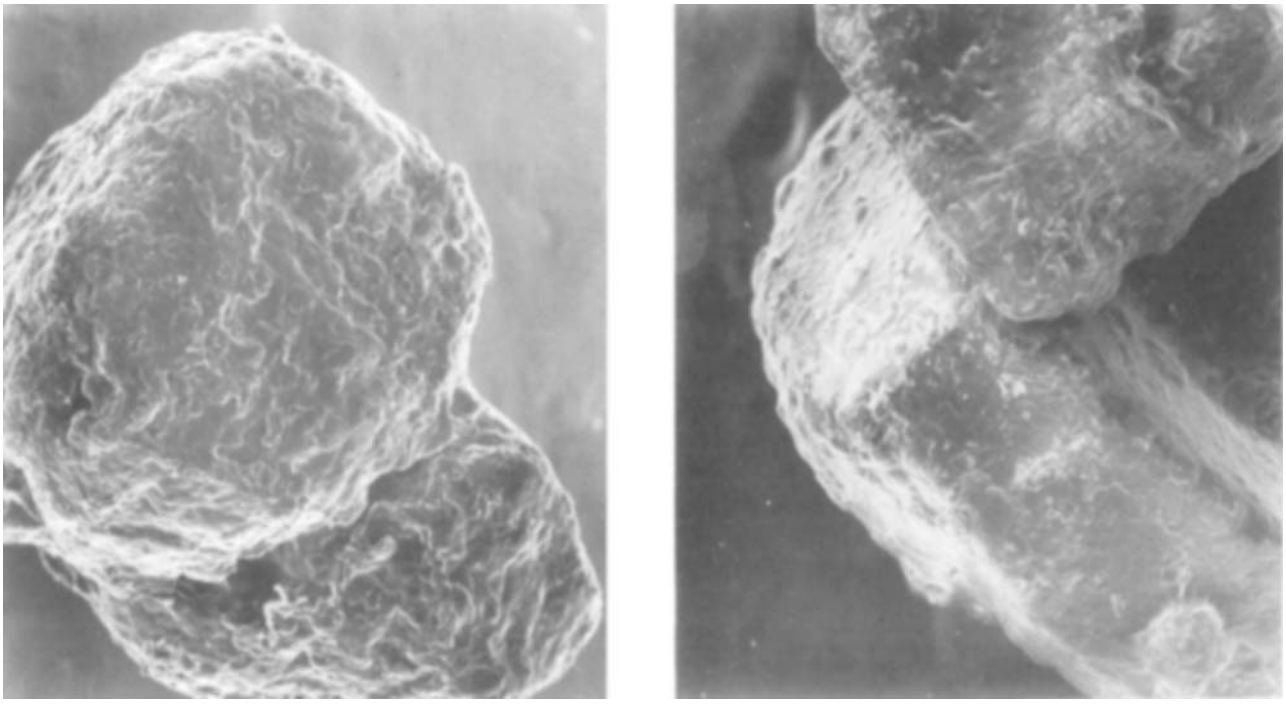
Figure 4. Diffusion reflectance spectra of microcapsules prepared by melt coating: a, coating level = 0%; b, coating level = 5%; c, coating level = 10%; d, coating level = 15%.

Figure 4 shows the diffusion reflectance spectra of the microcapsules prepared by melt method. The loss in the intensity of reflectance seems to be directly proportional to wall thickness.

A study on surface morphology of the microcapsules by scanning electron microscopy (SEM) shows significant differences between the coat morphologies of microcapsules prepared by the melt method and fluidization (Fig. 5). The melt method results in a coat without any discontinuity, in consequence of the continuous material transition between the solid core and the semisolid molten coat material. In the case of fluidization atomization, the coating material is applied onto the core in a form close to the solid state, because of the immediate evaporation of solvent.

CONCLUSIONS

By changing coating level, the drug release of the samples can be modified to a significant degree, according to the linear function found between the mean dissolution time (τ_d) values and the coating level. It can be established that the method of preparation markedly influences the drug release process from the micro-



(a) (b)

Figure 5. SEM (×70) photos of microcapsules, 10% coating level: (a) melt; (b) fluid.

capsules. The extent of coating can be checked by diffusion reflectance measurements, since the decrease of reflected energy follows the coat thickness.

The results demonstrate that melt coating is able to control the drug release and may serve as an advantageous solvent-free alternative to fluidization.

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