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A METHOD OF PREPARING GELATIN MICROCAPSULES

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ABSTRACT

In the pharmaceutical industry, microencapsulation has been applied to a variety of drug dosage forms. Usually a mechanical method produces a narrowly defined final product with a specific coating material and size of the core particles. Microcapsules were prepared by passing molten drug-gelatin mixture through a vibrating needle at a known frequency and amplitude. The microcapsules obtained were spherical, rigid, discrete, and had a narrow size range.

EXPERIMENTAL

Equipment and Materials: A VCG Function Generator; a speaker; Poineer amplifier; travelling microscope; Big Jack; Micromate

luer lock syringes; Spinal needle gauge 18 and 22; Shim Brass Stock 0.001 inch thick; U.S.P. gelatin, type B, grade 5A, jelly strength 202 gms, viscosity 44 mps., pH=5.3; sodium sulfamerazine; FD & C green No.3 and FD & C yellow No. 5; Cenco-Meinzer sieve shaker.

Apparatus for Microencapsulation: Of the several methods examined for the production of microcapsules of narrow size distribution, a method similar to that described by Madan et al. (1) was used.

A shim brass cone, CE, made by using a soldering gun was attached to the center of a speaker, SR, with clear silicone glue (Figure 1). A small piece of cork, CK, was attached to the tip of the cone. The speaker, enclosed in a styrofoam box, SB, was attached to micrometric device of a travelling microscope and a laboratory jack so that it could be moved precisely in the horizontal and the vertical directions. The speaker was connected to the amplifier, AM, which in turn was connected to the gererator, GR. A syringe, SE, with a spinal needle was connected to the lower end of a vacuum flask, EF, by a piece of tygon tubing. The assembly outside the vacuum flask up to near the tip of the needle was jacketed, SJ, for the flow of steam to keep it warm. The upper end of the flask was connected to a compressed air tank. The drug-gelatin mixture, GD, was heated in a flask on a water bath, WB, to 70°C. An evaporating dish, ED, containing approximately 3

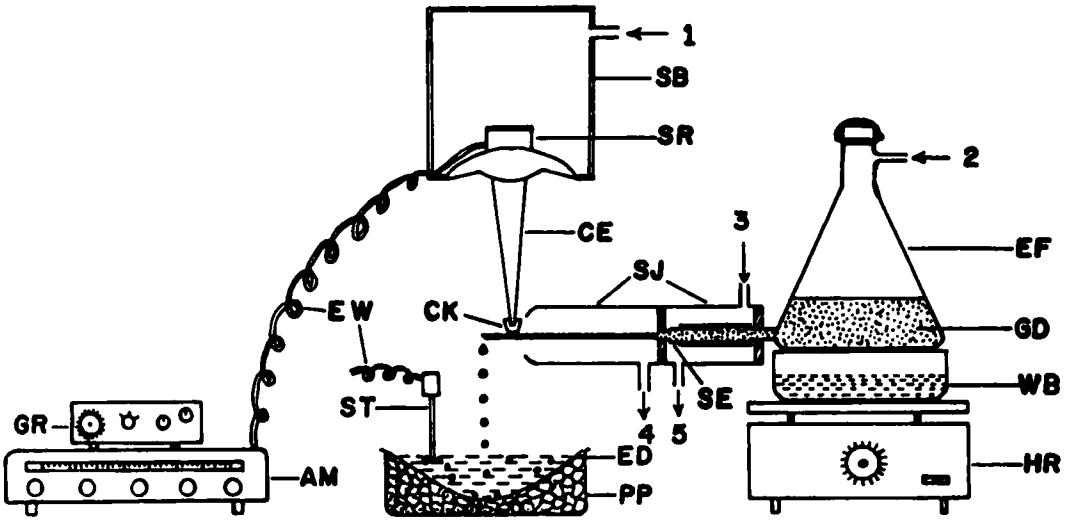


FIGURE 1.

Apparatus for Microencapsulation.

liters of light liquid petrolatum was cooled to 5° to 10°C by an ice-salt mixture.

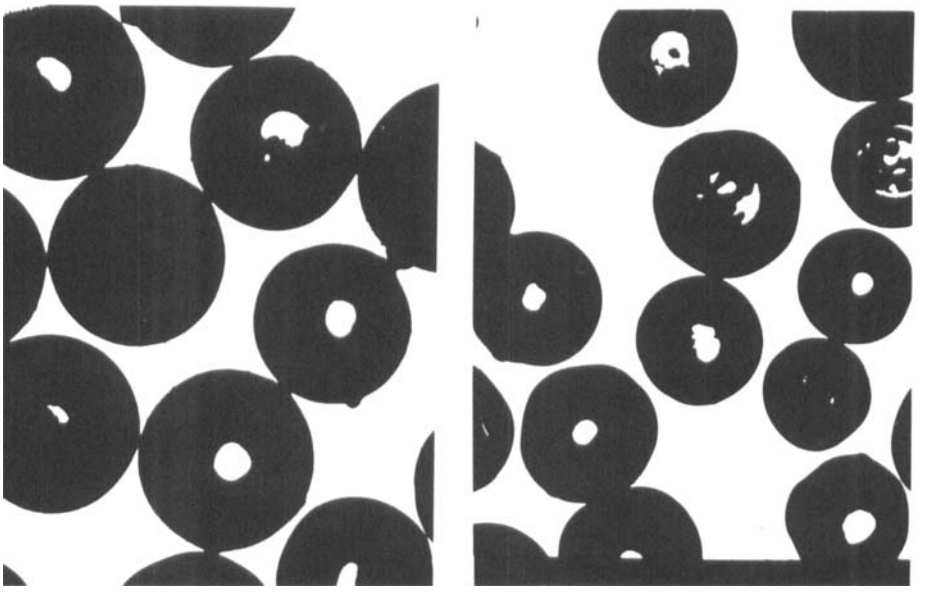
Preparation of Microcapsules: A mixture containing 12.6 ml. of 1 N-NaOH, 5 gm. of sodium sulfamerazine, 0.2 gm. of colorant, and 20 gm. of gelatin type B, grade 5A was heated on a steam bath. The volume of the mixture was adjusted to approximately 90 ml. The pH of the drug-gelatin mixture was adjusted between 8.7 and 8.9 by using a pH-meter calibrated at 70° C. The volume of the mixture was adjusted to 100 ml. The mixture was poured in the Erlenmeyer flask, stoppered securely and heated on steam bath.

The flask was adjusted so that the cork, CK, was 1 cm. away from the tip of the spinal needle. The cork was lowered by the jack to a distance of approximately 1 to 2 mm. The generator and the amplifier were turned on and adjusted to a known value so that the total displacement of the vibrating needle was about 5 mm. The homogeneous drug-gelatin mixture, while heated on steam bath, was pressurized as read from the pressure gauge attached to the air tank.

The microcapsules formed at and discharged from the needle tip were collected in the chilled mineral oil. At a given vibrational speed, the capsule size was increased as feed rate was increased. Increased vibrational speed produced smaller capsules. These two factors were balanced to obtain the desired size of the microcapsule. Careful reproduction of the conditions was required in order to obtain good results.

Conditions for 45/80-mesh size microcapsules were: 5% w/v sodium sulfamerazine, 0.2% w/v FD & C Green No. 3, 20% w/v gelatin B, grade 5A, pH = 8.7 to 8.9, spinal needle 3.5 inches long, 25 gauge, pressure 7.5 psi, frequency 1200 HZ, distance between needle and the oil surface in the receiver was approximately 15 cm.

After collecting a batch of approximately 100 to 500 gm. of microcapsules in the mineral oil bath, the microcapsules were collected on a 200-mesh size screen in a cold room maintained at 5° to 10°C to minimize aggregation. The

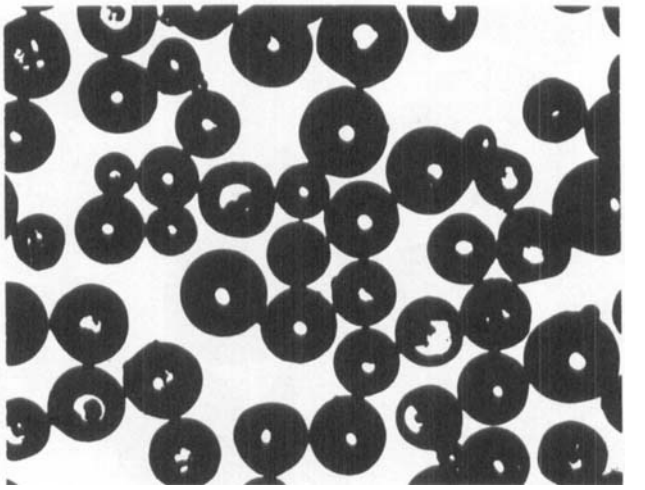


(a) (b)

FIGURE 2.

Photomicrographs of microcapsules under microscope
Magnification 35x
Key: (a) 20/30-mesh size microcapsules,
(b) 30/45-mesh size microcapsules.

microcapsules collected on screen were washed two times each with 500 ml. of isopropyl alcohol at 5° to 10°C for 10 min. The excess of mineral oil adhering to the microcapsules was carefully washed with a stream of cold chloroform. The microcapsules on the screen were hardened by immersion for 48 hours in a 10% solution of formaldehyde in isopropyl alcohol at 5° to 10°C. Ten milliliters of formaldehyde-isopropyl alcohol was used for each gm. of microcapsules. The hardened



(a)

FIGURE 3.

Photomicrographs of microcapsules under microscope.
Magnification 35x
Key: (a) 45/80-mesh size microcapsules.

microcapsules were alternately washed with methanol-acetone (1:1) mixture and air dried. The microcapsules were free flowing, and had a narrow range of particle size. Figures 2 and 3 show photomicrographs of the microcapsules.

Sieve Analysis of Microcapsules: A nest of sieves and Cenco Meinzer Sieve Shaker were employed for the separation of microcapsules into various size ranges. Microcapsules passing through one sieve and retained on the next finer sieve were assigned the arithmetic mean size of the two screen openings. Sieve numbers 20, 30, 45, and 80 were used to obtain

TABLE 1.

Sieve Analyses of Microcapsules:

Color of Microcapsules	Sieve Size	Average Diameter of Microcapsules (cm.)	Weight Retained (gm.)	Percent Retained
Blue	top/20	-	4.35	3.07
	20/30	0.0725	5.79	4.08
	30/45	0.0478	43.61	30.78
	45/80	0.0266	76.78	54.19
	80/pan	-	11.17	7.88
Yellow	top/20	-	11.93	5.57
	20/30	0.0725	98.55	46.00
	30/45	0.0478	88.65	41.38
	45/80	0.0266	13.65	6.37
	80/pan	-	1.46	0.68

microcapsules having average diameters of 725, 478, and 266 microns, respectively. The microcapsules thus obtained were spherical in shape and had a predictable narrow size distribution. The particle size analyses obtained are given in Table 1.

The density of microcapsules was determined by pycnometry by using n-heptane at 25°C as displacement fluid, given in Table 2.

TABLE 2.

Density of Microcapsules:

Sieve size	Density ($gm./cm.^3$)
20/30-mesh	1.428
30/45-mesh	1.428
45/80-mesh	1.371

The 20/30- and 30/45-mesh size yellow colored microcapsules and 45/80-mesh size blue colored microcapsules were used to conduct hindered settling studies described elsewhere (2).

ACKNOWLEDGEMENTS

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REFERENCES

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(2) K. C. Dhupar, Ph.D. Thesis, University of Iowa, Iowa City, Iowa, 1982.