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## NOTES

# Effect of Capsule Size on Permeability of Gelatin–Acacia Microcapsules toward Sodium Chloride

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**Abstract** □ The effect of capsule size on the permeability of gelatin–acacia microcapsules toward sodium chloride was investigated. Gelatin–acacia microcapsules containing olive oil were prepared by phase separation. The encapsulated olive oil was extracted with acetone and the acetone-loaded microcapsules dispersed in acetone were fractionated by a series of mesh screens. The core material of acetone then was replaced by water. The permeability of each capsule fraction toward sodium chloride was estimated from the change in electrical conductance with time of the mixture of microcapsule suspension and sodium chloride solution. The permeability decreased with decreasing capsule size. Structured water in and around the capsule wall may be the cause of the observed size effect.

**Keyphrases** □ Gelatin–acacia microcapsules—prepared by phase separation, capsule-size effect on permeability toward sodium chloride □ Permeability—gelatin–acacia microcapsules, evaluated for capsule-size effect □ Capsule size—effect on permeability of gelatin–acacia microcapsules □ Microcapsules, gelatin–acacia—capsule-size effect on permeability toward sodium chloride

Relatively few papers (1–4) have dealt with the permeability characteristics of microcapsules, and many uncertainties remain (5) in spite of their importance in the sustained release of encapsulated drugs and chemicals and the application of microcapsules in enzyme technology and therapy and in the removal of waste products by polymer-coated charcoal. Among the various permeability characteristics of microcapsules, the effect of capsule size seems to be the most ignored; only one paper (6) described the size effect on the permeability of ethylcellulose microcapsules toward electrolytes. This situation prompted the present study to see if capsule size affects the permeability of microcapsules made of polymers other than ethylcellulose. The observed size effect on the permeability of gelatin–acacia microcapsules toward sodium chloride is reported here.

## EXPERIMENTAL

**Preparation of Microcapsules**—The gelatin–acacia microcapsules were prepared as described earlier (7). Gelatin and acacia solutions were made by dissolving separately 5 g each of gelatin[1] (pI 5.0) and acacia[2] in 100 ml of distilled water. These solutions were allowed to hydrate for 10 min at room temperature and then for 30 min at ~47°. Coacervation was induced at 47°.

Fifty milliliters of olive oil was added in small portions to the gelatin solution with gentle stirring. The stirring rate then was increased for 15 sec. The acacia solution then was added in portions with moderate stirring to the newly formed emulsion. With this procedure, a favorable degree of emulsification and spherical mononuclear microcapsules were obtained. The system was adjusted to pH 3.5 by dropwise addition of 10% acetic acid after the addition of the acacia solution.

Coacervation was brought about by adding 170 ml of distilled water prewarmed at 47° in 3-ml portions during 20 min. The temperature was decreased to 5° at a rate of 0.3°/min. This cooling rate was found to be very important in obtaining spherical microcapsules. When the temperature reached 5°, a dilute formaldehyde solution was added to the microcapsule dispersion to make the final aldehyde concentration ~6 m*M*, and the pH was raised to 8.5 by the addition of 10% NaOH. After a 2-hr reaction time, the insolubilized microcapsules were separated by centrifugation in a low field of no higher than $100 \times g$ to avoid possible breakdown of the capsules.

**Fractionation of Microcapsules**—A wet mass of the microcapsules (~10 g) was transferred into 1000 ml of acetone to extract the encapsulated olive oil. The suspension was stirred vigorously by a magnetic stirrer to prevent capsule aggregation. Ten minutes later, the microcapsules were filtered and transferred into 200 ml of acetone. After this procedure was repeated four times, the acetone-loaded gelatin–acacia microcapsules dispersed in acetone were obtained.

The acetone-loaded microcapsules were fractionated in acetone by a series of mesh screens. Each capsule fraction of a given size was filtered through a coarse filter paper. The separated microcapsules of each fraction were transferred into a large volume of distilled water with vigorous stirring. In this way, acetone was replaced by water. The procedure was not repeated more than twice, because the water-containing gelatin–acacia microcapsules thus obtained were sticky to the surface of the filter paper.

**Determination of Microcapsule Size**—To determine the size of the microcapsules, a sample of each capsule fraction was placed on a hemocytometer, and the microcapsules were photographed under an optical microscope. The photographed film was projected on a large section of paper, and 500 enlarged capsule images were measured to the nearest 0.8 μm. The scale in the hemocytometer was used for calibration. Finally,

[1] Nippi Co., Tokyo, Japan.
[2] Gum acacia JP, Kokusan Chemicals, Tokyo, Japan.



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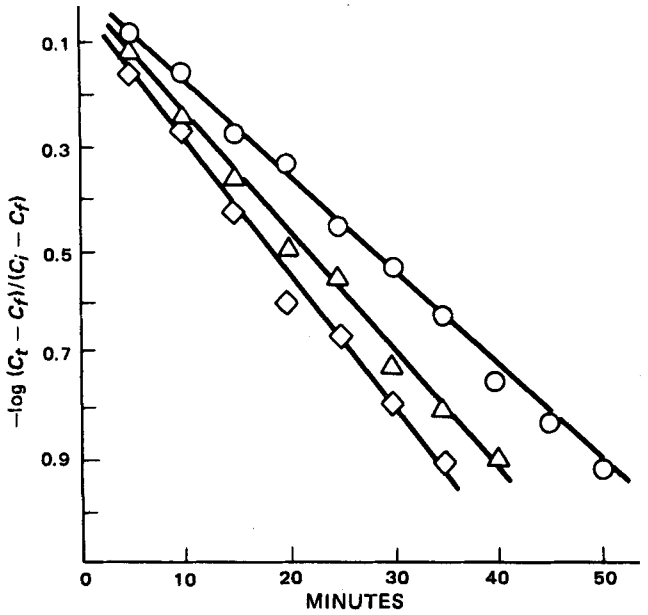


**Figure 1**—*Plot of log* $(C_t - C_f)/(C_i - C_f)$ *against time for the entry of sodium chloride into gelatin–acacia microcapsules. Key (capsule fraction):* ○, *A;* △, *B; and* ◇, *C.*

the mean diameter of the microcapsules was calculated using the measured diameters.

**Permeability Estimation**—As in previous work (2–4, 6), the permeability of the microcapsules was estimated from the change in electrical conductance with time of the microcapsule dispersion–electrolyte solution mixture. To 100 ml of 0.05 *M* NaCl solution in a conductance cell immersed in a constant-temperature bath was quickly added, with stirring, 100 ml of the microcapsule dispersion previously kept at the same temperature. The conductance reading was begun soon after mixing and was taken at suitable time intervals. The electrical conductance measurements were carried out at 10 ± 0.1°. The stirring was continued throughout the measurements.

The permeability coefficient for the electrolyte ($P$) was calculated from (3, 4, 6):

$$P = -\frac{2.303 C_f V_m}{C_i A t} \log \frac{C_t - C_f}{C_i - C_f} \qquad \text{(Eq. 1)}$$

where $C_i$, $C_t$, and $C_f$ are the initial, intermediary (at time $t$), and final concentrations of electrolyte in the dispersion medium, respectively, and $V_m$ and $A$ are the total volume and total surface area of the microcapsules, respectively. The validity of the equation can be checked by plotting log $(C_t - C_f)/(C_i - C_f)$ against time. If the plot is linear, the equation strictly holds and the permeability coefficient can be evaluated from the slope of the line.

## RESULTS AND DISCUSSION

Figure 1 shows plots of log $(C_t - C_f)/(C_i - C_f)$ against time for the entry of sodium chloride into the gelatin–acacia microcapsules of different sizes. For all fractions, the plot was a straight line 5 min after mixing the electrolyte solution and microcapsule dispersion. This finding seems to confirm the validity of the equation for the calculation of the permeability coefficient.

The permeability coefficients for sodium chloride calculated from the slope of the straight line are given in Table I. The permeability coefficient decreased with decreasing capsule size. The same trend was observed with other preparations of gelatin–acacia microcapsules, although the permeability coefficient value varied from one preparation to another.

**Table I—Mean Diameter, Total Volume, and Permeability Coefficient for Sodium Chloride of Gelatin–Acacia Microcapsules**

| Fraction | Mean Diameter, μm | Total Volume, % | Permeability Coefficient, × $10^6$ cm/sec |
|---|---|---|---|
| A | 79 | 13 | 0.95 |
| B | 115 | 12 | 1.86 |
| C | 151 | 12 | 3.12 |

In view of the highly hydrophilic nature of both gelatin and acacia, the wall of gelatin–acacia microcapsules can be assumed to be a hydrogel even after treatment with formaldehyde. Thus, sodium and chloride ions are transported through a capillary network filled with water of the microcapsule wall. Under these circumstances, the rate of ion transport is expected to depend on the wall thickness (extent of capillary network), total volume of the microcapsules (size of sink), and total surface area of the microcapsules.

The wall thickness was constant and independent of the capsule size for gelatin–acacia microcapsules obtained in one preparation (8), and the total microcapsule volume was approximately the same for all fractions (Table I). Hence, the observed size-dependent permeability should arise from the difference in the total surface area of the microcapsules. According to Fick's first law of diffusion, however, the rate of ion transport increases with increasing total surface area or decreasing capsule size. This concept is contrary to the observed capsule-size effect.

A recent paper (9) indicated that the water structure in and around the wall of polyamide microcapsules is different from that of the bulk, and this difference may be responsible for the decreasing permeability of the microcapsules toward electrolytes with decreasing capsule size. This effect occurs because the structured water in and around the capsule wall retards the movement of hydrated ions, and the amount of structured water is greater in a dispersion containing numerous microcapsules of a small size than in that containing few microcapsules of a large size, assuming that the total microcapsule volume is identical for both dispersions. This observation also may account for the size effect on the permeability of gelatin–acacia microcapsules toward sodium chloride observed in the present work.

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