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A METHOD TO ANALYZE THE SURFACE OF MICROCAPSULES USING DIFFUSE REFLECTANCE

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ABSTRACT

The diffuse reflectance of infra-red energy from microcapsules was shown to be a useful analytical technique to study the structural properties of microcapsules. The technique of diffuse reflectance is unique in that the anisotropic nature of reflected light enables spectral differences to be explained on the basis of molecular orientation. As a result of the collection and analysis of diffuse spectra, spectral differences that may correspond to structural differences in the capsule wall structure were found to be dependent on the core material. More specifically, in microcapsules of kaolin and talc, produced with a block copolymer of d-tartaric acid and 1,8-octanediol, the relative orientation of hydroxyl functional groups for the respective core materials differed by forty-nine degrees while carbonyl groups differed by 15 degrees.

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INTRODUCTION

A review of the literature indicates that investigators are interested in covalently coupling proteins or antibodies to microcapsule surfaces in order to improve the site specificity of medicinal agents (1-2) If the above attempts are to be successful it is important to be able to determine if functional groups have the appropriate orientation for future manipulations, i.e., coupling of targeting molecule. A more complete understanding of the structure and surface of microcapsule walls is needed before the surface of microcapsules can be successfully utilized.

Before the molecular description of microcapsule surfaces is feasible, new types of information must become available. Due to the nature of microcapsules, this analytical technique should be capable of evaluating the sample in the dry state and utilize minimal sample handling. Therefore, the purpose of this report is to introduce a new application of an established analytical technique for the analysis of microcapsule surfaces.

An analytical technique which fits this criteria is diffuse reflectance. In the past diffuse reflectance has been used to study the properties of powders as a function of the particle size and moisture as well as to determine the composition and interaction of two components (3-4). Diffuse reflectance has also been used to characterize interactions of adsorbed molecules (5-6). Diffuse reflectance spectroscopy enables the orientation from surface normal to be determined for a variety of functional groups (7). Others have also utilized diffuse reflectance to determine angles of orientation from surface normal for a series of adsorbed bifunctional organic disulfides on gold films (9) and to study the hydrogen bonding properties of synthetic fluorophlopite mica (10). The unique ability of diffuse reflectance to detect angles of alignment and various substrate-monolayer interactions is due to the unique properties of reflected plane polarized light (11).

While the relationship between transmittance and absorbance may be described by Beer's Law, the reflectance of light is described by the Kubleka-Monk relationship (12), Eq. 1.

$$F(R) = 2.303 \frac{C}{S} E \tag{1}$$

where,

F(R) = Reflectivity or apparent absorbance
C = Molar concentration
S = Scattering coefficient
E = Molar absorption coefficient

Since this study is concerned with determining the orientation of various functionalities on the microcapsule surface, the scattering coefficient (dependent on size) and the molar concentration are of no interest. Equation 1 was modified to separate the molar concentration and scattering coefficient from the variable of interest, ie. the molar extinction coefficient (Eq. 2).

$$\log F(R) = \log \left(2.303 \frac{C}{S}\right) + \log (E) \tag{2}$$

A plot of the logarithm of the apparent absorbance versus the wavelength of irradiation produces a profile in which the shape of the spectra is solely dependent on the various molar extinction coefficients (log E). The baseline for such a plot is dependent on the molar concentration and scattering coefficient and may be subtracted from the resultant spectra. The baseline remains constant between samples if the concentration of microcapsules and the particle size is maintained constant.

To determine the orientation of a functional group on a surface, the maximum magnitude of the molar extinction coefficient (E_{max}) for a particular functional group must first be determined, i.e., when the functional group is perpendicular to the reflecting surface. Ideally, E_{max} should be determined using a system with a defined surface orientation. Unfortunately, the lack of a defined molecule/surface system at this time represents a limitation. On this basis, the apparent absorbance spectra obtained using a pure polymer sample can be utilized by calculating an E_{max} value after assigning forty-five (45) degrees as the average bond orientation. It is important to note that the assignment of an average angle of orientation establishes a baseline for the comparison of relative orientations within a given polymer system, but does not enable the comparison of absolute orientations between different polymer systems to be made. Due to intra- and inter-molecular interactions producing bond orientations which tend to exhibit preferred orientations, the authors acknowledge that in reality the absolute bond orientations are probably different, but the relative differences would be the same. With the understanding of this limitation, the calculation of E_{max} for pure bulk polymer is shown by Eq. (3).

$$E_{max} = \frac{\text{Log Absorbance } (\lambda)}{\cos (45)} \tag{3}$$

E_{max} = Maximum absorption coefficient at 0° from surface normal for a given wavelength (λ).

Absorbance (λ) = Apparent absorbance of a given functional group at a given wavelength (λ).

cos (45)= Randomly chosen angle of orientation for pure bulk polymer.

The calculated value of E_{max} (Eq. 3) for bulk polymer, for a given functional group, is used to determine the orientation from surface normal of the polymer in the microcapsule polymer wall through the use of the following relationship.

$$\text{Cos } (\theta) = \frac{\text{Log Absorbance } (\lambda)}{E_{max}} \tag{4}$$

where, θ = Degrees from surface normal

MATERIALS AND METHODS

Materials. Kaolin (10-40 microns, 48 M^2/G) and talc (10-40 microns, 63 M^2/G) (both reagent grade, Allied Chemical Company) were sieved to the desired particle size, otherwise they were used as supplied. Due to the adsorption of even small amounts of atmospheric water interfering with the infra-red spectra, potassium bromide (IR grade, Sigma Chemical Co.) was obtained in chunks and ground to a fine powder (40-50 microns) at the time of use. The macromolecule which was used for encapsulation was a biodegradable block copolymer consisting of d-tartaric acid and 1,8-octanediol (13). The polymer was a fine (20 to 80 microns), white, semi-crystalline powder which had a molecular weight of approximately 1200 grams per mole and a melting point of 82-84°C.

Microencapsulation Procedure. Two hundred milliliters (200.0 ml) of an alcoholic polymer solution (0.036 mg polymer/ml ethanol) were added to a thermostatically controlled jacketed beaker at 25°C. A quantity of a core material, (kaolin or talc), was added to the jacketed beaker to establish a polymer to core ratio(PCR) of two to one (2:1), normalized to surface area. The normalization of the polymer to core ratio was required to ensure that the surface concentration of polymer was equivalent between the talc and kaolin microcapsules. Water was then infused into the jacketed beaker dropwise at a rate of 33 milliliters/hour to produce coacervation. The resulting microcapsules (10-50 microns) were filtered, dried and stored under vacuum.

FTIR Sample Preparation. A 0.05% w/w mixture of microcapsules and potassium bromide was produced by geometrically diluting a quantity of microcapsules with freshly ground potassium bromide with gently stirring or shaking (no grinding). Mixing of the reference material with the bulk polymer or microcapsules was kept to a minimum to prevent fractionation of the bulk polymer structure and the fracturing of microcapsules.

Diffuse Reflectance Collection. Using a modified (14) diffuse reflectance apparatus (Harrick Scientific, Inc., Ossling, New York) infra-red spectra were collected using a Fourier transform infra-red spectrometer (Nicolet, 60SX) with a liquid nitrogen cooled mercury cadmium telluride (MCT) detector. The resolution was comparable to conventional transmittance spectroscopy, ie. ± 2 cm^{-1}. The collected spectra represented an average of forty scans within ± 5% over the wavelength range of interest. The logarithm of the apparent absorbance was calculated using FTIR software.

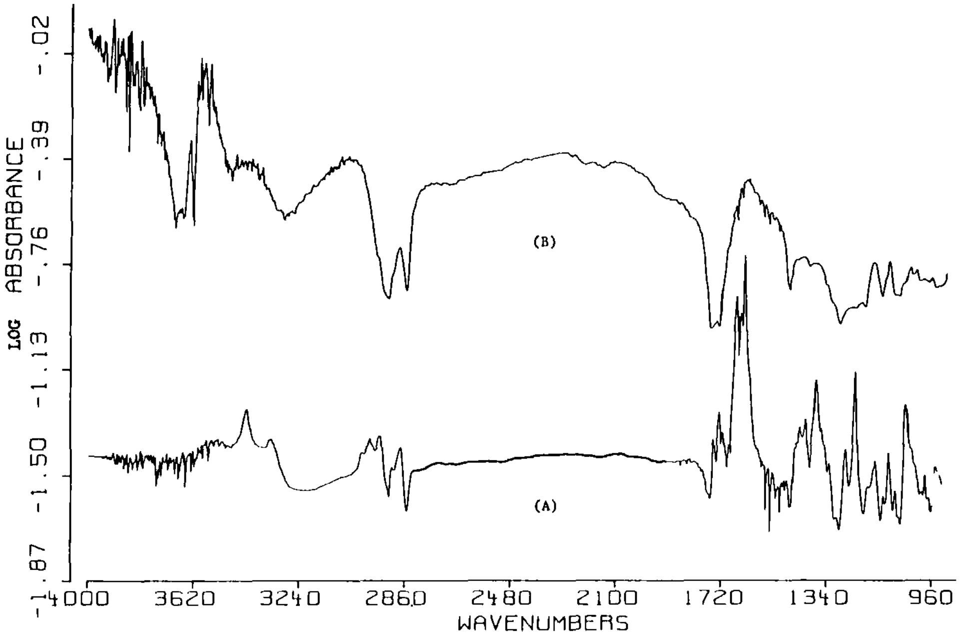

FIGURE 1:

Logarithm of the Diffuse reflectance Spectra for Microcapsules Produced with a Polymer to Core ratio of (2:1). Legend: (a)Talc Microcapsules; (b)Kaolin Microcapsules.

RESULTS AND DISCUSSION

Using kaolin and talc as core materials, microcapsules were produced under equivalent coacervation conditions and their diffuse reflectance infra-red spectra were collected. Representative plots of log F(R) or apparent absorbance as a function of the wavelength for kaolin and talc microcapsules are shown in Fig. 1.

When analyzing spectra of log apparent absorbance it is important to realize that spectral peaks in conventional plots are transposed into troughs when the log of the function is presented. The analysis of Fig. 1 indicates that the diffuse spectra for kaolin and talc microcapsules are distinctly unique. For example, the spectral region representing the

TABLE I

Relative Orientation from the Microcapsule Surface

	Angle of Functional Group*		
Core Material	Hydroxyl	Carbonyl	Methylene
Kaolin	11±10	15±5	18±7
Talc	60±11	30±6	49±9

*Angle in degrees from surface normal of microcapsules relative to bulk polymer

molar extinction coefficient (E) of the hydroxyl region (3200-3500 cm^{-1}) was different for each microcapsule core combination. The analogous observations were made by analyzing the spectral regions representing the polymer's methylene (ca. 2800-2900 cm^{-1}) and carbonyl (ca. 1700-1750 cm^{-1}) regions. For example, the methylene doublets are separate and relatively small for talc microcapsules compared to the overlapping large doublet troughs for kaolin microcapsules. Qualitative analysis of Fig. 1 indicates that the molar extinction coefficient which is related to the orientation of the polymeric functional groups is different between the two microcapsule/core combinations. Due to the use of pure polymer as a reference for orientation (E_{max}, Eq. 3), relative bond orientations were calculated from Eq.. 4.

Equations 3 and 4 were used to calculate the average relative orientation of the carbonyl, hydroxyl, and methylene groups of the polymer microcapsule wall. Representative relative orientations calculated from Fig. 1 are given in Table I. Analysis of Table I indicates that the relative orientation of the polymer's functional groups in the capsule wall was different for each core material. For talc microcapsules, Table I suggests that the hydroxyl groups of the polymer were approximately 60°±11 from surface normal, carbonyl groups were approximately 30°± 6 from surface normal.

For kaolin microcapsules, Table I suggests that the functional groups of the polymeric microcapsule coating had the following orientations: hydroxyl groups, 11±10 degrees; carbonyl groups, 15±5 degrees; methylene groups, 18±7 degrees.

Based on our assumption, the relative orientations between polymer of kaolin and talc microcapsules may be determined. Analysis of Table I in this manner indicates that the orientation of the functional groups in the talc microcapsules were oriented more parallel to the capsule surface (30-60° from the normal surface) compared to kaolin microcapsules (11-15° from the normal surface).

In summary, diffuse reflectance provides for the collection of unique information about the orientation of the various functional groups of this particular polymer on microcapsule surfaces. Several questions or concerns about this technique are yet to be answered such as the depth of penetration of infra-red and the effect on the resultant spectra (minimized in this study due to the use of polymer normalized to the surface area of kaolin and talc). Future studies will include studies that will investigate these issues as well as the effect of various polymer orientations on the diffusion characteristics of model drugs.

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