THE CHARACTERIZATION OF SURFACE GROUPS ON GELATIN-ACACIA MICROCAPSULES

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The lymphatic system acts as a route of absorption for lipophilic compounds which must first be incorporated into chylomicra before being discharged into the bloodstream. Long chain unsaturated fatty acids stimulate the production of chylomicra and several drugs have been co-administered with oils (Palin and Wilson, 1984) being absorbed concomitantly into the lymph. Microencapsulation of the drug dissolved in oil may overcome problems with patient compliance since a smaller amount of oil would be required to enhance absorption. Although gelatin microcapsules have been reputed to posess no mucoadhesive properties in vitro (Park and Robinson, 1985), it should be possible to link putative mucoadhesives onto the surface of the microcapsules in order to improve mucoadhesion. A knowledge of the density of functional groups available for linkage is thus essential and the purpose of this study was to determine the density of carboxyl and amino groups on the surface of gelatin-acacia microcapsules, employing 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide HCl (EDC).

Arachis oil was encapsulated by the complex coacervation of gelatin and acacia at pH 4.1 as reported by Helliwell et al (1989). Batch A was cross-linked with glutaraldehyde (12.5ml, 25%v/v) whereas Batch B was not cross-linked. Empty cross-linked microcapsules (Batch C) were also prepared.

Microcapsules (5 mg) were dispersed in nine samples of 0.9% w/v NaCl containing 1% Tween 20, using a submerged magnetic stirrer. ^{14}C labelled glycine ethyl ester (GEE) (0.05 mL; specific activity 46.5 mCi/mmol) was added. Increasing volumes (0 to 0.64 mL) of EDC (100 mg/mL) were added to produce final dispersion volumes of 1 mL. The samples were stirred at 4°C for 2.5 h, washed twice in distilled water, suspended in 5 mL Optiphase scintillation fluid and then left overnight before being counted in a liquid scintillation counter. Controls were prepared by employing the same procedure (using 0.64 mL of EDC (100 mg/mL)) except that no GEE was added. To determine the density of amino groups, the same methodology was adopted except that the EDC was mixed with 0.05 ml ^{14}C labelled sodium acetate (specific activity 56 mCi/mmol) for 5 min prior to the addition of the microcapsule suspension. In calculating the numbers of groups present, the DPM obtained in the absence of EDC was taken as an indication of any non-specific binding and this was subtracted from the maximum DPM obtained in the presence of EDC.

Relative numbers of carboxyl and amino groups detected (n = 3)

Microcapsule	COOH groups ($\times 10^{15}$)	NH_2 groups ($\times 10^{13}$)
Batch A	2.2	0.7
Batch B	2.2	3.1
Batch C	3.3	7.7

High levels of EDC induced microcapsule-microcapsule linking thus producing an under-estimation in the calculated numbers of groups present. Titration of Batch C microcapsules (5 mg) with NaOH revealed that there were 5.9×10^{17} COOH groups present which suggests that not all of the COOH groups, and possibly NH_2 groups, are available for linking. The observed reduction in the numbers of amino groups on the hardened microcapsules is attributable to their involvement in the cross-linking reaction with glutaraldehyde. EDC was employed to link poly(acrylic acid) [PAA], a putative mucoadhesive, onto the surface of empty microcapsules. The results obtained here suggest that uncross-linked microcapsules possess more binding sites available for the linkage of PAA which will hopefully improve their mucoadhesive properties.

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Park, H., Robinson, J.R. (1985) J. Controlled Release 2: 47 - 57
Helliwell, M. et al (1989) J. Pharm. Pharmac. 41: 117P