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Microencapsulation of Mammalian Cells in Polyacrylates

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Live mammalian cells have been encapsulated in water insoluble polyacrylates with the ultimate objective of transplantation of microencapsulated pancreatic islets for the treatment of insulin-dependent diabetes. Water-insoluble capsule membranes have the potential to be more biocompatible than the water soluble components used by others (*1*).

EUDRAGIT RL (Rohm Pharma Darmstadt, W. Germany), an acrylic–methacrylic acid ester copolymer with a low content of quarternary ammonium groups, and a noncrosslinked 2-hydroxyethyl methacrylate/methyl methacrylate copolymer (HEMA–MMA, 50% HEMA) have been investigated as potential microencapsulation membranes. EUDRAGIT RL was used as a 10% solution in diethyl phthalate, or as a 0.5% aqueous emulsion. The emulsion was used to coat calcium alginate-immobilized erythrocytes. Poly(HEMA-MMA) was prepared by solution polymerization in butanone to a low degree of polymerization and dissolved in polyethylene glycol 1540 (PEG). Details of the encapsulation methods have been presented elsewhere (*2–4*).

Histological sections of EUDRAGIT RL coated calcium alginate immobilized erythrocytes (Fig. 1) revealed a shell and core structure. The

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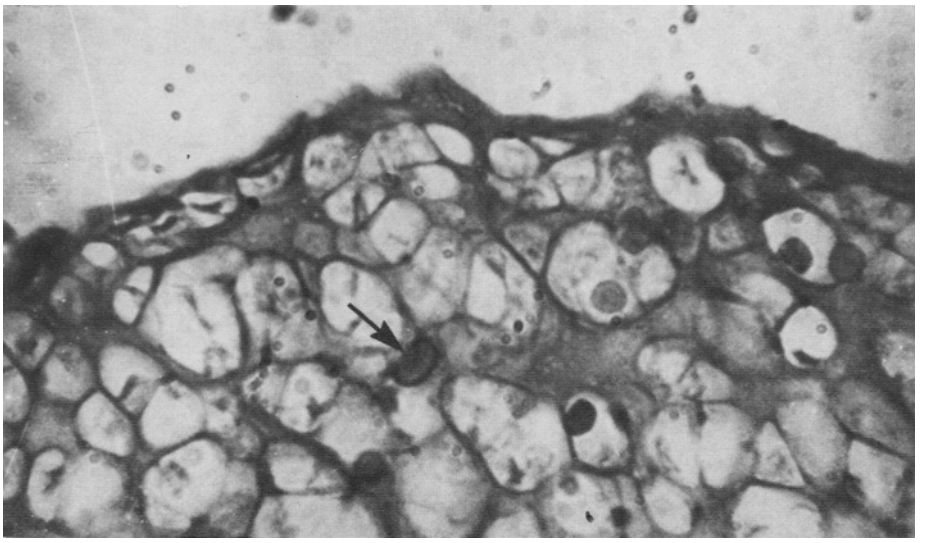

Fig. 1. Hematoxylin-eosin stained section of EUDRAGIT RL coated calcium alginate microcapsule. Calcium alginate beads were suspended in an isotonic Tris-buffered 1.5% (w/v) calcium chloride solution containing 0.5% (w/v) EUDRAGIT RL as an emulsion for 60 min.

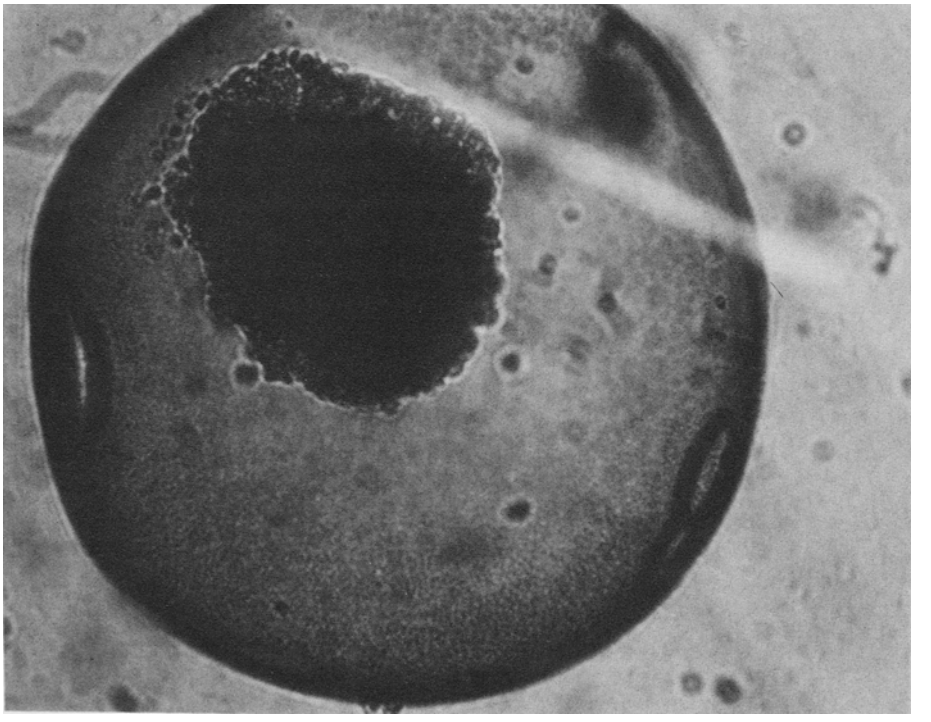

Fig. 2. EUDRAGIT RL microcapsules containing rat pancreatic islets produced by coextrusion and interfacial precipitation in a nonsolvent mixture of 1:1 glycerol trioleate/mineral oil.

capsule wall appeared as a dense band of material that arises as a consequence of polymer diffusion into the permeable sponge-like core. Microcapsules produced by coextrusion of a EUDRAGIT solution and a cell suspension were 300 μm in diameter with a 30 μm thick capsule wall (Fig. 2). Erythrocytes encapsulated by either process continued to consume glucose, and demonstrated normal oxygen-binding kinetics. Preliminary work with EUDRAGIT RL microencapsulated islets has demonstrated the absence of gross morphological changes and normal secretion of insulin after incubation with a high glucose medium. Further assessment of cell viability is underway.

Erythrocytes encapsulated in poly(HEMA-MMA) were fragile. Dropwise extrusion of a mixture of a 5% poly(HEMA-MMA) solution and cell suspension into an aqueous buffer yielded large capsules (~0.9 mm in diameter) surrounded by a 20 μm thick shell (Fig. 3). Stepwise rinsing of the capsules in isotonic buffer to harden the capsules failed to prevent cell lysis however. Coextrusion is being examined as a means of minimizing the contact time between the cell suspension and the solvent (PEG), and the consequent cell lysis.

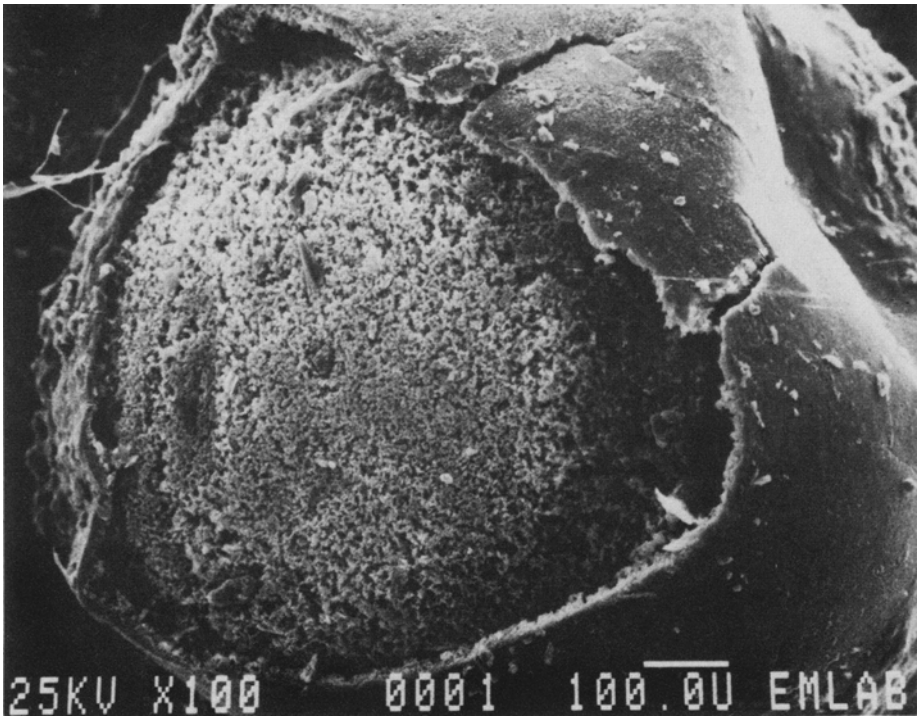

Fig. 3. Microencapsulated erythrocytes produced by extrusion of a mixture of poly(HEMA-MMA) solution and erythrocytes.

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