MICROENCAPSULATION OF HISTIDASE FOR ENZYME REPLACEMENT THERAPY

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Microencapsulated enzymes have potential applications in the therapy of enzyme deficiency diseases such as phenylketonuria (PKU) and histinaemia. The enzyme is constrained within the aqueous interior of the microcapsule while substrate may diffuse in and product may diffuse out through semipermeable polymer walls. Immunological reactions, which would occur with the unencapsulated enzyme, are avoided.

Histidase has beeen encapsulated in poly(piperazine terephthalamide) microcapsules by in situ interfacial polymerisation. In vivo studies (Bacon et al) with a strain of histidinaemic mice studied by Kacser et al (1973) have shown promise in reducing blood histidine levels. Loss of enzymic activity during encapsulation, important with expensive enzymes, has been investigated using ^{125}I - labelled proteins. In general, activity yields do not exceed 40% (e.g. Kondo & Muramatsu, 1976) and similar low yields were found in this work. Table 1 shows that ca. 65% of the labelled proteins become incorporated in poly (piperazine terephthalamide) microcapsules.

Table 1. Distribution of labelled proteins in polyamide microcapsules preparation.

	% Activity with:	
	^{125}I-HSA	^{125}I-Fibrinogen
Organic Phase	7	11
Total washings	29	13
Microcapsules	64	66

To determine the extent to which protein becomes chemically incorporated into the microcapsule membrane, microcapsules were broken. Retention of activity by the membrane fragments is given in Table 2 together with the activity which will adsorb onto membrane fragments.

Table 2. Incorporation and adsorption of labelled protein by microcapsule membrane.

	% retained with broken microcapsules	% adsorbed (5 min, 0.9% NaCl, pH 7.4)
^{125}I-HSA	35	1.2
^{125}I-Fibrinogen	71	92

Studies with nylon 4,10 and 5,10 microcapsules prepared using ^{14}C-labelled diamines have shown low degradability (~2% in 24 weeks at 37°C, pH 7.4). Similar experiments have been carried out with poly (butyl 2-cyanoacrylate) microcapsules which are potentially biodegradable (Florence et al, 1979).

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