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Applications of Polymers in Bioseparations and Delivery of Biomolecules

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=**Abstract**=

Polymers are widely applied in bioseparation processes as well as in drug delivery systems. These two fields have a certain commonality, in that they involve either removal or delivery of specific biomolecules from or to an aqueous environment. It is also to be noted that therapeutic toxin removal is an example of a bioseparation process. This presentation will focus on the use of polymers in physical as well as biospecific separations and delivery of biomolecules. Several new systems will also be described.

SUMMARY OF PRESENTATION

There are many separation systems available to the chemical engineering and bioengineer. The principles and some examples of the various separation systems are shown in Table 1. The most important applications of polymers in separation processes involve the use of membranes or particulates.

Table 1. Separation Technology

Basis of Separation	General Examples
Size	Filters, membranes, porous particles, gels
Density	Sedimentation, centrifugation, flotation
Charge, pH	Ion exchange solids, isoelectric focusing
Physico-Chemical Interactions	Adsorption, extraction, partitioning coacervation, precipitation
Biospecific Affinity	Particles, membranes, macromolecules with specific binding ligands
Biospecific Enzymolysis	Isomer separation

Membranes are used in physical separations as microfilters, ultrafilters or permselective membranes (as in reverse osmosis). Designs include flat plate, coiled or hollow fiber systems. There is an increasing trend towards synthesis and applications of membrane systems-especially hollow fiber devices-which separate on the basis of specific bioaffinity, in addition to the more common membrane separations based on size and charge.

Particulates refer to suspensions or packed columns, as in chromatographic separation systems. These latter systems can separate molecules on the basis of size, charge, pH, hydropohbicity and specific bioaffinity. Polymeric membranes and particulates have been extensively used in both bioseparation and delivery processes for therapeutics, diagnostics and industrial biotechnology proce-

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ssing in general.

We have recently developed a novel polymeric system which may be used for both delivery or separation of biomolecules as drugs and polypeptides from aqueous environments. Our system is based on a novel type of hydrogel. It is well known that hydrogels are hydrophilic polymer gels which may swell significantly but do not dissolve in water. The gels may be synthesized by copolymerizing selected monomers with minor amounts of crosslinking agents. The monomers may be chosen to yield water soluble polymers or copolymers which exhibit a phenomenon known as a lower critical solution temperature(LCST). Such polymers precipitate out of aqueous solution as the temperature is raised to the LCST. When a hydrogel is composed of a lightly crosslinked matrix of an LCST polymer, the gel will shrink significantly over a narrow temperature range as the temperature is raised to the LCST and above. This phenomenon reverses when the gel is cooled below the LCST, where the gel returns to its swollen state[1~3].

Since the deswelling or shrinking occurs over a narrow temperature range, one may release or "deliver" at these specific temperatures, substances which have been previously absorbed into the gel[2~4]. Furthermore, since the LCST phenomenon is reversible, a shrunken gel above its LCST may be used to absorb and remove substances from a solution simply by cooling below the LCST while in the solution[2,3]. These principles are illustrated in Fig 1 using drug absorption followed by delivery as an example.

In summary, in this paper we will describe the use of LCST gels for both delivery and removal of substances to and from surrounding aqueous environments. There are many exciting potential applications of this technology in biomedical engineering and biotechnology.

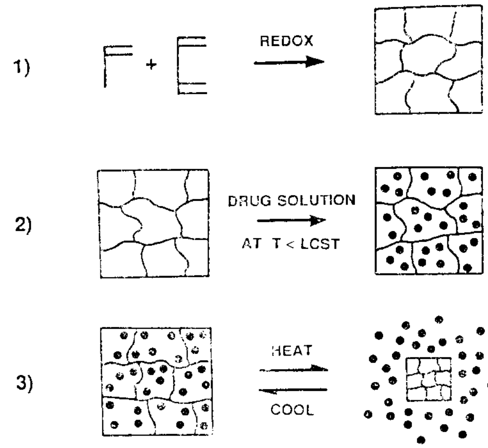

Fig. 1. Schematic illustration of the preparation and application of thermally reversible hydrogels for delivery or removal of substances to or from surrounding aqueous solutions[2,3].

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