CELLULOSIC SYSTEMS FOR DRUG DELIVERY

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CERTIFICATE

This is to certify that the thesis entitled "CELLULOSIC SYSTEMS FOR DRUG DELIVERY" being submitted by Mr. Maninder Singh to the Indian Institute of Technology, Delhi for the award of the Degree of Doctor of Philosophy of the Indian Institute of Technology, New Delhi, is a record of bonafide research work carried out by him under our supervision and guidance and to our knowledge it has reached the standard fulfilling the requirement of the regulations relating to the degree.

The results contained in this thesis have not been submitted in part or in full to any other University or Institute for the award of any degree or diploma.

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ABSTRACT

Alternatives to the conventional methods of drug delivery were analysed and modes of delivery using biodegradable and non-biodegradable polymers identified. Systems, based on cellulosic materials were chosen for the study because these are abundently occuring natural polymers made up of glucose units joined by β -1,4 linkages. Cellulose itself does not degrade enzymatically in the body. But it was proposed that on oxidizing it with periodate, formation of aldehyde groups at the 2- and 3 positions may facilitate a hydrolytic cleavage of the β-glucosidic bonds, thus making the matrix biodegradable. Further, the aldehyde groups would act as sites for anchoring drugs which may subsequently be released in the biological environment.

The in vitro degradation of the matrix was studied in solutions simulating the body fluids, using spectrophotometric as well as radio-labelling techniques. The biocompatibility and biodegradability of the matrix was assessed by subcutaneous implantation in rats ~~over a period of six months~~ and conducting histopathological studies over a period of six months. Toxicological tests on the products of

degradation were carried out in mice. It was found that the biocompatibility of oxidized cellulose was comparable to that of silastic, a well known non-irritant widely used as a control. The oxidised cellulose matrix degrades slowly, the rate of degradation increasing with increase in the degree of oxidation.

Feasibility of formulating a drug depot for sustained delivery using the oxidized cellulose matrix was examined by taking ∝- chymotrypsin as the model. The enzyme was immobilized by Schiff's base formation and the elution pattern was studied in Ringer's solution. The release of the enzyme sustained upto 10 days while retaining its activity. The period of release could be prolonged by reducing the Schiff's base with sodium borohydride. The possibility of using oxidized cellulose-based depots for therapeutic applications was examined with insulin as an example. Insulin depots were injected intraperitonially into rabbits and the resulting hypoglycemic effect was studied. Further, the delivery of insulin from such depots to rabbits diabetized with alloxan was taken up. The results indicated that sustained insulin delivery to diabetic subjects over a period of a few weeks could be achieved.

Drug delivery by diffusion from microcapsules was considered as an alternative mode for sustained release.

Among the cellulose derivatives, cellulose acetate was chosen as the wall material since it has good film forming properties. Conditions of microencapsulation with this polymer were examined. Good microcapsules with hydrocortisone as the core material were obtained. The release profile of the drug *in vitro* was determined indicating the possibility of using such a system for sustained delivery of drugs.

The overall results are summarized and critically analyzed. The limitations of the present systems and possible improvements are discussed and the scope for further work is outlined.

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