POLYMERS IN MEDICINE AND SURGERY : CELLULOSIC SYSTEMS

By

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C E R T I F I C A T E

This is to certify that the thesis entitled, "POLYMERS IN MEDICINE AND SURGERY: CELLULOSIC SYSTEMS" being submitted by Mr. T. JAI MANGAL SINHA for the award of the 'degree of 'DOCTOR OF PHILOSOPHY' in TEXTILE TECHNOLOGY of the INDIAN INSTITUTE OF TECHNOLOGY, DELHI is a record of bonafide research work carried out by him under my guidance and supervision. To my knowledge, it has reached the standard of fulfilling the requirements of the degree. The matter embodied in this thesis has not been submitted for the award of any degree or diploma of any other University or Institute.

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ABSTRACT

Various chemical modifications of cellulose having applications in Medicine and surgery are reviewed. Cellulosic derivatives based on different methods of oxidation viz. sodium meta-periodate, $NaClO_2$ as well as NO_2 oxidation are described. Conditions of synthesis, chemical characterization, bio-degradation and bio-compatibility of these cellulose derivatives are discussed. Most of the possible applications of these oxidation products for sustained drug delivery were examined.

Available modes of insulin delivery were critically analyzed. Alzet mini osmotic pump was used as a model for achieving prolonged insulin delivery in streptozotocin diabetised monkeys. Parameters like blood sugar, intravenous glucose tolerance test were monitored. Osmotic pump is able to maintain sustained normoglycemia in diabetic monkeys for a period of 8 days. The total dosage being less than that required when insulin is given free. The drawback of the method is that it requires surgical implantation of the pump.

DAC was studied as a biodegradable carrier for sustained release of insulin in diabetic rabbits. Insulin DAC (Insulin depot) was characterized by spectroscopy, gel permeation chromatography, and photon correlation

techniques. Amino acids of insulin involved in binding to DAC were determined by amino acid analysis, to be Phe, Lys, Arg and Tyr. Sustained insulin delivery upto a maximum period of 14 days was observed in diabetic rabbit as model.

Prolonged topical drug delivery using DAC as a carrier was also studied from cellulosic wound dressings. Various antimicrobial agents chosen for sustained topical delivery were acriflavin, bacitracin, neomycin, and dihydrostreptomycin. Different modes of binding were attempted. Binding by lyophilization was found to show both instantaneous and prolonged antimicrobial activity indicating the presence of free as well as bound antimicrobial agent and was thus more suitable for wound dressing than completely immobilized samples. Mixture of DAC bound acriflavin, bacitracin, neomycin and dihydrostreptomycin was found to have wide spectrum antimicrobial activity. Also effect of the polymer on wound healing was studied. 6-Carboxy cellulose (CC) and 2,3,6-tricarboxy cellulose (TCC) were evaluated for hemostatic activity. Various parameters for blood coagulation were studied. The hemostatic activity was related to the generation of low pH environment. Lastly the spermicidal activity of CC and TCC were evaluated. TCC was found to have very good spermidal activity which was again pH dependent.

C O N T E N T S