

Biodegradable adhesive composed of polysaccharide and polyamino acid

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Introduction : To improve the drawbacks of conventional and commercially available medical adhesives, such as cyanoacrylate, aldehyde-based, and fibrin glue, new type bioadhesive has been prepared using medical and food additive sources as starting materials. The present study was undertaken to develop novel surgical glue with high performance for clinical application, low toxicity, and without the risk of infection. Medical and food additive sources were selected as starting materials. Our glue is based on Schiff base formation between oxidized and aldehyded polysaccharides and ϵ -poly(L-lysine), a kind of antibacterial food additives.

Materials and Methods : Dextran with the molecular weight of 75K Da and dextrin hydrate were purchased from Wako Pure Chem. Ind. Ltd. (Osaka, Japan). ϵ -Poly(L-lysine) having the molecular weight ϵ was from Chisso Corporation (Tokyo, J). Aldehyde groups introduced in these polysaccharides was evaluated by simple iodometry.

Results and Discussion : Gel formation of aldehyded dextran (75K) with ϵ -poly(L-lysine) was investigated. The results were given in Fig.1 as a function of aldehyde introduction in dextran. Set time considerably shortened with an increase in aldehyde content, suggesting effective gel network between aldehyded dextran and ϵ -poly(L-lysine) molecules, though molecular weight of ϵ -poly(L-lysine) is large. Degradation of hydrogel consisting of aldehyded dextran and ϵ -poly(L-lysine) was observed in PBS at 37°C. The lower concentration of acetic anhydride showed slower degradation was observed in physiological condition, suggesting easy control of degradation speed of the glue *in vivo* as well as *in vitro*. Bonding strength to soft tissue was evaluated using cow skin sheet and the results were given in Fig. 2. In this study, commercial fibrin glue (Bolheal) was used as reference. Bolheal shows the bonding strength less than 500 g/cm², though set time of this glue was fast to handling. On the other hand, our glue shows 2 times higher strength than that of fibrin glue. Cytotoxicity of aldehyded dextran and ϵ -poly(L-lysine) was investigated using L929 cell line. Formaldehyde in GRF glue reveals extremely high toxicity lower than IC50, 4 μ g/ml. On the other hand, the toxicity of aldehyded dextran was quite low and only 1/1,000 of toxicity was observed, compared with these aldehyded low molecules, which might be due to

low reactivity of high molecule of aldehyded dextran. In addition, the cytotoxicity of ϵ -poly(L-lysine) was also quite low and almost no toxicity was observed.

Conclusion : Reaction of aldehyded polysaccharides, such as dextran with ϵ -poly(L-lysine) formed self-degradable hydrogel, which showed high bonding strength and low cytotoxicity. This finding suggests the development of novel bioadhesive without the risk of any virus infections.

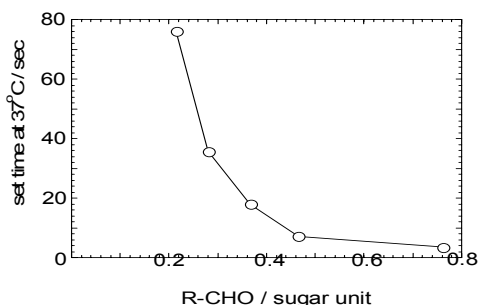


Fig.1 Effect of aldehyde introduction in dextran 75K on the gel formation with ϵ -poly(L-lysine) at 37°C. Dextran 75K (20 w/w%) and ϵ -poly(L-lysine) were used at the concentration 20 and 10 w/w %, respectively.

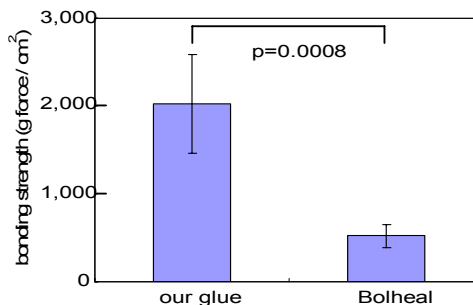


Fig. 2 Bonding strength of the glue to cow skin sheets. After loading 100 g force for 5 min at 25°C, shear strength was measured at 25°C and 10 mm/min. Error bar shows the standard deviations (n=5).