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WICHIT NOSOONGNOEN: THE STUDY OF PHARMACOKINETICS AND PHARMACODYNAMICS OF INTRANASAL AND INTRARECTAL INSULIN IN RAT USING VARIOUS SOURCES OF CHITOSANS AS A PERMEABILITY ENHANCER. THESIS ADVISORS: KORBTHAM SATHIRAKUL, Ph.D., SUWABUN CHIRACHANCHAI, Ph.D. 187 p. ISBN 974-664-361-4

The permeability enhancement of insulin by using chitosan from various sources, i.e., crab shells, squid pens, water soluble chitosan, and chitosan glutamate were studied in intranasal and intrarectal in a rat model. The plasma insulin concentration (pharmacokinetics) was quantitatively monitored by ELISA technique. Indirect pharmacodynamic sarrogate, which is the alteration in blood glucose level was also monitored. A comparison between intranasal and intrarectal insulin administration showed that the pharmacokinetic parameters, i.e., $AUC_{insulin}$ of intranasal insulin (4 IU/kg) with chitosan from various sources (0.25% w/v) were significantly ($p<0.05$) higher than that of intrarectal administration. The maximum insulin concentration (C_{max}) of intranasal insulin administration with chitosan obtained from crab shells, chitosan glutamate and water soluble chitosan were significantly different at ($p<0.05$) but chitosan obtained from squid pens was not significantly different at ($p>0.05$) from that of intrarectal administration. The pharmacodynamic response, i.e., $AUC_{glucose}$ and % reduction in glucose level of intranasal insulin with chitosan glutamate and water soluble chitosan were significantly different at ($p<0.05$) from that of intrarectal administration. The absolute bioavailability values of intranasal and intrarectal insulin in the various chitosan solutions were approximately 6.8-12.6% and 0.53-2.92%, respectively. The effects of the alteration in physiochemical properties, i.e., apparent viscosity, molecular weight, and percent degree of deacetylation of chitosan from various sources on the pharmacokinetic and pharmacodynamic effects of intranasal insulin administration were in a linear relationship. The intrarectal insulin administration did not show a relationship among each of the chitosan on pharmacokinetic and pharmacodynamic effects. It can be concluded that intranasal insulin administrations with various sources of chitosan are more feasible candidates for future safe and effective insulin absorption than intrarectal administration.