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L-valin conjugated PLGA nanoparticles for oral insulin delivery

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Oral delivery is the preferred route of administration because it offers several advantages over other routes. However, it is not an effective route for the delivery of peptides and proteins because of so many constraints. The small intestine has been shown to be able to transport the L-forms of amino acids against a concentration gradient and that they compete for the mechanism concerned. So L-Valine was used as a ligand for carrier mediated transport of insulin loaded PLGA nanoparticles. L-valine-conjugated PLGA-nanoparticles were prepared using double emulsion solvent evaporation method. The insulin bearing nanoparticles were also studied for size, drug entrapment efficiency, zeta potential and polydispersity index, *in vitro* insulin release. *Ex-vivo* studies on intestine revealed that conjugated nanoparticles showed greater insulin uptake as compared to non-conjugated nanoparticles. *In-vivo* studies were performed on streptozotocin induced diabetic rabbits. Oral suspension of insulin loaded PLGA nanoparticles reduced blood glucose level from 265.4±8.5 to 246.6±2.4 mg/dl within 4 hrs which further decreased to 198.7±7.1 mg/dl value after 8 hrs. The ligand conjugated formulation on oral administration produced hypoglycaemic effect within 4 hrs of administration, the hypoglycaemic effect prolonged till 12 hrs of oral administration. Simultaneously, the insulin concentration in withdrawn samples was also assessed and found that profile of insulin level is in compliance with the blood glucose reduction profile. Compared with formulation loaded with the drug, the valine conjugated nanoparticles produced a sustained hypoglycaemic response till 12 hrs than 8 hrs. Hence, it is concluded that the L-valine conjugated NPs bearing insulin are the promising carrier for the transportation of insulin across the intestine on oral administration.

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