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Multifunctional Nanoconstructs for peroral delivery of Insulin

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Objectives: India is fast on its way to becoming a global diabetes `hub` of the world. Insulin therapy is the most appropriate choice for treatment of diabetes mellitus, but has several disadvantages as I.V. injection of insulin results in its inactivation by proteolytic enzymes in liver, frequent hyperglycemia and hypoglycemia, local reactions like swelling, erythema. The aim of the present work was to prepare a biodegradable system to deliver insulin through Concanavillin-A anchored PEGylated-PLGA nanoparticles, which would possibly, lead to enhance the stability of system; prolong insulin fate in blood and enhance the oral bioavailability of insulin by enhancing its lymphatic uptake using targeted approach.

Methods: PLGA-Nanoparticles were prepared by Double Emulsification Method. Insulin loaded nanoparticles were characterized for their shape, size via electron microscopy. The prepared nanoparticles were activated and then conjugated to concanavillin-A. The conjugated system was again characterized *in-vitro* for conjugation efficiency with ligand, entrapment efficiency and stability. Studies like x–ray diffraction, differential scanning calorimetry & integrity of entrapped insulin was assessed using circular dichroism spectrum & *in-vitro* ligand agglutination assay were performed.

Results: *Ex-vivo* study was performed, which exhibited the higher intestinal uptake of Con-A conjugated nanoparticles. The system was found to be effective in protecting the drug in the GIT environment and with good release profile. *In-vivo* studies suggested that developed system lowered blood glucose levels within a safer limit over prolonged duration of action.

Conclusions: Con-A anchored PEGylated-PLGA nanoparticulate system can be a promising drug delivery carrier for oral insulin delivery in the treatment of diabetes mellitus. Targeted approach led to the better uptake of system and increasing the oral bioavailability of the drug as inferred from blood glucose profile, additionally it also prolongs circulation time due to PEG attachment. Thus the potential for the use developed system as oral drug delivery system can be further investigated.