

Oral nanotherapeutic formulation of insulin with reduced episodes of hypoglycaemia

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Abstract

Injectable insulin is an extensively used medication with potential life-threatening hypoglycaemic events. Here we report on insulin-conjugated silver sulfide quantum dots coated with a chitosan/glucose polymer to produce a responsive oral insulin nanoformulation. This formulation is pH responsive, is insoluble in acidic environments and shows increased absorption in human duodenum explants and *Caenorhabditis elegans* at neutral pH. The formulation is sensitive to glucosidase enzymes to trigger insulin release. It is found that the formulation distributes to the liver in mice and rats after oral administration and promotes a dose-dependent reduction in blood glucose without promoting hypoglycaemia or weight gain in diabetic rodents. Non-diabetic baboons also show a dose-dependent reduction in blood glucose. No biochemical or haematological toxicity or adverse events were observed in mice, rats and non-human primates. The formulation demonstrates the potential to orally control blood glucose without hypoglycaemic episodes.

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