PUBLICATION REVIEW

A polyphenol-metal nanoparticle platform for tunable release of liraglutide to improve blood glycemic control and reduce cardiovascular complications in a mouse model of type II diabetes

Source:

J. Control Release
February 2020

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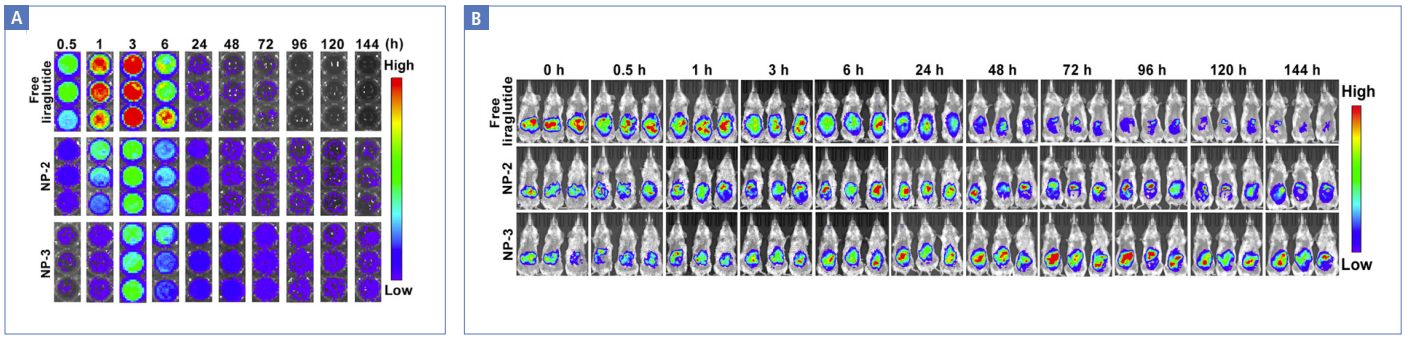
Approximately 80% of Type 2 diabetes (T2D) mortality is related to cardiovascular (CV) complications. Therefore, there is a critical need for novel therapeutics that not only manage blood glucose levels, but also reduce the risk of developing CV diseases. Liraglutide (Lira), a glucagon-like peptide-1 (GLP-1) receptor agonist, has reported benefits for risk reduction of major CV complications in T2D patients. However, the short half-life of Lira (~13h) requires daily injections, which could result in poor patient compliance and complications due to frequent injections. Therefore, the development of a long-lasting release system of Lira has great clinical significance for T2D patients.

Numerous strategies have been explored for the sustained release of Lira. However, each strategy tested has suffered from issues such as poor bioavailability and efficacy. In the present study, researchers developed a biocompatible Lira/tannic acid (TA)/Al3+ nanoparticle platform for the sustained, controlled release of GLP-1. IVIS® optical imaging technology, a powerful research tool for the non-invasive visualization of drug biodistribution, was utilized to evaluate Cy7.5-labelled Lira release *in vivo*. Results demonstrate that this nanoparticle system exhibits increased Lira bioavailability and long-acting glycemic control with improved CV function relative to free Lira in a T2D mouse model.

PUBLICATION HIGHLIGHTS:

Collectively, results demonstrate that a polyphenol-metal nanoparticle platform can extend the release of Lira and improve therapeutic outcomes relative to daily Lira injections in T2D mice. Further, this study demonstrates the utility of using PerkinElmer's IVIS® optical imaging platform to non-invasively visualize and quantify Cy7.5-labelled Lira in mice and highlights the value of IVIS technology for preclinical research surrounding metabolic disease drug development.



A) BALB/c mice were administered a single I.P. injection of free Lira (1mg/mL), NP-2 (1mg/ml [Lira], 1mg/mL [TA], 0.02 mg/ml [Al3+]) or NP-3 (2mg/ml [Lira], 1mg/mL [TA], 0.02mg/ml [Al3+]). Blood was collected at different time points (0-144h) and imaged on an IVIS® imaging system. Blood from mice injected with free Lira demonstrated a rapid increase in fluorescent intensity that peaked at 3h P.I. and quickly decreased within 24h. The nanoparticle formulations did not result in a rapid initial increase in blood Lira concentration, but rather significantly extended Lira persistence in blood circulation for up to 6 days. B) Mice were administered a single I.P. injection of free Lira, NP-2 or NP-3 and imaged at different time points (0-144h) via IVIS® imaging. The fluorescent signal in mice injected with free Lira was barely detectable after 48 h. In contrast, Lira administered in the NP-2 or NP-3 nanoparticles exhibited low fluorescence signal at early time points (likely due to quenching of Lira inside the nanoparticles) that grew stronger at later time points as Lira was gradually released.

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