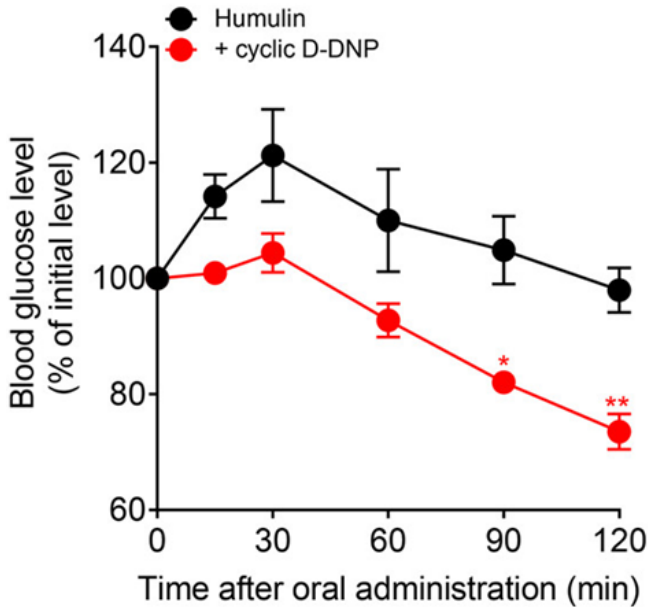


# Toward painless oral insulin administration

26 April 2021



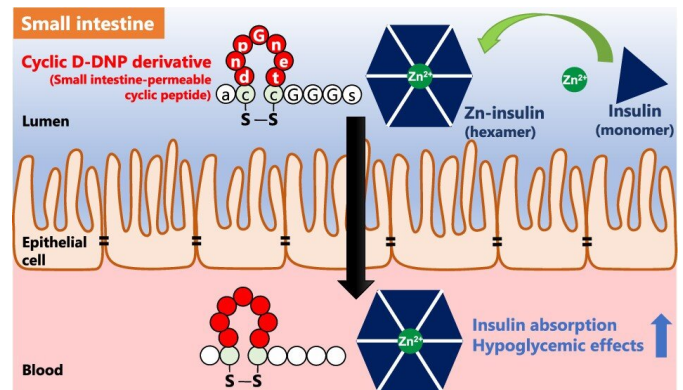
When the D-DNP peptide was added to an injectable insulin preparation (HumulinR3/7) and administered orally to mice, a hypoglycemic effect was observed, similar to that of the experimental zinc insulin hexamer. Credit: Associate Professor Shingo Ito

Researchers from Kumamoto University, Japan have found that DNP peptide, a small intestine-permeable cyclic peptide originally used as an insulin additive to improve absorption into the small intestinal, lowers blood glucose levels in mice. They also found that insulin can be administered orally by simply adding D-form DNP peptide (D-DNP) peptide to injectable insulin used in clinical practice. This study is expected to provide a basis for the development of oral insulin using DNP peptides.

Insulin therapy by self-injected insulin is currently the best way to control blood glucose. However, self-injection is painful and a major burden for many diabetics. The development of oral insulin is strongly desired to improve their quality of life. Although it has been over 100 years since the

discovery of insulin, oral insulin has yet to be developed. This is mainly because insulin is not absorbed in the [small intestine](#) and it is broken down in the [gastrointestinal tract](#). To solve this problem, researchers used a DNP peptide that can permeate large molecules across the small intestine, which they previously discovered, and an insulin hexamer that was created by adding zinc.

First, the research team synthesized a DNP peptide using D-amino acids (D-DNP peptide) to inhibit the gastrointestinal degradation of DNP. Then, to reduce the gastrointestinal degradation of insulin, researchers created an insulin hexamer (zinc insulin hexamer) by combining zinc chloride and insulin. A mixture of the D-DNP peptide and insulin hexamer was then administered into the intestinal tracts of mice to study the absorption rate. Five minutes after administration, insulin was detected in the portal blood, and blood glucose levels started decreasing between 15 to 60 minutes after administration. The reduced glucose levels were sustained until at least 120 minutes after administration. Additionally, when the mixture was administered orally, blood [glucose](#) level began decreasing after 15 minutes and was maintained for least 120 minutes. For both administration methods, the D-DNP peptide produced a stronger hypoglycemic effect than a L-DNP peptide synthesized from L-amino acids. Furthermore, when the mixture was administered intraintrastestinally and orally to diabetic model mice, [blood glucose levels](#) began decreasing after 30 minutes.



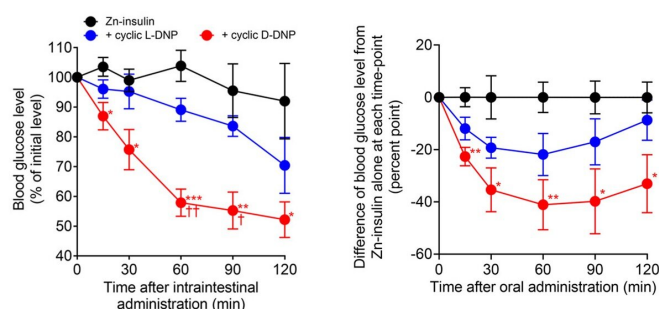
This study supports the concept that small intestinal absorption of insulin can be improved by mixing D-DNP peptide with an insulin hexamer. Credit: Associate Professor Shingo Ito

**More information:** Shingo Ito et al, Oral Coadministration of Zn-Insulin with d-Form Small Intestine-Permeable Cyclic Peptide Enhances Its Blood Glucose-Lowering Effect in Mice, *Molecular Pharmaceutics* (2021). DOI: [10.1021/acs.molpharmaceut.0c01010](https://doi.org/10.1021/acs.molpharmaceut.0c01010)

Based on their previous work, and the fact that many insulin injections already contain zinc insulin hexamers, the researchers hypothesized that oral insulin could be developed by adding the D-DNP peptide to insulin injections currently in use. Thus, they added the peptide to HumulinR3/7 (an injectable insulin) and tested it on mice orally.

Provided by Kumamoto University

Their positive results suggest that oral insulin development is possible by simply adding D-DNP peptide to existing insulin injection formulations because the combination of D-DNP peptide with a zinc insulin hexamer improves insulin absorption in the small intestine.



Left: blood glucose levels continued to decrease from 15 to 60 minutes after administration. This decrease in blood glucose levels persisted until at least 120 minutes after administration. Credit: Associate Professor Shingo Ito

"Our study shows that we were able to build a foundation for the development of oral insulin using D-DNP [peptides](#)," said Associate Professor Shingo Ito, leader of this study. "In the future, we expect to contribute to oral insulin drug discovery by developing a method to further enhance [insulin](#) absorption by the small intestine by optimizing the administration method."

APA citation: Toward painless oral insulin administration (2021, April 26) retrieved 20 July 2022 from <https://medicalxpress.com/news/2021-04-painless-oral-insulin-administration.html>

*This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.*