Nanotech opens door to future of insulin medication

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Research and development version of the oral insulin capsule. Credit: University of Sydney/ Stefanie Zingsheim.

An international team, led by researchers from Australia, have developed a system using nanotechnology that could allow people with

diabetes to take oral insulin in the future. The researchers say the new insulin could be eaten by taking a tablet or even embedded within a piece of chocolate.

The new nano carrier, tested in mice, rats and baboon animal models, could help people with diabetes avoid side-effects linked to insulin injections such as hypoglycemia (a low blood sugar event, when too much insulin has been injected).

These animal studies have shown that the greatest strength of the nano-scale material is that it can react to the body's blood sugar levels. The coating dissolves and releases the insulin when there is a high concentration of blood sugar and importantly does not release the insulin in low blood sugar environments.

The new oral insulin uses a type of nano-scale material that is 1/10,000th the width of a human hair. The material acts similarly to acid resistant coating on tablets, which protects it from being destroyed by stomach acid. But this new coating instead surrounds individual insulin molecules and becomes a "nano carrier"—acting like a courier to ferry insulin molecules in the body to the places it needs to act.

The findings are published in *Nature Nanotechnology*.

It is estimated 422 million people worldwide have diabetes, and approximately 75 million of these inject themselves with insulin daily. Around 1.5 million deaths are directly attributed to diabetes each year. In 2021, it was estimated more than 1.3 million Australians were living with diabetes.

Lead author Dr. Nicholas Hunt from the University of Sydney's School of Medical Sciences in the Faculty of Medicine and Health, says the development of a safe and effective oral insulin has been a challenge

since insulin was discovered over a century ago.

Research and development version of oral insulin capsule. Credit: University of Sydney/ Stefanie Zingsheim.

"A huge challenge that was facing oral insulin development is the low percentage of insulin that reaches the blood stream when given orally or with injections of insulin," says Dr. Hunt, who is also a member of the University of Sydney Nano Institute and Charles Perkins Center.

"To address this, we developed a nano carrier that drastically increases the absorbance of our nano insulin in the gut when tested in human intestinal tissue."

Preclinical testing in animal models found that, following ingestion, the nano insulin was able to control blood glucose levels without hypoglycemia or weight gain. There was also no toxicity.

"Our oral insulin has the added benefit of greatly reducing the risk of hypoglycemic episodes. For the first time we have developed an oral insulin that overcomes this major hurdle," said Dr. Hunt.

Human trials are expected to start in 2025 led by the spin out company Endo Axiom Pty Ltd.

Endo Axiom Pty Ltd was founded by Professor Victoria Cogger, Professor David Le Couteur AO and Dr. Nicholas Hunt, after 20 years of research.

Dr. Hunt and his team were driven to develop oral insulin technology given it could help lighten the economic, health and well-being burden related to diabetes management for patients.

Lead researchers Dr. Nicholas Hunt and Professor Victoria Cogger. Credit: University of Sydney/ Stefanie Zingsheim.

"We wanted to devote our time to develop successful oral insulin technology because we believe it will help people with diabetes have more control over their condition."

Senior author Professor Victoria Cogger, director of The ANZAC Research Institute, said the development of oral insulin is the culmination of many years of scientific endeavor and collaboration.

"It's wonderful to see our work published, supported by Endo Axiom and reaching clinical trials?—to be able to lead a change in the way we treat a disease that impacts so many people," she said.

Professor Cogger said when her work first began on creating an oral insulin it was a purely scientific question, but then a family member became impacted by type 1 diabetes.

"Life is strange and along the way my family was impacted by a type 1 diabetes diagnosis, and I really started to understand the reality of what life is like on injectable insulin therapy.

"Having that lived experience has driven the project in many ways and created an impetus to improve life for all people living with diabetes. My hope is we can reduce the multi-faceted burden of diabetes through easily accessible oral insulin."

More information: Nicholas J. Hunt et al, Oral nanotherapeutic formulation of insulin with reduced episodes of hypoglycaemia, *Nature Nanotechnology* (2024). DOI: 10.1038/s41565-023-01565-2

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