UCD Impact Case Study

No more needles: developing oral peptide treatments for diabetes

Professor David Brayden
UCD School of Veterinary Medicine and UCD Conway Institute

ECONOMIC HEALTH SCIENTIFIC SOCIAL TECHNO-LOGICAL

SUMMARY

Professor Brayden's lab, working with an industry partner, has developed a new nanoparticle that could allow diabetes patients to take insulin and other peptides orally, rather than with an injection.

This led to a wide range of outcomes: an award-winning international documentary film seen by thousands, a patent application, a presentation of the research at the first Keystone Symposium on Drug Delivery in Dublin, and an article in the top-tier journal, the *New England Journal of Medicine*.

Ultimately, if this discovery leads to a new treatment for diabetes, it will yield profound impacts on health: patients will no longer need injections and will opt to take oral peptides earlier in their disease to achieve better outcomes.

RESEARCH DESCRIPTION

Insulin is typically injected by patients with diabetes. If taken in a pill, peptides like insulin break down in the gut and do not cross the gut wall, and so they cannot reach the bloodstream. This is why they must be injected. To address this, Professor Brayden's lab is aiming to make convenient oral versions for patients.

In 2016, his team won an SFI TIDA grant to develop a nanoparticle, using silica as a coating, that can deliver insulin and other similar drugs orally. To do so, they trapped insulin in a core with two chemicals: a metal to preserve the insulin's structure, and an amino acid to help it cross the gut wall.

By 2019, Professor Brayden's lab proved that, in rats, the silica shell protected the insulin in the nanoparticle, and that the insulin was able to cross the gut wall with the help of other ingredients. This was the first time a nanoparticle had been combined with a so-called 'permeation enhancer'. Professor Brayden's team then used another anti-diabetic peptide, known as exenatide, to verify the effectiveness of this method in mice.

Professor Brayden in the documentary film Bittersweet.

The industry collaborator, Sanofi Pharma, provided peptides and analytical support, while four postdocs trained in the UCD School of Chemistry and Veterinary Medicine carried out the lab work.

RESEARCH IMPACT

This research[1] led to multiple impacts across society, with additional impacts on the horizon.

Economic and health impact

In 2016, Professor Brayden's lab filed a UK patent application describing the oral delivery system developed through their research.[2] Then, in 2019, they refined the nanoparticle and submitted a new invention disclosure. The team collaborated with Sanofi Pharma (Paris) regarding the research publication and patent application. If such a discovery for oral peptides leads to new medication, it will be a significant health impact, as patients will no longer need injections and will opt to go onto oral peptides earlier in their disease to achieve better outcomes. Patients would comply better with oral medications than with injections.

Social impact

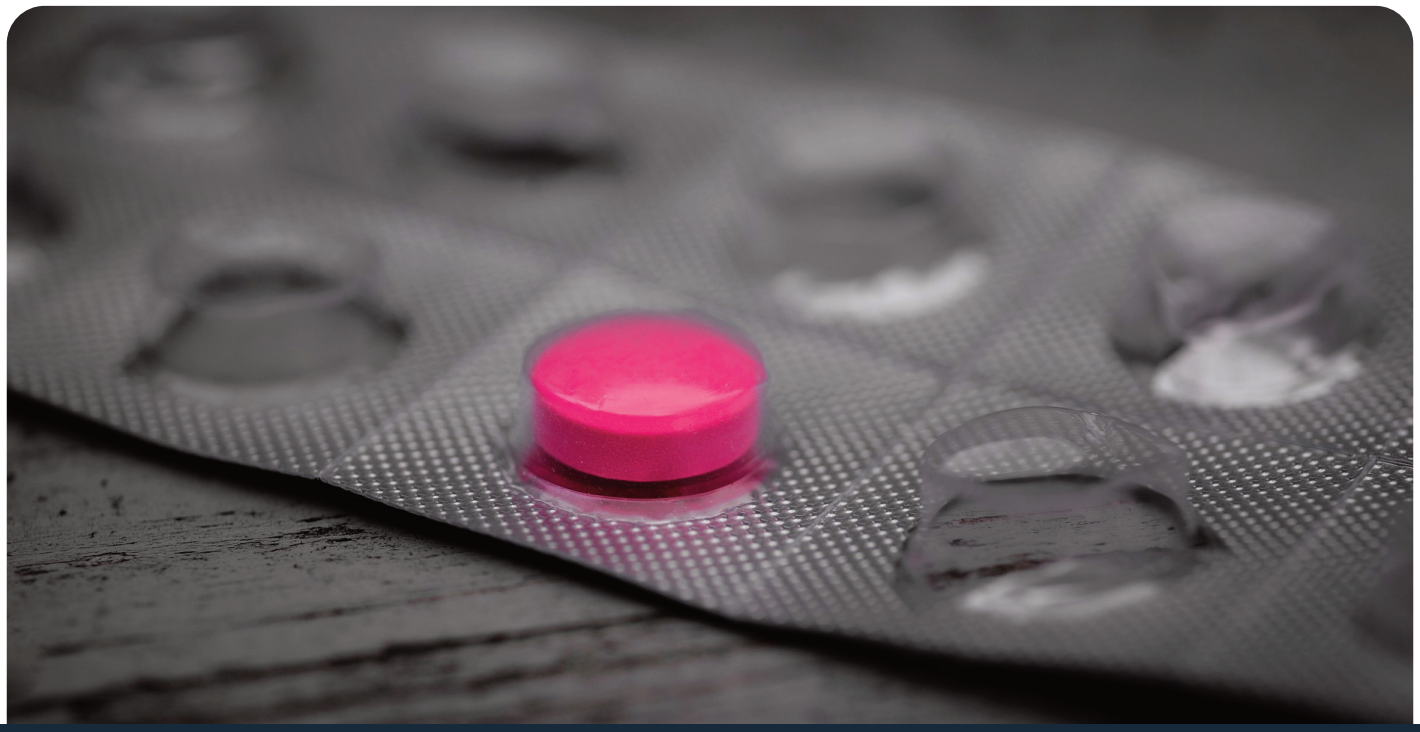
In 2017, responding to a documentary competition run by the SFI CURAM Centre, Professor Brayden designed a visual diabetes story, charting the journey from the discovery of injectable insulin to the possibility of an oral insulin. The documentary, Bittersweet,[3] describes his team's nanoparticle project and was screened at the 2017 Galway Film Festival, the 2018 UCD Festival, 10 secondary schools, and on RTÉ television.[4,5] It won the "Best Educational Media" Industry Award at the Raw Science Film Festival in Los Angeles in 2019,[6] and it has been seen by 88,000 people. The film highlighted the potential benefits of this discovery for diabetic patients who were coping with the disease at different stages of their lives.

Scientific and technological impact

Because the research identified a new mechanism for how a nanoparticle could enable oral peptide delivery, Professor Brayden and his team publicised it at conferences, with invited presentations at the Controlled Release Society[7] and American Chemical Society.[8] A paper is currently under review at *ACS Materials and Interfaces*. Four postdocs, one PhD, and one MSc were trained on the project. Each has gone on to a career in industry or academia.[9]

Following the publicity around these presentations, the influential *New England Journal of Medicine* (Impact Factor 79) approached Professor Brayden to write an article[10] assessing a ground-breaking Science paper on oral peptides.[11] The article currently has an Altmetric score of 150,[12] and is estimated to be in the top 5% of all published research outputs. Importantly, 74% of tweets regarding the article were from members of the public, indicating a broader social impact. Feedback from an ex-Deputy Commissioner of the US Food and Drug Administration is given in the References section below.

As a result of communicating this research, the group was asked to lead the hosting of a major conference. Professor Brayden co-chaired and presented the oral nanoparticle concept at the first ever Keystone Symposium on Drug Delivery in Dublin in 2019.[13] This prestigious conference was attended by 120 visitors at the Royal Dublin Society. Additional economic impact can be seen in the fact that each international conference visitor typically brings €2000 to Dublin. Attendee feedback is given in the references below.



REFERENCES

1. SFI Technology Innovation Development Award: *"Silica nanoshells for oral peptide delivery: widening the platform."*

2. *"An oral delivery system"*, UK Patent Application GB1605740.8. David Brayden, Sourav Battacharjee, Delyan Hristov, Eugene Mahon (filed 4th April, 2016).

3. https://www.rte.ie/player/movie/bittersweet/83918888259

4. https://scannain.com/irish/bittersweet-the-rise-of-diabetes-premiere/

5. https://presspack.rte.ie/2018/11/14/bittersweet/

6. https://www.imdb.com/title/tt7680912/awards

7. *"Oral peptide delivery: the potential of combining nanoparticle constructs with permeation enhancers,"* Controlled Release Society Symposium invited speaker. https://www.abstractsonline.com/pp8/#!/5717/presentation/14157 (New York, July 2018).

8. Hristov, D., McCartney, F., Beirne, J., Reid, S., Mahon, E., Bhattacharjee, S., Redmond, G., Brougham, D., Brayden D. (2018). *Insulin- containing silica nanoparticles with a high loading capacity and demonstration of bioactivity: potential for oral delivery.* Am. Chem. Soc. Abstract 256. 19 Aug 2018.

9. Dr Fiona McCartney (achieved PhD, 2017, current postdoc in UCD Vet School); Dr Delyan Hristov (current postdoc in University of Massachusetts Boston); Dr Jason Beirne (current researcher in Genzyme, Ireland); Dr Eugene Mahon (current researcher in Life Scientific, Ireland); Stephanie Reid (achieved MSc, 2017, current researcher in industry in Ireland); Dr Sourav Bhattacharjee (postdoc to Assistant Lecturer, UCD).

10. Brayden, D. J. & Baird, A. W. (2019). *Stomaching drug delivery*. Clinical Implications of Basic Research. New Eng., J. Med. 380 (17) 1671-1673. doi: 10.1056/NEJMcibr1901766.

11. Abramson A, et al. (2019). *An ingestible self-orienting system for oral delivery of macromolecules*. Science. 363(6427):611-615. doi: 10.1126/science.aau2277.

12. https://www.altmetric.com/details/59493308

13. http://www.keystonesymposia.org/19E1

Evaluations

Bittersweet documentary reach and reception:

- More than 100,000 viewers on RTÉ television and RTÉ Player
- Winner of the *Raw Science Festival Industry Award for Best Educational Media*
- 24 screenings in total: 5 festivals, 2 broadcast, 3 online platform, 3 health services, 10 schools, 1 Community

"Diabetes has reached epidemic proportions in Ireland … This short documentary by award-winning director Hugh Rodgers hears the stories of young people living with diabetes, and looks at the breakthroughs being made in diabetes research and in finding better ways to deliver insulin to patients."

– 9 of the best shows this week, Irish Times Weekend Magazine recommendation for *Bittersweet*

"I saw the NEJM article headline and thought of old Elan colleagues, then I read your name and felt happy and proud. Wonderful to see that you are still doing cutting edge work."

– Feedback from ex-Deputy-Commissioner of the US Food and Drug Administration (1990-1998), Dr Mary Pendergast

"I wanted to extend my congratulations to you (and Claus-Michael and Katie) in organizing a truly great Keystone Symposium! It was a fantastic few days of exceptionally high quality presentations and discussions, coupled with excellent opportunities to discuss and network with other attendees. And it being in Dublin made it a little extra special too. Moreover, I thoroughly enjoyed the opportunity to be able to share some perspectives on scientific publishing with the PhD and postdoc attendees at the meeting."

– Feedback on the Keystone Symposium from Stephen Buckley, Head of Department, Discovery ADME, Novo Nordisk