SSPC The Research Ireland Centre for Pharmaceuticals

Drug Delivery and Formulation Part 2

SSPC shines a spotlight on its' research initiatives in material, dosage form and process designs which work together to convert drug substances into stable, effective, and manufacturable drug products. Innovations in this space enable the clinical, regulatory, and commercial phases of drug development. Advancements in understanding disease pathologies and identifying targets to restore health have led to the design of complex therapeutics, with challenging properties, increasing the importance of formulation, drug delivery vehicles and drug product design. Here we highlight just a few examples of research projects and the talented SSPC researchers leading the work from across Ireland to showcase these initiatives. The selected projects focus on designing novel routes of administration for therapeutic molecules, ranging from biologics to hybrid and small molecules, developing medicines with increased therapeutic effectiveness and more patient friendly dosing regimens, ensuring better health outcomes and improved quality of life for patients.

Tumour Responsive Systems For Targeted Drug Delivery


Associate Prof. Joanna McGouran
Connor O'Leary
Trinity College Dublin

This research involves developing innovative model systems and proof-of-concept studies demonstrating an enzyme-targeted approach to inducing a response in the tumour microenvironment which can be harnessed for applications including targeted drug delivery. It investigates synthesising target molecules designed to form enzyme-responsive materials after polymerisation – glycoconjugates for use as monomers and crosslinkers to respond to β-glucuronidase and β-galactosidase glycosidases.

It incorporates the glycoconjugate monomers and crosslinkers into polymerisation cocktails and subsequently optimises the polymerisation conditions by two-photon polymerisation (2PP) and bulk methods (UV, white light). It looks at validating an enzyme-induced material response from the polymer using microscopy and establishes applications for the responsive materials and present proof-of-concept use cases.

Designing Food Independent Formulations for Oral Oncology Drugs


Prof. Brendan Griffin
Callum Ryan
University College Cork

Development of a food independent formulation for oral oncology drugs would result in improved patient compliance due to less restrictive dosage conditions. The team here are investigating the synthesis of lipophilic salts of a BCS IV drug which displays a pharmaceutical food effect, so that it can be incorporated into a lipid-based formulation. The salts are characterised and their performance in a lipid vehicle will be assessed using several *in vitro* tests. Computational tools with bio-predictive *in vivo* screening are being used to computationally inform formulation selection. The stability of the lipophilic salts and their impact on solubility are examined. A recently licensed oral oncology drug performance is being assessed using an *in vivo* porcine food effect model. Allowing typically inherently poorly soluble drugs to be incorporated into lipid-based formulations through conversion of the drug into a lipophilic salt, will allow for a bioenabling technique (lipid-based formulation) to be used.

Optimal Drug Loading and Stability

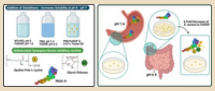
THERADEP


Prof. Abina Crean
Dr Katie Ryan
University College Cork


Chloe Frewen
Ethan Morrissey

This collaborative research between UCC-SSPC and TheraDep Technologies focuses on exploring the properties and performance of coatings applied using TheraDep's BioDep™ technology. Researchers are leveraging the benefits of BioDep™, a cold atmospheric plasma process, to directly deposit drugs and molecules with varying physicochemical characteristics onto different substrates. Our research is interested in customising drug loading and release, as well as creating packaging materials that stabilise biopharmaceuticals. Current projects are centred on cardiovascular applications and involve optimising the drug formulation and process parameters for coating various device substrates, including angioplasty balloons and drug-eluting stents. The goal is to achieve optimal drug loading and stability, and to achieve spatial and temporal control over drug release. This research is significant as it enables the application of coatings with high adhesion and integrity in a single-step process, eliminating the need for lengthy wet chemical methods and binders. Additionally, it holds promise to be deployed in a wide range of combination drug-device products.

Publication highlights



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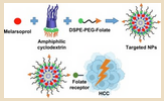

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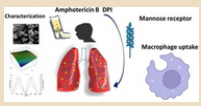

Targeting lung macrophages for fungal and parasitic pulmonary infections with innovative amphotericin B dry powder inhalers. De Pablo. E., O'Connell, P., Fernández-García, R., Marchand, S., Chauzy, C., Tewes, F., Dea- Ayuela, M. A., Kumar, D., Bolás, F., Ballesteros, M.P., Torrado, J. J., **Healy A. M.**, Serrano, D. R., 2023, 635, 122788, *International Journal of Pharmaceutics*

Enzyme Activated Peptides (EAP's) - Application of EAP's as disease specific biological probes and targeted drug delivery vectors


Assoc. Prof. Rob Elmes
Dr Conor Wynne
Maynooth University

Small molecules incorporating biological substrates, such as peptides or proteins, have been recognised as highly versatile structures that can function as exceptionally specific drug delivery agents. This combination of small molecule therapeutics with a biological targeting component in a single molecule is highly attractive to the pharmaceutical industry and is ever more recognised as a major way forward in designing intelligent and targeted drugs.

This project investigates developing a novel targeted drug-bioconjugates that also display site specific drug activation; an innovative design strategy that not only enables targeted drug delivery but also the site-specific activation of small molecule drugs in response to endogenous biological stimuli. The protocols developed - as part of this project - will give rise to novel drug delivery vehicles for a variety of diseases that could show a significantly improved efficacy profile while vastly reducing the risk of unwanted side effects leading to improved patient care & treatment.

Developing models to explore *in vivo* drug availability from long-acting injectable preparations


Assoc. Prof. Deirdre D'Arcy
Hannah Cleary
Trinity College Dublin

This project is exploring methods to improve prediction of bioavailability of long-acting injectable (LAI) preparations. It aims to develop in silico Physiologically Based Pharmacokinetic (PBPK) models predicting *in vivo* plasma concentration versus time profiles of LAIs and assess the effect varying inputs has on the models. It investigates dissolution methods that are more predictive of target dissolution profiles generated from in silico models of LAIs through exploration of hydrodynamic effects e.g. vary flow rate, viscosity, surfactants and their concentrations. It uses imaging to characterise particle behaviour of LAIs during *in vitro* dissolution testing and utilises modelling and simulations to assess the predictability of accelerated testing methods.

Meet the SSPC Researchers

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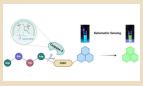
Non-invasive delivery of peptide and protein drugs via the skin route


Dr Sonja Vucen
Laura Koenitz
University College Cork

Making protein/peptide drugs available in a dissolvable microneedle (DMN) patch could enable non-invasive self-administration and thereby enhance patients' quality of life, compliance and therapeutic outcome. This programme of research focuses on making protein/peptide drugs available via the non-invasive skin route. It aims to get a better understanding of protein/peptide bioavailability in the skin following dissolvable microneedle (DMN) administration by assessing systemic and local bioavailability of protein/peptide drugs following DMN administration using *in vitro*, *ex vivo* and in silico methods.

A better understanding of DMN dosage forms and protein/peptide dermatopharmacokinetics could potentially facilitate the approval of DMN pharmaceutical products by regulatory authorities. Improving the stability of protein/peptide drugs by administrating them as a DMN can offer better drug stability, prolong a product shelf life and enhance transport and storage (potential elimination of cold chain).

Publication highlights



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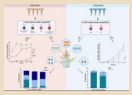

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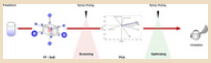

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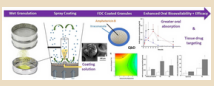

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