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| **Designing nanoparticles for the delivery of actives to and/or through skin** |
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| **Background:**  The skin provides a promising avenue for the delivery of active pharmaceutical ingredients (APIs). To overcome the skin barrier for transdermal API delivery, nanomedicines have emerged as a promising approach. FRET is an efficient imaging technique with the advantage of high sensitivity, good selectivity, non-radioactive, non-invasiveness and less expensive. For FRET to occur there must be the resonant transfer of electronic excitation energy from a donor fluorophore in the excited state to an acceptor molecule in the ground-state under the nano-spacing interaction between fluorophores. Thus, the technique is sensitive to the distance change in nanoscale; if the donor and acceptor dyes in the lipid nanoparticles (LNPs) dissolve then the FRET signal is lost. Such a probe in LNPs will provide a valuable tool to improve the understanding of the in vivo and in vitro dynamic biofate of LNPs, including structural and conformational changes, cargo release behaviour, and LNPs interaction with skin lipids, etc. Thus, in our project, we aim to develop new LNPs with a Förster resonance energy transfer (FRET) imaging-based system to monitor the location and integrity of LNPs. We also explore strategies for increasing the solubility and high entrapment of dyes loaded in LNPs, and develop simple and fast methods to test a large number of formulations and more detailed testing methods to give greater insight into the mechanism for dynamic biofate of LNPs. |
| **Methods:**  We are using nanoprecipitation to produce the LNPs and are exploring the growth mechanism of nanoparticles through increasing nucleation events and suppressing subsequent growth of the particles. The particles are characterised a by various techniques such as Dynamic Light Scattering (DLS) and Fluorescence Spectroscopy (FLS) and obtaining efficient FRET signals and colloidally stable particles. During the particle nucleation and growth phase, parameters such as the solvent to anti-solvent ratio, surfactant concentration, and mixing time significantly influence their size, stability and payload, and thus will be optimised to achieve the desired FRET nanoparticle characteristics. |
| **Results:**  Depending on the solvent to antisolvent ratio it was possible to obtain the smaller size range of dye nanoparticles that exhibited different degree fluorescence behaviour. As a continuation of this study, future work will focus on optimising the nanoparticle sizes and enhancing the FRET signal. |
| **Conclusions:**  The application of nanoparticles with efficient FRET signal as a promising tool for investigating the penetration of substrates, such as the skin, the corneum etc. Our work seeks to contribute to the development of this toolbox, which presents a valuable opportunity to deepen our understanding of the dynamic behaviour of nanoparticles and to facilitate the optimisation of their penetration into a wide range of substrates. |