#LoveIrish Research

"My Heart, Your Heart"

Hot melt enteric targeted therapeutic delivery platform

Enhancing drug solubility through advanced polymer extruded drug delivery system

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IRISH RESEARCH COUNCIL
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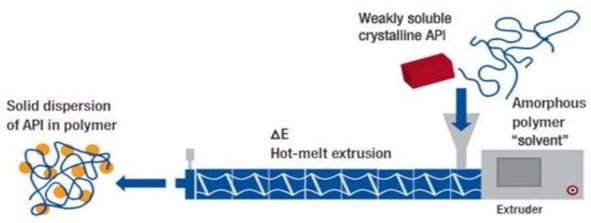
Introduction

Cardiovascular diseases (CVDs) are the number 1 cause of death globally. Fenofibrate has been shown an excellent treating effect on CVDs. However, Fenofibrate is a neutral, lipophilic compound that is practically insoluble in water, making it challenging to achieve therapeutic levels consistently. As a result, this project was using shellac material as the polymeric matrix to enhance the solubility of Fenofibrate by producing solid dispersion by hot melt extrusion.



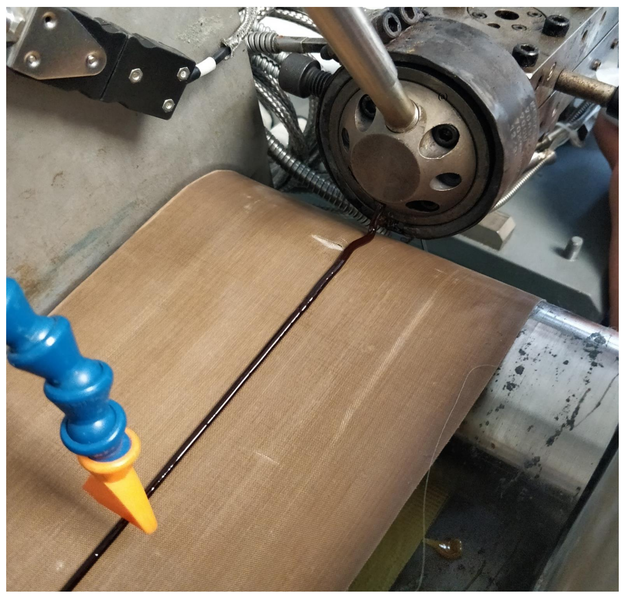
Aims

Enhance the solubility and bioavailability of Fenofibrate as an amorphous HME solid dispersion and develop a continuous downstream process to produce a finished, ready to package dosage form direct from the extruder.

Method

- Material Characterisation → Different type of shellac and Model Drug Fenofibrate
- Formulation Production → Prism™ twin-screw co-rotating extruder
- Characterisation of formulation → Formulation Analysis; Drug Stability; Drug recrystallization; Formulation uniformity
- Optimization of formulation → Release profile; Process condition; Screw design
- Screw design Simulation → Ansys Polyflow
- Optimised screw design production → Formulation Analysis; Formulation uniformity; Release profile

Result and discussion



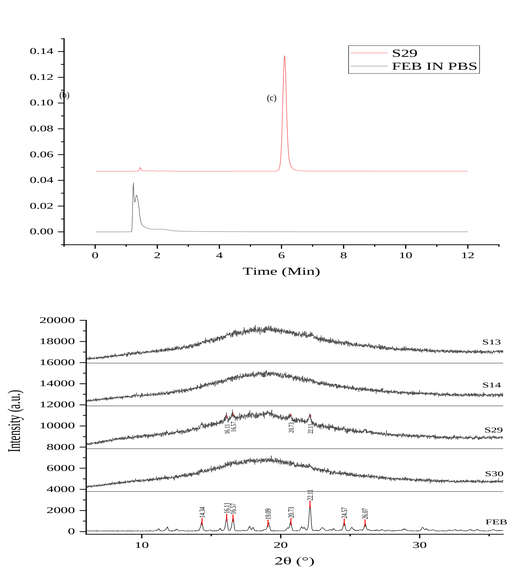


Fig. 1 (a) Formulation samples, (b) Overlay of HPLC response graph, (c) P-XRD result.

The extrudate can keep its shape well during processing, and the process condition has a noticeable impact on the extrudate and the state of the drug substance. Moreover, compared to origin Fenofibrate substance, the drug in the shellac base solid dispersion formulation existing as amorphous state and have significant higher solubility in phosphate buffer solution.

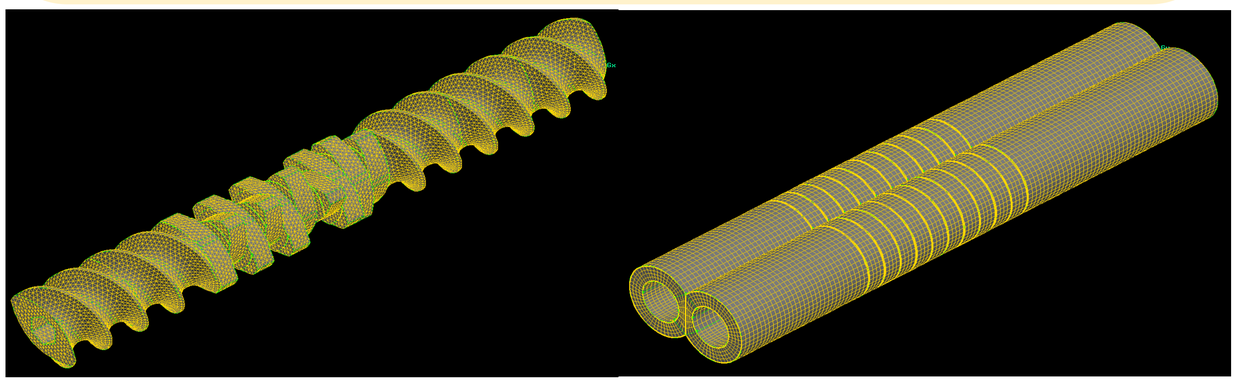


Fig. 2 (a) Screw solid moving mesh , (b)Screw set fluid domain mesh

The first production screw design can provide much less mixing performance than the other screw design from the simulation results. The 30-degree kneading block was used for the forwarding purpose. As a result, new designed screw combination was crated based on the simulation result. By using this new screw configuration, the new formulation have a much better uniformity.

Future Work

Formulation Optimise and downstream process study

- Deeper simulation of production line
- Downstream process development
- Downstream process simulation

Acknowledgment: This research was funded by Irish Research Council (GOIPG/2018/2067) and Athlone Institute of Technology, Presidents Seed Fund.

Reference

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