**A novel topical formulation of fenofibrate restores wound healing in diabetic mice.**

Aims:

To investigate the potential for TGA-approved, fenofibrate and mirabegron, to be topically repurposed in diabetic foot ulcers.

Methods:

After six weeks of high-fat diet (HFD), hyperglycaemia was induced by 5 intraperitoneal doses of 55mg/kg streptozotocin (STZ) to model diabetes in mice. After 4 weeks of hyperglycaemia and HFD, mice were subject to 5mm excisional wounds, secured with silicon splints, modelling human-like healing by preventing contraction of the panniculus carnosus. Wounds were measured and treated topically with vehicle or drug then redressed daily. Proteins and gene expression were analysed from ex-vivo wounds at day 14 and day 4 by western blot, histology and RT-qPCR. Wound healing data was analysed using a two-way mixed-effects model with Dunnett’s multiple comparisons post-hoc test.

Results:

We successfully induced diabetes in mice shown by dramatically increased random blood glucose and markedly impaired glucose tolerance. The diabetic mice healed significantly slower compared to non-diabetic vehicle mice on day 11 (p=0.0229), day 12 (p=0.0124), day 13 (p=0.0099), and 14 (p=<0.0001). Topical fenofibrate significantly improved diabetic wound healing compared to diabetic vehicle control at day 14 (p=0.0005).

Conclusion:

Our findings suggest that repurposing fenofibrate in a topical form may be an effective strategy for improving healing in humans with diabetic ulcers. This is a strong candidate for rapid clinical translation that can have a real impact for more than 100 million people with diabetic foot ulcers.