Doctoral Training Network in Technologies for Healthy Ageing

Dissolving Microneedle Array Patches: The Effects of Drug Incorporation on Polymer Physicochemical Properties

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Background

Dissolving microneedle array patches (DMAPs) provide a novel platform for ophthalmic drug delivery by increasing bioavailability compared to topical administration (TA) whilst remaining user-friendly.[1] DMAPs are fabricated from water soluble, biodegradable polymers, such as poly (vinyl pyrrolidone) (PVP), and require tailored mechanical strength for administration and fast dissolution for drug delivery.[2] Integration of plasticisers such as poly (ethylene glycol) (PEG) can tailor the physicochemical properties, therefore altering the surface behaviour and insertion efficiency to provide a sustained drug release.[3] Here, latanoprost (LAT) a first line therapeutic for glaucoma, is studied within DMAPs and compared to TA.[4]

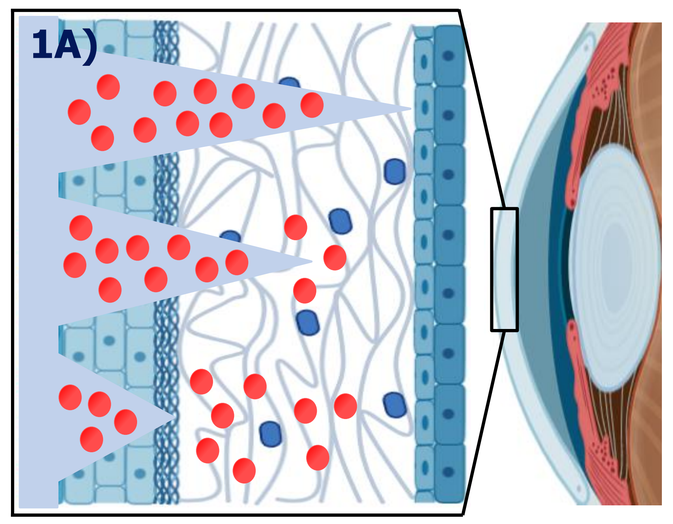

Figure 1: A) *DMAP penetration and dissolution (top to bottom) through corneal layers of the eye.* ***B)*** *Micro-CT imaging of a PVP_{100}·PEG_0 DMAP, scale bar = 200 µm.*

Surface Behaviour

The surface tension (ST) of a liquid can be evaluated *via* tensiometer analysis, and the degree of hydrophilicity/hydrophobicity *via* contact angle (CA) measurements. These were used to determine changes in the surface behaviour based upon LAT loading and plasticiser incorporation.

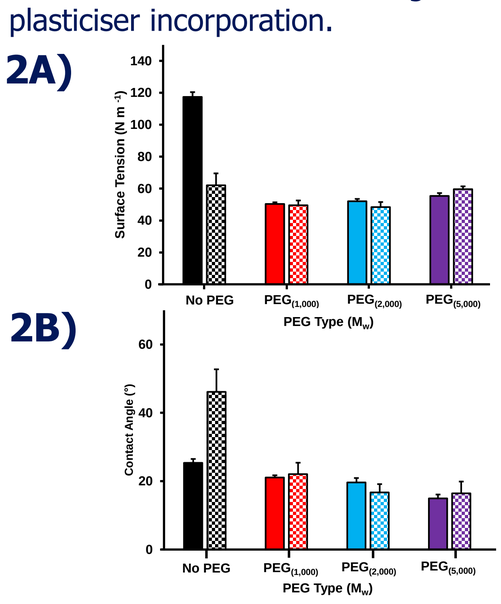

Figure 2: A) *ST and* ***B)*** *CA measurements of PVP_{90}·$PEG_{10(1,000\text{-}5,000)}$ relative to PVP (black); unloaded (bold) and drug loaded (tiled) formulations. n=5, error bars represent ± 1 SD.*

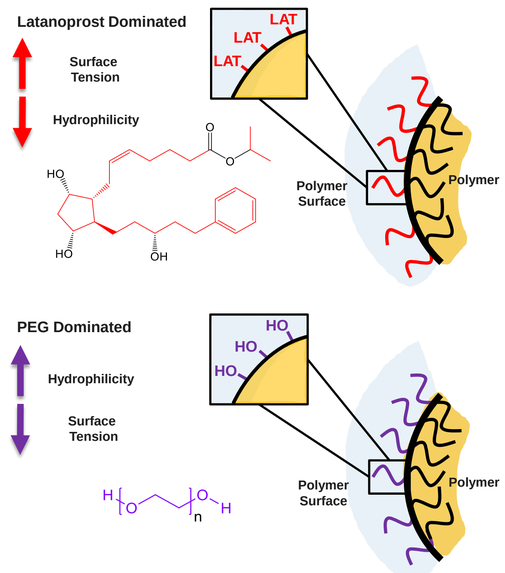

Figure 3: *Surface behaviour dominated by* ***A)*** *LAT and* ***B)*** *PEG.*

Mechanical Strength

DMAPs were inserted into an *ex vivo* porcine corneal model at a rate of 50 µm s^{-1}. Gradient increases were used to determine the force required for initial compression and complete insertion of PVP·PEG DMAPs into corneal tissue.

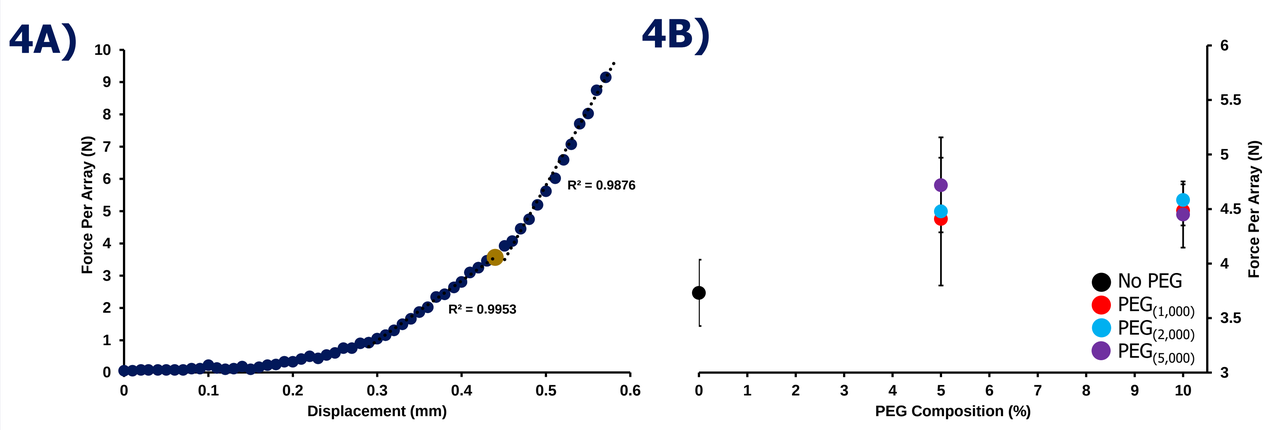

Figure 4: A) *PVP·PEG DMAP insertion profile using regression analysis to determine complete insertion (gold)* ***B)*** *Force required for complete insertion of PVP·PEG DMAPs, highlighting plasticising effects of $PEG_{(1,000\text{-}5,000)}$ relative to no PEG. n=3, error bars represent ± 1 SD.*

Dissolution

Dissolution of DMAPs was measured *via* their application to *ex vivo* porcine corneal tissue for fixed periods of time. Forces used for insertion were determined from insertion analysis.

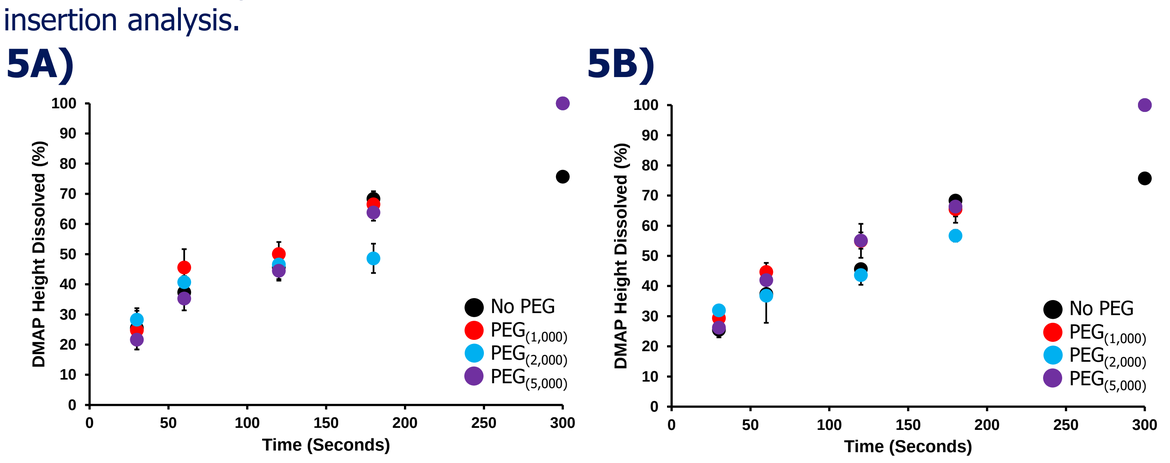

Figure 5: *Ex vivo dissolution studies of* ***A)*** *PVP_{95}·$PEG_{5(1,000\text{-}5,000)}$ and* ***B)*** *PVP_{95}·$PEG_{5(1,000\text{-}5,000)}$, both relative to PVP. n=9, error bars represent ± 1 SD.*

^{3}H-latanoprost (^{3}H-LAT) was used to determine drug deposition and permeation within an *ex vivo* porcine corneal model following TA and DMAP insertion.

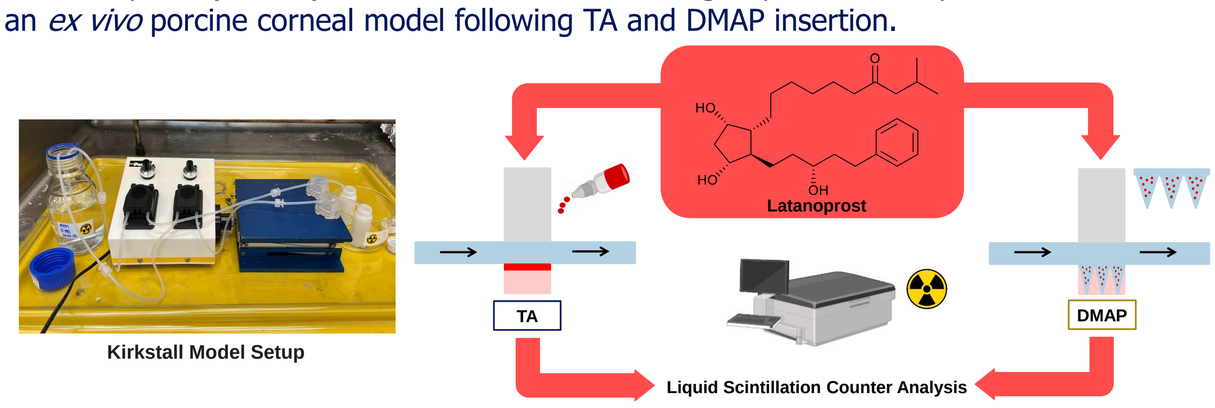

Figure 6: *Overview of ex vivo deposition and permeation studies of DMAP and TA application using a Kirkstall flow model.*

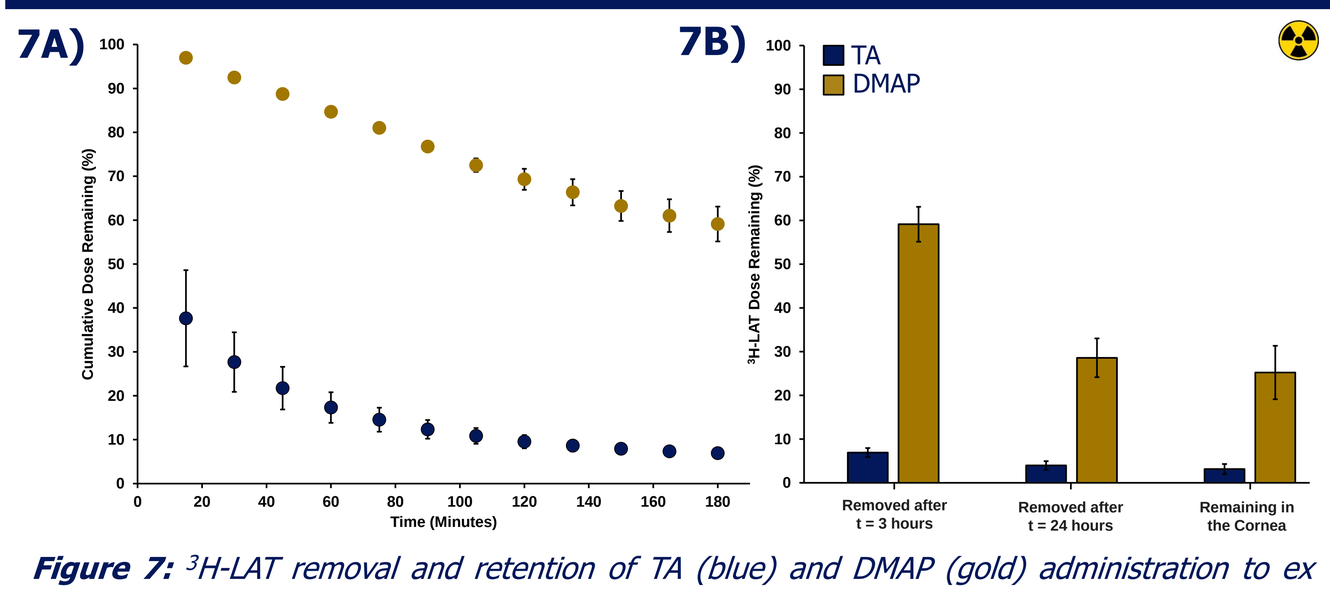

Figure 7: *^{3}H-LAT removal and retention of TA (blue) and DMAP (gold) administration to ex vivo corneal tissue using the Kirkstall model* ***A)*** *After 3 hours* ***B)*** *After 24 hours. n=3, error bars represent ± 1 SD.*

Conclusions

- The plasticising behaviour of PEG was successfully assessed through the evaluation of varying PVP·PEG compositions.
- Surface behaviour analysis determined the ability of PEG to dominate the surface of LAT loaded PVP·PEG formulations.
- Insertion testing highlighted increased forces were required for successful insertion of DMAPs *ex vivo* when PEG was present.
- Inclusion of $PEG_{(1,000\text{-}5,000)}$ resulted in faster dissolution relative to PVP DMAPs.
- Reduced removal and increased retention of ^{3}H-LAT was observed within *ex vivo* corneal tissue following DMAP administration compared to TA using radiometric analysis.

Acknowledgements

The authors would like to thank the University of Liverpool Doctoral Network for Healthy Ageing for supporting this research.

References

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