Transdermal Drug Delivery Via Bostik Adhesive Patches

Matthew Beech

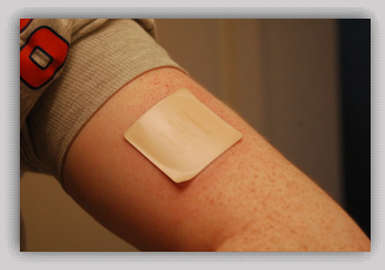
m.beech@warwick.ac.uk

THE UNIVERSITY OF WARWICK

URSS Undergraduate Research Support Scheme

Introduction

Transdermal drug delivery systems are widely used as an alternative to oral delivery. Many different types have been developed and numerous drugs have been approved for use in transdermal *systems.*[1]



We wished to develop and test methodologies to manufacture drug patches from a novel adhesive developed by Bostik.

The objective of this research was to determine whether single-layer, drug-in-adhesive transdermal patches could be produced using the adhesive with simple drugs, and further to monitor the rate of drug delivery from the patch across the skin.

Methodology

Adhesive and drug were weighed to give desired w/w percentage and stirred using industrial dissolver rig at 100°C for approx. 1 hour. Adhesive was cast onto polyethylene sheets to give uniform layers and cured in an oven at 60°C with 100% humidity for at least 24 hours. Patches were initially tested for drug uptake via extraction using THF and subsequent GC analysis.

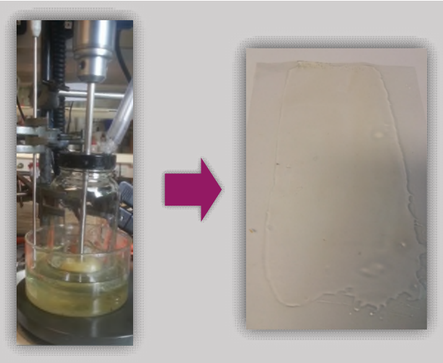


Figure 1 Experimental setup for manufacturing patches (left) and cured adhesive patch (right)

Release properties were tested using a Franz-type diffusion cell, using pig skin as the membrane and PBS (pH 7.4) as a receptor medium.[2] The size of the patch used in each case was 5cm in diameter or 19.6cm^2. The amount of drug diffusing across the membrane was determined by monitoring the integral of the corresponding peak in HPLC*.

Figure 2 Experimental setup for monitoring drug release properties

Results

- Patches were produced containing the drugs ibuprofen and diclofenac sodium of varying concentrations.
- Proof that drug was dissolved into the adhesive was obtained by comparing the GC traces of the pure drug to that extracted from the patch via THF. This was further proved by GCMS.
- An example using ibuprofen is shown in figure 3, where the corresponding ibuprofen peaks (~5.15 mins) suggest ibuprofen was present in the adhesive. This was later confirmed by mass spectrometry.

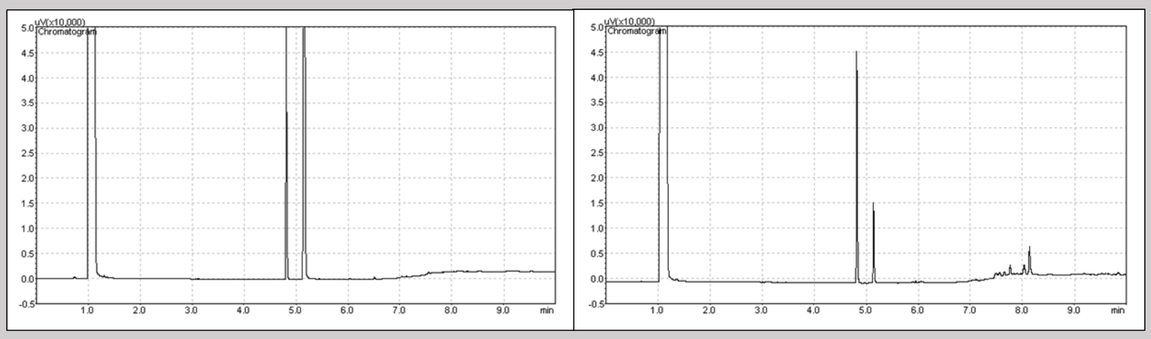


Figure 3 GC chromatograms of ibuprofen (left) and adhesive containing ibuprofen (right), with an eluent of THF.

- HPLC data proved that patch could deliver drug across the skin via diffusion, as HPLC integral is proportional to amount of drug.
- Increasing the amount of drug in the adhesive increased the amount and rate of drug delivery (figure 4).
- Rate of drug delivery was much slower than the commercial ibuprofen gel (figure 5), indicating it could be effective as a slow controlled delivery system for specific applications.
- From a calibration curve, it was estimated that ~0.5mg of ibuprofen was delivered by the 32.3% w/w patch over 24 hours. This suggested the adhesive would be most appropriate for delivery of drugs requiring only small doses, such as fentanyl.[3]

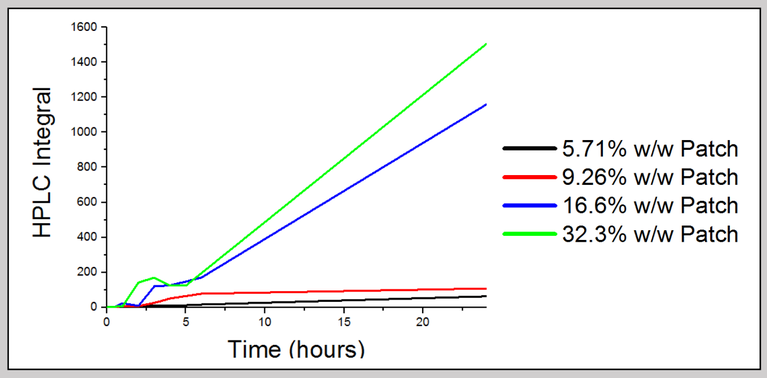


Figure 4 Plot of HPLC integral of the ibuprofen peak of the receptor medium against time of exposure of the receptor medium to the skin with transdermal patch for different concentrations of drug.

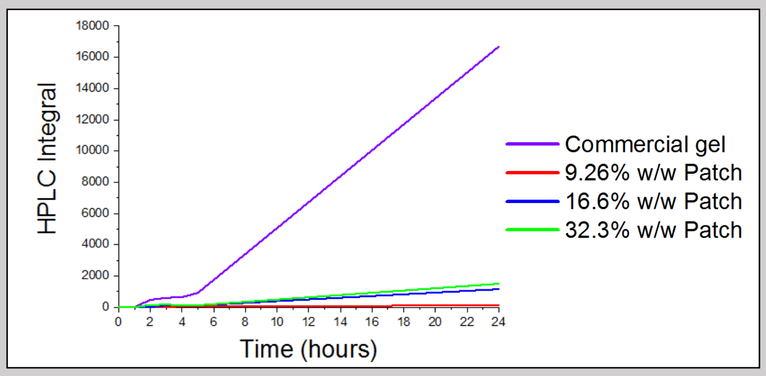


Figure 5 Plot of HPLC integral against exposure time comparing a commercially available 5% w/w gel (standard dosage) with the adhesive patches

Conclusions

- Methodology was developed to produce drug-containing patches of the adhesive using some bioavailable drugs and with varying concentrations of those drug.
- Proof by HPLC that drug is able to be provided by patches in a controlled release manner across the skin.
- Adhesive could potentially provide alternatives to current transdermal patches as it provides very slow release across the skin for small doses of drug.

Future Outlook

- Future research should focus upon the release properties of more complex and pharmacologically valuable drug molecules.
- Research should also be undertaken concerning the viability of upscaling or mass producing drug patches based upon the methodologies described here.

Acknowledgements

- The author would like to thank David Haddleton, the Haddleton group, Bostik and the URSS scheme.

(1) M. Prausnitz and R. Langer, *Nat. Biotechnol.*, 2008, **26**, 1261-1268
(2) J. Hadgraft, M. Whitefield and P. Rosher, *Skin Pharmacol. Appl. Skin. Physiol.*, 2003, **16**, 137-142.
(3) R. Muijsers and A. Wagstaff, *Drugs*, 2001, **61**, 2289-2307

*HPLC was run in 60/40 acetonitrile with a flow rate of 1 mL/min and detection at 225nm