# Microarray Patches for the Delivery of the Hydrophobic Drug Olanzapine

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## Introduction

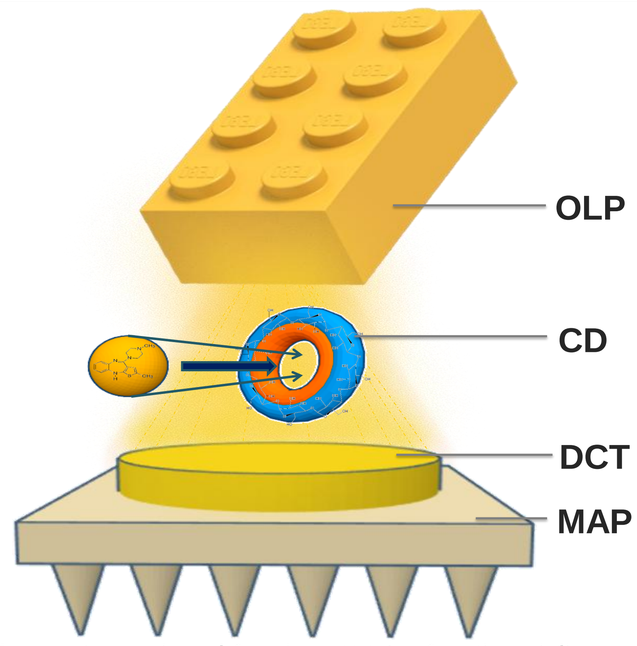


**Figure 1.** Hydrogel-forming MAPs for the delivery of a hydrophobic or "brick dust-like" drug.

- Olanzapine **(OLP)** is an atypical antipsychotic drug with indications for the treatment of schizophrenia, mania and bipolar disorder [1].
- As with 70% of emerging therapeutic agents, OLP displays poor aqueous solubility, and therefore reduced oral bioavailability; leading to frequent side effect occurrence and consequently poor patient adherence [2].
- **It is proposed that the rate-controlled delivery of the hydrophobic drug OLP *via* minimally-invasive, pain-free, hydrogel-forming Microarray patches (MAPs) will demonstrate reduced side effect incidence and increased patient acceptance [3].**

## Experimental

1. Initial screening of different solubility enhancing cyclodextrin **(CD)** molecules through phase solubility investigations to identify the most suitable CD for use with OLP.
2. Solid state OLP/ Hydroxypropyl-β-CD **(HP-β-CD)** inclusion complexes were then produced by spray drying **(SD).**
3. Directly compressed tablets **(DCTs)** with varying compositions, containing OLP, HP-β-CD and common oral excipients were formulated using Stat-Ease® Design Expert software.
4. Finally, *in vitro* delivery of OLP from DCTs *via* hydrogel-forming MAPs was evaluated using the modified Franz cell apparatus.

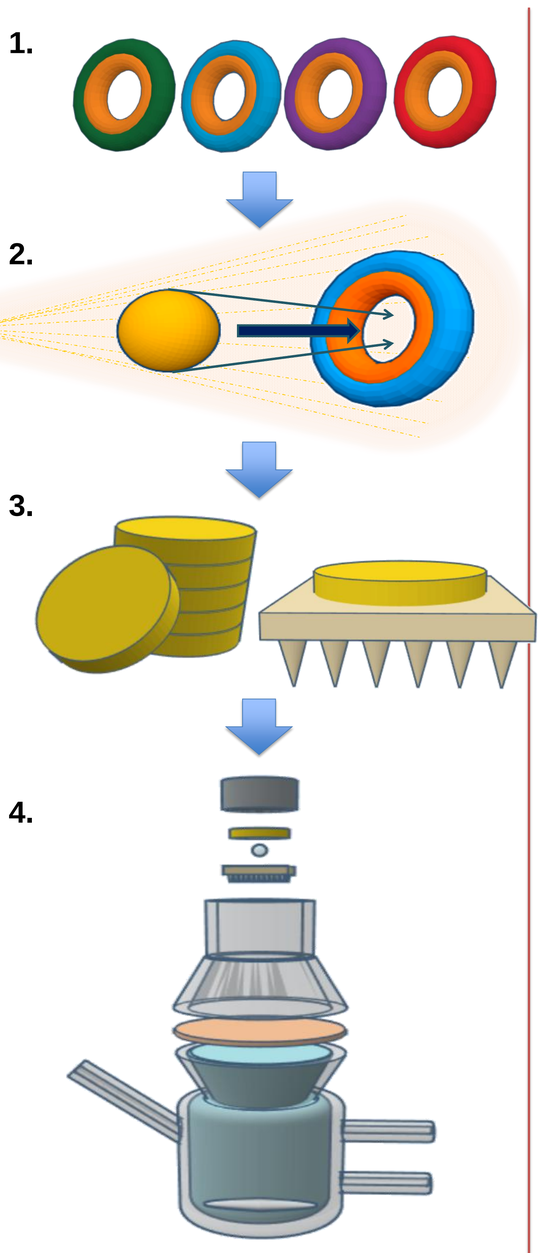


**Figure 2.** A summary of the experimental steps involved in this work.

- Two previously reported hydrogel-forming MAP formulations were tested *in vitro* using the Franz cell apparatus *i.e.* Gantrez-based [4] and PVA-based [5] formulations.

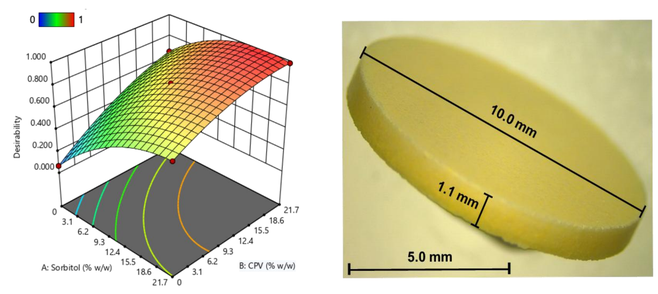


**Figure 4. (A)** Representative response surface plot used to optimise DCT formulation and **(B)** an image of a DCT.

- DCTs were formulated so that they contained 0.7% w/w OLP in all cases (**Table 1**).

**Table 1.** Formulation compositions of DCTs tested *in vitro* alongside hydrogel-forming MAPs.

| Formulation | Excipient composition (% w/w) | Processing method |
|---|---|---|
| **OLP** | Anhydrous glucose - 99.3 | Direct compression at 0.5 T for 20 s. |
| **CD** | HP-β-CD - 99.3 | See **OLP** |
| **DX** | HP-β-CD - 78.3, D-Sorbitol - 7.0, Crospovidone - 14.0 | See **OLP** |
| **SD** | See **SD** | OLP and HP-β-CD dissolved in Methanol (MeOH) and then spray dried, prior to excipient addition and direct compression as with OLP |
| **PEG-SD** | HP-β-CD - 78.3 PEG 3400 - 21.0 | OLP, HP-β-CD and PEG 3400 spray dried as with SD and then directly compress as with OLP |

- After 24 h, only those DCTs containing HP-β-CD had successfully delivered the hydrophobic drug OLP.
- The greatest amount of OLP was delivered using SD and PEG-SD DCTs in combination with PVA-based MAPs; 375.10 ± 68.02 µg (~ 54.13% total OLP content) and 473.27 ± 40.44 µg (~ 68.29% total OLP content) respectively.

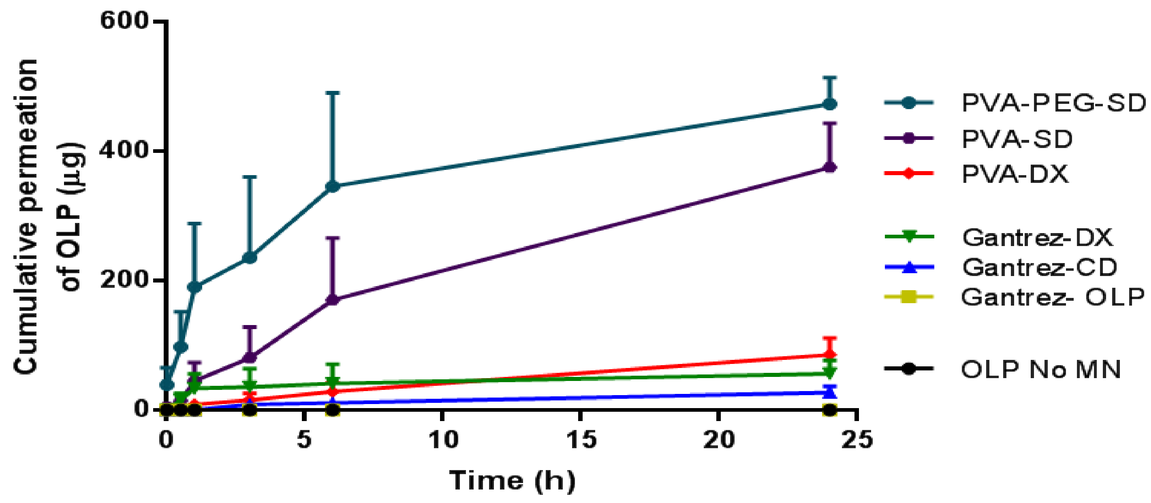


**Figure 5.** Cumulative permeation of OLP from formulated DCTs across dermatomed neonatal porcine skin *via* hydrogel-forming MAPs after 24 h. (means + SD, n = 6).

## Results

- HP-β-CD is the most suitable CD for use with OLP (6-fold enhancement of OLP's aqueous solubility).
- Further processing of OLP and HP-β-CD by SD facilitated a 42-fold improvement in the aqueous solubility of OLP.

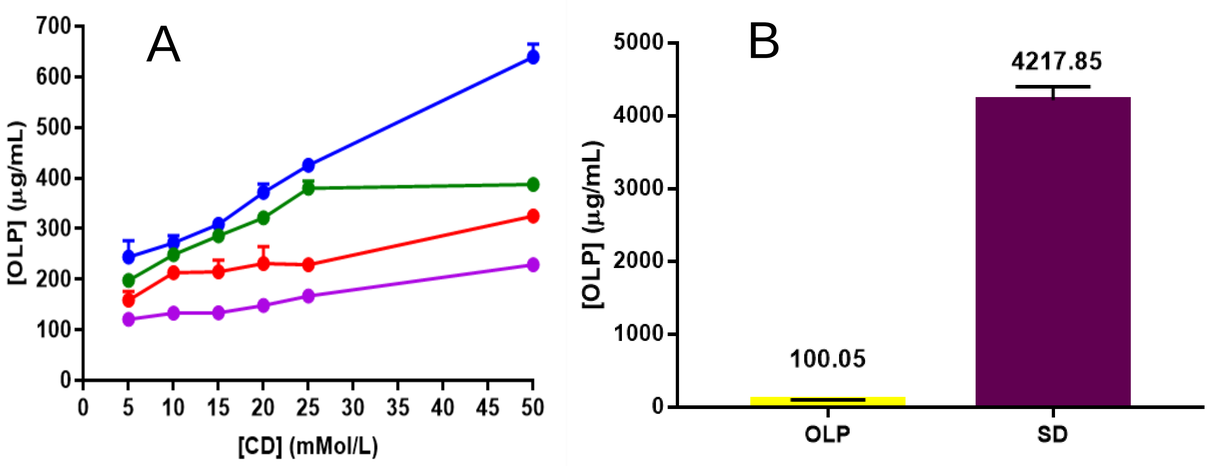


**Figure 3. (A)** Phase solubility data at 24 h for OLP with increasing concentrations of **HP-β-CD**, **β-CD**, **HP-γ-CD** and **γ-CD,** and **(B)** Saturation solubilities of OLP and OLP/ HP- β-CD inclusion complexes formed by SD in PBS. (means + SD, n = 5).

## Conclusions and Future work

**This work has proven that hydrogel-forming MAPs are a viable platform for the rate-controlled delivery of hydrophobic drugs. Future work will focus on the *in vivo* experimentation of this novel MAP platform.**

## References and Acknowledgements

[1] The British Medical Association and the Royal Pharmaceutical Society, BNF 78, 78th ed, 2019, pp. 398 - 399. [2] A. Siew, Pharm. Technol., vol. 39, no. 7, 2015, pp. 20 - 27. [3] R. F. Donnelly, T. R. R. Singh, M. J. Garland, K. Migalska, R. Majithiya and A. D. Woolfson, Adv. Funct. Mater., vol. 22, no. 1, 2012, pp. 4879 – 4890. [4] R. F. Donnelly, M. T. C. McCrudden, A. Z. Alkilani, E. Larrañeta, E.

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