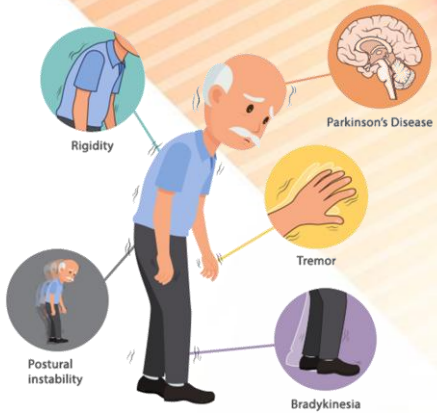
Is transdermal delivery achievable for levodopa? Microarray patch for Parkinson's disease treatment



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Background

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Background

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Parkinson's disease (PD)

- 2nd most prevalent neurodegenerative disease, affecting 10 million people globally (after Alzheimer's disease).
- Depletion or degeneration of dopaminergic neurons within the brain.
- Motor symptoms (e.g., movement difficulties) and non-motor symptoms (e.g., cognitive problems).
- Not curable, whereas treatment options are available for symptom management.

Levodopa

- A naturally-occurring amino acid dopamine precursor.
- The gold standard therapy for PD disease management (with carbidopa).
- Orally-administered LD – commonly associated with pulsatile delivery to the brain.
- Treatment 'off' period.

Using dissolving microarray patches (MAPs) to continuously deliver LD and CD, as the alternative to conventional oral LD formulations.

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Methods and results

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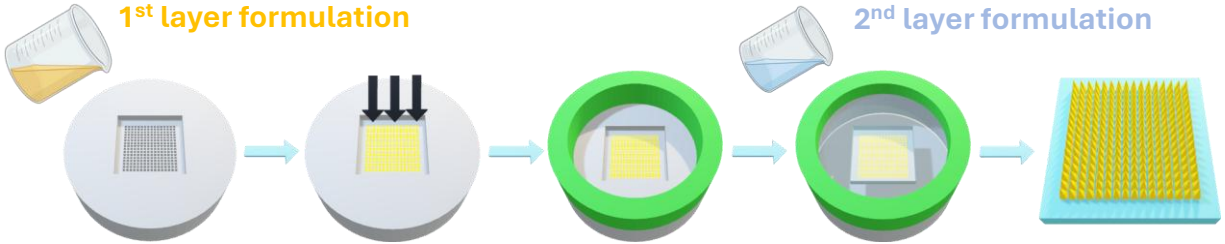
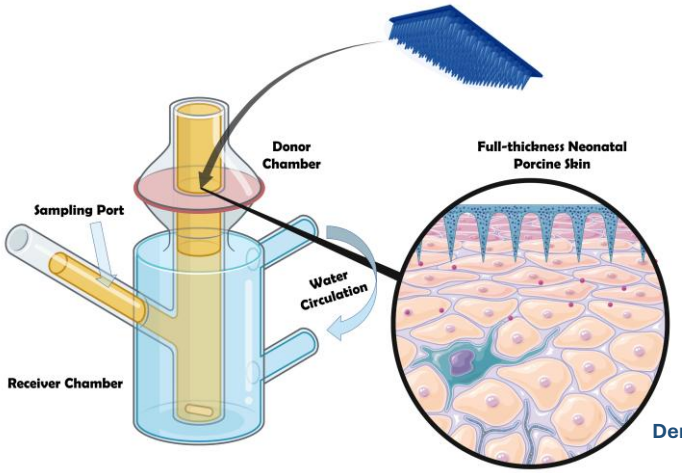
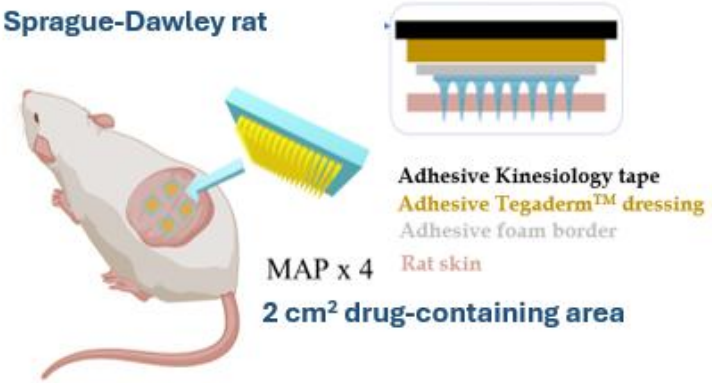
MAP fabrication and characterisations



- Formulation stability investigations.
- Mechanical characterisations.
- *In vitro* permeation studies.
- *In vivo* pharmacokinetic evaluations.



Dermatomed Neonatal Porcine Skin



In vitro characterisations of dissolving MAPs

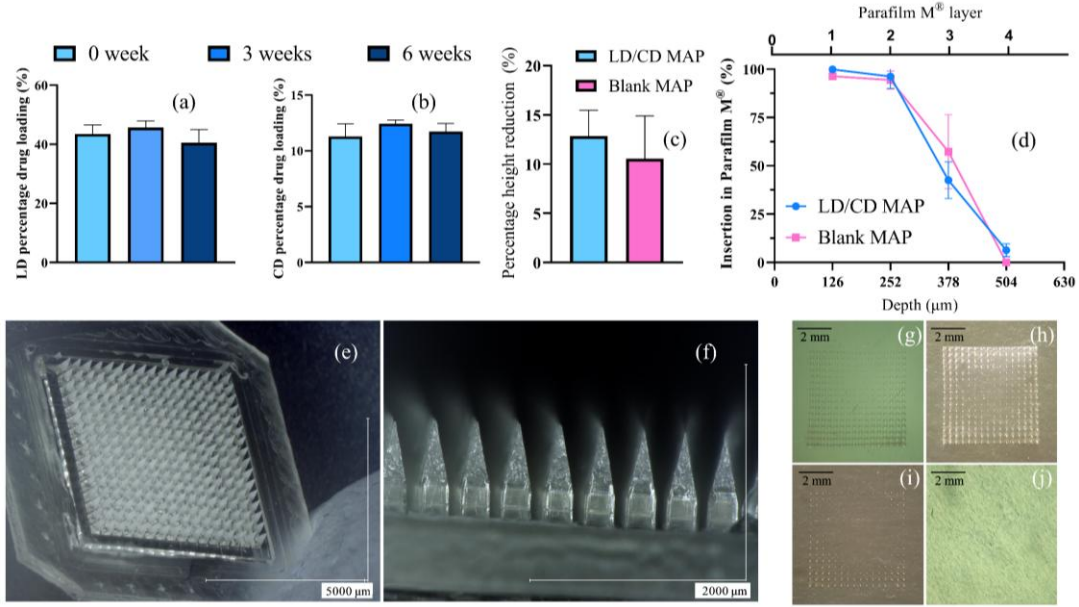


Figure 1. (a) LD content and (b) CD content in the LD/CD MAP 'drug-containing layer' formulation (means + S.D., *n* = 3). (c) Representative digital microscopic images of the LD/CD dissolving MAPs. (d) Drug distribution of the LD/CD dis-solving MAPs. (e) Percentage height reduction of MAP needles upon 32 N/cm2 pressure for 30 seconds (means + S.D., n = 5). (f) Insertion profiles of dissolving MAPs (means ± S.D., *n* = 3). Representative microscopic images of (g) 1st layer (h) 2nd layer (i) 3rd layer (j) 4th layer of Parafilm M® in the insertion studies.

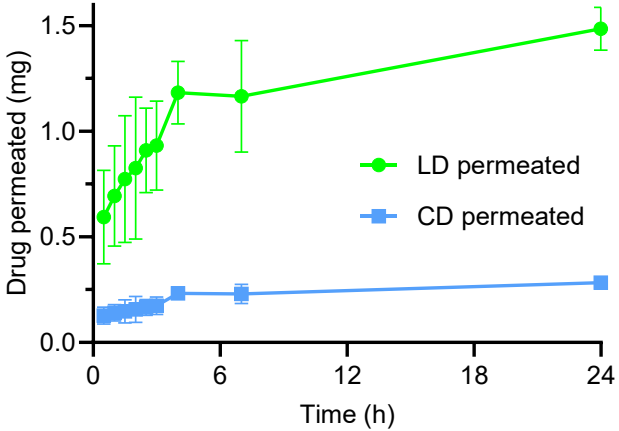


Figure 2. *Ex vivo* permeation profiles of LD and CD from the dissolving MAPs (Means ± S.D., *n* = 3).

API	Drug delivered (mg)	Drug content (mg/0.5 cm^2)	Drug delivery efficiency (%)
LD	1.49 ± 0.10	1.82 ± 0.24	81.82 ± 5.66
CD	0.28 ± 0.02	0.47 ± 0.04	60.15 ± 1.88

In vivo pharmacokinetic profiles

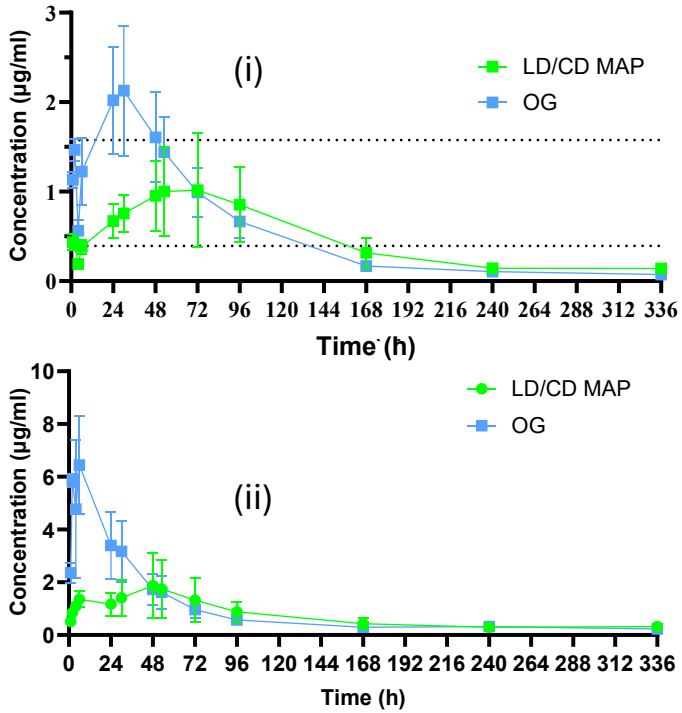


Figure 3. *In vivo* pharmacokinetic profiles of (i) LD and (ii) CD (means ± S.D., *n* = 5).

Table 2. *In vivo* pharmacokinetic profiles of LD and CD.

	Parameter	LD/CD MAPs (means ± S.D., *n* = 5)	Oral gavage (means ± S.D., *n* = 5)
LD	C_{max} (µg/ml)	1.016 ± 0.639	2.129 ± 0.727
	T_{max} (hour)	72	30
	AUC (ng.h/ml)	149.400 ± 21.970	179.500 ± 14.390
CD	C_{max} (µg/ml)	1.871 ± 1.232	6.443 ± 0.601
	T_{max} (hour)	48	6
	AUC (ng.h/ml)	232.900 ± 29.070	309.500 ± 28.250

- *The in vivo bioavailability of LD from the dissolving MAPs was calculated to be ~ 37%.*

Figure 3. *In vivo* pharmacokinetic profiles of (i) LD and (ii) CD (means ± S.D., *n* = 5).

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Summary

MAP fabrication and characterisations

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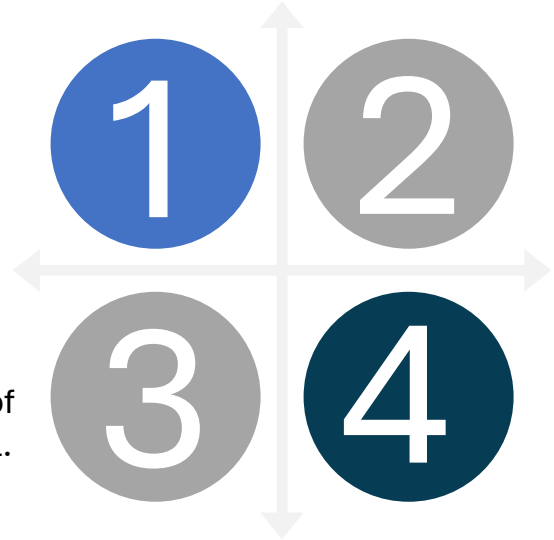
A transdermal approach using dissolving MAPs to deliver LD and CD simultaneously was introduced.



A single 24 h application can provide therapeutic LD level for at least 4 days.

The pharmacokinetic profile of the dissolving MAPs indicated the potential of avoiding unnecessarily high plasma level.

Such strategy offers an alternative LD long-acting formulation which can potentially avoid the influence of the varied gastric emptying time with PD patients.

- Continuous delivery from hydrogel-forming MAPs, by keeping the patch on site over a few days.

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Thanks!
Q&A session

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