Electronic Supplementary Information

Calculation of Sample Concentrations

The concentrations of the samples (LD-1, LD-2, and LD-3) were determined by UV-Vis spectrophotometry using a standard calibration curve and corrected for the experimental dilution factor.

1. Calibration Curve Equation

Separate calibration curves were generated for acid-based quantification (encapsulation efficiency) and plasma-based quantification (release studies). Reported R^2 values, therefore, correspond to independent regressions.

A series of standards with known LD concentrations in 0.1 M hydrochloric acid was measured to establish a linear relationship between absorbance and concentration. Based on the linear regression of the calibration data, the following equation was derived:

Absorbance = 2.674 x Concentration (mM) + 0.0049

- Slope (m): 2.674 (Absorbance units per mM)
- Intercept (c): 0.0049 (Background absorbance)
- Correlation Coefficient (R^2): 0.9996

2. Step-by-Step Calculation Procedure

To determine the actual concentration of the LD samples in mM, the following steps were applied to every raw absorbance reading:

Step A: Solve for the Concentration in the Cuvette (C-cuvette)

The raw absorbance was rearranged using the calibration equation to find the concentration of the diluted liquid measured in the spectrophotometer:

C-cuvette (mM) = (Measured Absorbance - 0.0049) / 2.674

Step B: Correct for the Dilution Factor (DF)

Since the original samples were diluted by a factor of 5 before measurement, the concentration in the cuvette was multiplied by the dilution factor to find the actual sample concentration (C-sample):

C-sample (mM) = C-cuvette x 5

3. Representative Sample Calculation

For sample LD-1 at 0.5 hours (Absorbance = 0.8393):

1. Calculate Cuvette Conc: (0.8393 - 0.0049) / 2.674 = 0.312 mM
2. Multiply by Dilution Factor: 0.312 x 5 = 1.56 mM

Concentration/ mM	Absorbance	SEM
0.000233	0.0009	6.00E-05
0.000467	0.00578	0.00066
0.0007	0.004663333	0.003353333
0.000933	0.005173333	0.000423333
0.00233	0.0008	9.00E-05
0.00467	0.017333333	0.002666667
0.007	0.01803	0.00061
0.00933	0.055596667	0.076843333
0.0233	0.06015	0.0033
0.0467	0.12025	0.00083
0.07	0.1916	0.00117
0.0933	0.2541	0.00072
0.233	0.637483333	0.004876667
0.467	1.25176	0.00428

Table S1: Calibration data used for UV–Vis quantification of LD in 0.1 M HCl. The table reports standard concentrations, measured absorbance values, and regression parameters.

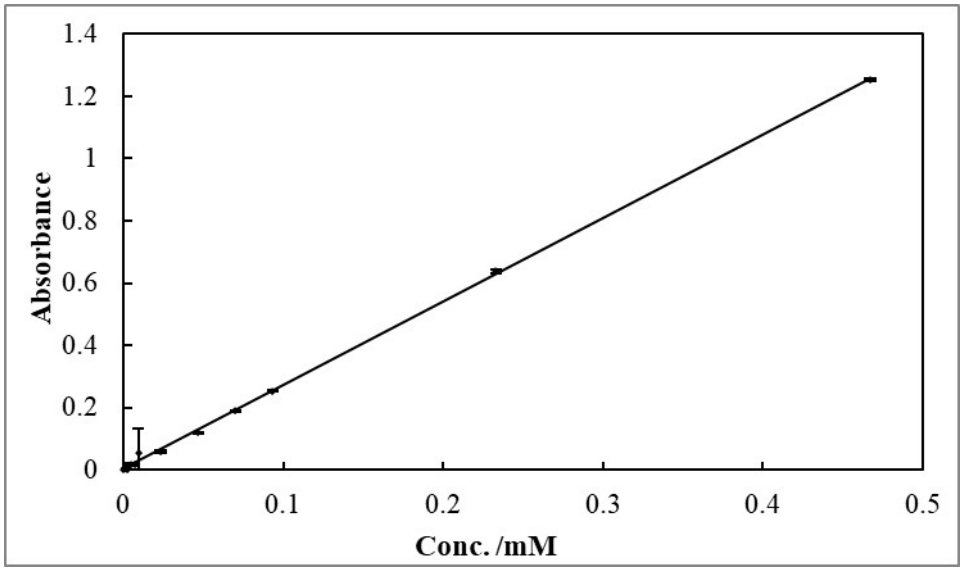

Figure S1: UV–Vis calibration curve for levodopa (LD) in 0.1 M HCl. The linear regression (Abs = 2.674 C + 0.0049) shows excellent linearity over the investigated concentration range (R^2 = 0.9996). To minimise stray-light effects at high absorbance, all samples with A > 1.8 were diluted with blank plasma before measurement, and dilution factors were applied in all calculations. To ensure strict adherence to the UV–Vis spectrophotometer's validated linear range, only calibration standards with absorbance values ≤ 1.8 were included in the final regression analysis. Higher-concentration standards were measured during method development but excluded from the reported calibration to minimise potential stray-light deviations at high absorbance. All release samples exceeding this threshold were diluted with blank plasma before quantification, and the dilution factors were applied accordingly.

Time (hr)	LD-1 Abs	Conc-1 (mM)	LD-2 Abs	Conc-2 (mM)	LD-3 Abs	Conc-3 (mM)
0	0.1332	0.24	0.1439	0.26	0.1332	0.24
0.5	0.8393	1.56	0.866	1.61	0.8446	1.57
1	0.8713	1.62	0.8767	1.63	0.8713	1.62
1.5	0.882	1.64	0.882	1.64	0.8874	1.65
2	0.8981	1.67	0.8927	1.66	0.9034	1.68
2.5	0.9088	1.69	0.9195	1.71	0.9248	1.72
3	0.9195	1.71	0.9254	1.721	0.9302	1.73
3.5	0.9302	1.73	0.9302	1.73	0.9355	1.74
4	0.9302	1.73	0.9409	1.75	0.9355	1.74
4.5	0.9307	1.731	0.9345	1.738	0.935	1.739
5	0.9312	1.732	0.9318	1.733	0.9339	1.737
6	0.9361	1.741	0.9382	1.745	0.9398	1.748
7	0.9387	1.746	0.9414	1.751	0.943	1.754
8	0.9403	1.749	0.9425	1.753	0.9446	1.757
9	0.9414	1.751	0.943	1.754	0.9452	1.758
10	0.9419	1.752	0.9436	1.755	0.9457	1.759
11	0.9425	1.753	0.9441	1.756	0.9457	1.759
12	0.9425	1.753	0.9441	1.756	0.9462	1.76

Table S2: Raw UV–Vis absorbance values and calculated LD concentrations for release samples. Measurements were corrected using a dilution factor of 5 and converted to concentration values using the validated calibration equation.

Determination of Encapsulation Efficiency (EE%)

A carrier mass of 0.5 g of dry sporopollenin exine microcapsules (SECs) was suspended in 90 mL of 0.1 M HCl containing an initial Levodopa (LD) mass of 2.076 g. The suspension was subjected to vacuum-assisted passive diffusion and stirred at room temperature for 2 hours to ensure maximum drug penetration into the hollow exine cores.

The mixture was filtered under vacuum. The resulting filtrate, containing the non-encapsulated (waste) drug, was collected, and its volume was maintained at 90 mL. 1 mL aliquot of this waste filtrate was diluted to 125 mL (DF = 125) with 0.1 M HCl for spectrophotometric quantification.

The recovered drug-loaded SECs were washed and dried. To quantify the internal drug content, the microcapsules were resuspended in 50 mL of 0.1 M HCl and stirred vigorously for 2 hours to trigger a complete release. 1 mL aliquot of this extract was diluted to 500 mL (DF = 500) with 0.1 M HCl for measurement.

All concentration measurements were derived from a validated linear regression model in 0.1 M HCl:

Abs = 2.674 x C (mM) + 0.0049

- Correlation Coefficient (R^2): 0.9998
- Molecular Weight (LD): 197.19 g/mol

Analysis of Non-Encapsulated LD (Waste)

- Waste Volume: 90 mL
- Dilution Factor: 125
- Measured Absorbance: 0.570
- Cuvette Concentration: (0.570 - 0.0049) / 2.674 = 0.2114 mM
- Calculated Waste Mass = 0.2114 mM x 125 x 0.090 L x 197.19 g/mol / 1000 = 0.469 g.

Verification of Encapsulated LD (Actual Mass)

- Extraction Volume: 50 mL
- Dilution Factor: 500
- Measured Absorbance: 0.575
- Cuvette Concentration: (0.575 - 0.0049) / 2.674 = 0.2132 mM
- Actual Encapsulated Mass = 0.2132 mM x 500 x 0.050 L x 197.19 g/mol / 1000 = 1.051 g
- Theoretical encapsulated mass = Initial LD mass - Waste mass = 2.076 g - 0.469 g = 1.607 g

EE % = [1.051 g / 1.607 g] x 100 = 65.40 %

Given the significant dilution factors involved, EE values should be interpreted with an estimated uncertainty of ±3–5%, dominated by absorbance measurement error and dilution propagation.

Sporopollenin Mass	0.5 g
Initial LD Mass	2.076 g
LD Waste Mass	0.469 G
Theoretical Loaded LD	1.607 g
Actual Encapsulated LD	1.051 g
Encapsulation Efficiency	65.40%

Table S3: Summary of encapsulation efficiency (EE %) calculations for LD-loaded sporopollenin microcapsules. The table reports initial LD mass, non-encapsulated (waste) LD mass, encapsulated LD mass, and calculated EE%.

Linearised Kinetic Model Validation Plots:

Time (hr)	Replicate	[LD] (mM)	Mt/M∞	1−Mt/M∞	ln(1−Mt/M∞)	sqroot t	log(t)	log(Mt/M∞)
0.5	LD-1	1.5696	0.0147	0.9853	-0.0148	0.707	-0.301	-1.832
	LD-3	1.5796	0.0148	0.9852	-0.0149	0.707	-0.301	-1.829
	Mean ± SD	1.5899 ± 0.027	0.0149 ± 0.0003	0.9851 ± 0.0003	-0.0150 ± 0.0003	0.707	-0.301	-1.826 ± 0.007
1	LD-1	1.692	0.0159	0.9841	-0.016	1	0	-1.799
	LD-2	1.7052	0.016	0.984	-0.0161	1	0	-1.796
	LD-3	1.6924	0.0159	0.9841	-0.016	1	0	-1.799
	Mean ± SD	1.6965 ± 0.008	0.0159 ± 0.0001	0.9841 ± 0.0001	-0.0160 ± 0.0001	1	0	-1.798 ± 0.002
1.5	LD-1	1.7768	0.0167	0.9833	-0.0168	1.225	0.176	-1.778
	LD-2	1.78	0.0167	0.9833	-0.0168	1.225	0.176	-1.777
	LD-3	1.7865	0.0168	0.9832	-0.0169	1.225	0.176	-1.776
	Mean ± SD	1.7811 ± 0.005	0.0167 ± 0.0001	0.9833 ± 0.0001	-0.0168 ± 0.0001	1.225	0.176	-1.777 ± 0.001
2	LD-1	1.8724	0.0176	0.9824	-0.0177	1.414	0.301	-1.755
	LD-2	1.8656	0.0175	0.9825	-0.0177	1.414	0.301	-1.757
	LD-3	1.8841	0.0177	0.9823	-0.0178	1.414	0.301	-1.753
	Mean ± SD	1.8740 ± 0.009	0.0176 ± 0.0001	0.9824 ± 0.0001	-0.0177 ± 0.0001	1.414	0.301	-1.755 ± 0.002
3	LD-1	2.0469	0.0192	0.9808	-0.0194	1.732	0.477	-1.717
	LD-2	2.0607	0.0193	0.9807	-0.0195	1.732	0.477	-1.714
	LD-3	2.0691	0.0194	0.9806	-0.0196	1.732	0.477	-1.712
	Mean ± SD	2.0589 ± 0.011	0.0193 ± 0.0001	0.9807 ± 0.0001	-0.0195 ± 0.0001	1.732	0.477	-1.714 ± 0.003
4	LD-1	2.2045	0.0207	0.9793	-0.0209	2	0.602	-1.684
	LD-2	2.2267	0.0209	0.9791	-0.0211	2	0.602	-1.68
	LD-3	2.2175	0.0208	0.9792	-0.021	2	0.602	-1.682
	Mean ± SD	2.2162 ± 0.011	0.0208 ± 0.0001	0.9792 ± 0.0001	-0.0210 ± 0.0001	2	0.602	-1.682 ± 0.002
6	LD-1	2.4232	0.0227	0.9773	-0.023	2.449	0.778	-1.643
	LD-2	2.4305	0.0228	0.9772	-0.0231	2.449	0.778	-1.642
	LD-3	2.4341	0.0228	0.9772	-0.0231	2.449	0.778	-1.641
	Mean ± SD	2.4293 ± 0.006	0.0228 ± 0.0001	0.9772 ± 0.0001	-0.0231 ± 0.0001	2.449	0.778	-1.642 ± 0.001
8	LD-1	2.5707	0.0241	0.9759	-0.0244	2.828	0.903	-1.618
	LD-2	2.5784	0.0242	0.9758	-0.0245	2.828	0.903	-1.616
	LD-3	2.5831	0.0242	0.9758	-0.0245	2.828	0.903	-1.616
	Mean ± SD	2.5774 ± 0.006	0.0242 ± 0.0001	0.9758 ± 0.0001	-0.0245 ± 0.0001	2.828	0.903	-1.617 ± 0.001
10	LD-1	2.7137	0.0255	0.9745	-0.0258	3.162	1	-1.594
	LD-2	2.7207	0.0255	0.9745	-0.0259	3.162	1	-1.593
	LD-3	2.7256	0.0256	0.9744	-0.0259	3.162	1	-1.592
	Mean ± SD	2.7200 ± 0.006	0.0255 ± 0.0001	0.9745 ± 0.0001	-0.0259 ± 0.0001	3.162	1	-1.593 ± 0.001
12	LD-1	2.8549	0.0268	0.9732	-0.0271	3.464	1.079	-1.572
	LD-2	2.8621	0.0268	0.9732	-0.0272	3.464	1.079	-1.571
	LD-3	2.8674	0.0269	0.9731	-0.0273	3.464	1.079	-1.57
	Mean ± SD	2.8615 ± 0.006	0.0268 ± 0.0001	0.9732 ± 0.0001	-0.0272 ± 0.0001	3.464	1.079	-1.571 ± 0.001

Table S4: Derived kinetic variables used for release-model fitting of levodopa (LD) from sporopollenin microcapsules (SECs) in human blood plasma at 37 °C. Replicate-resolved concentrations (LD-1, LD-2, LD-3), corresponding fractional release values, and the transformed variables required for Higuchi, Korsmeyer–Peppas, and Peppas–Sahlin analyses are reported as mean ± SD. Each replicate was treated independently before statistical summarisation.

Time (hr)	LD-1 (mM)	LD-2 (mM)	LD-3 (mM)	LD-1 Cum (mM)	LD-2 Cum (mM)	LD-3 Cum (mM)	Mean Cum (mM)	SEM x 10	Higuchi fit (mM)	KP fit (mM)	106.6	M∞ (mM)	Peppas–Sahlin fit (mM)
0	0.24	0.26	0.24	0.24	0.26	0.24	0.2467	0.067	1.23123		0.004442	Higuchi k	
0.5	1.56	1.61	1.57	1.5696	1.6204	1.5796	1.5899	0.156	1.566057223	1.445965367	0.01155	Higuchi intercept	1.440180538
1	1.62	1.63	1.62	1.692	1.7052	1.6924	1.6965	0.043	1.7047472	1.671488	0.01568	KP k	1.6665844
1.5	1.64	1.64	1.65	1.7768	1.78	1.7865	1.7811	0.028	1.811167762	1.819382216	0.2091	KP n	1.815317799
2	1.67	1.66	1.68	1.8724	1.8656	1.8841	1.874	0.054	1.900884446	1.932184684	0.01551	PS kd	1.928899463
2.5	1.69	1.71	1.72	1.9593	1.9822	1.9915	1.9777	0.096	1.979926432	2.02447547	0.000124	PS kr	2.021917312
3	1.71	1.721	1.73	2.0469	2.0607	2.0691	2.0589	0.065	2.051385849	2.103145492	0.2091	PS m	2.101270726
3.5	1.73	1.73	1.74	2.1353	2.1376	2.1479	2.1403	0.039	2.117099565	2.172040361			2.170812171
4	1.73	1.75	1.74	2.2045	2.2267	2.2175	2.2162	0.064	2.1782644	2.233541402			2.23292834
4.5	1.731	1.738	1.739	2.2747	2.2848	2.2862	2.2819	0.036	2.235711669	2.28923301			2.289207849
5	1.732	1.733	1.737	2.345	2.3492	2.3536	2.3493	0.025	2.290046648	2.34022649			2.340765373
6	1.741	1.745	1.748	2.4232	2.4305	2.4341	2.4293	0.032	2.391105524	2.431166426			2.432772274
7	1.746	1.751	1.754	2.4979	2.5063	2.51	2.5047	0.036	2.484038753	2.510806609			2.51341112
8	1.749	1.753	1.757	2.5707	2.5784	2.5831	2.5774	0.036	2.570538893	2.581899773			2.58544647
9	1.751	1.754	1.758	2.6427	2.6495	2.6544	2.6489	0.034	2.6517816	2.646277424			2.65071857
10	1.752	1.755	1.759	2.7137	2.7207	2.7256	2.72	0.035	2.728622863	2.705224195			2.710518728
11	1.753	1.756	1.759	2.7848	2.7919	2.796	2.7909	0.033	2.801708884	2.759678395			2.76579049
12	1.753	1.756	1.76	2.8549	2.8621	2.8674	2.8615	0.036	2.871541697	2.810347744			2.817245779

Table S5: Replicate-resolved cumulative LD concentrations and corresponding model-fitted concentration values. Experimental data (LD-1, LD-2, LD-3), corrected cumulative concentrations, mean ± SEM values, and fitted profiles generated using Higuchi, Korsmeyer–Peppas, and Peppas–Sahlin models are provided. These data underpin the kinetic overlays shown in Figure 1 of the main manuscript.

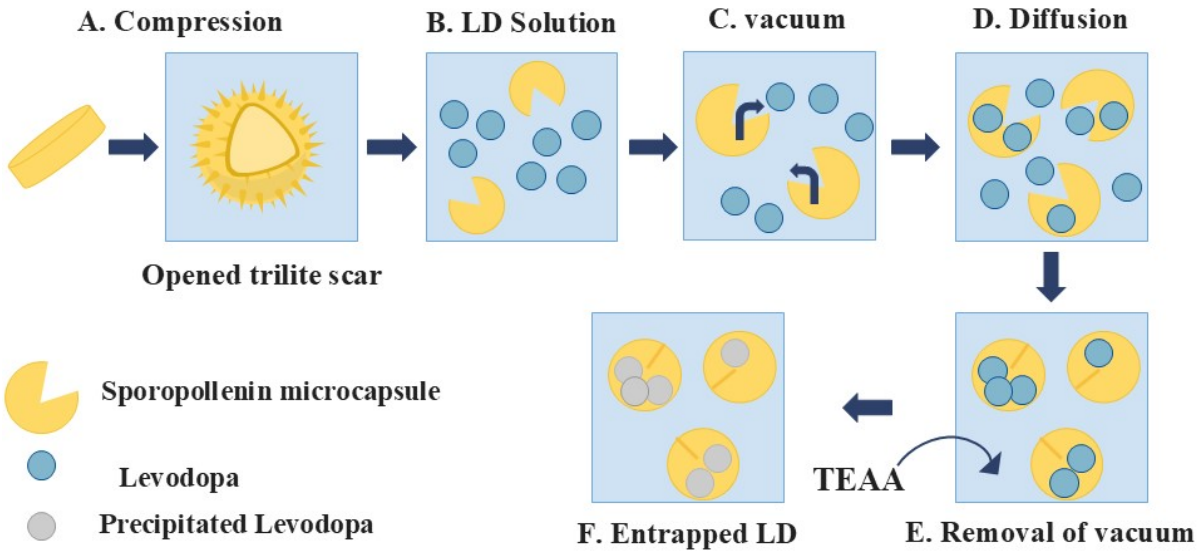

Figure S2: Schematic illustration of the vacuum-assisted, pH-triggered encapsulation process used to load LD into sporopollenin exine microcapsules.

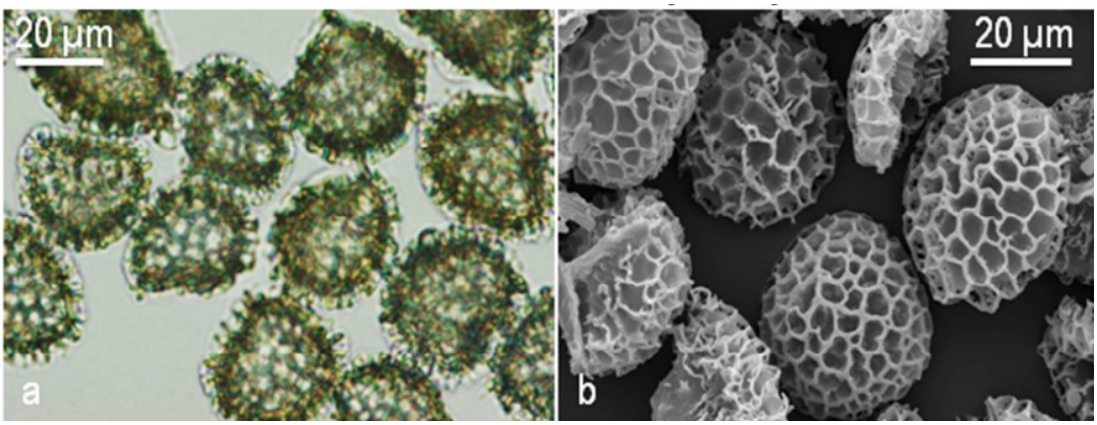

Figure S3: (a) Optical microscopy and (b) scanning electron microscopy (SEM) images of LD-loaded sporopollenin microcapsules following encapsulation, showing preservation of capsule morphology, absence of surface-deposited LD crystals, and an average capsule diameter of 20–35 µm. *Reproduced from Ref. [33] with permission. © Journal of Zankoy Sulaimani – Part A, 2019.*