

Table S1: DPI formulation optimization parameters

S. No.	Parameters	Values
1	Volume	1%
2	Nozzle	4 μm
3	Pump	3
4	Gas flow	119 to 136 L/min
5	Inlet temperature	120 °C
6	Outlet temperature	48–51 °C
7	Spray	100%
8	Head temperature	127 °C
9	Pressure	37 to 43 mbar
10	Aspirator	37.95

Table S2: Solubility of drugs in solutions of different pH

S. No.	pH	Solubility (mg/ml)	
		L-tryptophan	L-tyrosine
1	4.0	4.79	0.091
2	6.8	8.83	0.272
3	7.4	11.56	0.397
4	Water	13.75	0.432

The data for the solubility study is provided in Table 4.

Table S3: pH and logP value for L-tryptophan and L-tyrosine

S. No.	Drug	pH (1%)	logP value
1	L-tryptophan	5.7	-0.99
2	L-tyrosine	5.2	-1.71

Table S4: Drug-to-carrier ratio for DPI formulation

S. No.	Ingredients	Ratio (mg)
1	L-tyrosine	5
2	L-tryptophan	1
3	Lactose	4

Table S5: Determination of moisture content

S. No.	Weight (initial) (g)	Weight (final) (g)	% Moisture
1	1	0.98	2.0

2	1	0.98	2.0
3	1	0.98	2.0
4	1	0.98	2.0
5	1	0.99	1.0

Table S6: Drug stability studies following ICH recommendations

Stability conditions	Sampling days	Drug content L-tryptophan mean $\pm$ SD	Drug content L-tyrosine mean $\pm$ SD
60	98.98 $\pm$ 0.05	99.81 $\pm$ 0.24	100.00 $\pm$ 0.10
90	98.96 $\pm$ 0.11	99.00 $\pm$ 0.10	99.98 $\pm$ 0.11
0	99.29 $\pm$ 0.10	99.98 $\pm$ 0.22	99.81 $\pm$ 0.24
30	99.25 $\pm$ 0.22	99.90 $\pm$ 0.18	99.00 $\pm$ 0.10
60	98.95 $\pm$ 0.17	98.79 $\pm$ 0.17	99.98 $\pm$ 0.22
90	98.89 $\pm$ 0.14	97.56 $\pm$ 0.22	99.90 $\pm$ 0.18

Table S7: Evaluation parameters of capsules

S. No.	Evaluation parameters	Values
1	Physical appearance	Smooth and elegant
2	Locking length	15 $\pm$ 0.08 mm [$n = 20$]
3	Weight uniformity	19.95 $\pm$ 0.17 mg [$n = 20$]

Table S8: Percentage of drug content of L-tryptophan and L-tyrosine

S. No.	Drug	Wavelength (nm)	Absorbance	Drug content (%)
1	L-tryptophan	287.40	1.367	99.53
2	L-tyrosine	274.60	0.959	100.00

Table S9: ACI results for DPI formulation ($n = 6$)

Parameters	Results
Emitted dose (%)	88.56 $\pm$ 2.96
Respiratory fraction (%)	19.6 $\pm$ 3.53
Total recovery	95.5 $\pm$ 0.92
Mass median aerodynamic diameter (μ m)	1.92 $\pm$ 0.01

*Respiratory fraction calculated as the ratio of total drug deposited in the lower stages of the ACI (stages 2–8) to total theoretical dose

Table S10: In-vitro drug release for L-tryptophan in DPI formulation

Time (min)	Absorbance	Drug concentration	Amount released	% Released
		(mg/L)	(mg)	(%)

2	0.0096	10.2128	2.5532	25.5
4	0.0109	11.5957	2.8989	29.0
6	0.0126	13.4043	3.3511	33.5
8	0.0145	15.4255	3.8564	38.6
10	0.0198	21.0638	5.2660	52.7
12	0.0211	22.4468	5.6117	56.1
14	0.0231	24.5745	6.1436	61.4
16	0.0245	26.0638	6.5160	65.2
20	0.0300	31.9149	7.9787	79.8
25	0.0354	37.6596	9.4149	94.1
30	0.0370	39.3617	9.8404	98.4
45	0.0384	40.8511	10.2128	102.1
60	0.0386	41.0638	10.2660	102.7

Table S11: In-vitro drug release for L-tyrosine in DPI formulation

Time (min)	Absorbance	Drug concentration	Amount released	% Released
		(mg/L)	(mg)	(%)
2	0.2890	61.7962	15.4490	30.9
4	0.2990	63.9344	15.9836	32.0
6	0.3590	76.7641	19.1910	38.4
8	0.3840	82.1098	20.5274	41.1
10	0.3990	85.3172	21.3293	42.7
12	0.4890	104.5617	26.1404	52.3
14	0.5990	128.0827	32.0207	64.0
16	0.6540	139.8432	34.9608	69.9
20	0.7890	168.7099	42.1775	84.4
25	0.8950	191.3756	47.8439	95.7
30	0.9350	199.9287	49.9822	100.0
45	0.9540	203.9914	50.9979	102.0

60	0.9680	206.9850	51.7463	103.5
----	--------	----------	---------	-------

Table S12: Percentage delivered dose

S. No.	Loaded dose (mg)	Remained dose (mg)	Delivered dose (%)
1	10	1.6	84.0
2	10	1.1	89.0
3	10	0.5	95.0
4	10	1.2	88.0
5	10	1.6	84.0
6	10	1.3	87.0
Average		1.216 (12.166%)	87.83

Table S13: Drug concentration in lung tissue

Time (in minutes)	Drug concentration in lung tissue ($n = 6$) ($\mu\text{g/ml}$)
30	4.971 ± 0.04
60	3.524 ± 0.07
120	2.074 ± 0.04
180	0.726 ± 0.07
240	0.310 ± 0.05

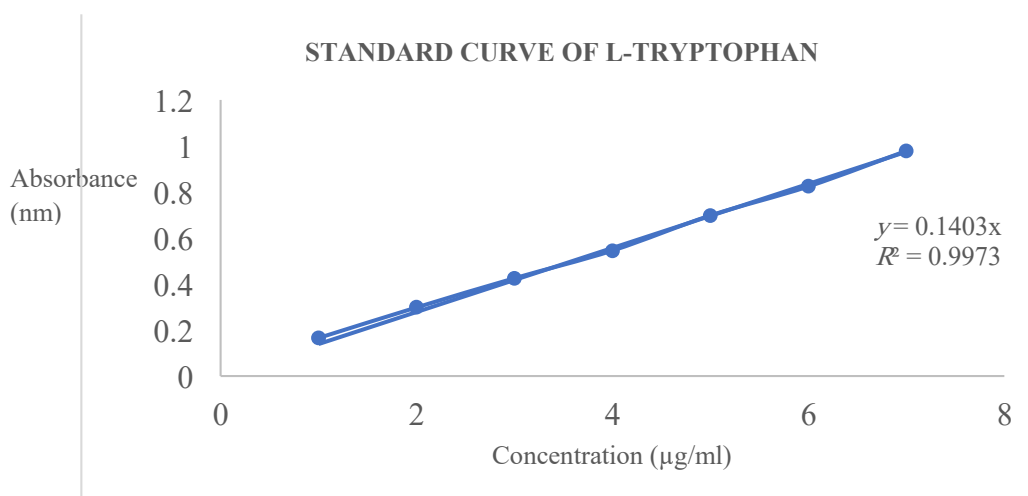


Figure S1: Standard curve of L-tryptophan

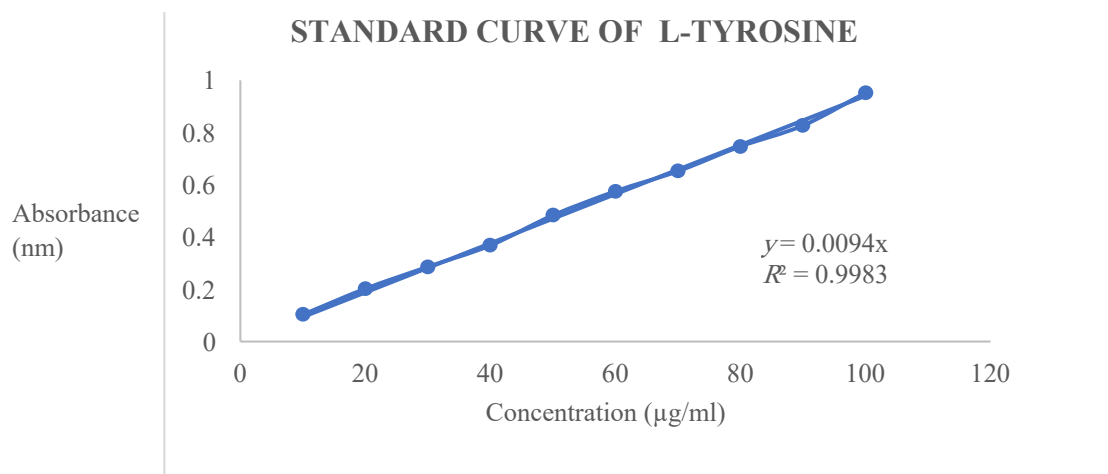


Figure S2: Standard curve of L-tyrosine

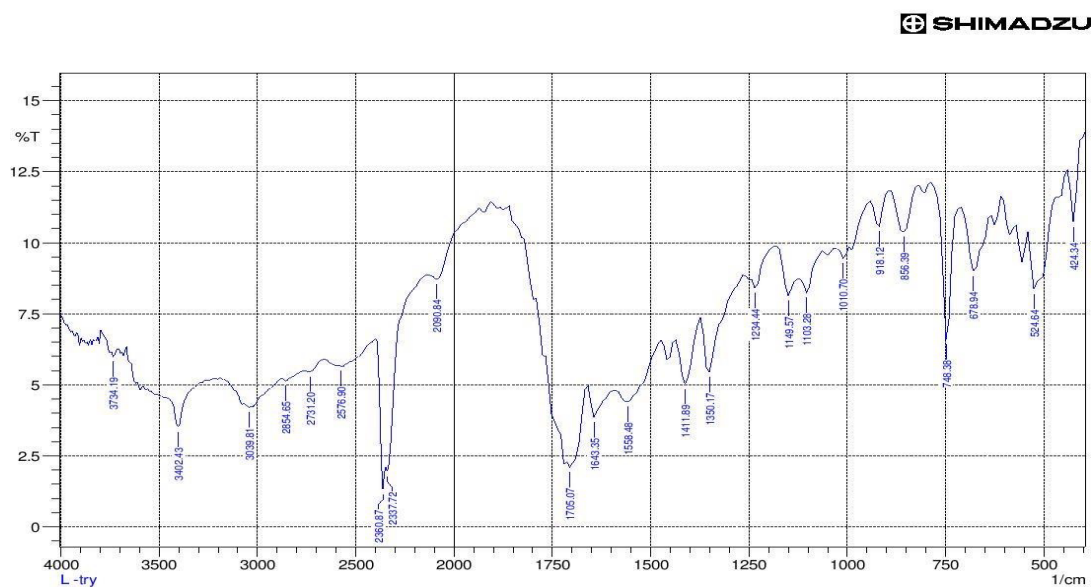


Figure S3: FT-IR spectrum of L-tryptophan FT-IR analysis of L-tyrosine:

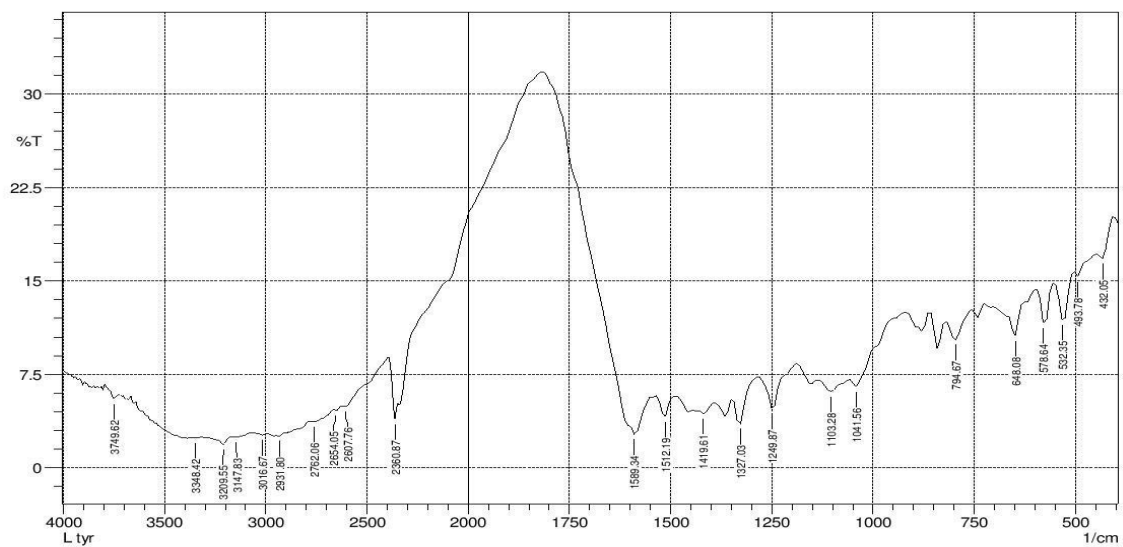


Figure S4: FT-IR spectrum of L-tyrosine

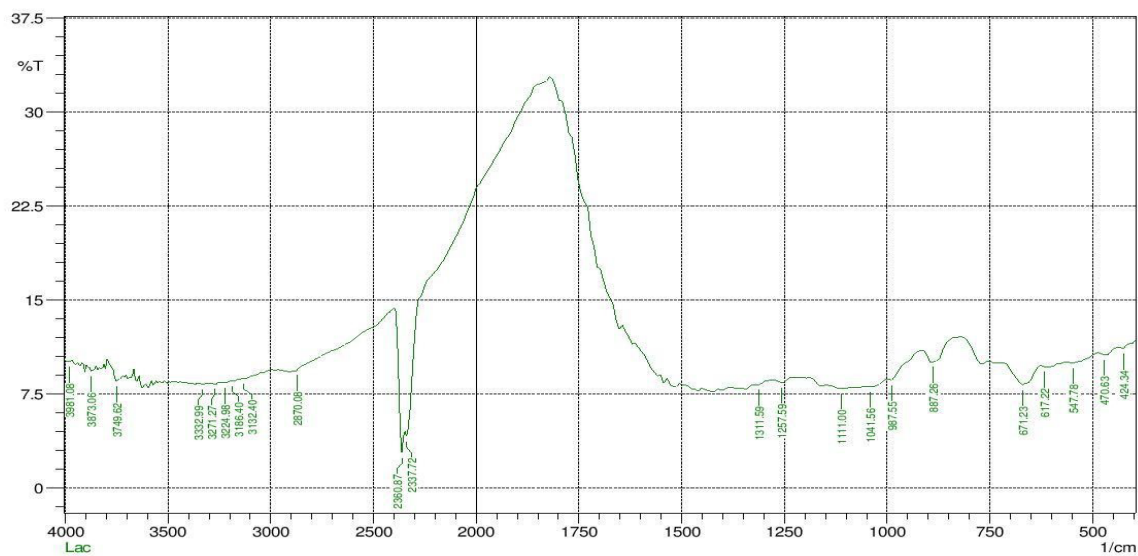


Figure S5: FT-IR spectrum of lactose

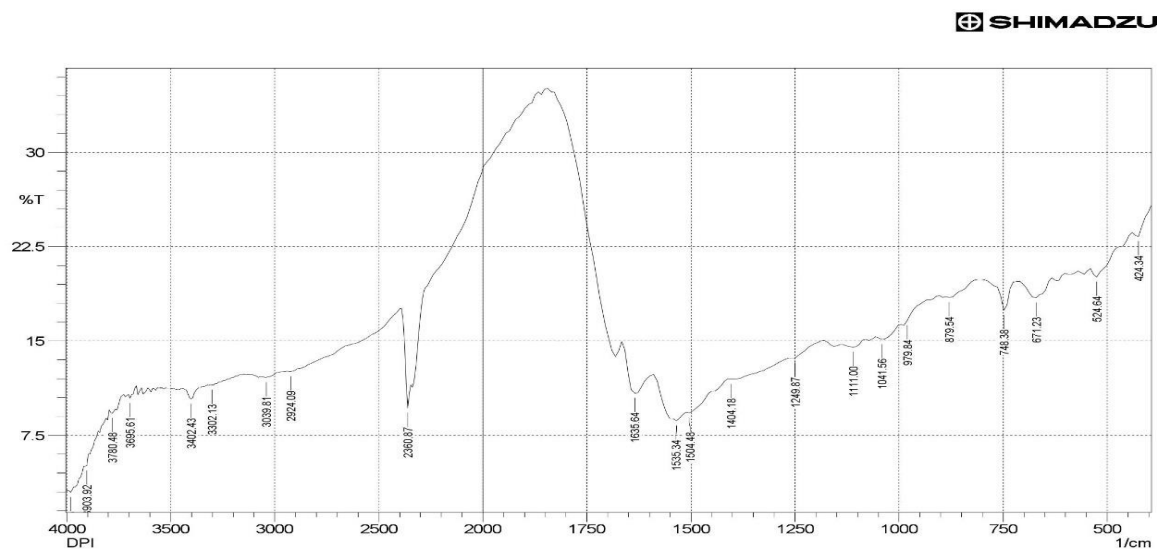


Figure S6: FT-IR spectrum of DPI formulation

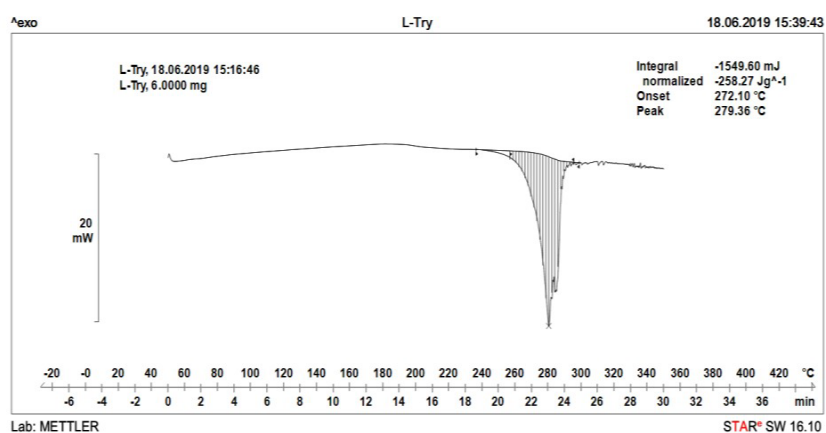


Figure S7: DSC spectrum of L-tryptophan

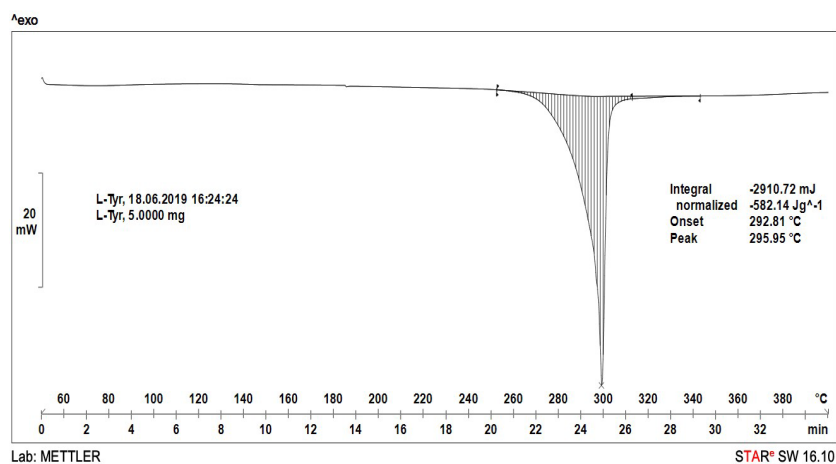


Figure S8: DSC spectrum of L-tyrosine

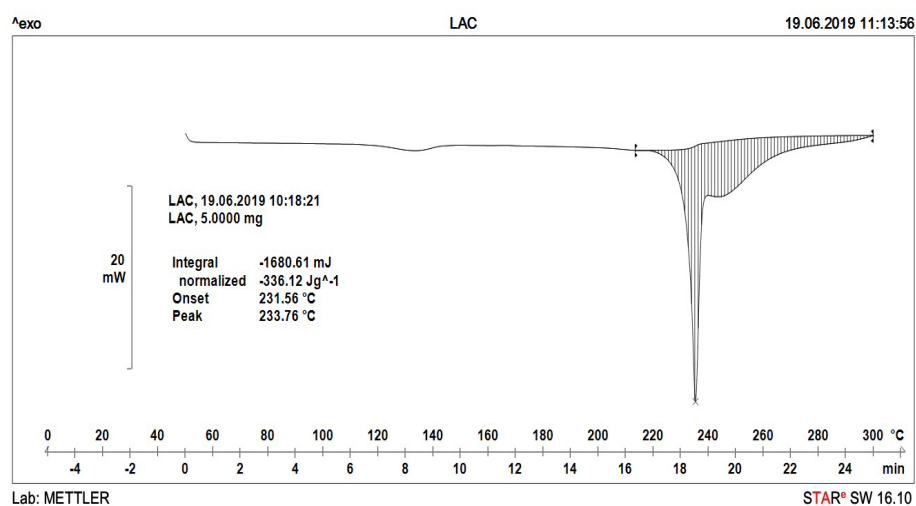


Figure S9: DSC spectrum of lactose

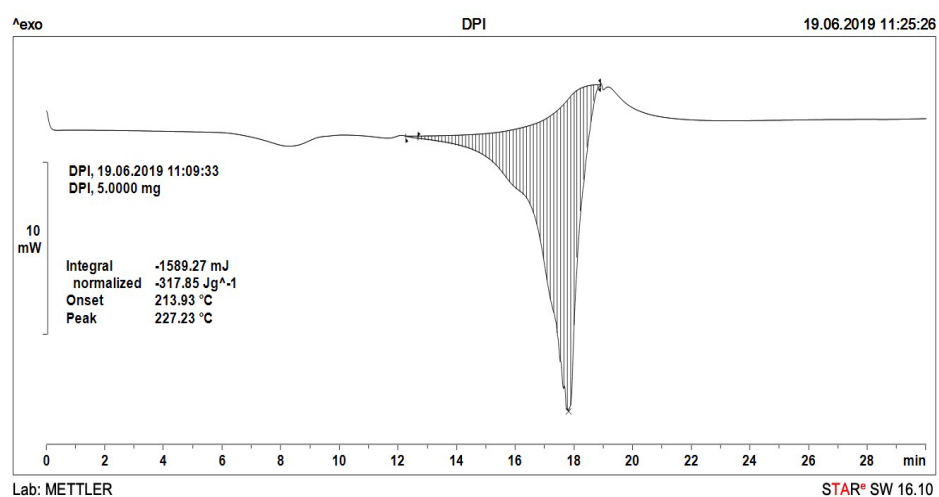


Figure S10: DSC spectrum of DPI formulation

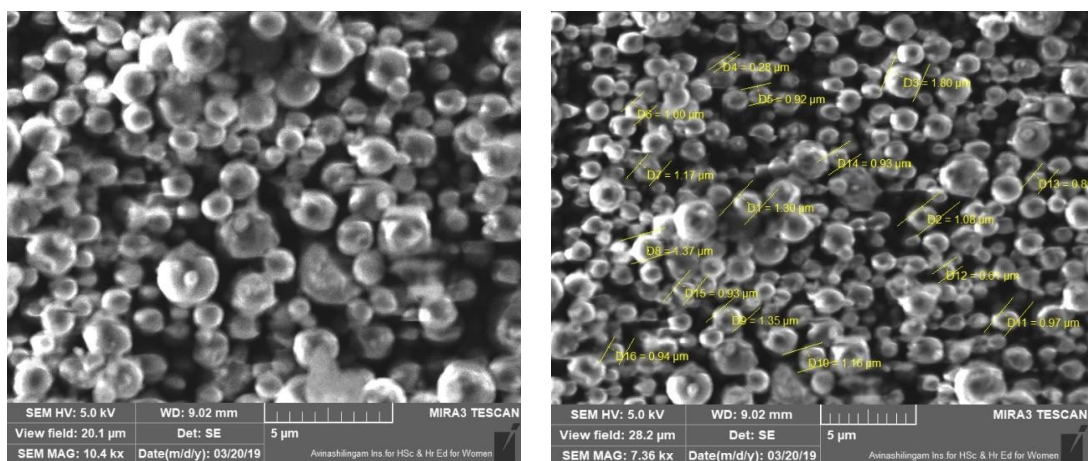


Figure S11: SEM photographs of L-tryptophan

Scanning electron microscope photograph of L-tyrosine

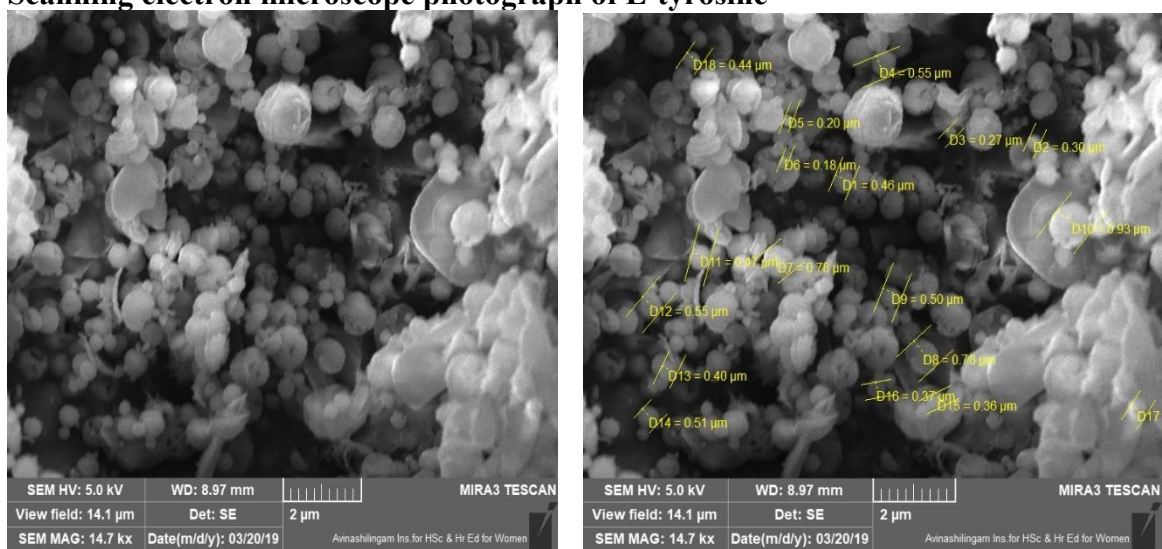


Figure S12: SEM photographs of L-tyrosine

Scanning electron microscope photograph of lactose:

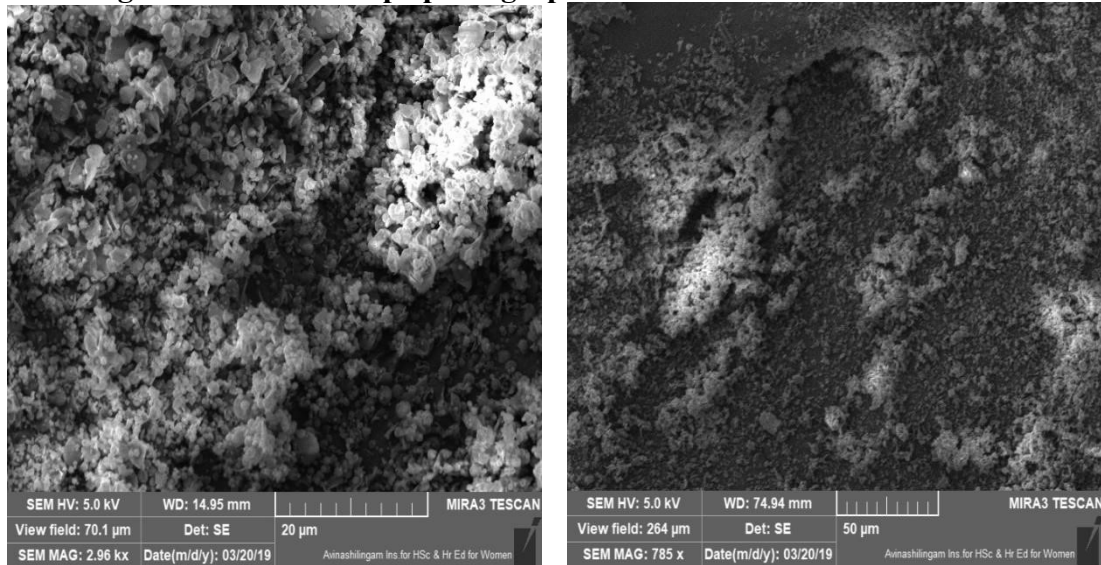


Figure S13: SEM photographs of lactose



Figure S14: Energy dispersive spectroscopy graph of L-tryptophan

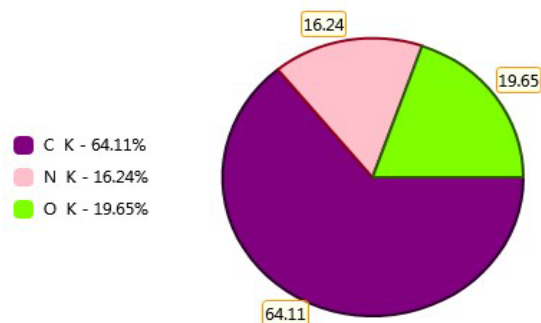


Figure S15: Elemental analysis graph of L-tryptophan



Figure S16: Energy dispersive spectroscopy graph of L-tyrosine

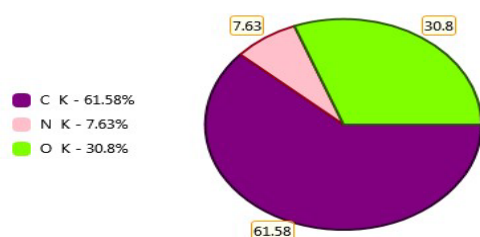


Figure S17: Elemental analysis graph of L-tyrosine

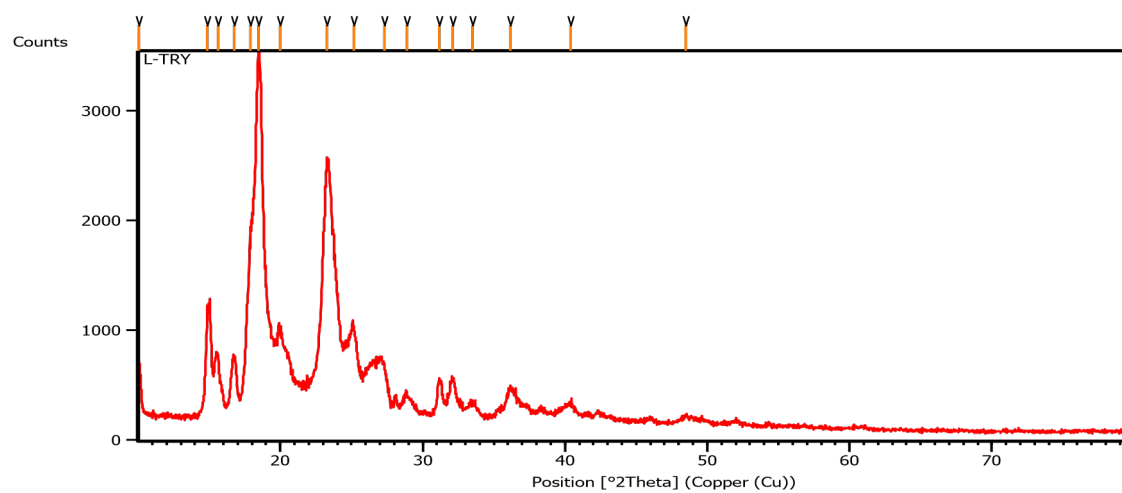


Figure S18: X-ray diffraction image of L-tryptophan

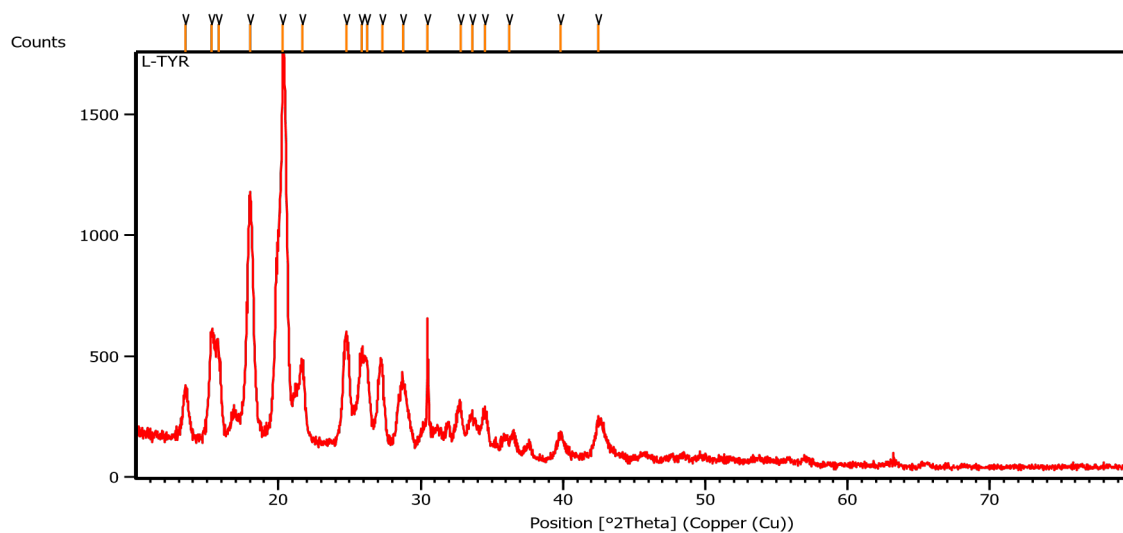


Figure S19: X-ray diffraction image of L-tyrosine

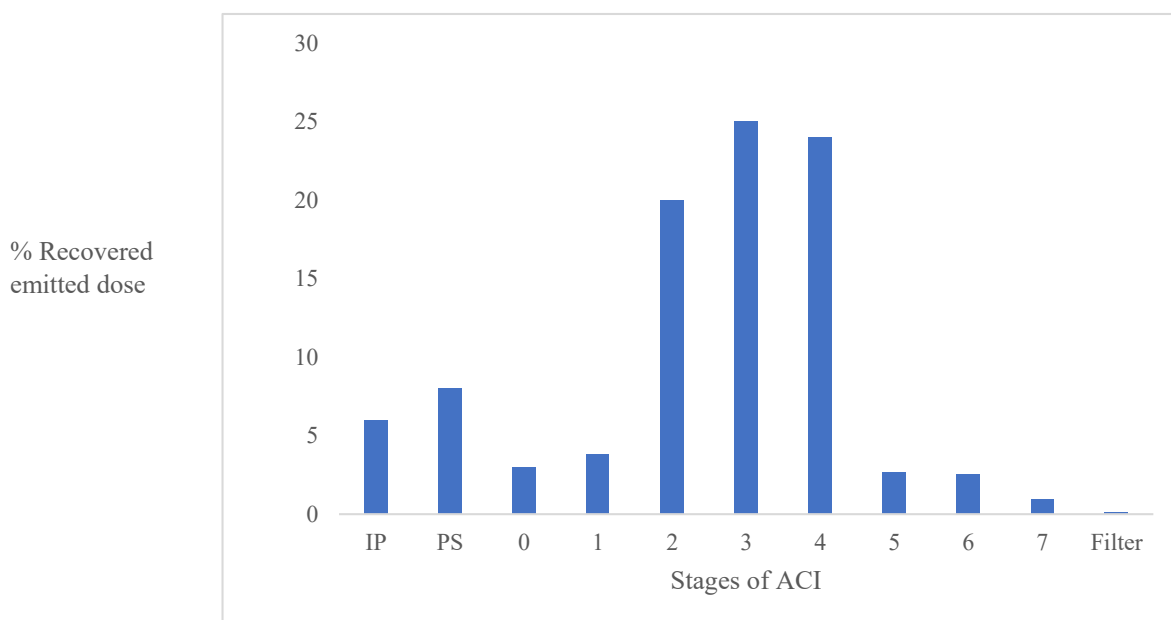


Figure S20: ACI histogram for percentage deposition profiles in all seven stages of DPI formulation

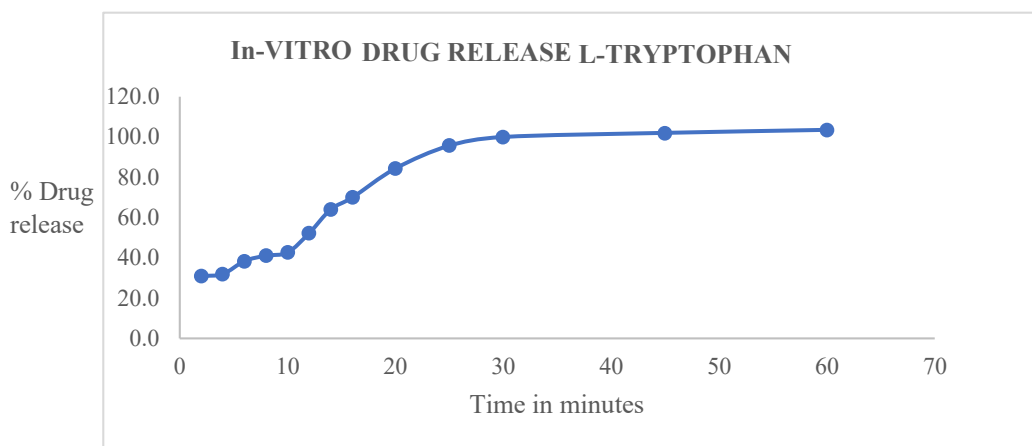


Figure S21: In-vitro drug release of L-tryptophan in DPI formulation

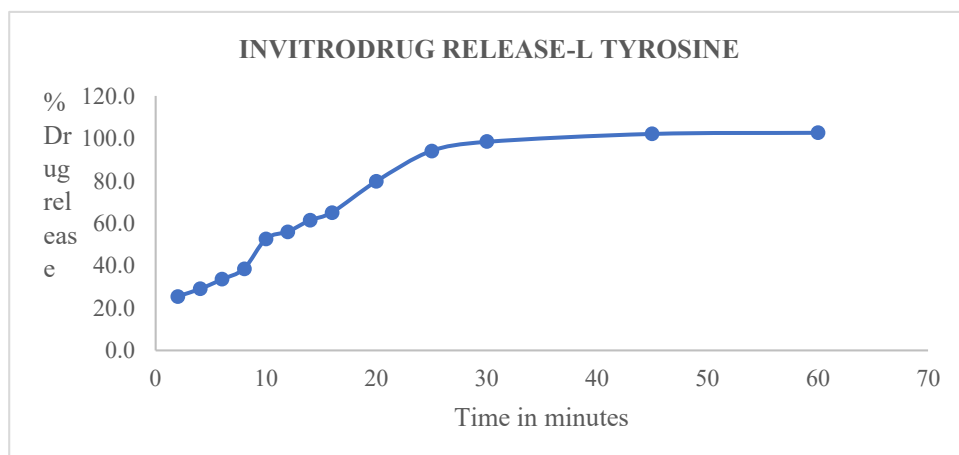


Figure S22: In-vitro drug release for L-tyrosine in DPI formulation

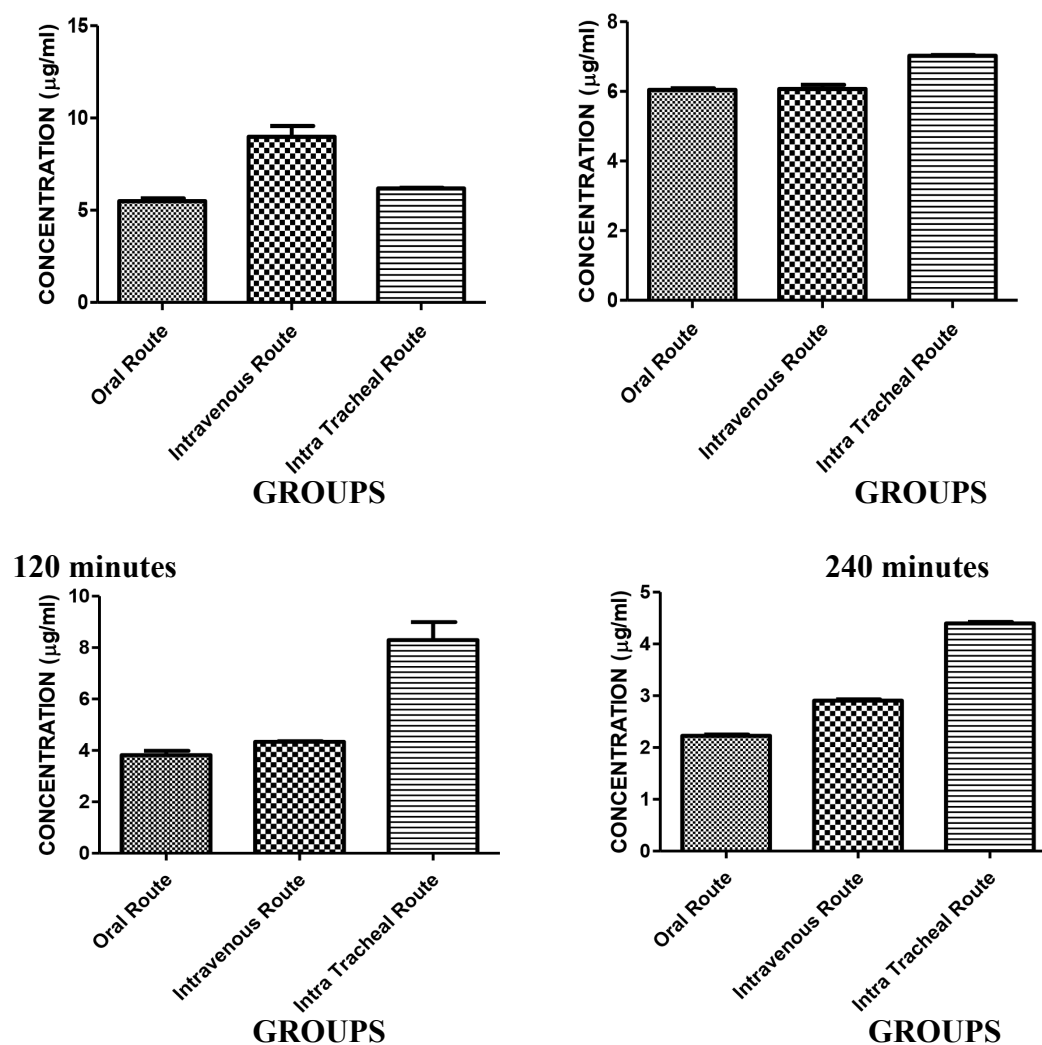


Figure S23: Plasma concentration at various time intervals for Oral, IV and IT routes of drug administration