Supplementary File

Rebamipide Nanocrystal with Improved Physicomechanical Properties and its assessment through bio-mimicking 3D intestinal permeability model

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Table S1. Apparent Permeability of Standard drugs: (A) Metoprolol, (B) Acyclovir, (C) Prazosin, (D) Digoxin, (E) Verapamil, (F) Digoxin in presence of verapamil

(A) Metoprolol (Dose: 2.99 µM)				
Time (min)	**Apical to Basal Papp * 10^{-6} (cm/s)**	**Basal to Apical Papp * 10^{-6} (cm/s)**	**Efflux Ratio**	**Reference**
15	5.94	19.9	3.350168	[1]
30	4.05	18.5	4.567901	
60	2.15	12.2	5.674419	
90	1.75	10.6	6.057143	
120	1.39	10.1	7.266187	
150	1.27	8.28	6.519685	
180	1.12	6.93	6.1875	
Metoprolol Reported (Dose: 100 mg/250 mL or 9.35 µM)	14.6* 10^{-6}	12.7* 10^{-6}	0.869863014	
(B) Acyclovir (Dose: 2.66 µM)				
15	4.69	10.8	2.302772	[2]
30	8.55	12.0	1.403509	
60	6.21	13	2.093398	
90	7.15	12.1	1.692308	
120	6.54	13.5	2.06422	
150	6.21	11.8	1.900161	
180	5.79	10.1	1.744387	
Reported Acyclovir (Dose: 2.5 mM)	0.352* 10^{-6}			
(c) Prazosin (Dose: 10 µM)				
15	57.7	1781	30.86655	[3]
30	68.5	1303	19.0219	
60	64.1	951	14.83619	
90	65.6	787	11.99695	
120	181	685	3.78453	
150	73.1	683	9.343365	
180	77.8	616	7.917738	
Reported Prazosin HCl polyhydrate (Dose: 500 µM)	3.7* 10^{-6}	38.2* 10^{-6}	10.32432	
(D) Digoxin (Dose: 10 µM)				

15	1019	3569	3.502453	4
30	630	2201	3.493651	
60	373	1744	4.675603	
90	275	453	1.647273	
120	240	1159	4.829167	
150	195	924	4.738462	
180	165	779	4.721212	
Reported Digoxin (Dose: 1μM)	$1.45 \pm 0.71 \times 10^{-6}$	$23.27 \pm 2.17 \times 10^{-6}$	16.02	
(E) Verapamil (Dose: 10 μM)				
15	37.4	98.4	2.631016	5
30	22.8	76.7	3.364035	
60	11	37.4	3.4	
90	7.97	47.9	6.010038	
120	5.36	33.9	6.324627	
150	4.28	20.4	4.766355	
180	4.45	25.3	5.685393	
Reported Verapamil (Dose: 75mg/250mL or70 μM)	$32.1 \pm 12.4 \times 10^{-6}$	$28.6 \pm 5.1 \times 10^{-6}$	0.9	
(F) Permeability of Digoxin (10 μM) in presence of Verapamil				
15	380	1338	3.521053	
30	276	1260	4.565217	
60	186	905	4.865591	
90	122	838	6.868852	
120	110	666	6.054545	
150	89.4	437	4.888143	
180	80.5	383	4.757764	

Table S2. Apparent Permeability of Rebamipide and its Formulations.

(A) REB				
Time (min)	**Apical to Basal Papp * 10^{-4} (cm/s)**	**Basal to Apical Papp * 10^{-4} (cm/s)**	**Efflux Ratio**	**Reference**
15	58.79	21.62	0.36775	6
30	38.01	74.5	1.960011	
60	27	5.27	0.195185	
90	22.11	3.54	0.160109	
120	18.54	2.7	0.145631	
150	13.87	1.75	0.126172	
180	13.02	1.66	0.127496	
Reported value (Dose:)	$1.51 \pm 0.13 \times 10^{-5}$ cm/s	$2.50 \pm 0.15 \times 10^{-5}$ cm/s	1.66 ± 0.11	
(B) **REB-Man-NC**				
15	6.17	60.9	9.87034	
30	18.87	75.75	4.014308	
60	14.84	31.95	2.152965	
90	13.82	18.12	1.311143	
120	17.81	27.74	1.557552	
150	13.59	25.01	1.840324	
180	17.12	38.04	2.221963	

Table S3. Chromatographic conditions for different standard drugs

Drug	Metoprolol	Acyclovir	Prazosin	Digoxin	Verapamil
Standard Curve	y=11.56x-3.16 (5-25µg/mL, R^2 =0.997)	y=21.428x+6.6847 (2-10µg/mL, R^2 =0.999)	y=28.237x +7.6647 (2-10µg/mL, R^2 =0.999)	y=300.16x + 58.213 (2-10µg/mL, R^2 =0.997)	y=9.0166x - 2.75 (100-500ng/mL, R^2 =0.998)
Mobile phase	A: acetonitrile; B: 10 mM Phosphate buffer (adjusted pH to 3 by 1M phosphoric acid) (A: B = 25:75)	A: orthophosphoric acid (pH 4.2); B: Methanol (A: B = 50:50)	A: Water (0.5%v/v acetic acid); B: Methanol (A: B = 54:46)	A: water; B: Acetonitrile (A: B = 74:26)	A: 10mM sodium acetate buffer; B: Acetonitrile (A: B = 56:44)
Flow rate (ml/min)	1.0	1.0	1.0	0.8	1.0
Wavelength (nm)	280	254	250	218	278
Injection Volume (µL)	10	10	5	10	10
Column Temperature	Room Temperature	Room Temperature	33°C	Room Temperature	Room Temperature
Retention Time (Min)	5.1	2.5	6.2	2.3	5.4
Reference	7	8	9	10	11

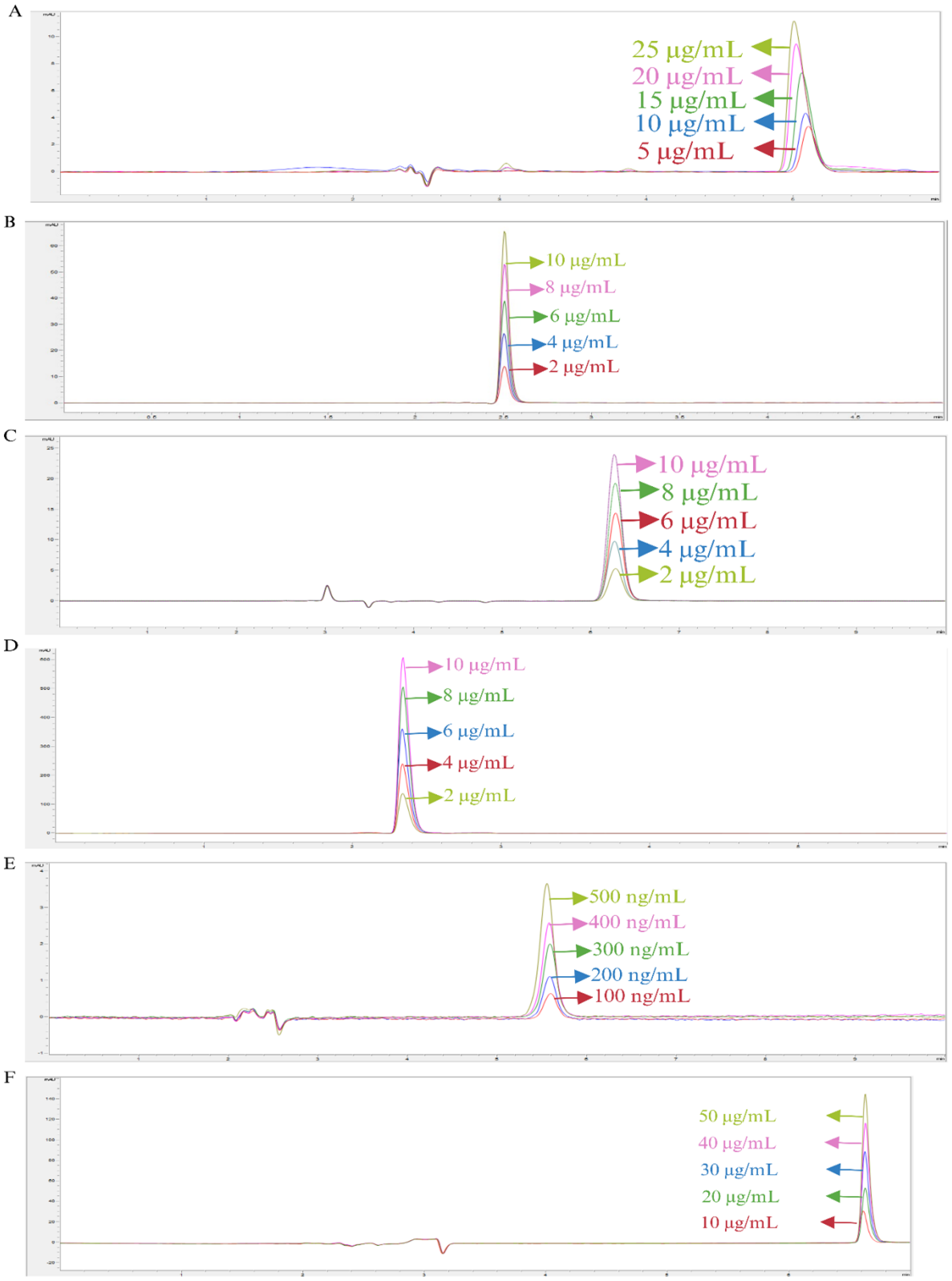

Fig. S1 Chromatogram of different drugs. (A) Metoprolol, (B) Acyclovir, (C) Prazosin, (D) Digoxin, (E) Verapamil, (F) Rebamipide

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