Supplementary Information

Non-Systemic Oral Cellulose-Based Superabsorbent Hydrogels for Weight Management: Potential Drug-Device Interactions Estimated by a Simplified In Vitro Assay

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Supplementary Table S1. Compositions of stock solutions prepared for the simplified in vitro assay. Simulated Gastric Fluid (SGF) and Simulated Intestinal Fluid (SIF).

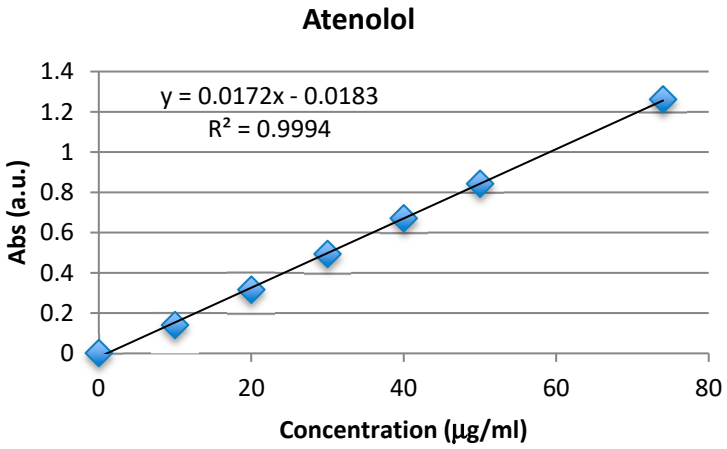
	SGF	SIF
COMPOSITION		
Sodium chloride (g)	2.0	-
Hydrochloric acid 1 M (mL)	84.0	-
Purified water (mL)	-	750.0
Monobasic potassium phosphate (g)	-	6.8
Sodium hydroxide 0.2 N (g)	-	117.0
Adjust pH and/or volume		
Sodium hydroxide 0.2 N to (or hydrochloric acid 0.2N)	-	pH 6.8
Purified water to (L)	1.0	1.0
PROPERTIES		
pH	1.1	6.8
Ionic strenght (mM)	118	72

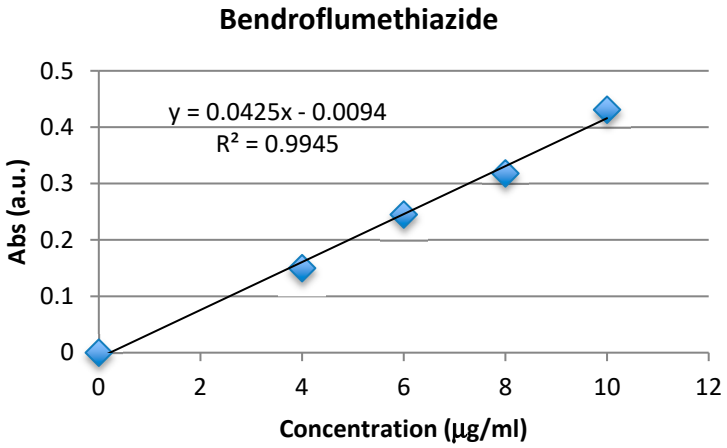
Supplementary Table S2. Experimental parameters utilized for drug dissolution and UV-Vis quantification.
For each drug substance, pre-dissolution in organic solvents (before dissolution in diluted SGF, i.e., SGF/water 1/8 v/v) and/or the use of surfactants is indicated, if any, along with the wavelength (λ) and the dilution ratio adopted for detection and quantification, under simulated gastric and intestinal conditions. Where noted, the UV-Vis absorbance of the CMC released by a given CB-SAH (either GelA or GelB) was subtracted from the absorbance of the experimental sample (at Steps 3 and 4) to correctly estimate the drug amount. SLS = sodium lauryl sulfate; PP = potassium permanganate.

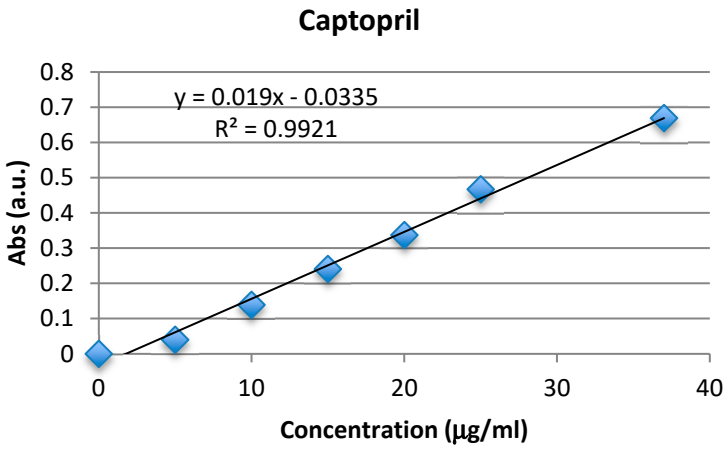
Therapeutic Indication	**Drug substance**	**Changes to dissolution medium**	**Dissolution time (min)**	**UV-Vis detection and quantitation**				
				Gastric conditions (Step 1)		**Intestinal conditions (Steps 3 and 4)**		**Additional notes**
				Dilution ratio	**λ (nm)**	**Dilution ratio**	**λ (nm)**	
Hypertension	Atenolol	/	30	/	275	1:1.5	230	CMC interference
	Bendroflumethiazide	Pre-dissolution (5 ml methanol, sonication 40kHz, 10 min, 37°C)	15	/	275	/	275	/
	Captopril	/	30	1:3	205	1:2	205	CMC interference
	Carvedilol	/	60	1:2	285	/	285	/
	Diltiazem	/	30	1:15	235	1:3	235	/
	Furosemide	1% w/w Tween80	120	1:5	275	1:1.5	275	CMC interference
	Hydrochlorothiazide	Pre-dissolution (5 ml methanol, sonication 40kHz, 10 min, 37°C)	30	1:20	270	See notes	270	- Dilution 1:20 at Step 3 - Dilution 1:10 at Step 4
	Lisinopril	/	45	1:10	205	/	210	CMC interference
Dyslipidemia	Gemfibrozil	Pre-dissolution (5 ml methanol, sonication 40kHz, 10 min, 40°C) + 1% w/w Tween80	60	1:20	275	1:4	275	/
	Lovastatin	1% w/w SLS	120	1:10	240	1:2	240	CMC interference
	Rosuvastatin	/	60	1:5	240	/	240	/
Blood clotting	Clopidogrel	0.1% w/w SLS	60	/	270	/	230	/
	Rivaroxaban	1.6% w/w SLS	60	1:2	250	/	250	CMC interference
	Ticlopidine	1% w/w SLS in SIF only	30	/	270	/	270	CMC interference

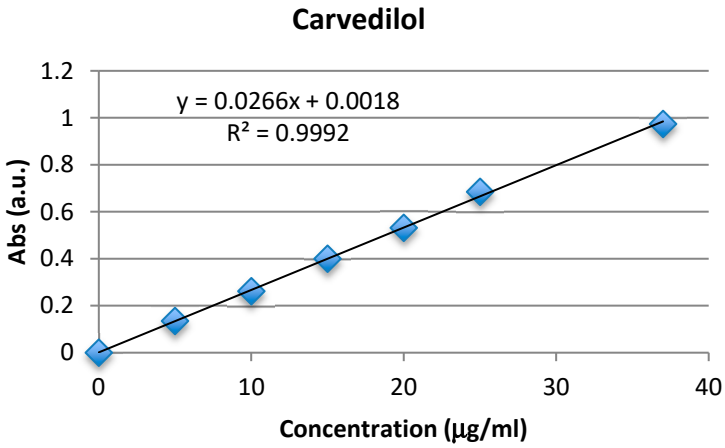
Therapeutic Indication	Drug substance	Changes to dissolution medium	Dissolution time (min)	UV-Vis detection and quantitation				
				Gastric conditions (Step 1)		Intestinal conditions (Steps 3 and 4)		Additional notes
				Dilution ratio	λ (nm)	Dilution ratio	λ (nm)	
Type 2 diabetes	Acarbose	/	60	1:20	430	3:10	430	- Need of PP for detection, as described by Ibrahim et al., Int J Biomed Sci 3(1): 20-30, 2007 - CMC interference
	Metformin	/	60	1:100	230	1:100	235	/
	Repaglinide	/	30	/	240	/	240	/
	Sitagliptin	/	60	/	265	/	265	/
Pain	Acetaminophen	/	60	1:200	245	1:40	245	/
	Ibuprofen	1% w/w SLS	120	1:2	265	1:5	230	CMC interference
Hypothyroidism	Levothyroxine	1% w/w SLS	120	/	230	/	230	CMC interference
Contraception	Drospirenone	1% w/w SLS	Overnight	1:4	275	See notes	275	- Simultaneous analysis of both active principles, with CMC interference (especially at 220 nm) - GelA: dilution 1:2 at Step 3 and no dilution at Step 4 - GelB: no dilution at both Steps 3 and 4
	Ethinyl Estradiol	1% w/w SLS	Overnight	1:4	220	See notes	220	

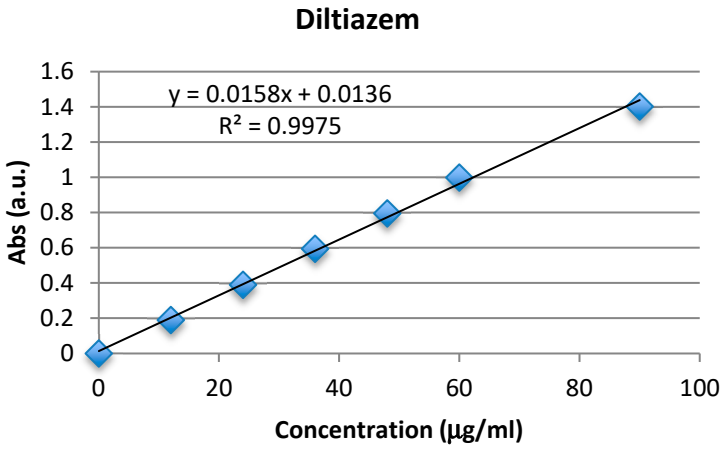
Supplementary Figure S1. Calibration curves used for UV-Vis drug quantification under simulated intestinal conditions. Unless otherwise specified, for each drug the same calibration curve was used at Steps 3 and 4 of the simplified in vitro assay, with both GelA and GelB. Further information on the UV-Vis analytical method is provided in the Supplementary Table S2.

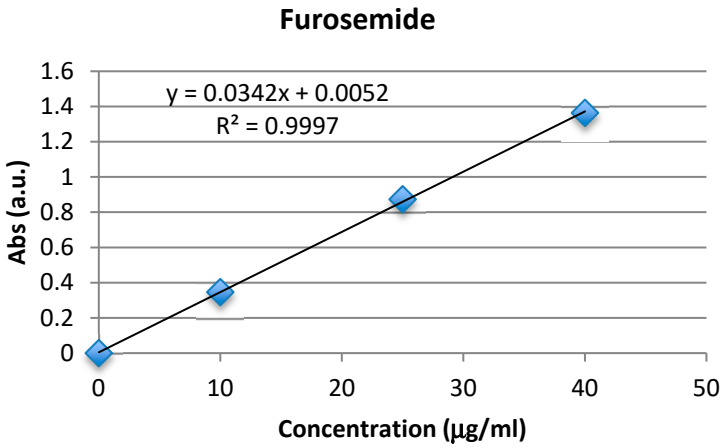


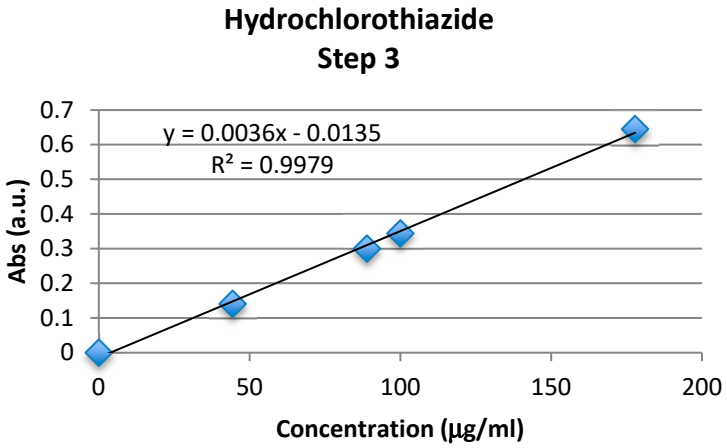


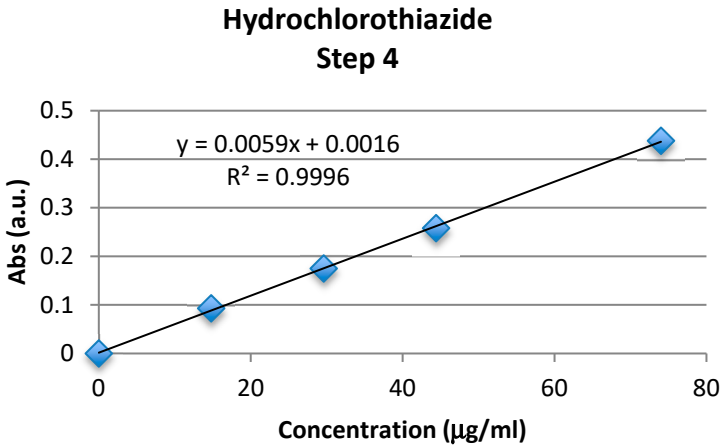


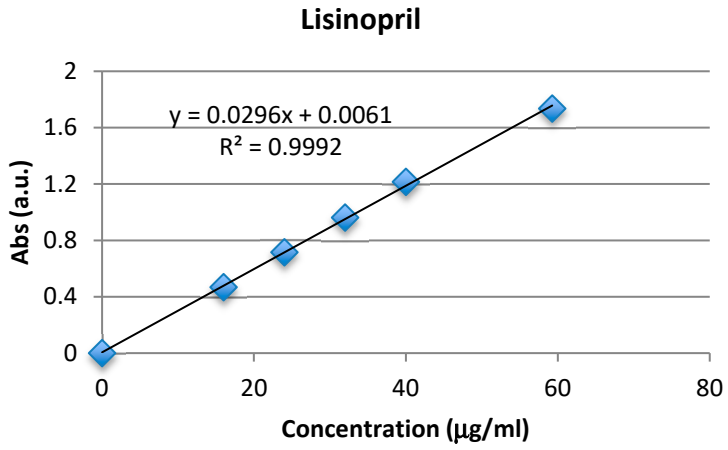

Carvedilol
y = 0.0266x + 0.0018
R² = 0.9992
Abs (a.u.)
Concentration (µg/ml)
0
0.2
0.4
0.6
0.8
1
1.2
0
10
20
30
40

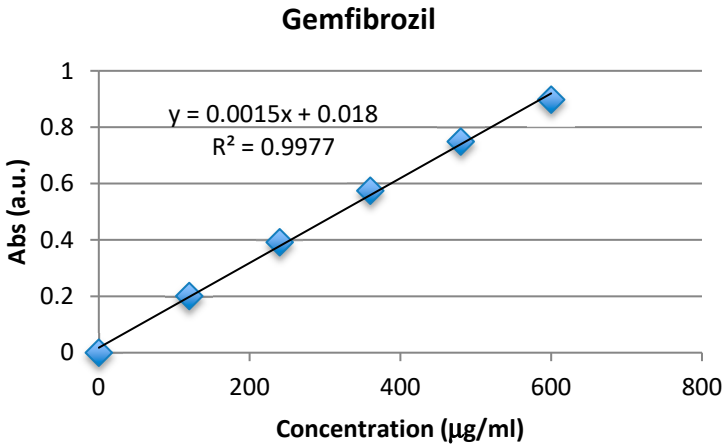

Diltiazem
y = 0.0158x + 0.0136
R² = 0.9975
Abs (a.u.)
Concentration (µg/ml)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
0
20
40
60
80
100

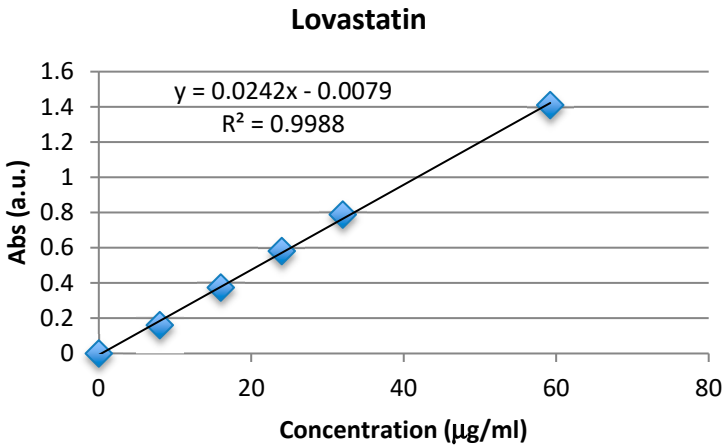

Furosemide
y = 0.0342x + 0.0052
R² = 0.9997
Abs (a.u.)
Concentration (µg/ml)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
0
10
20
30
40
50

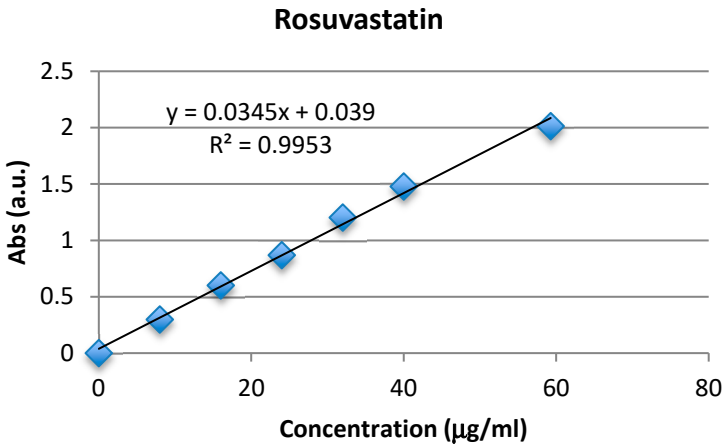

Hydrochlorothiazide
Step 3
y = 0.0036x - 0.0135
R² = 0.9979
Abs (a.u.)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
50
100
150
200
Concentration (µg/ml)

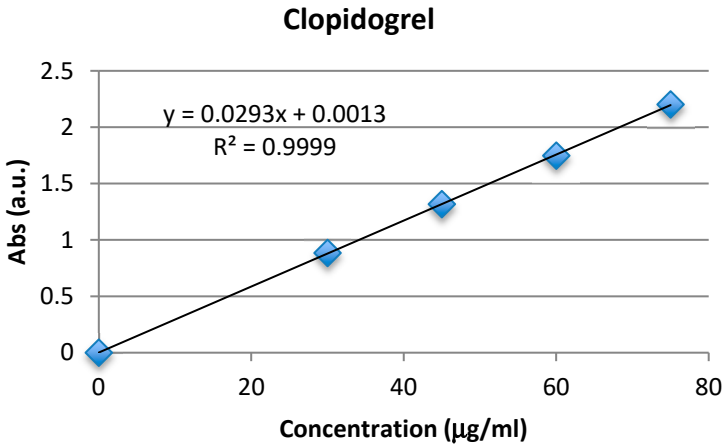

Hydrochlorothiazide
Step 4
y = 0.0059x + 0.0016
R² = 0.9996
Abs (a.u.)
0.5
0.4
0.3
0.2
0.1
0
0
20
40
60
80
Concentration (µg/ml)

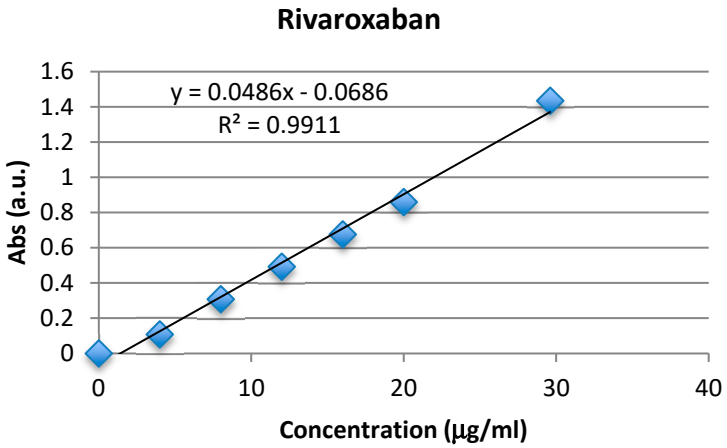

Lisinopril
y = 0.0296x + 0.0061
R² = 0.9992
Abs (a.u.)
2
1.6
1.2
0.8
0.4
0
0
20
40
60
80
Concentration (µg/ml)

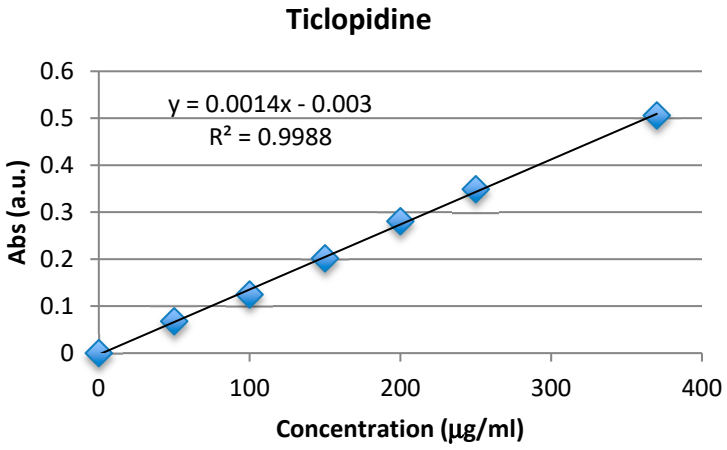

Gemfibrozil
y = 0.0015x + 0.018
R² = 0.9977
Abs (a.u.)
Concentration (µg/ml)
0
0.2
0.4
0.6
0.8
1
0
200
400
600
800

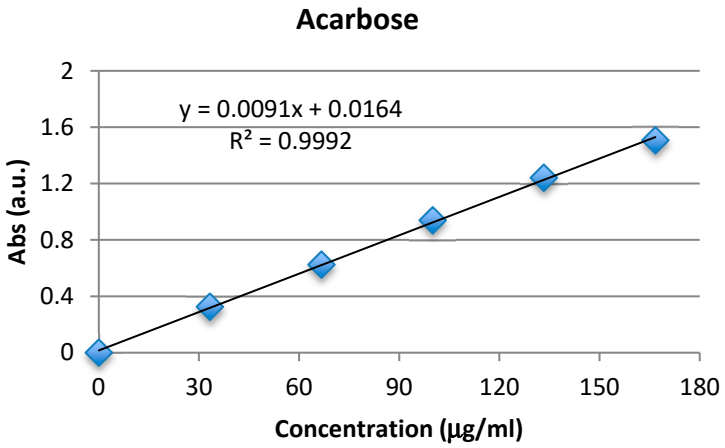

Lovastatin
y = 0.0242x - 0.0079
R² = 0.9988
Abs (a.u.)
Concentration (µg/ml)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
0
20
40
60
80

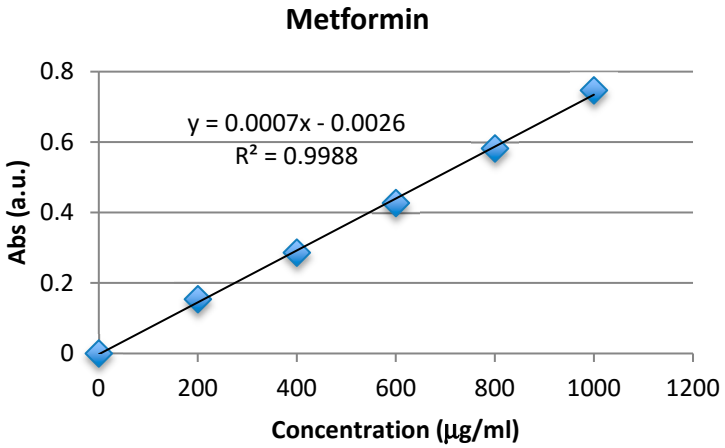

Rosuvastatin
y = 0.0345x + 0.039
R² = 0.9953
Abs (a.u.)
Concentration (µg/ml)
0
0.5
1
1.5
2
2.5
0
20
40
60
80

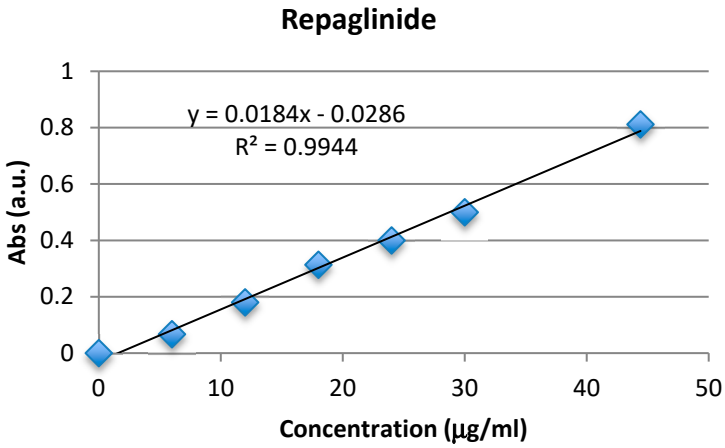

Clopidogrel
y = 0.0293x + 0.0013
R² = 0.9999
Abs (a.u.)
Concentration (µg/ml)
0
0.5
1
1.5
2
2.5
0
20
40
60
80

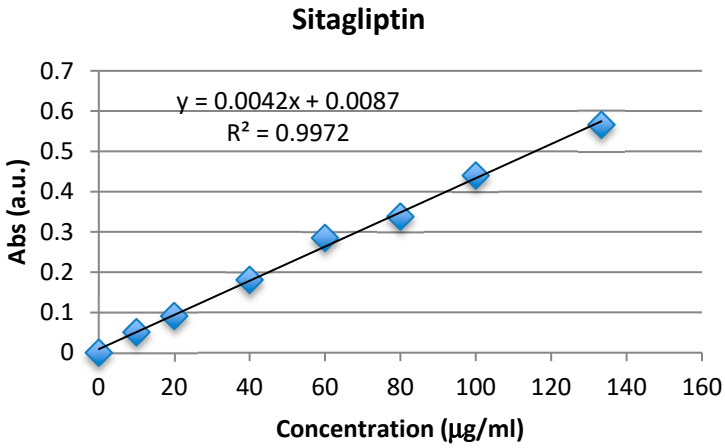

Rivaroxaban
y = 0.0486x - 0.0686
R² = 0.9911
Abs (a.u.)
Concentration (µg/ml)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
0
10
20
30
40

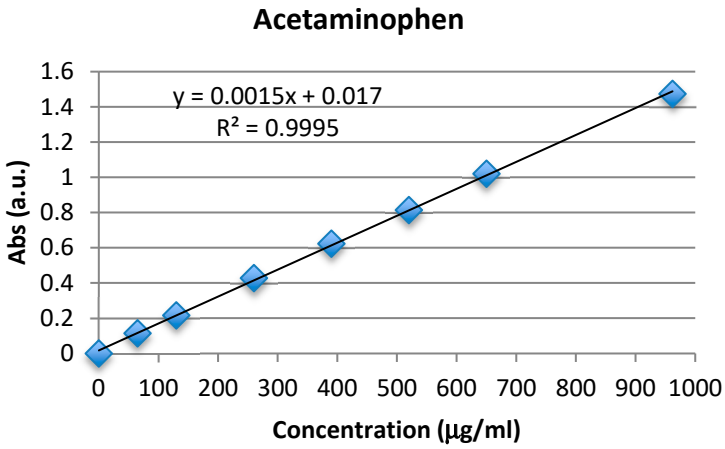

Ticlopidine
y = 0.0014x - 0.003
R² = 0.9988
Abs (a.u.)
Concentration (µg/ml)
0
0.1
0.2
0.3
0.4
0.5
0.6
0
100
200
300
400

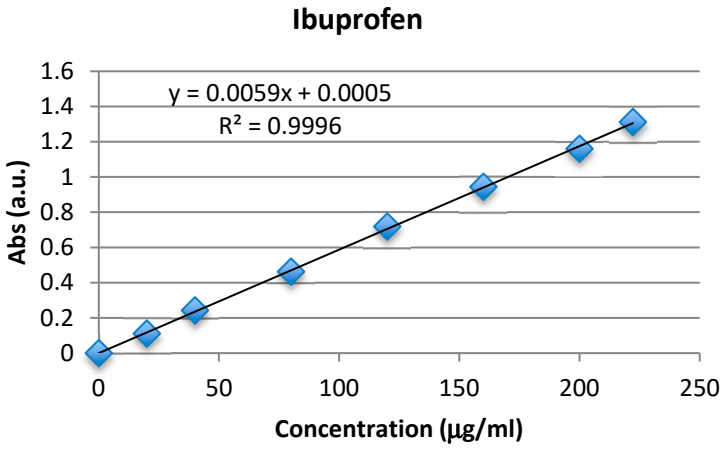

Acarbose
y = 0.0091x + 0.0164
R² = 0.9992
Abs (a.u.)
Concentration (µg/ml)
0
0.4
0.8
1.2
1.6
2
0
30
60
90
120
150
180

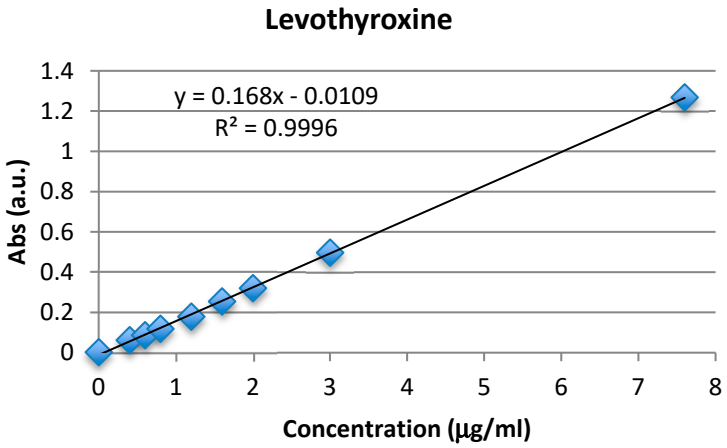

Metformin
y = 0.0007x - 0.0026
R² = 0.9988
Abs (a.u.)
Concentration (µg/ml)
0
0.2
0.4
0.6
0.8
0
200
400
600
800
1000
1200

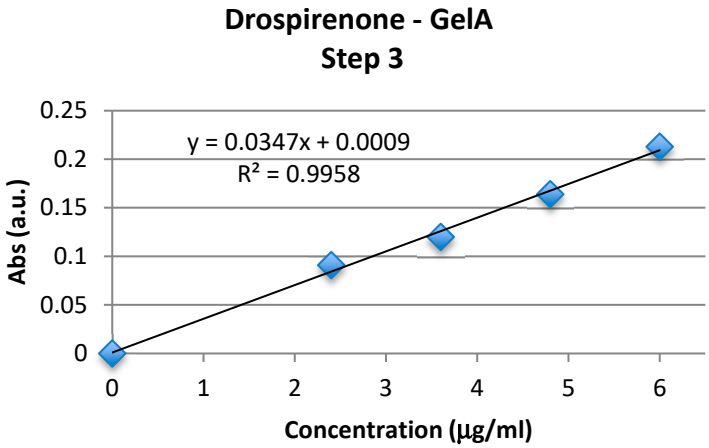

Repaglinide
y = 0.0184x - 0.0286
R² = 0.9944
Abs (a.u.)
Concentration (µg/ml)
0
0.2
0.4
0.6
0.8
1
0
10
20
30
40
50

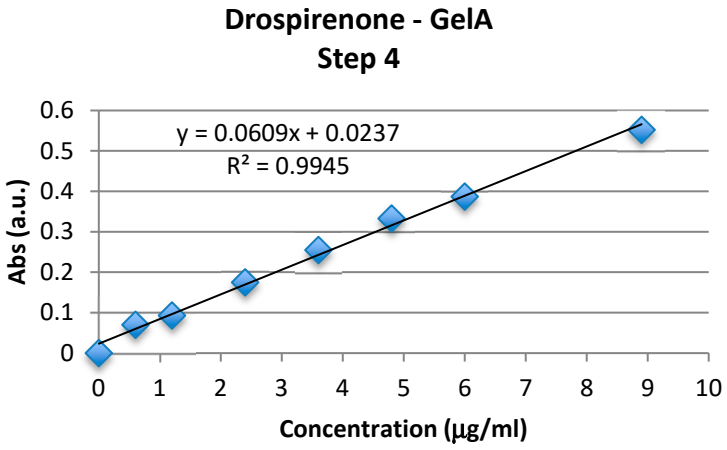

Sitagliptin
y = 0.0042x + 0.0087
R² = 0.9972
Abs (a.u.)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
20
40
60
80
100
120
140
160
Concentration (µg/ml)

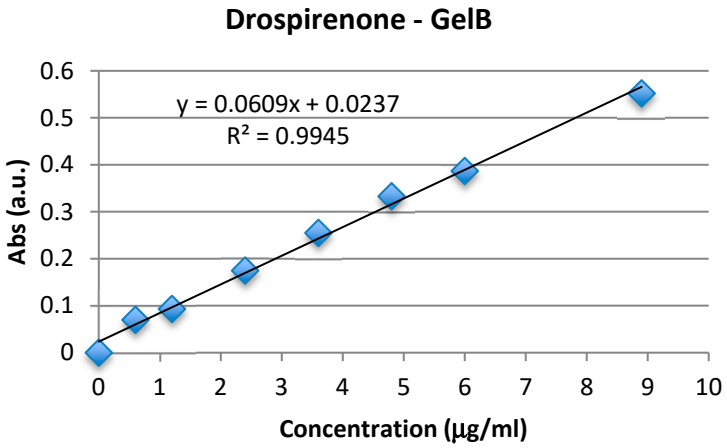

Acetaminophen
y = 0.0015x + 0.017
R² = 0.9995
Abs (a.u.)
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
100
200
300
400
500
600
700
800
900
1000
Concentration (µg/ml)

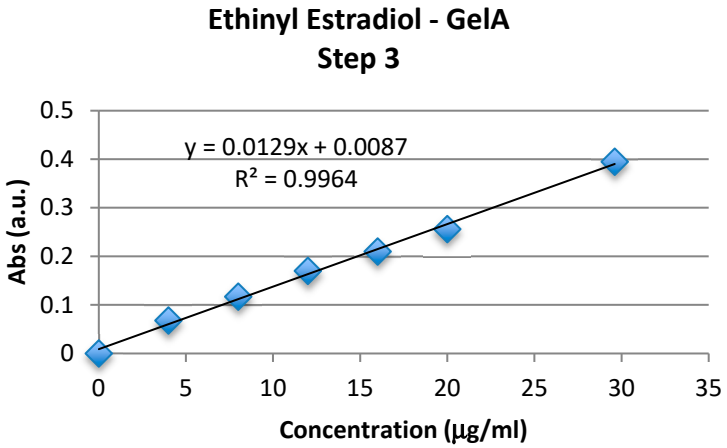

Ibuprofen
y = 0.0059x + 0.0005
R² = 0.9996
Abs (a.u.)
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
50
100
150
200
250
Concentration (µg/ml)

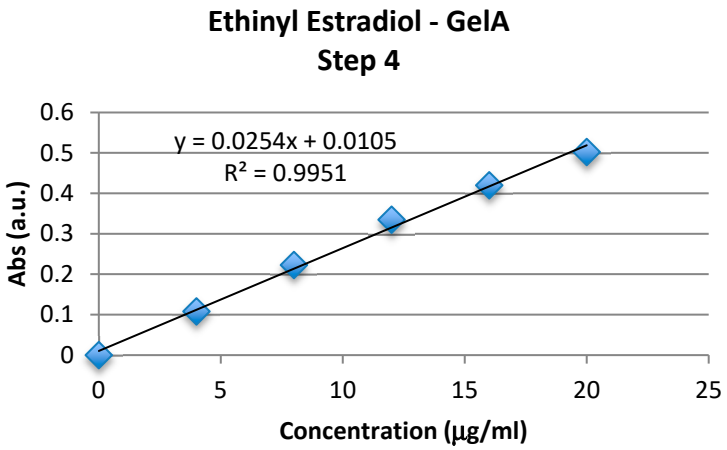

Levothyroxine
y = 0.168x - 0.0109
R² = 0.9996
Abs (a.u.)
Concentration (µg/ml)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
0
1
2
3
4
5
6
7
8

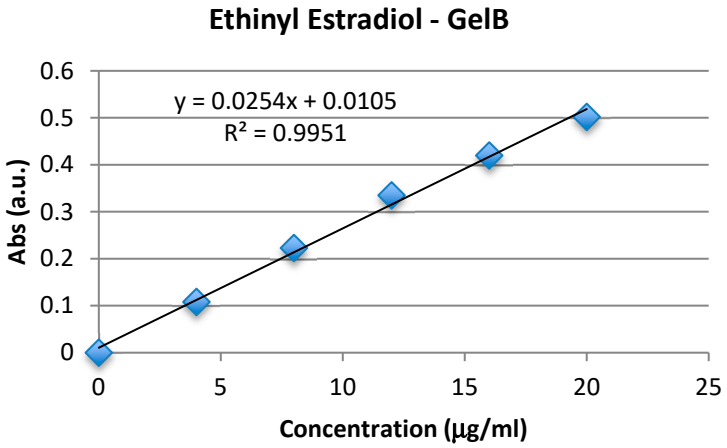

Drospirenone - GelA
Step 3
y = 0.0347x + 0.0009
R² = 0.9958
Abs (a.u.)
Concentration (µg/ml)
0
0.05
0.1
0.15
0.2
0.25
0
1
2
3
4
5
6


Drospirenone - GelA
Step 4
y = 0.0609x + 0.0237
R² = 0.9945
Abs (a.u.)
Concentration (µg/ml)
0
0.1
0.2
0.3
0.4
0.5
0.6
0
1
2
3
4
5
6
7
8
9
10

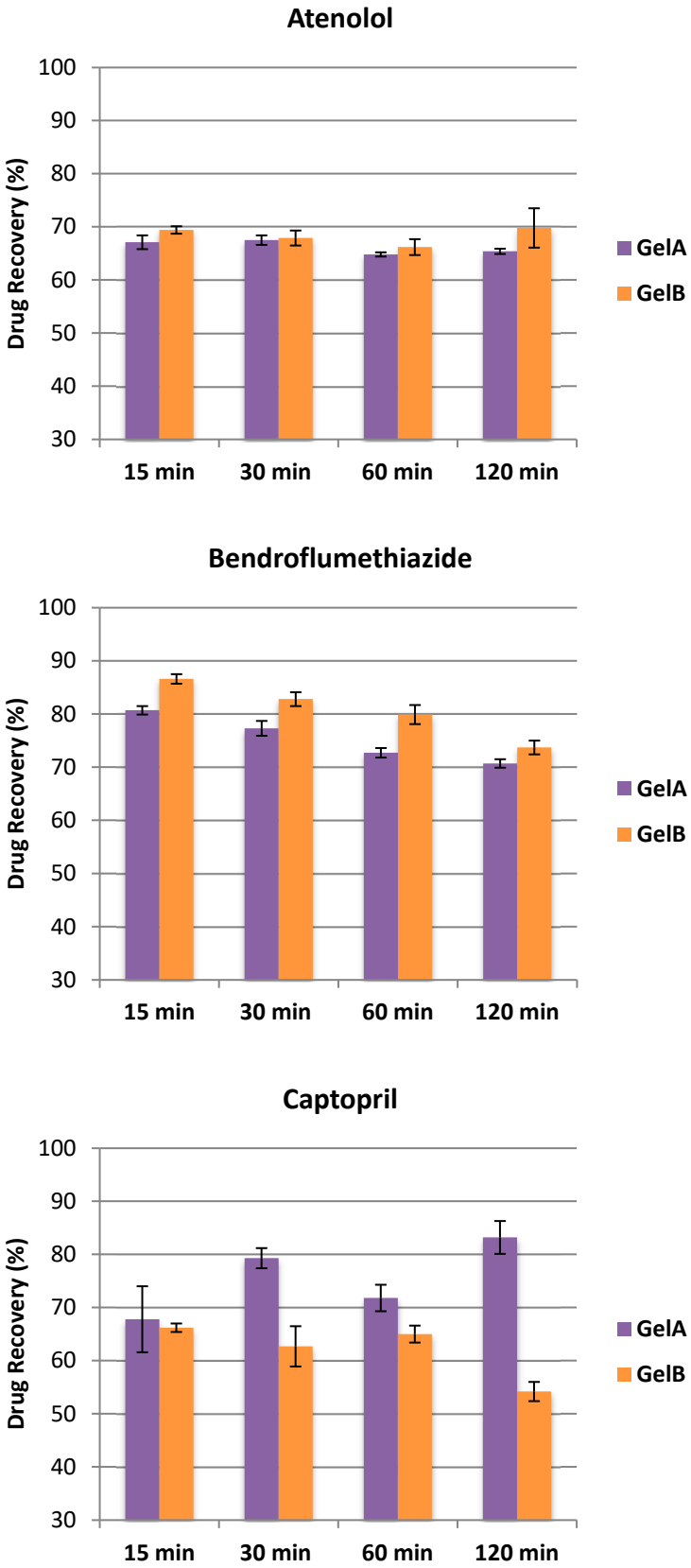

Drospirenone - GelB
y = 0.0609x + 0.0237
R² = 0.9945
Abs (a.u.)
0
0.1
0.2
0.3
0.4
0.5
0.6
0
1
2
3
4
5
6
7
8
9
10
Concentration (µg/ml)

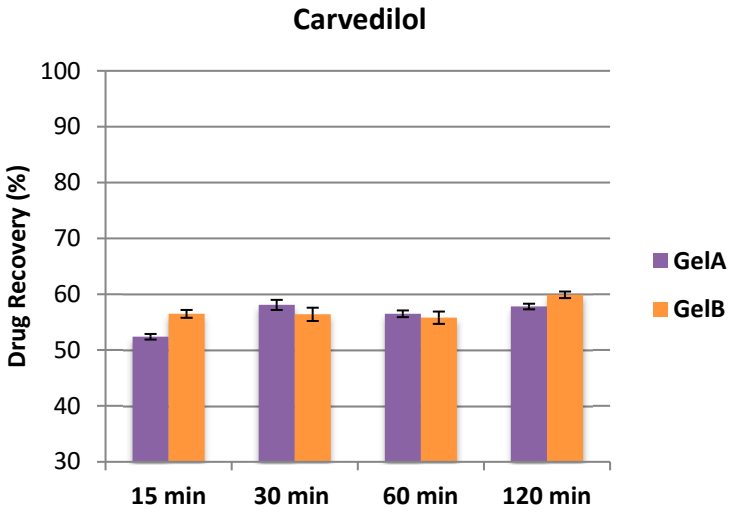

Ethinyl Estradiol - GelA
Step 3
y = 0.0129x + 0.0087
R² = 0.9964
Abs (a.u.)
0
0.1
0.2
0.3
0.4
0.5
0
5
10
15
20
25
30
35
Concentration (µg/ml)

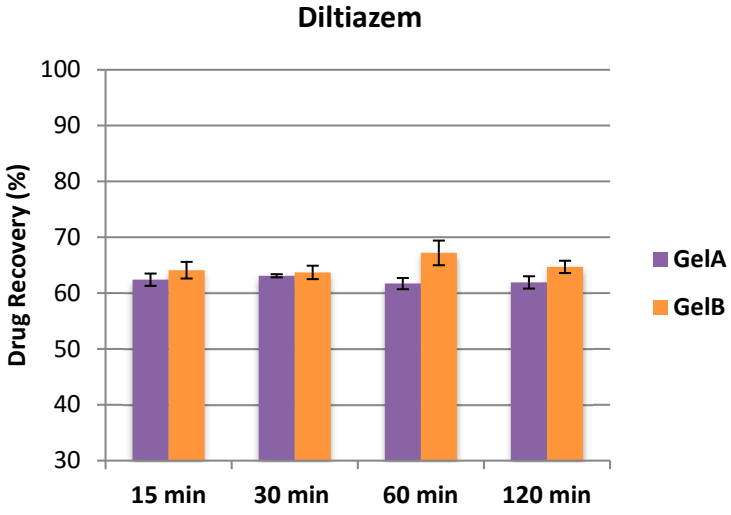

Ethinyl Estradiol - GelA
Step 4
y = 0.0254x + 0.0105
R² = 0.9951
Abs (a.u.)
0
0.1
0.2
0.3
0.4
0.5
0.6
0
5
10
15
20
25
Concentration (µg/ml)

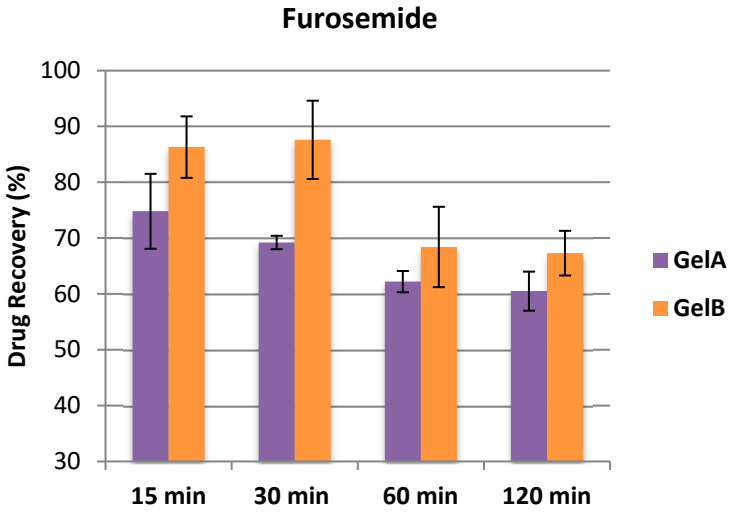

Ethinyl Estradiol - GelB
y = 0.0254x + 0.0105
R² = 0.9951
Abs (a.u.)
0.6
0.5
0.4
0.3
0.2
0.1
0
0
5
10
15
20
25
Concentration (µg/ml)

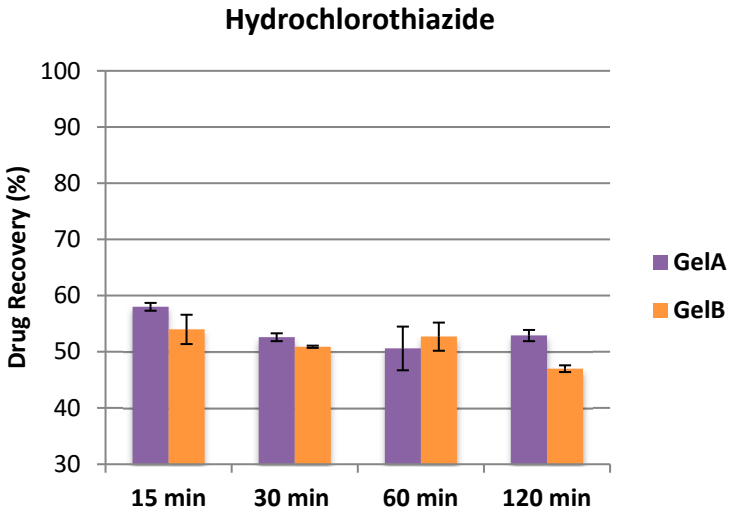
Supplementary Figure S2. Drug recovery over time measured at Step 3 of the simplified in vitro assay. For each drug, direct comparison between GelA and GelB is provided. Results are reported as mean ± SD (n=3).

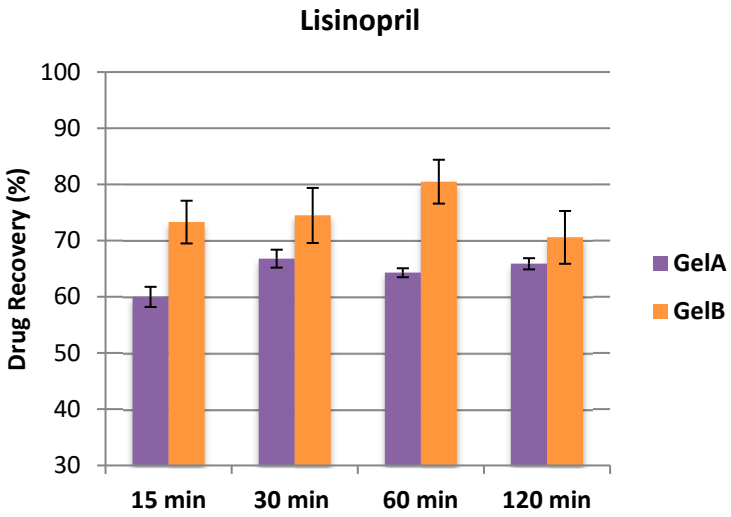


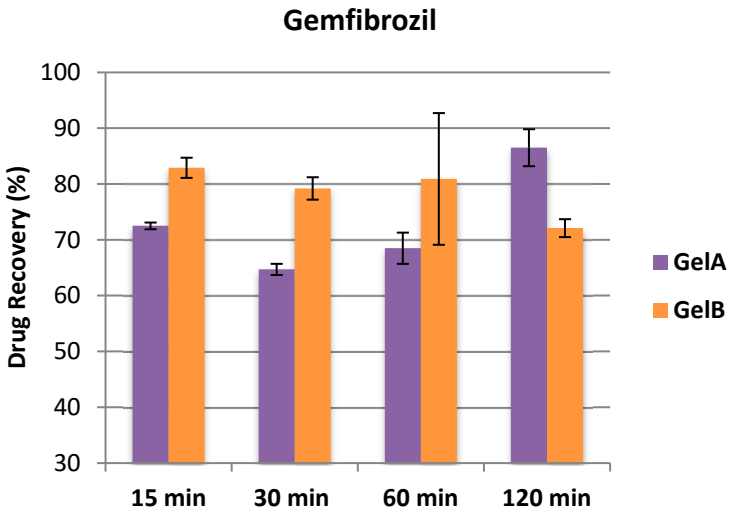

Carvedilol
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB

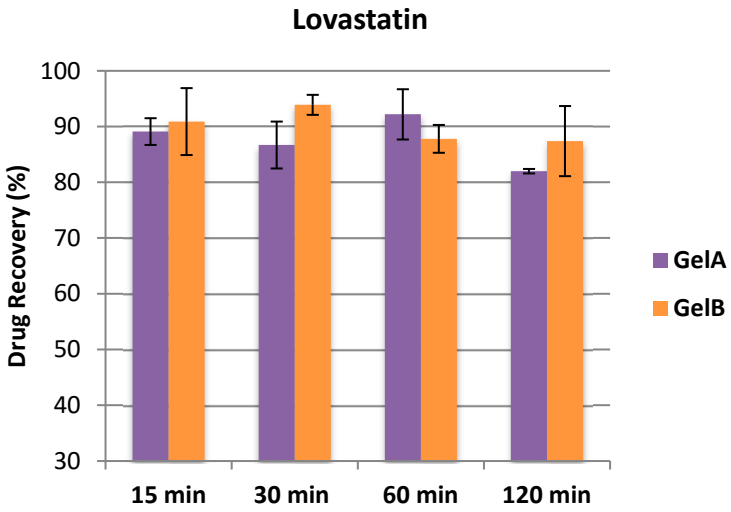

Diltiazem
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB

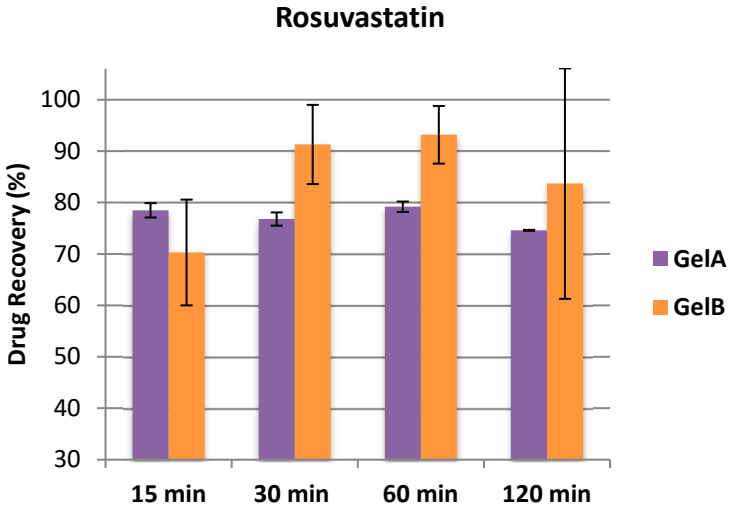

Furosemide
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB

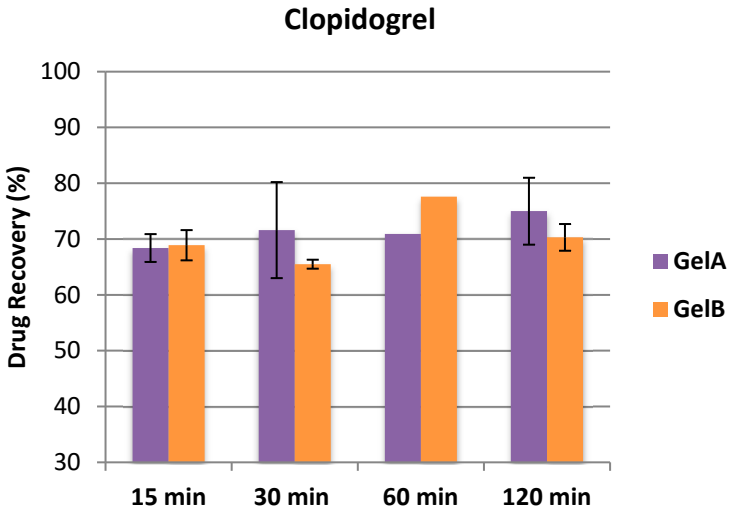

Hydrochlorothiazide
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB

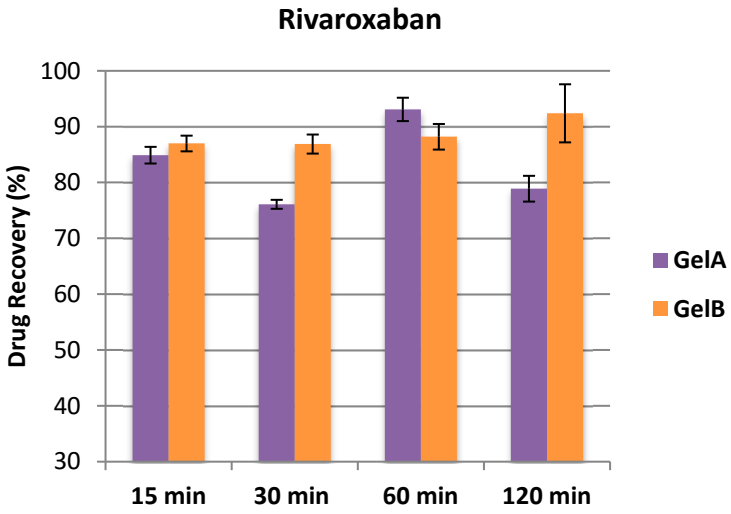

Lisinopril
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB

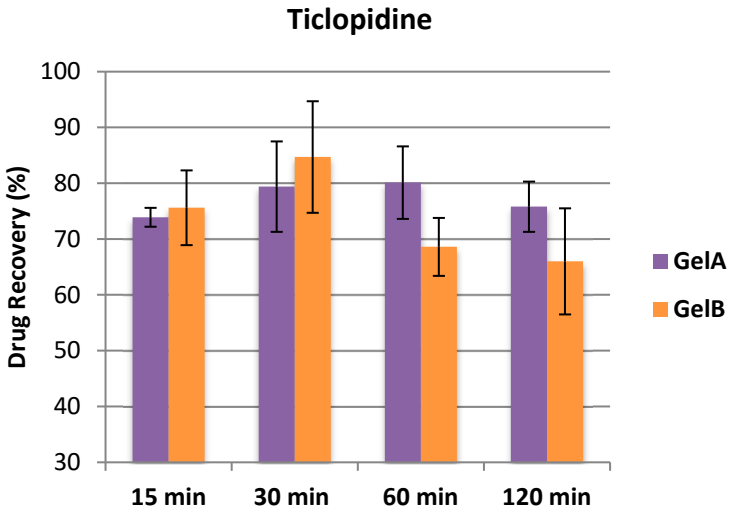

Gemfibrozil
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB

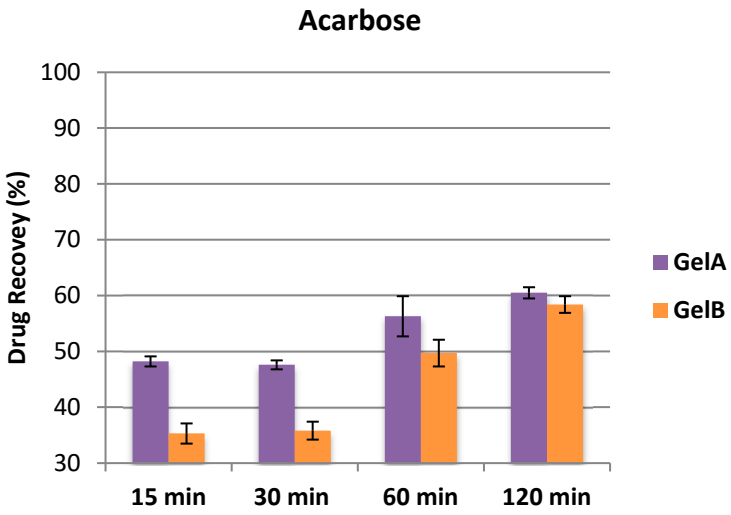

Lovastatin
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB

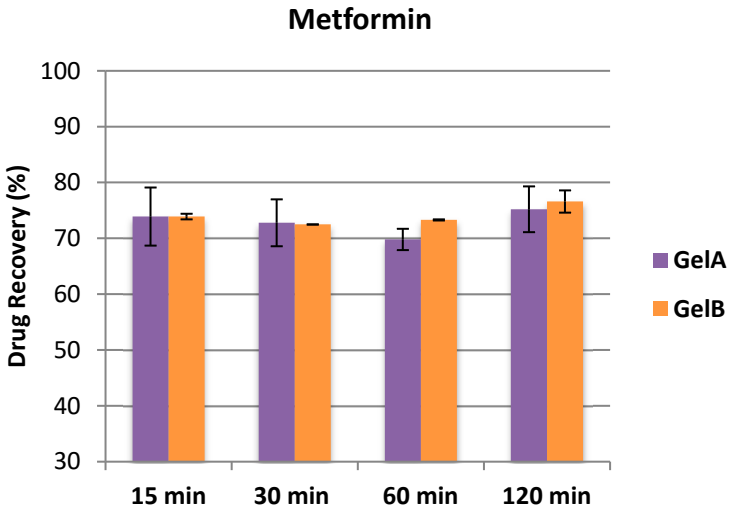

Rosuvastatin
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB

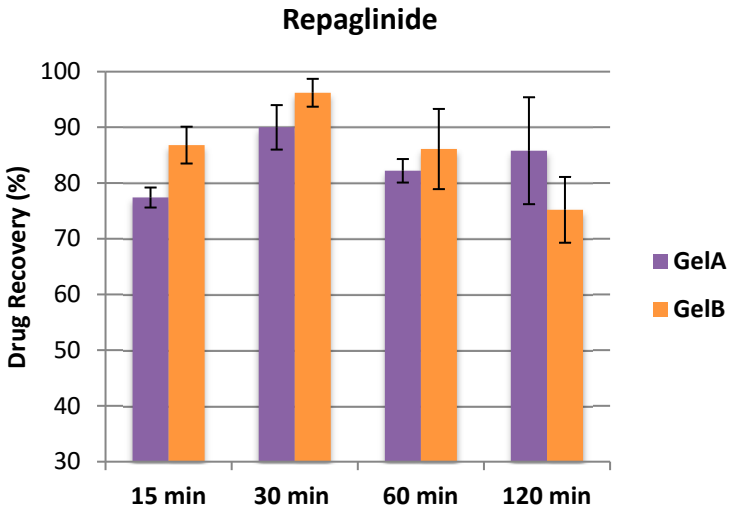

Clopidogrel
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB

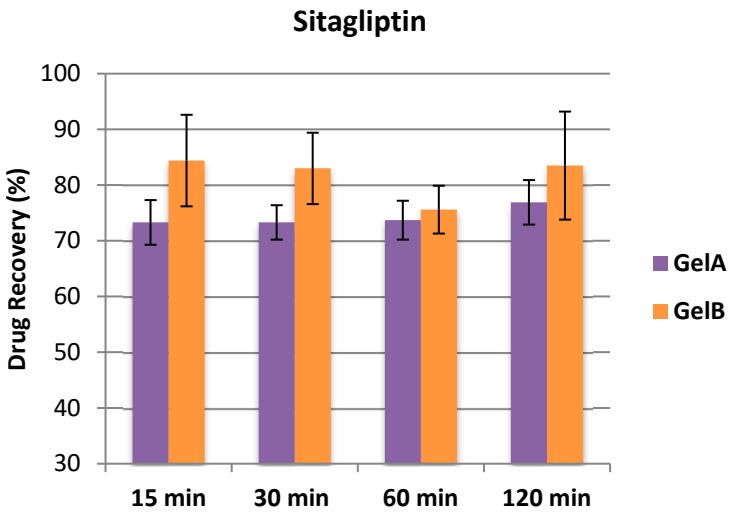

Rivaroxaban
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB

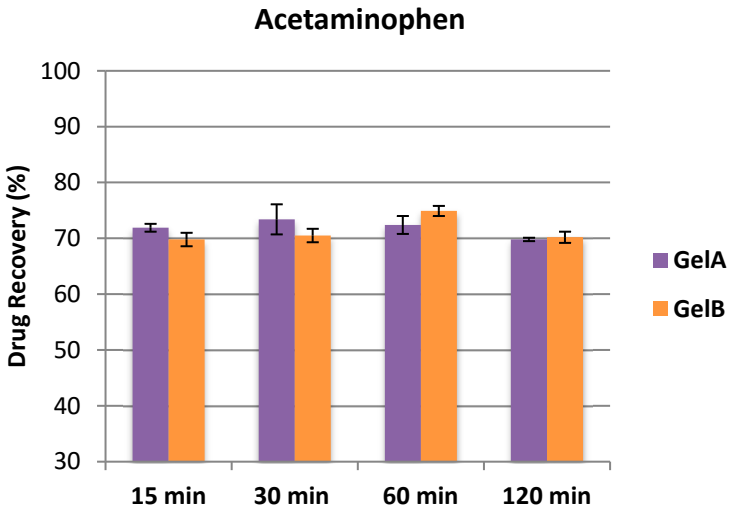

Ticlopidine
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB

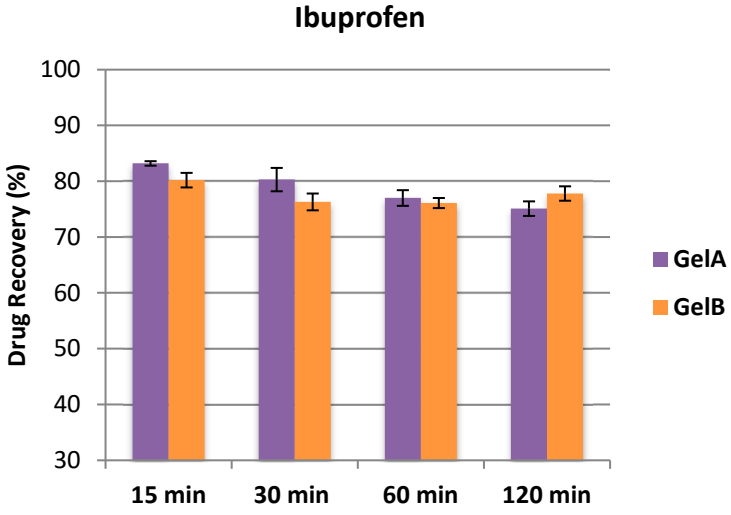

Acarbose
Drug Recovey (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB

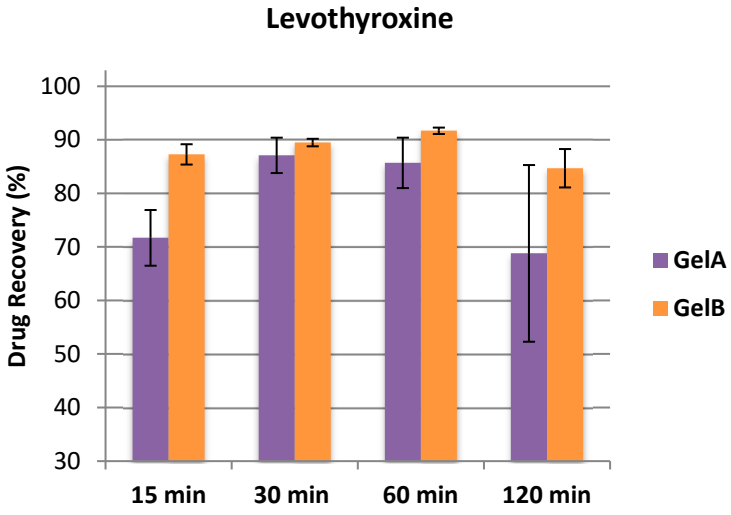

Metformin
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB

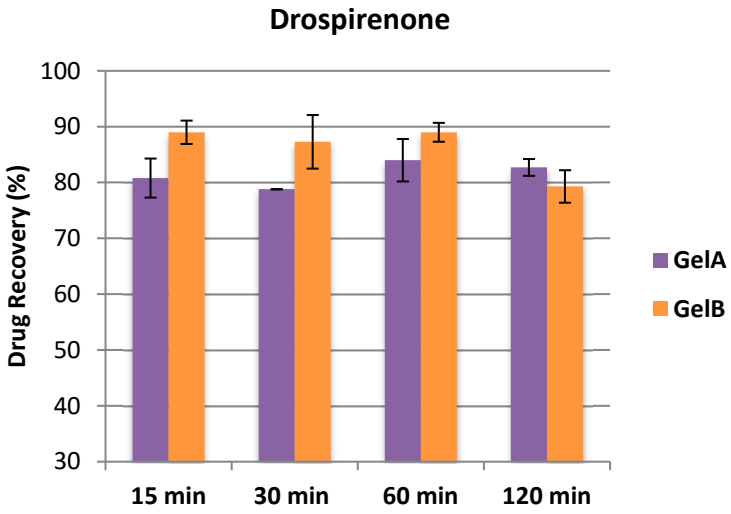

Repaglinide
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB

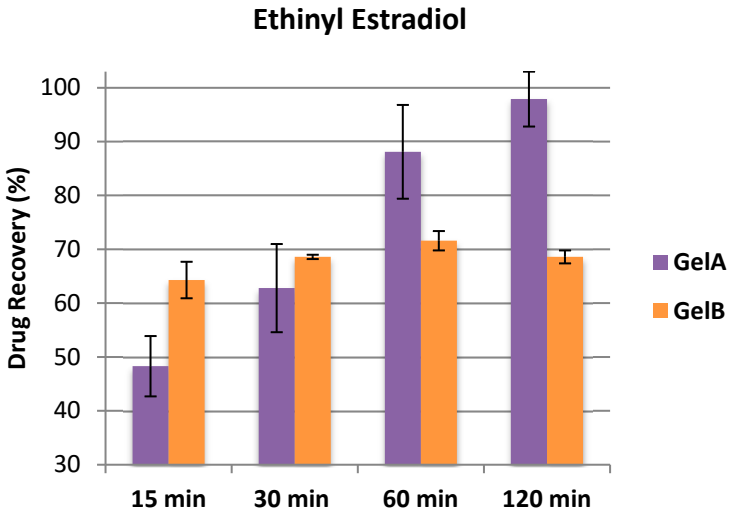

Sitagliptin
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB


Acetaminophen
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB


Ibuprofen
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB


Levothyroxine
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB


Drospirenone
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB


Ethinyl Estradiol
Drug Recovery (%)
100
90
80
70
60
50
40
30
15 min
30 min
60 min
120 min
GelA
GelB