

Supplementary Materials

Table S1. Standards of PGZ to analyze the linearity

Standards ($\mu\text{g/mL}$)	Area 1 ($\mu\text{V}\cdot\text{sec}$)	Area 2 ($\mu\text{V}\cdot\text{sec}$)	Area 3 ($\mu\text{V}\cdot\text{sec}$)	A(Average) ($\mu\text{V}\cdot\text{sec}$)	SD
1.5	34167	31506	32387	32387	1355.57
3	48311	46324	48380	48311	1167.62
5	65374	64878	63891	64878	754.92
10	124741	116434	119389	119389	4210.74
15	189224	171933	170119	171933	10545.69
30	366468	314375	329348	329348	26819.66
60	702444	665092	678080	678080	18962.52
80	972119	921532	943514	943514	25365.65
110	1292669	1309338	1314170	1309338	11280.49

SD: Standard deviation

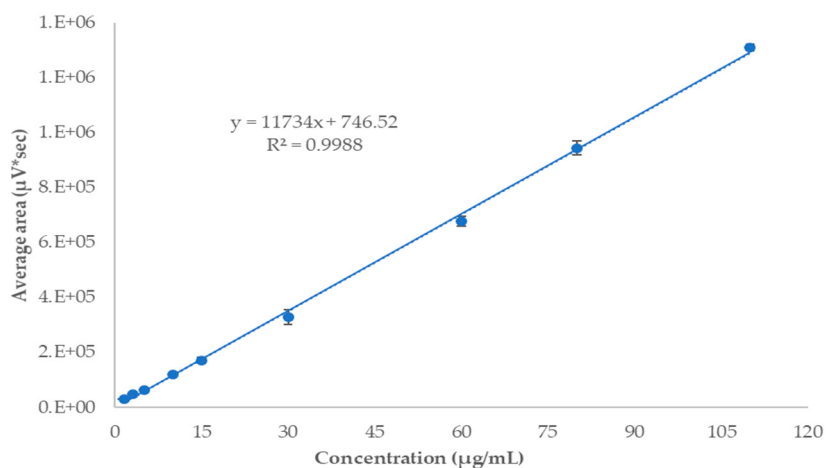


Figure S1: Linearity of the average of 3 calibrate curve. Runs test showed that deviation from linearity is not significant ($p=0.1071$)

Table S2. Precision inter-day

Day 1		Day 2		Day 3		SD	CV	Method Precision
Area ($\mu\text{V}\cdot\text{Sec}$)	C ($\mu\text{g/mL}$)	Area ($\mu\text{V}\cdot\text{Sec}$)	C ($\mu\text{g/mL}$)	Area ($\mu\text{V}\cdot\text{Sec}$)	C ($\mu\text{g/mL}$)			
45104	3	42679	3	43376	3	1248.49	2.87	97.15
713066	60	711243	60	702444	60	5679.97	0.79	99.19
1295099	110	1293630	110	1292669	110	1223.81	0.09	99.90

C: Concentration; SD: Standard deviation; CV: Coefficient of variation

Table S3. Accuracy of the analytical method

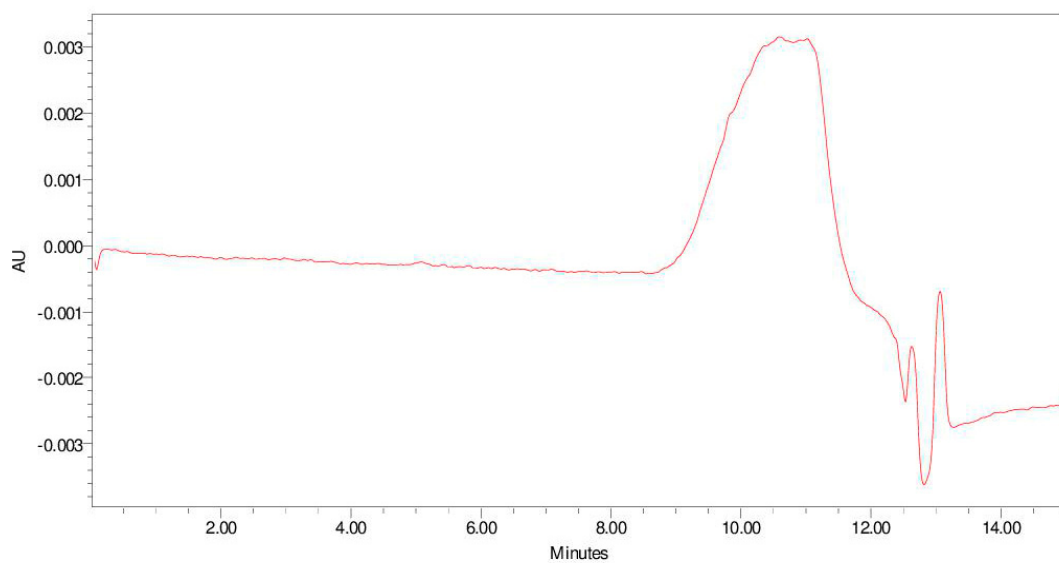
Theor. C. ($\mu\text{g/mL}$)	Tested C. ($\mu\text{g/mL}$)	Theor. C. ($\mu\text{g/mL}$)	Tested C. ($\mu\text{g/mL}$)	Theor. C. ($\mu\text{g/mL}$)	Tested C. ($\mu\text{g/mL}$)	Average ($\mu\text{g/mL}$)	SD	CV (%)	Relative error (%)	Accuracy (%)
3	3.263	3	3.057	3	3.116	3.145	106.086	3.40	-4.83	104.83
30	30.088	30	29.957	30	30.178	30.074	111.132	0.36	-0.24	100.24
60	59.897	60	59.742	60	57.442	59.027	1374.83	2.30	1.62	98.38
110	109.245	110	109.121	110	110.656	109.674	852.693	0.78	0.29	99.71

SD: Standard deviation; CV: Coefficient of variation

Table S4. Robustness of the analytical method: Effect of the change of flow (mL/min) and variations in the concentration (V/V) of the mobile phase to determine robustness.

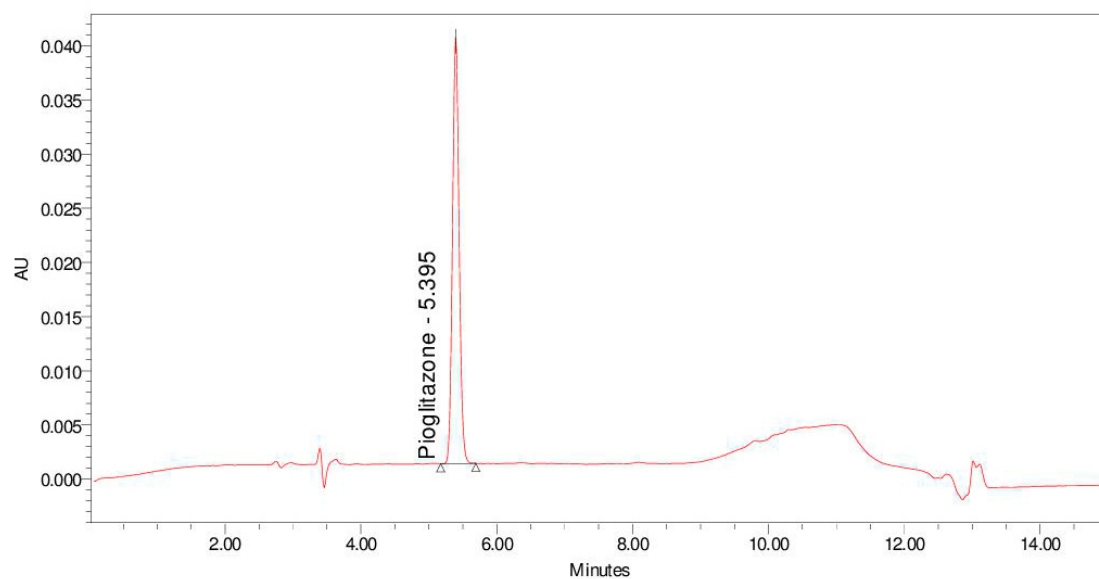
Flux (mL/min)	C ($\mu\text{g/mL}$)	Average retention time (min) $\pm$ SD	C (v/v)	Average retention time (min) $\pm$ SD
0.6	30	6.2 $\pm$ 0.002	A:78	5.1 $\pm$ 0.002
	60	6.2 $\pm$ 0.007	B:22	5.1 $\pm$ 0.002
0.7	30	5.3 $\pm$ 0.004		
	60	5.4 $\pm$ 0.016		
0.8	30	4.6 $\pm$ 0.008	A:72	6.1 $\pm$ 0.002
	60	4.5 $\pm$ 0.016	B:22	6.1 $\pm$ 0.002

SD: Standard deviation



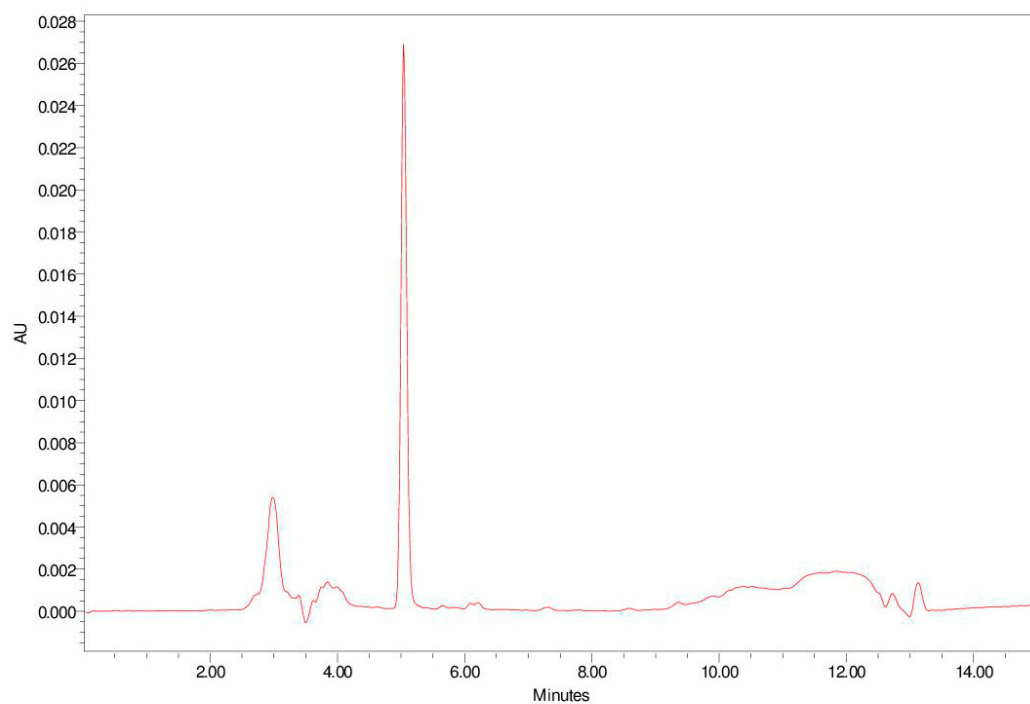
Peak Results						
	SampleName	Name	RT	Height	Amount	Units Area ($\mu\text{V}\cdot\text{sec}$)
1	Blank_control	Pioglitazone	5.390		Missing	

Figure S2: Chromatogram of blank control sample (Mobile phase)



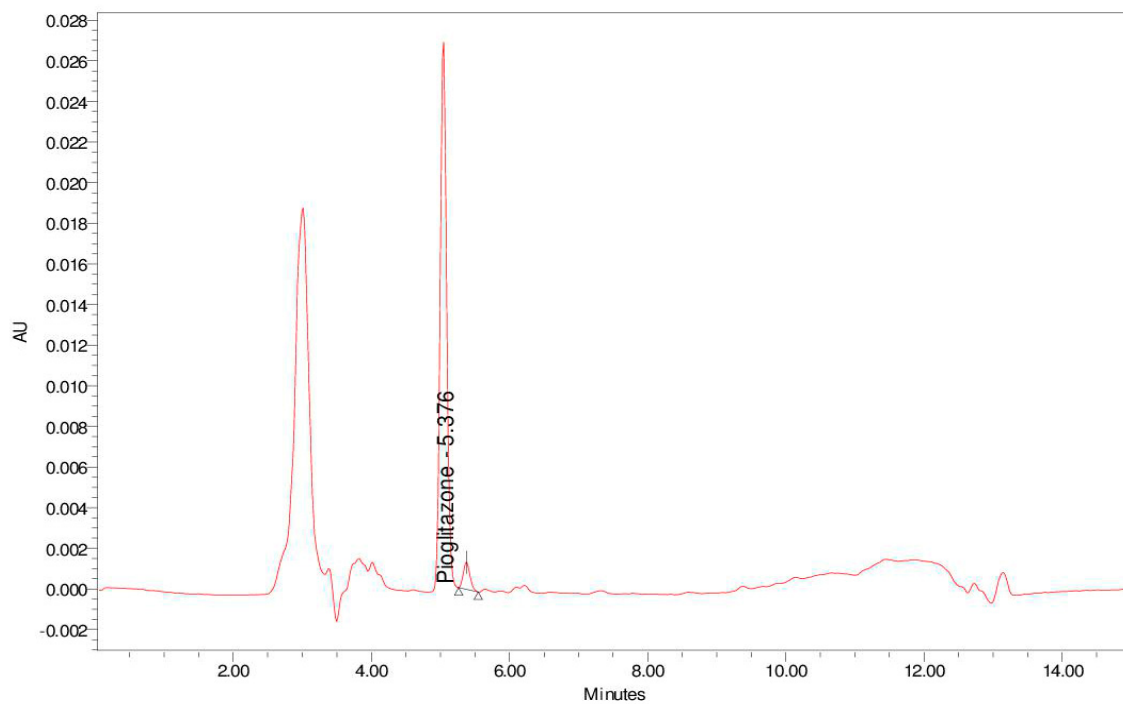
Peak Results							
	SampleName	Name	RT	Height	Amount	Units	Area ($\mu V \cdot sec$)
1	30 ppm	Pioglitazone	5.395	39301	30.000	ppm	268716

Figure S3: Standard sample 30 ppm.



Peak Results						
	SampleName	Name	RT	Height	Amount	Units
1	Time_0_skin	Pioglitazone	5.390		Missing	

Figure S4: Skin blank sample of permeation study as control.



Peak Results							
	SampleName	Name	RT	Height	Amount	Units	Area (μV*sec)
1	Limonene_skin_2	Pioglitazone	5.376	1335	0.088	ppm	8967

Figure S5: Skin sample permeation study of PGZ-limonene.



Figure S6.: Evolution of erythema shown as skin color sequence, using PGZ-limonene, limonene, compared with positive control. Colors are reproduced from the average values of RGB codes.