

SUPPLEMENTARY MATERIAL

Flavonoid C11

Nonlinear regression using SOLVER

x values	0,0625	9,21	y values	concentrations of the inhibitor	7,985	10,219	7,789	10,837	8,857	9,594	1,22	
	0,125	11,50			0	11,256	11,228	10,891	11,576	12,305	11,743	0,49
	0,25	15,52			0	14,618	14,912	15,03	15,908	16,872	15,809	0,83
	0,0625	6,75			37,5	5,924	7,179	5,714	7,466	6,915	7,318	0,75
	0,125	8,29			37,5	8,135	8,455	7,999	7,999	8,842	8,338	0,32
	0,25	11,45			37,5	10,817	11,491	10,873	11,278	13,305	10,956	0,94
	0,0625	6,29			50	5,416	6,774	5,472	6,932	6,623	6,496	0,67
	0,125	7,61			50	7,503	7,179	7,391	7,593	8,352	7,658	0,40
	0,25	10,49			50	10,359	9,929	10,698	9,701	11,966	10,268	0,80
	0,0625	5,20			75	4,083	5,549	4,532	5,985	5,469	5,556	0,73
	0,125	5,92			75	5,333	5,721	5,624	5,573	7,325	5,958	0,72
	0,25	7,93			75	7,094	6,018	8,255	8,433	9,632	8,169	1,24
	0,0625	4,12			100	3,29	3,946	3,658	4,384	4,895	4,541	0,60
	0,125	4,90			100	4,288	4,729	4,474	4,638	6,287	4,999	0,72
	0,25	6,01			100	5,512	5,313	5,328	6,529	7,146	6,261	0,75
	0,0625	2,88			150	2,206	3,011	2,498	3,57	2,692	3,281	0,51
	0,125	3,29			150	2,613	2,789	3,166	3,46	4,197	3,488	0,57
	0,25	4,08			150	3,309	3,54	4,17	4,842	4,399	4,241	0,57
										standard deviations y_{exp}		

Figure 1S: Mean values of the slopes (y values) and respective standard deviations as results of the *in vitro* inhibition of DPP-4 (38 U/mL) by flavonoid **C11** (0 - 150 μ M) using three concentrations of the substrate (x values: 0.0625; 0.125 and 0.25 mM).



Figure 2S: Sum of the squares (sum) of the different models (without inhibition, competitive inhibition, noncompetitive inhibition, uncompetitive inhibition and mixed inhibition) from the results obtained from DPP-4 inhibition by flavonoid **C11**.

Comparison based on F test:

	(Y _{exp} - Y _{calc}) ²	p	N	N-pB	f _{0,05}	F _{calc}	ΔSS	Δ df	Δ SS/Δ df	p (%)
Without inhibition	968,8068	2	108	106						
Competitive inhibition	183,9564	3	108	105	1,380	447,98	0,871	0,010	90,536	0%
Noncompetitive inhibition	99,6898	3	108	105	1,381	915,41	0,014	0,010	1,423	24%
Uncompetitive inhibition	109,3686	3	108	105	1,381	825,11	0,112	0,010	11,659	0%
Mixed inhibition	98,3440	4	108	104	1,382	460,26				

Comparison based on Akaike test:

	AIC c	ΔAICc			
Without inhibition	243,1713	↓			
Competitive inhibition	65,8982	-177,27	↓		
Noncompetitive inhibition	-0,2664	-243,44		↓	
Uncompetitive inhibition	9,7409	-233,43			↓
Mixed inhibition	0,4617	-242,71	-65,44	0,73	-9,28

Figure 3S: Comparison of the different models (without inhibition, competitive inhibition, noncompetitive inhibition, uncompetitive inhibition and mixed inhibition) applying the F test and the Akaike test, obtained from DPP-4 inhibition by flavonoid **C11**.

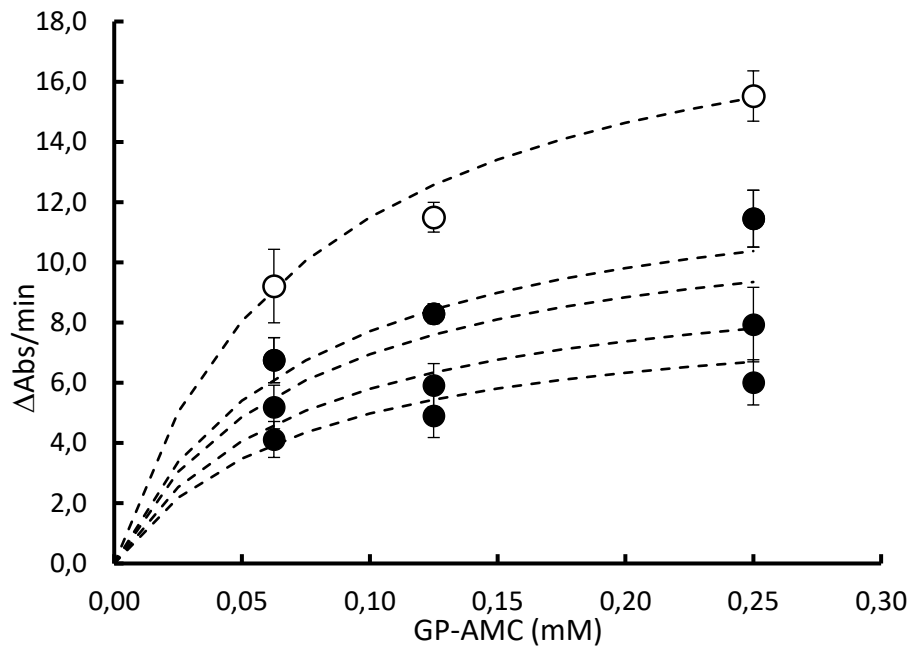


Figure 4S: Michaelis-Menten representation of the noncompetitive inhibition model of flavonoid **C11**.

Sitagliptin

Nonlinear regression using SOLVER

x values	0,0625	8,88	y values	0	concentration of the inhibitor	8,019	9,369	7,259	8,892	10,846	1,37
	0,125	11,64		0		11,649	11,753	10,586	11,229	12,986	0,88
	0,25	15,17		0		14,638	15,24	13,771	14,854	17,326	1,32
	0,0625	6,99		0,0125		6,501	8,199	5,306	7,18	7,776	1,14
	0,125	9,44		0,0125		9,674	10,21	8,259	8,886	10,151	0,85
	0,25	13,93		0,0125		13,34	14,66	12,36	13,4	15,918	1,38
	0,0625	5,92		0,025		5,234	7,066	4,704	6,186	6,413	0,95
	0,125	8,18		0,025		8,057	9,341	7,297	7,712	8,516	0,79
	0,25	11,87		0,025		11,732	12,91	11,009	11,65	12,062	0,69
	0,0625	4,41		0,05		4,088	5,184	3,363	4,583	4,811	0,71
	0,125	6,51		0,05		6,455	7,249	5,911	6,536	6,423	0,48
	0,25	9,59		0,05		9,988	10,564	8,62	9,268	9,49	0,74
	0,0625	3,01		0,1		2,715	3,654	2,418	3,002	3,242	0,48
	0,125	4,51		0,1		4,596	5,145	4,114	4,532	4,143	0,42
	0,25	7,48		0,1		7,277	8,023	6,823	7,366	7,935	0,50
	0,0625	1,90		0,2		1,642	2,327	1,553	2,02	1,938	0,31
0,125	2,89	0,2	2,956	3,296	2,716	2,858	2,606	0,27			
0,25	5,02	0,2	4,89	5,512	4,945	4,958	4,803	0,28			
									standard deviation y_{exp}		

Figure 55: Mean values of the slopes (y values) and respective standard deviations as results of the *in vitro* inhibition of DPP-4 (38 U/mL) by **sitagliptin** (0 - 0.2 μ M) using three concentrations of the substrate (x values: 0.0625; 0.125 and 0.25 mM).



Figure 6S: Sum of the squares (sum) of the different models (without inhibition, competitive inhibition, noncompetitive inhibition, uncompetitive inhibition and mixed inhibition) from the results obtained from DPP-4 inhibition by sitagliptin.

Comparison based on F test:

	(Y _{exp} - Y _{calc}) ²	p	N	N-pB	f _{0,05}	F _{calc}	Δ SS	Δ df	Δ SS/Δ df	p (%)
Without inhibition	861,8555	2	90	88						
Competitive inhibition	60,1335	3	90	87	1,424	1159,92	0,017	0,012	1,495	22%
Noncompetitive inhibition	72,7273	3	90	87	1,426	943,99	0,230	0,012	19,819	0%
Uncompetitive inhibition	117,6024	3	90	87	1,426	550,58	0,990	0,012	85,113	0%
Mixed inhibition	59,1059	4	90	86	1,427	584,01				

Comparison based on Akaike test:

	AIC c	ΔAICc			
Without inhibition	209,6077				
Competitive inhibition	-27,8321	-237,44	↓		
Noncompetitive inhibition	-10,7186	-220,33	↓	↓	
Uncompetitive inhibition	32,5347	-177,07			↓
Mixed inhibition	-27,1455	-236,75	0,69	-16,43	-59,68

Figure 7S: Comparison of the different models (without inhibition, competitive inhibition, noncompetitive inhibition, uncompetitive inhibition and mixed inhibition) applying the F test and the Akaike test, obtained from DPP-4 inhibition by sitagliptin.

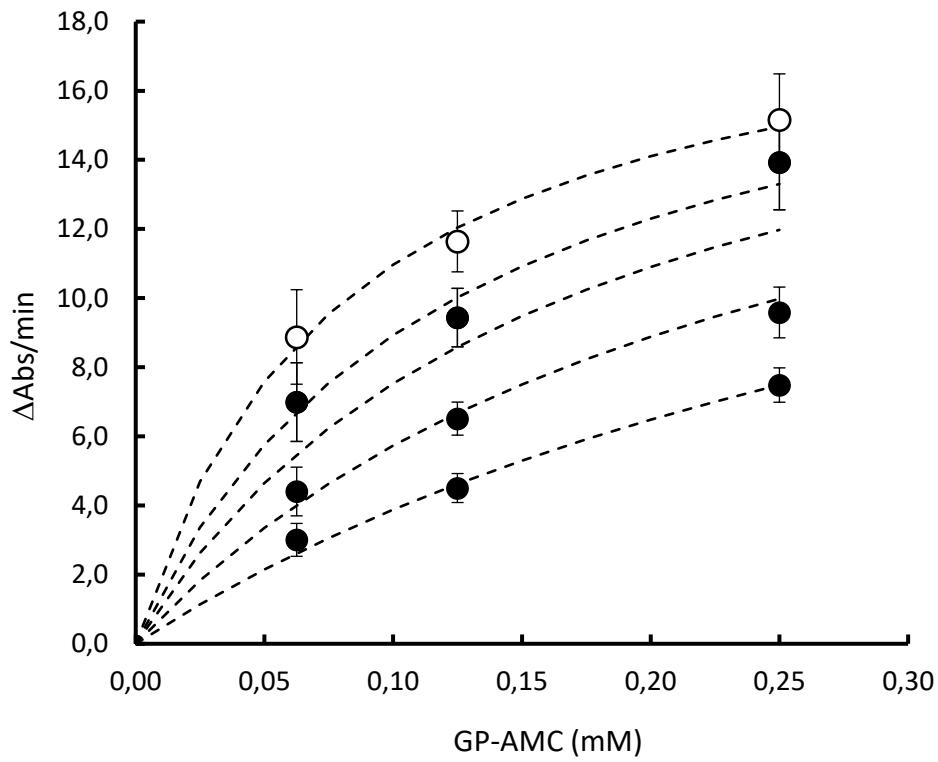


Figure 85: Michaelis-Menten representation of the competitive inhibition model of sitagliptin.

Diprotin A

Nonlinear regression using SOLVER

x values	0,0625	9,15	y values	0	concentration of the inhibitor	10,089	8,902	10,261	8,131	8,359	0,98	standard deviation y_{exp}
	0,125	12,28		0		11,9	13,302	12,323	11,988	11,9	0,60	
	0,25	16,43		0		15,856	16,972	16,52	16,347	16,442	0,40	
	0,0625	7,24		7,8		7,752	6,913	8,004	6,795	6,718	0,60	
	0,125	9,99		7,8		9,823	9,38	10,21	10,17	10,348	0,39	
	0,25	14,67		7,8		14,14	14,69	14,75	14,97	14,773	0,31	
	0,0625	6,09		15,6		6,887	5,655	7,089	5,433	5,381	0,83	
	0,125	8,55		15,6		8,439	8,692	8,75	8,764	8,096	0,28	
	0,25	12,54		15,6		12,265	12,624	12,432	13,339	12,063	0,49	
	0,0625	4,46		31,3		5,055	4,104	5,079	4,088	3,996	0,55	
	0,125	6,57		31,3		6,646	6,566	6,492	6,898	6,27	0,23	
	0,25	10,29		31,3		10,148	10,196	10,257	11,164	9,69	0,54	
	0,0625	2,93		62,5		3,37	2,701	3,309	2,83	2,438	0,40	
	0,125	4,61		62,5		4,661	4,486	4,541	5,134	4,224	0,33	
	0,25	7,51		62,5		7,575	7,38	7,366	8,224	6,989	0,45	
	0,0625	1,73		125		1,921	1,593	1,87	1,706	1,54	0,17	
0,125	2,86	125	2,733	2,809	2,84	3,234	2,673	0,22				
0,25	4,78	125	4,756	4,784	4,651	5,283	4,436	0,31				

Figure 9S: Mean values of the slopes (y values) and respective standard deviations as results of the *in vitro* inhibition of DPP-4 (38 U/mL) by **diprotin A** (0 - 125 μ M) using three concentrations of the substrate (x values: 0.0625; 0.125 and 0.25 mM).



Figure 10S: Sum of the squares (sum) of the different models (without inhibition, competitive inhibition, noncompetitive inhibition, uncompetitive inhibition and mixed inhibition) from the results obtained from DPP-4 inhibition by **diprotin A**.

Comparison based on F test:

	(Y _{exp} - Y _{calc}) ²	p	N	N-pB	f _{0,05}	F _{calc}	Δ SS	Δ df	Δ SS/Δ df	p (%)
Without inhibition	1002,8949	2	90	88						
Competitive inhibition	26,6457	3	90	87	1,424	3187,52	-0,519	0,012	-44,628	25%
Noncompetitive inhibition	37,8039	3	90	87	1,426	2221,01	-0,317	0,012	-27,303	0%
Uncompetitive inhibition	90,4150	3	90	87	1,426	878,02	0,632	0,012	54,385	0%
Mixed inhibition	55,3884	4	90	86	1,427	735,58				

Comparison based on Akaike test:

	AIC c	ΔAICc			
Without inhibition	223,2480				
Competitive inhibition	-101,0866	-324,33	↓		
Noncompetitive inhibition	-69,6061	-292,85	↓	↓	
Uncompetitive inhibition	8,8738	-214,37	↓	↓	↓
Mixed inhibition	-32,9919	-256,24	68,09	36,61	-41,87

Figure 11S: Comparison of the different models (without inhibition, competitive inhibition, noncompetitive inhibition, uncompetitive inhibition and mixed inhibition) applying the F test and the Akaike test, obtained from DPP-4 inhibition by **diprotin A**.

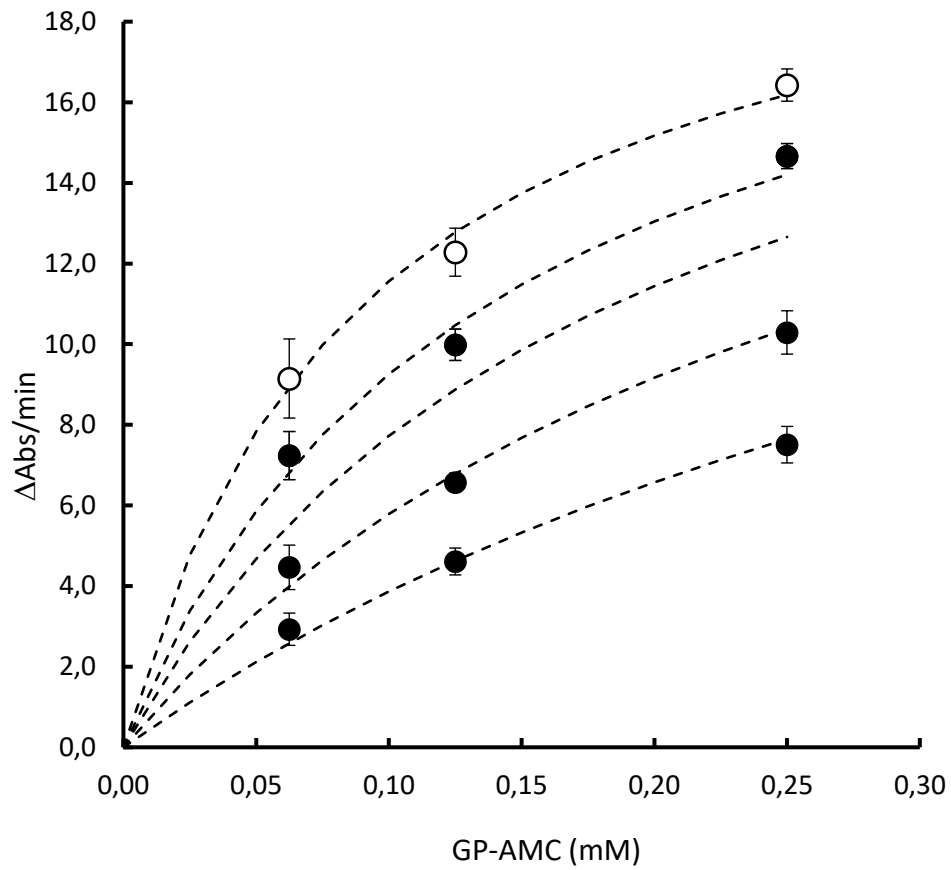


Figure 12S: Michaelis-Menten representation of the competitive inhibition model of **diprotin A**.