

S U P P L E M E N T A R Y M A T E R I A L S

QSAR, Structure-Based Pharmacophore Modelling and Biological Evaluation of Novel Platelet ADP Receptor (P2Y₁₂) Antagonist

Belal O. Al-Najjar^{a,b,*}, Manal A. Abbas^{b,c}, Obada A. Sibai^{a,b}, Fadi G. Saqallah^d and Aya Y. Al-Kabariti^{e,f}

^a Department of Pharmaceutical Sciences, Faculty of Pharmacy, Al-Ahliyya Amman University, 19328 Amman, Jordan.

^b Pharmacological and Diagnostic Research Centre, Al-Ahliyya Amman University, 19328 Amman, Jordan.

^c Department of Medical Laboratory Sciences, Faculty of Allied Medical Sciences, Al-Ahliyya Amman University, 19328 Amman, Jordan.

^d Discipline of Pharmaceutical Chemistry, School of Pharmaceutical Sciences, Universiti Sains Malaysia, 11800 Penang, Malaysia.

^e Department of Biopharmaceutics and Clinical Pharmacy, Faculty of Pharmacy, Al-Ahliyya Amman University, 19328 Amman, Jordan.

^f Institute of Cancer Therapeutics, Faculty of Life Sciences, University of Bradford, BD7 1DP Bradford, United Kingdom.

* **Corresponding author:** Belal O. Al-Najjar, Department of Pharmaceutical Sciences, Faculty of Pharmacy, Al-Ahliyya Amman University, 19328 Amman, Jordan; +962-5-350-0211(ext. 2053); b.najjar@ammanu.edu.jo, najjar.belal@gmail.com

CONTENTS

	Page
Table S1. Pharmacophore models generated by Receptor-ligand pharmacophore generation protocol embedded in Discovery Studio.	2
Fig. S1. Histograms representing the Area under the curve from the platelet aggregation test for (a) NSC380323, (b) NSC617595 and (c) NSC618159 with ADP.	4

Table S1. Pharmacophore models generated by Receptor-ligand pharmacophore generation protocol embedded in Discovery Studio.

#	Pharmacophore Model	Maximum Features	Minimum I.D. ^a	Maximum E.V.D. ^b	ROC ^c – AUC ^d	Sensitivity	Specificity
1	T1D1P1	6	1	5	0.831	1	0.63889
2	T1D1P2				0.726	0.98901	0.38889
3	T1D1P3				0.894	1	0.5
4	T1D1P4				0.702	0.98901	0.38889
5	T1D1P5				0.828	1	0.5
6	T1D1P6				0.637	1	0.36111
7	T1D1P7				0.674	1	0.52778
8	T1D1P8				0.539	0.98901	0.27778
9	T1D1P9				0.546	1	0.22222
10	T1D1P10				0.505	0.98901	0.36111
11	T1D3P1	6	3	5	0.805	1	0.44444
12	T1D3P2				0.842	1	0.47222
13	T1D3P3				0.544	1	0.30556
14	T1D3P4				0.629	1	0.25
15	T1D3P5				0.746	1	0.33333
16	T1D3P6*				0.909	1	0.30556
17	T1D3P7				0.637	1	0.33333
18	T1D3P8*				0.901	1	0.27778
19	T1D3P9				0.814	1	0.38889
20	T1D3P10				0.867	1	0.27778
21	T2D3P1	7	3	5	0.805	1	0.44444
22	T2D3P2				0.842	1	0.47222
23	T2D3P3				0.544	1	0.30556
24	T2D3P4				0.629	1	0.25
25	T2D3P5				0.746	1	0.33333
26	T2D3P6*				0.909	1	0.30556
27	T2D3P7				0.637	1	0.33333
28	T2D3P8*				0.901	1	0.27778
29	T2D3P9				0.814	1	0.38889
30	T2D3P10				0.867	1	0.27778
31	T2D1P1	7	1	5	0.657	0.98901	0.5
32	T2D1P2				0.831	1	0.61111
33	T2D1P3				0.851	1	0.63889
34	T2D1P4				0.837	1	0.58333
35	T2D1P5				0.63	0.97802	0.52778
36	T2D1P6				0.705	0.97802	0.52778
37	T2D1P7				0.774	0.98901	0.47222
38	T2D1P8				0.801	0.96703	0.63889
39	T2D1P9				0.831	1	0.63889
40	T2D1P10				0.539	0.98901	0.27778

41	T3D1P1	10	1	5	0.803	0.96703	0.66667
42	T3D1P2				0.657	0.98901	0.5
43	T3D1P3				0.831	1	0.61111
44	T3D1P4				0.851	1	0.63889
45	T3D1P5				0.837	1	0.58333
46	T3D1P6				0.63	0.97802	0.52778
47	T3D1P7				0.705	0.97802	0.52778
48	T3D1P8				0.774	0.98901	0.47222
49	T3D1P9				0.801	0.96703	0.63889
50	T3D1P10				0.831	1	0.63889
51	T3D3P1	10	3	5	0.805	1	0.44444
52	T3D3P2				0.842	1	0.47222
53	T3D3P3				0.544	1	0.30556
54	T3D3P4				0.629	1	0.25
55	T3D3P5				0.746	1	0.33333
56	T3D3P6*				0.909	1	0.30556
57	T3D3P7				0.637	1	0.33333
58	T3D3P8*				0.901	1	0.27778
59	T3D3P9				0.814	1	0.38889
60	T3D3P10				0.867	1	0.27778
61	T4D1P1	10	1	4	0.838	0.97802	0.63889
62	T4D1P2				0.705	0.98901	0.47222
63	T4D1P3				0.82	1	0.58333
64	T4D1P4*				0.928	1	0.55556
65	T4D1P5*				0.921	1	0.55556
66	T4D1P6				0.652	0.98901	0.52778
67	T4D1P7				0.778	0.98901	0.47222
68	T4D1P8				0.858	1	0.44444
69	T4D1P9				0.818	0.97802	0.58333
70	T4D1P10				0.871	1	0.61111
71	T4D3P1	10	3	4	0.852	1	0.41667
72	T4D3P2				0.856	1	0.44444
73	T4D3P3				0.568	1	0.30556
74	T4D3P4				0.755	1	0.25
75	T4D3P5				0.832	1	0.33333
76	T4D3P6*				0.915	1	0.27778
77	T4D3P7				0.723	1	0.33333
78	T4D3P8				0.887	1	0.27778
79	T4D3P9*				0.916	1	0.36111
80	T4D3P10				0.891	1	0.27778

^a Minimum interference distance.

^b Maximum exclusion volume distance.

^c Receiver operating characteristic curve.

^d Area under the curve.

* Selected pharmacophore models for ligand mapping.

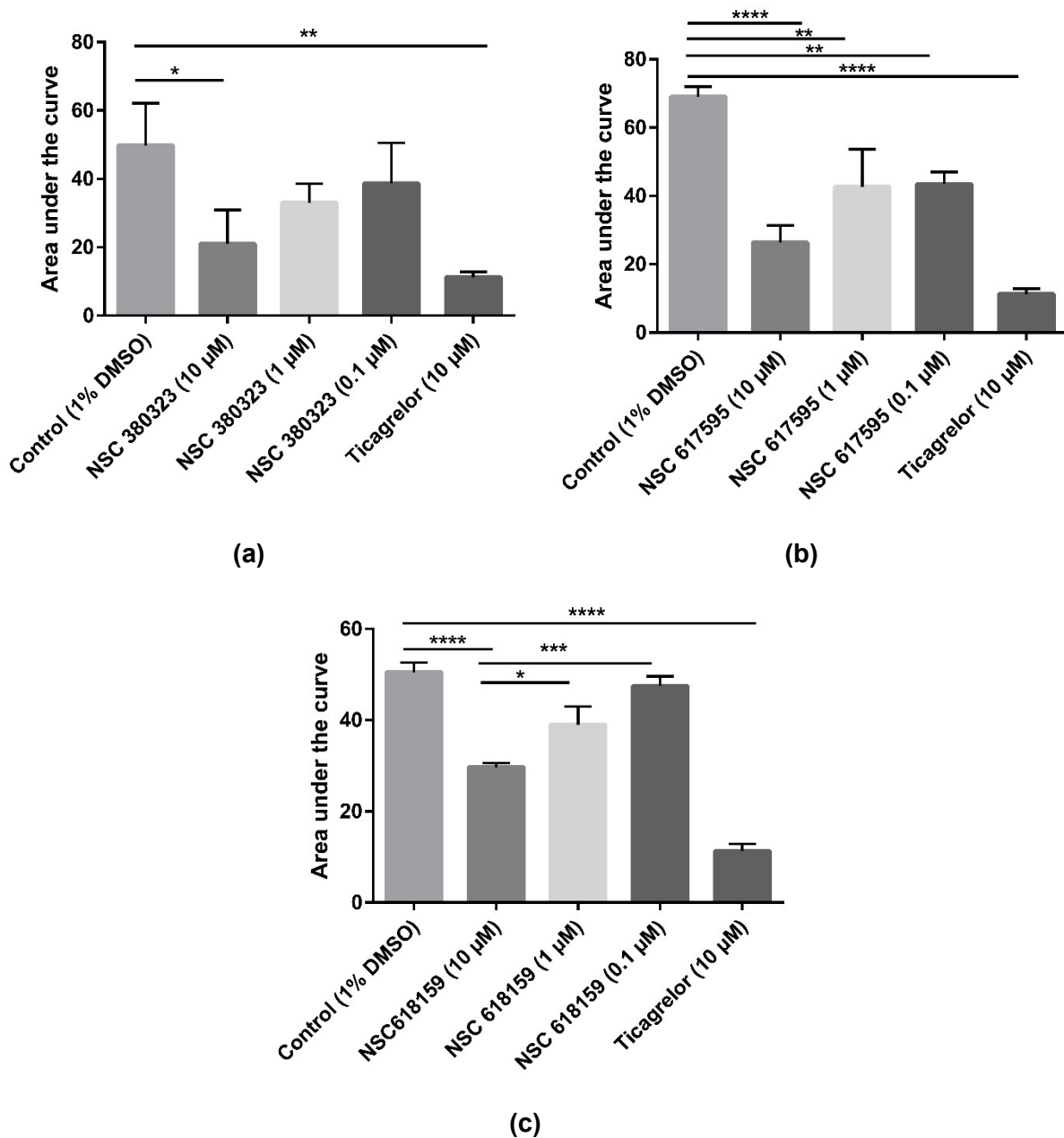


Fig. S1. Histograms representing the Area under the curve from the platelet aggregation test for **(a)** NSC380323, **(b)** NSC617595 and **(c)** NSC618159 with ADP.

* $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$; **** $p \leq 0.0001$