Electronic Supplementary Information

Exploring the supramolecular profile of 5-phenylhydantoins

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Table S1 Selected bond lengths (Å) and angles (°) in the investigated compounds.

	1	**2**	**3**	**4**
N1 C2	1.334(2)	1.333(2)	1.332(3)	1.336(2)
C2 O1	1.228(2)	1.216(2)	1.214(3)	1.223(2)
C2 N3	1.384(2)	1.395(2)	1.392(3)	1.390(3)
N3 C4	1.369(2)	1.349(2)	1.348(3)	1.359(2)
C4 O2	1.201(2)	1.216(2)	1.220(2)	1.208(2)
C4 C5	1.534(2)	1.529(2)	1.534(3)	1.538(3)
C5 N1	1.460(2)	1.452(2)	1.458(3)	1.459(2)
C5 C6	1.527(2)	1.530(2)	1.531(3)	1.522(2)
C2–N1–C5	113.3(1)	113.7(1)	113.5(2)	112.7(2)
O1–C2–N1	127.8(1)	129.1(2)	128.1(2)	127.4(2)
O1–C2–N3	124.7(1)	124.3(1)	124.7(2)	125.1(2)
N1–C2–N3	107.6(1)	106.5(1)	107.2(2)	107.5(2)
C2–N3–C4	111.9(1)	112.4(1)	112.1(2)	112.3(2)
O2–C4–N3	126.7(1)	126.8(1)	127.0(2)	127.0(2)
O2–C4–C5	126.7(1)	126.2(1)	125.6(2)	126.6(2)
N3–C4–C5	106.6(1)	107.0(1)	107.3(2)	106.4(2)
N1–C5–C4	100.3(1)	100.3(1)	99.9(2)	100.7(1)

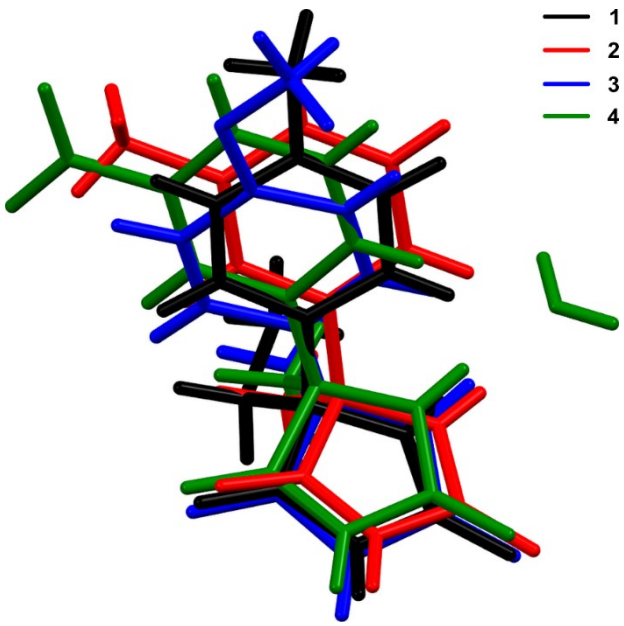

Fig. S1 A structural overlay highlighting the differences of the conformations of **1**–**4**.

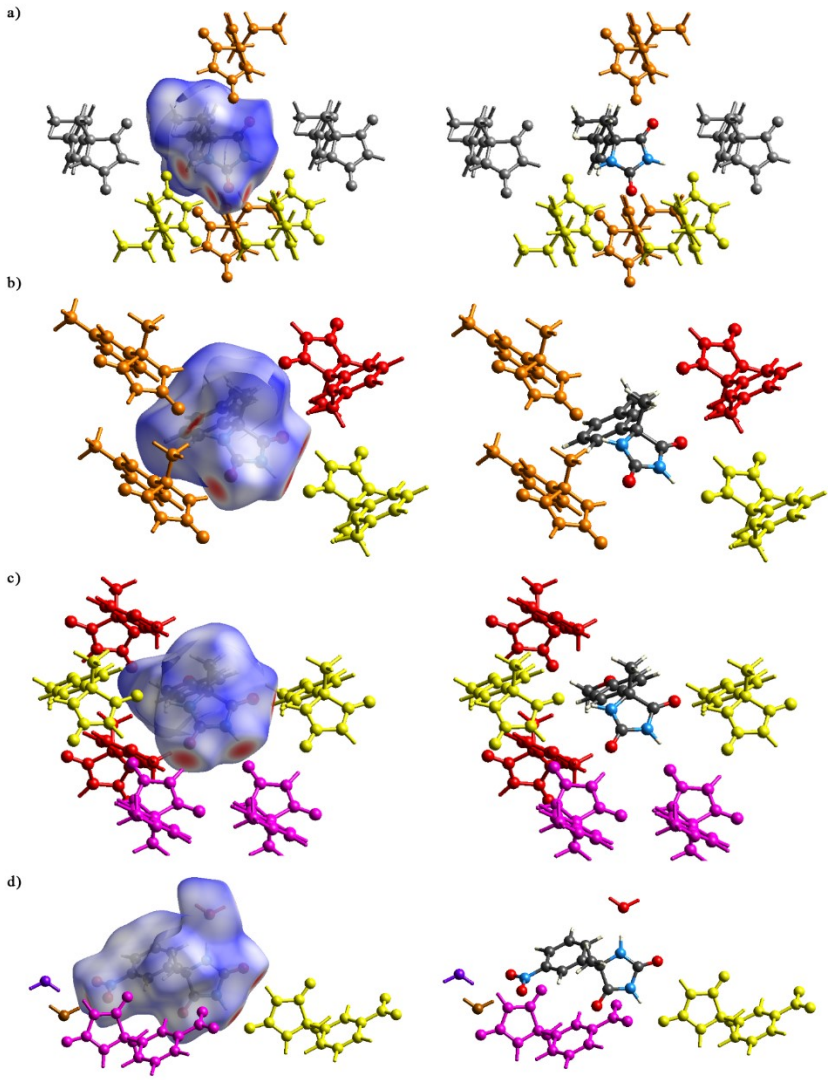

Fig. S2 The three-dimensional Hirshfeld surface showing intermolecular interactions of **1**–**4** (a–d) plotted over d_{norm}. The pair of molecules colored by the same color interacts with the central unit through the same type of interaction. a) Yellow-coloured pairs of molecules are in contact with the central unit through interaction labelled as A and A' in Fig. 3; orange-coloured pairs of molecules are in contact with the central unit through interaction labelled as B and B' in Fig. 3; grey-coloured pairs of molecules are in contact with the central unit through interaction labelled as C and C' in Fig. 3. b) Orange-coloured pairs of molecules are in contact with the central unit through interaction labelled as A and A' in Fig. 3; the yellow-coloured molecule is in contact with the central unit through the interaction labelled as B in Fig. 3; the red-coloured molecule is in contact with the central unit through interaction labelled as C in Fig. 3. c) Yellow-coloured pairs of molecules are in contact with the central unit through interaction labelled as A and A' in Fig. 3; red-coloured pairs of molecules are in contact with the central unit through interaction labelled as B and B' in Fig. 3; cyclamen-coloured pairs of molecules are in contact with the central unit through interaction labelled as C and C' in Fig. 3. d) Yellow-coloured molecule is in contact with the central unit through interaction labelled as A in Fig. 3; cyclamen-coloured molecule is in contact with the central unit through interaction labelled as B in Fig. 3; violet-coloured molecule is in contact with the central unit through interaction labelled as C in Fig. 3; brown-coloured molecule is in contact with the central unit through interaction labelled as D in Fig. 3.

Table S2. Calculated surface minima and maxima (kcal/mol) for compounds **1**–**4**.

	1		**2**		**3**		**4**	
	min	max	min	max	min	max	min	max
1	–35.80	43.24	–35.33	44.12	–35.58	43.74	–30.74	51.20
2	–31.74	41.89	–30.95	42.54	–32.30	41.77	–30.59	48.54
3	–11.71	16.31	–12.32	18.55	–18.03	21.79	–29.77	26.22
4	–8.09	16.31	–9.91	17.35	–11.20	19.20	–27.84	25.68
5		15.31		15.96	–9.68	19.00		23.52
6		15.18		15.88	–8.39	18.59		20.98
7		15.09		15.86		17.92		20.97
8		14.87		13.03		17.51		20.70
9		14.19		12.25		16.49		16.86
10		13.49		12.18		15.08		14.60
11		12.77		8.97		12.77		8.00
12		10.07		7.65		7.75		4.96
13		8.18				7.39		
14		7.26						

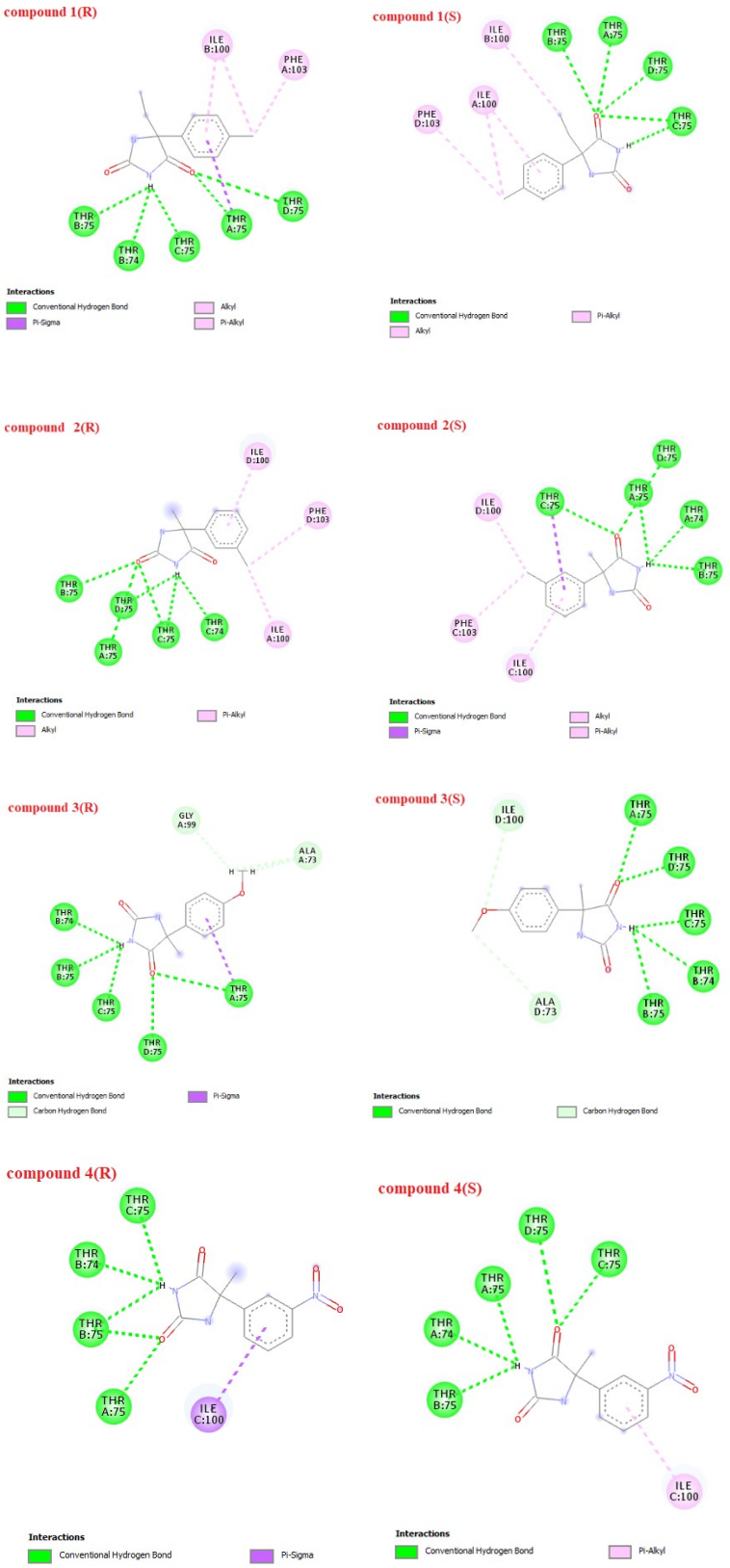

Fig. S3 The amino-acid environment at the first binding site of investigated compounds in a closed state of VGSC, predicted by molecular docking study.

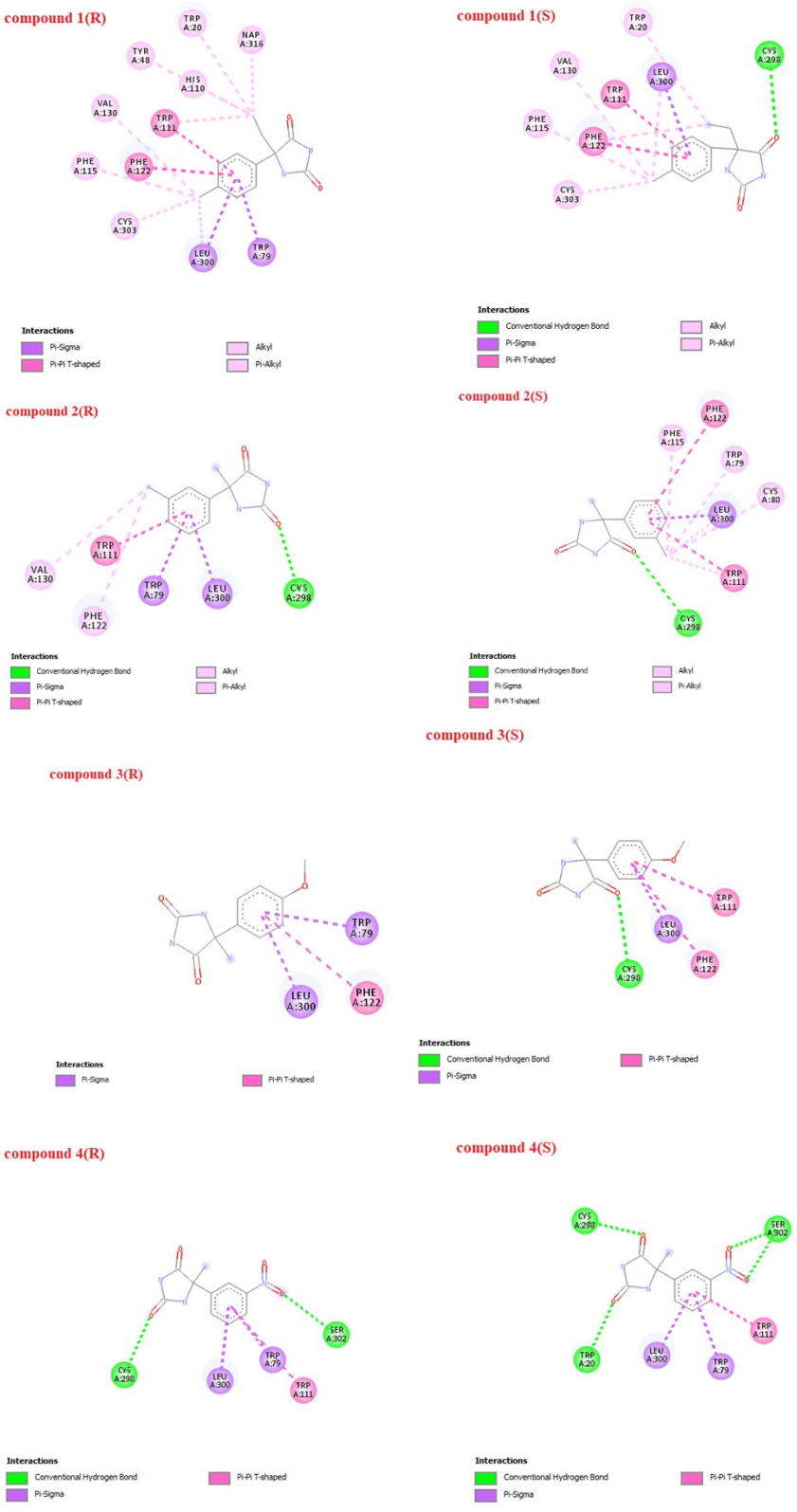

Fig. S4 The amino-acid environment at the first binding site of investigated compounds in AR predicted by molecular docking study.

Table S3 Binding energies (in kcal/mol) of the investigated compounds for selected enzymes, obtained by docking studies.

Compound / Target	voltage–gated ion channel (1BL8)		MMP–12 (3F15)		Aldose reductase (2FZD)	
	Δ*E*(BS1)	Δ*E*(BS2)	Δ*E*(BS1)	Δ*E*(BS2)	Δ*E*(BS1)	Δ*E*(BS2)
1(*R*)	–7.2	–	–8.0 (bm1) –7.8 (bm2)	–	–7.9	–7.1
1(*S*)	–7.0	–	–8.6 (bm2)	–	–7.6	–6.6
2(*R*)	–7.2	–	–7.8 (bm1) –7.8 (bm2)	–	–7.9	–6.6
2(*S*)	–7.0	–	–8.2 (bm1) –7.5 (bm2)	–	–7.9	–
3(*R*)	–6.6	–	–7.9 (bm2)	–	–7.4	–
3(*S*)	–6.5	–	–8.2 (bm2)	–	–7.3	–
4(*R*)	–7.0	–	–7.5 (bm3) –7.1 (bm2)	–	–7.6	–
4(*S*)	–6.8	–	–8.4 (bm3) –7.1 (bm2)	–	–7.6	–