Supporting Information

Molecular docking and 3D-QSAR CoMFA studies on indole inhibitors of GIIA secreted phospholipase A_2

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Table of contents

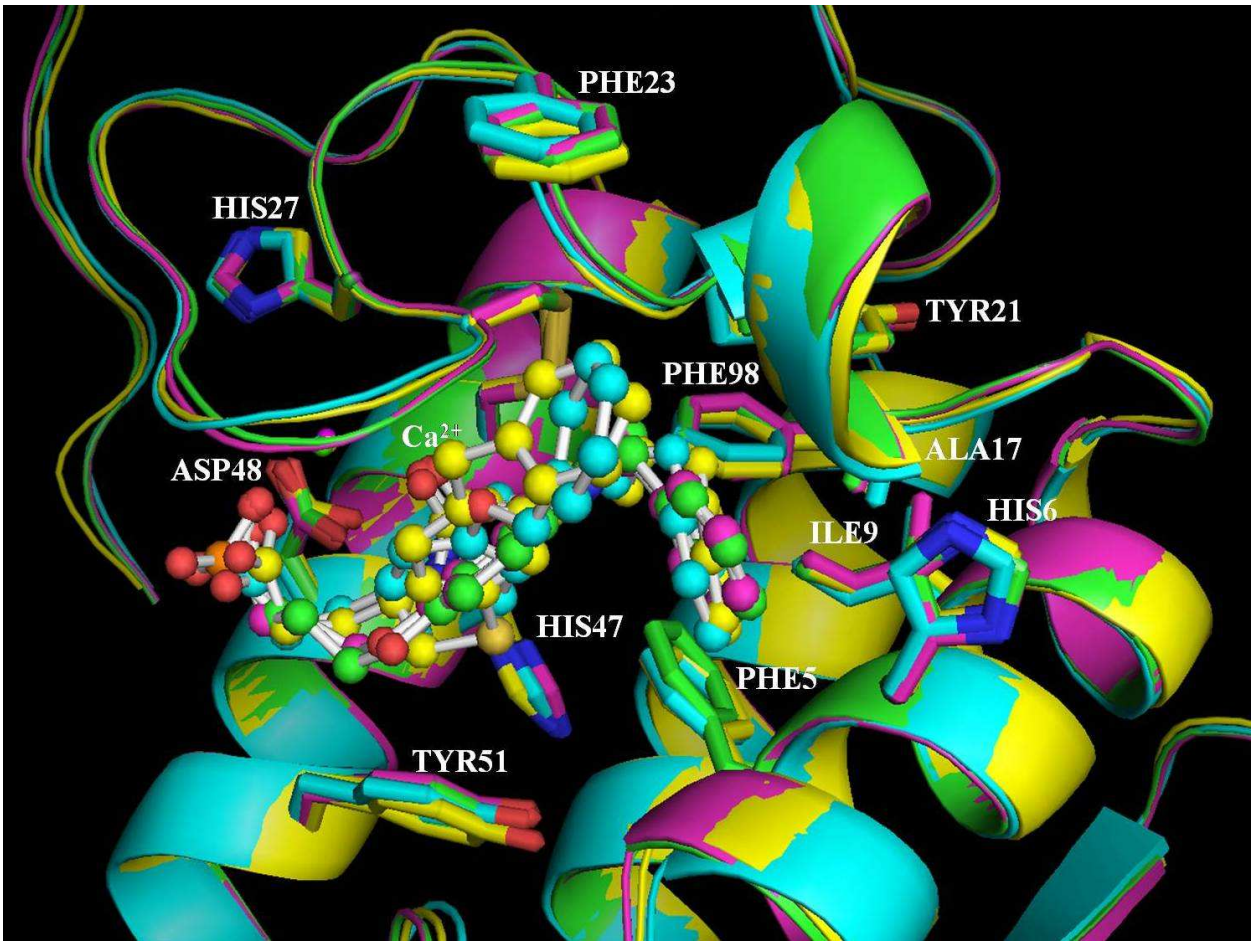


Figure 1. The superimposition of the four crystal structures of the GIIA $sPLA_2$ enzyme co-crystallised with four different ligands. The crystal structure with PDB ID: 1DB4 is highlighted in green colour; the crystal structure with PDB ID: 1DB5 is highlighted in magenta colour; the crystal structure with PDB ID: 1J1A is highlighted in cyan colour and the crystal structure with PDB ID: 1KVO is highlighted in yellow colour.

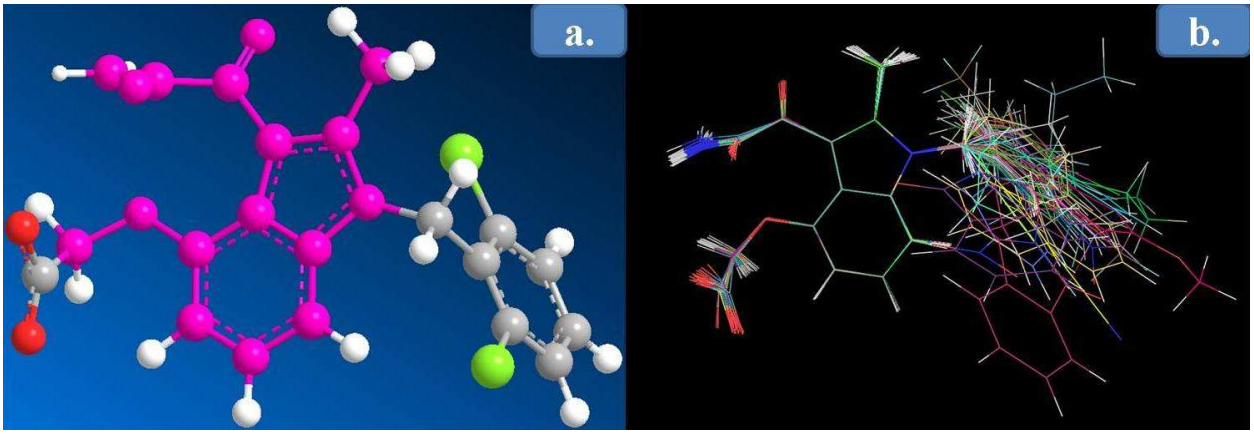


Figure 2. (a) The common atoms used for the alignment of the data set are highlighted in magenta colour in compound **1**; (b) The alignment results of the data set are presented.

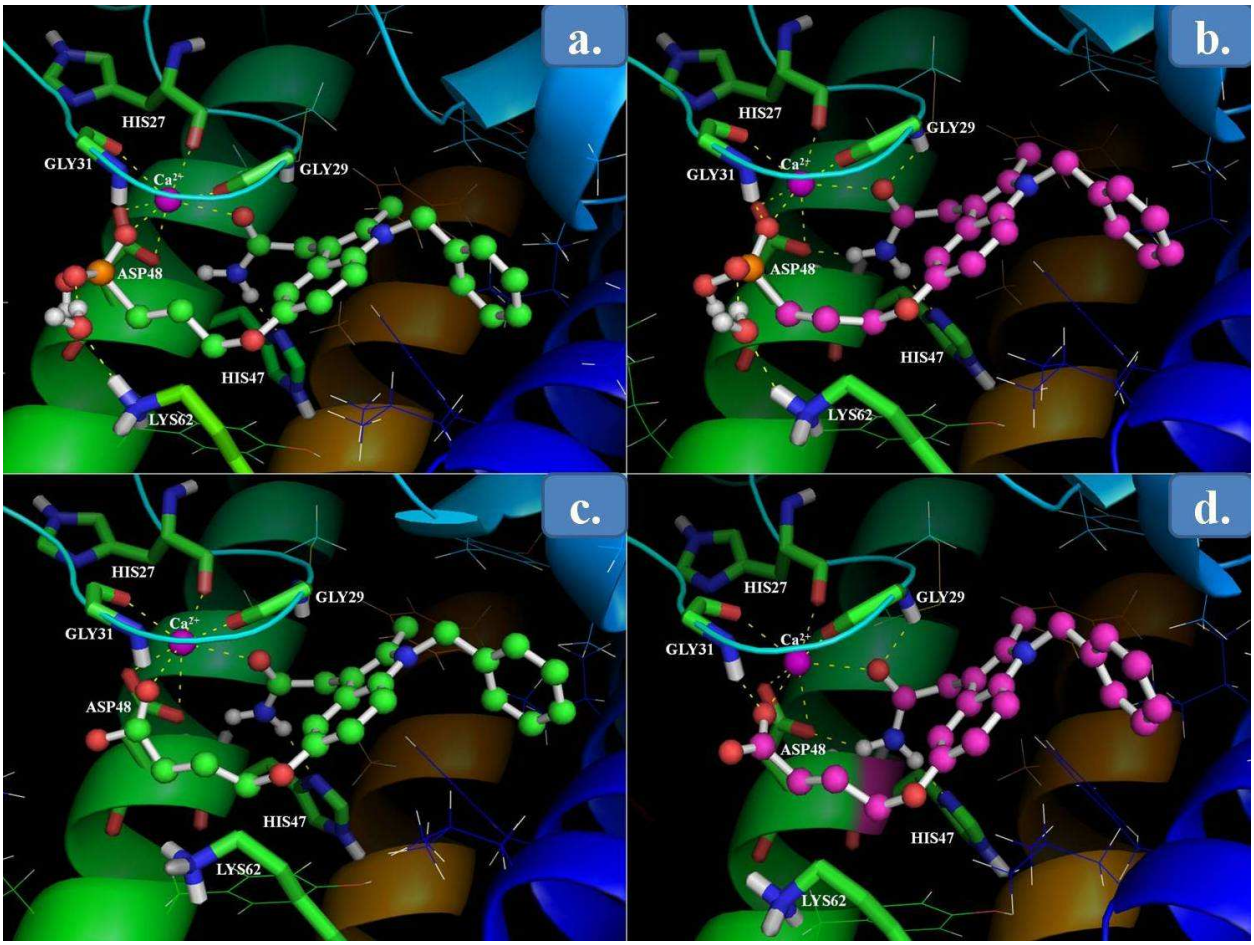
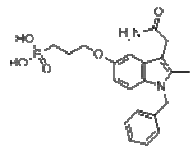
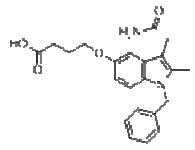


Figure 3. (a) The binding of indole8 in the active site of the GIIA $sPLA_2$ enzyme as revealed by the crystal structure, PDB ID: 1DB4; (b) the binding of indole8 in active site of the GIIA $sPLA_2$ as predicted by GLIDE; (c) The binding of indole6 in the active site of the GIIA $sPLA_2$ enzyme as revealed by the crystal structure, PDB ID: 1DB5; (d) the binding of indole6 in the active site of the GIIA $sPLA_2$ as predicted by GLIDE.

Table 1. The XP binding score, the distances of the interactions in Å and the RMSD values in Å for the crystallographic inhibitors indole8 and indole6.

Code	Molecular Structure	XP GScore	Interaction	Crystallographic distance	Glide Distance	RMSD
Indole8		-15.90	Ca^{2+}…O (Ca^{2+}-$PO(OH)_2$)	2.40	2.20	0.318
			Ca^{2+}…O (Ca^{2+}-CONH)	2.60	2.70	
			N…H-N N…N (His47-NHCO)	1.90 3.00	1.90 2.90	
			O…H-N O…N (Asp48-NHCO)	1.80 2.50	1.60 2.60	
			N-H…O N…O (Gly29-CONH)	2.20 2.90	2.10 2.90	
			N-H…O N…O (Gly31-$PO(OH)_2$)	1.90 2.70	1.90 2.80	
			N-H…O-H…O N…O…O (Lys62-H_2O-$PO(OH)_2$)	1.90, 1.70 2.90, 2.60	1.90, 1.50 2.90, 2.50	
Indole6		-14.34	Ca^{2+}…O (Ca^{2+}-COOH)	2.60	2.20	0.581
			Ca^{2+}…O (Ca^{2+}-CONH)	2.60	2.60	
			N…H-N N…N (His47-NHCO)	2.10 3.00	1.90 2.80	
			O…H-N O…N (Asp48-NHCO)	2.00 2.90	1.90 2.70	
			N-H…O N…O (Gly29-CONH)	2.20 3.00	2.30 3.00	
			N-H…O N…O (Gly31-COOH)	1.60 2.50	2.10 3.00	

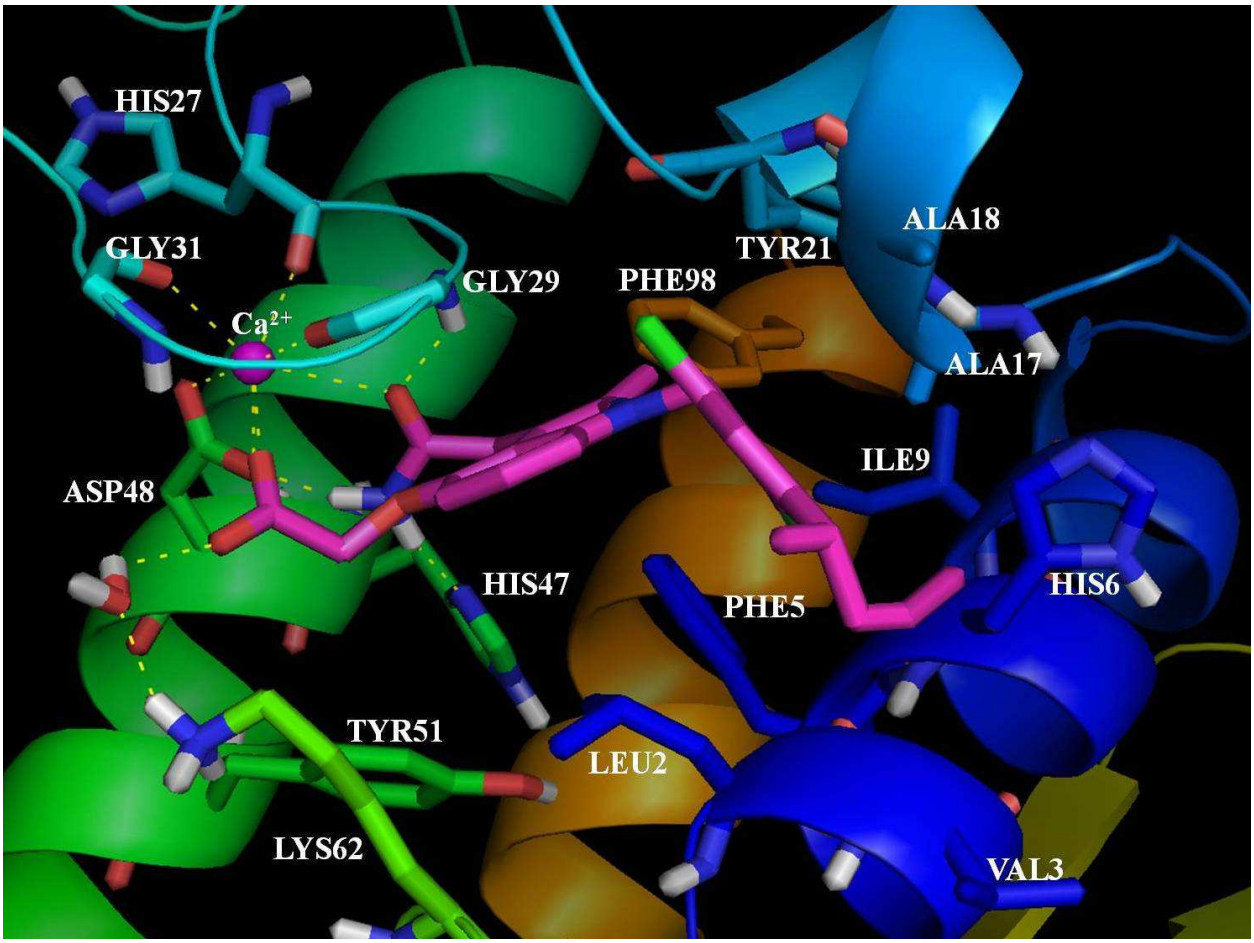


Figure 4. The binding of compound **N2** in the active site of the GIIA $sPLA_2$ enzyme. The enzyme-ligand complex was obtained by automated molecular docking of the compound in the enzyme active site using GLIDE.

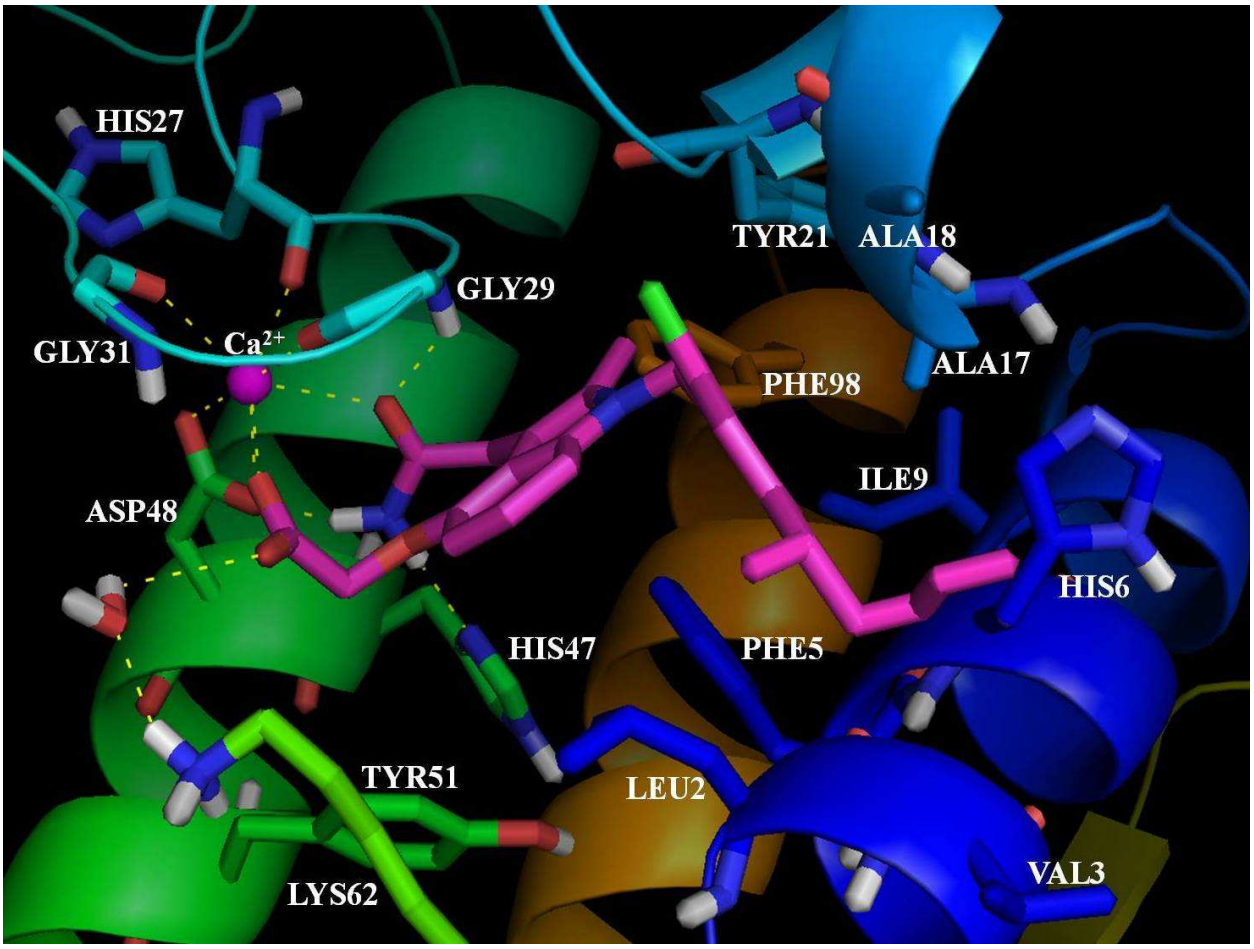


Figure 5. The binding of compound **N3** in the active site of the GIIA $sPLA_2$ enzyme. The enzyme-ligand complex was obtained by automated molecular docking of the compound in the enzyme active site using GLIDE.