Supplementary material

In Silico Mapping of Essential Residues into the Catalytic Domain of PDE5 Responsible for Stabilization of Its Commercial Inhibitors

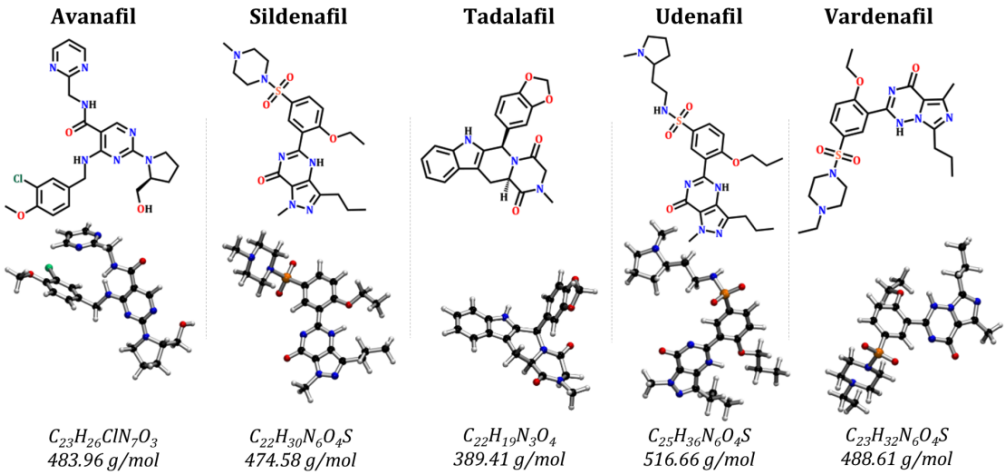

Figure S1. Chemical structures of the commercial inhibitors of phosphodiesterase type 5 (PDE5) enzyme and conformational arrangements after energy minimization of contacts between atoms.

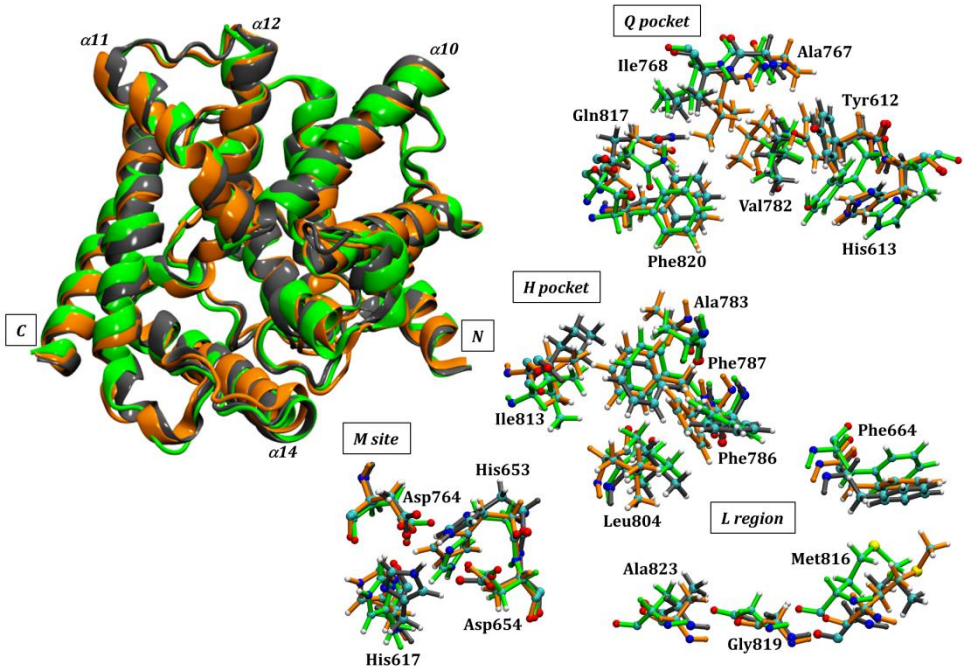

Figure S2. Details of the three-dimensional structure of the PDE5 enzyme showing an overlapping of the protein structures of the PDE5 enzyme used in the molecular docking studies. Some catalytic domain residues are highlighted: crystallographic 1XOZ (grey), structures MD1 (green) and MD2 (orange).

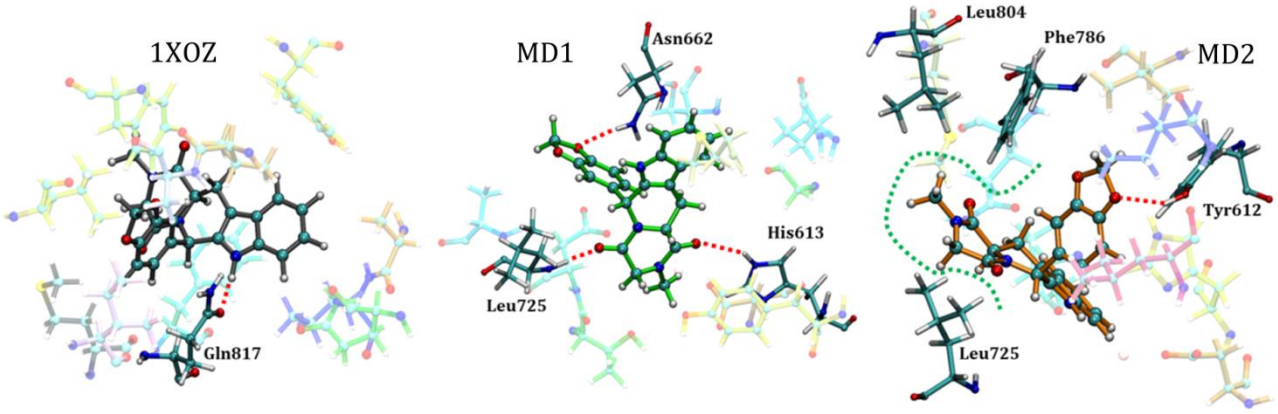

Figure S3. Residues identified in molecular docking were responsible for stabilizing the tadalafil inhibitor in the crystallographic structure and in two independent structures after 80 ns of Molecular Dynamics simulation (MD1 and MD2). Residues considered only at distance equal to or greater than 3.0 Å of the ligand (r ≤ 3.0 Å). Legend of interactions, red: hydrogen bond (and dipole-dipole); green: hydrophobic.

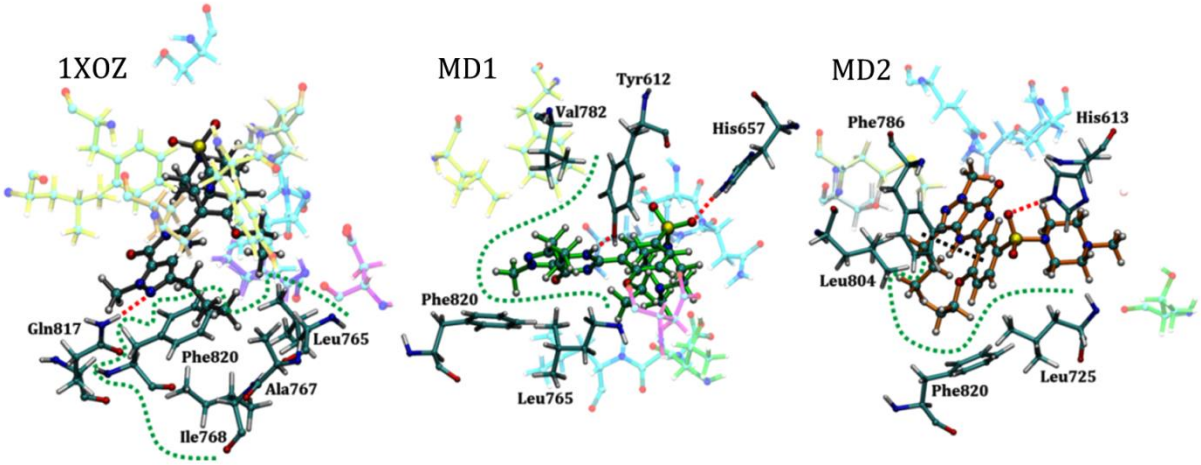

Figure S4. Residues identified in molecular docking were responsible for stabilizing the sildenafil inhibitor in the crystallographic structure and in two independent structures after 80 ns of Molecular Dynamics simulation (MD1 and MD2). Residues considered only at distance equal to or minor than 3.0 Å of the ligand (r ≤ 3.0 Å). Legend of interactions, red: hydrogen bond (and dipole-dipole); green: hydrophobic; black: π-stacking.

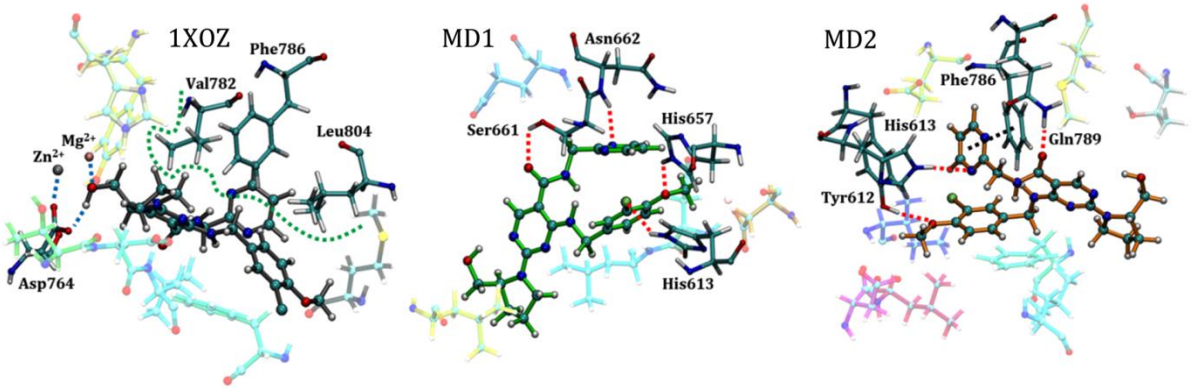

Figure S5. Residues identified in molecular docking were responsible for stabilizing the avanafil inhibitor in the crystallographic structure and in two independent structures after 80 ns of Molecular Dynamics simulation (MD1 and MD2). Residues considered only at distance equal to or minor than 3.0 Å of the ligand (r ≤ 3.0 Å). Legend of interactions, red: hydrogen bond (and dipole-dipole); green: hydrophobic; black: π-stacking; blue: metal-ligand.

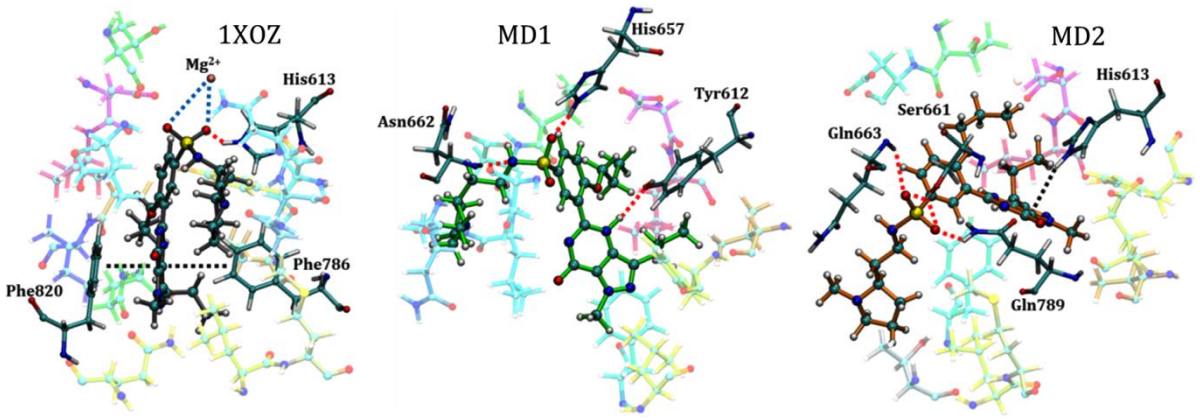

Figure S6. Residues identified in molecular docking were responsible for stabilizing the udenafil inhibitor in the crystallographic structure and in two independent structures after 80 ns of Molecular Dynamics simulation (MD1 and MD2). Residues considered only at distance equal to or minor than 3.0 Å of the ligand (r ≤ 3.0 Å). Legend of interactions, red: hydrogen bond (and dipole-dipole); black: π-stacking; blue: metal-ligand.

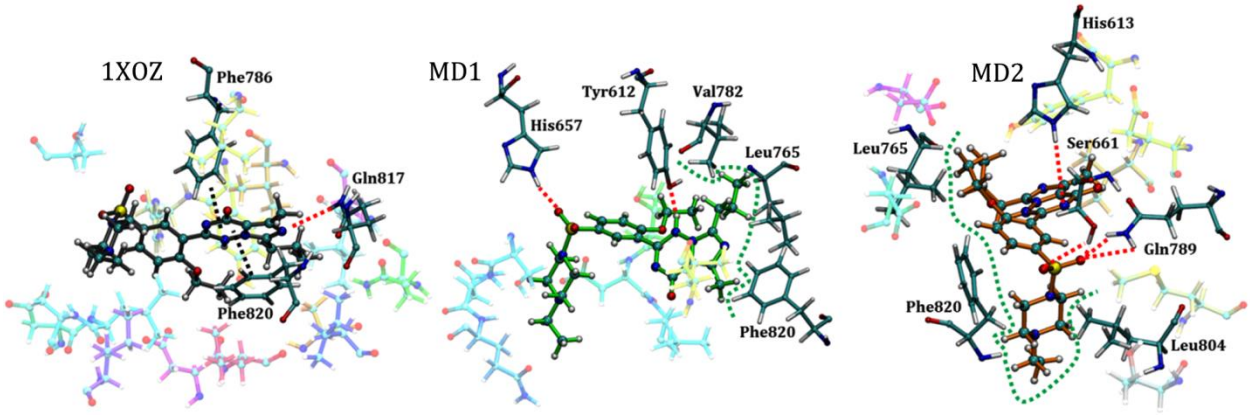

Figure S7. Residues identified in molecular docking were responsible for stabilizing the vardenafil inhibitor in the crystallographic structure and in two independent structures after 80 ns of Molecular Dynamics simulation (MD1 and MD2). Residues considered only at distance equal to or minor than 3.0 Å of the ligand (r ≤ 3.0 Å). Legend of interactions, red: hydrogen bond (and dipole-dipole); black: π-stacking; green: hydrophobic.

Table S1. RMSD values calculated for the structures used in molecular docking studies, obtained after 80 ns of Molecular Dynamics simulation. The crystallographic structure of PDE5 was used as a reference (PDBid:1XOZ).

RMSD / Å	**Structure MD1**	**Structure MD2**
All atoms of the PDE5 enzyme	1.8168	1.5478
Only Cα atoms of the backbone	1.2780	1.0791
Atoms of catalytic domain residues	1.6308	1.0085