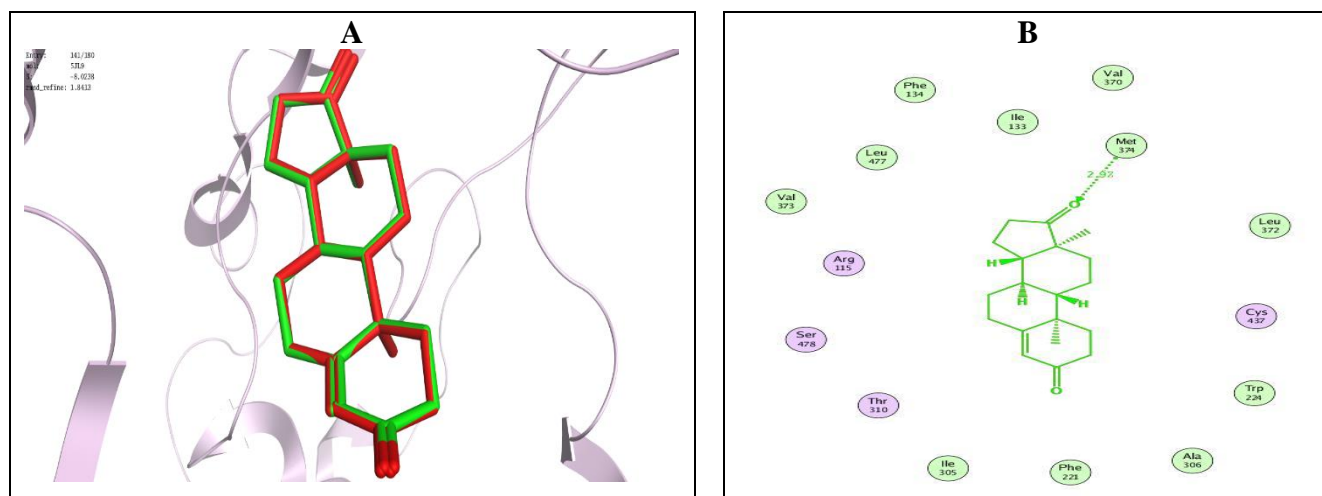
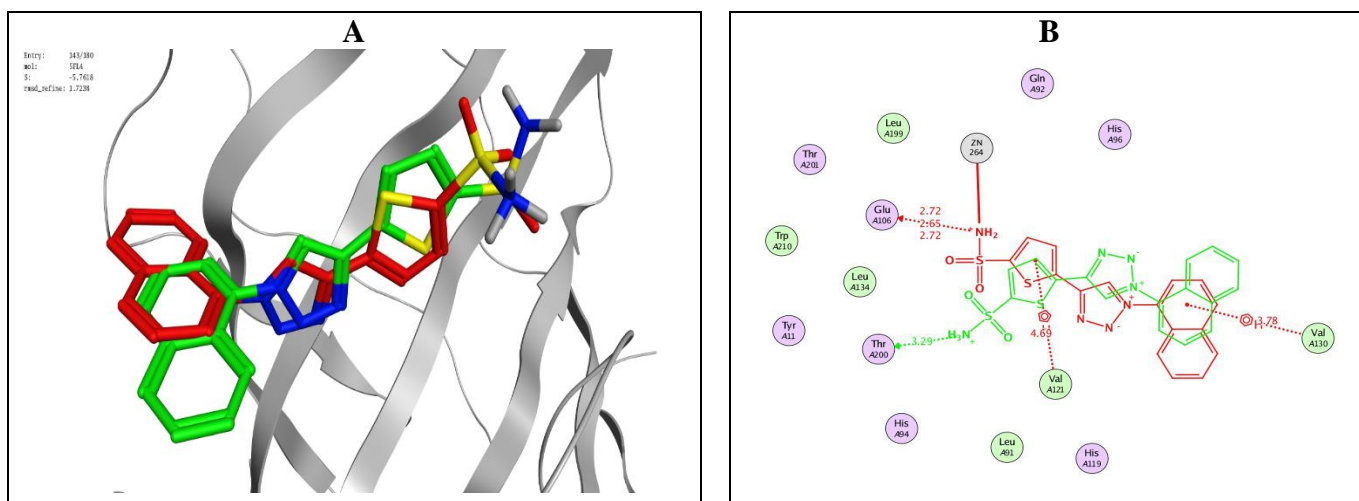


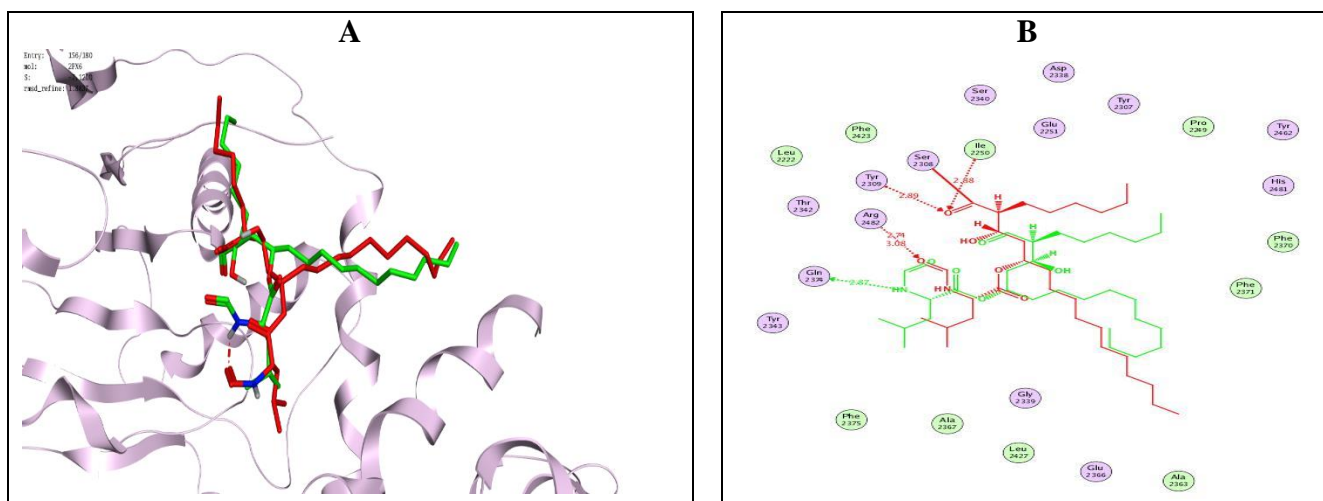
# Supplementary Materials



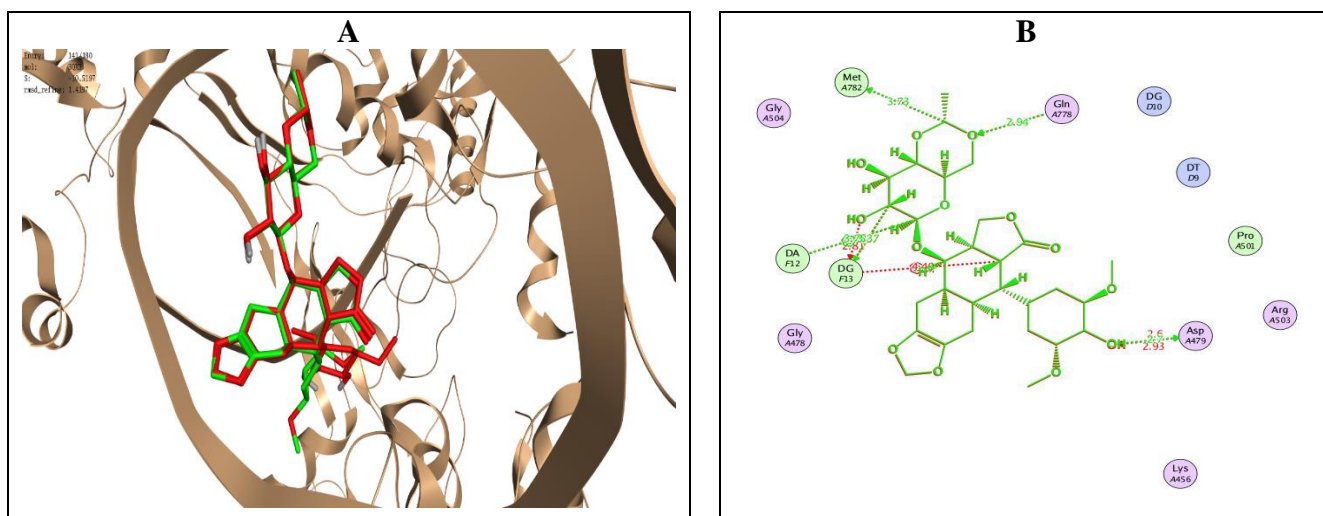
**Figure S1:** (A) 3D diagram and (B) 2D overlay disclosing the superimposition of the native co-crystallized ligand (green), and the redocked co-crystallized ligand (Red) at aromatase enzyme with RMSD value of 1.84 Å for docking program validation.



**Figure S2:** (A) 3D diagram and (B) 2D overlay disclosing the superimposition of the native co-crystallized ligand (green), and the redocked co-crystallized ligand (Red) at **CA IV** with RMSD value of 1.72 Å for docking program validation.



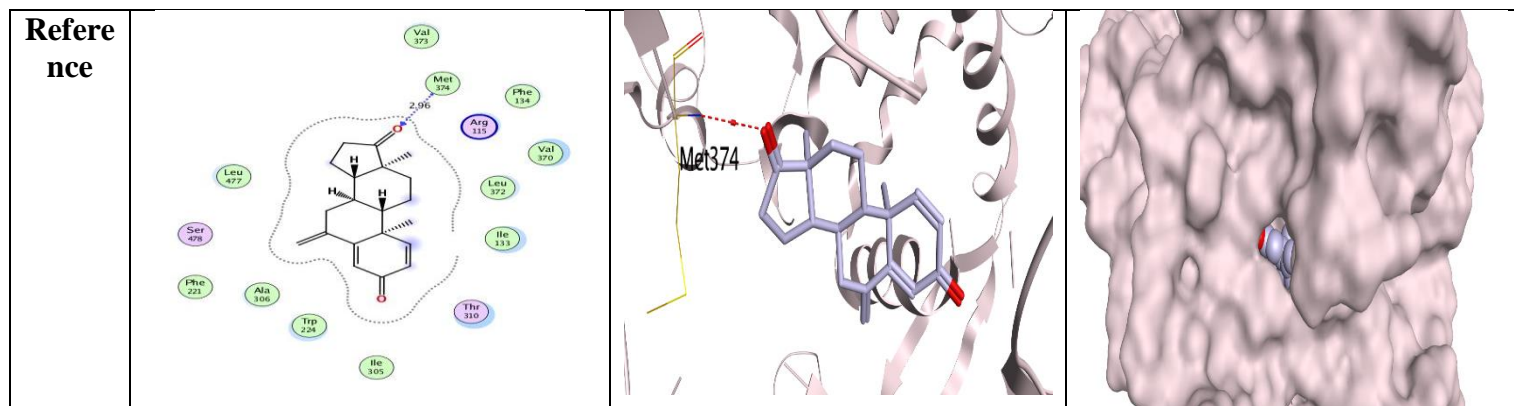
**Figure S3:** (A) 3D diagram and (B) 2D overlay disclosing the superimposition of the native co-crystallized ligand (green), and the redocked co-crystallized ligand (Red) at **FAS** with RMSD value of 1.88 Å for docking program validation.



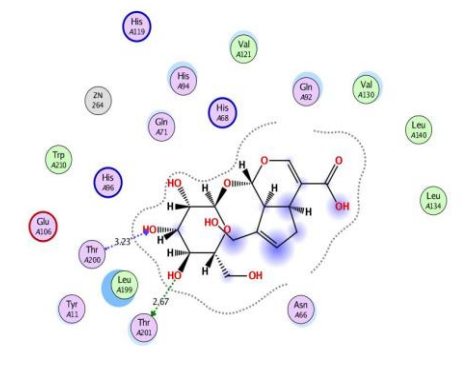
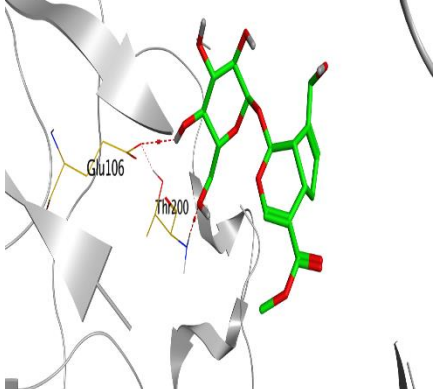
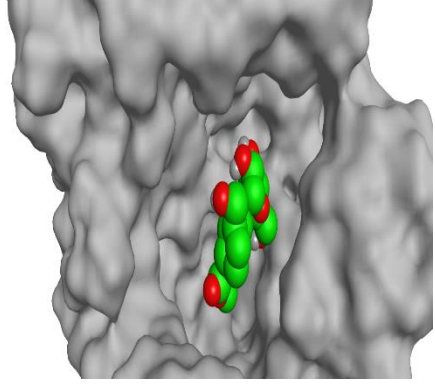
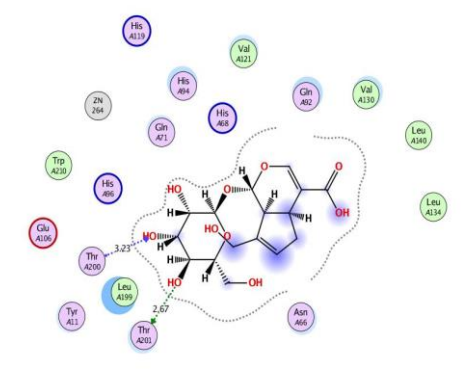
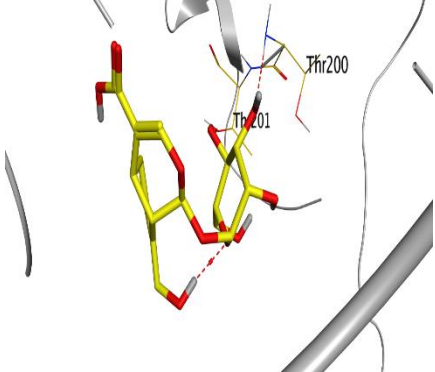
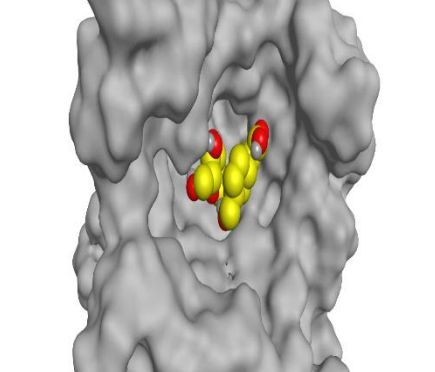
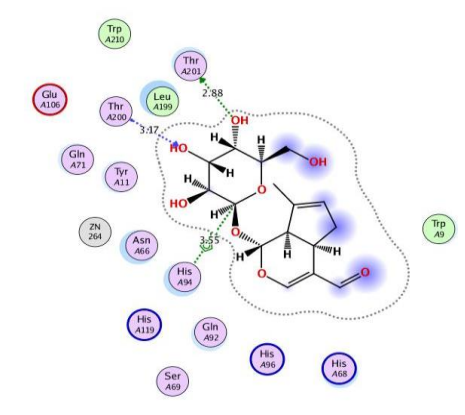
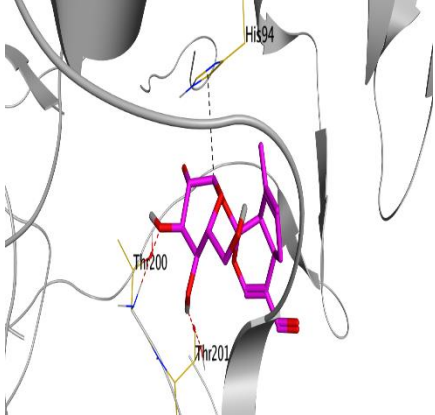
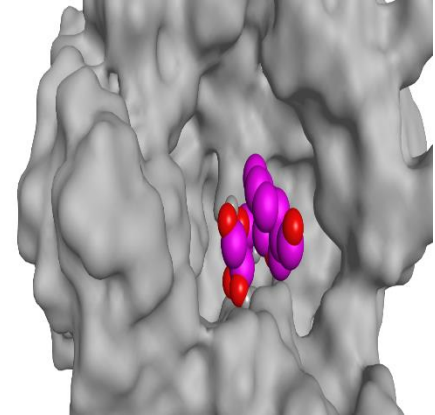
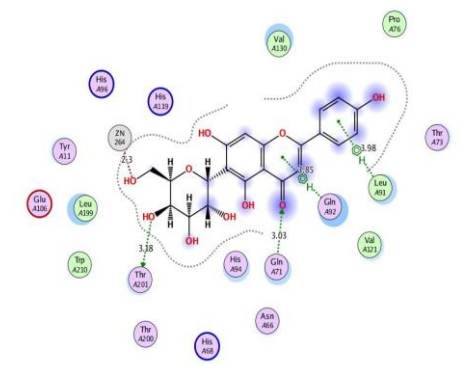
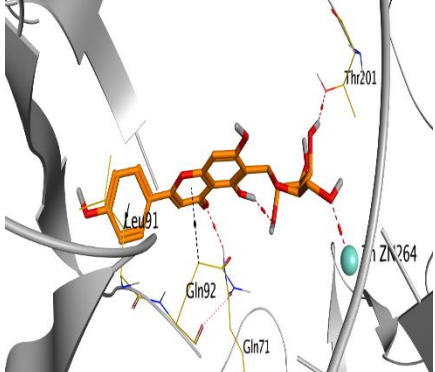
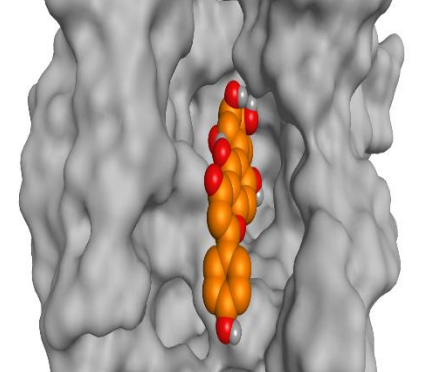
**Figure S4:** (A) 3D diagram and (B) 2D overlay disclosing the superimposition of the native co-crystallized ligand (green), and the redocked co-crystallized ligand (Red) at **TOP II** with RMSD value of 1.42 Å for docking program validation.

Aromatase			
Comp no.	2D	3D	3D protein
1			
2			
3			
4			

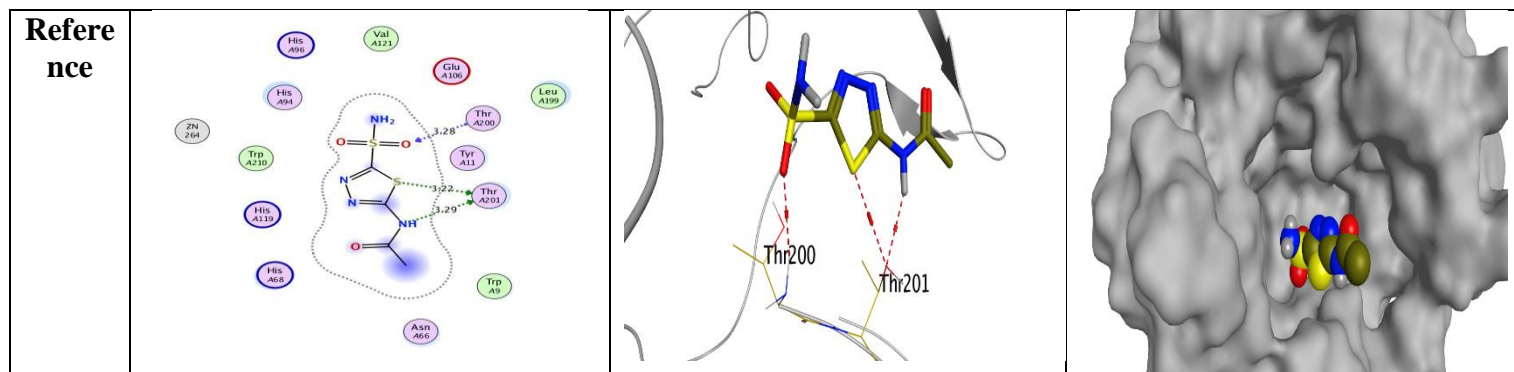
<p>5</p>			
<p>6</p>			
<p>7</p>			
<p>Co-crystallized</p>			



**Figure S5:** the 2D, 3D, and 3D protein positioning of all investigated compound at the biological target, aromatase.

CA IX			
Comp no.	2D	3D	3D protein
1			
2			
3			
4			

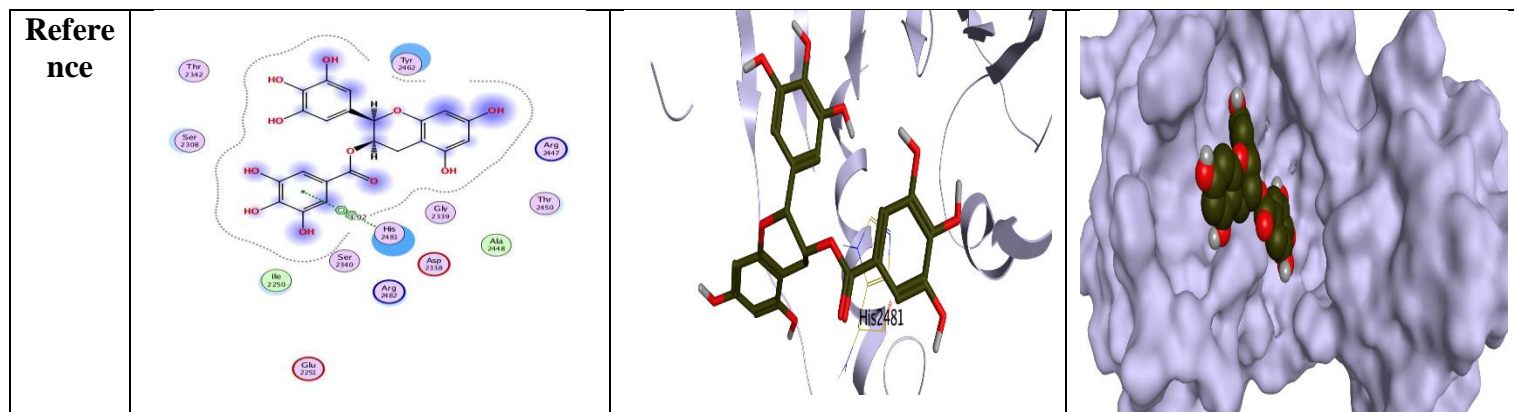
5			
6			
7			
Co-crystallized			



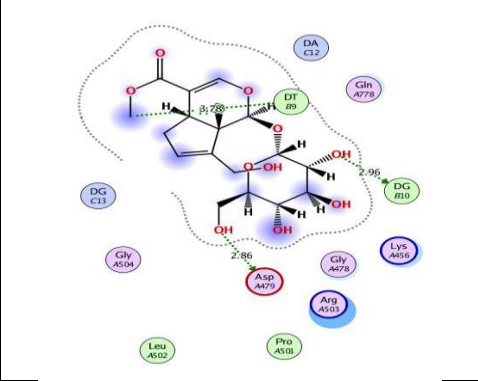
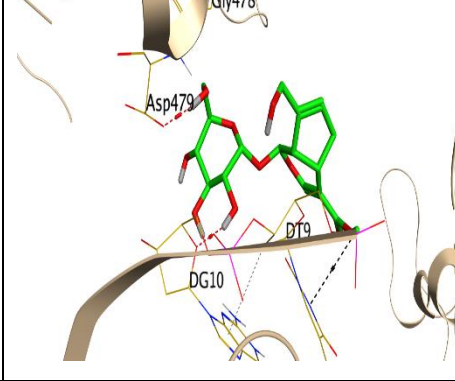
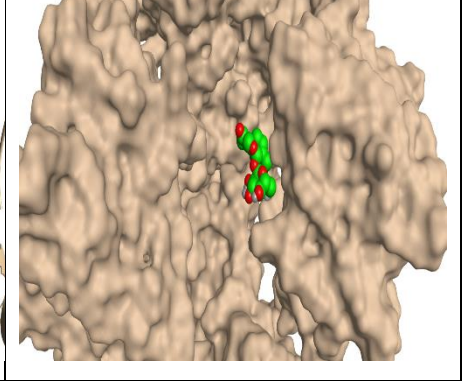
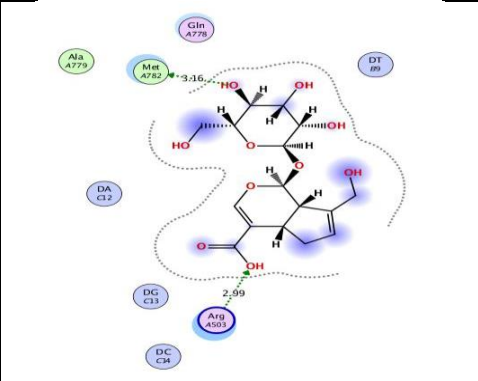
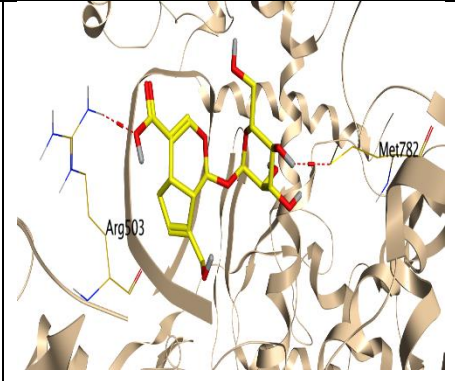
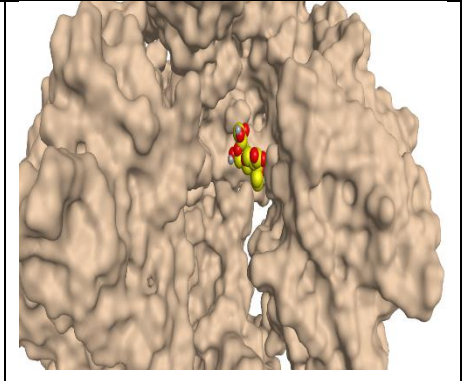
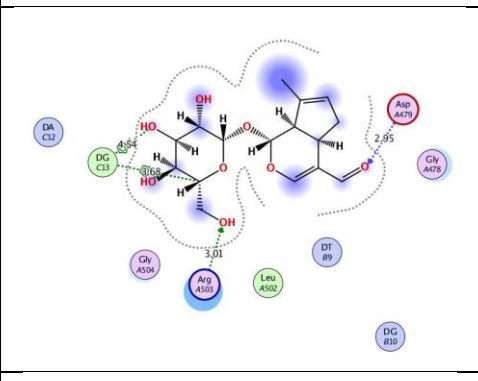
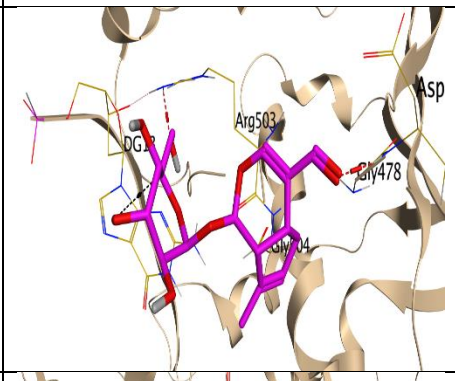
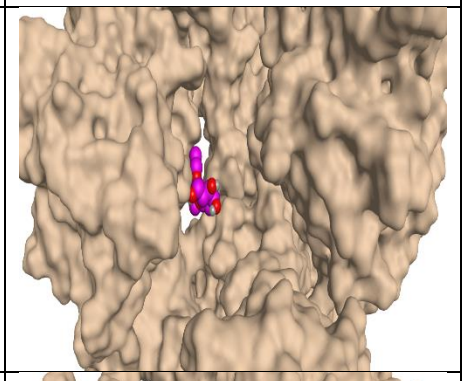
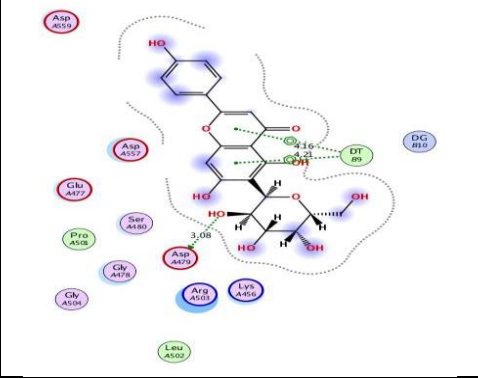
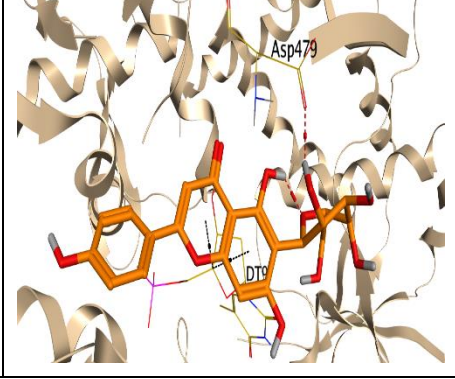
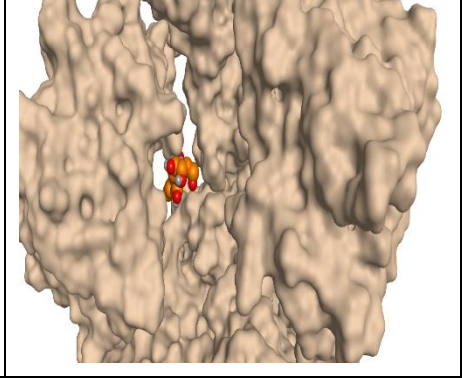
**Figure S6:** the 2D, 3D, and 3D protein positioning of all investigated compound at the biological target, CA IX.

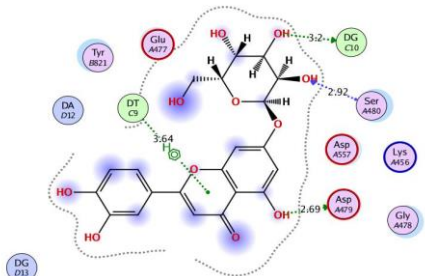
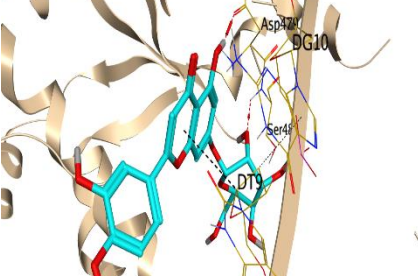
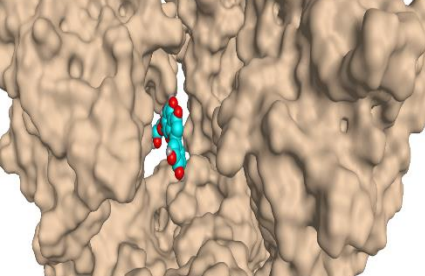
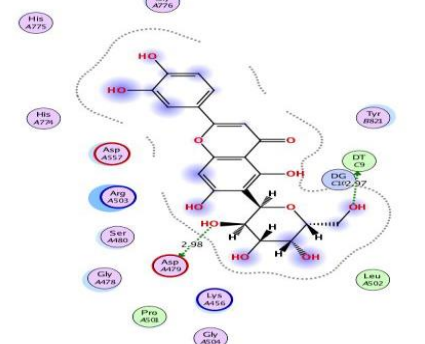
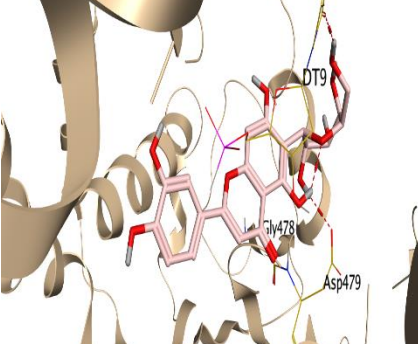
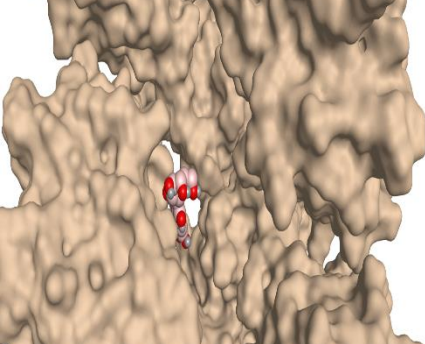
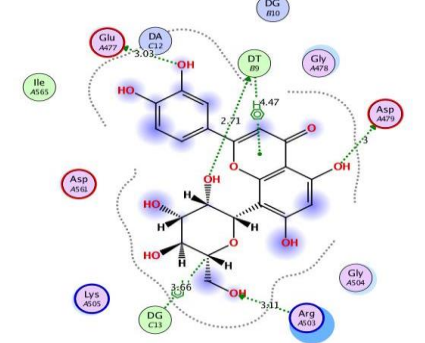
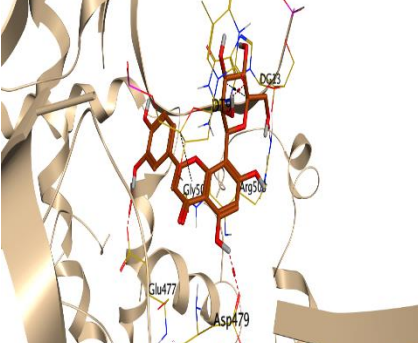
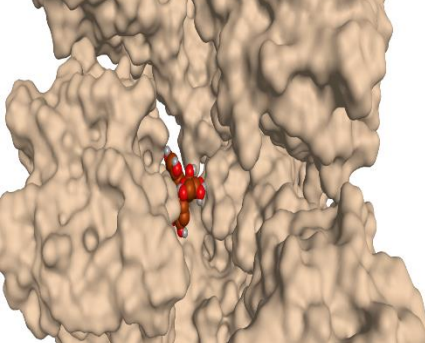
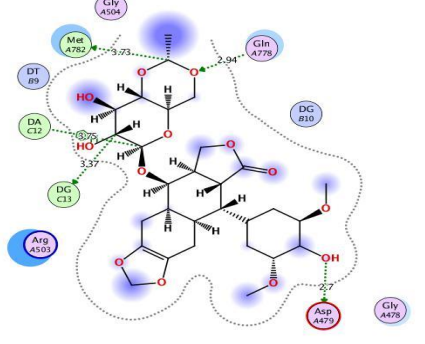
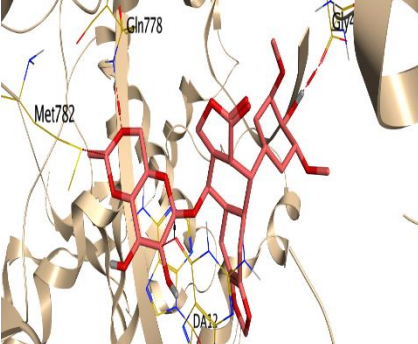
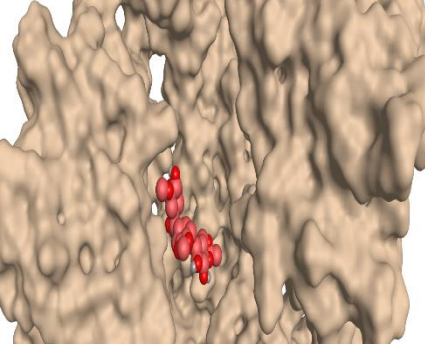
FAS			
Comp no.	2D	3D	3D protein
1			
2			
3			
4			

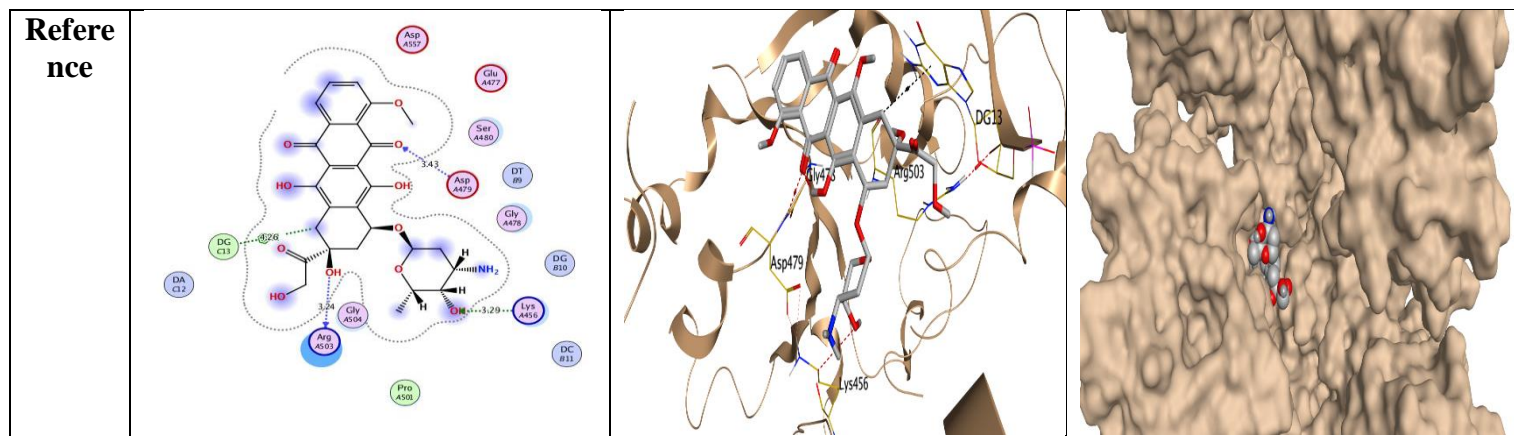
<p>5</p>			
<p>6</p>			
<p>7</p>			
<p>Co-crystallized</p>			



**Figure S7:** the 2D, 3D, and 3D protein positioning of all investigated compound at the biological target, FAS.

TOP II			
Comp no.	2D	3D	3D protein
1			
2			
3			
4			

5	 <p>Chemical structure of a flavonoid molecule (likely a flavan-3-ol) showing interactions with residues: Glu A477, Tyr B621, DA D12, DT C9, Ser A480, Asp A455, Lys A456, Asp A479, Gly A478, and DG D11. Distances are indicated: 3.2, 2.92, 3.64, 2.69.</p>	 <p>3D ribbon diagram of the protein structure showing the binding site with residues Asp479, Ser480, and DT9.</p>	 <p>Surface representation of the protein structure showing the binding site.</p>
6	 <p>Chemical structure of a flavonoid molecule (likely a flavan-3-ol) showing interactions with residues: His A478, Glu A776, Tyr B621, Asp A455, Ser A480, Gly A478, Asp A479, Lys A456, Pro A458, Glu A454, and DG C10. Distances are indicated: 2.98, 3.03, 4.47, 3.96, 3.31.</p>	 <p>3D ribbon diagram of the protein structure showing the binding site with residues DT9, Gly478, and Asp479.</p>	 <p>Surface representation of the protein structure showing the binding site.</p>
7	 <p>Chemical structure of a flavonoid molecule (likely a flavan-3-ol) showing interactions with residues: Glu A477, DA D12, DT C9, Glu A478, Asp A479, Asp A455, Lys A456, DG C10, and Arg A450. Distances are indicated: 3.03, 4.47, 3.96, 3.31.</p>	 <p>3D ribbon diagram of the protein structure showing the binding site with residues Glu477, Asp479, and Arg450.</p>	 <p>Surface representation of the protein structure showing the binding site.</p>
Co-crystallized	 <p>Chemical structure of a flavonoid molecule (likely a flavan-3-ol) showing interactions with residues: Glu A504, Met A782, DT C9, DA D12, DG C10, Asp A479, Gly A478, Lys A456, and Pro A458. Distances are indicated: 3.73, 3.94, 3.31, 3.96.</p>	 <p>3D ribbon diagram of the protein structure showing the binding site with residues Glu778, Met782, Asp479, and DA12.</p>	 <p>Surface representation of the protein structure showing the binding site.</p>



**Figure S8:** the 2D, 3D, and 3D protein positioning of all investigated compound at the biological target, TOP II.