Supporting Information

HOMOLOGY MODELING OF LEISHMANOLYSIN (gp63) FROM *Leishmania panamensis* AND MOLECULAR DOCKING OF FLAVONOIDS

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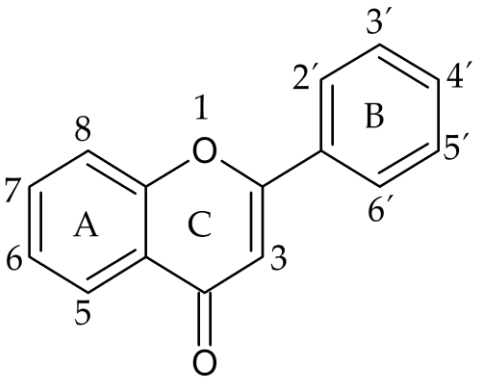
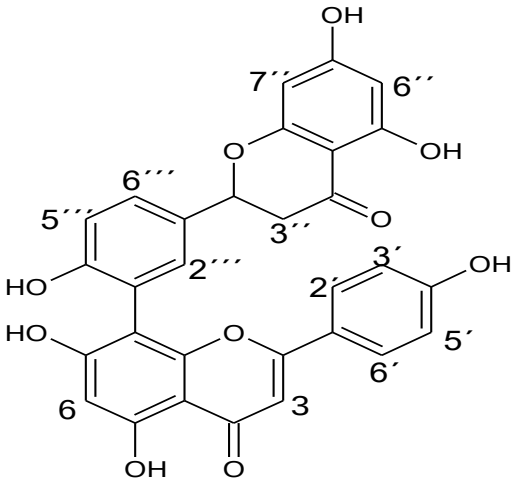
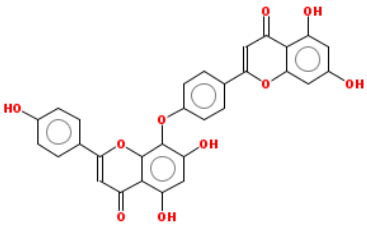
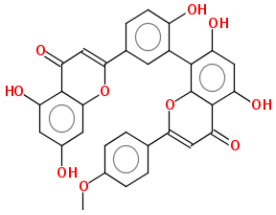
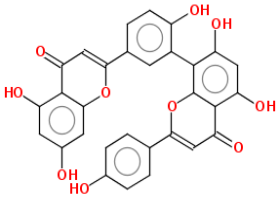
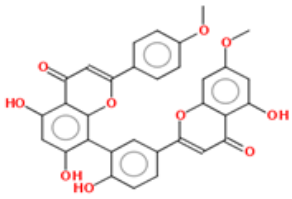
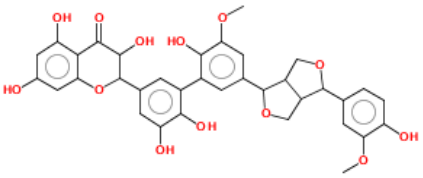
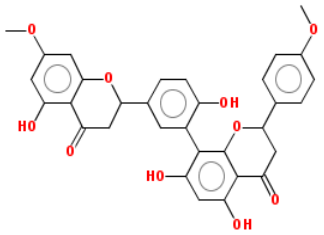
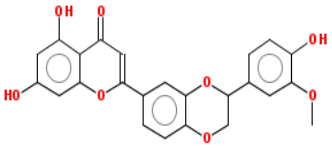
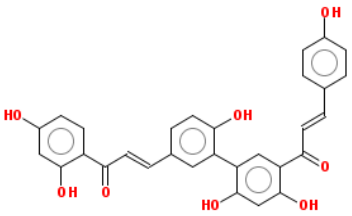
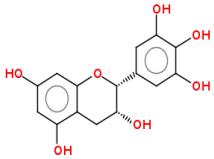
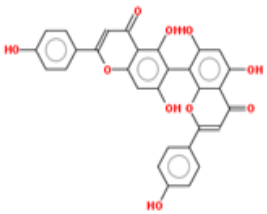
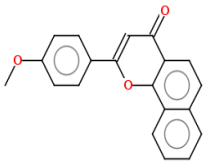
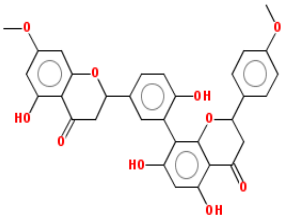
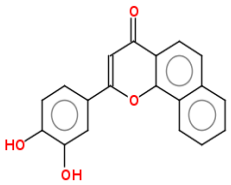
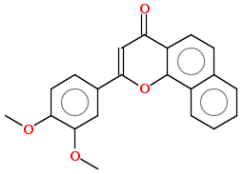
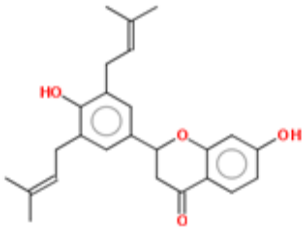
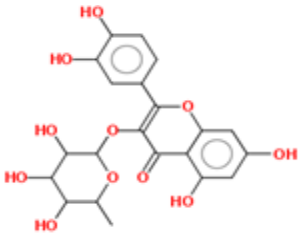
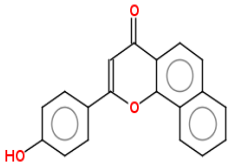
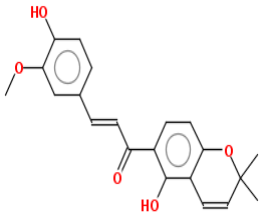
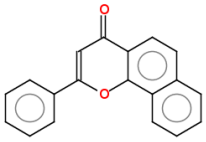
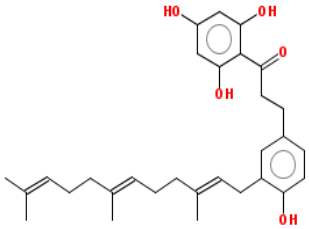
Table S1. The chemical structure of the 24 molecules that resulted from the virtual screening with the best free binding energy.





Structure	Name	Reference
	Lanaroflavone	Ramirez et al. (2010)
	Podocarpusflavone A	Nisha et al. (2014)
	Amentoflavone	Nisha et al. (2014)
	Podocarpusflavone B	Nisha et al. (2014)

	Pseudotsuganol	Ogungbe et al. (2014)
	Tetrahidrorobustaflavone	Ogungbe et al. (2014)
	2,3-Dehidrosolibinin	Banerjee et al. (2015)
	Rhuschalcone VI	Ogungbe et al. (2014)
	Epigallocatechin	Ramirez et al. (2010)
	Agathisflavone	
	SN00000577	Banerjee et al. (2015)
	Metyltetrahydroamentoflavone	Ogungbe et al. (2014)

	SN00000355	Banerjee et al. (2015)
	SN00000558	Banerjee et al. (2015)
	Abyssinone IV	Banerjee et al. (2015)
	Quecitrin	Ramirez et al. (2010)
	SN00000365	Banerjee et al. (2015)
	4-hidroxylanchocarpin	Ramírez et al. (2010)
	SN00000328	Banerjee et al. (2015)
	Bipinnatone A	Banerjee et al. (2015)

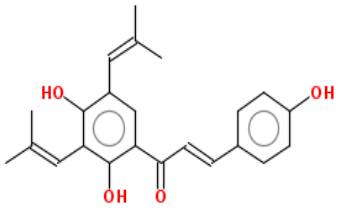
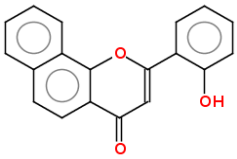
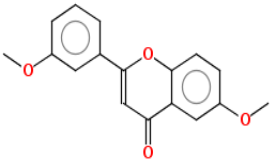
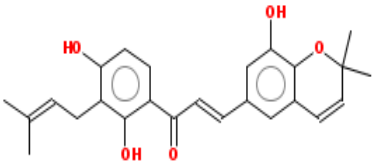
	Medicagenina	Ramirez et al. (2010)
	SN00000367	Banerjee et al. (2015)
	SN00000357	Banerjee et al. (2015)
	SN00157618	Banerjee et al. (2015)

Table S2. The solvent-Surface area accessible of the main amino acid residues of the proteins that interact with the docked flavonoids.

1LML (ASA Area, Å²)					
Amino acid	**Native**	**Amentoflavone**	**Lanaroflavone**	**Podocarpusflavone A**	**Podocarpusflavone B**
LEU224	30.564	10.899	9.197	5.451	14.190
HIS264	14.481	4.672	4.382	4.382	6.289
GLU265	17.318	8.621	7.235	8.082	9.005
HIS268	17.513	17.513	17.513	17.513	17.513
HIS334	4.085	2.840	3.048	3.151	3.255
GLN341	18.376	3.031	2.569	8.210	1486
ALA346	1.029	1.029	1.029	1.029	1.029
ALA349	59.531	9.987	9.987	11.296	11349
ZN	20.655	9.760	9.420	9.760	8.739
lpgp63 (ASA Area, Å²)					
LEU222	33.532	9.874	11.916	6.355	16.002
ALA223	9.242	0.462	0.000	0.231	3.233
HIS262	8.641	2.834	2.834	2.834	2.834
GLU263	18.241	8.709	7.389	8.164	9.478
HIS266	12.398	12.398	12.398	12.398	12.398
HIS332	2.904	1.763	1.763	1.763	1.970
LYS339	16.213	6.513	6.059	9.918	4.244
ZN	20.655	9.647	9.306	9.647	8.625

Table S3. Validation data for the proteins studied.

Parameter	1LML	lpgp63
AUC[a]	0.926 ± 0.026	0.928 ± 0.017
EF[1%]	45	44
R[b]	0,794	0,775

[a] Expressed as the mean standard deviation.

[b] P value < 0.05

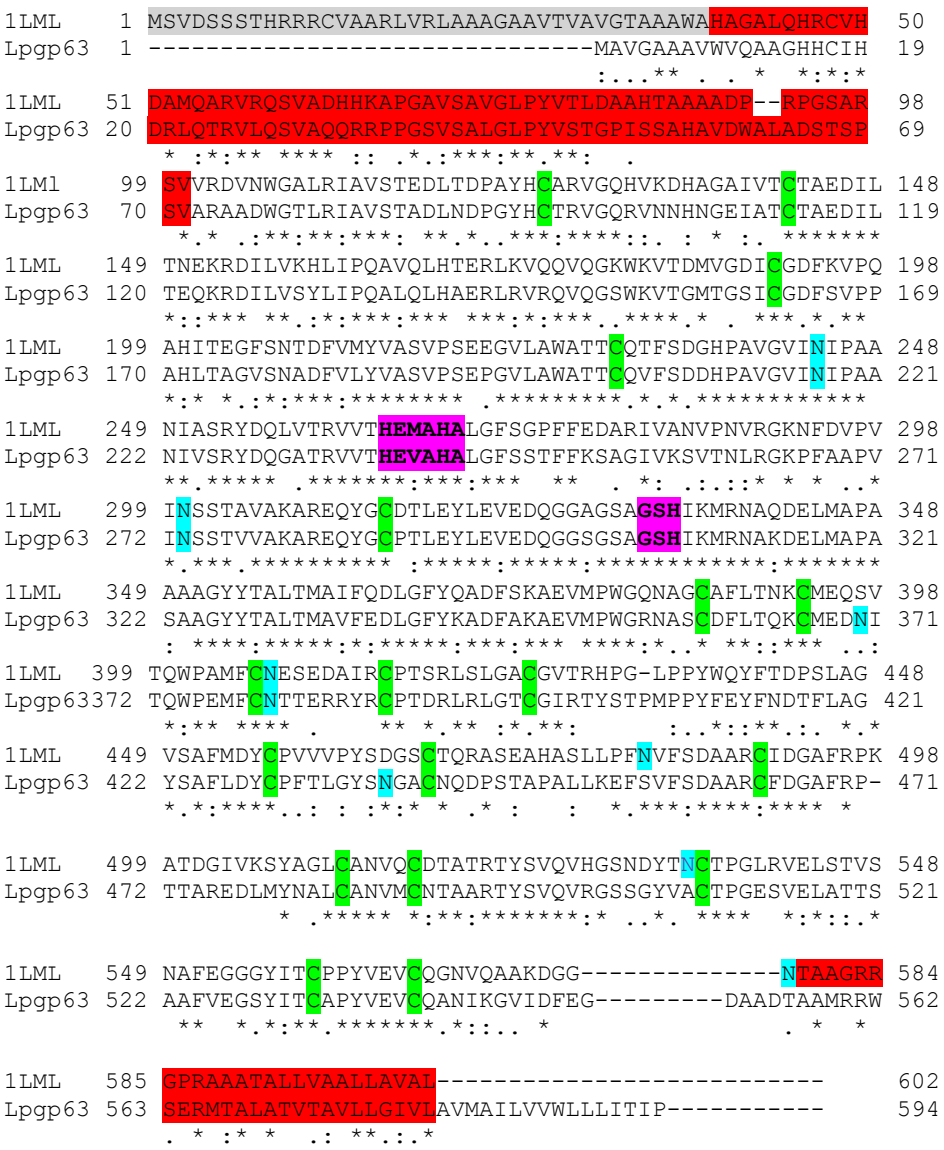


Figure S1. Alignments of leishmanolysin of *L. major* (1LML) and *L. panamensis* (Lpgp63). The catalytic residues are highlighted in magenta; nine disulfides bond in green; glycosylation sites in blue; signal peptide and propeptide in gray and red, respectively.

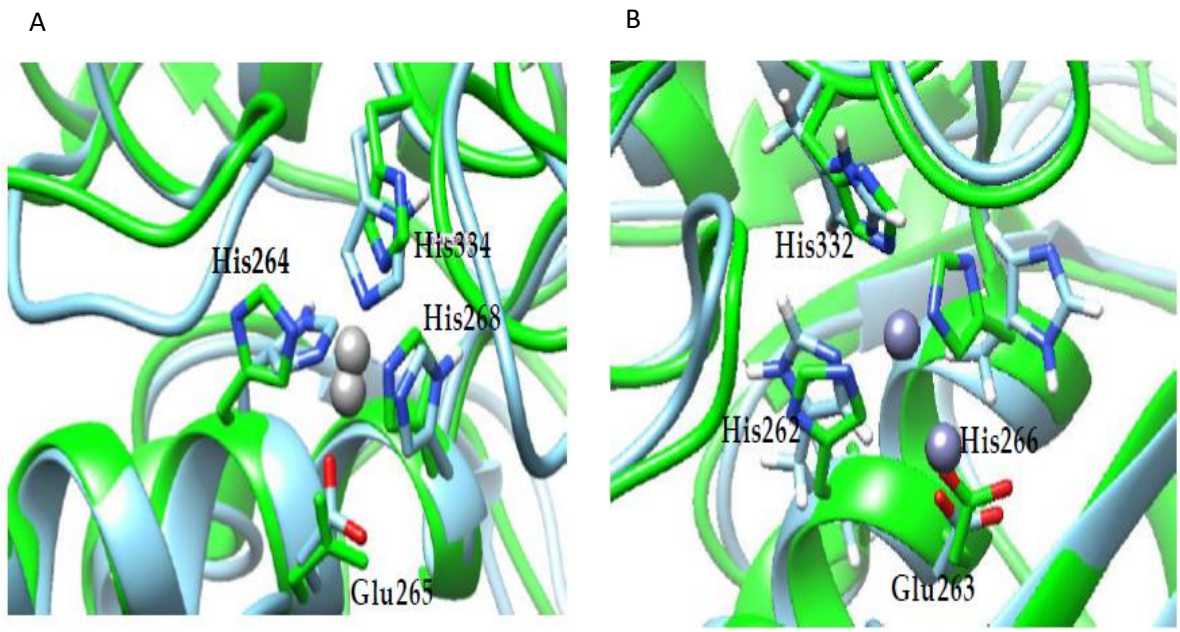


Figure S2. Superimposition between the MD-simulated structures and Initial Model. Average structures from the last 200 ns of the MD simulations in the residues of the active site are displayed. Initial models are in green and those optimized in cyan. A) 1LML, B) and B) Lpgp63. The change in the distance between the nitrogen-ε and the zinc atom is observed, as well as the approximation to the Glu residue.

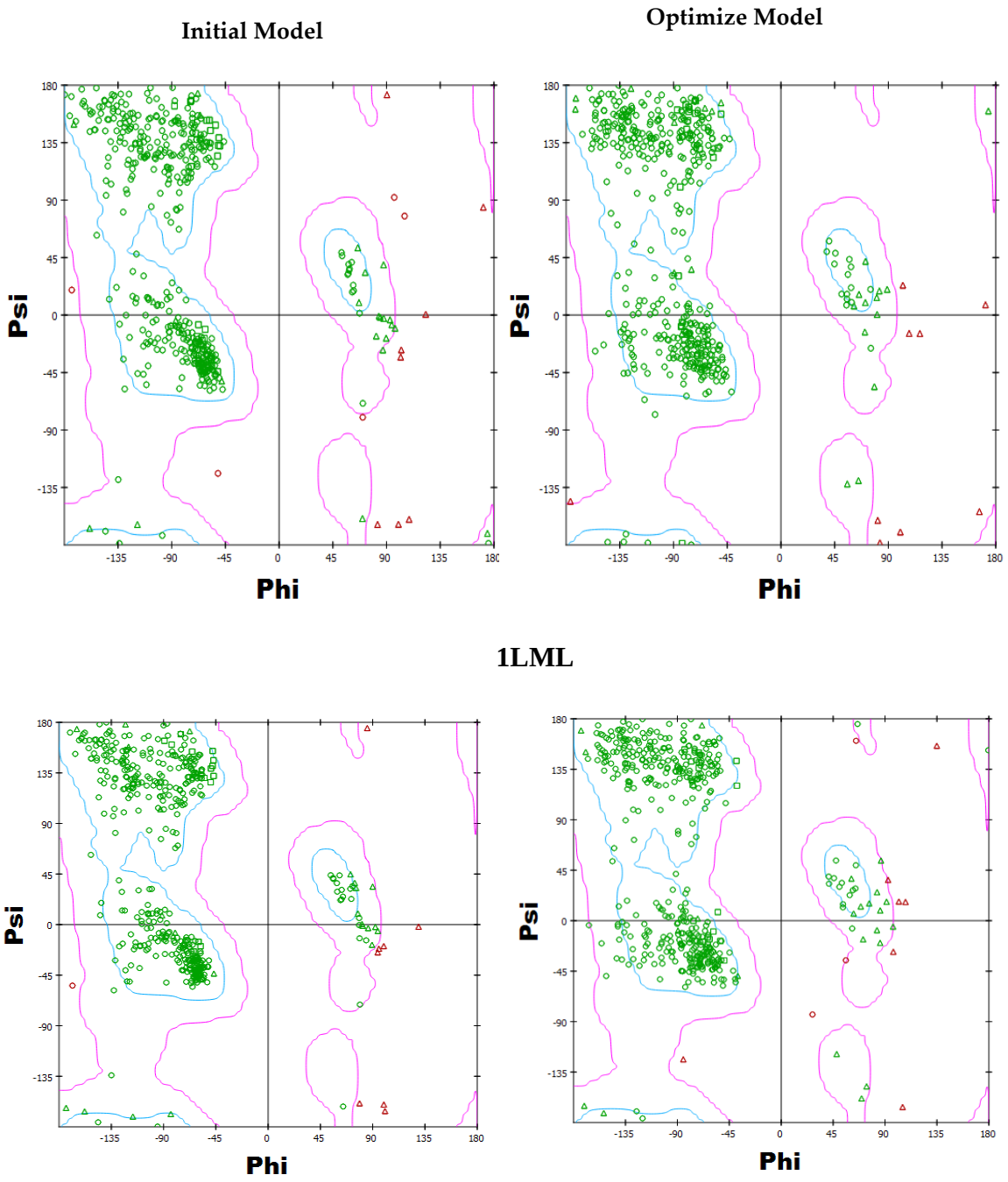
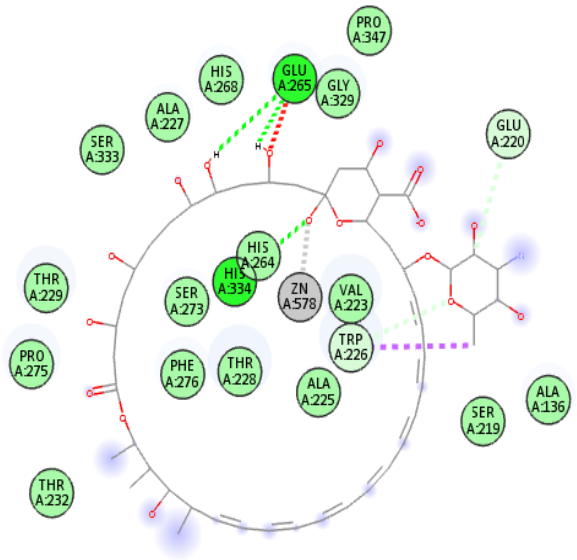


Figure S3. The Ramachandran plots of the initial and the optimized models after 200 ns of MD simulation.

1LML



Lpgp63

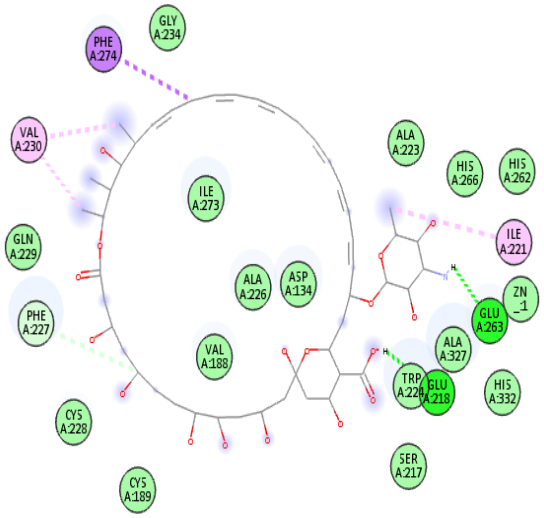


Figure S4. Interactions of amphotericin B with amino acid of the active site from leishmanolysin of 1LML and lpgp63.

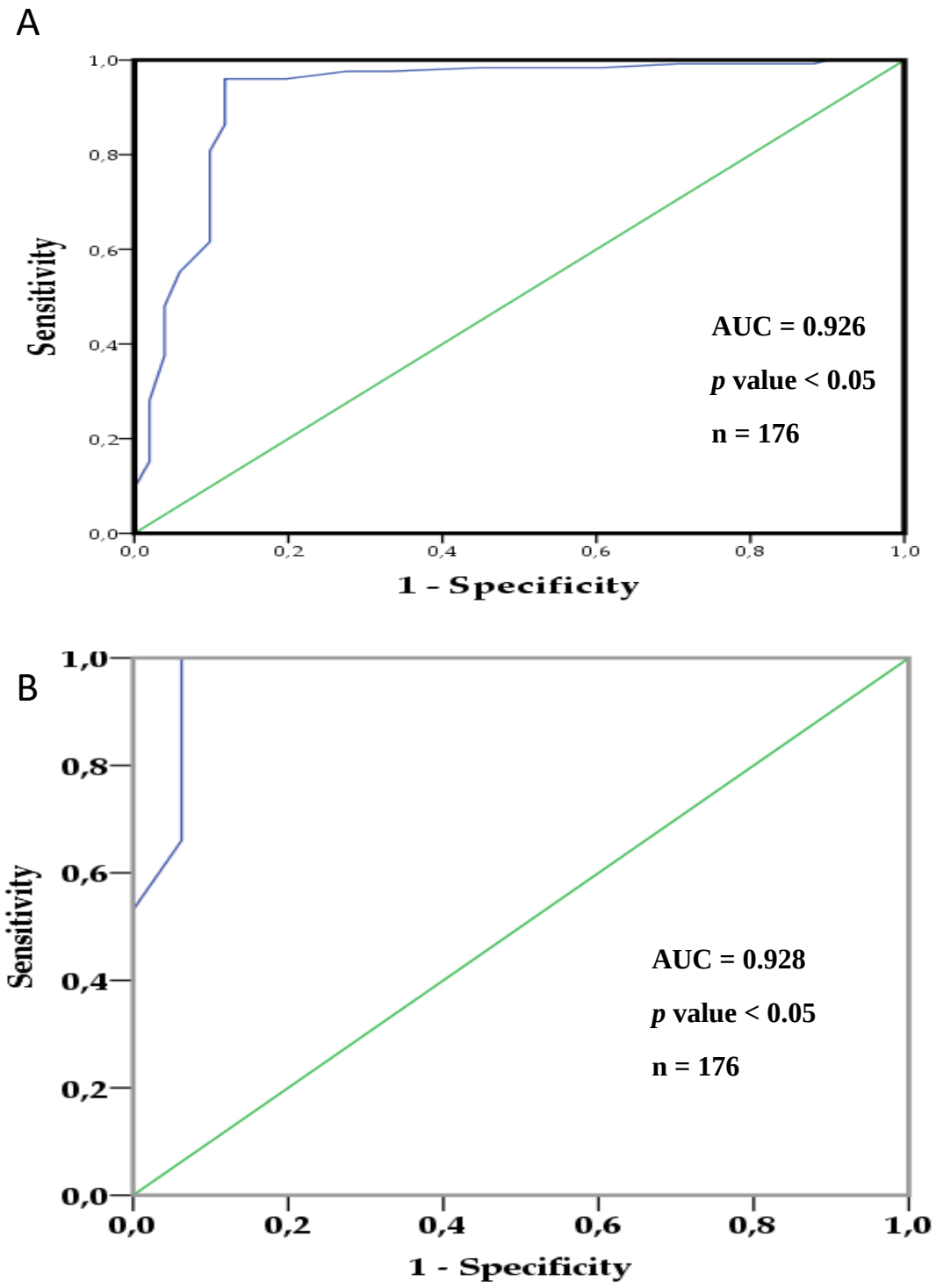
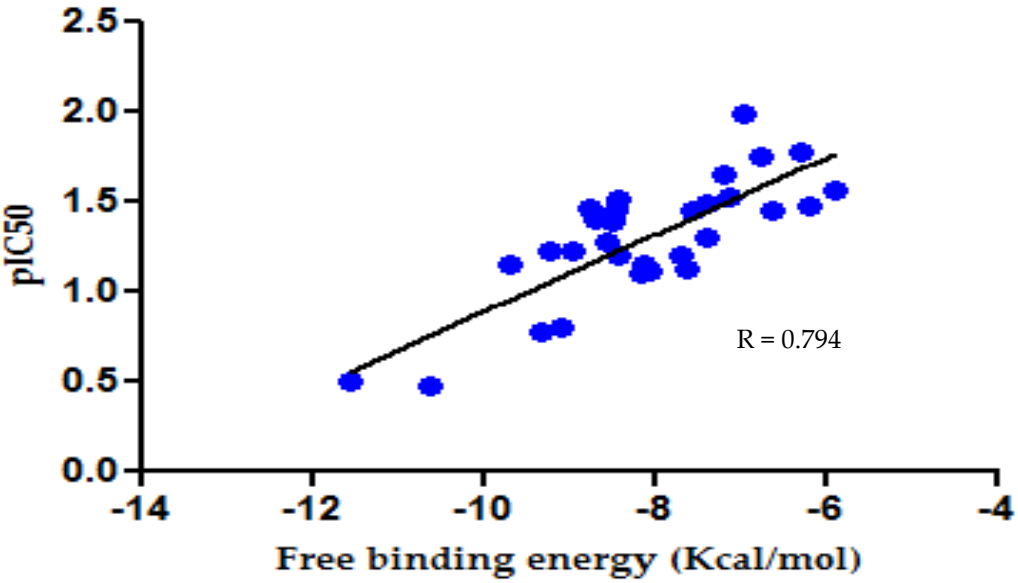


Figure S5. The ROC curve generated by screening virtual of flavonoids ligands from (A) 1LML (B)LpGp63.

A



B

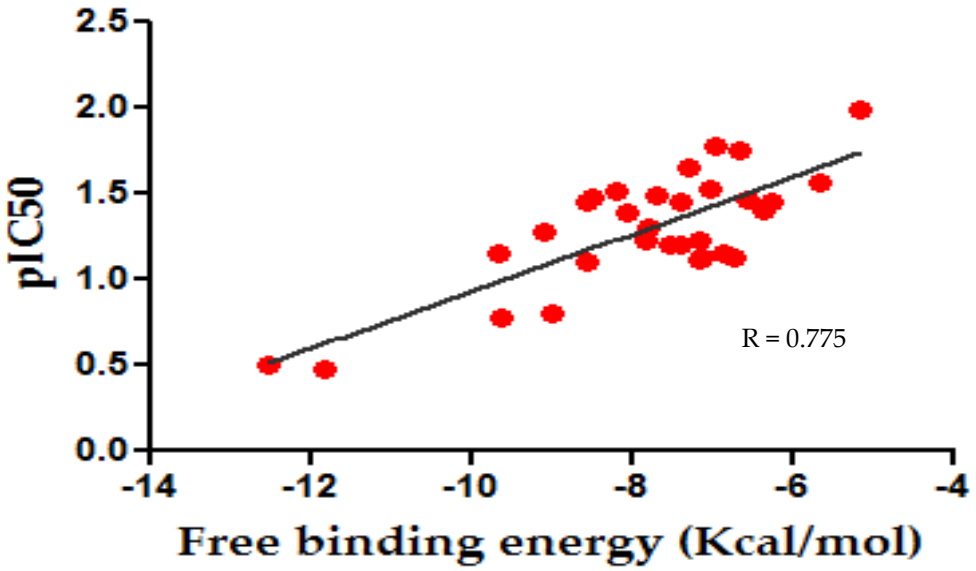


Figure S6. Analysis of correlation between affinities versus pIC50 of flavonoids with antileishmanial activity for modeled proteins. A) 1LML B) LpGp63.