

## Supporting Information

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

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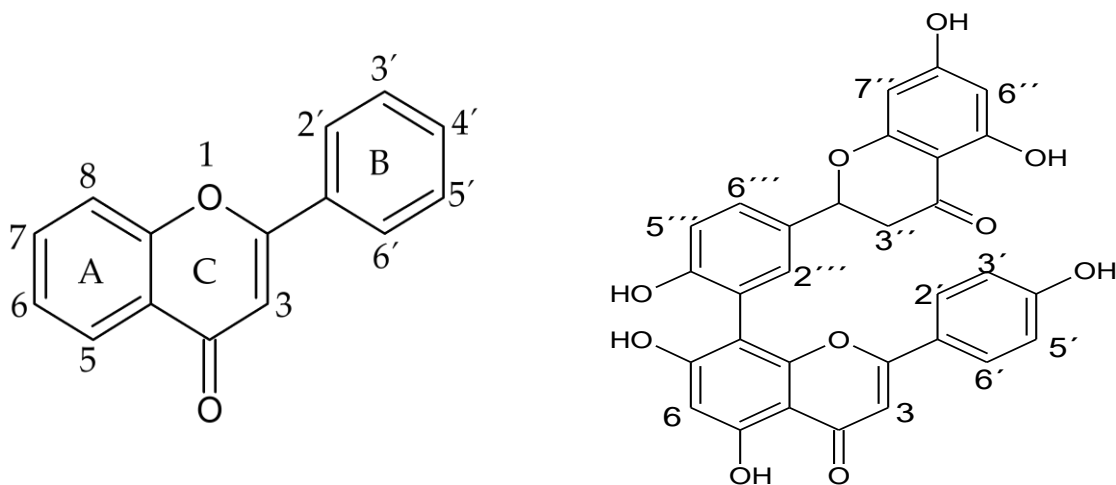
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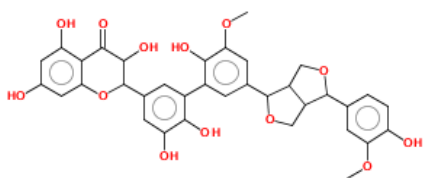
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**Table S1.** The chemical structure of the 24 molecules that resulted from the virtual screening with the best free binding energy.

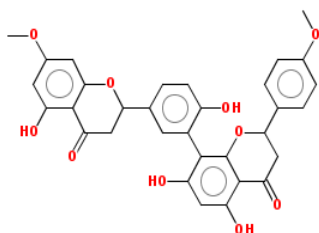


Structure	Name	Reference
	Lanaroflavone	Ramirez et al. (2010)
	Podocarpusflavone A	Nisha et al. (2014)
	Amentoflavone	Nisha et al. (2014)
	Podocarpusflavone B	Nisha et al. (2014)



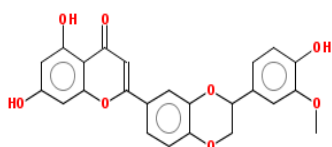
Pseudotsuganol

Ogungbe et al. (2014)



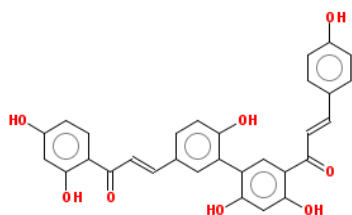
Tetrahidrorobustaflavone

Ogungbe et al. (2014)



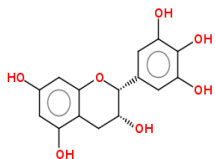
2,3-Dehidrosolibinin

Banerjee et al. (2015)



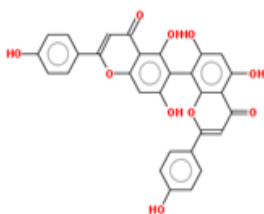
Rhuschalcone VI

Ogungbe et al. (2014)

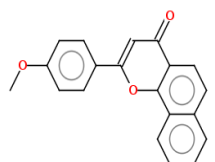


Epigallocatechin

Ramirez et al. (2010)

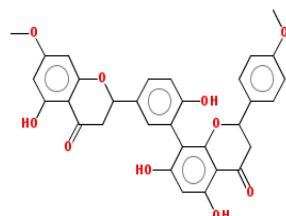


Agathisflavone



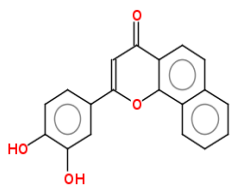
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Banerjee et al. (2015)



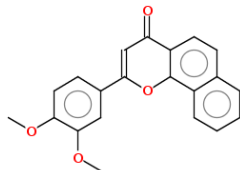
Metyltetrahydroamentoflavone

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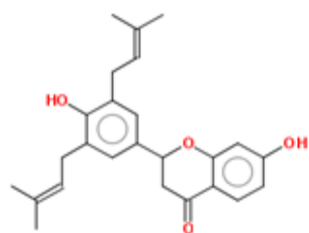
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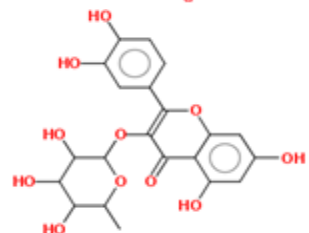
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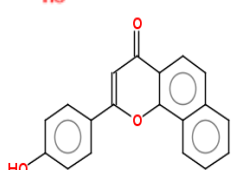
Abyssinone IV

Banerjee et al. (2015)



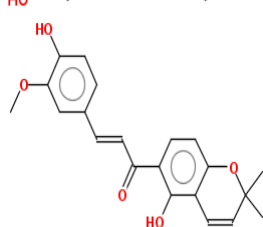
Quecitrin

Ramirez et al. (2010)



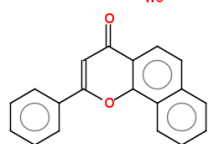
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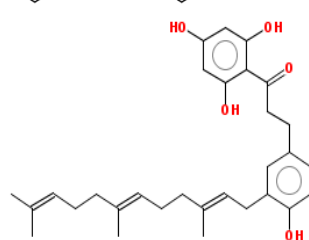
4-hydroxylanchoarpin

Ramírez et al. (2010)



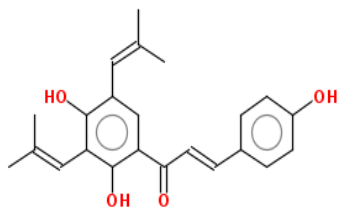
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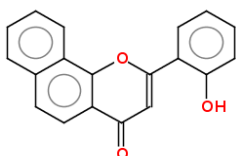
Bipinnatone A

Banerjee et al. (2015)



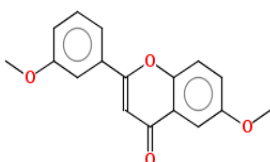
Medicagenina

Ramirez et al. (2010)



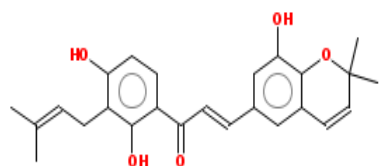
SN00000367

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.

<b>1LML (ASA Area, Å<sup>2</sup>)</b>					
<b>Amino acid</b>	<b>Native</b>	<b>Amentoflavone</b>	<b>Lanaroflavone</b>	<b>Podocarpusflavone A</b>	<b>Podocarpusflavone B</b>
<b>LEU224</b>	30.564	10.899	9.197	5.451	14.190
<b>HIS264</b>	14.481	4.672	4.382	4.382	6.289
<b>GLU265</b>	17.318	8.621	7.235	8.082	9.005
<b>HIS268</b>	17.513	17.513	17.513	17.513	17.513
<b>HIS334</b>	4.085	2.840	3.048	3.151	3.255
<b>GLN341</b>	18.376	3.031	2.569	8.210	1486
<b>ALA346</b>	1.029	1.029	1.029	1.029	1.029
<b>ALA349</b>	59.531	9.987	9.987	11.296	11349
<b>ZN</b>	20.655	9.760	9.420	9.760	8.739
<b>lpgp63 (ASA Area, Å<sup>2</sup>)</b>					
<b>LEU222</b>	33.532	9.874	11.916	6.355	16.002
<b>ALA223</b>	9.242	0.462	0.000	0.231	3.233
<b>HIS262</b>	8.641	2.834	2.834	2.834	2.834
<b>GLU263</b>	18.241	8.709	7.389	8.164	9.478
<b>HIS266</b>	12.398	12.398	12.398	12.398	12.398
<b>HIS332</b>	2.904	1.763	1.763	1.763	1.970
<b>LYS339</b>	16.213	6.513	6.059	9.918	4.244
<b>ZN</b>	20.655	9.647	9.306	9.647	8.625

**Table S3.** Validation data for the proteins studied.

<b>Parameter</b>	<b>1LML</b>	<b>lpgp63</b>
<b>AUC<sup>a</sup></b>	0.926 ± 0.026	0.928 ± 0.017
<b>EF<sup>1%</sup></b>	45	44
<b>R<sup>b</sup></b>	0,794	0,775

<sup>a</sup> Expressed as the mean standard deviation.

<sup>b</sup> P value < 0.05

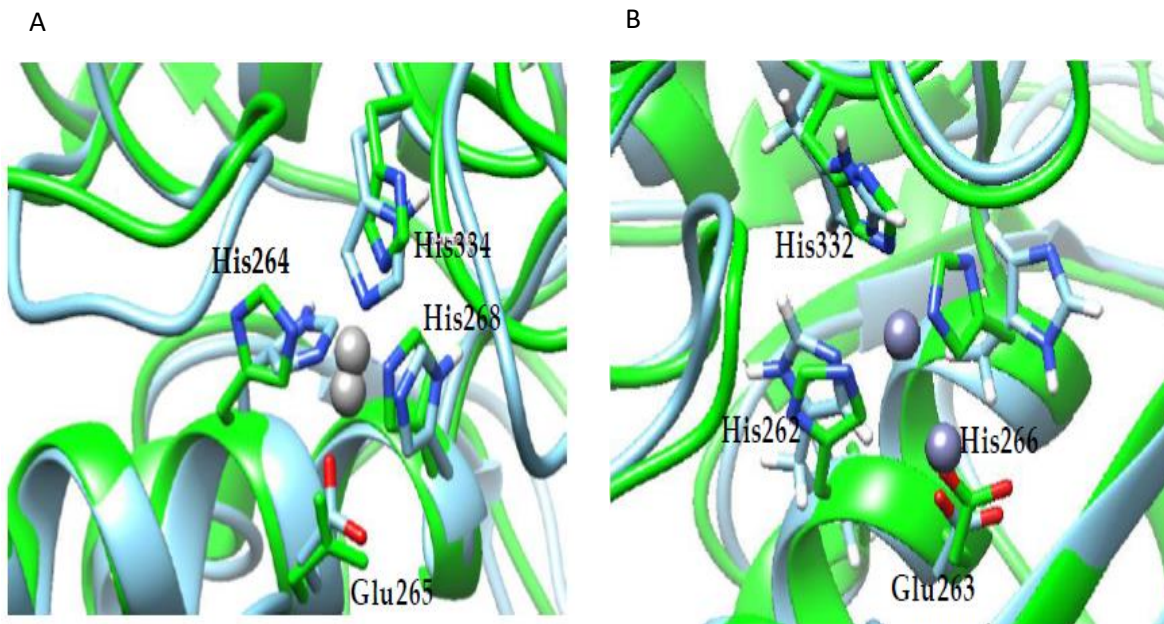


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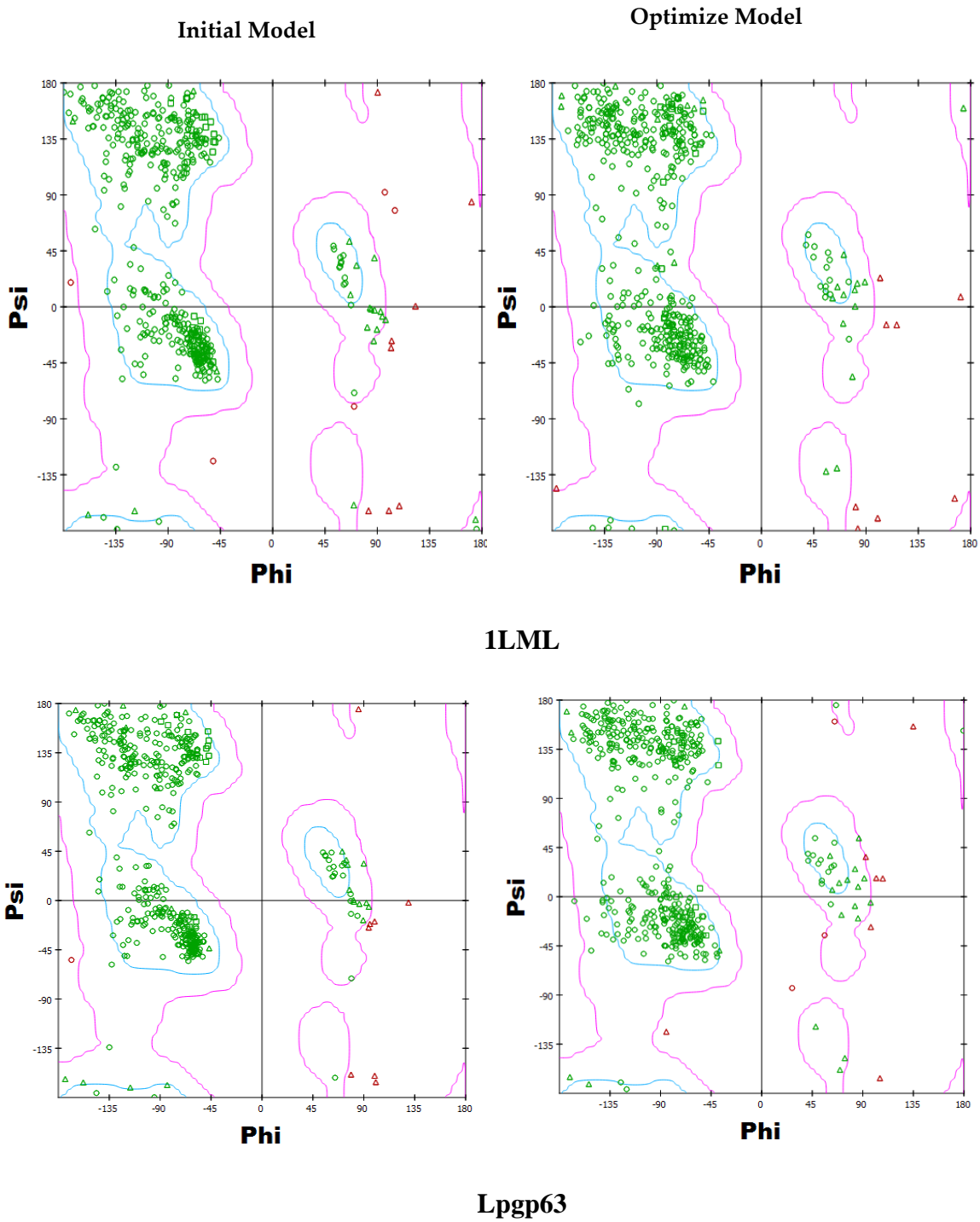
1LML 1 MSVDSSSTHRRRCVAARLVRLAAAGAAVTAVGTAAAWA HAGALQHR CVH 50
Lpgp63 1 -----MAVGAAAVVWQAAGHHC IH 19
          :...** . . * *:*:*
1LML 51 DAMQARVRQSVADHHKAPGAVSAVGLPYVTLDAHAHTAAAADP--RPGSAR 98
Lpgp63 20 DR LQTRVLQSV AQRRPPG SVSALGLPYVSTGPISSAHAVDWALADSTSP 69
          * :*:** ***** : : .*.:***:*.** : .
1LML 99 SVVRDVNWGALRIAVSTEDLTDPAYH CARVGHVQVVDHAGAIVT CTAEDIL 148
Lpgp63 70 SVARAADWGT LRIAVSTADLNDPGYH CTRVGRVNNHNGEIAT CTAEDIL 119
          *. * .:***:***:***: *. * .***:***:***: : . * :. *****
1LML 149 TNEKRDILVKHLIPQAVQLHTERLKVQVQGWKVTDMVGDICGDFKVPQ 198
Lpgp63 120 TEQRDILVSYLIPQALQLHAERLRVQVQGSWKVTGMTGSI CGDFSVPP 169
          *::** * .:***:***:*** *****:*.***.***.***. * . ***.***
1LML 199 AHITEGFSNTDFVMYVASVPSEEGVLAWATTCQTFSDGHPAVGVINIPAA 248
Lpgp63 170 AHLTAGVSNADFVLYVASVPSEPGVLAWATTCQVFSDDHPAVGVINIPAA 221
          *:* * .:***:***:*** ***** .*****.***.*****
1LML 249 NIASRYDQLVTRVVTHEMAHALGFSGPF FEDARIVANV PNVRGKNFDVPV 298
Lpgp63 222 NIVSRYDQ GATRVVTHEVAHALGFSSTFFKSAGIVKSVTNLRGKPF AAPV 271
          **.* ** .*****:***:*** ** . * : .:***:*** * * .**
1LML 299 INSSTAVAKAREQYGDPTLEYLEVEDQGGAGSAGSHIKMRNAQDELMAPA 348
Lpgp63 272 INSSTVAVAKAREQYGDPTLEYLEVEDQGGSGSAGSHIKMRNAKDELMAPA 321
          *.***.***** :*****:*****:*****:*****:*****
1LML 349 AAAGYYTALTMAIFQDLGFYQADFSKAEVMPWQONAGCAFLTNKMEQSV 398
Lpgp63 322 SAAGYYTALTMAVFEDLGFYKADFAKAEVMPWGRNASCDFLTQKCMEDNI 371
          : *****:*.*****:***:*** *****:*. * **:*:* * .:
1LML 399 TQWPAMFCNESEDAIRPTSRLSLGAGVTRHPG-LPPYQYFTDP SLAG 448
Lpgp63 372 TQWPAMFONTTERRYRPTDRLRLGTGIRTYSTPMPYFEYFNDTFLAG 421
          *:* * ** . * * .** :*:* : .:***:***. * *
1LML 449 VSAFMDYCPVVVPYSDGSC TQRASEAHASLLPFNVFSDAARCIDGAFRPK 498
Lpgp63 422 YSAFLDYCPFTLGYSNGACNQDPSTAPALLKEFSVFSDAARCFDGA FRP- 471
          *.*:***. .: : :*:* * . * : : * .***:***:*** *
1LML 499 ATDGI V KSYAGLCANVQCDTATRYSVQVHGSNDYTNCTPGLRVELSTVS 548
Lpgp63 472 TTAREDLMYNALCANVMCNTAARTYSVQVRGSSGYVACTPGESVELATTS 521
          * .***** *:*:*:*****:*. * . * ** * *:*:* *
1LML 549 NAFEGGGYITCPPYVEVQGNVQA AKDGG-----NTAAGR 584
Lpgp63 522 AAFVEGSYITCAPYVEVQANIKGVIDFEG-----DAADTAAMRRW 562
          ** * .:***:***:***.***:.. * . * *
1LML 585 GPRAAATALLVAALLAVAL----- 602
Lpgp63 563 SERMTALATVTAVLLGIVLAVMAILVVWLLLITIP----- 594
          . * :* * .: * * .: *

```

**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.

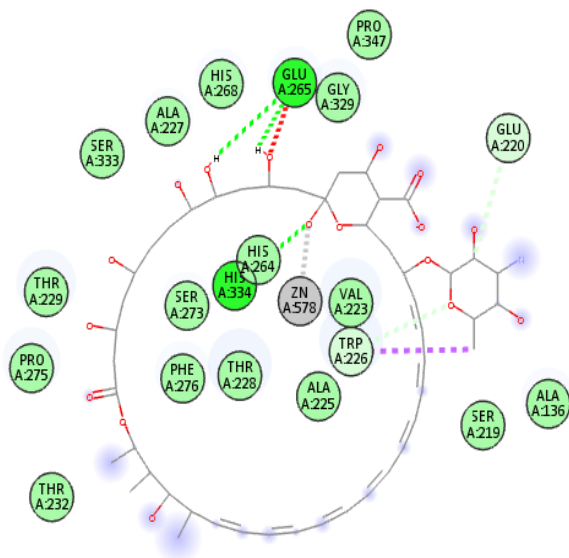


**Figure S2.** Superimposition between the MD-simulated structures and Initial Model. Average structures from the last 200 ns of the MD simulations in the residues of the active site are displayed. Initial models are in green and those optimized in cyan. A) 1LML, B) and B) Lpgp63. The change in the distance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

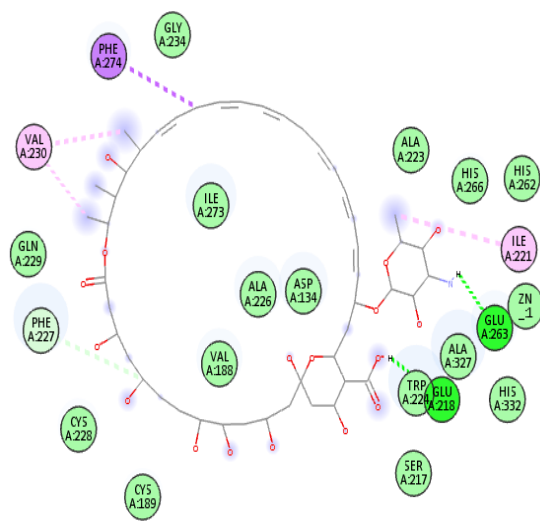


**Figure S3.** The Ramachandran plots of the initial and the optimized models after 200 ns of MD simulation.

**1LML**

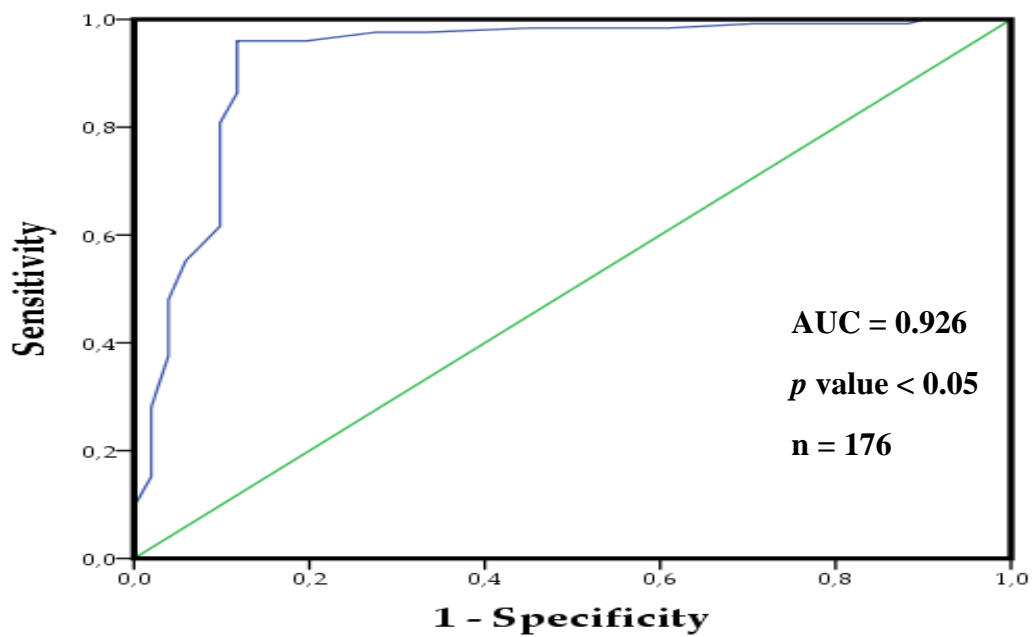


**Lpgp63**

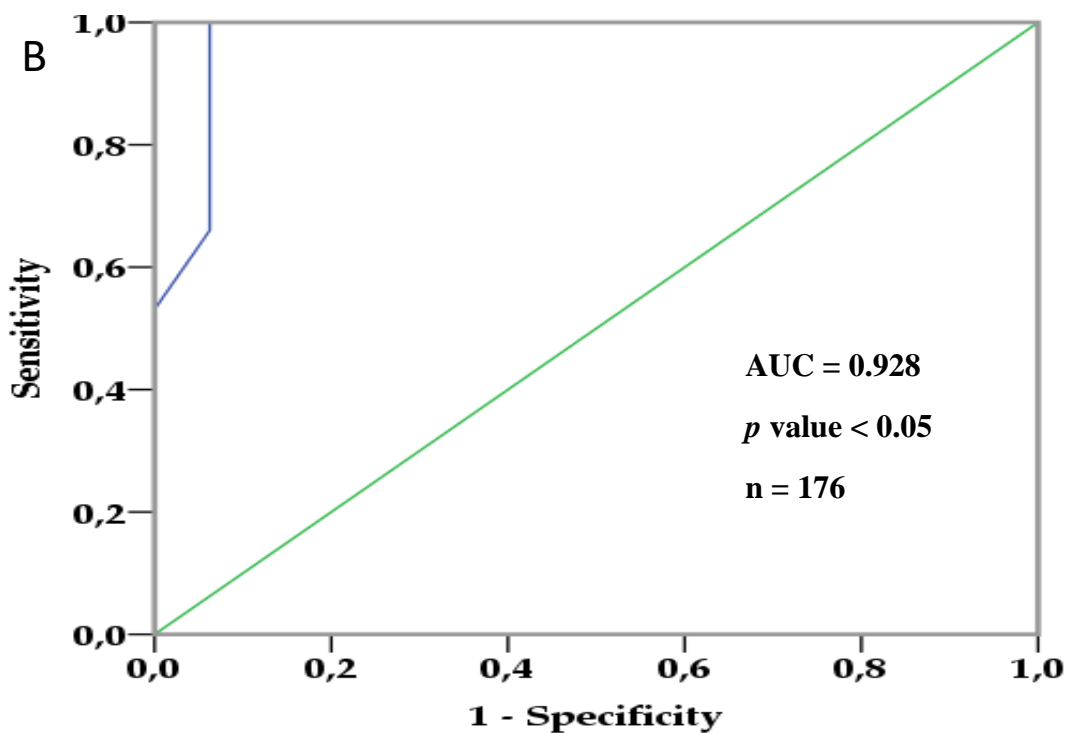


**Figure S4.** Interactions of amphotericin B with amino acid of the active site from leishmanolysin of 1LML and lpgp63.

A

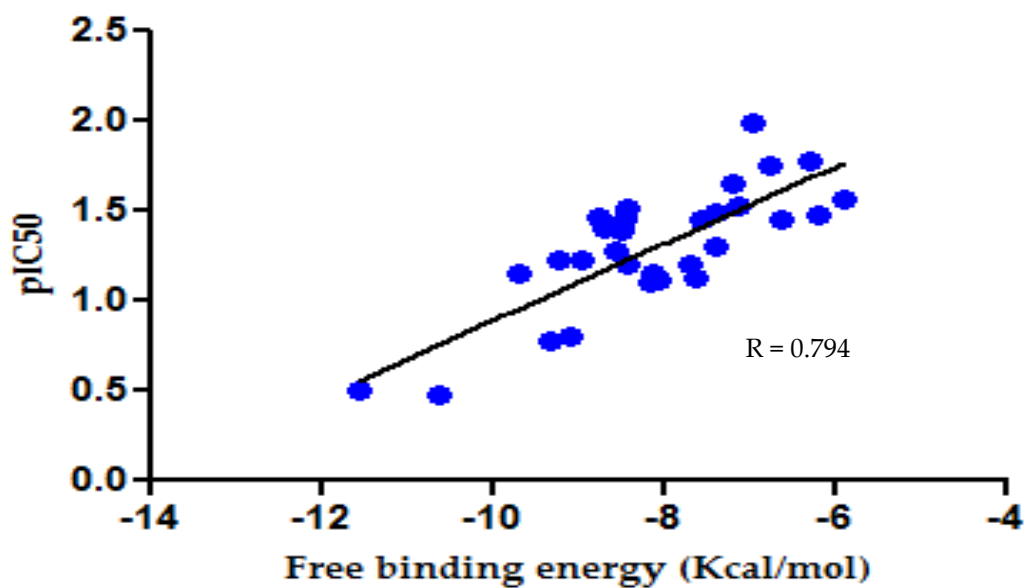


B

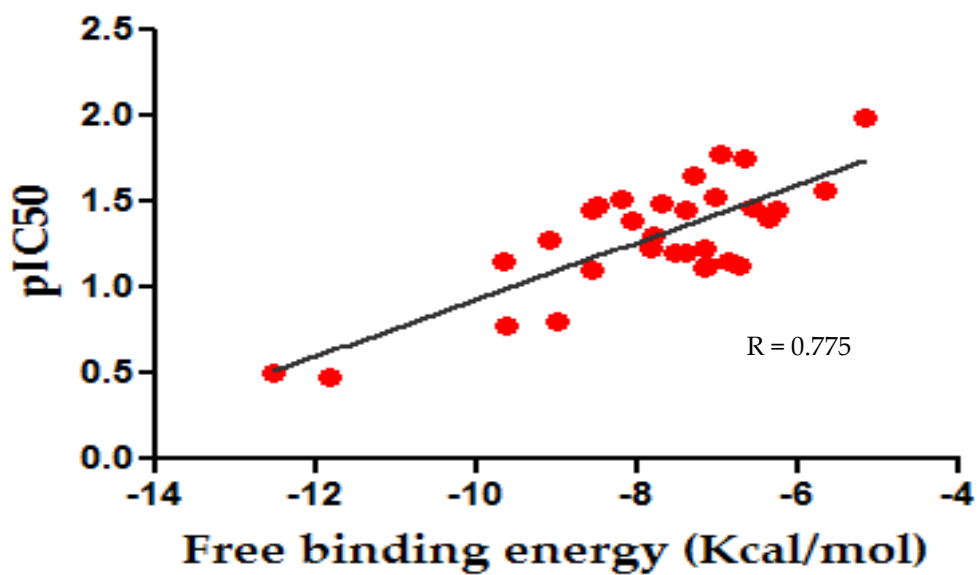


**Figure S5.** The ROC curve generated by screening virtual of flavonoids ligands from (A) 1LML (B)LpGp63.

A



B



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

