Supplementary Materials

Virtual Screening and the In Vitro Assessment of the Antileishmanial Activity of Lignans

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Table S1. Lignans with good ADMET profiles.

	Pharmacokinetics							
ID	**GI[1]**	**BBB[2]**	**P-gp[3]**	**CYP1A2**	**CYP2C19**	**CYP2C9**	**CYP2D6**	**CYP3A4**
01	High	No	Yes	No	No	No	No	No
08	High	No	Yes	No	No	No	No	No
20	High	No	Yes	No	No	No	Yes	No
30	High	No	Yes	No	No	No	Yes	No
31	High	No	Yes	No	No	No	Yes	No
32	High	No	Yes	No	No	No	Yes	No
44	High	No	Yes	No	No	No	Yes	No
57	High	No	Yes	No	No	No	Yes	No
58	High	No	Yes	No	No	No	Yes	No
59	High	No	Yes	No	No	No	Yes	No
60	High	No	Yes	No	No	No	Yes	No
61	High	No	No	No	No	No	Yes	No
76	High	No	No	No	No	No	Yes	No
77	High	No	No	No	No	No	Yes	No
83	High	No	Yes	No	No	No	Yes	No
84	High	No	Yes	No	No	No	Yes	No
86	High	No	Yes	No	No	No	No	No
87	High	No	Yes	No	No	No	Yes	No
88	High	No	Yes	No	No	No	No	No
90	High	No	Yes	No	No	No	No	No
91	High	No	Yes	No	No	No	Yes	No
121	High	No	Yes	No	No	No	No	No
124	High	No	Yes	No	No	Yes	No	No
131	High	No	No	No	No	No	Yes	Yes
132	High	No	Yes	No	No	No	No	No
139	High	No	Yes	No	No	No	No	No
140	High	No	Yes	No	No	No	No	No
151	High	No	Yes	No	No	No	Yes	No
156	High	No	Yes	No	No	No	Yes	No
157	Low	No	Yes	No	No	No	No	No
158	Low	No	Yes	No	No	No	No	No
159	Low	No	Yes	No	No	No	No	No
160	Low	No	Yes	No	No	No	No	No

[1]GI: Gastrointestinal absorption; [2]BBB: Blood–brain barrier; [3]P-gp: P-glycoprotein.

Table S2. Predictive assessment of lignan toxicity for the evaluated parameters.

ID	Mutagenic	Tumorigenic	Reproductive Effective	Irritant
1	No	No	No	No
8	No	No	No	No
20	No	No	No	No
30	No	No	No	No
31	No	No	No	No
32	No	No	No	No
44	No	Low	No	No
57	No	No	No	No
58	No	No	No	No
59	No	No	No	No

60	No	No	No	No
61	No	No	No	No
76	No	No	No	No
77	No	No	No	No
83	No	No	No	No
84	No	No	No	No
86	No	No	No	No
87	No	No	No	No
88	No	No	No	No
90	No	No	No	No
91	No	No	No	No
121	No	No	No	No
124	No	No	No	No
131	No	No	No	No
132	Low	Low	No	No
139	No	No	No	No
140	No	No	No	No
151	No	No	No	No
156	No	No	No	No
157	No	No	No	No
158	No	No	No	No
159	No	No	No	No
160	No	No	No	No

Table S3. Average of all energy values (EM) obtained from the five scoring functions, for each lignan, and the probability value of potential consensus docking activity (P_{DC}), for each studied enzyme in *L. major*. Absent values indicate the molecules that were eliminated during this evaluation.

ID	GPDH		DHODH		PTR1		TR		UGPase	
	EM	**P_{DC}**	**EM**	**P_{DC}**	**EM**	**P_{DC}**	**EM**	**P_{DC}**	**EM**	**P_{DC}**
44	58.90	0.82	43.43	0.69	68.81	0.83	63.96	0.91	63.96	0.91
60	63.50	0.89	46.47	0.67	67.38	0.82	62.45	0.89	62.45	0.89
83	63.94	0.90	59.44	0.67	73.90	0.89	64.63	0.92	64.63	0.92
86	63.53	0.89	60.87	0.72	72.16	0.87	63.19	0.90	63.19	0.90
87	63.39	0.89	58.81	0.70	-	-	63.95	0.91	63.95	0.91
124	57.36	0.64	68.34	0.67	75.47	0.91	69.58	1	69.58	1
132	64.43	0.90	49.07	0.66	-	-	62.21	0.89	62.21	0.89
157	67.91	0.95	41.51	0.81	72.03	0.87	-	-	50.43	0.72
158	66.48	0.93	54.86	0.75	77.00	0.93	-	-	49.97	0.71
159	63.43	0.89	53.39	0.87	83.63	1	53.32	0.76	65.55	0.94
160	71.03	1	-	0.81	82.16	0.98	53.58	0.77	53.58	0.77
PDB inhibitor	37.72	0.53	35.75	0.58	63.94	0.77	37.38	0.53	37.38	0.53

Table S4. Average of all energy values (EM) obtained from the five scoring functions, for each lignan, and the probability value of potential consensus docking activity (P_{DC}), for each studied enzyme in *L. braziliensis*. Absent values indicate the molecules that were eliminated during this evaluation.

ID	GPDH		DHODH		PTR1		TR		UGPase	
	EM	**P_{DC}**	**EM**	**P_{DC}**	**EM**	**P_{DC}**	**EM**	**P_{DC}**	**EM**	**P_{DC}**
8	59.21	0.86	43.99	0.58	72.53	0.80	-	-	-	-
20	58.17	0.85	50.00	0.66	74.64	0.83	56.19	0.76	-	-
31	60.39	0.88	48.93	0.65	78.41	0.87	57.66	0.78	62	0.77

32	59.15	0.86	48.32	0.64	78.54	0.87	55.41	0.75	63	0.78
44	45.54	0.66	48.07	0.64	82.79	0.92	55.57	0.75	64	0.80
57	55.88	0.81	47.32	0.63	80.91	0.90	54.14	0.73	64	0.80
58	50.37	0.73	46.09	0.61	68.36	0.76	53.10	0.72	64	0.80
59	49.23	0.72	44.79	0.59	70.40	0.78	-	-	64	0.80
60	56.97	0.83	46.11	0.61	77.81	0.86	54.06	0.73	66	0.83
61	56.56	0.82	52.94	0.70	-	-	55.24	0.75	-	-
76	-	-	44.90	0.59	-	-	-	-	-	-
83	59.50	0.87	54.88	0.73	77.25	0.86	64.98	0.80	61	0.77
87	60.87	0.89	49.12	0.65	71.98	0.80	59.44	0.80	62	0.78
91	61.54	0.90	48.37	0.64	78.16	0.87	57.35	0.77	61	0.77
121	61.30	0.89	47.32	0.63	76.26	0.85	-	-	-	-
124	56.49	0.82	51.88	0.69	81.29	0.90	65.78	0.89	-	-
156	53.24	0.78	51.39	0.68	74.87	0.83	54.11	0.73	66	0.83
157	58.25	0.85	63.68	0.84	89.59	1	60.59	0.82	66	0.83
158	68.18	1	55.11	0.73	77.40	0.86	62.11	0.84	68	0.85
159	68.07	0.99	55.19	0.73	82.16	0.91	73.53	1	79	1
160	57.54	0.84	74.97	1	79.52	0.88	-	-	76	0.95
PDB inhibitor	36.26	0.53	32.40	0.43	67.31	0.75	53.15	0.72	61	0.76

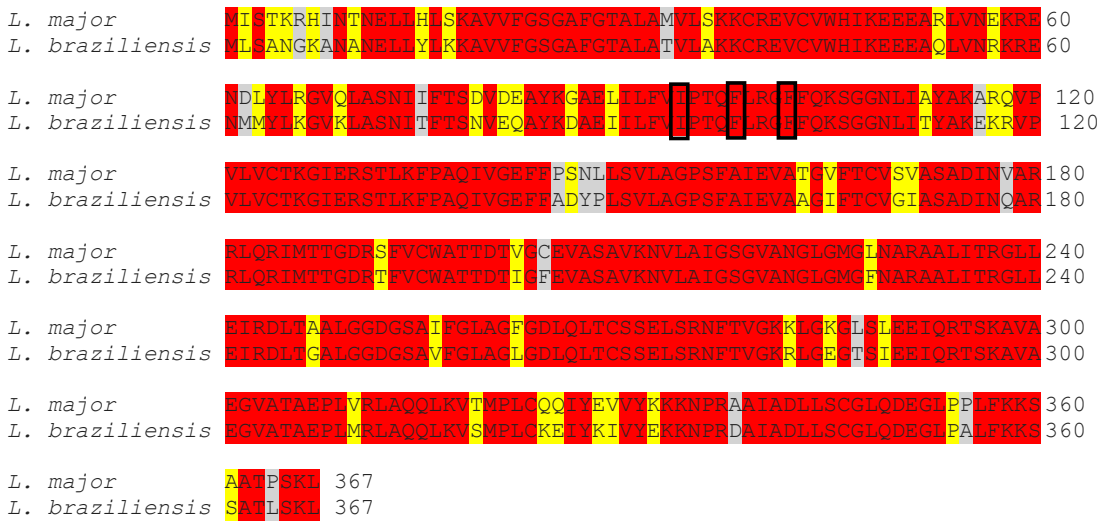

Figure S1. Alignment of the GPDH protein sequences. The gray regions show non-similar and non-identical amino acids. The red regions show identical amino acids. The yellow regions show similar amino acids. The black boxes indicate the active site.

Figure 2. Alignment of the DHODH protein sequences. The gray regions show non-similar and non-identical amino acids. The red regions show identical amino acids. The yellow regions show similar amino acids. The black boxes indicate the active site.

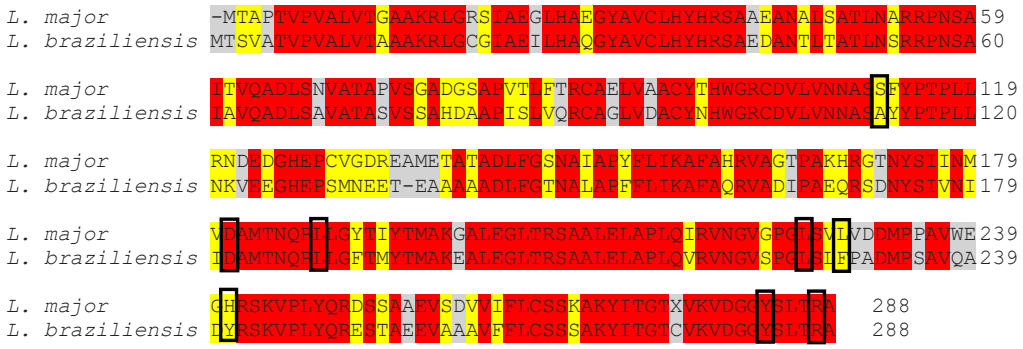

Figure 3. Alignment of the PTR1 protein sequences. The gray regions show non-similar and non-identical amino acids. The red regions show identical amino acids. The yellow regions show similar amino acids. The black boxes indicate the active site.

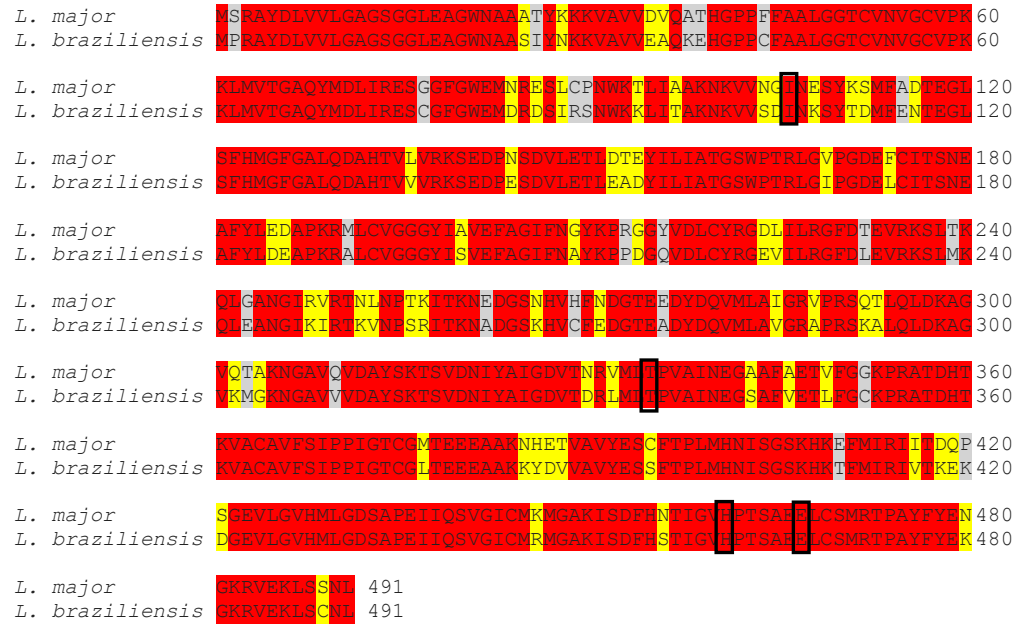

Figure S4. Alignment of the TR protein sequences. The gray regions show non-similar and non-identical amino acids. The red regions show identical amino acids. The yellow regions show similar amino acids. The black boxes indicate the active site.

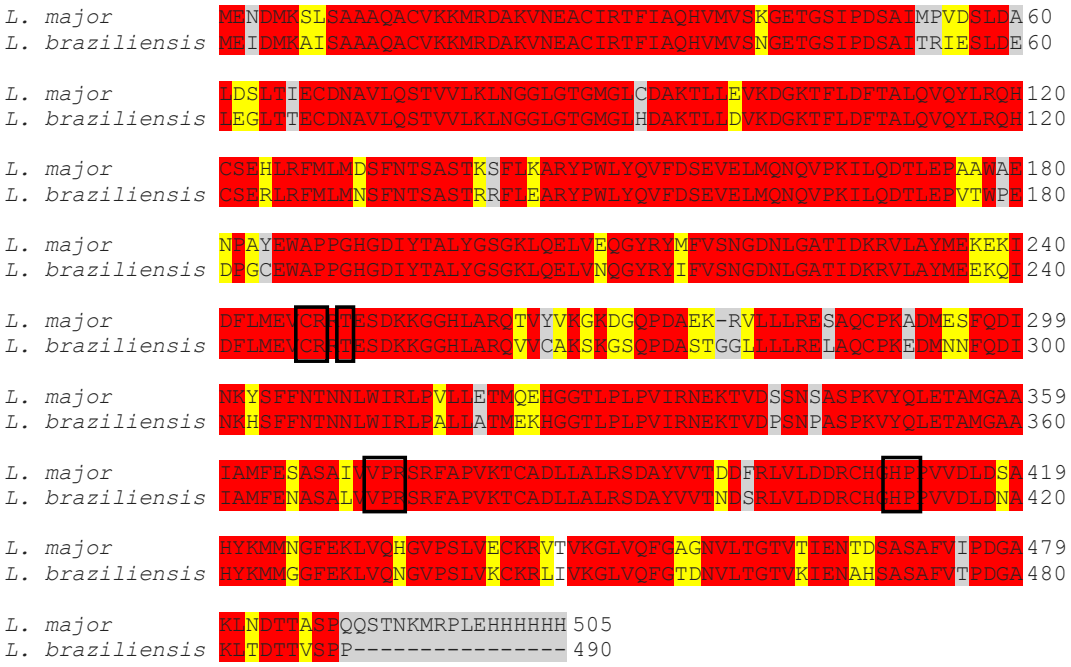

Figure S5. Alignment of the UGPase protein sequences. The gray regions show non-similar and non-identical amino acids. The red regions show identical amino acids. The yellow regions show similar amino acids. The black boxes indicate the active site.