Virtual screening applied in the search for inhibitors of *Trypanosoma cruzi* trypanothione reductase using the of the Natural Products database from State of Bahia (Brazil)

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Keywords: *Virtual Screening, Chagas disease, Trypanosoma cruzi, Trypanothione reductase, NatProDB.*

Introduction

Chagas disease, caused by *Trypanosoma cruzi*, affects 21 countries in the Latin America, and is considered a serious public health issue.[1] There is not currently treatment for this disease, especially in its chronic phase. Thus, the search for inhibitors of Trypanothione Reductase *Trypanosoma cruzi* (TCTR) through the Virtual Screening is crucial, because this enzyme is a validated target for rational drug design. In this way, we applied the Virtual Screening in the database of the natural products from Bahia aiming to search for molecules that can act against this parasite.

Results and Discussion

A Virtual Screening in Natural Products Database of Bahia was performed (http://natprodb.uefs.br/) employing the Autodock4[2] program. In our results, we selected the TcTR-ligand complexes according to the best interaction energy values (Table 1).

Table 1. The best binding energies (kcal/ mol) of TcTR and Natural Products NatProDB complexes.

#	NatProDB Code	Binding Energy (kcal/mol)
1	TCA	- 12, 41
2	CGA	- 10, 59
3	REA	- 10, 05
4	CLA	- 9, 61
5	EAA	- 9, 48

From binding energy values, we noted that the TCA compound was better classified followed by CGA, REA, CLA and EAA.

The automatic analysis of conformations screening using a self-organizing map (AuPosSOM)[3], allowed the comparison of the interactions of the active compounds with the residues present at TcTR site (Table 2).

Table 2. Residues of TcTR active site that interact with the NatProDB compounds (http://natprodb.uefs.br/).

Site[4]	TcTR Residues	NatProDB Code
Site Z	Phe^{396}	TCA
	Pro^{398}	TCA, REA, EAA e CLA
	Leu^{399}	
Site γ-Glu	His^{461}	TCA, REA, EAA e CLA
	Glu^{466}	TCA, CLA e CGA
	Glu^{467}	TCA, REA, EAA e CLA

The TCA interacted with all the residues of γ-Glu site and site Z of TcTR[4] which reinforce its best binding energy (Table 1). CLA interacts with all sites, except Phe^{396}, showing an intermediate activity. REA and EAA interacted with the site same, except with Phe^{396} and Glu^{466}, indicating a lower potency of these compounds.

Conclusions

The Virtual Screening based on the target structure allowed us to evaluate the most prevalent interactions with NatProDB molecules and TcTR. Finally, we noted the interactions which are useful for the development of most potent inhibitors of TcTR.

Acknowledgements

FAPESB (APP0072/2011, JCB0039/2013, RED 0008/2013), CAPES, CNPq.

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