

# In Silico Study of *Cucurbita maxima* Compounds as Potential Therapeutics Against Schistosomiasis

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**ABSTRACT:** Schistosomiasis, a disease usually related to poverty and poor sanitation, affects more than 200 million people worldwide. Since the 1970s, the medical sector has depended on a single drug, praziquantel, for the treatment of the disease. The emerging evidence of resistance of the *Schistosoma* parasite to praziquantel and the drug's inefficacy against juvenile stages of the parasite makes the need to find alternative drugs an urgent matter. In this study, we explored the inhibition potential of compounds from *Cucurbita maxima* using molecular docking studies on *Schistosoma mansoni* purine nucleoside phosphorylase (*Sm*PNP) and *Schistosoma haematobium* 28-kDa glutathione S-transferase (*Sh*28kDaGST). Following molecular docking studies and analysis of the active sites, the primary amino acids that were observed and shown to be involved in the *Sm*PNP-ligand interaction are CYS 33, ARG 86, HIS 88, TYR 90, ALA 118, ALA 119, PRO 200, TYR 202, GLU 203, VAL 219, MET 221, THR 244, ASN 245, PRO 257 and HIS 259. For the *Sh*28kDa-ligand interaction, the primary amino acids were PHE 11, ARG 16, TRP 41, LEU 53, GLU 70 and SER 71. Momordicoside I aglycone binds to *Sm*PNP with the lowest binding affinity of -7.9 kcal/mol by pi sigma bond interactions with HIS 88. Balsaminoside B binds to *Sh*28kDaGST with a binding affinity of -7.6 kcal/mol by hydrogen bond interaction with TRP 41, LEU 53 and SER 71. Pharmacokinetic studies showed favourable drug-like properties for the 10 compounds that exhibited the lowest binding energies. Therefore, we propose that bioactive compounds from *C. maxima* be considered as potential novel drug hits in the treatment of schistosomiasis.

**KEYWORDS:** Schistosomiasis, *Cucurbita maxima*, purine nucleoside phosphorylase, 28-kDa glutathione S-transferase, pharmacokinetics

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## Introduction

*Schistosoma* species are digenetic blood trematodes and are the causal agents of schistosomiasis.<sup>1</sup> The annual estimated number of deaths due to the disease varies between 24 000 and 200 000 globally.<sup>2</sup> The 6 species responsible for morbidity are *Schistosoma mansoni*, *S. haematobium*, *S. japonicum*, *S. guineensis*, *S. mekongi*, and *S. interlacum*.<sup>1</sup> The most common species in sub-Saharan Africa are *S. mansoni* and *S. haematobium*.<sup>3</sup> Since 1970, the treatment of schistosomiasis has greatly relied on the drug praziquantel.<sup>4</sup> The reliance on a single drug for the treatment of the disease poses a threat to the medical sector as this can lead to drug resistance. Reduced efficacy of the drug following mass drug administration programmes and the reported laboratory-based resistance<sup>5</sup> necessitates the need for the search for potential novel drug candidates.

Research in drug discovery based on natural products has been practised for a long time.<sup>6</sup> Various plants have been investigated for anti-schistosomal activity *in vitro* and *in vivo*. These include *Zizinger officinale*,<sup>2</sup> *Anonidium mannii*,<sup>7</sup> *Rauwolfia vomitoria*,<sup>8</sup> *Pulsatilla chinensis*,<sup>9</sup> and *Artemisia annua*.<sup>10</sup> *Cucurbita* cultivars such as *Cucurbita pepo* and *Cucurbita moschata* have also been tested for anti-schistosomal activity. *C. pepo* seed oil has been shown to induce microsatellite instability

and tegumental damage to *S. mansoni in vitro*,<sup>11</sup> while the curative effect of *C. moschata* was observed when patients infected with schistosomiasis were treated with daily doses of the powdered seeds.<sup>9</sup>

*Cucurbita maxima* are rich in alkaloids, flavanoids, phenolics, carbohydrates, tannins, saponins, terpenoids, and proteins. The plant is cultivated for nutritional and medicinal purposes.<sup>12</sup> For centuries, the plant has been used to treat intestinal infections,<sup>13</sup> renal failure,<sup>14</sup> constipation, hyperplasia, and parasite infestation.<sup>15</sup> Oral consumption of the seeds has also been used for blood pressure regulation.<sup>16</sup> The molluscicidal potential and potency of *C. maxima* has been studied and successfully determined.<sup>17</sup> However, there is a dearth of literature on the plant's anti-schistosomal properties. Currently, 17 compounds from the plant are available on online databases such as PubChem (<https://pubchem.ncbi.nlm.nih.gov/>) and ChEMBL (<https://www.ebi.ac.uk/chembl/>). However, data on *in silico* studies on the anti-schistosomal activities of the plant is currently unavailable in the public domain.

Various schistosome protein and kinetic parameters have been studied as potential drug targets. Presently, 238 schistosome protein structures are registered in the Protein Data Bank and most of the proteins were obtained through X-ray



**Table 1.** The Pyrx grid box coordinates.

PROTEIN	CENTRE X COORDINATES	CENTRE Y COORDINATES	CENTRE Z COORDINATES
<i>Sm</i> PNP		-6.4363	1.5792
<i>Sh</i> 28kDaGST	15.6356		0.7630
			26.34

Abbreviations: *Sh*28kDaGST, *Schistosoma haematobium* 28-kDa glutathione S-transferase; *Sm*PNP, *Schistosoma mansoni* purine nucleoside phosphorylase.

crystallography.<sup>18</sup> *S. mansoni* purine nucleoside phosphorylase (*Sm*PNP) and *S. haematobium* 28-kDa glutathione S-transferases (*Sh*28GST) are crucial targets in schistosomes.

Purine nucleoside phosphorylase (PNP) also known as inosine phosphorylase,<sup>19</sup> plays a fundamental role in the maintenance of proper cellular function and metabolism, acting both in the *de novo* purine synthesis and the purine nucleotide salvage pathway.<sup>20</sup> One crucial component of the salvage pathway is the catalysis of the reversible phosphorolysis of the N-ribosidic bond of 6-oxopurine deoxynucleosides and nucleosides delivering their correspondent base and ribose-1-phosphate.<sup>21</sup> PNP facilitates the metabolism of inosine into hypoxanthine, adenosine into adenine and guanosine into guanine, and in each case, a ribose phosphate is created. Mutations in the PNP enzyme lead to severe combined immunodeficiency (SCID).<sup>22</sup>

The *Sh*28GST are enzymes associated with parasite metabolic cycles and host immune adjustment.<sup>23</sup> In schistosomes, 28GST have been shown to revoke the development of host epidermal Langerhans cells to the depleting lymph nodes.<sup>24</sup> The protein is uncovered on the outer layer of the cercaria in the same manner as in adult worms, suggesting its inclusion in the parasite-host communication. First discovered in the 1980s, the protein is considered a promising candidate for a schistosomiasis vaccine, having undergone successful phases 1 and 2 clinical trials.<sup>25</sup> It is hypothesised that the enzymes assist the schistosomes by protecting them from membrane damage and from toxins circulating in the host blood.<sup>24</sup> This is achieved through immune-effector cells at the parasite surface, yielding lipid peroxidation products. Also, the increase in the solubility of haematin in the schistosome gut aids in the reduction of the 'constipation' of worms.<sup>24</sup>

There is a need to control morbidity and eventually eliminate schistosomiasis as well as to attain the Sustainable Development Goal 3 'achieve health for all'.<sup>26</sup> To achieve this goal, computational biology studies can be carried out to speed up drug discovery efforts against schistosomiasis. In this work, we screened the library of 17 *Cucurbita maxima* bioactive compounds to determine their anti-schistosomal properties using molecular docking against *Sm*PNP and *Sh*28GST. Our results show that momordicoside I aglycone and Balsaminoside B have the lowest binding affinity of -7.9 and -7.6 kcal/mol, respectively.

## Materials and Methods

### Protein preparation

The crystal structures of *Sm*PNP (3FAZ) and *Sh*28GST (1OE7) were retrieved from the PDB (<https://www.rcsb.org/>)

in complex with co-crystallised ligands. The proteins were prepared using Biovia Discovery Studio Visualiser v21.1.0.20298 (<http://www.accelrys.com>) through deletion of water molecules and addition of missing hydrogen atoms. The metal ionisation was corrected to certify formal charge and force field treatment using Autodock tools. All co-crystallised ligands were cut from the protein complexes and used in validating the molecular docking protocol through calculation of root mean square deviation (RMSD) using Biovia Discovery Studio. The proteins were optimised and refined for docking analysis using the Pyrx v 2008 to 2012 (Sargis Dallakyan, The Scripps Research Institute).

### Ligand preparation

The phytochemicals of *C. maxima* were retrieved from published literature,<sup>27</sup> their structures were downloaded from the ChEMBL database (<https://www.ebi.ac.uk/chembl/>). The ligands were prepared using the Open Babel module of the Pyrx tool by using the force field uff.

### Molecular docking

Molecular docking simulations were done using Autodock Vina integrated with the Pyrx software. *C. maxima* phytochemicals were docked into the active sites of *Sm*PNP<sup>28</sup> and *Sh*28GST<sup>24</sup> proteins. The grid was generated using the receptor grid generation module of the Pyrx tool (coordinates are shown in Table 1). The grid box was adjusted to cover the catalytic site residues for *Sm*PNP and *Sh*28GST proteins.

The best 10 ligands according to the binding energy  $\Delta G$  binding and RMSD values in each trial were chosen as novel inhibitors. The 17 compounds were docked against the catalytic site of the proteins using the binding pocket of the co-crystallised ligands which had been removed before docking. Visualisation of the protein-ligand complex was performed using Biovia Discovery Studio 2021.

### Toxicity analysis

The SMILE structures of 10 compounds with the lowest binding energy were retrieved from ChEMBL. Using Lipinski's rule of 5, the prediction of absorption, distribution, metabolism, elimination and toxicity (ADMET) analysis was done using the pkCSM server (<http://biosig.unimelb.edu.au/pkcsml/>).<sup>29</sup> The following parameters were considered: human intestinal absorption (%), blood-brain barrier permeability

(log BB), metabolic interactions with cytochromes CYP2D6 and CYP3A4, total clearance (log mL/min/kg), Ames toxicity; human ERG I inhibition, oral rat acute toxicity (LD50) in mol/kg and oral rat long-term toxicity lowest adverse effect levels (LOAEL) in log mg/kg body weight/day. ADMET properties of praziquantel were also predicted for comparative studies.

## Results and Discussion

### Molecular docking

Virtual screening of a library of compounds from *C. maxima* was done using molecular docking against the targeted proteins *SmPNP* and *Sb28kDaGST*. Each of the generated docked complexes was observed centred on minimum binding energy values (kcal/mol). Pharmacokinetic profiling of the phytocompounds was further done to predict their drug-likeness properties. The interactions of the ligands within the binding pockets of *SmPNP* and *Sb28kDaGST* are shown in Table 3.

The amino acid residues involved in the interactions and each of their position in their ligand-binding site were identified. Hydrophobic, pi-pi stacking, hydrogen bonding and many other interactions between the protein and the ligands were demonstrated through molecular docking. The primary amino acids that were observed and shown to be involved in the *SmPNP*-ligand interaction are CYS 33, ARG 86, HIS 88, TYR 90, ALA 118, ALA 119, PRO 200, TYR 202, GLU 203, VAL 219, MET 221, THR 244, ASN 245, PRO 257, and HIS 259. For the *Sb28kDa*-GST-ligand interaction, the primary amino acids were PHE 11, ARG 16, TRP 41, LEU 53, GLU 70 and SER 71.

Among the 10 compounds docked against proteins, Momordicoside I aglycone and Balsaminoside B were predicted to have the lowest binding energy values when bound to *SmPNP* and *Sb28kDaGST*, respectively. Momordicoside I aglycone is a triterpenoid saponin found in the Cucurbitaceae family and previous studies have shown the compounds' anti-diabetic properties and anti-obesity properties through reduction of fat accumulation.<sup>31-33</sup> Following the docking of Momordicoside I aglycone against *SmPNP*, it displayed pi sigma bonding with amino acid residue HIS 88 with a binding affinity of -7.9 kcal/mol. Balsaminoside B is a triterpene that has been shown to have antimalarial and anticancer activity.<sup>34</sup> The docking results from Balsaminoside B docked against *Sb28kDaGST* displayed a binding affinity of -7.69 kcal/mol. Hydrogen bond interactions with the amino acid residues TRP 41, LEU 53, SER 77 and carbon-hydrogen bonds with ARG 16 were observed. Our results are in agreement with studies that have shown the *in vitro* anti-schistosomal activity of triterpenes in plants such as *Argemone mexicana*,<sup>35</sup> *Momordica balsamina*, *Actinopyga echinites*, and *Holothuria polii*.<sup>10,36</sup>

Balsaminol E showed affinity on both *SmPNP* and *Sb28kDaGST* with binding energies of -7.6 and -7.5 kcal/

mol, respectively. For *SmPNP*, the amino acid residue interactions observed with Balsaminol E were hydrogen bonds with ARG 86 and ASN 244, alkyl and pi alkyl bonds with TYR 202, VAL 219 and PRO 257. For *Sb28kDaGST*, the interactions observed with Balsaminol E were hydrogen bonds with TRP 41, pi sigma bonds with PHE11, pi alkyl and alkyl bonds with LEU 53 and carbon-hydrogen bonds with ARG16.

CHEMBL468165 binds to *SmPNP* with a binding affinity of -7.0 kcal/mol by hydrogen bond interactions with PRO 200 and pi sigma bond interactions with TYR 90 and HIS 259. Charantadiol A interacts with *SmPNP* through hydrogen bonds with amino acid residues at CYS 33, VAL 219; alkyl and pi alkyl bonds at TYR 202 and MET 221. 3beta,25-diol had a binding affinity of -6.6 kcal/mol exhibiting pi sigma bonds with *SmPNP* amino acid residues at HIS 259 and pi alkyl and alkyl bonds at TYR 202 and MET 221.

Neither visible interactions nor Lipinski violations were observed between Balsaminol C and *Sb28kDaGST*. Balsaminol E and Balsaminoside C, both triterpenoids, had the same binding affinities of -7.5 kcal/mol with *Sb28kDaGST* amino acid residues exhibiting pi sigma and hydrogen bonds. CHEMBL249658 binds to *Sb28kDaGST* with a binding affinity of -7.1 kcal/mol showing pi sigma bond interaction with PHE 11 and TRP 41. Docking results showed that compounds generally exhibited good docking energy values with the highest binding energy values of -6.6 kcal/mol for *SmPNP* and -7.1 kcal/mol for *Sb28kDaGST*. Table 1 shows the Pyrx grid box coordinates; Table 2 shows the drug-like properties of the 10 best ligands and Table 3 shows the interactions between the ligands and the proteins in three-dimensional images.

### Pharmacokinetic Studies

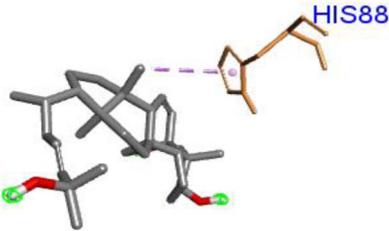
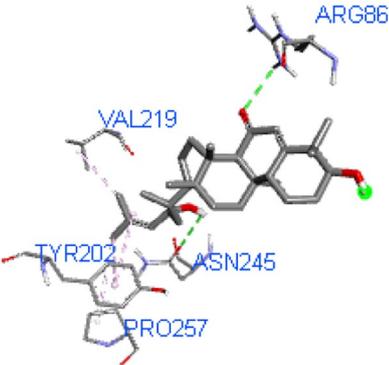
Tables 4 and 5 show the pharmacokinetics and drug-likeness parameters of each experimental compound. Momordicoside I aglycone's toxicity study confirms that it has an excellent intestinal absorption of 96,373% and acceptable blood-brain barrier permeability of log BB -0.117. The log BB value of Momordicoside I aglycone and all the compounds were less than the standard (log BB 0.3) which suggests that the compounds do not readily cross the blood-brain barrier. The compounds do not inhibit the cytochrome P3A4 and cytochrome 2D6 enzymes and can be easily excreted. The pharmacokinetic predictions suggest that none of the compounds was Ames toxic and none inhibited the potassium channels encoded by the human ether- a -go-go gene 1 (herG1). The pharmacokinetic properties of the favourable compounds were comparable to that of praziquantel with 70% of the compounds showing better intestinal absorption than praziquantel. The predicted intestinal absorption of all the 10 compounds was greater than the set standard of 30%. All of the compounds exhibited a total drug clearance prediction that was greater than 0. Also, all the compounds showed maximum tolerated values that were less than the standard (0.477 mg/kg/day) and in the same range as praziquantel. The highest predicted rat LD50 value of the

**Table 2.** The drug-likeness properties and binding affinities in kcal/mol of the 10 best ligands.

PROTEIN-LIGAND COMPLEX	MOLECULAR WEIGHT	LOG <i>P</i>	ROTATABLE BONDS	ACCEPTORS	DONORS	SURFACE AREA	LIPINSKI VIOLATIONS	BINDING AFFINITY IN kcal/mol
<i>Sm</i> PNP ChEMBL3264665 Momordicoside I aglycone	456.711	6.2946	4	3	2	201.616	1	-7.9
<i>Sm</i> PNP ChEMBL1254849 Balsaminol E	456.711	6.4848	4	3	2	201.670	1	-7.6
<i>Sm</i> PNP ChEMBL 468165	440.712	7.2259	4	2	2	7.2259	1	-7.0
<i>Sm</i> PNP Charantadiol A ChEMBL3264664	454.695	6.4182	4	3	2	201.616	1	-6.7
<i>Sm</i> PNP ChEMBL3264663 3beta,25-diol	486.737	6.2671	5	4	2	213.095	1	-6.6
<i>Sh</i> 28kDaGST ChEMBL1928850 Balsaminoside B	620.868	4.1008	7	8	6	264.096	2	-7.6
<i>Sh</i> 28kDaGST ChEMBL1254849 Balsaminol E	456.711	6.4848	4	3	2	201.670	1	-7.5
<i>Sh</i> 28kDaGST ChEMBL1928851 Balsaminoside C	620.868	4.1008	7	8	6		2	-7.5
<i>Sh</i> 28dkaGST ChEMBL1254762 Balsaminol	470.694		5	4	2	205.832	0	-7.2
<i>Sh</i> 28dkaGST ChEMBL249658	468.722	7.0723	5	3	1	207.611	1	-7.1

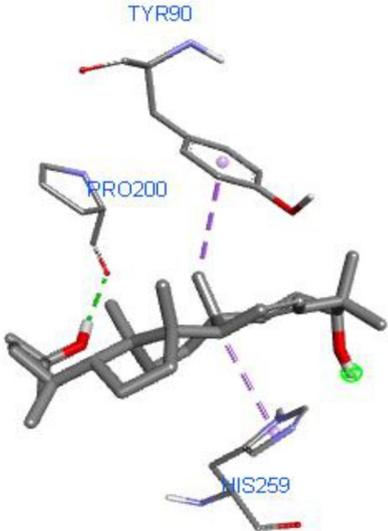
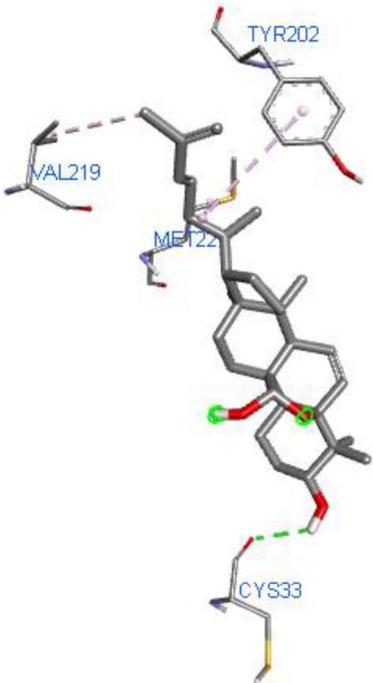
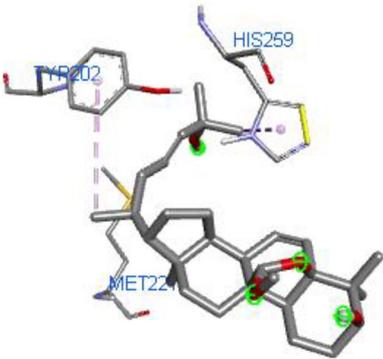
Abbreviations: *Sh*28kDaGST, *S. haematobium* 28-kDa glutathione S-transferase; *Sm*PNP, *S. mansoni* purine nucleoside phosphorylase.

**Table 3.** Shows the interaction between the docked ligands and the proteins in 3-dimensional images.

PROTEIN-LIGAND COMPLEX	3D INTERACTION
<i>Sm</i> PNP Momordicoside I aglycone (ChEMBL3264665)	
<i>Sm</i> PNP Balsaminol E (ChEMBL1254849)	

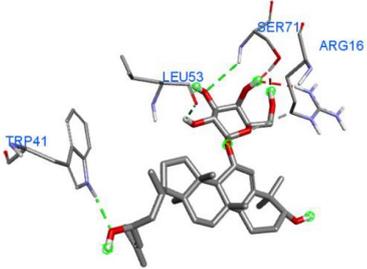
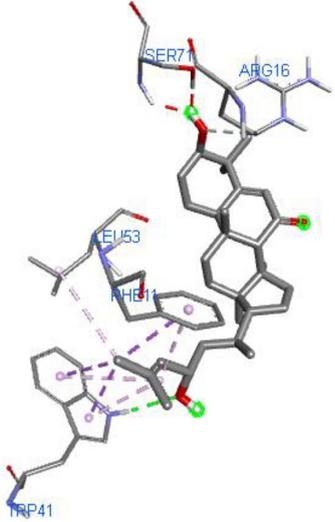
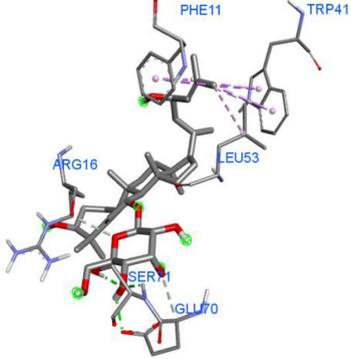
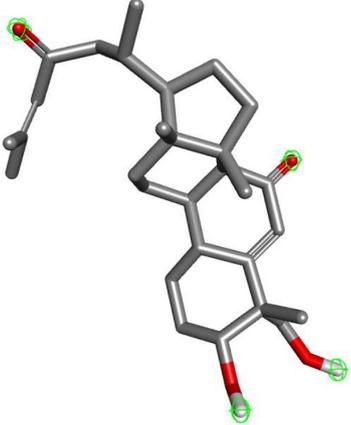
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Table 3. (Continued)

PROTEIN-LIGAND COMPLEX		3D INTERACTION
SmPNP	CHEMBL468165	
SmPNP	Charantadiol A (CHEMBL3264664)	
SmPNP	3beta,25-diol (CHEMBL3264663)	

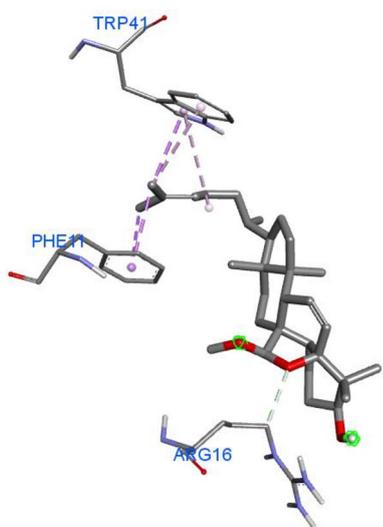
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Table 3. (Continued)

PROTEIN-LIGAND COMPLEX		3D INTERACTION
Sh 28kDaGST	Balsaminoside B (CHEMBL1928850)	
Sh28kDaGST	Balsaminol E (CHEMBL1254849)	
Sh28kDaGST	Balsaminoside C (CHEMBL1928851)	
Sh 28dkaGST	Balsaminol C (CHEMBL1254762)	

(Continued)

Table 3. (Continued)

PROTEIN-LIGAND COMPLEX		3D INTERACTION
Sh 28dkaGST	CHEMBL249658	

Abbreviations: Sh28kDaGST, *S. haematobium* 28-kDa glutathione S-transferase; SmpNP, *S. mansoni* purine nucleoside phosphorylase.

Table 4. The pharmacokinetic properties of the best 10 compounds.

COMPOUND	INTESTINAL ABSORPTION, %	BLOOD-BRAIN BARRIER PERMEABILITY, LOGBB	CYP3A4 INHIBITOR	CYP2D6 INHIBITOR	TOTAL CLEARANCE LOG (MIL/MIN/KG)
CHEMBL3264665	96.373	-0.117	NO	NO	0.292
CHEMBL1254849	96.753	-0.644	NO	NO	0.334
CHEMBL468165	95.149	-0.207	NO	NO	0.33
CHEMBL3264664	97.319	-0.001	NO	NO	0.401
CHEMBL3264663	97.757	-0.424	NO	NO	0.32
CHEMBL1928850	50.312	-1.118	NO	NO	0.492
CHEMBL1928851	50.312	-1.118	NO	NO	0.492
CHEMBL1254762	99.995	0.254	NO	NO	0.359
CHEMBL249658	98.037	0.107	NO	NO	0.423
Praziquantel	93.386	0.3	NO	NO	1.182

compounds was 4.256 mol/kg exhibited by the compounds CHEMBL1928850 and CHEMBL19288.

The calculated RMSD values and the superimposed co-crystallised and docked ligands are shown in Figures 1 and 2.

Our results are in agreement with studies that have shown that Balsaminol F, a closely related tripetene to the promising compounds from this study, has anti-anthelmintic properties against *S. mansoni* *in vitro*<sup>37,38</sup> with an LC50 value of 15  $\mu$ M.

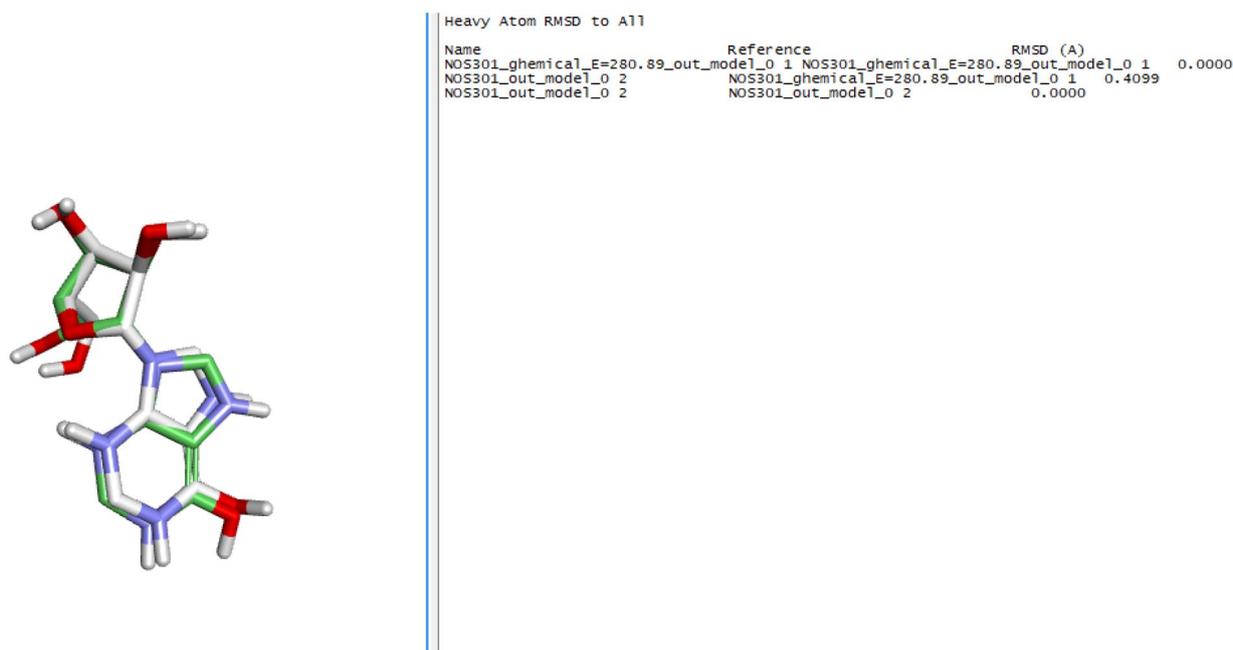
Balsaminoside B and Balsaminoside C had similar pharmacokinetic properties. The compounds had the lowest intestinal

absorption of 50.312%. This can be attributed to the fact that they are both triterpenes with similar molecular formulae and their differentiation is difficult as also observed by Serala et al<sup>36</sup>. The ligands Momordicoside I aglycone, Balsaminol E, CHEMBL468165, Charantadiol A, 3 $\beta$ ,25-diol, Balsaminol E and CHEMBL249658 violated the ROF with log *P* values greater than 5. Although the log *P* value, which affects the compound's lipophilicity, is a major determining factor in a compound's penetration across vital membranes and biological barriers, some researchers<sup>39</sup> argue that these rules can be done away with at least during a virtual screening protocol, because

**Table 5.** Pharmacokinetic properties of the best 10 compounds.

COMPOUND	AMES TOXICITY	MAX. TOLERATED DOSE (HUMAN) LOG (mg/kg/day)	HERG I INHIBITOR	ORAL RAT ACUTE TOXICITY (LD50) (MOL/KG)	ORAL RAT LONG-TERM TOXICITY (LOAEL) (mg/kg_bw/day)
CHEMBL3264665	NO	-0.869	NO	3.398	1.796
CHEMBL1254849	NO	-0.734	NO	3.996	1.949
CHEMBL468165	NO	-0.976	NO	3.548	2.26
CHEMBL3264664	NO	-0.863	NO	3.085	1.818
CHEMBL3264663	NO	-0.441	NO	3.104	1.376
CHEMBL1928850	NO	-1.559	NO	4.256	2.923
CHEMBL1928851	NO	-1.559	NO	4.256	2.923
CHEMBL1254762	NO	-0.426	NO	3.45	1.693
CHEMBL249658	NO	0.072	NO	2.251	1.752
Praziquantel	NO	-0.554	NO	2.469	1.248

Abbreviation: LOAEL, lowest adverse effect levels.



**Figure 1.** Superimposed SmPNP co-crystallised, docked ligand and RMSD values used as a validation of docking protocol. RMSD indicates root mean square deviation; SmPNP, *S. mansoni* purine nucleoside phosphorylase.

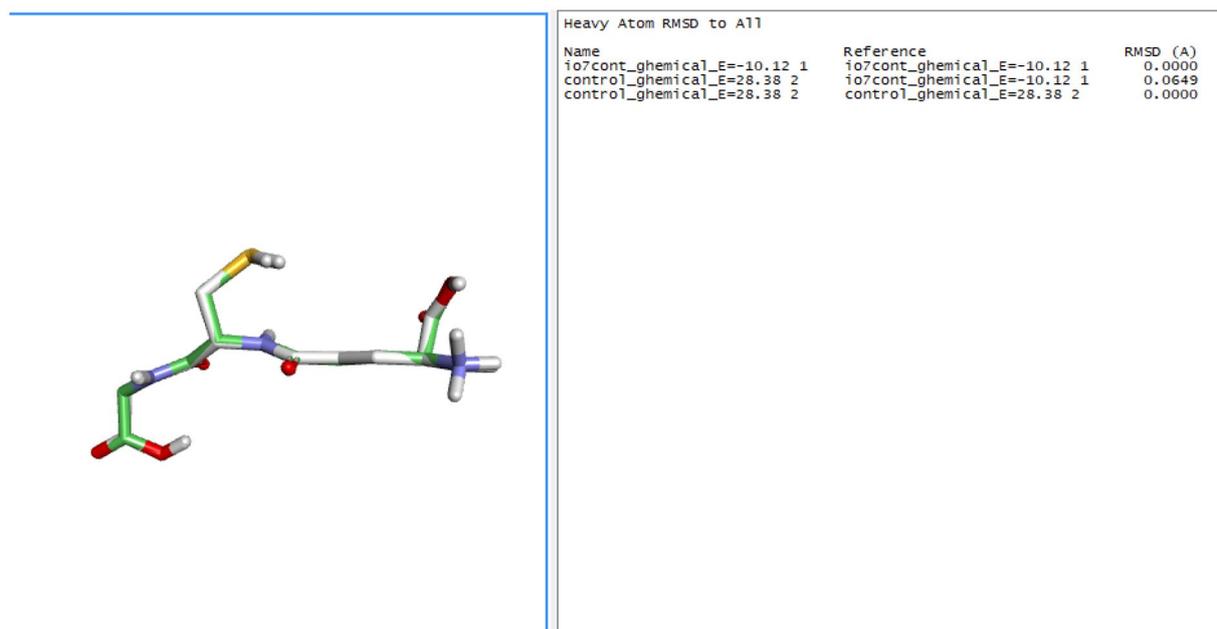
it is essential to first look for a potent molecule and once potency is validated, improved kinetics can then be sought.

Hit to lead compound identification may take time, making it impossible for most current hit compounds to reach the market. However, various approaches are being brought forward in coming up with novel anti-schistosomal agents. An interesting iterative drug development process successfully identified derivatives of the OXA drug that are effective against all three species of the *Schistosoma* parasite.<sup>40</sup> Evaluation of 6-Gingerol and its modified analogues as therapeutic candidates against *S.*

*mansoni* phosphofructokinase<sup>41,42</sup> has also been done. Molecular docking methods showed oxadiazole-2-oxides derivatives furoxan exhibiting significant anti-schistosomal activity against *S. japonicum*.<sup>43</sup> These *in silico* studies, including ours, lay a crucial foundation in the development of novel drugs against schistosomiasis.

## Conclusion

Praziquantel has been the only drug used to treat schistosomiasis since 1970 making it vital to look for novel drugs to treat the



**Figure 2.** Superimposed 28kDaGST co-crystallised, docked ligand and RMSD values used as a validation of docking protocol. 28kDaGST indicates 28-kDa glutathione S-transferase; RMSD, root mean square deviation.

disease. *C. maxima* seeds have been used in different parts of the world as traditional medicine for treatments of gastrointestinal parasites such as anthelmintic, urinary dysfunctions, hyperplasia of prostate, dysuria, cardiovascular disease, enuresis, and lowering blood glucose. This *in silico* study was aimed at exploring *Cucurbita maxima* compounds as potential therapeutics against schistosomiasis. We used computational modelling techniques to predict the inhibitory potential of *C. maxima* against *SmPNP* a crucial protein in purine synthesis and *Sb28kDaGST* which is involved in parasite metabolic cycles. The binding of *C. maxima* compounds with *SmPNP* and *Sb28dKa*, pharmacokinetic properties as established by docking studies, demonstrate that the *C. maxima* ligands are promising anti-schistosomal agents. Momordicoside I aglycone and Balsaminoside B exhibited the highest binding affinities with favourable drug-like properties. The ADMET properties of the compounds favour their consideration as drug candidates. We propose that *C. maxima* compounds be considered as potential therapeutics against schistosomiasis. We suggest that future research should involve molecular dynamic simulations to validate the structural stability of the selected ligands. Thereafter, *in vitro* and *in vivo* assays are required to get a more detailed analysis of the activity of the compounds within live organisms.

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### Author Contributions

All authors contributed to the study conception and design. Primary investigation, formal analysis and data interpretation were carried out by FLM. The first draft of the manuscript was written by FLM and all authors commented on the previous

versions of the manuscript. RS obtained funding and supervised the study. All authors have read and agreed to submit the final version of the manuscript.

### Data Availability Statement

Data can be made available upon request.

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