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Epolactaene-derived identification of potential inhibitors of S. mansoni Hsp60 towards anti-schistosomal drug discovery

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Human schistosomiasis has heavily plagued the destitute of various tropical and sub-tropical countries of the world, particularly in sub-Saharan Africa and South America, with devastating effects in various health and economic areas [1]. Globally, the burden of schistosomiasis has been controlled by using a single chemotherapeutic drug, Praziquantel [2]. However, the drug has recently displayed various shortcomings, including its inability to destroy juvenile schistosome worms, as well as drug resistance in response to its extensive use. This has prompted efforts concentrated on the discovery and design of new anti-schistosomal drugs [3].
In this study, in silico techniques and tools were used to elucidate the structural binding and interaction between the S. mansoni heat shock protein 60 (SmHsp60) and epolactaene-based inhibitors. The upregulation of heat shock proteins in the schistosome lifecycle is significant in overcoming the proteotoxic environment experienced within the human host. Through the creation of SmHsp60 complexes with pharmacophore-derived inhibitors with the lowest binding energies, molecular dynamic (MD) simulations were performed.
Post-MD analyses of the trajectories indicates various energetic, structural and conformational changes, as well as the identity of amino acid residues involved in the interaction with the inhibitors. Our results further showed that inhibitor 2 and inhibitor 3 exhibited enhanced inhibitory activity against SmHsp60, thus suggesting their potential as “lead compounds” in the design of new anti-schistosomal drugs.

References
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