STRUCTURAL FEATURES OF 24-C-STEROL-METHYLTRANSFERASE FROM *TRYPANOSOMA BRUCEI*

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Ergosterol and 24-alkylated sterols are major cell membrane components of parasites like *Trypanosoma brucei* (*T. brucei*), in contrast to cholesterol in mammals. Their biosynthesis requires an alkylation, catalyzed by a S-adenosyl-L-methionine:Δ24-sterol methyltransferase (24-SMT), a key difference between cholesterol and ergosterol biosynthesis, presenting an opportunity for the rational design of anti-infective agents. Protonated azasterols (AZA) inhibit 24-SMT, arresting parasite development production of selective inhibitors. This model could elucidate the catalytic site and guide the rational drug design. Our goals consists of building 3D models for *T. brucei’s* 24-SMT using threading, comparative modeling and map its active site to build a pharmacophoric model. We built 100 models based on the structure of 4′-O-methyltransferase *L. aerocolonigenes* (PDB ID 3BUS) with 60% coverage, 23% identity and 41% similarity. After validation, the active site was mapped for the best model. Docking parameters were optimized by redocking S-Adenosyl-L-Homocysteine to 3BUS structure. After that, three different AZA were docked with 24-SMT. Comparative modeling showed the best model to have the following parameters: Ramachandran plot where the highest value R1 is 95.2%, RMSD with template is 0.37Å and the DOPE score is -23404. Active site residues were predicted to be G58, C59, N80, Q85, D108, F109 and I125.
The docking for all the azasterols tested showed over 55% of the ranking poses in the same cluster with a binding energy below -10.40 kcal/mol. We can conclude that our model have reasonable quality. The selected active residues were conserved between template and model and the docking study showed correlation with the experimental data.

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24-SMT, Three-dimensional structure and Trypanosoma brucei