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Screening of PDE inhibitors for antischistosomal potential using *in vitro Schistosoma mansoni* worm killing

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Background: Schistosomiasis is a worldwide health problem and Praziquantel is the only drug currently used for the treatment. There is some evidence that extensive monotherapy of Praziquantel may be leading to drug resistance in the parasite.

Method: A total 146 compounds were examined *in vitro* for antischistosomal potential against adult and early mature *Schistosoma mansoni* worms using a well cultured medium. Worms were treated with different concentrations of phosphordiesterase inhibitors and after 5 days, worm was assayed in terms of viability, motility, death of worms, female ovipositing capacity and worm coupling.

Result: Findings of one or two repeat experiments revealed potential anti schistosomal activities against adult mature schistosomes, expressed as worm killing/and or sluggish worm movement, worm pairing and female ovipositing capacity for 52 compounds. However, the effect was recorded at high concentrations, resulting in worm killing for 26% of the compounds (13) with the survivors showing sluggish worm movement. All compounds showed worm killing at high concentrations of 100 μM and 50 μM revealed, worm uncoupling with absence of ova. At the concentrations of 25 μM and 10 μM, 4% and 8% out of a total of 13 compounds showed the same profile. Reduction in number of eggs was recorded for most of the compounds (34%) with less concentrations in the presence of living intact couples. 33% of the compounds showed no worm killing, uncoupling with absence of eggs was recorded. In four out of 52 compounds (7%), no worm killing with absence of ova was recorded despite presence of intact couples. In 46 out of 52 promising compounds, only male worms were affected where 100% of them were killed. Meanwhile, insult to early mature worms was more pronounced. Expression and cloning analysis of PDEs in *S. mansoni* adult and early mature worms revealed higher expression of Sm4A, Sm4C and Sm11 in adult and early mature male worms than in female worms. Sm9C is highly expressed in juvenile male.

Conclusion: PDE inhibitors showed potential against schistosomiasis In vitro with insult mainly targeting worm ovipositing.

Biography

Samia William is a Professor in Theodor Bilharz Research Institute, Egypt. As a Senior Scientist, she conducted several research studies in evaluating several antischistosomal drugs and spearheaded many research teams since joining TBRI in evaluation of the antischistosomal activity (*in vivo*) and *in vitro* culture assays for the effect of new drugs (synthetic & natural) on schistosome worms, in performing worm muscle tension, isotopic estimation of calcium uptake and transmission &amp and Scanning Electron Microscopy. She has shared and worked in eight research projects sponsored by international and national agencies; published more than 22 research articles in peer reviewed international journals and supervised four MSc and three PhD theses.

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