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Potential antischistosomal activity of PDE inhibitors using *in vitro Schistosoma mansoni* worm killing

We report the testing of 135 non-toxic phosphodiesterase inhibitors developed at Vrije Universiteit Amsterdam (VUA), University of Antwerp (UA) and CSIC, with molecular weights between 234 and 606, for their potential antischistosomal activity. The compounds were assessed for killing of adult mature and early mature *Schistosoma mansoni* worms *in vitro*; female ovipositing capacity and worm coupling. Findings of one or two repeat experiments revealed potential antischistosomal activities against adult mature schistosomes, expressed as worm killing/and or sluggish worm movement or exaggerated spastic worm contractions for 25 compounds. However, the effect was recorded at high concentrations of 100 µM and 50 µM, resulting in worm killing of 20%-100% and 27%-50% respectively for 56% of the compounds (14) with the survivors showing sluggish movement. Sluggish worm movement without killing was recorded for five of the compounds (20%) with absence of ova for two compounds. 24% of the compounds (six) revealed exaggerated spastic worm contractions. In 24 out of 25 promising compounds, only male worms were affected and 100% of those were killed. Meanwhile insult to early mature worms was more pronounced. The percentage worm killing recorded at 25 µM of test compounds was 0%-44%, with the insult still directed against male worms only. This was contrary to 0%-27% killing when mature worms were examined. All compounds (14) showing worm killing at high concentrations of 100 µM and 50 µM (56%) revealed, worm uncoupling with absence of ova. At the concentrations of 25 µM and 10 µM, 4% and 8% out of a total of 25 compounds showed the same profile. NPD0223 (VUA) was the most promising compound; 100%, 50%, 25% and 7% worm killing at concentrations of 100 µM, 50 µM, 25 µM and 10 µM were recorded. 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.

Biography

Sanaa S Botros is a professor of pharmacology at Theodor Bilharz Research Institute (TBRI), Egypt. She has been carrying research work on efficacy/resistance and pharmacokinetics of antischistosomal drugs since >30 years. She has shared her work in several international projects and initiatives. She is the Director of WHO-ANDI Excellence Center on antitrematodal R&D. She is a winner of several national and regional awards in life sciences.

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