Turning the untapped stones of the repurposed drug Auranofin

Drug repurposing is an affordable and sustainable way of using the existing approved drugs to alternatively utilize it for treatment of other ailments. Auranofin is an antirheumatic agent, repurposed for its antibacterial (1, 2) and antiprotozoal activity (3, 4). Auranofin targets a class of enzymes called Thiol-reductases (TRs) which are involved in maintaining reactive oxygen species (ROS) or oxygen free radicals homeostasis in the cell. Build up of these ROS can cause damage to nucleic acid content of cell i.e. DNA and RNA, and proteins which can eventually lead to cell death. Auranofin is a metal (Gold or Au) conjugated drug which transfers its Au atom to the target enzyme in turn permanently inhibiting its catalytic function. Although how this transfer of metal atom actually occurs was unknown. Comparing the amino acid sequences and analyzing the docking and simulation results of TRs from different parasitic organisms against Auranofin we have mapped the binding site of the drug and proposed the plausible mechanism of transfer of Au which forms a basis for understanding the formation of metal coordinated adducts (5). This mechanistic understanding can further assist in repurposing of the drug. We also designed some of the Auranofin analogues which were showing better in silico results compared the parent molecule, Auranofin, which can be optimized and tested in future as potential drugs against TRs (5).

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