SILVER DIPHOSPHINE COMPLEXES AS ANTIMITOCHONDRIAL AGENTS

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Like their Au(I) counterparts, silver complexes of the type $[M(R'_2P(CH_2)_nPR''_2)_2]^+$ exhibit potent cytotoxicity towards cancer cells *in vitro*,^{1,2} in addition, they show antifungal and modest antibacterial properties.² However, none of these has reached clinical trials because of extreme mitochondrial toxicity related to uncoupling of oxidative phosphorylation for the gold(I) analogues.³ We now report that the Ag(I) complex, $[Ag(Et_2PCH_2CH_2PPh_2)_2]NO_3$, (I), inhibits the growth of yeast selectively in non-fermentable media, indicating a primary effect on mitochondrial function. Yeast cells in a fermentable medium (containing glucose) show a high frequency of the mitochondrial mutation *petite*, while toxicity (measured as cell death) is low. Aspirin in the growth medium largely reverses the antimitochondrial effects of the complex. The chemistry of this complex and the implications for drug design will be discussed.

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References

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