

***IN VITRO* NEUROTOXICITY OF ANTIMALARIALS AS MEASURED BY INHIBITION OF MITOCHONDRIAL FUNCTION**

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artemisinin compounds are very potent antimalarials that have been used for the treatment of drug resistant and severe malaria. However, there were many reports of artemisinin neurotoxicity in animals. A rapid screening method to predict the potential neurotoxicity of newly developed artemisinin-related antimalarial drugs is needed. Electron microscopy confirms that one of the targets in the neuronal cell for dihydroartemisinin (DHA) are mitochondrial membranes. We have developed an *In vitro* neurotoxicity test based on the measurement of the mitochondrial function in neuroblastoma cells (NG108). The technique is based on the measurement of the reduction of ATP levels by the drugs in the presence of 100 μ M ADP after 4 hr incubation. The ATP levels in NG108 in the presence of ADP increases about 90%. Upon addition of the known mitochondrial enzyme inhibitors, rotenone (100 μ M) and antimycin (25 μ M), the ATP levels were reduced to 13.2% and 29.4% respectively. Artelinic acid (an artemisinin compound developed by the US Army) and DHA at 100 μ M showed a reduction of ATP levels to 66.5% and 48.1%, respectively. Interestingly, other classes of compound such as mefloquine (25 μ M) and tafenoquine (5 μ M) reduced the ATP production of NG108 to 2.2% and 27.9%, respectively. This technique is a very rapid method and may prove valuable in the neurotoxicity screening of new antimalarials.

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