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Chloroquine is a zinc ionophore

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Abstract

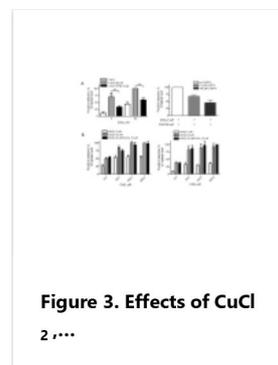
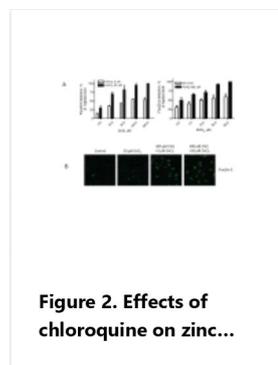
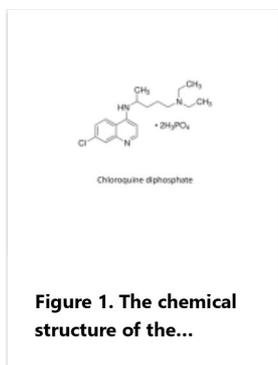
Chloroquine is an established antimalarial agent that has been recently tested in clinical trials for its anticancer activity. The favorable effect of chloroquine appears to be due to its ability to sensitize cancerous cells to chemotherapy, radiation therapy, and induce apoptosis. The present study investigated the interaction of zinc ions with chloroquine in a human ovarian cancer cell line (A2780). Chloroquine enhanced zinc uptake by A2780 cells in a concentration-dependent manner, as assayed using a fluorescent zinc probe. This enhancement was attenuated by TPEN, a high affinity metal-binding compound, indicating the specificity of the zinc uptake. Furthermore, addition of copper or iron ions had no effect on chloroquine-induced zinc uptake. Fluorescent microscopic examination of intracellular zinc distribution demonstrated that free zinc ions are more concentrated in the lysosomes after addition of chloroquine, which is consistent with previous reports showing that chloroquine inhibits lysosome function. The combination of chloroquine with zinc enhanced chloroquine's cytotoxicity and induced apoptosis in A2780 cells. Thus chloroquine is a zinc ionophore, a property that may contribute to chloroquine's anticancer activity.

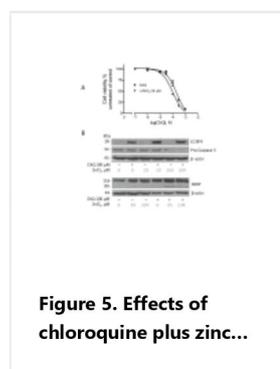
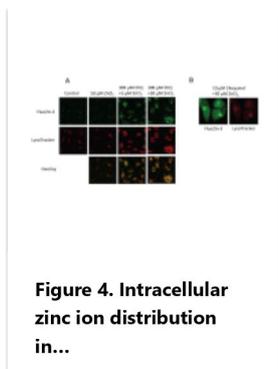
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