PROTECTIVE EFFECT OF TEMPAMINE ON THE PLASMA MEMBRANE OF CELLS TREATED WITH DOXORUBICIN

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Anthracycline drug doxorubicin (DOX) is widely used in treatment of a number of cancers but its use is limited by both acute and delayed dose-dependent side effects such as cardiotoxicity or hepatotoxicity. It has been shown that side effects of anthracyclines are mainly attributed to their ability to generate superoxide and hydroxyl radicals in targeted tissue, which takes place during metabolic activation of these drugs inside the cells. According to different authors DOX targets the cell membrane mainly at the anionic phospholipid level and degradation of these structural lipids of the plasma membrane is considered as one of the main factor for the toxic effects of this anticancer drug.

The objective of this work was to assess the capacity of the piperidine nitroxide Tempamine, TE, to attenuate the changes in plasma membrane fluidity induced by Doxorubicin and thus to protect plasma membrane against the damage induced by this drug. Tempamine, cell permeable stable radical of low molecular weight, has been shown to protect cellular macromolecules from oxidative damage. Fluorescence spectroscopic analysis of fluidity of hydrophobic core of plasma membrane was determined on the basis of fluorescence anisotropy of the hydrophobic fluorescent probe 12-AS [12-(9-anthroyloxy)-stearic acid]. We have found that low concentration of DOX (0.5 and 1.0 μM) caused significant increase in plasma membrane fluidity. Tempamina did not change fluidity of the hydrophobic core of lipid bilayer at both low (1 and 10 μM) and high (100–500 μM) concentrations. Middle concentrations (20 and 50 μM) of the nitroxide caused however modest membrane fluidization, while concentrations higher than 1 mM provoked membrane rigidification. In combined treatment Tempamine depending on the concentration range used protected either fully (1–20 μM; 500–1000 μM) or partially (50–200 μM) plasma membrane against damage caused by 0.5 μM DOX. The nitroxide was fully protecttive (except concentration of 50 μM) in cells treated with 1 μM DOX. Slight decrease in membrane fluidity was observed at high concentration of TE (2 mM) applied together with low concentrations of DOX (0.5 and 1.0 μM).

These results suggest that Tempamine could be an efficient protector against damage to plasma membrane caused by Doxorubicin.