

**THE NITROXIDES PIROLIN AND PIROLID PROTECT THE PLASMA
MEMBRANE OF RAT CARDIOMIOCYTES AGAINST DAMAGE
INDUCED BY ANTHRACYCLINES**

ANETA KOCEVA-CHYŁA¹, ADAM SOKAL², KATARZYNA KANIA¹,
KRZYSZTOF GWOŹDZIŃSKI³ and ZOFIA JOŹWIAK¹

¹Department of Thermobiology, University of Łódź, ²First Department and
Clinic of Cardiology, Silesian Medical Academy, Zabrze, Poland, ³Department
of Molecular Biophysics, University of Łódź, Łódź, Poland

The Anticancer anthracycline drugs DOX and ACL have been shown to enhance the production of reactive oxygen species in cancer cells, which is considered one of the main mechanisms of the toxicity of these drugs. At the same time, long-term treatment with DOX and other anthracyclines is limited by their acute and chronic cardiotoxicity. A major role in the development of cardiotoxicity has been assigned to the free radical production generated by anthracyclines, leading to lipid peroxidation and damage to the cell nucleus. In this study, we investigated the protective effect of two water-soluble and cell-permeable stable radicals-antioxidants – the nitroxides PIROLIN and PIROLID – on the toxic effects induced by doxorubicin (DOX) and aclarubicin (ACL) in isolated rat cardiomyocytes. We analysed the modification of membrane fluidity of isolated rat cardiomyocytes treated with DOX and ACL alone and in the presence of nitroxides PIROLIN and PIROLID. The analysis was performed at the hydrophobic core of the lipid bilayer via the fluorescence spectroscopy technique using the fluorescent probe 12-(9-anthroyloxy)-stearic acid (12-AS). We demonstrated that both anthracycline drugs influence the hydrophobic core of the lipid bilayer and cause a significant increase in membrane rigidity at concentrations of 5-20 μM . PIROLIN alone did not significantly change the structure of membrane lipids in contrast to PIROLID, which at doses higher than 50 μM caused an increase in membrane fluidity. The protective effect of PIROLIN and PIROLID on plasma membrane damage was observed in cells pretreated with both nitroxides before incubation with doxorubicin and aclarubicin.