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Isfahan University of Medical Sciences

Iron chelation afforded cardioprotection against H2O2-induced H9C2 cell injury: Application of novel 3-hydroxy pyridine-4-one derivatives

R. Sabet[1,*], M. Behjati[2], A. Fassihi[3], L. Saghaie[3], R. Miri[4]

[1]Department of Medicinal Chemistry, Faculty of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Department of Cardiology, School of Medicine , Isfahan University of Medical Sciences, Isfahan, Iran
[3]Department of Medicinal Chemistry, School of Pharmacy and Pharmaceutical Sciences and Isfahan Pharmaceutical Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.
[4]Medicinal and Natural Product Chemistry Research Center, Shiraz University of Medical Sciences

Background and Aims: Intracellular iron chelation is the only well-established strategy for cardioprotection. Chelators administrated at optimal dose supposedly shield the labile iron pool inside the cardiomyocytes and thereby prevent the excessive formation of ROSs. So, the aim of this study is to evaluate the cardioprotective potential of some novel analogues of 3-hydroxy-4-pyridinone on a rat myoblast cell line.
Methods: In order to make an in vitro model of cardiotoxicity, H2O2-treated H9C2 rat cardiac cells were used. These cells were exposed to various concentrations of either of four novel L1 (1,2-dimethyl-3-hydroxy-4-pyridinone) derivatives or L1, as a positive control. The cardioprotective effect of the compounds was evaluated by their capability to prevent the release of LDH from H9C2 cells. Potential cytotoxicity of the compounds and their effect on cell survival were also assessed using cell proliferation XTT assay and annexinV/PI staining, respectively.
Results: The obtained data demonstrated that 5a and 5b inhibited apoptosis and necrosis without in vitro cytotoxic effects. These compounds are potential novel iron chelators comparable with L1 ($P<0.5$).The synthesized compounds had log p greater than L1. These lipophilic compounds exerted cardioprotection through the enhancement of the cell survival.
Conclusions: The overall results obtained in this study are very promising in preventing cardiac injury directing to apoptosis pathway. Further investigations including in vivo studies are needed to introduce them as candidates for perquisite evaluations for clinical applications.

Keywords: Iron chelation; H9C2 cell injury; Cardioprotection; 3-Hydroxy-4-pyridinone