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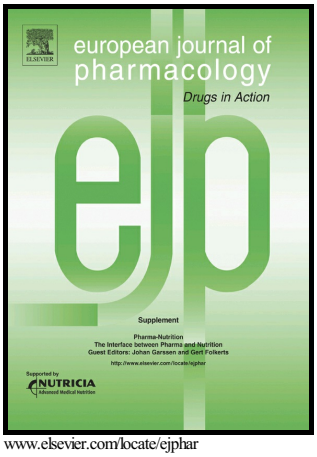

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Small molecules exert anti-apoptotic effect and reduce oxidative stressaugmenting insulin secretion in stem cells engineered isletsagainst hypoxia

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Abstract

Transplantation of pancreatic islets is the most reliable treatment for Type 1 diabetes. However cell death mediated by hypoxia is considered as one of the main difficulties hindering success in islet transplantation. The aim of our experiment was to investigate the role of small molecules in survival of Islet like cell aggregates (ICAs) engineered from umbilical cord matrix under oxygen deprived condition (<5%O_2).ICAs were analyzed for cell death via fluorosceindiacetate/propidium iodide (FDA/PI) staining, estimation of Caspase 3 and free radical release in presence and absence of small molecules. The samples were also analysed for the presence of hypoxia inducible factor 1α (HIF1α) at both transcriptional and translational level. The addition of small molecules showed profounddefensive effect on ICAs under hypoxicenvironment as evidenced by their viability and insulin secretion compared to untreated ICAs. The combinations of Eicosapentaenoic acid (EPA), Docosahexaenoicacid(DHA) and metformin and EPA,DHAandγ amino butyric acid (GABA) acted as anti-apoptotic agentsforhuman ICAs when exposed to 1% O_2 for 48h.The combinations of the small molecules reduced the total reactive oxygen species and malonaldehyde (MDA) levels and enhanced the