

Role of recombinant human erythropoietin loading chitosan-tripolyphosphate nanoparticles in busulfan-induced genotoxicity: Analysis of DNA fragmentation via comet assay in cultured HepG2 cells

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Abstract:

Busulfan is one of the most effective chemotherapeutic agents used for the treatment ofchronic myeloid leukemia. Busulfan is involved in secondary malignancy due to its genotoxic potential in normal tissues. As an alkylating agent busulfan can cause DNA damage by cross-linking DNAs and DNA and proteins, induces senescence in normal cells via transient depletion of intracellular glutathione (GSH) and subsequently by a continuous increase in reactive oxygen species (ROS) production. Erythropoietin, a glycoprotein widely used against drug induced anemia in cancerous patients and regulates hematopoiesis, has been shown to exert an important cyto-protective effect inmany tissues. Recombinant human erythropoietin has been demonstrated to directly limitcell injury and ROS generation during oxidative stress. Furthermore, rhEPO decreasedlevels of pro-apoptotic factor (Bax) and also increased expression of the anti-apoptoticfactor Bcl2. According to EPO's short half-life and requirements for the frequentlyadministration, finding the new strategies to attenuate its side effects is important. Theaim of this study was to explore whether rhEPO loading chitosan – tripolyphosphatenanoparticles protects against busulfan-induced genotoxicity in HepG2 cells. For this purpose cells were incubated with busulfan alone, regular rhEPO alone and regularrhEPO and CS-TPP-EPO nanoparticles along with busulfan in pre and co-treatmentcondition. Our results showed that busulfan induced a noticeable genotoxic effects inHepG2 cells ($p<0.0001$). Both regular rhEPO and CS-TPP-EPO nanoparticles reduced the effects of busulfan significantly ($p<0.0001$) by reduction of the level of DNA damage via blocking ROS generation, and

enhancement intracellular glutathione levels. CS-TPPEPO nanoparticles were more effective than regular rhEPO in both pre and co-treatment conditions. In conclusion,our results show that administration of rhEPO and CS-TPPEPO nanoparticles especially in the pre-treatment conditions, significantly decreased the level of DNA damage induced by busulfan, measured with the comet assay, in HepG2 cells compared to the regular rhEPO group.

Biography

Nasrin Ghassemi Barghi was born in Ardabil (Iran) at 1989. She is a PhD candidate of toxicology at Mazandaran University of medical sciences. She accomplished her M.s in toxicology from Isfahan University and BS of laboratory sciences from Kerman University of medical sciences. Scientifically, she has been interested in genotoxicity and comet assay and erythropoietin tissue protective effects. she is also interested in cancer chemotherapy and secondary malignancy induced by anticancer drugs. She works on antioxidants such as melatonin and EPO and … She has outstanding records of scientific and academic accomplishments with multiple research, publications in highly prestigious journals and various presentations in both national and international conferences.

Research interests: Cell culture; Apoptosis; Nanotoxicology; Synthsis of Chitosan nanoparticle; Western blotting; Genotoxicity; Comet and Micronucleus assay; HPLC, in vivo Organ Toxicity

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