CHARACTERIZATION OF A NEW HEME IRON BASED DIETETIC SUPPLEMENT: FROM THE QUALITATIVE-QUANTITATIVE ANALYSIS TO THE BIOCHEMICAL AND TOXICOLOGICAL EVALUATION

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ABSTRACT

Iron therapy components are essential in disease states or in states of iron deficiency. Furthermore, given that iron can catalyze the formation of free radicals and therefore potentially be detrimental to cells or tissues by this route. The aim of my PhD was addressed to obtain, through a new extractive method, a dietetic iron-heme supplement and to evaluate its toxicological end biochemical interaction in vitro.We obtain a compound of iron-heme (Fe-eme) standard final product, which was then subjected to various in vitro toxicological tests. We proceeded to assess the toxicity on Caco-2 cell lineswith different concentration of Heme-iron/Hemin/FeSO4.The results on cell viability (MTS) and cell proliferation (BrdU) showed a very low toxicity of this new compoundcompared with Hemin and FeSO4.

In particular, Fe-eme increased the cell toxicity in a time dependent manner only at the higher concentrations tested whereas hemin, a structural analog, produce a inhibition of cell viability in a dose and time related fashion reaching the peak of activity after 24h. $FeSO_4$ maintains the same pattern of activity throughout all the time points tested, increasing cell death at the higher concentrations tested. In addition, given the controversial role of HO-1 in cell survival and/or death and take into account the role of the mitochondrial 18kDa translocator protein (TSPO) on cell metabolism, we addressed our studies to evaluate a possible modulation of these proteins by Fe-eme.

The obtained results showed an involvement of TSPO rather than HO-1, in the activity elicited by Fe-eme and hemin. In particular the result obtained with Fe-eme and hemin alone or in association with PK11195,a specific TSPO antagonist, suggest that Fe-eme and Hemin act as agonist on TSPO, probably trough an increase of the level of intracellular ROS, leading to a decrease of cell viability and cell proliferation. Our results in vitro, suggest that Fe-eme has no toxic effects at the concentrations thought by an oral assumption. A nutrition based preparation of heme-iron at low doses in the absence of side effects in terms of induction of cytotoxicity and oxidative stress may allow the maintenance of body iron status.Moreover the finding regarding the possible role of TSPO as a scavenger of porphyrin-based compounds, suggest that the receptor might contribute in protecting cells from potential toxic effect of free tetrapyrroles.

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