International Journal of Radiation Biology ›
Volume 86, 2010 - Issue 2

Radiation Effects on Rat Brain

Metalloporphyrin antioxidants ameliorate normal tissue radiation damage in rat brain

Robert D. Pearlstein, Yoshinori Higuchi, Maria Moldovan, Kwame Johnson, Shiro Fukuda, Daila S. Gridley, ...show all

Pages 145-163 | Received 22 Sep 2008, Accepted 31 Aug 2009, Published online: 11 Feb 2010

Cite this article https://doi.org/10.3109/09553000903419965

Full Article | Figures & data | References | Citations | Metrics
Reprints & Permissions | Read this article | Share

Abstract

Purpose: We examined the effects of manganese (III) meso-tetrakis (diethyl-2-5-imidazole) porphyrin, a metalloporphyrin antioxidant (MPA), on neural tissue radiation toxicity in vivo and on tumour cell radiosensitivity in vitro.

Materials and methods: MPA was administered directly into the right lateral ventricle of young adult, male Sprague-Dawley rats (0 or 3.4 µg) 3 h before treatment with a single fraction, 100 Gy radiation dose delivered to the left brain hemisphere. The effects of treatment on radiation responses were assessed at different time points following irradiation.

Results: MPA treatment prior to brain irradiation protected against acute radiation-induced apoptosis and ameliorated delayed damage to the blood-brain barrier and radiation necrosis, but without producing a discernible increase in tissue superoxide

disumtase (SOD) activity. In vitro, MPA pretreatment protected against radiation-induced apoptosis in primary neuronal cultures and increased clonogenic survival of irradiated rat glioma C6 cells, but had no discernible effect on radiation-induced DNA double-strand breaks. MPA, a low molecular weight SOD mimic, significantly increased mitochondrial SOD activity in C6 cells, but not total cellular SOD activity. MPA up-regulated C6 expression of heme-oxygenase 1 (HO-1), an endogenous radioprotectant, but had no effect on HO-1 levels in human astrocytoma U-251 cells, human prostatic carcinoma LNCaP cells, or primary rat brain microvascular endothelial cells in vitro, nor on brain tissue HO-1 expression levels in vivo.

Conclusions: Metalloporphyrin antioxidants merit further exploration as adjunctive radioprotectants for cranial radiotherapy/radiosurgery applications, although the potential for tumour protection must be carefully considered.

Keywords:

antioxidant | radioprotection | normal tissue complication probability | pre-conditioning

Acknowledgements

Manganese (III) meso-tetrakis (diethyl-2-5-imidazole) porphyrin (AEOL-10150) was supplied by Incara Pharmaceuticals (Durham, NC, USA).

Declaration of interest: One of the authors JDC is a patent holder for the compound manganese (III) meso-tetrakis (diethyl-2-5-imidazole) porphyrin used in this study. None of the other authors report any conflicts of interest.

An Orally Active Catalytic Metalloporphyrin Protects against 1-Methyl-4-Phenyl-1,2,3,6-Tetrahydropyridine NeurotoxicityIn Vivo

Source: Journal of Neuroscience

Cytoprotective Effect of Podophyllum hexandrum Against Gamma Radiation is Mediated via Hemopoietic System Stimulation and Up-Regulation of Heme-oxygenase-1 and the Prosurvival Multidomain Protein Bcl-2

Source: Integrative Cancer Therapies

Heme Oxygenase-1: Molecular Mechanisms of Gene Expression in Oxygen-Related Stress

Related research

People also read | Recommended articles | Cited by 36