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Comments on the mechanisms of action of radiation protective agents: basis components and their polyvalence

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Abstract

Purpose: These comments suggest a division of radiation protective agents on the grounds of their mechanism of action that increase the radio resistance of an organism.

Conclusion: Given below is the division of radiation protective agents on the basis of their mechanism of action into 3 groups: 1) Radiation protective agents, with the implementation of radiation protective action taking place at the cellular level in the course of rapidly proceeding radiation-chemical reactions. At the same time, when the ionizing radiation energy is absorbed, these agents partially neutralize the "oxygen effect" as a radiobiological phenomenon, especially in the radiolysis of DNA; 2) Radiation protective agents that even their effect at the system level by accelerating the post-radiation recovery of radiosensitive tissues through activation of a number of pro-inflammatory signaling pathways and an increase in the secretion of hematopoietic growth factors, including their use as mitigators in the early period after irradiation prior to the clinical development of acute radiation syndrome (ARS), 3) Radiomodulators including drugs and nutritional supplements that can elevate the resistance of the organism to adverse environmental factors, including exposure to ionization by means of modulating the gene expression through a hormetic effect of small doses of stressors and a "substrate" maintenance of adaptive changes, resulting in an increased antioxidant protection of the organism. Radiation protective agents having polyvalence in implementation of their action may simultaneously induce radioprotective effect by various routes with a prevalence of basis mechanisms of the action.

Keywords: Radioprotector, Radiomitigator, Radiomodulator, Mechanism of action

Introduction

Clinical radiotherapy of tumors demands a knowledge of the potential effectiveness of radiation protective agents to reduce radiation damage to healthy tissues, as well as knowledge of their impact on the radiosensitivity of tumor tissues. A theoretical understanding of the mechanisms of the radiation protective action of the agents may contribute to this knowledge.

The key aspects of radiation protective agents are the practical need to use them in specific scenarios of radiation exposure and the corresponding tactical and technical requirements for medical preparations. These aspects are related to the indications for use (depending on the nature and severity of a radiation injury), possible routes of administration, acceptable side effects in certain situations, pharmacodynamic characteristic, as well as the possibility of expected scheme of repeated administration.

A recent monograph (Arora et al. 2008) and a review (Weiss and Landauer 2009) provide a contemporary view of the pharmacological measures against the harmful effects of ionizing radiation, as well as comprehensive information about radiation protective agents — their classification, the history of discovery, pharmacological and radiation protective properties, data on tolerability, and their current use. Based on the current knowledge of the mechanism of action of radiation protective agents, in particular gene regulation induced by the increased radiation resistance of the organism, this commentary mainly focuses on some of the common features typical for their mechanism of action. For most of these agents applied in practical medicine it is possible to distinguish three main pathways for the

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Radiation-protective Drugs and Their Reaction Mechanisms J. C. Livesey, D. J. Reed, L. F. Adamson, 1985 Radiation and Human Health Michael R. Quastel, John R. Goldsmith, 1997 **Biochemical Modulation of** Anticancer Agents: Experimental and Clinical Approaches Frederick A. Valeriote, L.O. Baker, 2012-12-06 Biochemical Modulation at the present time defines an area of study in which the intracellular metabolism of a given anti cancer agent is modulated usually by a noncytotoxic agent or a cytotoxic agent at sufficiently low dosage to make it non cytotoxic in order to either increase the effectiveness of the particular agent against tumor cells or decrease its cytotox icity against normal cells The major focus of modulation has been the agents 5 fluorouracil FUra arabinofuranosylcytosine ara C methotrexate MTX and a few alkylating agents The major thrust of the studies has been to increase the flow of the anticancer agent along the pathway responsible for the formation of the cytotoxic species for example FUra to FUTP or ara C to ara CTP While in most cases the application of research re sults to clinical trials does not require the subsequent exper tise of the laboratory researchers application of biochemical modulatory schemes to clinical protocols necessitate a dramatic break with the past procedures As shown in the laboratory clinical loop below close collaboration between the laboratory and clinical investigator is essential While the laboratory REDEFINE TECHNOLOGY TESTS OR QUESTIONS FOR FURTHER THERAPEUTIC ADVANCE CLINICAL EXPERIMENTAL PROTOCOL LABORATORY RESEARCH STUDIES DEFINE AND TEST APPROPRIATE SCIENTIFIC PARAMETERS results define rationally based regimens it is essential that the clinical protocols contain the requirement that clinical material either tumor or normal tissues be sampled to deter mine whether the biochemical modulation being proposed is in fact being accomplished Radioprotectors Edward A. Bump, Kamal Malaker, 2021-12-24 It is essential to minimize damage to normal tissues during radiation therapy and many strategies have been employed in finding the best methods for radioprotection This book integrates chemical biological and clinical perspectives on these strategies and developments providing a comprehensive treatise It emphasizes new concepts in radioprotection aiming to inspire further basic science and clinical progress in radioprotector research Radioprotectors Chemical Biological and Clinical Perspectives includes the following topics Early research on radioprotectors WR 2721 an aminothiol prodrug as a radioprotector New results with naturally occurring thiols Nitroxides as effective radioprotectors in vitro and in vivo Radioprotection observed with radical scavengers or antioxidants Bone marrow radioprotection with cytokines and biological modifiers Multiple mechanisms of altering radiation response by eicosanoids Vascular response to radiation and the importance of vascular damage to normal tissue Modifiers of radiation induced apoptosis Survey of clinical trials with radioprotectors Radiation biologists and oncologists cancer researchers and toxicologists will benefit from the findings discussed and strategies for future research **Environmental Health Perspectives** ,1993 **Research Grants Index** National Institutes of Health (U.S.). Division of Research Grants, 1968 National Library of Medicine Current Catalog

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