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ORIGINAL ARTICLE

Protective effect of sesamol against ^{60}Co γ-ray-induced hematopoietic and gastrointestinal injury in C57BL/6 male mice

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Abstract

Protection of γ-ray-induced injury in hematopoietic and gastrointestinal (GI) systems is the rationale behind developing radioprotectors. The objective of this study, therefore, was to investigate the radioprotective efficacy and mechanisms underlying sesamol in amelioration of γ-ray-induced hematopoietic and GI injury in mice. C57BL/6 male mice were pre-treated with a single dose (100 or 50 mg/kg, 30 min prior) of sesamol through the intraperitoneal route and exposed to $LD_{50/30}$ (7.5 Gy) and sublethal (5 Gy) dose of γ-radiation. Thirty-day survival against 7.5 Gy was monitored. Sesamol (100 mg/kg) pre-treatment reduced radiation-induced mortality and resulted survival of about 100% against 7.5 Gy of γ-irradiation. Whole-body irradiation drastically depleted hematopoietic progenitor stem cells in bone marrow, B cells, T cell subpopulations, and splenocyte proliferation in the spleen on day 4, which were significantly protected in sesamol pre-treated mice. This was associated with a decrease of radiation-induced micronuclei (MN) and apoptosis in bone marrow and spleen, respectively. Sesamol pre-treatment inhibited lipid peroxidation, translocation of gut bacteria to spleen, liver, and kidney, and enhanced regeneration of crypt cells in the GI system. In addition, sesamol pre-treatment reduced the radiation-induced pattern of expression of p53 and Bax apoptotic proteins in the bone marrow, spleen, and GI. This reduction in apoptotic proteins was associated with the increased anti-apoptotic-Bcl-x and PCNA proteins. Further, assessment of antioxidant capacity using ABTS and DPPH assays revealed that sesamol treatment alleviated total antioxidant capacity in spleen and GI tissue. In conclusion, the results of the present study suggested that sesamol as a single prophylactic dose protects hematopoietic and GI systems against γ-radiation-induced injury in mice.

Keywords: sesamol, γ-radiation, hematopoietic progenitor stem cell, bone marrow cells, spleen, gastro-intestine, p53, PCNA, B cells, CD4/CD8, apoptosis

Introduction

Exposures to ionizing radiation cause oxidative injury to almost all organs depending upon the radiosensitivity of the organs, radiation dose, and dose rate [1,2]. These damages result in multi-organ dysfunction, which can lead to acute radiation syndrome (ARS) and long-term health effects, for example, cancer or pulmonary fibrosis [3,4]. ARS includes hematopoietic (2–6 Gy), gastrointestinal (6–8 Gy), and cerebrovascular (>8 Gy) sub-syndromes [5]. The hematopoietic and gastrointestinal (GI) subsyndromes are manifested by enormous loss of hematopoietic progenitor stem cells (HPSCs) in bone marrow and impairment of crypt cell regeneration in the GI tract, respectively. Therefore, strategies for developing prophylactic agents as radioprotectors necessarily require an investigation of hematopoietic and GI injury [5].

The possibility of occurrence of ARS during planned radiation exposure exists in critical operations, military warfare, radiation environment, nuclear reactors, and radiotherapy. At present, no radioprotector is available to prevent radiation-induced injuries to hematopoietic and GI systems. Therefore, there is an urgent necessity to develop radioprotectors for human use. Even though the research in this direction was started about five decades ago and amifostine (WR 2721) had emerged as a radioprotector, due to toxicity in human, this molecule was not approved as radioprotector. US FDA has approved amifostine as a cytoprotective agent for patients undergoing radiotherapy of head and neck cancers [6]. Till date, several thousand different chemical and biological compounds have been investigated *in vitro* and *in vivo* [5,7,8]. Because of the complex nature of radiation effects in biological systems, all potential molecules have showed lower efficacy, and therefore the possibility of toxicity at higher doses in humans is one of the impediments for the development of radioprotectors. No prophylactic agents are approved by the FDA (USA) to alleviate ARS in humans [9]. Thus, the search for safe, less toxic, or nontoxic prophylactic agents as radioprotectors is continuing [9,10].

Sesamol (3, 4-methylenedioxyphenol) is a natural dietary antioxidant present in processed sesame oil [11],

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