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Nicotynic Acid Derivatives as New Potential Radio-Protective and Radio-Remedial Agents

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Disorders caused by the short-term absorption of moderate-to-high doses of ionizing radiation are often associated with suppressed heamatopoiesis as well as primary and secondary inflammation and thrombosis. Nicotinamide (NA), a derivative of nicotinic acid (NAc) and a precursor of nicotinamide adenine dinucleotide (NAD+), is metabolized in the body to 1-methylnicotinamide (MNA) which exerts both anti-thrombotic and anti-inflammatory activities based on its effects on the vascular endothelium. Also, 1,4-dimethylpyridine (1,4-DMP), a pyridinium salt formed during coffee roasting, and 1-methyl-3-acetylpyridine (1,3-MAP), a synthetic analogue of NAD+, may exert similar properties. Hence, the aim of the present study was to assess potential radio-protective and radio-remedial effects of NAc, NA, MNA, 1,4-DMP, and 1,3-MAP.
The 30-day survival of BALB/c mice was assessed after whole body irradiation (WBI) with γ-rays at a dose of 7.5 Gy. NAc, NA, MNA, 1,4-DMP, and 1,3-MAP were given to the animals in drinking water at 100 mg/kg b.w. daily, starting 7 days before, on the day of, or 7 days after the exposure to ionizing radiation and continued until the animals'death or the end of observation. Another group of mice was exposed (WBI) to X-rays at 6.5 Gy and on the selected days thereafter spleen and bone marrow cell as well as the peripheral blood leukocyte and thrombocyte counts were estimated.
Application of the derivatives of NAc significantly increased the survival of mice from the groups in which administration of these compounds started 7 days before (NAc, MNA, 1,4-DMP), on the day of (1,4-DMP), and 7 days after (NAc, MNA, 1,4-DMP, 1,3-MAP) the irradiation. Inconsistent results obtained in mice exposed to X-rays indicate that stimulation of haematopoiesis does not seem to be the underlying mechanisms of the enhanced survival and other possibilities, such as reversal of the radiation-induced inflammatory and/or thrombotic reactions in association with the modulated endothelial function, need to be considered.

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