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The scavengers of reactive oxygen species TEMPOL and reactive nitrogen species cPTIO enhance chromosome aberrations induced by low-dose γ-irradiation

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There is significant evidence that, in living systems, the overproduction of reactive oxygen species (ROS) and nitrogen species (RNS) can damage DNA, proteins, cellular membranes and leads to tissue dysfunction. Ionizing radiation is a strong inducer of ROS and RNS. The SOD-mimetic TEMPOL and nitric oxide scavenger cPTIO were found to detoxify efficiently ROS and RNS, correspondingly, protecting cells from the mutagenic and cytotoxic effects of radiation. In the present study, we investigated the effect of these compounds on chromosome aberration induction in human breast carcinoma cells Cal51 exposed to γ-radiation at low and high doses. At high doses (1 and 2 Gy), treatment with TEMPOL resulted in an about twofold decrease in the yield of aberrant cells, which is in agreement with its declared properties. At the same doses of γ-exposure, the nitric oxide scavenger cPTIO had no effect on chromosome aberration yield compared with untreated and TEMPOL-treated cells. However, an inverse effect was observed at a low-dose irradiation (10 cGy). Both scavengers enhance chromosome aberration induction, and this effect was most pronounced when TEMPOL and cPTIO were used simultaneously. In this case, the frequency of chromosome aberrations increased more than 1.5 times. A measurement of the ROS level with CM-H2DCFDA-staining in cells exposed to this dose showed that in the presence of Tempol ROS yield increased rather than decreased. However, at the dose 1 Gy this compound efficiently detoxified ROS and it can explain pronounced protective effect of TEMPOL on chromosome aberrations induction which was observed at high doses. A pro-oxidant effect of nitroxides like TEMPOL was reported and ascribed to the formation of strongly oxidizing oxoammonium derivatives that can be responsible for its genotoxic effect at low doses of γ-irradiation. Hence, reactions with superoxide overproduced at high doses can reduce oxoammonium cation back to its respective nitroxide are anticipated to improve the antioxidative effect of nitroxides.

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