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Tempol prevents genotoxicity induced by vorinostat: role of oxidative DNA damage.

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Abstract: Vorinostat is a member of histone deacetylase inhibitors, which represents a new class of anticancer agents for the treatment of solid and hematological malignancies. Studies have shown that these drugs induce DNA damage in blood lymphocytes, which is proposed to be due to the generation of oxidative lesions. The increase in DNA damage is sometimes associated with risk of developing secondary cancer. Thus, finding a treatment that limits DNA damage caused by anticancer drugs would be beneficial. Tempol is a potent antioxidant that was shown to prevent DNA damage induced by radiation. In this study, we aimed to investigate the harmful effects of vorinostat on DNA damage, and the possible protective effects of tempol against this damage. For that, the spontaneous frequency of sister chromatid exchanges (SCEs), chromosomal aberrations (CAs), and 8-hydroxy-2-deoxy guanosine (8-OHdG) levels were measured in cultured human lymphocytes treated with vorinostat and/or tempol. The results showed that vorinostat significantly increases the frequency of SCEs, CAs and 8-OHdG levels in human lymphocytes as compared to control. These increases were normalized by the treatment of cells with tempol. In conclusion, vorinostat is genotoxic to lymphocytes, and this toxicity is reduced by tempol. Such results could set the stage for future studies investigating the possible usefulness of antioxidants co-treatment in preventing the genotoxicity of vorinostat when used as anticancer in human.