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Pronounced synergistic cytotoxicity, but not genotoxicity, on human peripheral lymphocytes induced by a particular combination of pemetrexed and cefixime

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In this study, the genotoxic and cytotoxic effects of a particular combination of pemetrexed (Pmx, a novel antimetabolite antineoplastic agent) and cefixime (Cfx, a beta-lactam ring-containing cephalosporin agent) were investigated in human peripheral blood lymphocytes. Chromosome aberration (CA), sister chromatid exchange (SCE) and micronucleus (MN) tests were used to assess genotoxicity, and the cytotoxicity was evaluated using mitotic index (MI), proliferation index (PI) and nuclear division index (NDI). Human peripheral blood lymphocytes were treated with 12.5 + 450, 25 + 800, 37.5 + 1150, and 50 + 1500 microg/ml of Pmx+Cfx, respectively, for 24 and 48 h. The combination of Pmx + Cfx did not induce the CA or SCE in human peripheral blood lymphocytes when compared with both the control and solvent control. MN formation in human peripheral blood lymphocytes was not significantly increased after treatment with the particular combination of Pmx+Cfx. However, the combination treatment of Pmx+Cfx caused a significant reduction in the MI, PI and NDI at all concentrations for 24- and 48-hr treatment periods. Generally, the Pmx+Cfx combination inhibited cell proliferation more than positive control (MMC), and showed a higher cytotoxic/cytostatic effect than MMC at both treatment periods. Furthermore, in this study, the results of combined effects of Pmx+Cfx were compared with the results of single effects of Pmx (Istifli and Topaktas, 2012) or Cfx. Taken together, the particular combination of Pmx+Cfx synergistically induced the cytotoxicity in human peripheral blood lymphocytes.

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