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Title: 3-Aminobenzamide – a PARP inhibitor enhances the sensitivity of peripheral blood micronucleus

and comet assays in mice

Authors: Kansara, B.R. (/jspui/browse?type=author&value=Kansara%2C+B.R.)

Keywords: DNA damage

Genotoxicity

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Weak genotoxins

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Abstract:

Context: DNA repair is an essential outcome of DNA damage, which may compromise the end point of various in vitro and in vivo test systems of the genotoxicity evaluation. poly(ADP-ribose) polymerase (PARP) enzymes have an essential role in DNA repair. Here, we investigated the effect of 3-AB, a PARP inhibitor on the sensitivity of comet and PBMN assays. Objective: This study aimed to enhance the sensitivity of the comet and peripheral blood micronucleus (PBMN) assays using 3-aminobenzamide (3-AB), a well-characterized PARP inhibitor. Materials and methods: Cyclophosphamide (CP, 50mg/kg), 5-flourouracil (5-FU, 25mg/kg), zidovudine (AZT, 400mg/kg) and furosemide (FUR, 60mg/kg) were selected as genotoxins. 3-AB was given every 8h with the first dose given 2h before the genotoxin treatment. For the PBMN assay, small amount of blood was taken from the tail tip of each animal and smears were prepared. The comet assay was performed in PBL, bone marrow and liver. Results: In the comet as well as PBMN assay, 3-AB pre-treatment enhanced the extent of DNA damage in all the combination groups (3-AB+CP, 3-AB+5-FU and 3-AB+AZT) compared to CP, 5-FU and AZT per se. 3-AB also enhanced the DNA damage caused by FUR in the bone marrow and liver. Discussion: This study results clearly demonstrate that the pretreatment with 3-AB (30mg/kg) significantly enhances the sensitivity of the PBMN and comet assays. This model may be useful for the detection of marginally active DNA damaging agents.

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