OS1-4

Radio- and chemoprotective effects of Zhu-Ling Mushroom (*Polyporus umbellatus*) in human cultured cells and in mice

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Zhu-Ling Mushroom (*Polyporus umbellatus*) is a commonly used Chinese Medicine in the treatment of renal and liver disease. We examined the radio- and chemoprotective effects of PUPs in human lymphoblastoid TK6 cells and in ICR mice. The pretreatment of PUPs 30 min before irradiation significantly reduced radiation-induced micronuclei (MN) formation and tk mutant frequencies in TK6 cells. Pretreatments of PUPs at a dose of 50 mg/kg by i.p. injection 30 min or 45 min before 6 Gy irradiation caused a significant decrease in the frequencies of MN in the peripheral blood reticulocytes of irradiated mice. Comparative studies showed that PUPs may be a better radioprotective agent with a higher inhibition ratio of radiation-induced micronuclei and tk mutant frequencies than a well-known radioprotective agent amifostine. Mechanistic study showed that administration of PUPs at a dose of 50 mg/kg 30 min before irradiation significantly reduced the Comet tail length in the peripheral blood leucocytes and decreased the formation of the oxidative DNA damage (8-hydroxy-2′-deoxyguanosine) and lipid peroxidation in irradiated mouse liver, implying that the antioxidant activity of PUPs may contribute to its radioprotective effect. Furthermore, PUPs caused a dose-dependent inhibition of cyclophosphamide-induced MN formation in TK6 cells. Pretreatments of PUPs at a dose of 50 mg/kg by i.p. injection 30 min before CP treatment resulted in statistically significant decrease in the frequencies of MN in the peripheral blood reticulocytes in mice. Our results suggest that the potential us of PUPs as a useful radio- and chemoprotective agent.

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OS1-5

Genotoxicity of safrole oxide in HEPG2 cells and in mice

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Safrole oxide (SAFO) is an electrophilic metabolite of the carcinogen safrole, the main constituent of sassafras oil. There is little or no data available on the genotoxicity of SAFO in mammalian systems. We investigated the cytotoxicity and genotoxicity of SAFO by MTT assay, Comet assay and Micronucleus test in HepG2 human hepatoma cells in vitro and in FVB mice in vivo. SAFO exhibited a time- and dose-dependent cytotoxic effect in HepG2 cells. SAFO produced a marked increase in comet tail length and in the frequency of micronucleated binucleated cells at doses of 125 μM and higher. Furthermore, repeated intraperitoneal injections of SAFO to mice caused a significantly increase in mean comet tail length of peripheral blood leukocytes and in the frequency of micronucleated reticulocytes in a dose-dependent manner. Our present data have demonstrated for the first time that SAFO exhibited significant genotoxicity in human cells in vitro and in vivo.

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OS1-6

TiO_2 nanoparticles exhibit genotoxicity and impair both NER and BER DNA repair pathways in A549 cells

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Impact of titania nanoparticles (TiO_2-NPs) is now largely reported, yet published results are often contradictory. A panel of deeply characterized TiO_2-NPs was used to study the influence of physicochemical parameters on their impact on A549 cells. All the tested cytotoxicity assays led to the same conclusion: the cytotoxic impact of TiO_2-NPs is moderate, with a maximum of 25% of cells death after exposure for 48 h to 100 $\mu g\,ml^{-1}$ of NPs. Trypan blue staining and clonogenic assay led to the lowest interference between NPs and the test. NPs were internalized into cells, where they located mostly in the cytoplasm, entrapped in vesicles and vacuoles. Their accumulation caused oxidative stress and oxidative lesions to DNA, mainly 8-oxodGuo. It also induced DNA strand breaks, visualized by Comet assay, which increased between 4 h and 24 h exposure timepoints, then decreased. Conversely the number of gamma-H2AX foci or micronuclei did not increase. This kinetics may be significant of DNA repair processes. However, we also showed that TiO_2-NPs drastically impair DNA repair processes, both nucleotide excision repair (NER) and base excision repair (BER) pathways. These data prove that TiO_2-NPs do not induce severe lethality but cause genotoxic damage to A549 cells, but also impair DNA repair processes, which may preclude their mutagenicity.

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OS1-7

Micronuclei frequency of a pesticide exposed population

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A wide range of chemical products known to be acutely toxic is nowadays used in the agricultural sector – a large number of pesticides with different compositions. Nevertheless, the effects in human health as result of long-term exposure to low levels are not yet completely understood. Human biomonitoring is an extremely useful tool that provides an efficient and effective mean of measuring human exposure to hazardous agents. The methodology for determination of micronuclei in lymphocytes (CBMN) is well validated and accumulating data have shown its relationship to cancer