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Cytotoxicity and Genotoxicity Study of CKD-712 in Mammalian Cell System

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CKD-712, named S-YS49 is a chiral compound derived from higenamine (one component of *Aconite spp.*) derivatives. To compare the cytotoxicity of CKD-712 between in the absence and in the presence of S9 metabolic activation system, we performed trypan blue dye exclusion assay in Chinese hamster lung (CHL) cell. In CHL cells, the cytotoxicity (IC50) of CKD-712 was 92.9 μg/ml and 186.1 μg/ml in the absence and presence of S9 metabolic activation, respectively. And we also investigated the induction of DNA damages in mammalian cells. To perform the single cell gel electrophoresis, we determined optimum concentration in mouse lymphoma L5178Y cells using trypan blue dye exclusion assay. Each IC20 of CKD-712 was determined the concentration of 23.4 μg/ml and 24.8 μg /ml in the absence and presence of S9 metabolic activation, respectively. In the comet assay, DNA damage was not observed at the concentration range from 23.4 μg/ml to 5.9 μg/ml in the absence of S9 metabolic activation system. In the presence of S9 metabolic activation system, DNA damage was not observed at the concentration range from 24.8 μg/ml to 6.2 μg/ml. From these results, it is assumed that CKD-712 may be metabolized to less cytotoxic metabolite(s).