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DNA Conformation Assay: Determination of *In Vitro* DNA Adduct Formation and Strand Breaks

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ABSTRACT

The appearance of DNA strand breaks as detected by the conversion of supercoiled plasmid DNA (pBR322) to its relaxed open circular conformation was used to test the genotoxic potential of 28 nonmutagenic and mutagenic (including direct- and indirect-acting) model chemicals. This very rapid and simple in vitro assay is shown to be useful for the detection of chemicals which do or do not require metabolic activation for their interaction with DNA, because DNA nuclease-depleted microsomes in the presence of ethylendiaminetetraacetic acid (EDTA) were found to efficiently activate indirect-acting chemicals to ultimate reactive species. The results showed that the DNA conformation assay is at least as sensitive and specific as the Salmonella reverse mutation (Ames) assay. A comparison to in vivo carcinogenicity data (obtained from the Gene-Tox data base, Nesnow et al., 1986) indicated that an accuracy of 74 % (17 out of 23 chemicals were correctly identified as carcinogens or noncarcinogens) was achieved. The accuracy together with its quick and easy performance make the DNA conformation assay a useful method for the short-term screening of chemicals for their genotoxic potential.

Keywords: genotoxic chemicals, short-term assay, DNA strand breaks, metabolic activation