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Nicotine, cotinine, and β-nicotyrine inhibit NNK-induced DNA-strand break in the hepatic cell line HepaRG

Patricia Ordonez [a], Ana Belen Sierra [a], Oscar M. Camacho [b], Andrew Baxter [b], Anisha Banerjee [b], David Waters [b], Emmanuel Minet [b,*]

[a] Vivotecnia Research S.L., Santiago Grisolia 2, Tres Cantos, Madrid, Spain
[b] BAT, Group Research and Development, Regents Park Road, Southampton SO15 8TL, UK

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ABSTRACT

Recent *in vitro* work using purified enzymes demonstrated that nicotine and/or a nicotine metabolite could inhibit CYPs (CYP2A6, 2A13, 2E1) involved in the metabolism of the genotoxic tobacco nitrosamine NNK. This observation raises the possibility of nicotine interaction with the mechanism of NNK bioactivation. Therefore, we hypothesized that nicotine or a nicotine metabolite such as cotinine might contribute to the inhibition of NNK-induced DNA strand breaks by interfering with CYP enzymes. The effect of nicotine and cotinine on DNA strand breaks was evaluated using the COMET assay in CYP competent HepaRG cells incubated with bioactive CYP-dependent NNK and CYP-independent NNKOAc (4-(acetoxymethylnitrosoamino)-1-(3-pyridyl)-1-butanone). We report a dose-dependent reduction in DNA damage in hepatic-derived cell lines in the presence of nicotine and cotinine. Those results are discussed in the context of the *in vitro* model selected.