ENG.3 17.4.91

LDPA 17.4.91

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DNA adducts formed by urinary extracts from smokers, passive smokers and non-smokers

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It has been assumed that the elevated mutagenic activity in smokers' urine is predominantly caused by aromatic amines. Pyrolysis products of proteins such as 3-amino-1,4-dimethyl-5H-pyrido[4,3-b]indole (Trp-P1), 3-amino-1-methyl-5H-pyrido[4,3-b]indole (Trp-P2), 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP), 2-amino-6-methyldipyrido[1,2-a:3',2'-d]imidozole (Glu-P1), 2-aminodipyrido[1,2-a:3',2'-d]imidazole (Glu-P2) and 2-amino-3-methyl-9H-pyrido[2,3-b]indole (MeAαC) are possible candidates for this activity. An in vitro assay for detecting DNA-binding capacity of complex mixtures has been established according to published methods. The assay includes incubation of the test substance with calf thymus DNA in the presence of rat liver S9, cofactors and 3'-phosphoadenosine-5'-phosphosulfate (PAPS), subsequent isolation of the DNA and ^{32}P-postlabelling analysis (P1 version) for DNA adducts. This method has been applied to benzo(a)pyrene (BaP), some aromatic amines (4-aminobiphenyl, MeAαC, Trp-P1, Trp-P2, Glu-P2) and condensates of cigarette smoke (CSCs, both from mainstream smoke and from environmental tobacco smoke). The major DNA adducts of BaP and most of the aromatic amines seem to be visually similar to those reported in the literature. The autoradiographs obtained with CSCs show the characteristic diagonale radioactive zone (DRZ) observed with DNA isolated from smokers or from mice treated with CSC. Presently urine extracts from smokers, passive smokers and non-smokers from a study with controlled diet are under investigation. The adducts obtained with urine extracts so far do not match with those of any of the aromatic amines tested.