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Biomarkers of DNA Damage and Repair, Exposure, and Phenotype 2: Poster Presentations - Proffered Abstracts

Abstract #1883

Pyridyloxobutylated DNA adducts in oral mucosa of nonsmokers, smokers and snuff dippers in relation to other biomarkers of exposure

Anne-Kathrin Heling, Katharina Schutte-Borkovec, Christopher Heppel, Karl Fagerstrom and Elmar Richter

Walther Straub Inst. for Pharm. & Tox., Munich, Germany, Fagerstrom Consulting AB, Helsingborg, Sweden

Pyridyloxobutylated (POB) DNA adducts releasing 4-hydroxy-1-(3-pyridyl)-1-butanone (HPB) have been implicated in 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) induced lung cancer and N'-nitrosonornicotine (NNN) induced esophageal tumors. However, biomonitoring studies of these adducts have not shown the expected specificity for smoking in either lung tissue or esophageal mucosa. NNK and NNN are also implicated in oral cancer of both smokers and snuff dippers. At present, the concept that currently available smokeless tobacco products (SLT) should be used as a substitute for cigarette smoking is controversely discussed. If at all, SLT should have low concentrations of NNN and NNK as is the case of Swedish snus. In the present study, POB DNA adduct were determined in buccal cells from 45 nonsmokers, 24 smokers, and 33 users of Swedish snus. Samples of oral mucosa were collected by Cytobrush Plus® from the left and right cheek, and from the site where snus was normally placed. Subjects filled in a questionnaire on smoking and dietary habits. Saliva and 1-2 mm clippings of the toenails were sampled for estimation of short- and long-term exposure to tobacco alkaloids. HPB-releasing adducts were determined after acid hydrolysis of DNA and derivatization by high-resolution gas chromatography/mass spectrometry with negative chemical ionization. Cotinine and myosmine in saliva and, together with nicotine, in toenails were determined by gas chromatography/mass spectrometry in the EI mode. Highly significant ($p < 0.0001$) differences in POB DNA adduct levels were detectable in all three groups. The levels were lowest in nonsmokers (2.00 ± 2.31 pmol HPB/mg DNA), four-fold higher in smokers (7.40 ± 3.82 pmol HPB/mg DNA), and nine-fold higher in snus users (17.61 ± 7.10 pmol HPB/mg DNA). So far, saliva and toenails

have been analysed in a subset of 11 nonsmokers and 15 smokers. Cotinine was not detectable in toenails from nonsmokers. Myosmine was about three-fold higher in both toenails (0.058±0.052 versus 0.021±0.014 ng/mg, $p < 0.01$) and saliva (2.54±2.68 versus 0.73±0.65 ng/ml, $p < 0.01$) from smokers compared to nonsmokers. Much higher differences were observed for nicotine in toenails (0.128±0.079 versus 1.789±0.964 ng/mg, $p < 0.001$) and cotinine in saliva (1.85±4.50 versus 84.14±54.30 ng/mg, $p < 0.001$) of smokers and nonsmokers, respectively. These findings support our hypothesis that a significant fraction of human myosmine exposure comes from sources other than tobacco. The same holds true for POB DNA adducts in oral mucosa because of the small differences between smokers and nonsmokers. Higher adduct levels in snuff dippers may be explained by prolonged exposure of the mucosa to NNN and NNK. However, they do not correspond to the inherent risk of oral cancer which is considerably lower in Swedish snus users than in smokers.