P003 Analysis of aminophenylnorharman (APNH) in human hair samples

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Mutagenic/carcinogenic 9-(4'-aminophenyl)-9*H*-pyrido[3,4-*b*]indole (aminophenylnorharman, APNH) is formed from norharman and aniline in the presence of CYP3A4/CYP1A2. APNH is detected in human urine, suggesting that humans are continuously exposed to APNH. To investigate chronic exposure of APNH to humans, amounts of APNH in human hair samples were estimated. Hair samples from volunteers were washed with 0.1% SDS and methanol, then treated with 1N NaOH at 100℃ for 45 min after spiking with a tetradeuterated derivative of APNH as an internal standard. Sample solutions were neutralized, and APNH was adsorbed on a Blue-Chitin column. APNH was extracted with methanol:ammonia water (50:1, v/v), and analyzed by LC-ESI/MS/MS. The detection limit of APNH was 50 fg/g hair. When nine samples collected from healthy volunteers (5 males, 4 females) were analyzed, APNH could be detected in all hair samples at levels of 200-500 pg per g hair. Moreover, norharman and aniline were analyzed by HPLC and GC in the same samples, respectively, and they were detected in all the samples. Amounts of norharman were 190-900 ng and those of aniline were 70-230 ng per g hair. To estimate the exposure levels of APNH to humans, we are now quantifying APNH incorporation rate into hair using experimental animals.

ヒト毛髪中のアミノフェニルノルハルマン (APNH) の測定

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P004 Simultaneous Analysis of Urinary 4,4'-Methylenebis (2-Chloroaniline) and N-acetyl 4,4'-Methylenebis (2-Chloroaniline) Using Solid-Phase Extraction and Liquid Chromatography Tandem Mass Spectrometry

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Analysis of 4,4'-methylenebis (2-cholroaniline) (MOCA) or its metabolites in urine has been considered as the appropriate method to assess MOCA exposures through inhalation and skin absorption. MOCA and its metabolites N-acetyl 4,4'-methylenebis(2-cholroaniline) (acetyl-MOCA) were analyzed using methods either limited by sensitivity or sample preparation. Therefore, a solid-phase extraction (SPE) and liquid chromatography tandem mass spectrometry (LC-MS/MS) method was developed to simultaneously analyze MOCA and acetyl-MOCA in urine to serve as biomarkers for MOCA exposures. Protein was precipitated by using acetonitrile, and SPE were applied to clean up samples to eliminate the matrix effect and to improve the recovery. The limit of quantitation of this method was at 1.0 ng/mL for MOCA and 0.03 ng/mL for acetyl-MOCA (S/N=10). Urinary MOCA and acetyl-MOCA levels in MOCA-exposed workers were analyzed and quantitated to be 191.9±373.2 (mean±SD) and 11.79±23.8 ng/mL (N=54), respectively. MOCA concentrations are significantly correlated with their corresponding acetyl-MOCA levels in urine (Spearman correlation coefficient $r=0.916$, $p<0.001$). These results show that this method has been successfully developed and provides high throughput potential to analyze MOCA and acetyl-MOCA not only to serve as exposure biomarkers for future study of the potential health effects associated with MOCA exposures, but also to elucidate the mechanisms related to the health effects.

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