

Estimation of α -pinene absorption in the Japanese resident based on toxicokinetic analysis in rats by inhalation exposure

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日本の住宅内での α -ピネン吸収量の推定 —吸入曝露ラットにおける体内動態の薬物動力学解析から—

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Abstract

α -Pinene is a major compound contributing to indoor air pollution in Japanese residences together with many aliphatic or aromatic hydrocarbons. In the present study, the amounts of each enantiomer of α -pinene ((+)- and (-)- α -pinene) absorbed by a resident in a Japanese home were estimated by evaluating their inhalation toxicokinetics in rats. Measured amounts of the substances were injected into a closed chamber system in which a rat had been placed, and the concentration changes in the chamber were examined. The toxicokinetics of the substances were evaluated based on concentration-time courses using a nonlinear compartment model. The absorption amounts per unit time in rats exposed to the substances at constant concentration were simulated using the estimated values of the toxicokinetic parameters. The estimated amounts for the two enantiomers showed approximate agreement. When the values were compared with those for aliphatic or aromatic hydrocarbons examined in our previous studies, α -pinene was estimated to be absorbed more easily by inhalation than *n*-hexane, *n*-heptane, *n*-nonane, *n*-decane, toluene, xylenes, ethylbenzene and styrene, and to be absorbed about the same level as 1,2,4-trimethylbenzene. Their absorption amounts in human residents were extrapolated from the results for rats and the residential concentrations found in our previous study. The total amount of the two enantiomers absorbed was estimated to be 31 $\mu\text{g}/60$ kg of human body-weight while at home for 16 h (residential concentration: 4.4 $\mu\text{g}/\text{m}^3$ as median value). The value was the highest after that for toluene. Similarly, in a residence where air pollution was marked, the absorption amount of α -pinene (13 mg for 16 h in a residence with an indoor maximum concentration of 1.8 mg/m^3) was estimated to be much more than those of other substances. The value (13 mg) was the same level as the tolerable daily intake (TDI) calculated from the No Observed Adverse Effect Level (NOAEL) proposed by the Environmental Protection Agency (EPA).

要旨

α -ピネンは、多くの脂肪族及び芳香族炭化水素と同様に日本の住宅内の空気汚染に関与する主要な化学物質である。本研究では、 α -ピネンの2つの異性体(+)-及び(-)- α -ピネンのラットにおける体内動態をそれぞれ薬物動力学的に解析し、ヒトにおける経気道吸収量を外挿した。ラットを入れた閉鎖系曝露装置内に一定量の α -ピネンを注入後気化させ、ラットへの吸入による装置内濃度推移を調べ、薬物動力学的に解析した。得られた結果から、一定濃度の α -ピネンに一定時間曝露されたラットにおける吸収量を推定したところ、異性体間で差は認められなかった。ラットにおける炭化水素類の経気道吸収量について過去に我々が得た結果と比較すると、同一の曝露濃度下において α -ピネンは*n*-ヘキサン、*n*-デカン、トルエン、キシレン、エチルベンゼン、スチレンなどよりも吸収されやすく、1,2,4-トリメチルベンゼンと同程度であると推定された。ラットから得た結果及び日本の住宅における各物質の室内濃度に関する過去の調査結果をもとに、居住者(体重60 kg)における α -ピネンおよび各炭化水素類の吸収量を推定した。16時間の在宅時間中の α -ピネン吸収量(住宅内濃度中央値4.4 $\mu\text{g}/\text{m}^3$ において31 μg)は、トルエンに次いで多かった。また、各物質による空気汚染の著しい住宅居住者の α -ピネン吸収量(住宅内濃度1.8 mg/m^3 において13 mg)は他の物質の吸収量よりもはるかに多く、米国環境保護庁(EPA)の提案する α -ピネンの無毒性量(NOAEL)から算出した耐容一日摂取量(TDI)と同レベルであった。

Key words: α -pinene(α -ピネン), indoor air pollution(室内空気汚染), extrapolation(外挿), closed chamber system(閉鎖系曝露装置), residence(住宅), toxicokinetics(毒物動力学)