Triazolam disposition

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Triazolam (T) is a new, potent hypnotic with a short duration of action in man. After an 0.88 mg oral dose of $T^{14}C$ in six male subjects, mean recovery of ^{14}C radioactivity was 85% in urine and 8% in feces. The major urinary metabolites were α–hydroxytrizolam (α-HT) and 4-hydroxytrizaolma (4-HT) accounting for 69% and 11% of the urinary ^{14}C, and these were mostly in conjugated from. A, 4-Dihydroxytrizolam and three dichtorotriazoltylbenzophenone analogs were minor metabolites. At least 85% of the dose was rapidly absorbed: mean absorption half-life ($t\,½_{A}$) was 2.8 min. After reaching a mean peak plasma level (C_{max}) of 8.8 ng/ml at mean time (1_{max}) of 1.3 hr, plasma T decreased rapidly with a mean elimination half-life ($1\,½_{F}$) of 2.3 hr. The remainder of the plasma ^{14}C consisted predominantly of glucuronides of α-HT and 4-HT. Mean plasma parameters for these metabolites were as follows: α-HT-glucuronide, $1\,½_{E}$ = 3.9 hr, 1_{max} = 1.3 hr, C_{max} = 6.1 ng/ml: 4-HT-glucuronide, $1\,½_{E}$ = 3.8 hr, 1_{max} = 2.5 hr, C_{max} = 6.1 ng/ml. Nonconjugated α-HT and 4-HT were present in plasma but in insufficient amounts for kinetic analysis. The results were consistent with the short duration of action.