Triazolam disposition


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 form. A, 4-Dihydroxytrizolam and three dichlorotriazolylbenzophenone 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 (t_{max}) of 1.3 hr, plasma T decreased rapidly with a mean elimination half-life (1 ½ E) 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, t_{max} = 1.3 hr, C_{max} = 6.1 ng/ml: 4-HT-glucuronide, 1 ½ E = 3.8 hr, t_{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.