# A Dose-Dependent Pharmacokinetic Study of Levodopa by Intramuscular Administration in Rabbits

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## Abstract

The dose-dependent pharmacokinetics of levodopa (L-dopa) was studied in rabbits by intramuscular administration. Three different doses of L-dopa/carbidopa (2/0.5, 5/1.25, and 10/2.5 mg/kg) were administered to six male rabbits via an intramuscular (IM) route, and one dose of L-dopa/carbidopa (2/0.5 mg/kg) was administered via an intravenous (IV) route with a washout period of 1-week between different doses. Plasma samples were collected after each treatment and the concentrations of L-dopa and 3-O-methyldopa (an L-dopa metabolite, 3-OMD) were measured by a sensitive high-performance liquid chromatographic (HPLC) method. Subsequently, these measurements were used to determine the pharmacokinetic behavior of L-dopa and 3-OMD. The results indicated that the absorption of L-dopa was fast with the time to the peak within 30 min, but the formation of 3-OMD was slow with the time to the peak of 120-180 min after IM administration. The IM bioavailability of L-dopa was in the range of 0.70-1.21, and the relative ratios of the formation of 3-OMD at different doses of L-dopa were in the range of 0.79-1.24. No statistically significant difference could be observed for IM bioavailability of L-dopa or for the relative ratios of the formation of 3-OMD in this dose range. The elimination half-lives of L-dopa and 3-OMD also exhibited no significant differences for each dose after IM administration. In addition, both the area under the curve (AUC) and maximum plasma concentration (Cmax) values of L-dopa and 3-OMD increased proportionally over the dose range of 2/0.5-10/2.5 mg/kg for L-dopa/carbidopa, suggesting that L-dopa and 3-OMD obeyed dose-independent pharmacokinetics.