

# Pharmacokinetic Modeling of Nitrate, Nitrite and N-Nitroso Compounds

by

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## **Abstract**

A theoretical and experimental investigation of the pharmacokinetics of nitrate, nitrite, and N-nitroso compounds was undertaken. Nitrate was found to have a half-life in humans of about 5 hours. Sixty percent of the removal of nitrate is due to renal clearance. Using a mathematical model developed in this work, it was estimated that roughly half of the metabolism of nitrate which occurs is due to the bacteria inhabiting the large bowel. Supporting evidence was obtained in an experimental study using both germfree and conventional rats.

The fate of nitrite in the stomach was investigated with the use of a dog with a surgically-implanted gastric fistula. Comparison of the time course of gastric nitrite in vivo with that observed in incubations of nitrite in gastric fluid in vitro revealed that nitrite is rapidly absorbed by the gastric mucosa. Of the nitrite entering the stomach which does not pass into the duodenum, 96% is absorbed and 4% undergoes reaction. Between 40 and 90 percent of the reactive loss of nitrite was found to be due to oxidation of nitrite to nitrate.

The amino acid proline was used as the precursor in experiments designed to study the nitrosation reaction. Formation of nitrosoproline from nitrite and proline was found to be catalyzed by an unknown substance in canine gastric juice. This catalytic effect, which was observed in both in vitro and in vivo experiments, was not due to thiocyanate or chloride ions.

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