

# Disposition of Nifurtimox and Metabolite Activity Against *Trypanosoma cruzi* using Rat Isolated Perfused Liver

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**Abstract** Nifurtimox disposition was investigated using the rat isolated perfused liver method after administration of 25 mg mL<sup>-1</sup> nifurtimox, and its disappearance was monitored by analysing the perfusate sample at various times. Biliary excretion was also measured. The drug concentration profile underwent a biexponential decline over the 2-h study period, with a terminal half-life of 62.76 ± 17.56 min. Nifurtimox is a high clearance compound (15.23 ± 5.53 mL min<sup>-1</sup>). The extraction ratio was 0.621 ± 0.159. Biliary excretion accounted for 0.05% of the dose, the remainder consisting of highly polar metabolites. By 2 h, a minimal fraction of unchanged nifurtimox was recovered from the perfusate. Nifurtimox activity against *Trypanosoma cruzi* (clone CA-1) during the perfusion was also determined. Epimastigotes isolated from continuous culture were exposed to the samples of perfusate at different perfusion times in a microtitre plate. After an incubation time of 72 h at 27°C, the parasite number