

The disposition of nifurtimox in the rat isolated perfused liver: effect of dose size

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Abstract? The disposition of nifurtimox was studied in the rat isolated perfused liver using a recirculating system. The drug was administered as a bolus (5.0, 15.0 or 30.0 $\mu\text{g mL}^{-1}$), and its disappearance was monitored by analysing perfusate samples. In all experiments perfusate disappearance was monoexponential, and no significant difference was found between the three doses for the elimination constant (0.016, 0.011 and 0.012 min^{-1} , respectively), half-life (46.6, 65.8 and 66.8 min, respectively), extraction rate (0.128, 0.091 and 0.099, respectively) and distribution volume (41.1, 47.3 and 30.7 mL g^{-1} , respectively). At 30 $\mu\text{g mL}^{-1}$ the hepatic clearance was lower than the other concentrations of nifurtimox (0.66, 0.51 and 0.34 $\text{mL min}^{-1} \text{g}^{-1}$, respectively). Relatively little parent drug was recovered from the liver at the end of the perfusions. In summary, nifurtimox is cleared slowly from the rat isolated perfused liver, is poorly extracted by hepatocyte cells and is completely metabo