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PDF...Investigation of the role of
cytochrome P450 enzymes in the
metabolism of a new oral potassium
sparing agent, levosimendan, in
healthy volunteers. Levosimendan is an
effective and safe inotropic drug and
its pharmacokinetic characteristics
(e.g., absorption, distribution,
metabolism and excretion) have been
examined in humans. Additionally,
there is a need for a more thorough
understanding of its metabolism, as
reflected by its poor oral bioavailability
in humans, which requires enhanced
oral exposure for optimal therapeutic
effectiveness. Levosimendan

undergoes primary hepatic metabolism to form its predominant glucuronide metabolite, M4. The aim of the present study was to examine the role of two cytochrome P450 enzymes, CYP2C19 and CYP3A4 in the metabolism of levosimendan in vitro. Metabolic stability of levosimendan was assessed using human liver microsomes (HLMs) in comparison with recombinant cytochrome P450 enzymes CYP2C19 (including its genetic polymorphisms), and CYP

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