Pharmacokinetics and Metabolism of Fimasartan, a Novel Angiotensin II Receptor Blocker in Rats
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Purpose
Fimasartan is a novel angiotensin II receptor blocker with a selective type I receptor (AT1) blockade effect. This study was conducted to characterize the pharmacokinetics and metabolism of fimasartan in rats.

Methods
[14C]fimasartan and unlabeled fimasartan were given to rats by i.v. injection and oral administration. Total radioactivity was determined by liquid scintillation counting and radioactivity associated with the metabolites was assayed by the radiochemical detection method. Unlabeled fimasartan concentrations in biological samples were quantified by LC/MS/MS, and metabolite identification was conducted by product ion scanning using LC/MS/MS.

Results
Following oral administration of [14C]fimasartan, total radioactivity was found primarily in feces (92.4 - 2.1%), with a minimal radioactivity found in urine (0.42 - 0.04%). In bile duct cannulated rats, 58.8 - 14.4% of the radioactive dose was excreted via bile. Major metabolites of fimasartan including the active metabolite, desulfo-fimasartan, were identified. None of these metabolites represented more than 7.2% of the exposure of the parent drug. After i.v. administration, plasma concentrations of fimasartan were decreased multi-exponentially. After oral administration, a secondary peak was observed (8 - 12 h). The oral absorption of fimasartan was rapid, with the bioavailability ranging of 32.7 - 49.6%.

Conclusion
Fimasartan was excreted primarily via feces as an unchanged drug. The major active metabolite was identified, and its amount in the systemic circulation was insignificant compared to the parent drug. The extent of biliary and fecal excretion was similar between i.v. injection and oral administration, indicating efficient gastrointestinal absorption which did not limit the oral bioavailability.