pharmacokinetics.(B. Rosenkranz, V. Profozic, Z. Metelko, V. Mrzljak, C. Lange, V. Malerczyk. 1996)

In healthy subjects, the intra- and inter-individual variability of glimepiride pharmacokinetic parameters were 15-23% and 24-29%, respectively. After intravenous dosing in healthy subjects, the volume of distribution was 8.8 L (113 ml/kg), and the total body clearance was 47.8 mL/min (J DeRUITER, 2003). Protein binding was greater than 99.5%. Glimepiride is completely metabolized by oxidative biotransformation after either an intravenous or oral dose. The major metabolites are the cyclohexyl hydroxy methyl derivative (Ml) and the carboxyl derivative (M2). Cytochrome P450 2C9 is involved in the biotransformation of glimepiride to Ml. Ml is further metabolized to M2 by one or several cytosolic enzymes. M2 is inactive. In animals, Ml possesses about one-third of the pharmacological activity of glimepiride, but it is unclear whether Ml results in clinically meaningful effects on blood glucose in humans. When ^{14}C-glimepiride was given orally to 3 healthy male subjects, approximately 60% of the total radioactivity was recovered in the urine in 7 days. Ml and M2 accounted for 80-90% of the radioactivity recovered in the urine (J DeRUITER, 2003). The ratio of Ml to M2 in the urine was approximately 3:2 in two subjects and 4:1 in one subject. Approximately 40% of the total radioactivity was recovered in feces. Ml and M2 accounted for approximately 70% (ratio of Ml to M2 was 1:3) of the radioactivity recovered in feces. No parent drug was recovered from urine or feces. After intravenous dosing in patients, no significant biliary excretion of glimepiride or its Ml metabolite was observed. (J DeRUITER, 2003)

1.5.4 Amlodipine besylate and atorvastatin calcium combination tablets

Following oral administration of amlodipine besylate/ atorvastatin calcium tablets, peak plasma concentrations of amlodipine and atorvastatin are seen at 6 to 12 hours and 1 to 2 hours post dosing, respectively. The rate and extent of absorption (bioavailability) of