1.5 Pharmacokinetics of amlodipine, atorvastatin, and glimepiride

Pharmacokinetic is the action of drugs in the body over a period of time; including the processes of absorption, distribution, localization in tissues, biotransformation, and excretion and its primary goal is to enhance efficacy and decrease toxicity in patient. **(**LZ Benet, DL Kroetz, LB Sheiner.1996)

1.5.1 Amlodipine

Amlodipine is a dihydropyridine calcium antagonist drug with distinctive pharmacokinetic characteristics which appear to be attributable to a high degree of ionization. Following oral administration, bioavailability is 60 to 65% and plasma concentrations rise gradually to peak 6 to 12 h after administration (Peter A. Meredith, Dr Henry L. Elliott. 1992). Amlodipine is extensively metabolised in the liver (but there is no significant presystemic or first-pass metabolism) and is slowly cleared with a terminal elimination half-life of 40 to 50h. Volume of distribution is large (21 I/kg*)* and there is a high degree of protein binding (98%) (Peter A. Meredith, Dr Henry L. Elliott. 1992).. There is some evidence that age, severe hepatic impairment and severe renal impairment influence the pharmacokinetic profile leading to higher plasma concentrations and longer half-lives. There is no evidence of pharmacokinetic drug interactions. Amlodipine shows linear dose-related pharmacokinetic characteristics and, at steady-state, there are relatively small fluctuations in plasma concentrations across a dosage interval (Brown BG, Zhao XQ, Sacco DE, et al. 1993) (Pedersen TR, Kjekshus J, Berg K, et al. 1994). Thus, although structurally related to other dihydropyridine derivatives, amlodipine displays significantly different pharmacokinetic characteristics and is suitable for administration in a single daily dose. Finally, the elimination of amlodipine from the plasma is biphasic with a terminal elimination half-life of about 30-50 hours. Ten percent of the