

parent amlodipine compound and 60% of the metabolites of amlodipine are excreted in the urine. interval (Brown BG, Zhao XQ, Sacco DE, et al. 1993) ( Pedersen TR, Kjekshus J, Berg K, et al. 1994)

### *1.5.2 Atorvastatin*

Atorvastatin is an inhibitor of HMG-CoA reductase and thus it reduces LDL production levels. The clinical dosage range for atorvastatin is 10-80 mg/day, and it is given in the acid form. Atorvastatin acid is highly soluble and permeable, and the drug is completely absorbed after oral administration. After oral administration alone, atorvastatin is rapidly absorbed; maximum plasma concentrations occur within 1 to 2 hours. Extent of absorption increases in proportion to atorvastatin dose (Hans Lennernäs,2003). The absolute bioavailability of atorvastatin (parent drug) is approximately 14% and the systemic availability of HMG-CoA reductase inhibitory activity is approximately 30%. The low systemic availability is attributed to presystemic clearance in gastrointestinal mucosa and/or hepatic first-pass metabolism. Plasma atorvastatin concentrations are lower (approximately 30% for C<sub>max</sub> and AUC) following evening drug administration compared with morning. However, LDL-C reduction is the same regardless of the time of day of drug administration. Mean volume of distribution of atorvastatin is approximately 381 liters. Atorvastatin is >98% bound to plasma proteins. A blood/plasma ratio of approximately 0.25 indicates poor drug penetration into red blood cells. The total plasma clearance of atorvastatin acid is 625 mL/min and the half-life is about 7 hours. (Hans Lennernäs,2003)

Based on observations in rats, atorvastatin calcium is likely to be secreted in human milk.

Food decreases the absorption rate of atorvastatin acid after oral administration, as indicated by decreased peak concentration and increased time to peak concentration. Women appear to