CHAPTER V

CONCLUSIONS

1. For *in vitro* study, the formulations produced drug release profiles similarly to that of Cardil® based on difference factor and similarity factor were those with 7% mixed polymers (3.5% HPMC and 3.5% XG) in Emcompress® (7% P/E), 10% mixed polymers (5% HPMC and 5% XG) in Emcompress® and Tablettose® (2:1) (10% P/E+T) and 15% mixed polymers (7.5% HPMC and 7.5% XG) in Tablettose® (15% P/T). All three formulations had difference factor less than 15 and similarity factor closed to 100. The formulation with 10% P/E+T was the most similar to Cardil®.

2. Combination of XG and HPMC in formulation could reduce initial drug release more than only HPMC in formulation because XG produced gel layer greater than HPMC.

3. For soluble filler (lactose), release profiles of tablet with 15% P/T was the most similar to that of Cardil®. On the other hand, for insoluble filler (dibasic calcium phosphate), release profiles of the drug with 7% P/E was the most similar to that of Cardil®.

4. All three formulations were subjected for *in vivo* study. Rabbits were employed as subjects for comparative bioavailability study. The average AUC values of the formulations with 7% P/E, 10% P/E+T, 15% P/T and Cardil® were 5451.63 ± 2166.42, 3364 ± 1630.10, 3825.08 ± 1521.89 and 2626.76 ± 1735.66 ng-hr./mL, respectively. The average peak plasma concentration of formulations with 7% P/E, 10% P/E+T, 15% P/T and Cardil® were 1246.05 ± 598.57; 777.86 ± 591.68, 960.33 ± 509.49 and 430.99 ± 209.67 ng/mL, respectively. The average time to peak plasma concentration were 4.50, 3.10, 78 and 3.17 hr. for 7% P/E, 10% P/E+T, 15% P/T formulations and Cardil®, respectively. The elimination half-life ($t_{1/2}$) of 7% P/E, 10%

P/E+T, 15% P/T formulations and Cardil® were 1.36 ± 0.52, 1.52± 0.52, 1.17± 0.33 and 1.74 ± 0.52 hr, respectively.

5. The three formulated 120 mg diltiazem hydrochloride controlled release tablets were not bioequivalent to Cardil® with respect to both the rate and the extent of drug absorption. However, it was found that 10% P/E+T formulation was as closely bioavailable as Cardil® based on both *in vitro* and *in vivo* data. It was suggested that the test formulation should be modified further to have a better *in vitro* result. Moreover, the experiment should be also done in human being to establish its availability relative to Cardil®.