CHAPTER V

CONCLUSIONS

Development of multiple-unit sustained release tablets of film-coated diltiazem hydrochloride resinates could be successfully prepared. Diltiazem hydrochloride resinates were suitably prepared by batch method. The 4 % crosslinkage resin had higher percentage of drug loading (28.80 %) than of 8 % crosslinkage resin (5.51 %). This was due to decreasing in resin crosslinkage increased the drug binding. The percentage of drug loading also increased when the quantity of resin was decreased or when the initial drug amount in the drug loading solution was increased. Although at the equilibrium of system, increasing initial drug amount presented no increase in drug loading. From the result of this study, the drug to resin ratio of 1:1, prepared in 8 % w/v loading solution, were more suitable for preparing resinates. However, increasing in temperature to 50°C not only increased the percentage of drug loading but also reduced the time required for system equilibrium. In conclusion, the loading of drug onto resins was found to be influenced by resin crosslinkage, the quantity of resins and the temperature during drug loading while the concentration of drug solution had less effect on the percentage of drug loading.

The drug release kinetic of resinates followed the Higuchi model. The release rate was influenced by the ionic strength of dissolution medium, while the pH of dissolution medium did not. This indicated that their exchange capacity tended to be independent of pH.

Coating of resinate to modify drug release by using the fluidized bed technique appeared to be the most useful and versatile. However, the agglomeration of resinates could found during coating process. Addition of talcum which was the antiadherent in the film coating solution reduced tackiness problem and the 20 % triethyl citrate was used as plasticizer for the polymer. Coating of resinates with acrylate polymer, Eudragit®RL and Eudragit®RS, presented the slower release rate than uncoated resinates. Increased the coating level and amount of Eudragit®RS decreased drug

release rate but did not affect the drug release kinetic. The release of drug from coated resinates was also best described by the Higuchi model.

The tablets formulated from MCC granules which contained 30-50 % coated resinates could not be compressed to tablet form. They were too soft to handle. The optimal quantity of resinates in tablets was about 20 % w/w and needed some excipients to improve cohesion force within the tablet such as PEG. Compression of coated resinates with MCC and PEG produced tablets with good physical properties. The plastic and soft material could also protect resinates from compression pressure. Addition of PEG presented the tablets with high hardness property but presented long disintegration time. To solve this problem, the addition of 8 % sodium starch glycolate was used as disintegrating agent in tablets. The tablets formulated from granules which had 20 % of PEG 4000 seemed to be the most suitable because the tablets presented acceptable characteristic and dissolution profile. The similarity factor (f_2) of this tablets was 65.71 when compared with the dissolution profile of coated resinates before formulating into tablets. The release kinetic of drug from tablets was best fitted by the Higuchi model.

Comparing dissolution profile between tablets compressed at various compression pressures, 340-1,022 pound, found indifference in drug release from tablets prepared from coated resinates. The single punch tableting machine produced the tablets with acceptable physical properties. The comparison of dissolution profile between tablets compressed by the hydraulic press and the single punch tableting machine presented indifference in drug release profile (f_2=78.48). This indicated that the development of multiple-unit sustained release tablets of film-coated diltiazem hydrochloride resinates provided the useful information for further development to industrial scale.