CHAPTER V

SUMMARY

1. Four organic salts of lidocaine; lidocaine adipate, lidocaine maleate, lidocaine malonate and lidocaine tosylate were synthesized. The structures were confirmed by ^{1}H NMR, IR, mass spectroscopy and elemental analysis. Approximate solubility of the products was also determined. The synthesized compounds were regarded as prodrugs of lidocaine and were expected to enhance skin permeability by ion pair mechanism.

2. **In vitro** skin permeation study of synthesized compounds were accomplished in comparison with lidocaine and lidocaine hydrochloride. Lidocaine adipate and lidocaine malonate gave satisfactory results. The skin permeabilities after 12 hours of application were of the same order as lidocaine, not significantly different at $\alpha < 0.05$. In addition, the permeabilities at this time interval were significantly higher than lidocaine hydrochloride. The skin permeabilities at 24 hours after application of all synthesized compounds were lower than lidocaine, the permeability of lidocaine adipate was still greater than lidocaine hydrochloride and other salts. For lidocaine maleate and lidocaine tosylate, the skin

permeation were not significantly different from lidocaine hydrochloride at any observed time intervals.

The synthesized compounds also showed different profile of permeation. The transportation was rapid at the beginning and declined after 24 hours of application.

3. Apparent partition coefficients (P) of the synthesized compounds were determined and compared with P of lidocaine and lidocaine hydrochloride. The rank order of the compounds ranged from the highest value of P to the lowest was lidocaine, lidocaine hydrochloride, lidocaine adipate, lidocaine malonate, lidocaine maleate and lidocaine tosylate.

The results indicated that the increase in permeability of proposed prodrugs from lidocaine hydrochloride may relate to the chemical structure and the apparent partition coefficient of the synthesized salts contributing ion-pair mechanism of transportation.