CHAPTER IV

DISCUSSION

In therapeutic ointment the maximum extent and rate of drug absorption are generally desired. The drug is transported from the ointment to the skin by diffusion. The pharmaceutical scientists assume that the diffusion process is passive; i.e., it is not energetically associated with a biological transport process., (11, 15) though an experimental procedure used diffusion technique (6) to measure the release of drug from an ointment base. This is a simple and convenient way to study. The significance of this method has also been critically examined. (4). In vitro release of drug found to correlated with in vivo method (2)

In all cases, the amount of dexamethasone released to the aqueous phase was plotted versus the time over $1\frac{1}{2}$ hr.

In selection of ointment base, it appeared from figure 4 that white ointment and hydrophilic petrolatum which are insoluble in water, did not release dexamethasone significantly from the base. Polyethylene glycol ointment however gave the maximum release, while hydrophilic ointment gave only small release. Therefore polyethylene glycol ointment base was chosen for this experiment.

The rate of drug release could be promoted by adding materials into the base to modify the epidermal sorption barrier and alteration of the physical properties of the ointment base. These agents have came to be known as additives, accelerants, sorption promoters or penetration enhancers such as water, alcohol, surfactants. These additives will effect the solubility and dispersibility of dexamethasone in ointment base, and alter the viscosity of the base.(11)

Figure 5 Compared the effect of various additives. Their efficiency for releasing dexamethasone was in the following order when used the additives in 5% V/W concentration, benzalkonium chloride 1 : 10,000 > water > alcohol > cetylpyridinium chloride

1 : 1000 . From the results shown in Figure 6,7,8,9,10 for high concentration of 13% v/w the efficiency for the releasing dexamethasone was in the following order, benzalkonium chloride 1:10,000 > alcohol > water > cetylpyridinium chloride 1:1,000.

Figure 6 showed the effect of alcohol on diffusion,the amount of the dexamethasone increased as the concentration of alcohol increased. As seen in the figure.

Figure 7 showed the effect of water on diffusion , the amount of dexamethasone increased as the concentration of water increased. As seen in the figure.

When alcohol was added to the base., the viscosity of the base decreased. The maximum amount of alcohol added was 13% V/W. Dexamethasone was sparingly soluble in alcohol (1 : 30 - 100) and practically insoluble in water (> 1 : 10,000) Dexamethasone is more soluble in alcohol than in water therefore the solution of dexamethasone in alcohol has a strong affinity for the ointment base than the solution of dexamethasone in water, a drug that has a strong affinity for a vehicle shows a low activity coefficient therefore, the thermodynamic activity of the drug in that vehicle is low and its rate of release from the vehicle will be slow. (26)

In low concentration of alcohol the release of dexamethasone is less than the release in water probably because of a strong affinity of drug in vehicle. But in high concentration of alcohol and water the release of dexamethasone from the base which contained alcohol was equal or higher than water because organic solvents such as alcohol may act involving the hole formation (5). Thus after $1\frac{1}{2}$ hours the drug in base containing the alcohol can be diffused through the membrane more than the drug in base containing the water.

Slightly swelling of membrane, occurred during the diffusion experiment when polyethylene glycol base was used, was due to the water up take into the dialysis cell. This result can be accounted for by the high osmotic pressure of the polyethylene glycol base, initially inducing water molecules to penetrate the membrane and

enter into the cell (25). This effect would explain the " lag " period of approximately 30 minutes before the drug released rate become constant.

Benzalkonium chloride 1 : 10,000 solution and cetylpyridinium chloride 1 : 1000, are often included in pharmaceutical formulation as antiseptic or preservative. They are cationic surface active agent. In figure 8 showed the release of dexamethasone from the base containing various concentration of cetylpyridinium chloride 1 : 1000. As the concentration of cetylpridinium chloride increased the release of dexamethasone increased.

Figure 9 showed similar results, as the concentration of benzalkonium chloride increased, the released of dexamethasone also increased. Comparing the drug released from these two additives, the solution of dexamethasone in cetylpyridinium cholride has a strong affinity for the base than benzalkonium chloride solution . Therefore dexamethasone could be released from the base containing benzalkonium chloride better than the base containing cetylpyridinium chloride as shown in the figure 5,8,9, On skin permeation, they probably have little effect which may be the changing of the physical state of water in the skin in such a way as to permit greater freedom to the passage of charged, hydrophilic substance (11)

The total amount of dexamethasone released from polyethylene glycol ointment base in $1\frac{1}{2}$ hour by using various additives, 13% V/W of benzalkonium chloride 1 : 10,000 was approximately 5.5 times greater than that observed from the base without additives. Cetylpyridinium chloride and water was approximately 4 times. Alcohol was approximately 4.5 times.