Chapter 5

CONCLUSION

There were several important factors which regulated the effectiveness of preservatives in combating microbial growth in pharmaceutical preparations. Preservative action was dependent on the solubility of the preservative in the aqueous-phase, and its partition between water-phase and oil-phases. In an emulsion, a preservative would partition itself depending on its relative solubility in the phases. In some specific emulsion, the equilibrium distribution of a stable preservative in the different phases would depend on the nature of the phases (i.e., on the partition coefficient), the solubility of the preservative and the volumes of the different phases.

Another factor regulating preservative activity was the number of microorganisms challenging the preservative system. Since there was an absorption of preservative by microorganism, a preservative could be exhausted by excessive microbial contamination. Microorganisms grew in the water-phase or at the water-oil interface. The continuous water-phase of an oil-in-water emulsion permitted their multiplication more readily than the discontinuous water-phase of a water-in-oil emulsion. Therefore, the preservative should be in the water-phase if it supposed to be effective.

Other constituents in the formula might interfere the anitmicrobial action of a preservative. Nonionic surface active agents were commonly used in pharmaceutical preparation, but we often found that they might cause the uneffectiveness of preservatives. At low concentrations, they were not significant but at high concentration more than the critical micelle concentration they were usually employed in the preparations. Rosen and Berke (50) stated that above this critical micelle concentration, the nonionic surface active agent form aggregates, called "micelles" which constitute a new phase in the system and actually extract preservatives out of the other phases.

The effect of pH on the activity of preservatives was not performed in this project. However, the pH of a pharmaceutical formation ought to be considered in designing a preservative system. Many preservatives became less effective or unstable at certain pH's. The other related problem was the absorption of preservative by the container. Rubber and plastics, especially plyethylene containers or caps, were always suspected to be concerned with the stability of the preparations because lipid-soluble preservatives were capable on migrating into them.

There are many other problems ought to be investigated to know how most effectiveness of preservatives concerned during storage.