CHAPTER I

INTRODUCTION

In the pharmaceutical industry, the research for novel techniques used for the modifying of drug properties is necessary. Microencapsulation, which is one of those techniques, has been widely investigated for several years and it is still of great interest and useful today.

Microencapsulation is a process of applying relatively thin coatings to small particles of solids or droplets of liquids. There are many advantages of this useful technique; one of these is the stabilization of drugs sensitive to environmental conditions (Luzzi, 1970; Bakan and Sloan, 1972; Madan, 1978b; Deasy, 1984; Bakan, 1986, 1994). Microcapsules may be prepared by a number of methods. Coacervation is the most widely used method of microencapsulation. For water soluble and moisture sensitive drugs such as ascorbic acid and aspirin, the coacervation method using an organic vehicle (e.g. ethylcellulose-cyclohexane solution) and a change in temperature is a useful method (Samejima, Hirata, and Koida, 1982; Deasy, 1984). The non-aqueous solvent evaporation is another technique which is particularly suitable for microencapsulating the above-mentioned drugs (Watts, Davies, and Melia, 1990; Bodmeier, Wang, and Herrmann, 1994). Ethylcellulose is a water insoluble polymer that is used as a wall-forming material on account of its safety, stability, hydrophobicity and compact film-forming nature (Wade and Weller, 1994c; Rekhi and Jambhekar, 1995).

The principle of coacervation technique is the solubility reduction of ethylcellulose in cyclohexane to form coacervates by cooling the solution of ethylcellulose. As temperature drops, solvated ethylcellulose develops as a separate phase due to its lowered solubility in cyclohexane. The solvated ethylcellulose, which is distributed in cyclohexane as droplets, tends to wet and envelope the core particles. As the droplets coalesce, they lose solvent and develop into solid encapsulating walls. Plasticization of polymer material is necessary to lower the softening point and to improve thermoplasticity of the polymer (Deasy, 1984). Plasticizers may also be used to control drug release from polymeric films.

Microencapsulation by solvent evaporation is a simple procedure (Bakan, 1986; Watts et al., 1990). It involves the emulsification of a polymer solution containing drug into an immiscible liquid phase containing an emulsifier to form a dispersion of drug-polymer-solvent droplets. The solvent is removed from the dispersed droplets by allowing evaporation at room temperature to leave a suspension of drug-containing polymer microcapsules or microspheres. There are many production variables that should be taken into consideration for the microencapsulation by this technique and one of these variables is the emulsifier.

Ascorbic acid is essential for normal human metabolism. It has specific effects in the treatment of scurvy and also has antioxidant properties which is useful to pharmaceutics, foods, and cosmetics (Ovesen, 1984; Block, Henson, and Levine, 1991). In an aqueous solution, however, ascorbic acid is easily oxidized to give dehydroascorbic acid (Connors, Amidon, and Stella, 1986). The oxidation rate is dependent on pH and oxygen concentration, and is catalyzed by metal ions. Ascorbic acid is also susceptible to degradation under anaerobic conditions giving furfural and carbon dioxide. In solid dosage forms, ascorbic acid is stable but storage conditions

must be controlled at a relative humidity of 55 to 65%. Moisture, silica gel, and other tablet excipients affect the decomposition rate of ascorbic acid (Rubin, DeRitter, and Johnson, 1976). Samejima et al. (1982) investigated microencapsulation of ascorbic acid by temperature induced coacervation technique to examine the effect of coacervation-inducing agent. However, the stability of ascorbic acid microcapsules prepared by this technique had not been studied. Kirby et al. (1991) reported the stability enhancement of ascorbic acid by microencapsulation in liposomes prepared by the dehydration/rehydration procedure. In this form, its stability is enhanced compared with that in an aqueous solution, particularly in the presence of a number of factors (e.g. metal ion) which normally lead to its rapid degradation. However, ascorbic acid in the liposomes degrades faster than that in dry powder.

Therefore, ascorbic acid was selected as a model core material due to its water soluble property and its sensitivity to moisture. In addition, microencapsulation by temperature induced coacervation and non-aqueous solvent evaporation techniques was used for reducing the degradation rate of ascorbic acid. Other techniques using water as the manufacturing vehicle can not be used for microencapsulation of drugs sensitive to moisture.

The aims of this study were:

1. To prepare ascorbic acid microcapsules by temperature induced coacervation and non-aqueous solvent evaporation techniques.

2. To investigate the effects of core to wall ratios, and types and amounts of plasticizers on properties of the ascorbic acid microcapsules prepared by temperature induced coacervation technique.

3. To investigate the effects of polymer concentrations in organic solvent, core to wall ratios, and types and amounts of emulsifier on properties of the ascorbic acid microcapsules prepared by solvent evaporation technique.

4. To evaluate properties of the prepared microcapsules, namely morphology, yield, size and size distribution, drug content and drug entrapment, and release rate of ascorbic acid from the microcapsules.

5. To investigate stability of ascorbic acid microcapsules prepared from both techniques.