

CHAPTER I

INTRODUCTION

Centella asiatica is a medicinal plant with a long history of therapeutic use. It is a creeping plant which has its origin in tropical and subtropical climates. In India and Indonesia, it has a long history of use, healing wounds and slowing the progression of leper. Furthermore, it is considered to prolong life and to increase energy and sexual potency. Based on many indications of the traditional medicine, it is accepted in France in 1880. In the 70s, Italian and European investigators found evidences that this plant may significantly improve the symptoms caused by hemorrhoids and varicose veins (Adaptogen Medical Center, 1996). Rigorous clinical investigations of *Centella asiatica* have been conducted on chronic venous insufficiency and varicose veins such as enhanced connective tissue integrity, elevated antioxidant levels in wound healing, and improved capillary permeability (Shukla, Rasik, and Dhawan, 1999; Belcaro, Grimaldi and Guidi, 1990). For most clinical studies, *Centella asiatica* are used in oral form. However, Allegra et al. (1981) has been studied topical form of centella extract for various venous disorders (including hemorrhoids and varicose veins). Moreover, there is a patent in United States Patent about topical form of centella extract for treatment of hemorrhoids (Borod and Murray, 2000). From previous knowledge *Centella asiatica* has ability as topical dosage form for hemorrhoids. So, in this research *Centella asiatica* extract in suppository dosage form is designed. However, conventional solid suppositories which melt or soften in the rectum, may give a feeling of discomfort, pain and refusal to the patients, possibly lowering patients compliance. To solve the problems of conventional solid suppositories, it would be desirable to develop a liquid suppository which forms gel at body temperature and has mucoadhesive force to the rectal mucous membranes (Choi et al., 1998; Ryu et al., 1999). In this investigation, it was aimed to prepare the formulation of *Centella asiatica* extract liquid suppositories. For an active substance, centella extract, was modified by spray-dried with chitosan. The microsphere type was positively charged in order to enhance the mucoadhesive property.

Poloxamers, known as a surfactant are ABA-type triblock copolymers composed of poly (oxyethylene) (A) and poly (oxypropylene) (B) units. Poloxamer solutions are known to exhibit the phenomenon of reverse thermal gelation; remaining as solution at low temperature and gelling when temperature increases. Furthermore, poloxamers were reported not to cause any damage on mucosal membranes (Lenaerts et al., 1987; Dumortier et al., 1991).

Spray drying technique transforms liquid feed into dry powder in a one step, continuous particle processing operation and could be applied to a wide variety of materials (Broadhead et al., 1994). Despite the main advantages of spray-drying, processing variables must be well controlled to avoid difficulties such as low yields, sticking, or high moisture content, which were often encountered with laboratory scale spray-dryers (Masters, 1979). So, statistically designed experiments have been used as they allow the evaluation of both different factors and their interaction to process efficiency.

The purposes of this study were:

1. To prepare the rectal suppositories containing microspheres of *Centella asiatica* extract and suppository bases which have appropriate *in situ* gel property.
2. To prepare the microspheres of *Centella asiatica* extract with chitosan by spray drying technique.
3. To evaluate physiochemical properties of prepared microspheres and *in situ* gelling suppositories containing microspheres of *Centella asiatica* extract.