CHAPTER I

INTRODUCTION

Nowadays botanical *Centella asiatica* extracts play an increased role in pharmaceutical applications. The beneficial effects of this plant have been known for a long time such as treatment of wound healing, burns, leprous ulcers, hypertrophic eschars, keloids and venous lymphatic disorders (Loiseau and Mercier, 2000). The active constituents of this plants of therapeutic interest are asiatic acid, madecassic acid and asiaticoside (Bonte et al., 1993; Kim et al., 1997, 2001). Centella preparations used in conventional medicine are prepared in oral form (tablets and drops), topical form (ointments and powder) and in the form of injections (s.c., i.m. and i.v.) (Brinkhaus et al., 2000). For skin treatment, topical delivery of active constituents of *Centella asiatica* may provide better patient compliance. The ability of drug in a topical formulation to permeate the skin is dependent on two consecutive events. The drug must first release from the vehicle to the skin surface and then it must permeate this barrier to the site of action. One of factors on both steps is dependent upon the physicochemical properties of the vehicle (Kriwet and Muller-Goymann, 1995). In an attempt to improve the skin permeation of these constituents, there has been interest in the development of new effective vehicle.

Microemulsions have received a great attention in recent years for various application, including topical delivery of drug. Microemulsions are colloidal dispersions of oil and water stabilized by an interfacial film of surfactant molecules either alone or combination with cosurfactant (Sirotti et al., 2002). Several

mechanisms have been proposed to explain the advantage of microemulsion for the topical delivery. First, a large amount of drug in formulation can be incorporated due to the high solubilizing capacity. Microemulsions have been shown to exert a high capacity for incorporating both lipophillic or hydrophilic substances. Second, the diffusional barrier of the stratum corneum may be modified depending on the surfactant and cosurfactant in the microemulsion. Third, an increased thermodynamic activity of the drug may favor its partitioning into the skin (Baroli et al., 2000; Rhee et al., 2001). The penetration of drugs from microemulsions into human skin has been the objective of numerous studies. The in vitro permeation across skin membranes as well as the in vivo penetration of drug from microemulsions was higher than from conventional systems (Bronaugh and Maibach, 1999).

However, it is known that microemulsions exert irritative effects, often by their high content of surfactants (Bronaugh and Maibach, 1999). In order to make these systems for pharmaceutically acceptable formulation using non-toxic and safe ingredients is required. Many nonionic surfactants e.g. polysorbates have suitable properties for topical administration (Aboofazeli and Lawrence, 1994). Many studies have shown that the use of short chain alcohols in the preparation of microemulsions can decrease surfactant concentration (Aboofazeli et al., 1995; Alany et al., 2000). Many of the short chain alcohols are regarded as non-toxic. 1,2-alkanediols have similar properties to aliphatic alcohols, but are reported to be less toxic. Due to this advantage, 1,2-alkanediols are regarded as suitable substitutes for use in the formulation of microemulsions. In this study, it has been aimed to develop the

formulation of *Centella asiatica* microemulsions using very low concentration of non-toxic excipients and to study the effects of composition in microemulsions on the pseudoternary phase diagram and permeation through shed snake skin membrane.

The objectives of the present study were as follows:

1. To study the effects of oils, surfactants and cosurfactants on the pseudoternary phase diagram of microemulsion
2. To develop the formulation of *Centella asiatica* microemulsions
3. To study the effects of oils, surfactants and cosurfactants on the skin permeation of *Centella asiatica* microemulsions