CHAPTER I

INTRODUCTION

Indomethacin was a product of a laboratory search for drugs with antiinflammatory property. It was introduced in 1963 for the treatment of rheumatoid arthritis and related disorders. Although indomethacin is widely used and is effective, toxicity often limits its use (details in Appendix 1). One way to avoid this problem is to use this drug in an external form such as ointments, creams, gels and solutions. However, there is only one manufacturer in Thailand that produces an external dosage form of indomethacin. That is a solution sprays which is known as " Elmetacin™ ".

Indomethacin decomposes by alkaline hydrolysis and its water solubility is poor (Windhol, 1983). The formulation of indomethacin in an external dosage form is interesting and challenging especially in a solution form from the stability point of view. A dosage form of which ingredients are similar to the solution is gels. Gels is an interesting dosage form for antiinflammatory drugs because it often releases drugs easily and it is also an elegant dosage form. Antiinflammatory drugs in the gel form that have already been available in the market are piroxicam gel and diclofenac emulgel. It was expected that

the gel form can improve the stability of this drug.

In formulation work, the stability testing of a pharmaceutical dosage form usually begins during the early stages of its development and the main purpose is establishing a product shelf life. Because room temperature shelf lives may range up to several years in duration, the stability tests are often performed under exaggerated conditions (e.g., elevated temperature) to accelerate the degradation process. The shelf life is usually predicted by monitoring the decomposition rate at several higher temperatures and the data are then extrapolated to the room temperature using the Arrhenius equation (Garret, 1962).

In summary, the objectives of this study were to:

1. formulate topical indomethacin solution in order to obtain a stabilized preparation.

2. formulate topical indomethacin gel in order to obtain a stabilized preparation.

3. study the stability of a topical indomethacin solution available in Thailand, Elmetacin™, in comparison with the prepared solutions.

4. compare the stability of the prepared topical indomethacin solution with the stability of the prepared topical indomethacin gel.