CHARTER I

INTRODUCTION

The electrochemical definition of oxidation is the reaction involving the electron-transfer mechanism. Several factors influencing are, for the most part, environmental factors such as concentration of oxygen, intensity of light and amount of heavy metal impurity which are ubiquitous and difficult to control. Oxidation reactions can create obvious stability problems of many drugs and pharmaceutical substances which most exist in a reduced from and tend to be converted to a more oxidized state (Connors, Amidon and Stella, 1986). Thus, the shelf life of many pharmaceutical products is limited by susceptibility of the active drug to undergo oxidative decomposition (Kaufman, 1990). Degradation products occurring, although in a very low level, can cause the rancidity and discoloration in pharmaceutical products (Stewart and Tucker, 1985). Kinetically, however, there is a sufficient energy barrier to many oxidative reactions that not all molecules can oxidize spontaneously. The radiation from the sun and artificial light, which give the absorptible molecules the energy, can cause oxidative reactions to occur more easily (Connors et al., 1986). Moreover, the heavy metal impurities and reaction products accumulating can act as catalysts and make the oxidative reaction more complex in kinetic behavior (Kaufman, 1990).

Ranitidine is a histamine H_2-receptor antagonist. It has been used for treatment of duodenal and gastric ulceration, Zollinger-Ellison syndrome and inhibition of gastric acid secretion in gastrointestinal tract. The furan ring and amino-alkyl substitute structure make ranitidine more potent in inhibition of gastric acid secretion induced by various stimuli and less anti-androgenic and hepatic microsomal enzyme inhibition effects than other drugs in the same group, such as cimetidine, which contains an imidazole ring (Hohnjec et al., 1986).

The hydrochloride salt of ranitidine is the most popular form because of its high water solubility which leads to an increase in its bioavailability. Almost all the stability studies of ranitidine HCl have been reported in the field of intravenous admixture. There are only a few publishing reported involving the chemical stability of ranitidine HCl. In Kanokwan Thiengthawat's Master thesis, degraded products occurred in a change of color of solutions from clear-colorless to dark-red (Kanokwan, 1994). The color occurred indicated that oxidation reaction may be one of the decomposition pathway of ranitidine hydrochloride. As a consequence, the oxidative degradation kinetics of ranitidine HCl solutions were studied here by addition of various kinds of antioxidants. The solutions were placed in the presence and absence of light and / or oxygen.

Objectives

The objectives of this study are the following:

1. to study oxidative degradation kinetics of ranitidine HCl in solutions,
2. to study the effect of light on the degradation rate of ranitidine HCl in solutions,
3. to study the effect of oxygen on the degradation rate of ranitidine HCl in solutions,
4. to study the effect of antioxidants on the degradation rate of ranitidine HCl in solutions.