CHAPTER I

INTRODUCTION

Cimetidine is an H_2-receptor antagonist which is used to antagonise the effects of histamine on the acid-secreting cells in the gastric mucosa. It is used to reduce gastric acid secretion in conditions associated with hyperacidity such as duodenal and peptic ulceration and Zollinger-Ellison syndrome. Cimetidine is used in the form of cimetidine base and hydrochloride salt and marketed in the form of tablet, capsule and injection (1,2,3).

Cimetidine is a new product discovered by Smith Kline and French (SKF) Research Laboratories(4), the analytical method developed by SKF is not an official one. However, some assay methods of cimetidine have been reported which depend on the characteristic functional groups. Because of the basic property, cimetidine has been analysed by potentiometric non-aqueous titration with perchloric acid in glacial acetic acid and end point was determined by plotting electrode potential changing against volume of acid used (5,6,7). When crystal violet was used as indicator, the observation of the end point is rather difficult. A spectrophotometric method(8) which was reported by SKF has disadvantage, as for some spectrophotometers cannot measure the

absorbance accurately at the wavelength 218 nm (9). A colorimetric method for the analysis of cimetidine via reaction with diazotized sulfanilic acid on imidazole ring, reported by Mehta and Chainani(10), was time consuming and disagree with the theory of Ehrlich diazo reaction(11,12). Randolph et al(13) recently proposed the high-pressure liquid chromatograph method for the analysis of cimetidine in blood and urine. Leonard et al(8) also determined cimetidine by high-pressure liquid chromatography in the bioavailability study of cimetidine capsule and tablet formulation. This stimulated the need for a satisfactory, rapid and sensitive method for determination of cimetidine in pharmaceutical preparations.

The purpose of this thesis is to develope a convenient assay method which can be used in the determination of cimetidine. With the advent of high-pressure liquid chromatography and its wide application in pharmaceutical analysis, it was considered worthy of consideration for the analysis of cimetidine. The work described in this study is an attempt to develope a specific assay method for cimetidine, and the results are compared with those from the potentiometric non-aqueous titration and the spectrophotometric method.