CHAPTER I

Introduction

Piperazine (diethylenediamine), an anthelmintic drug, was first introduced medicinally in the treatment of gout and rheumatism because of their possible value in dissolving uric acid. The clinical results, however, were almost nil because the distribution of therapeutic doses could not be expected to furnish efficient concentration. Its anthelmintic activity was not recognize untild the 1950 s,experimental and clinical studies have established and found that piperazine was a nearly ideal drug for the treatment of oxyuriasis (pinworm infestation) and ascariasis (roundworm infestation) in humans and domestic animals. It appears to function by inducing a state of narcosis in the worms. Piperazine posses a high order of activity, the treatment is relatively simple, toxicity is virtually absent at therapeutic dosage levels and the cost is relatively low - all formidable criteria for any competitive anthelmintic to satisfy. Various salts of piperazine, such as the citrate, adipate and phosphate, have been prepared and utilized in therapy, in addition to the hexahydrate which was the natural crystal form of piperazine. All of the derivatives have similar efficacy. Piperazind and its salts are available by brand names, usually in the form of a syrup or tablet.

With the rapidly increasing use of piperazine and its

salts in anthelmintics, both in human and domestic animals, the need has arisen for a rapid, simple and yet accurate method for routine quality control of piperazine in pharmaceutical preparations. The official method in U.S.P.XX and N.F.XV[18], B.P.C. 1973[50] and B.P. 1980[51], picric acid or trinitrophenol is used to form yellow precipitate, piperazine dipicrate, and determined gravimetrically. The official gravimetric methods are tedious, expensive, time consuming and use a large amount of sample. Picric acid is also harmful to human body and have difficulty in purchasing and storage. Several methods for the analysis of piperazine and its salts in pharmaceutical products have been published such as volumetric[29-36], near infrared[46,57-59] and colorimetric methods[24,25,61-65] Most of them lack of reproducibility and had several critical factors which must be carefully controlled especially time, temperature and pH of the reaction. Some methods gave satisfactory results in raw material but not in pharmaceutical preparations. Some required special equipments which were not available in common laboratory in drug industry. This stimulated the need for a satisfactory, simple, rapid, accurate, sensitive and stability-indicating method. The purpose of this thesis was to find the best and simple method which could be employed in quality control laboratory for analyzing piperazine and its salts in pharmaceutical dosage forms.

The method was based on selective complex formation of piperazine and sulfonphthalein dye in chloroform. Piperazine

was first easily extracted from aqueous strong alkaline solution with chloroform and then reacted with sulfonphthalein dye. A yellow complex was formed and determined spectrophotometrically. The procedure described required a minimum of time and of sample handling for analysis. Sulfonphthalein dye was a common reagent, inexpensive and easy to purchase. Its prepared solution was stable at room temperature for a long period of time. It was also safety and could be used without special precaution. The color reaction was specific for piperazine and was hardly interfered by other related materials. It is hoped that the proposed method will be useful in routine quality control of piperazine and its salts in pharmaceutical preparations.