

Chapter V

Summary and Conclusion

All experimental data indicated that piperazine and its salts could be detected in minute quantities from anthelmintic preparations of various dosage forms. Piperazine free base was extracted from its salts with chloroform in aqueous strong alkaline medium. The chloroform extracts were treated with four sulfonphthalein dyes : bromcresol green, bromthymol blue, bromcresol purple and bromphenol blue, produced yellow complex which were measured spectrophotometrically. The effects of various conditions on the stability of the complex, e.g., linear absorbance-concentration relationship, concentration of color forming agent used, mole ratio of complex formed, time and temperature were studied. BTB was found the best color forming agent and applied to the estimation of piperazine and its salts in commercial available pharmaceutical preparations. Slight modifications were required in some instances. For tablet or capsule, the powder or pasty content were stirred magnetically 1 hour to disintegrate compounds. In the case of sugar coated tablet, the coated sugar was washed out with distilled water and dried over silica gel before assays . It was observed that other excipients used in pharmaceutical preparations such as glycerin, methyl paraben, propyl paraben, coloring agent,

starch, talc, magnesium stearate, etc. did not interfere in the estimation of piperazine.

Bromthymol blue method showed high accuracy and good reproducibility compared to those **obtained by the tedious and** time consuming official gravimetric methods^(18,50,51). The proposed method was also faster, simpler and cheap. The great advantages of this procedure were summarized as below :

1). The procedure was very sensitive to minute amounts of piperazine in formulations and was easily adaptable to the various types of dosage forms, e.g. syrup, tablet, elixir, capsule. The official methods required large amount of sample and unapplicable to all piperazine containing preparations.

2). The proposed bromthymol blue method could be applied to various forms of piperazine, e.g., citrate, hydrate, adipate with slight modification while the official assays^(18,50,51) required different method for each salt.

3). High in accuracy was obtained, with per cent recoveries equalled to or better than 98.99 % for the prepared syrups. Reproducible results were obtained with individual sample.

4). **The method was simple and rapid.** One analyst could perform five to eight samples simultaneously per day on a routine basis. Although the official gravimetric methods^(18,50,51) gave highly consistent results but their procedures were tedious and time consuming. Since piperazine dipicrate formed in official gravimetric method was appreciably soluble in

water^(48,87), but in BPC 1973⁽⁵⁰⁾, the mixture of equal volume of saturated solution of trinitrophenol and water was required for removing sulfate impurity hence the washing solution was minimum as possible and should be constant, otherwise variable results were obtained.

5) Only one reagent was required in the proposed method. Bromthymol blue was available commercial or easily synthesized. The solution prepared could be stored for a long time without appreciable change. The reagent was used in small quantities and its cost was very low. Trinitrophenol, a reagent used in the official method was hazardous, difficult in purchasing and storage, and also expensive.

6). Conventional laboratory glasswares were required. Spectrophotometer was a common equipment which found easily in any laboratory.

7). The interferences on the procedure by common excipients in pharmaceutical dosage forms were found to be negligible.

Owing to other amines, quaternary ammonium compounds were known to react with BTB under the stipulated conditions, such compounds were tested for possible interference, but the commonly encountered formulations of piperazine salts, however, did not contain any of the above mentioned drugs, therefore no such interferences were expected. Caution must be taken with

the laboratory glasswares because the present of traces of detergent could react with BTB and caused large error in analysis, the glasswares used must be scrupulously cleaned with special attention paid to ground-glass surfaces.

The proposed bromthymol blue method has been used with complete satisfaction in quality control of piperazine and its salts in pharmaceutical preparations. Since analysis could be performed rapidly and economically with high accuracy and good reproducibility. It was usually more reliable for routine determinations.