INTRODUCTION
1. INTRODUCTION

Calorimetry is a fast emerging tool, which is finding extensive use in modern drug discovery, as it is non-invasive and non-destructive technique. Although the development of microcalorimetry for use in cell biology has been going on for long time in academic world, it was not until very recently that pharmaceutical industry began to show an interest in this field. Recent developments in the technique of calorimetry have allowed direct determination of both kinetic and thermodynamic parameters using native materials for long slow reactions. It has been found to be extremely useful during preformulation studies. It does not require optically transparent solution and can be used to study the cloudy or turbid solutions or suspensions directly.

Nitroimidazoles are important category of drugs and are their efficacy against anaerobic bacteria (Bacteroides species) and protozoans, such as Trichomonas, Entamoeba species and Giardia has led to these agents becoming well-established in the treatment of infections caused by these micro-organisms. Besides this, they are reported to have other interesting biological profiles. There are nitroimidazoles employed as radiosensitizers, in cancer therapy. The antifertility potential of ornidazole and antitubercular profile of certain nitroimidazopyrans have been explored. Nitroimidazoles may often be prescribed along with proton pump inhibitors and macrolides employed in the treatment of gastric and duodenal ulcers. Although a single agent is effective in vitro at killing H. pylori, eradication of the organism in patients with single agents is poor. Combination therapy probably attacks the organism through different mechanisms of action producing at least additive or perhaps synergic effect. But the compatibility of drugs in a combined preparation or combined therapy is critical factor for the development of pharmaceutical formulations. Therefore, it is important that the drugs do not interact in a way that is likely to reduce their efficacy and increase the toxicity because interactions in the solid or liquid state between the active ingredients in pharmaceutical dosage forms can give rise to changes in stability, solubility, dissolution rate and bioavailability of drugs.
Metronidazole

Tinidazole

Ornidazole

Secnidazole

Omeprazole

Lansoprazole
Literature survey has revealed that these 5-nitroimidazoles are not much water-soluble and show poor bioavailability. Literature survey also revealed that for drugs with low solubility in the crystalline state, the possibility of improving their solubility, dissolution rate and bioavailability based on the formation of an amorphous state using the polymers is a very attractive approach. Therefore, it is proposed to start systematic studies on drug-carrier systems of these drugs with polyvinylpyrrolidone and various cyclodextrins in binary as well as in ternary systems, with the aim to increase their water-solubility, using the technique of calorimetry. Equilibrium constant, standard enthalpy changes ($\Delta H^0$) standard free energy ($\Delta G^0$) and standard entropy ($\Delta S^0$) accompanying the formation of ternary complexes are calculated using non-linear least square method. Derivative
spectroscopy and HPLC techniques have been utilized by previous workers to study the stability of metronidazole and tinidazole. But very little literature is available about the stability studies of other nitroimidazoles. Moreover, no literature is available about the degradation enthalpy of these drugs. Therefore, calorimetric technique has been explored to study the degradation profile of these drugs. The enthalpy of degradation have also been measured at various pH and temperatures.

The present work is also aimed to predict any specific and non-specific interaction between the drugs prescribed in triple regimen therapy involving nitroimidazoles, macrolides and omeprazole in combined dosage forms using the technique of solution calorimetry. Magnitude of excess molar enthalpy of solution are used to correlate the extent of interaction between the various drugs in a combined formulation. The excess molar enthalpy of solution of binary and ternary systems are determined by comparing the experimental values of heat of solution of binary and ternary systems with the theoretically predicted values.