Preface

Extensive research is undergoing for developing controlled and prolonged intrapocket delivery systems of antimicrobials for achieving better therapeutic modalities than existing ones in periodontal disease. Intrapocket delivery is highly desirable as it bypasses systemic side-effects, attains higher concentration of drug at the infection site, prevents bacterial resistance and reduces drug dose along with improved patient compliance. These systems are particularly beneficial for deep seated periodontal pocket (> 5 mm) infections. Use of natural, non-toxic, biocompatible, biodegradable polymers *viz.* chitosan, produces prolonged and controlled release of drugs and decreases the overall cost of therapy with promising potential for controlling the periodontal diseases in poor patients of developing and underdeveloped countries.

This research was undertaken to statistically screen and develop multiparticulate based delivery systems with feasible characteristics for intra-pocket delivery. Chitosan microspheres were formulated, screened and evaluated for their safety and efficacy. The screening of process was done by Plackett-Burman Factorial Design and the final optimizations of formulations based on screened characteristics were done by Box-Behnken Experimental Design. Optimized *in-situ* gel formulations incorporated with optimized microspheres were evaluated for their physicochemical properties, preclinical and clinical efficacy for their safety and utility.

The whole thesis is presented by dividing into eight chapters. **Chapter one** provides introduction to the current understanding of potential and challenges associated with antimicrobial therapy of periodontal infections and basis of undertaking this work. **Chapter two**, illustrates an overview of the current background of knowledge and concepts related to periodontal disease, treatment methods, drugs and polymers. In addition, outline of the anatomical and physiological conditions of periodontal disease has been elaborated. Recent literatures and ideas related to disease, technologies, physicochemical properties of drugs and polymers have been included discussing their applicability in periodontal disease management.

Chapter three includes main objective and plan of research work as embodied in this thesis. **Chapter four** describes the preformulation studies including UV method development for the simultaneous routine analysis and solubility studies of ornidazole and doxycycline hyclate. **Chapter five** is divided into three parts based on the type of crosslinkers; alginate (A), tripolyphosphate (B) and vanillin (C) used for the formulation of chitosan crosslinked microspheres. Further, it deals with the application of quality by design approach for microsphere development, optimization and characterization. **Chapter six** deals with the design and optimization of microspheres loaded *in-situ* gel formulations. The optimized microspheres obtained in chapter five were incorporated into Pluronic® based thermosensitive gels and evaluated for their preclinical and clinical efficacy. **Chapter seven** outlines the summary of main findings of this research work and conclusions. The contents of this thesis bridges between the multiple disciplines needed to successfully design multiparticulate carrier systems for delivery of antimicrobials in periodontal drug delivery.