ABSTRACT

This dissertation presents the designing of novel, optimized polyamide 6,10 monolithic matrix systems synthesized using a modified interfacial polymerization process and formulated by direct compression for rate-controlled delivery of model soluble and insoluble drugs. The modification strategy employed included varying reaction stoichiometry, volume ratio and the inclusion of solvent phase modifiers. This was guided through the statistical and mathematical principles of robust experimental designs. A general introduction to this dissertation is presented at the beginning. The initial phase of this investigation employed the Plackett-Burman screening experimental design to evaluate the effects of a partial modification strategy utilized (varying reaction stoichiometry and volume ratio) on the physicochemical and physicomechanical properties of polyamide 6,10. Subsequently, a higher performance, Box-Behnken design using the full modification strategy (varying reaction stoichiometry, volume ratio and the inclusion of solvent phase modifiers) was applied to the optimization of the physicochemical and physicomechanical properties of polyamide 6,10 to achieve the desired drug release characteristics after the competence of the statistical designs in generating effective chemical transformations were established. From this analysis, optimized, directly compressed polyamide 6,10 monolithic matrix systems were developed. The monolithic matrix systems developed in this study demonstrated slow, intermediate and controlled drug release rates. Furthermore, the influences of formulation variables on the drug release performances of the respective optimized monolithic matrices were assessed. In addition, the potentials of the slow and controlled release monolithic matrix formulations to function as implantable and gastroretentive drug delivery systems respectively were also explored. Mathematical models showed that drug release from the three optimized monolithic matrix systems were predominantly regulated by matrix relaxation and lower levels of Fickian diffusion and was observed to follow zero-order kinetics. Also, a close relationship existed between the experimental and predicted data revealing the stability of the mathematical models employed. All dissolution studies in this work employed either amitriptyline hydrochloride or theophylline as model soluble or insoluble drugs respectively. Finally, the optimized polyamide 6,10 variants were characterized based on their physicochemical and physicomechanical properties. A direct relationship was observed between the physicochemical and physicomechanical characteristics and the drug release behaviour of the optimized polyamide 6,10 variants.