MODIFYING THE THREE-DIMENSIONAL NETWORK OF POLYAMIDE 6,10 FOR DESIGNING A NOVEL DRUG DELIVERY SYSTEM

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of

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DECLARATION

I, Oluwatoyin A. Kolawole declare that this dissertation is my own work. It is being submitted for the degree of Master of Pharmacy in the Faculty of Health Sciences at the University of the Witwatersrand, Johannesburg, South Africa. It has not been submitted before for any degree or examination at this or any other University. The abstracts and copies of paper(s) included are part of this work.

……..

Signature

……..

Date

DEDICATION

This dissertation is dedicated to my brothers, Ayokunle, Ayoyinka and Ajibola and parents Ibidayo and Ayowole Kolawole, for their love, support, encouragement and prayers that inspired me to face all the past and present challenges of my life.

PRESENTATIONS, PUBLICATION AND PATENT APPLICATION

PRESENTATIONS

1. Micromechanical Characterization of Polyamide Variants as Potential Polymeric Materials for Tissue Engineering, 26th Annual Conference of the Academy of Pharmaceutical Sciences, Port Elizabeth, South Africa, 2005.

2. Synthesis, Characterization and Preliminary Evaluation of Linear Polyamides for Controlled Drug Delivery, 26th Annual Conference of the Academy of Pharmaceutical Sciences, Port Elizabeth, South Africa, 2005.

3. Modifying the 3-D network of nylon for designing a novel drug carrier, Therapeutic Science Research Afternoons, University of the Witwatersrand, Johannesburg, South Africa, 2005.

4. Modifying the physical properties of polyhexamethylene sebacamide (PS) for the design of a novel drug delivery system, 1st Symposium on Biomaterials Sciences and Applications in South Africa, Johannesburg, South Africa, 2006.

5. Development of a novel gastroretentive mono-dispersed matrix system for rate-controlled drug delivery, 4th International Conference on Pharmaceutical and Pharmacological Sciences, Johannesburg, South Africa, 2006.

6. Design of a novel polyamide drug carrier for intracranial implantation in the treatment of depression, American Association of Pharmaceutical Scientists annual meeting and exposition, Texas, USA, 2006.

PUBLICATION

A paper titled “Novel polyamide 6,10 variants synthesized by modified interfacial polymerization for application as a rate-modulated monolithic drug delivery system” by Oluwatoyin A. Kolawole, Viness Pillay, Yahya E. Choonara and Michael P. Danckwerts accepted by the *Journal of Bioactive and Compatible Polymers*, 2006 (**In press**).

PATENT APPLICATION

South African Patent Application titled “Polyamide Rate-Modulated Monolithic Drug Delivery System” by Oluwatoyin A. Kolawole, Viness Pillay, Yahya E. Choonara and Michael P. Danckwerts, 2006.

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.

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