UNIVERSIDADE FEDERAL DE ITAJUBÁ – UNIFEI

INSTITUTO DE FÍSICA E QUÍMICA

PROGRAMA DE PÓS-GRADUAÇÃO EM MATERIAIS PARA ENGENHARIA

Microesferas de Poliglicerol Contendo Fumarato de Dimetila e Curcumina para Aplicação na Terapia da Esclerose Múltipla

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Priscila Veloso da Silva

Microesferas de Poliglicerol Contendo Fumarato de Dimetila e Curcumina para Aplicação na Terapia da Esclerose Múltipla

Defesa de Tese submetida ao Programa de Pós-Graduação em Materiais para Engenharia como requisito para a obtenção do título de Doutor em Ciências em Engenharia de Materiais.

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Resumo

A esclerose múltipla é uma doença autoimune e crônica caracterizada pela desmielinização dos neurônios no sistema nervoso central. Trata-se de uma doença incapacitante ao longo do tempo e cujas terapias podem provocar diversos efeitos colaterais. Este trabalho propõe uma alternativa ao tratamento da esclerose múltipla a partir do desenvolvimento de microesferas de dendrímero de poliglicerol carreadoras de fumarato de dimetila e de curcumina. Inicialmente, as microesferas foram caraterizadas por meio de MEV, FTIR, TGA e DSC. Foram determinados o grau de intumescimento e a energia de ativação das microesferas de PGLD (G10, G25, G50, G100 e G200). Os resultados dessas análises mostraram que as microesferas porosas, G100 e G200, de menor e maior tamanho, respectivamente, eram as mais adequadas para a formação dos compostos. Foram avaliadas a porosimetria desses grupos e a biocompatibilidade por meio de ensaios de citotoxicidade e hemocompatibilidade *in vitro*. O estudo teórico de ancoragem molecular mostrou que a formação dos compostos foi espontânea, sendo que, o composto com curcumina (-23,8 kJ/mol) apresentou maior afinidade em comparação ao composto com fumarato de dimetila (-11,3 kJ/mol). Os compostos, DMF-PGLD e CUR-PGLD, foram preparados e, posteriormente, caracterizados por FTIR e avaliados os perfis de liberação. Os espectros de FTIR sugeriram a interação dos compostos devido ao aparecimento de bandas de absorção características das moléculas precursoras nos compostos. Em geral, o estudo de liberação determinou o mecanismo de transporte super caso II. Foi observada uma retenção maior nos compostos com curcumina, isso porque as curvas se apresentaram menos acentuadas ou com liberação mais tardia. Em conclusão, sugere-se que a formação de compostos entre microesferas porosas de dendrímero de poliglicerol (G100 e G200) e os ativos (fumarato de dimetila e curcumina) seja uma alternativa para a liberação controlada no tratamento da esclerose múltipla, com o intuito de diminuir os efeitos colaterais. Entretanto, os compostos com curcumina tiveram resultados mais favoráveis a sua aplicação, em virtude de sua maior afinidade e retenção.

Palavras-chave: Esclerose múltipla, sistemas de liberação controlada, dendrímero de poliglicerol, fumarato de dimetila, curcumina.

Abstract

Multiple sclerosis is autoimmune and chronic disease characterized for neurons demyelinating and formation of sclerotic lesions within central nervous system. It is a disabling disease over time and whose therapies can cause several side effects. This work proposes an alternative to the treatment of multiple sclerosis from the development of carrier system using microspheres of polyglycerol dendrimer with dimethyl fumarate and curcumin. Initially, the microspheres were characterized by SEM, FTIR, TGA and DSC. The swelling degree and the activation energy of the polyglycerol dendrimer microspheres (G10, G25, G50, G100 and G200) were determined. The results of these analyzes showed that the smaller and larger porous microspheres G100 and G200, respectively, were the most suitable for the formation of the compounds. It was evaluated porosimetry of these groups and biocompatibility by *in vitro* cytotoxicity and hemocompatibility assays. The theoretical study of molecular anchoring showed that the formation of the compounds was spontaneous, the compound with curcumin (-23.8 kJ/mol) had higher affinity compared to the compound with dimethyl fumararte (-11.3 kJ/mol). The compounds, DMF-PGLD and CUR-PGLD, were prepared and subsequently characterized by FTIR and evaluated the release profiles. FTIR spectra suggested the interaction of the compounds due to the appearance of absorption bands characteristic of the precursor molecules in the compounds. The release study determined the super case II transport mechanism. A higher retention was observed in the compounds with curcumin, because the curves were less pronounced or with later release. In conclusion, it is suggested that the formation of compounds between polyglycerol dendrimer (G100 and G200) porous microspheres and active (dimethyl fumarate and curcumin) are an alternative for controlled release in the treatment of multiple sclerosis. However the compounds with curcumin had more favorable results to their application, due to affinity and retention.

Key-words: Multiple sclerosis, controlled release system, polyglycerol dendrimer, dimethyl fumarate, curcumin.

APÊNDICE A - Produção Científica

1) SILVA, P. V.; QUEIROZ, A. A. A. Long term multiple sclerosis drug delivery using dendritic polyglycerol flower-like microspheres. *Journal of Biomaterials Science-Polymer Edition*, v. 1, p. 1-13, 2019.

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