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Síntese e Caracterização de Nanopartículas de Prata Aplicadas à Detecção de Imunoglobulinas G Autorreativas

Dissertação apresentada ao Instituto de Medicina Tropical de São Paulo da Universidade de São Paulo para obtenção do título de Mestre em Ciências.

Área de concentração: Doenças Tropicais e Saúde Internacional
Orientador: Prof. Dr. Fabio de Lima Leite

São Paulo

2017

RESUMO

Higa AM. Síntese e caracterização de nanopartículas de prata aplicadas à detecção de imunoglobulinas G autorreativas (dissertação). São Paulo: Instituto de Medicina Tropical de São Paulo da Universidade de São Paulo; 2017.

Esta dissertação analisa a aplicação de nanopartículas de prata na detecção de imunoglobulinas G reativas aos epítopos da glicoproteína oligodendrocítica da mielina e da proteína básica da mielina, que são duas proteínas que compõem a estrutura da bainha de mielina, alvo de processos inflamatórios em doenças desmielinizantes. Há uma busca por marcadores biológicos para a diferenciação das doenças dentro desse espectro em seus estágios iniciais, anteriormente à disseminação de placas de desmielinização no sistema nervoso central, estágio no qual a detecção é realizada por exames de imagem no diagnóstico clínico. Nessa fase, porém, a bainha de mielina já apresenta alterações em nível molecular. Assim, a nanotecnologia oferece a possibilidade de investigação de processos biológicos em nanoescala, por meio de nanoestruturas biocompatíveis. Neste trabalho, o sistema desenvolvido foi o de nanopartículas de prata conjugadas aos epítopos da bainha de mielina, para detecção de anticorpos reativos às sequências peptídicas, com o objetivo de estabelecer os protocolos de síntese, funcionalização e de interação molecular, utilizando epítopos que são imunogênicos nos modelos experimentais das doenças desmielinizantes. As nanopartículas de prata foram obtidas por um processo de redução química e suas superfícies foram quimicamente modificadas para a funcionalização covalente dos epítopos da bainha de mielina. Esse processo foi caracterizado por técnicas de espectroscopia e microscopia. Os resultados de morfologia e diâmetro das nanopartículas foram obtidos pelas técnicas de microscopia de força atômica e difratometria de raios-X. A atividade das nanopartículas funcionalizadas em resposta aos anticorpos foi avaliada por espectrofotometria na região do ultravioleta-visível e por espectroscopia de força atômica. Os resultados obtidos por essas técnicas mostraram que o processo de funcionalização dos epítopos nas superfícies das nanopartículas de prata foi efetivo, já que o complexo foi responsivo aos anticorpos de forma específica. A resposta do sistema foi observável por sinais ópticos detectáveis na espectrofotometria na região ultravioleta-visível, por alterações visíveis de cor da suspensão de nanopartículas e por meio da quantificação das forças de interação por espectroscopia de força atômica. O conjugado nanopartícula-peptídeo apresenta, portanto, potencial para ser aplicado em estudos de investigação de biomarcadores para as doenças desmielinizantes.

Descritores: Nanopartículas. Nanotecnologia. Manifestações Neurológicas. Imunoglobulinas. Peptídeos.

ABSTRACT

Higa, AM. *Synthesis and characterization of silver nanoparticles applied to immunoglobulin G detection* (dissertation). São Paulo: Instituto de Medicina Tropical de São Paulo da Universidade de São Paulo; 2017.

This dissertation addresses the immunoglobulins G detection using silver nanoparticles. The chosen molecules are reactive to myelin oligodendrocyte glycoprotein and myelin basic protein epitopes, which are important components of myelin sheath structure, the main target of inflammatory processes in demyelinating diseases. In the context of demyelinating disorder spectrum, there is an effort in searching for biological markers that enable early differential diagnosis, prior to the spread damage in the white matter of the central nervous system, when lesions are usually seen on magnetic resonance imaging. At this stage, however, the myelin sheath has already undergone changes at the molecular level. Thus, nanotechnology offers the possibility of investigating biological processes at the nanoscale, using biocompatible nanostructures. In this work, silver nanoparticles were functionalized with myelin sheath epitopes to detect the antibodies reactive to these peptide sequences, aiming to establish protocols for the synthesis, functionalization and molecular interaction processes, using the immunogenic epitopes of experimental autoimmune encephalomyelitis model. The silver nanoparticles were chemically synthesized using a reduction method and the peptide sequences were covalently conjugated to the modified nanoparticle surfaces. This process was characterized with spectroscopy and microscopy techniques. The nanoparticle morphology and diameter results were obtained by atomic force microscopy and X-ray diffraction techniques. The activity of the functionalized nanoparticles in response to the antibodies was evaluated by spectrophotometry in the ultraviolet-visible electromagnetic region and by atomic force spectroscopy. The results obtained by these techniques showed that the functionalization process was effective since the nanoparticle-peptide complexes were specifically responsive to the antibodies. This response was observable by detectable optical signals in spectrophotometry in the ultraviolet-visible region, by the suspensions visible color changes and by interaction forces quantification by atomic force spectroscopy. The nanoparticle-peptide conjugate has, therefore, the potential to be applied in researches for biomarkers involved in the demyelinating diseases.

Descriptors: Nanoparticles. Nanotechnology. Neurological Manifestations. Immunoglobulins. Peptides.

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