Cytotoxicity and selectivity against cancer cells of chitosan oligosaccharides and gold nanoparticle-loaded carboxymethyl chitosan prepared by solution plasma treatment

Chayanaphat Chokradjaroen[a], Ratana Rujiravanit[a,b,c*], Sewan Theeramunkong[d], Nagahiro Saito[e]

[a)]The Petroleum and Petrochemical College, Chulalongkorn University, Bangkok 10330, Thailand
[b)]NU-PPC Plasma Chemical Technology Laboratory, Chulalongkorn University, Bangkok 10330, Thailand
[c)]Center of Excellence on Petrochemical and Materials Technology, Chulalongkorn University, Bangkok 10330, Thailand
[d)]Faculty of Pharmacy, Thammasat University, Pathumthani 12120, Thailand
[e)]Department of Chemical Systems Engineering, Graduate School of Engineering, Nagoya University, Nagoya 4648603 Japan

Chitosan is a cationic, linear polysaccharide consisting of two monomeric units that are *D*-glucosamine unit as a major component and *N*-acetyl-*D*-glucosamine unit as a minor component. Chitosan possesses some interesting molecular weight-dependent biological properties such as antimicrobial, antitumor and anticancer activities. Accordingly, degradation of chitosan by various approaches has been intensively studied. Solution plasma is an electrical discharge plasma generated between a pair of electrodes submerged in a liquid phase. During the discharge of plasma in an aqueous solution, a variety of highly active species including hydrogen radical and hydroxyl radical have been generated as a result of dissociation of water molecules. These radicals can cause bond cleavage in polymer chains, leading to the formation of lower molecular weight products. In this study, solution plasma was used to reduce molecular weight of chitosan. To achieve effective reduction of molecular weight of chitosan, solution plasma was used in combination with some chemicals, e.g. oxidizing agents, organic acids and inorganic salts, in order to get fast degradation rates and high production yield of low-molecular-weight products of degraded chitosan, i.e. chitosan oligosaccharides. Cytotoxicity against cancer cells of the as-prepared chitosan oligosaccharides was investigated. Selectivity to cancer cells in comparison with normal cells was also evaluated. Moreover, to attain better selectivity against cancer cells, carboxymethyl chitosan (CM-chitosan), a water-soluble derivative of chitosan, was degraded by solution plasma in the presence of gold nanoparticles to form gold nanoparticle-loaded CM-chitosan. Cytotoxicity against human breast adenocarcinoma cancer cell (MCF-7), human cervical cancer cell (HeLa), human lung cancer cell (H460) and normal cells of the gold nanoparticle-loaded CM-chitosan after plasma treatment was examined by using MTT assay. It was found that the presence of gold nanoparticle inside CM-chitosan matrix dramatically enhanced the cytotoxicity against cancer cells through the induction of the apoptosis which was analyzed by flow cytometry. However, the cytotoxicity against cancer cells was slightly improved by increasing the amount of gold nanoparticles loaded in the CM-chitosan matrix.

Corresponding author: ratana.r@chula.ac.th