21st Iranian Pharmacy Students Seminar
6-9 March, 2018, Ahvaz Jondishapour University of Medical Sciences, Faculty of Pharmacy

IPSS 21

Mitoxantrone-loaded aptamer-quantum dot nanoconjugates for cancer theranostics

Ata ahmadi Beiragh[1], Mohammad Johari-Ahar[1]

[1]Department of Medicinal Chemistry, School of pharmacy, Ardabil University of Medical Sciences, Ardabil, Iran

Introduction and background: Among advanced nanoparticles, fluorescent semiconductor nanocrystals known as quantum dots (QDs) have revolutionized the research areas of bio-sensing. a vast variety of bio-recognition elements, such as aptamers, monoclonal antibodies, and enzymes, have been loaded on the surface of QDs, and the developed nano platforms have been employed in bio-imaging studies. the conjugation reaction via an esteric bond between hydroxyl moieties of Mitoxantrone and carboxyl groups of Apt-conjugated QDs make the development of multiplexed nano-carriers possible for delivering to tumor sites via esterase enzymes or an acidic pH. To the best of our knowledge, this is the first report of MTO-Apt-QD synthesis for the development of a theranostic tool releasing a drug load by an esteric bond cleavage strategy.

Methods: In the conjugation of MUC-1 Apt to L-cys capped QDs (Apt-QD NPs), first, carboxyl groups of the CdSe QDs were activated using EDC and NHS (molar ratios of QDs:EDC:NHS were 1:10:10). After 1 h activation time, amine modified MUC-1 Apt was added to a succinimide ester of QDs and the conjugation reaction was completed with stirring within 48 h. unreacted chemicals were removed by dialysis (molecular weight cutoff 10 kilodaltons (kd)) against a borate buffer solution for 24h. the solution containing the photoluminescent Apt-QD NPs were freeze-dried for 48 h.

Results: The conjugation of Apt molcules to QDs NPs has been evaluated using agarose gel electrophoresis. The successful conjugation of MUC-1 Apt to L-cys capped QDs was validated by gel electrophoresis accomplished using 2.5% Metaphor agarose by which better resolution was obtained compared to that of results using conventional agarose. The Mitoxantrone-loaded aptamer-quantum dot nanoconjugates were applied successfully for concurrent imaging and therapy in cancer bearing mouse.

Discussion and Conclusion: In this study, we prepared multiplex MTO-Apt-QD NPs for theranostic applications. In vitro and in vivo assays indicated this nanoconjugate has the capability to specifically detect MUC-1 positive cancer cells and release their MTO molecules into the cells. Apt-QD NPs, which quench their photoluminescence after MTO molcules conjugation, reproduce a bright emission after MTO molecules release, which can be used for sensing of the targeted drug release of the NPs.

Keywords: Theranostics; Mucin-1 aptamer; Mitoxantrone; animal imaging

References: 1 Alivisatos, P .(2004)."The use of nanocrystals in biological detection." Nat Biotech 22(1) 47-52

2 Bagalkot, V., et al. (2007). "Quantum dot-aptamer conjugates for synchoronous cancer imaging, therapy, and sensing of drug delivery based on bi fluorescence resonance energy transfer." Nano Lett 7(10) 3056-3070

3 Nam, J., et al. (2013). "Surface engineering of inorganic nanoparticles for imaging and therapy."Advanced Drug Delivery Reviews 65(5) 622-648

Corresponding author Email address: Ataahb99@yahoo.com