Doxorubicin-loaded magnetic nanorods with temperature-dependent encapsulation behaviors

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Statement of Purpose: In order to confer multi functionalities to drug carriers such as site- specific targeting, diagnostic, release controllable properties, and low side effects. Gold-nickel multi-segmented nanorods were fabricated by electrodeposition and were endowed with multi-functionality for anti-cancer drug delivery. Furthermore the nanorod is expected to enhance tumor-specific contrasts in MRI.[1,2] In this study a gold segment was modified with doxorubicin or Pluronic F-127 to encapsulate more amounts of doxorubicin and a nickel segment was modified with folate to targeting for tumor cell. Pluronic F-127 was modified thiol groups using traut's reagent to be bound to gold segment and carboxyl group of folate was bound to nickel segment.

Methods: Nanorods were fabricated using an Al_2O_3 membrane as a template with 100nm of a pore diameter. A silver layer was sputted on one side of template played as the working electrode in a three-electrode configuration. A small segment of nickel was pre-deposited into the template so that the fully-deposited nanorod can be easily dissociated from the template. The segment of gold was first deposited, which was followed by a deposition of nickel segments A silver layer and the pre-deposition layer were carefully removed by 70vol% nitric acid and the template was dissolved by 3M potassium hydroxide[3].

Results: The length of each segment could be precisely adjusted controlled by modulating the applied coulombs, which was confirmed by SEM as shown in Figure1.

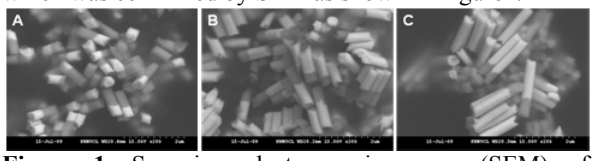

Figure 1. Scanning electron microscope (SEM) of nanorod according to different coulombs. (A) Au:Ni=500nm:500nm, (B) Au:Ni=1000nm:500nm, (C) Au:Ni=2000nm:500nm.

A gold segment was chemically modified with Pluronic F-127 to incorporate excessive amounts of doxorubicin on the nanorods and a nickel segment was decorated with folate to confer an active targeting moiety to the nanorod toward cancer cells. Thiol-modified doxorubicin was conjugated to the gold segment and a carboxyl group of folate was attached to nickel segment. In Figure 2, modification with two different molecules on the surface of each segments were confirmed by confocal scanning laser microscopy (CLSM).

In Pluronic F-127 modified rods, doxorubicin was reversibly encapsulated to the rods according to temperature change from 4°C to 37°C. However, in unmodified rods, doxorubicin was bound to rods irreversible (data not shown).

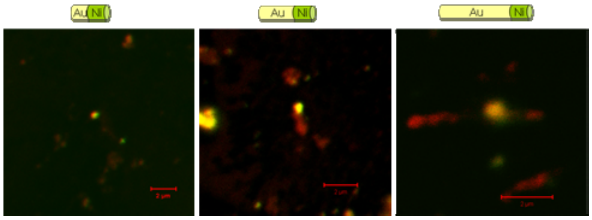

Figure 2. CLSM of the modified nanorods with multisegments. Red: doxorubicin encapsulated within Pluronic F-127 of gold segments, Yellow: carboxylate functionalized quantum dots (for visualization)

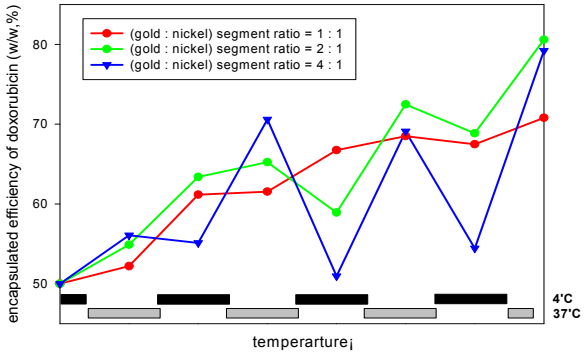

Figure 3. Reversible encapsulation of doxorubicin according to temperature changes

Conclusion: Doxorubicin was maximally incorpoated on the modified nanorods at 37◦C and a full extent of doxorubicin release was observed at 4◦C. Further studies are required to determine amounts of drug loading according to gold segment length, targeting effects of folate. Thus, nanorods should be employed nanorods as multifunctional anti-cancer drug carriers.

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