

# TRIGGERED RELEASE OF ANTICANCER DRUG AND THERANOSTICS FROM MICROSPHERICAL VEHICLES MADE BY COAXIAL ELECTROSPRAY

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**INTRODUCTION:** Current cancer treatment includes chemotherapy, radiotherapy, and surgery. But they have respective limitations. Developing novel theranostics, the nanodevices for cancer detection and treatment, is a major focus for nanotechnology in oncology<sup>[1]</sup>. Gold nanoparticles (AuNPs) are attractive for theranostics due to their unique properties, including surface enhanced Raman scattering (SERS)<sup>[2]</sup>, which can provide high-sensitivity signals for cancer detection. Composite NPs based on AuNP can be made as drug carriers but the amount of drug incorporated in this type of theranostics is limited. Furthermore, for some applications, timed release of theranostics and drug is needed. This study investigated the encapsulation and release of theranostics and drug in microspherical delivery vehicles.

**MATERIALS AND METHODS:** Folic acid-chitosan-capped gold NPs (Au@CS-FA) were synthesized<sup>[3]</sup>. Coaxial electrospay was investigated for making core-shell structured PLGA microspheres as delivery vehicles for Au@CS-FA NPs and DOX (anticancer drug). A coaxial electrospay nozzle was used: the outer capillary for a PLGA solution, the inner capillary for aqueous suspension/solution of Au@CS-FA and DOX. Theranostics and PLGA microspheres with or without theranostic and drug encapsulation were characterized. Timed release of theranostic and drug from microspheres was studied using immersion tests with or without laser irradiation. Laser irradiation was performed on the first day and every other day during the degradation period.

**RESULTS AND DISCUSSION:** Au@CS-FA NPs had a highly branched AuNP core and a CS-FA shell (Fig.1a). Highly branched AuNPs would enable generating strong SERS signals for cancer detection<sup>[4]</sup>; FA in CS-FA would provide tumor targeting ability for theranostics<sup>[5]</sup>. Core-shell structured PLGA microspheres were produced via coaxial electrospay and had a uniform size of 4 micron (Fig.1b and 1c). Au@CS-FA NPs were encapsulated in the core of microspheres. In coaxial electrospay, different polymer solution concentrations, flow rate ratios of polymer solution to aqueous solution, and Au@CS-FA concentrations were used to study their effects on microsphere formation and encapsulation efficiency of theranostics. Au@CS-FA NP concentration was the dominant factor. With an increasing concentration of theranostics in suspensions, microspheres formed became more distorted and more concomitant fine fibers formed

due to unstable electrostatic field caused by higher concentrations of theranostics. In in vitro release tests, laser irradiation did not show significant effect on microspheres without Au@CS-FA NPs. However, with laser irradiation, polymer shells of theranostics-containing microspheres were largely broken down due to heat generated by AuNP in theranostics (Fig.2a), which caused increased release of DOX from microspheres (Fig.2c). The Au@CS-FA NPs released from breakdown microspheres retained their original highly branched morphology (Fig.2b).

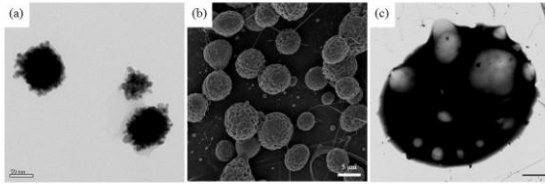


Fig. 1. (a) TEM image of as-synthesized Au@CS-FANPs; (b) SEM image of drug and Au@CS-FANP-encapsulated PLGA microspheres; (c) TEM image of a drug and Au@CS-FANP-encapsulated PLGA microsphere.

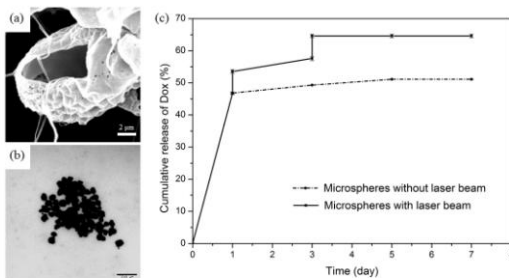


Fig. 2. (a) Drug and Au@CS-FANP-encapsulated PLGA microsphere after laser irradiation; (b) Au@CS-FANPs released from PLGA microspheres; (c) Release of drug from PLGA microspheres.

**CONCLUSION:** Core-shell structured polymer microspheres could be made via coaxial electrospay for drug and theranostics encapsulation and their timed in vitro or in vivo release later. This investigation showed triggered release of drug from theranostics-encapsulated microspheres, which was attributed to heat generation by the theranostics upon laser irradiation. Such delivery system and delivery mechanism can be useful in new anticancer therapy.

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