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# 学 位 論 文 内 容 の 要 旨

博士の専攻分野の名称　　博士（理学）　　氏名　OZBILGIN IREM NUR GAMZE

## 学 位 論 文 題 名

Synthesis and Characterization of Water-Soluble Silicon Quantum Dots for Photothermal Therapy and Fluorescence Imaging of Cancer Cells
（がん細胞の蛍光イメージングと光温熱治療を指向した水溶性シリコン量子ドットの合成と分析）

Quantum dots (QDs) are seen as a strong candidate as theranostic agents, which require to perform simultaneous imaging and therapy, due to their efficient interaction with incident excitations. Current QDs for theranostic applications have some challenges especially by means of toxicity. Silicon QDs (SiQDs), on the other hand, are intrinsically non-toxic thus they are promising candidate for bioapplications. So far, utilization of SiQDs were mostly focused on its photophysical properties. Whereas, controlling the nonradiative incidents in the structure remain scarce. In this work, we aim to investigate the use of SiQDs for theranostic applications. For this purpose, we conducted set of experiments to understand the mechanism of its photothermal response, its optical and photothermal properties in vitro.

Chapter 1 includes introductory information on target application area, theranostics and requirements for this field were addressed. Together with this, basic understanding to SiQDs were introduced Finally, current situation of quantum dots as fluorescence guided photothermal therapy and recent developments in SiQDs as theranostic agents were explained.

In Chapter 2, synthesis of stable, water soluble SiQDs that was used for these experiments was explained. Water-soluble SiQDs were prepared by thermal hydrosilylation of 10-undecenoic acid on their hydrogen-terminated surfaces, which are provided by thermal disproportionation of triethoxysilane hydrolyzed and subsequent hydrofluoric etching. SiQDs were characterized in terms of XRD, FTIR, TGA, zeta potential, UV-visible absorption, PL and PLQY. Prepared SiQDs were observed to have good surface properties also evidenced by enabling preparation of clear solutions up to 4 mg/mL. The 10-undecanoic acid functionalized SiQDs showed a long-term photostability when compared to commercial staining dye DAPI. Synthesis parameters were examined based on the PLQY and PL peak position values. It was seen that water soluble SiQDs with good PLQY could be obtained by at least 45 minutes of hydrosilylation and 160 °C. Findings from this chapter will contribute to the realization of stable water soluble SiQDs which is one of the main challenges for bioapplications.

In Chapter 3, photothermal effect of freestanding SiQDs were investigated. Hydrogen terminated SiQDs were prepared so as to be in three different sizes under Bohr exciton radius. Photothermal response was measured by irradiation of SiQDs with 532 nm Raman laser at three different powers. In Raman laser experiments, temperature of large sized QDs could be increased up to the temperatures as high as 275 °C. This behavior is correlated with increasing defect amount in the structure of larger particles. To explain defects structure of each SiQD, temperature dependent photoluminescence (PL) spectroscopy was conducted. 10-fold, 70-fold and 440-fold PL intensity decrease for small, medium and large particle size, respectively, was observed by increasing temperature. This behavior is due to the amount of nonradiative channels increased with increasing particle size. Calculated activation energies by Arrhenius plots show decreasing trend with increasing particle size which implies the presence of high density of defect states for large particles. Exciton-phonon interaction in the structure was examined by corresponding from temperature dependent broadening of peak linewidths were fitted by Bose-Einstein equation. Results show that exciton-phonon coupling increased with particle size which may lead photothermal heating. It is concluded that temperature of SiQDs can be strictly controlled by particle size and tuning the laser power. This behavior of SiQDs could be used for bioapplications where local heating in nanoscale is crucial.

In Chapter 4, photothermal performance of SiQD aqueous solutions were evaluated by calculating their photothermal conversion efficiencies. Photothermal conversion efficiency of SiQDs were seen to be size dependent, for instance, 25.6% and 37.1% for small and large particles, respectively, as confirmed by previous chapter. Obtained photothermal conversion efficiencies were comparable with counterpart materials for photothermal therapy applications. Furthermore, laser irradiation of HeLa cells with 50 and 400 μg/mL SiQDs were demonstrated and cell death depending on concentration was provided. It is concluded that water soluble SiQDs are potential candidates for theranostics with their good optical properties enabling imaging for more than 18 days and photothermal response having 25.6% photothermal conversion efficiency together with the direct evidence on cell death by laser irradiation.

In Chapter 5, interaction of water soluble SiQDs with live cells were investigated by using HeLa cell lines. Confocal microscopy analyses showed successful uptake of SiQDs by cell lines. Also, long term imaging studies show that SiQDs can be traced in HeLa cells for more than 18 days. Then, short term and long-term cytotoxic effects of water soluble SiQDs were investigated. No significant toxicity was observed for 1 day experiments up to 400 μg/mL. In the long term, cytotoxicity of SiQDs were at acceptable level for 14 days incubation of 50 μg/mL SiQD concentration. It was seen that prepared SiQDs have sufficient properties for bioimaging with low toxicity.

In Chapter 6, overall summary of this work was presented. This thesis conducted a systematic study on applicability of SiQDs as theranostic biomarkers. This thesis reveals the utilization of photonic and phononic properties of SiQDs, together with investigating their long-term stability in practical use. Deeper understanding on the photothermal heating mechanism was investigated. Furthermore, photothermal heating of aqueous SiQDs was performed and effectiveness of their photothermal response was demonstrated in vitro. With the findings of this thesis, merits for using SiQDs as theranostic agents were highlighted.