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Biodegradable black phosphorus-based nanospheres for *in vivo* photothermal cancer therapy

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Introduction: Photothermal therapy (PTT) based on the interaction between tissues and near infrared (NIR) radiation offers many advantages such as high efficiency and minimal invasiveness. However, currently used photothermal therapy agents have poor biodegradability and stay in the body for a long time accentuating the risk of deleterious effects [1]. As a new member of 2D materials, atomically thin black phosphorus (BP) with good photothermal performance and biocompatibility are potential therapeutic agents [2]. But, their actual clinical application still suffers from rapid renal excretion and degradation of the optical properties during circulation in the body. In this work, a kind of BP-based polymer nanospheres with high therapeutic efficacy and desirable biodegradation was prepared.

Materials and Methods: The BP quantum dots/ Poly (lactic-co-glycolic acid) nanospheres (BPQDs/PLGA NSs) were prepared by an oil-in-water emulsion solvent evaporation method. Briefly, BPQDs suspension was dispersed in the PLGA solution in DCM with a concentration of 10 mg/mL. After sonicating using a probe sonicator, the mixture was dispersed in PVA aqueous solution and sonicated for 5 min. The emulsion was stirred overnight at room temperature to evaporate the residual DCM. Then, washed twice with deionized water and re-suspended in the aqueous solution.

Results and Discussion: Fig. 1 reveals the uniform morphology of the BPQDs (3 nm) and the uniform spherical shape of BPQDs/PLGA NSs (~100 nm) with a smooth surface. BPQDs are incorporated into each nanosphere and most of them are located inside and protected by the PLGA shells. The hydrophobic PLGA not only isolates the interior BPQDs from oxygen and water to enhance the photothermal stability (Figure 2), but also control the degradation rate of the BPQDs (Figure 3). The *in vivo* experiments demonstrate that the BPQDs/PLGA possess excellent PTT efficiency and tumor targeting ability as evidenced by highly efficient tumor ablation under near infrared (NIR) laser illumination.

Conclusion: BPQDs/PLGA NSs with highly efficient photothermal performance are fabricated using PLGA loaded with 3 nm BPQDs by an oil-in-water emulsion solvent evaporation method. Owing to the strong hydrophobicity of PLGA, rapid degradation of the BPQDs is prevented so that the photothermal performance of the BPQDs/PLGA NSs in the physiological environment is improved significantly. Compared to other nanoagents, these BP-based nanospheres with the unique combination of biodegradability and biocompatibility are highly efficient PTT agents having immense clinical potential.

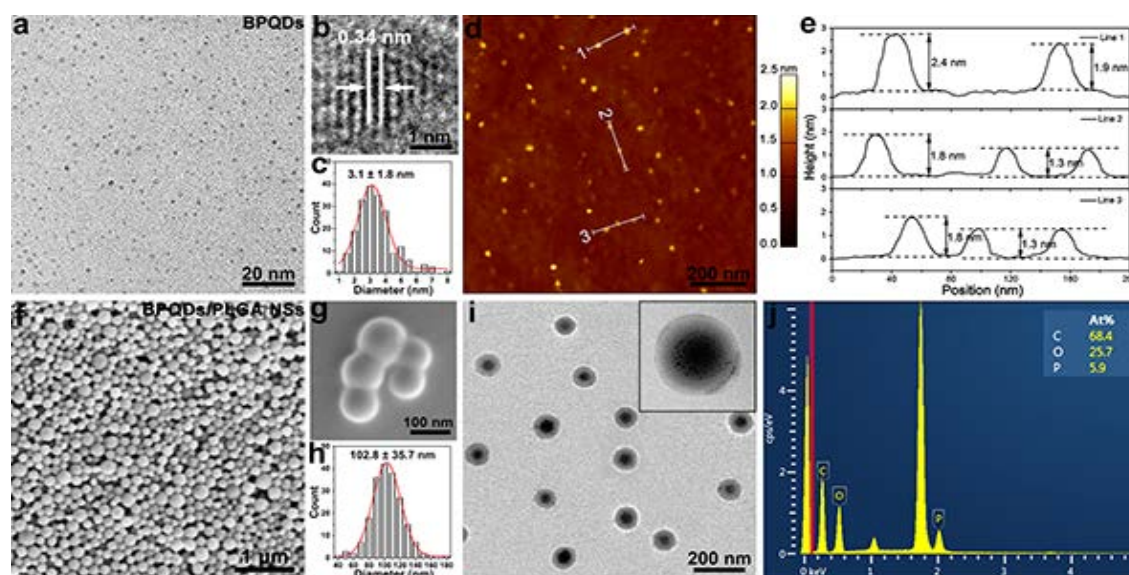


Figure 1. Morphology and characterizations of BPQDs and BPQDs/PLGA NSs.



Figure 2. Photographs of the BPQDs and BPQDs/PLGA NSs after storing in water for different periods of time.

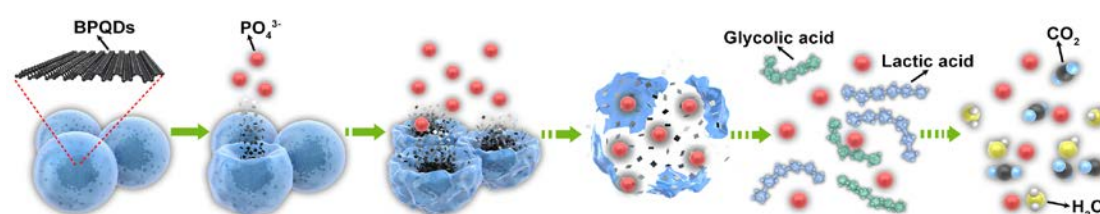


Figure 3. Schematic representation of the degradation process of the BPQDs/PLGA NSs in physiological environment.

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