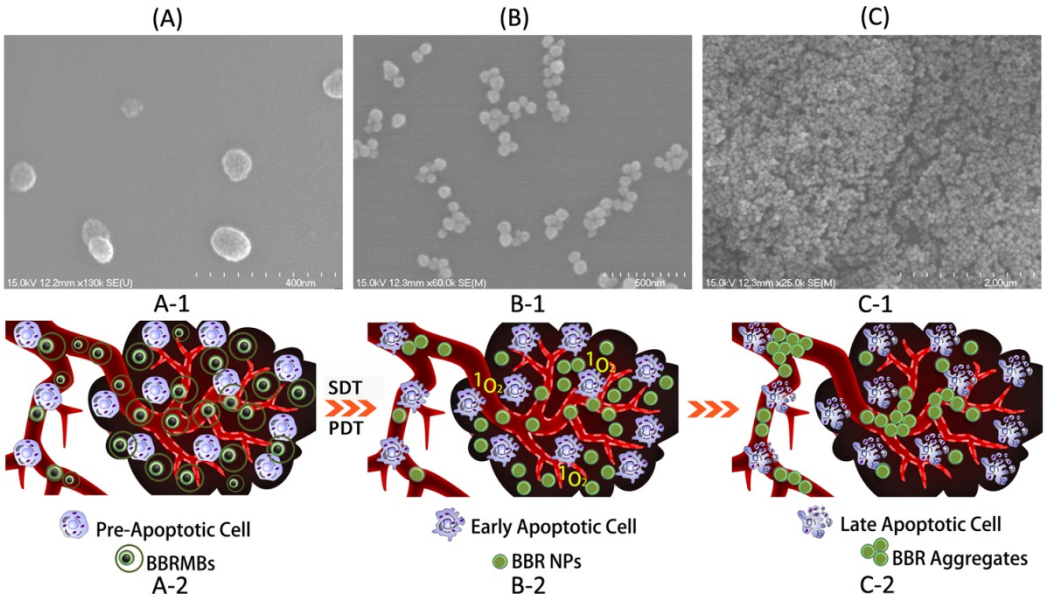
Tumor Vascular Embolization Therapy Triggered via BBR Nanoparticle Aggregation

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Abstract

Here we announce that berberine (BBR) nanostructure is a promising vascular embolization agent for tumour therapy. It has been reported that BBR contributes to tumour cells apoptosis by releasing reactive oxygen species (ROS) which triggers PI3K-AKT-mTOR signaling pathway. This triggering step succeeds with either focused laser beam (FLB) or focused ultrasound (FUS) under performances of photodynamic or sonodynamic therapy (PDT *or* SDT), respectively. Moreover, ultrasonic diagnosis shows that tumour vessels have been blocked after BBR-PDT or -SDT treatment *in vivo*. Further, we investigate what's behind and results point to self-assembly of BBR nanostructure, from nano- to micro- and macro-size. Finally, tumour vascular embolization occurs. Amphiphilic BBR chlorate tends to assemble into randomly nanostructures at room temperature in aqueous. However, spherical BBR nanostructures increase with growing temperature and BBR nanoparticles (BBRNPs) tends to monodisperse when we perform FLB or FUS. After treatment above, BBRNPs start to aggregate when temperature going down. Morphology studies from dynamic light scattering (DLS), scanning electron microscopy and optical microscopy show that BBRNPs aggregation is continuously taking place and finally ends up with macro-scale floccules. Though BBR is a commonly known photo- or sono-sensitizer for ROS-tumour therapy, rare is reported about what is going on after PDT or SDT therapy. Therefore, here we address BBRNPs aggregates as a promising vascular embolization which can assist PDT or SDT cancer therapy in preclinical studies.



Scheme 1. Progress schematic diagram of berberine nanoparticle induced tumour vascular embolization. (A) to (C) shows morphologies of berberine nanoparticles from monodispersed to oligo-aggregation and poly-aggregation. Group 1 shows BBR scanning electron microscopy images of BBR nanoparticles in different stages of self-assembly. Group 2 illustrates process of BBR nanoparticles self-assembly in tumour, following by early and late cell apoptosis. UTMD technonics

Keywords: *berberine nanoparticles, photodynamic therapy, sonodynamic therapy, tumour vascular embolization.*

Professional Biography (100-150 words)

Dr. Tingting Zheng obtained her PhD degree from Leiden University in Dec. 2014, and continue with postdoctoral studies at Wageningen University. She is currently associate professor at Peking University Shenzhen Hospital. She has published more than 25 papers in top journals and has been serving as an editor of *Open Chemistry* since 2015.



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