Analysis of Titanium Monocarbide Quantum Dots Synthesized via Cryo-Assisted Fragmentation as Potential Photothermal Agents for Cancer Hyperthermia

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ABSTRACT
Photothermal therapy (PTT) has gained significant attention in cancer treatment due to its ability to precisely ablate tumours using laser radiation, offering benefits such as minimal invasiveness, short treatment duration, and rapid recovery. PTT relies on photothermal agents that absorb near-infrared (NIR) light and convert it into heat, thereby inducing tumour cell destruction. While much progress has been made in developing photothermal agents, the development of efficient and biocompatible agents remains a critical challenge. Titanium monocarbide (TiC) is a refractory ceramic material known for its superior mechanical, thermal, and biocompatible properties, yet its potential as a photothermal agent for cancer treatment has not been explored. In this study, we demonstrate the remarkable light-to-heat conversion properties of TiC quantum dots, synthesized via a cryo-assisted fragmentation method. When an aqueous dispersion of TiC quantum dots was irradiated with NIR laser (808 nm, 1.5 W/cm^2), the temperature of the dispersion increased by approximately 65°C within 12 minutes, indicating the high efficiency of photothermal conversion. This rapid temperature rise, coupled with the biocompatibility and non-toxicity of TiC quantum dots, makes them a promising candidate for photothermal therapy, particularly in cancer hyperthermia applications.

KEYWORDS Photothermal therapy , Titanium carbide, photothermal conversion

INTRODUCTION

Photothermal therapy (PTT) using NIR laser radiation has attracted considerable attention due to its ability to precisely heat and ablate tumours, allowing for accurate temporal and spatial control over the heating process while minimizing side effects [1,2]. PTT depends on photothermal agents that absorb light (near-infrared (NIR)) and convert it into heat, which is concentrated within the tumour, resulting in the destruction of cancer cells. PTT offers various benefits, such as a straightforward procedure, short treatment duration, minimal invasiveness, and rapid recovery, making it an attractive cancer treatment option [3,4]. However, the development of highly efficient photothermal agents is crucial for optimizing the practical application of this technology. One of the essential requirements for effective tumour ablation through PTT is the high photothermal conversion efficiency of the agents [5]. Significant efforts have been dedicated to finding novel photo-absorbers with superior optical absorption and excellent photothermal performance. Another critical challenge is ensuring the biocompatibility of these PTT agents. For efficient renal clearance, the photothermal agents must be smaller than 10 nm, as particles above this size are unable to pass through the kidney's glomerular filtration system [6,7]. While metal nanoparticles, nanorods, and 2D materials like Bi_2Se_3 offer better biocompatibility and enhanced functionalization , their photothermal efficiency is limited by lower light-to-heat conversion ability.

Titanium monocarbide (TiC), with a metal-to-carbon ratio of 1:1, is a refractory ceramic material recognized for its high melting point, superior flexural strength, exceptional elastic modulus, low density, impressive Vickers hardness, excellent thermal conductivity, remarkable resistance to corrosion and oxidation in addition to showing outstanding biocompatibility [8,9]. These properties make TiC a versatile material for a broad range of applications, including high-stress components in aerospace, wear-resistant coatings, cutting tools, and biocompatible materials [10].It is also valued in electronics for its thermal conductivity and in chemical processing for its corrosion and oxidation resistance [11,12]. Additionally, TiC is used as a reinforcing phase in composites and as a hardening agent in superalloys, enhancing the mechanical properties like hardness, and tensile strength under extreme conditions[13]. TiC has a face-centred cubic (FCC) structure with a NaCl-type arrangement (space group Fm-3m), where Ti atoms occupy the cube corners and face centres, and C atoms are at the centre of each edge [14]. The material's unique properties arise from a combination of metallic, covalent, and ionic bonds present in it. Metallic bonds result from Ti-Ti interactions, covalent bonds form between Ti-d and C-2p orbitals, and ionic bonds stem from charge transfer between Ti and C [15]. The ultra-hardness of TiC is largely due to the hybridization of Ti-3d and C-2p electrons, as confirmed by first-principles calculations [16]. Recently, titanium carbide nanomaterials like TiC nanosheets, nanorods, quantum dots etc. have attracted considerable attention for their outstanding properties, making them well-suited for a wide range of applications, including energy conversion, catalysis, microwave absorption, electromagnetic shielding, and lightweight manufacturing [17]. However, the strong bonding patterns in TiC make the production of nanostructures from bulk TiC through scalable and generic top-down approaches, such as electrochemical, microwave and ultrasonic shearing processes, quite challenging [18]. These methods often involve multiple steps, require strict conditions, and utilize harsh chemicals, such as concentrated acids or high temperatures and pressures [19]. In this context, cryo-mediated fragmentation is a technique that can be employed to downsize bulk TiC powder. It involves repeatedly pre-treating the bulk TiC in liquid nitrogen before subjecting them to sonication in a liquid medium. The repeated low-temperature pretreatments induce thermal shocks that disrupt the intermolecular bonds in the bulk material, which when followed by sonication facilitates the formation of nanostructures [18]. Additionally, cryo-pretreatment only requires the use of pristine raw powders as precursors, without introducing any impurities or additional chemicals [19, 20]. As a result, the process produces high-quality QDs directly, without the need for surfactants or chemical contaminants, and avoids the complexity and harsh conditions of traditional methods.

To date, the exceptional thermal and mechanical properties of TiC have been extensively studied, but its optical characteristics and potential for photothermal behaviour remain largely unexplored. Though, MXene TiC quantum dots have been reported to exhibit photothermal conversion, TiC (Ti : C in the ratio 1:1)quantum dots are yet to be identified or demonstrated as a material suitable for photothermal transduction [1]. In this study, we highlight the remarkable light-to-heat conversion capabilities of titanium monocarbide (TiC) quantum dots, which were synthesized using a cryo-assisted fragmentation method. When an aqueous dispersion of the TiC quantum dots was exposed to NIR laser beam (with a wavelength of 808 nm and a power density $1W/cm^2$), the temperature of the dispersion increased by approximately 65°C within just 12 minutes. This rapid temperature rise demonstrates the efficiency of the photothermal effect in TiC quantum dots. This photothermal conversion capability combined with its biocompatibility and non-toxicity makes it a promising material in photothermal therapy especially for cancer hyperthermia applications.

MATERIALS AND METHODS

MATERIALS

Titanium carbide (TiC-325 mesh size, 98% purity, Aldrich) was used without any further purification in this study. Dialysis tubing having molecular weight cut–off 1kDa was supplied by Spectrum Laboratories, USA. The ultrapure water provided by Labostar TWF water purification system (18.2 MΩ.cm, Siemens Ultrapure Water Systems) was used for all experiments.

SYNTHESIS

The synthesis of Titanium carbide (TiC) quantum dots was carried out as follows: 500 mg of bulk TiC powder was initially heated to nearly 100°C and then transferred into a Teflon beaker. The beaker was then placed inside a thermo-insulated box, and 50 mL of liquid nitrogen was added. The box was sealed to prevent heat exchange with the surrounding environment. The rapid cooling induced by the liquid nitrogen caused a drastic temperature drop, leading to thermal shock. This heating-cooling cycle was repeated twenty times to further break down the TiC powder. Following the cryogenic treatment, the fine, dry TiC powder was transferred into a glass beaker and dispersed in 50 mL of deionized (DI) water. The resulting suspension was subjected to bath sonication for 5 minutes to ensure uniform dispersion of the particles. The dispersion was then centrifuged at 1000 rpm for 15 minutes, allowing for the separation of larger particles. The supernatant, which contained the nanostructured TiC particles, was carefully collected. The supernatant was dialyzed for 24 hours using a dialysis membrane with a molecular weight cutoff of 1 kDa, under continuous agitation by magnetic stirring. After the dialysis process, the deionized (DI) water containing the quantum dots outside the dialysis tubing was collected. To increase the concentration of the quantum dots in the aqueous medium, the collected solution was lyophilized. The lyophilized dispersion was then used for further characterizations.

CHARACTERISATION

The structural characterisation of bulk TiC powder were analyzed using X-ray diffraction with a PANalytical X'Pert powder diffractometer, operated at 45 kV and 40 mA, using Cu Kα radiation with a wavelength of 1.5406 Å. The sample morphology was examined using a Field Emission Scanning Electron Microscope (FESEM) (ZEISS Gemini 1 Sigma 300), operating at an accelerating voltage of 3 kV. The optical absorption spectrum of the powder was measured using a UV-diffuse reflectance spectrophotometer equipped with an integrating sphere (Ocean Insight FLAME Scientific-Grade spectrometer, Model: FLAME-UV-VIS-ES, Serial No. FLMT08457), with Barium sulfate ($BaSO_4$) as the reference material.

Photothermal Experiment

The photothermal studies of of the aqueous dispersion TiC quantum dots was evaluated through a detailed experimental procedure. In this setup, the aqueous dispersion was irradiated using NIR laser beam of wavelength 808 nm for a period of 12 minutes. The rise in temperature was measured using a K-type thermocouple, which was initially calibrated. This thermocouple was connected to a MAX6675 IC to record the temperature of the dispersion. A data acquisition device captured the data from the MAX6675 and transferred it through USB to a PC for analysis.

RESULTS AND DISCUSSION

Analysis of bulk TiC powder

Structural and morphological characterisation

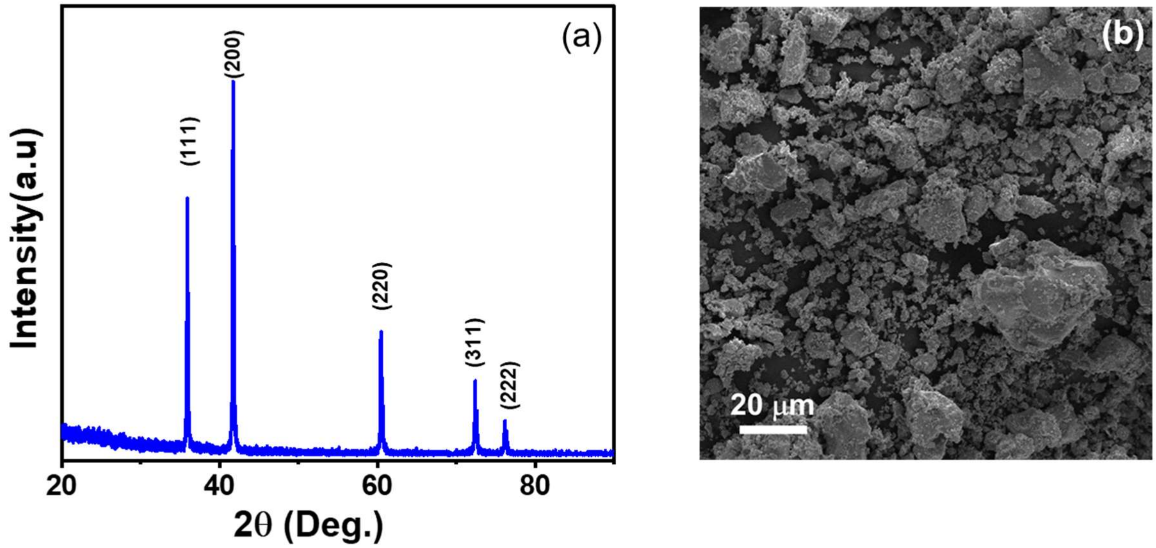

Fig. 1(a) XRD pattern **(b)** FESEM image of bulk TiC powder sample

The structural and phase purity of the bulk TiC powder was analyzed using X-ray diffraction. The XRD pattern shown in Fig. 1(a) confirmed the cubic crystalline structure of TiC, with five prominent peaks at 35.89°, 41.72°, 60.47°, 72.49°, and 76.1°, corresponding to the (111), (200), (220), (311), and (222) crystal planes, respectively, in accordance with ICDD No. 00-032-1383. The absence of impurity peaks further confirmed the purity of the TiC powder.

The morphology of the TiC powder was examined using FESEM. The SEM images in Fig. 1(b) show irregular, grainy particles with a size range spanning from a few hundred nanometers to several micrometers.

Analysis of TiC quantum dots

Microstructural studies

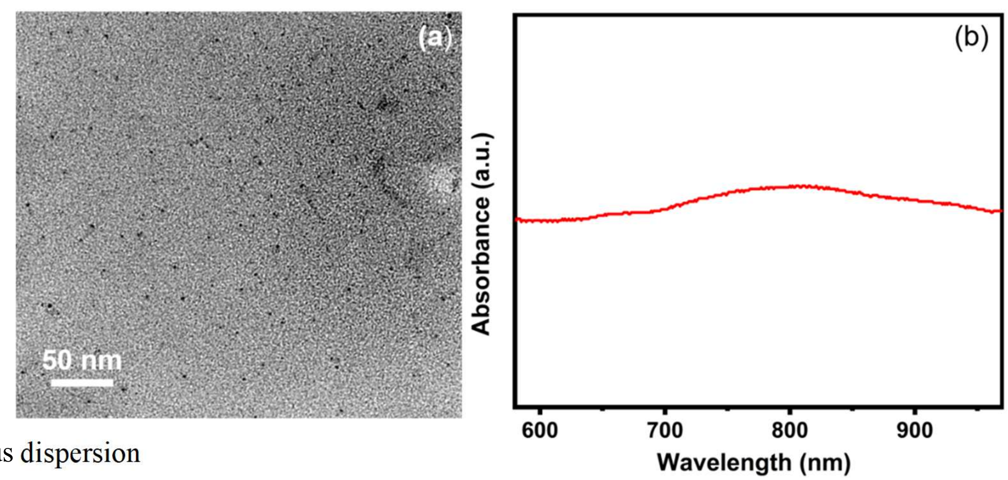

Fig. 2 (a) TEM image of aqueous dispersion of TiC quantum dots (b) UV-Vis spectra of the aqueous dispersion o TiC quantum dots

The formation of the TiC quantum dots in the aqueous dispersion was confirmed through transmission electron microscopy (TEM). The TEM images shown in Fig. 2(a) clearly demonstrate the successful formation of quantum dots with an average lateral size of less than 5 nm. This characterization confirms that the synthesis method successfully produced TiC quantum dots with sizes appropriate for renal clearance following photothermal therapy.

Optical absorption studies

The absorption properties of the TiC quantum dots were examined using UV-vis spectroscopy in Fig. 2(b), with DI water serving as the reference. The strong and broad absorption in the NIR region indicates the potential of TiC quantum dots as highly effective photothermal agents.

Photothermal studies

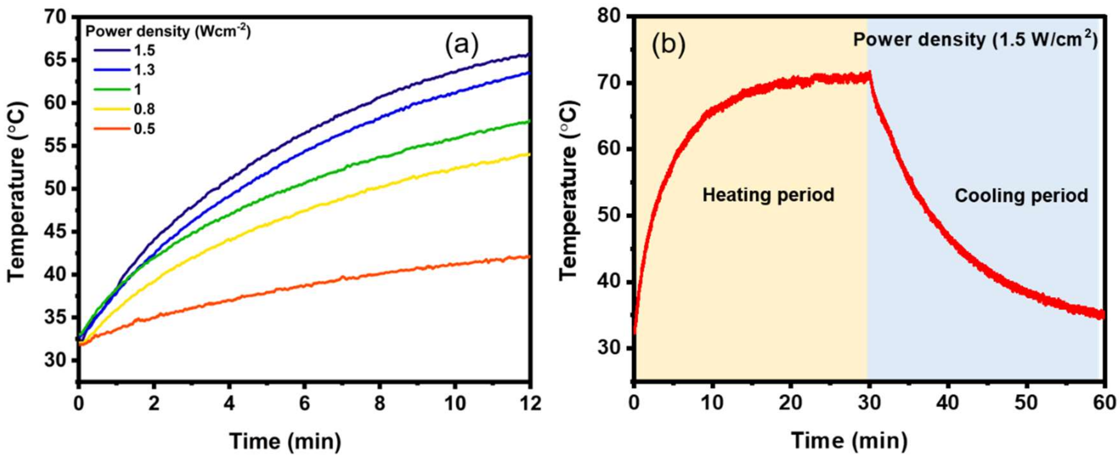

Fig. 3 (a) Photothermal heating curves of TiC quantum dots dispersed aqueous suspensions under the irradiation with 808 nm at varied power densities (b) Heating cooling curve at power density 1.5 Wcm$^{-2.}$

The photothermal studies of the sample are displayed in Fig. 3(a) and (b). TiC quantum dots were tested for their photothermal performance by exposing them to laser irradiation at 808 nm, at varying power densities (0.5, 0.75, 1.0, 1.25, and 1.5 W cm^{-2}). The objective was to evaluate the efficiency of TiC quantum dots in converting near-infrared (NIR) light into thermal energy. At a relatively low concentration of TiC (40 µg mL^{-1}), exposure to 808 nm laser beam at the highest power density of 1.5 W cm^{-2} led to a rapid and significant increase in the solution temperature, reaching approximately 65°C within just 12 minutes. This rapid heating response demonstrates the high photothermal conversion efficiency of the TiC quantum dots. The results indicate that TiC quantum dots are highly effective in utilizing laser light for localized heating, making them a promising candidate for applications such as photothermal therapy, where precise and controlled heating is crucial for targeting tumours or other specific tissue types without causing damage to surrounding healthy cells.

CONCLUSION

In summary, an aqueous dispersion of TiC quantum dots, exhibiting remarkable near-infrared (NIR) photothermal conversion capabilities, was successfully prepared through a cryo-assisted fragmentation technique. Transmission electron microscopy (TEM) analysis confirmed that the quantum dots have a size of less than 5 nm, which is ideal for renal clearance, ensuring their biocompatibility and minimizing potential toxicity. These TiC quantum dots demonstrated significant absorption in the NIR region, a key characteristic for efficient photothermal conversion. Upon exposure to NIR laser irradiation (808 nm, 1W/cm^2), the temperature of the aqueous dispersion increased by approximately 65°C within just 12 minutes, validating their high efficiency as photothermal agents. This study not only highlights the potential of TiC quantum dots as a photothermal agent but also underscores their suitability for practical application in cancer treatment, given their small size, excellent photothermal response, and biocompatibility.

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