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Development of Chemically Synthesized Spherical Plasmonic LaB₆

Nanoparticles for Biomedical Applications

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Abstract

LaB₆ is a unique plasmonic material, for which the localized surface plasmon resonance (LSPR) absorption band intrinsically lies in the near infrared (NIR) region. In this work, we synthesized spherical LaB₆ nanoparticles with a tunable size within 50–200 nm. The optical properties of these LaB₆ nanospheres were found to be sensitive to the thickness of surface oxide layer that was formed during the synthesis, purification and dispersion processes. In order to enhance the stability of LaB₆ nanoparticles in aqueous environment, LaB₆@SiO₂ with a core-shell structure was successfully prepared. Both LaB₆ and LaB₆@SiO₂ demonstrated low cytotoxity in biomedical tests when their concentrations were limited to 0.2 mg mL⁻¹. The in vitro photothermal therapy experiment showed that 4T1 cancer cells were eventually apoptotic after being exposed to a 980 nm laser for 5 min at a considerably low power density of 0. 82 W cm⁻² and a low dose of 0.1 mg mL⁻¹ for LaB₆@SiO₂. The results suggest that these LaB₆ nanospheres are viable photothermal agents for biomedical applications.

Keywords:

LaB₆, core-shell LaB₆@SiO₂, plasmonic NIR absorption, cytotocity, photothermal therapy.

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1. Introduction:

 LaB_6 is a plasmonic material that can absorb the near infrared (NIR) light around 1000 nm while with visible transparency. It is thus used as a smart window material for solar control [1-4]. Compared with other plasmonic materials, LaB₆ is unique because its light absorption band due to the localized surface plasma resonance (LSPR) effect locates intrinsically in the NIR region as a result of its suitable free carrier density of 1.45×10^{22} cm⁻³ [5], a value lower than those of elemental metals but higher than those of doped seminconductors. Due to this intrinsic free carrier density, the peak position of plasmonic NIR absorption for LaB₆ is not as strongly dependent on its nanoparticle geometry as that for other plasmonic materials [3,4]. It is well known that the NIR absorption of Au or Ag is highly sensitive to their nanoparticle geometry including size and shape [6-9]. Only some special shapes such as nanorods with large aspect ratios (length divided by width) can tune the LSPR absorption of Au or Ag to the NIR region [6,7]. On the other hand, the NIR absorption wavelengths of conducting oxides such as indium tin oxides (ITO) and antimony tin oxide (ATO) are commonly beyond 1000 nm. Only WO_{3-x}, Cs_xWO₃, and chalcogenides Cu_{2-x}S, Cu_{2-x}Se are reported to exhibit NIR absorption around 1000 nm, which is highly dependent on doping levels as well as nanoparticle shape and size [10]. Compared with semiconductor plasmonic materials, LaB₆ exhibits much high extinction coefficient (a maximum of 12142 M⁻¹ cm⁻¹ at 975 nm), which is an order of magnitude larger than that of ITO (1065 $M^{-1} cm^{-1}$) [2].

In recent years, materials with the plasmonic NIR absorption property attracted considerable attentions because they can be used in various applications including

surface-enhanced molecular spectroscopy, cancer cell imaging and photothermal cancer therapy [8-13]. For example, Au nanorods with large aspect ratios were used as agents for both molecular imaging and photothermal cancer therapy by A. EI-Sayed et al. [8]. WO_{3-x}, Cu_{2-x}S and Cu_{2-x}Se nanocrystals were also successfully used for similar purposes [11-13]. Though LaB₆ is an intrinsic and intense plasmonic NIR absorber, it is not yet well studied for the above-mentioned biomedical applications. One possible reason is the lack of convenient, reliable and well-established synthesis methods for LaB₆ nanoparticles with tunable sizes and shapes [14]. As LaB₆ can not be prepared through wet processes in aqueous solutions like other plasmonic materials, its synthesis is usually via solid-state processes that are commonly at high temperatures beyond 1000 °C [14,15]. The high synthesis temperature resulted in particles of micron or submicron scales [16]. The trials to prepare LaB₆ nanoparticles at lower temperatures are still not good at tuning the size and shape easily [17-19]. As a result, the common practice to obtain LaB₆ nanoparticles is via the breakdown of micron particles by media agitation milling [1-4,20]. The physical cleavage of hard LaB₆ particles resulted in irregular particle shapes and inevitable contaminations by the bead material $ZrO_2[4,20]$. Another reason is the uncertainty of biomedical safety for LaB_6 . Unlike Au nanoparticles with well confirmed biocompatibility [21], the cytotoxity of LaB₆ nanoparticles is not well studied. Due to these possible reasons, up till now, only Lai et al. [22] reported the use of bead milling derived and then C-SiO₂ coated LaB₆ nanoparticles for fluorescence imaging and NIR photothermal therapy of HeLa cancer cells. Their research demonstrated promising results regarding the

cytotocity and photothermal therapy effects of LaB₆.

In our previous study [23], we found that nearly spherical LaB₆ nanoparticles can be successfully prepared through the reaction between La(OH)₃ or La₂O₃ and lithium borohydride LiBH₄ at a low temperature of 352 °C. Considering that the optical properties for chemically prepared spherical LaB₆ nanoparticles are not yet well documented [24], it is thus interesting for us to study its NIR absorption and resulting photothermal properties in order to explore its viability in biomedical applications. Based on this preparation method, we investigated approaches to adjusting the size and surface condition of LaB₆ nanoparticles, as well as to making LaB₆ dispersions in ethanol and water to improve its compatibility with biomedical environments. This research is expected to explore the viability of using the chemically synthesized LaB₆ nanoparticles as the photothermal agent in biomedical applications, and find out the key factors influencing their NIR absorption performance and photothermal effects in these applications.

2. Experimental details

2.1 Synthesis of LaB₆ nanoparticles

The chemicals and raw materials used in this study were LiBH₄ (Acros, 97%), La(OH)₃ (Aladdin, 99.9%), La₂O₃(Macklin, 99.99%, 50 nm), polyvinylpyrrolidone (PVP) (Sinopharm., GR) and tetraethoxysilane (TEOS) (Sinopharm., GR). Commercial LaB₆ powder (Alfa Aesar, 99.5%, around 2μ m) was used as a reference.

The typical synthesis process of LaB_6 nanoparticles was as follows: a stoichiometric mixture of $La(OH)_3+6LiBH_4$ or $La_2O_3+12LiBH_4$ was put in a 100 mL

stainless steel vessel and ball milled in a planetary mill at 400 rpm for several hours. The ball milled mixture was then transferred to a stainless steel reactor in a glove box filled with high purity argon gas. The reactor was first evacuated and then heated from room temperature to 450 °C at a rate of 2 °C min⁻¹ and held at 450 °C for 1 h. After the synthesis reaction, the mixture was taken out of the reactor and washed by a dilute HCl solution and rinsed by deionized water for several times. The final product of LaB₆ nanoparticles was obtained by drying at 60 °C in a vacuum oven.

2.2 Preparation of LaB_6 dispersions and SiO_2 encapsulation

The dispersions of LaB₆ nanoparticles were prepared by milling the synthesized LaB₆ nanopowder with 0.3 mm yttrium-stablized ZrO_2 beads at 400 rpm. in dehydrated ethanol or deionized water with the addition of PVP as the dispersant (LaB₆:PVP=5:1 in weight).

For the preparation of LaB₆@SiO₂, LaB₆ suspension in ethanol with the PVP dispersant was first prepared by ultrasonically dispersing 50 mg LaB₆ in 40 mL ethanol with 10 mg PVP for 4 h. Then the LaB₆ dispersion was added with 2.5 mL 25% NH₃·H₂O and 100 μ L TEOS successively and stirred magnetically for 2 h at room temperature. The SiO₂ encapsulated LaB₆ was rinsed by ethanol for three times and then stored in ethanol or dried in the vacuum oven at 60 °C for use.

2.3 Characterization of LaB₆ and LaB₆@SiO₂ nanoparticles and dispersions

The characterization of LaB_6 nanoparticles and dispersions was performed using transmission electron microscopy TEM (HT-7700, Hitachi, Japan or CM200UT, Philips, the Netherland), and high resolution transmission electron microscopy

HRTEM (Tecnai G2 F30, FEI, USA) equipped with an energy dispersive spectroscope. The oxygen content in LaB₆ nanopowder was analyzed by the TC500 oxygen-nitrogen analyzer (Leco, USA). The size distribution of LaB₆ nanoparticles in dispersions was analyzed by Nanotrac Wave (Microtrac Inc., USA). The UV-Vis-NIR absorption of LaB₆ dispersions was measured on UV-3600 spectrophotometer (Shimadzu, Japan) using glass cells. The linear sweep voltammetry measurements for LaB₆ electrodes were carried out on a CHI1140C electrochemical workstation (Shanghai Chenhua, China). The electrodes of LaB₆ powder were prepared by hand milling a mixture of LaB₆ powder with carbon black and polytetrafluoroethylene (PTFE) at a weight ratio of 8:1:1 and then pasting on a carbon or nickel sheet. The counter electrode was a Pt plate electrode and the reference electrode was a Hg/HgO electrode in the electrolyte of 30 wt% KOH.

2.4 Photothermal and biomedical experiments

The photothermal heating experiments were carried out by irradiating 2 mL $LaB_6@SiO_2$ ethanol dispersion in wells (1.56 cm in diameter) of a cell culture plate using a fiber-coupled laser with a wavelength of 980 nm and a focus spot of 1.6 cm in diameter at a distance of 2 cm. The temperature of the dispersion was measured using a FLIR E40 infrared thermometer.

The in vitro experiments were performed by using $LaB_6@SiO_2$ as a photothermal agent to destroy 4T1 cancer cells. At first, $LaB_6@SiO_2$ suspensions in superpure water with a concentration of 1.0 mg mL⁻¹ was prepared and dispersed ultrasonically, and then the dispersion was diluted by the culture fluid. The cytotoxicity of LaB_6 and

LaB₆@SiO₂ was tested by incubating 4T1 tumor cells in the culture medium blended with different LaB₆ concentrations for 24 and 48 hours at 37 °C under 5% CO₂ atmosphere and then the cell viability was tested by the standard MTT assay. In the photothermal therapy tests, tumor cells were first incubated in the fluid blended with LaB₆@SiO₂ dispersions for 4 h, and then were irradiated by the 980 nm infrared light under different power densities and durations of time. The cells after light exposure were cultured for another 1 h and then stained by two dyes (Caicein-AM and PI). The cell viability was then monitored under an inverted fluorescence microscope.

Considering that only superpure water can be used to prepare dispersions in the above mentioned biomedical experiments, the freshly prepared LaB_6 or $LaB_6@SiO_2$ samples were dispersed in superpure water right before the biomedical tests to minimize possible surface oxidation.

3. Results and Discussion

3.1 Synthesis and characterization of LaB₆ nanoparticles

Based on our previous study [23], the synthesis reaction of LaB_6 is as follows:

$$La(OH)_3 + 6LiBH_4 = LaB_6 + 3Li_2O + 13.5H_2$$
(1)

or
$$La_2O_3 + 12LiBH_4 = 2LaB_6 + 3Li_2O + 6LiH + 21H_2$$
 (2)

The formation of LaB_6 occurs at a low temperature of 352 °C, accompanied with a characteristic endothermic effect, as shown in ref. [23]. Pure spherical LaB_6 nanoparticles could be obtained through washing off the Li-containing byproducts.

As the LSPR effect is dependent on the size of nanoparticles, it is thus important to synthesize LaB_6 nanoparticles with desirable and tunable sizes. The synthesis

conditions were thus varied to prepare LaB₆ nanoparticles with varying sizes. Due to a fast kinetics for the present synthesis approach, the nucleation-growth process occurred fast within a narrow temperature range. It was found that two synthesis conditions could effectively change the size of resulting LaB₆ nanoparticles. First, the average size of LaB₆ particles was found to reduce from 200 nm to 100 nm if the ball milling time of the reactant mixtures of La(OH)₃+6LiBH₄ varied from 1 h to 6 h. However, the increase in ball milling time from 6 h to 24 h did not significantly reduce LaB₆ size further. Then, it was found that the use of nanosized La₂O₃ of 50 nm as the precursor produced LaB₆ nanoparticles within 50-100 nm. The SEM and HRTEM images shown in Fig. 1 demonstrate the resulting LaB₆ nanoparticles. Larger spherical nanoparticles around 150 nm shown in Fig. 1(a) were obtained by using La(OH)₃ as the precursor and ball milling for 2 h. Smaller nanoparticles less than 100 nm was synthesized by using nanometric La₂O₃ and ball milling for 16 h. As shown by HRTEM images in Fig. 1(c)-(f), the LaB₆ nanoparticles produced at such a low synthesis temperature still revealed good crystallinity. Also most of these LaB₆ nanospheres seemed to be single crystals, as illustrated by the SAED pattern in Fig.1(f).

The preparation of LaB_6 dispersions in suitable media is another prerequisite to achieve good plasmonic performance. In this study, LaB_6 dispersions in ethanol or water was prepared by bead milling a mixture of LaB_6 nanopowder and polymer dispersant PVP at a low speed of 400 rpm. During the dispersion process, it was expected to separate the aggregated nanoparticles from each other rather than to break them down. As shown in Fig. 2, a homogeneous dispersion of LaB_6 in ethanol could be obtained after 4 h bead milling, in which the size distribution showed a peak at 100 nm. The TEM image in Fig. 2 suggests that LaB_6 nanoparticles could be individually and homogeneously dispersed in the solvent. In comparison, a bead milling time of 1 h seemed to be not yet enough to separate agglomerated or even coagulated nanoparticles, resulting in a size distribution peak at 230 nm.

Fig. 3 reveals the NIR absorption properties of LaB₆ dispersions in ethanol and water respectively. The LaB₆ dispersion in ethanol demonstrated strong NIR absorption within a broad band ranging from 600 nm to 1600 nm with a peak at 1032 nm. The absorption was intensified with the increases in LaB₆ concentration. Even low LaB₆ concentrations below 0.1 mg mL⁻¹ could induce strong NIR absorption. However, LaB₆ dispersed in water demonstrated very weak NIR absorption instead. The significant decrease in NIR absorption performance was ascribed to the severe oxidation of LaB₆ nanoparticles in water during bead milling because the initial black LaB₆ powder turned into white after milling. A further study indicated that the surface oxidation layer of LaB₆ nanoparticles exerted a dominant influence on the optical property when the size was below 100 nm. As shown in Fig.4, a considerable decrease in absorption intensity can be observed when the thickness of surface oxide layer increased from around 1 nm to about 2-3 nm. The oxygen content analysis revealed that the total oxygen content in the sample increased from 2.5% to 8.7% correspondingly. The thick oxide layer also induced a red-shift of peak from 1032 nm to 1132 nm. A similar behavior was observed by Kim et al. [25] during the NIR

absorption study of h-Cs:WO₃ nanocrystals. They found that the intensity of LSPR absorption for h-Cs:WO₃ diminished greatly due to its surface oxidation. A model of a fully depletion shell and a shinking core with unchanged carrier density was used to explain the change of NIR absorption. In this model, the moderate peak shift was due to the change of dielectric environment induced by the oxide shell, rather than due to the change of carrier density. This model may also applicable to explain the effects of LaB₆ surface oxidation on its NIR absorption. But a more detailed study is needed to confirm its validity.

Though bulk LaB₆ shows considerable chemical stability towards air and water, nanometric LaB₆ seems to be not stable enough in these oxidizing environments due to the enhanced surface activity of nanoparticles. As shown in Fig.5, a negative shift of -400 mV can be seen for the anodic oxidation peak of LaB₆ in 30 wt% KOH when the particle size was reduced from 2 μ m to 200 nm. As a result, the synthesized LaB₆ nanoparticles were subject to surface oxidation during the synthesis, purification, dispersion and storage in oxidizing environments such as air and water. Moreover, the high-speed collision and shear during bead milling might induce localized high temperature on nanoparticle surface [3], which is supposed to exacerbate the surface oxidation of LaB₆ in water. Consequently, unprotected bare LaB₆ nanoparticles would be susceptible to severe surface oxidation during bead milling in water, resulting in reduced optical properties. Considering these facts, a size of around 100 nm for the synthesized LaB₆ nanoparticles was thus preferred in this study because smaller size below 100 nm would be more vulnerable to surface oxidation.

3.2 Synthesis and characterization of LaB6@SiO₂ and its dispersions

To improve the stability of LaB_6 nanoparticles in aqueous environments that are required in biological applications, the encapsulation of LaB_6 nanoparticles by SiO₂ was thus performed considering that SiO₂ is not only with high biocompatibility but also transparent for visible and NIR light [21, 26]. Fig. 6 shows the HRTEM image and EDS elemental mappings of the prepared $LaB_6@SiO_2$ nanoparticles. The LaB_6 nanosphere, as shown by the HRTEM image in Fig. 6, was evenly coated by a thin layer of SiO₂. The EDS analysis clearly confirmed that the LaB_6 core was completely encapsulated by an amorphous SiO₂ shell of about 15 nm.

Fig. 7(a) shows the NIR absorption properties of $LaB_6@SiO_2$ dispersed in ethanol and water respectively. It can be seen that $LaB_6@SiO_2$ dispersed in water demonstrated much enhanced NIR absorption compared with bare LaB_6 nanoparticles shown in Fig. 3, indicating that the SiO₂ shell could effectively protect LaB_6 from excessive oxidation. However, the optical property of $LaB_6@SiO_2$ in water was still inferior to that in ethanol. This result suggests that the SiO₂ encapsulation could only provide partial protection for LaB_6 in water due to a porous structure of the deposited SiO₂ shell [27]. Therefore, a long-term storage of $LaB_6@SiO_2$ in water should be avoided. Moreover, the absorption peak of $LaB_6@SiO_2$ in ethanol lies at 1054 nm, which is slightly red-shifted as compared with 1032 nm of the bare LaB_6 . The absorption intensity of $LaB_6@SiO_2$ also decreased as compared with that of bare LaB_6 under the same concentration, as shown by Fig. 7(b). Lai et al. [22] reported similar effects of SiO₂ encapsulation on the LaB₆ NIR absorption performance. This is mainly because the presence of SiO_2 shell resulted in the change of dielectric environment for the plasmonic core and then influenced the optical properties [28].

Fig.8 demonstrates the photothermal transition in dispersions as functions of the LaB₆@SiO₂ concentration and laser power density. Under the irradiation of the laser at a wavelength of 980 nm, significant temperature rises resulting from the photothermal effect can be observed. The photothermal effect was enhanced with the increase in LaB₆@SiO₂ concentration and laser power output. Only a low LaB₆@SiO₂ concentration of 0.1 mg mL⁻¹ in the dispersion could result in significant temperature rises. Consequently, the temperature reached 47.8 °C under a power density of 0.24 W cm⁻², and rose up to 65.1 °C under 0.43 W cm⁻² after 3 min irradiation. These results indicate that LaB₆@SiO₂ was an efficient plasmonic photothermal material.

3.3 Cytotoxicity tests of LaB₆ and LaB6@SiO₂ and the use for photothermal therapy

The cytotocity of LaB₆ and LaB₆@SiO₂ nanoparticles was examined by the standard MTT assay. As shown in Fig. 9, both LaB₆ and LaB₆@SiO₂ nanoparticles seemed to be nontoxic during 24 h and 48 h cell culture if their concentrations were not high than 0.2 mg mL⁻¹. Though bare LaB₆ nanoparticles also seemed to be with low cytotoxicity, the LaB₆@SiO₂ sample is expected to be more biosafe due to the protection of SiO₂ shell.

After the cytotoxity tests, $LaB_6@SiO_2$ dispersed supersonically in superpure water was tested as the photothermal agents to destroy 4T1 cancer cells. Fig. 10 illustrates the results after laser irradiation at 980 nm under varied $LaB_6@SiO_2$ concentrations and irradiation time. It can be seen that most of cancer cells became apoptotic after 5 min exposure to the NIR light at a power density of 0.82 W cm⁻² when the concentration of $LaB_6@SiO_2$ exceeded 80 µg mL⁻¹. In comparison, cells were intact under the same irradiation without addition of the photothermal agents. In another experiment, the irradiation time of 5 min was found to be needed to eventually kill cancer cells under the laser power density of 0.82 W cm⁻² using $LaB_6@SiO_2$ of 100 µg mL⁻¹, as illustrated in Fig. 11. These results suggest that $LaB_6@SiO_2$ nanoparticles could be used as efficient photothermal agents for cancer therapy.

The above results demonstrated that LaB_6 is a promising plasmonic material for the biomedical applications. Being one of the very few materials that possess intrinsic plasmonic NIR absorption around 1000 nm, LaB₆ demonstrated broad and strong NIR absorption and remarkable photothermal effect. Only a low concentration of 0.1 mg mL^{-1} for LaB₆@SiO₂ and low laser power density below 1 W cm⁻² could realize the eventual destroy of cancer cells. Its broad absorption band overpasses both the first (700-950 nm) and the second (1000-1350 nm) biological transparency window. The NIR absorption of LaB₆ is less sensitive to its nanostructure geometry than that of Au or Ag. Also LaB_6 is much cheaper than the precious metal counterparts. The noncytotoxity of LaB₆ under a concentration of 0.2 mg mL⁻¹ has been demonstrated in this study, which is similar to the results shown by Lai et al. [22]. Moreover, our photothermal tests under milder conditions of laser irradiation exhibited similar therapy effects as theirs, suggesting that our chemically synthesized LaB₆@SiO₂ nanospheres were more effective photothermal agents due to their homogeneous morphology. The SiO₂ shell also facilitates further surface ligand decorations for multiple purposes such as tracing, targeting and imaging of cancer cells. LaB_6 , as a plasmonic material with intrinsic NIR aborption has been proven in this study to be a promising photothermal material in biomedical applications.

4. Conclusions

In this research, nearly spherical LaB₆ nanoparticles were synthesized with a tunable size within 50–200 nm. The LaB₆ dispersion in ethanol demonstrated good NIR absorption property with a peak centered at 1032 nm. However, the thickness of surface oxide layer on LaB₆ nanoparticles had a significant impact on their LSPR effect. LaB₆@SiO₂ core-shell structure was successfully prepared to improve its stability in the aqueous environment and to achieve better biocompatibility. The cytotoxity test revealed that LaB₆ or LaB₆@SiO₂ were nontoxic when their concentrations were limited to 0.2 mg mL⁻¹. The in vitro photothermal therapy experiment showed that 4T1 cancer cells were eventually apoptotic after being illuminated by a 980 nm laser for 5 min at a considerably low power density of 0.82 W cm⁻² and a low dose of 0.1 mg mL⁻¹ for LaB₆@SiO₂. The results suggest that LaB₆ or LaB₆@SiO₂ nanoparticles are promising plasmonic photothermal agents for biomedical applications.

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Figure captions:

- Fig. 1 SEM and HRTEM images of the synthesized LaB₆ nanoparticles.
 - a. SEM image of LaB₆ prepared by ball milling La(OH)₃+6LiBH₄ mixture for

2 h;

 b. SEM image of LaB₆ prepared by ball milling La₂O₃+12LiBH₄ mixture for 16 h;

c-f: HRTEM images and SAED pattern of LaB₆ nanoparticles.

- Fig. 2 Particle size distribution and TEM image of LaB₆ dispersion in ethanol
 - a: particle size distribution after bead milling of aggregated LaB_6 nanopowder with 0.3 mm ZrO₂ beads for 1h or 4h;

b: TEM image of dispersed LaB₆ nanoparticles.

- Fig. 3 NIR absorption properties of LaB_6 dispersed in ethanol and water prepared through bead milling for 3h.
- Fig. 4 The effect of surface oxide layer on NIR absorption performance of LaB_6 dispersions in ethanol.
 - a: NIR absorption spectra of LaB₆ nanoparticles dispersed in ethanol;
 - b, c: HRTEM images of LaB_6 nanoparticles with a low oxygen content of 2.5%;
 - d, e: HRTEM mages of LaB_6 nanoparticles with a high oxygen content of 8.7%.
- Fig. 5 Comparison of the linear potential sweep voltammograms between the synthesized LaB_6 nanoparticles with the commercial micron LaB_6 powder.

Fig. 6 HRTEM image and EDS analysis result of LaB₆@SiO₂ nanoparticles

- Fig. 7 (a) NIR absorption properties of $LaB_6@SiO_2$ dispersed in ethanol and water;
 - (b) Comparison of NIR absorption properties for LaB₆ and LaB₆@SiO₂dispersed in ethanol.
- Fig. 8 Photothermal transition experiment results of $LaB_6@SiO_2$ dispersion in ethanol.

a: under different LaB $_6@SiO_2$ concentrations

b: under different laser power output.

- Fig. 9 Cell viability under different LaB₆ and LaB₆@SiO₂ concentrations a: after 24 h; b: after 48 h.
- Fig. 10 Cell viability after irradiation of 980 nm laser under 0.82 W cm⁻² for 5 min using different concentrations of LaB₆@SiO₂.
 a-d: LaB₆@SiO₂; e: control

a: 20 mg mL⁻¹; b: 40 mg mL⁻¹; c: 80 mg mL⁻¹; d: 120 mg mL⁻¹.

Fig. 11 Cell viability after irradiation of 980 nm laser under 0.82 W cm⁻² for different durations using 0.1 mg mL⁻¹ LaB₆@SiO₂. a-e: LaB₆@SiO₂; f: control

a: 1 min; b: 2 min; c: 3 min; d: 4 min; e: 5 min



Fig. 1 SEM and HRTEM images of the synthesized LaB_6 nanoparticles. a. SEM image of LaB_6 prepared by ball milling $La(OH)_3+6LiBH_4$ mixture for 2 h; b. SEM image of LaB_6 prepared by ball milling $La_2O_3+12LiBH_4$ mixture for 16 h; c-f: HRTEM images and SAED pattern of LaB_6 nanoparticles.



- Fig. 2 Particle size distribution and TEM image of LaB₆ dispersion in ethanol a: particle size distribution after bead milling of aggregated LaB₆ nanopowder
- with 0.3 mm ZrO₂ beads for 1h or 4h; b: TEM image of dispersed LaB₆ nanoparticles.



Fig. 3 NIR absorption properties of LaB_6 dispersed in ethanol and water prepared through bead milling for 3h.



Fig. 4 The effect of surface oxide layer on NIR absorption performance of LaB_6 dispersions in ethanol.

a: NIR absorption spectra of LaB₆ nanoparticles dispersed in ethanol;

b, c: HRTEM images of LaB₆ nanoparticles with a low oxygen content of 2.5%;

d, e: HRTEM mages of LaB_6 nanoparticles with a high oxygen content of 8.7%.



Fig. 5 Comparison of the linear potential sweep voltammograms between the synthesized LaB_6 nanoparticles and the commercial micron LaB_6 powder.



Fig. 6 HRTEM image and EDS analysis result of $LaB_6@SiO_2$ nanoparticles



Fig. 7 (a) NIR absorption properties of $LaB_6@SiO_2$ dispersed in ethanol and water.



Fig. 7 (b) Comparison of NIR absorption properties for LaB_6 and $LaB_6@SiO_2$ dispersed in ethanol.





a: under different $LaB_6@SiO_2$ concentrations b: under different laser power output.



Fig. 9 Cell viability under different LaB_6 and $LaB_6@SiO_2$ concentrations a: after 24 h; b: after 48 h.



Fig. 10 Cell viability after irradiation of 980 nm laser under 0.82 W cm⁻² for 5 min using different concentrations of $LaB_6@SiO_2$. a-d: $LaB_6@SiO_2$; e: control a: 20 µg mL⁻¹; b: 40 µg mL⁻¹; c: 80 µg mL⁻¹; d: 120 µg mL⁻¹.



Fig. 11 Cell viability after irradiation of 980 nm laser under 0.82 W cm⁻² for different durations using 0.1 mg mL⁻¹ LaB₆@SiO₂. a-e: LaB₆@SiO₂; f: control a: 1 min; b: 2 min; c: 3 min; d: 4 min; e: 5 min

Research Highlights

Bullet points:

- 1. Spherical LaB₆ nanoparticles were chemically synthesized.
- 2. The NIR light absorption of LaB_6 was sensitive to the surface oxide layer.
- 3. Core-shell LaB₆@SiO₂ was prepared for biomedical compatibility.
- 4. Low concentrations of LaB₆ and LaB₆@SiO₂ were biosafe.
- 5. LaB₆@SiO₂ was effective agent for photothermal therapy.