ACS Biomaterials SCIENCE & ENGINEERING

Article

Cite This: ACS Biomater. Sci. Eng. 2018, 4, 3072−3077

Blue-Light -Activated Nano-TiO_2@PDA for Highly Effective and Nondestructive Tooth Whitening

Feng Zhang,[†] Chongxue Wu,[†] Ziyu Zhou,[†] Jiaolong Wang,[†] Weiwei Bao,[‡] Lina Dong,[‡] Zihao Zhang,[‡] Jing Ye,[§] Lan Liao,*[,†] and Xiaolei Wang*[,‡]

[†]The Key Laboratory of Oral Biomedicine, The Affiliated Stomatological Hospital of Nanchang University, Nanchang, Jiangxi 330006, China

[‡]Institute of Translational Medicine, Nanchang University, Nanchang, Jiangxi 330088, China

[§]The Second Affiliated Hospital of Nanchang University, Nanchang, Jiangxi 330006, China

Supporting Information

ABSTRACT: The application of polydopamine (PDA)-modified titanium dioxide nanoparticles (nano-TiO_2@PDA) as a new blue-light-activated tooth whitening material was discussed for the first time. Compared with the classical clinical whitening agent (peroxide, hydrogen peroxide, and carbamide peroxide), nano-TiO_2@PDA-based treatment not only had a similar whitening effect but also showed remarkably less damage on the enamel structure. Essentially, a highly effective and nondestructive tooth whitening treatment could thus be realized accordingly. The toxicity and antibacterial properties of this material were also evaluated systematically.

KEYWORDS: *nano-TiO_2, visible light, nondestructive tooth whitening, photocatalysis, reactive oxygen species*

INTRODUCTION

Tooth whitening material is a widely used healthcare material. Tooth discoloration could be classified as intrinsic, extrinsic, or both according to its location and etiology.[1,2] Extrinsic discoloration is caused by chromogens derived from habitual intake of dietary sources such as coffee, tea, chocolate, tobacco, and so on,[3] whereas intrinsic discoloration typically results from systemic or local causes, such as drug-related (tetracycline) and fluorosis.[4] The technologies of tooth whitening are roughly divided into invasive whitening and noninvasive whitening in clinical.[5] Invasive whitening includes full-crown restoration and laminate veneer restoration. These technologies have to grind and cut enamel which cause irreversible damage to the teeth. In comparison, noninvasive whitening refers to bleaching teeth through chemical method.[6] At present, hydrogen peroxide is the most commonly used tooth bleaching agent. Hydrogen peroxide can be used at lower levels (6−12%) and high concentration (30−40%) to bleach teeth. In our area, we often used a high concentration of hydrogen peroxide to bleach teeth in clinic.[7] This treatment is, an apparently nondestructive whitening technology.[8] However, in fact, the utilization of high concentration of H_2O_2 can bring on a series of problems, such as enamel demineralization,[9,10] tooth sensitivity,[11] gingival irritation,[12] cytotoxicity,[13,14] and acute pulpitis.[15,16] The mechanism of hydrogen peroxide for tooth whitening is on the basis of releasing ROS (reactive oxygen species) to clean pigment by oxidation, which can be accelerated under blue light.[17,18] Theoretically speaking, if we could find a new photocatalytic biomedical material with low stimulation and low toxicity to release ROS, the purpose of real nondestructive whitening of teeth could be achieved.

In the present study, the feasibility of nano-TiO_2 composite as an alternative material of H_2O_2 to realize blue-light-activated nondestructive tooth whitening is discussed for the first time.

EXPRIMENTAL SECTION

1. Preparation of Nano-TiO_2@PDA. Nano-TiO_2 (0.08 g) and dopamine hydrochloride (DA) (0.01 g) were added to 50 mL of ultrapure water to form a suspension. Then, 0.1 g of hexamethylenetetramine (HMTA) was dissolved in the suspension. After 3 min of ultrasonic dispersing, the mixture was incubated at 90 °C water for 3 h. Afterward, the mixture was centrifuged at 10 000 rpm for 2 min. Then, the supernatant was removed and the rest of the concentrated particles were washed by ultrapure water and absolute ethyl alcohol 2 times each, and the rest of the concentrated particles were washed by ultrapure water another 2 times. We obtained the wet nano-TiO_2@PDA after discarding the supernatant liquid and the nano-TiO_2@PDA powder can be obtained by using vacuum freeze-drying.

2. Morphological Characterization of Nano-TiO_2@PDA. Polydopamine (PDA) was coated and modified on the surface of nano-TiO_2 particles. The morphological characterization of the structure was observed by transmission electron microscope (TEM).

3. Physicochemical Features. Nano-TiO_2@PDA was characterized by energy-dispersive spectroscopy (EDS), X-ray diffraction

Received: May 10, 2018
Accepted: June 19, 2018
Published: June 19, 2018

DOI: 10.1021/acsbiomaterials.8b00548
ACS Biomater. Sci. Eng. 2018, 4, 3072−3077

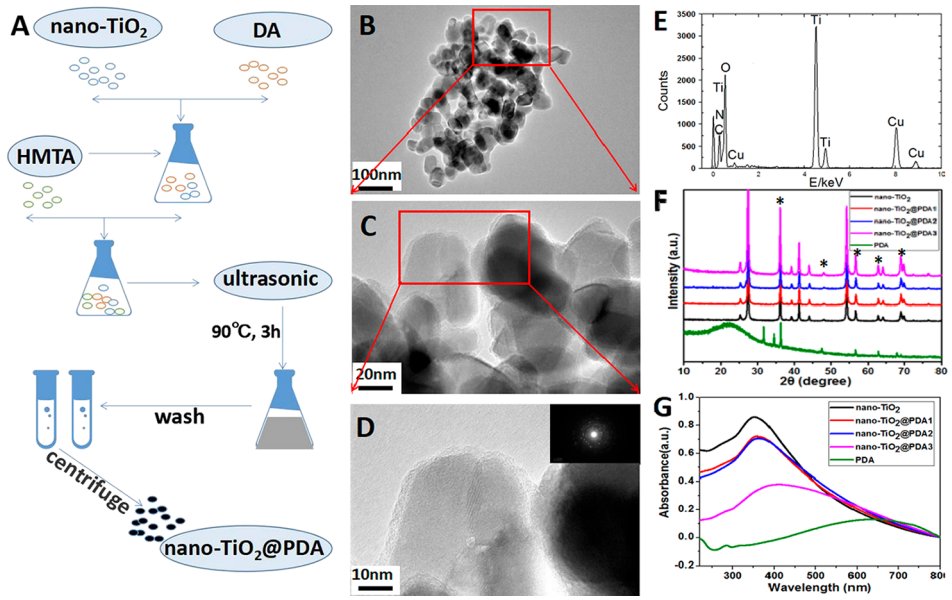

Figure 1. (A) Preparation process of nano-TiO_2@PDA. (B–D) TEM images of nano-TiO_2@PDA with different magnification. (E) EDS of nano-TiO_2@PDA. (F) XRD and (G) UV absorption spectroscopy of five different nano-TiO_2@PDA nanocomposites with increased PDA contents.

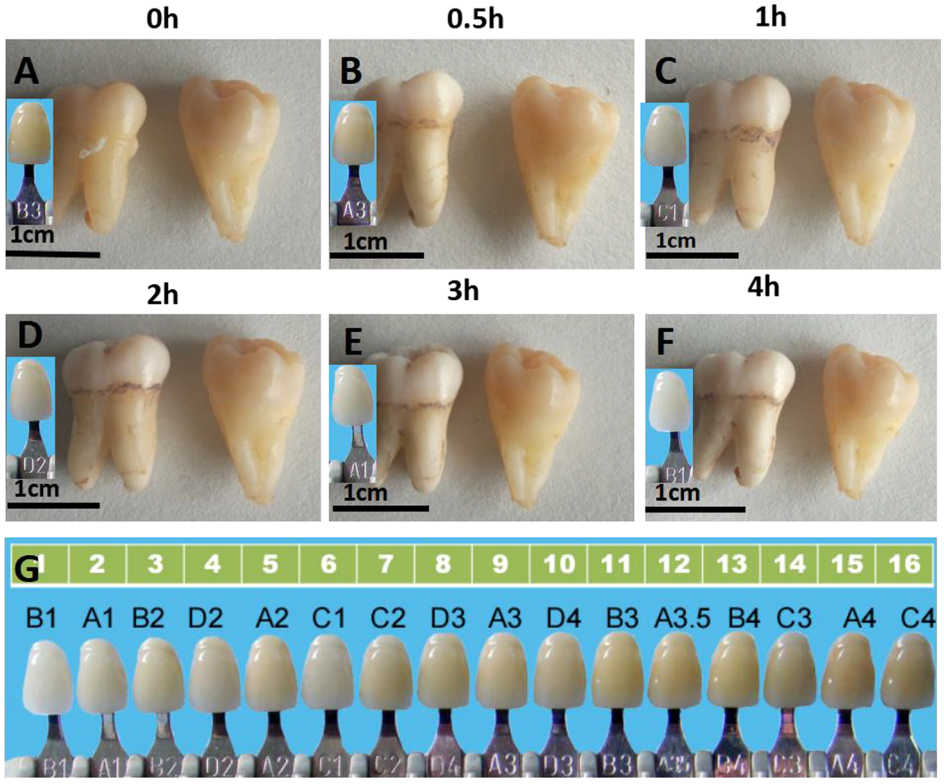

Figure 2. Left tooth was whitened by nano-TiO_2@PDA for 0.5h, 1h, 1.5h, 2h, 3h and 4h respectively. (A–F) The right tooth was used as the control. Professional Color order sorting was shown in picture G, which can be used to evaluate the effect of whitening.

(XRD), and UV–vis spectrophotometer. The PH was measured by PH meter.

4. Nano-TiO_2@PDA was Used for Tooth Whitening. The wet nano-TiO_2@PDA (494.10g/L, pH 7.72 ± 0.18) was coated on the surface of enamel evenly, the device was irradiated by blue light-emitting diode (LED). Dental professional color card was then applied to contrast the change of color after 0.5, 1, 1.5, 2, 3, and 4 h on irradiation, respectively.

5. Effect on Enamel after Tooth Whitening. We prepared two in vitro teeth and observed their enamel by scanning electron microscope (SEM) before whitening. One tooth was whitened by nano-TiO_2@PDA under blue light for 0.5h and the other one was whitened by 30% hydrogen peroxide (H_2O_2) under blue light for 0.5 h. Then, after whitening, we observed their enamal by SEM.

6. Cytotoxicity Testing. Human fibroblasts were cultured to logarithmic phase and inoculated in 60 mm culture plate, the cell dens ity was 10 000/cm^2, after 24 h, nano-TiO_2@PDA and 30%H_2O_2 were added, respectively. In addition, we set up a control group. All the three groups were cultured at 37 °C incubator for 1, 4, and 7 days. At each time point, we washed the cells by HBSS for 3 times and

DOI: 10.1021/acsbiomaterials.8b00548
ACS Biomater. Sci. Eng. 2018, 4, 3072–3077

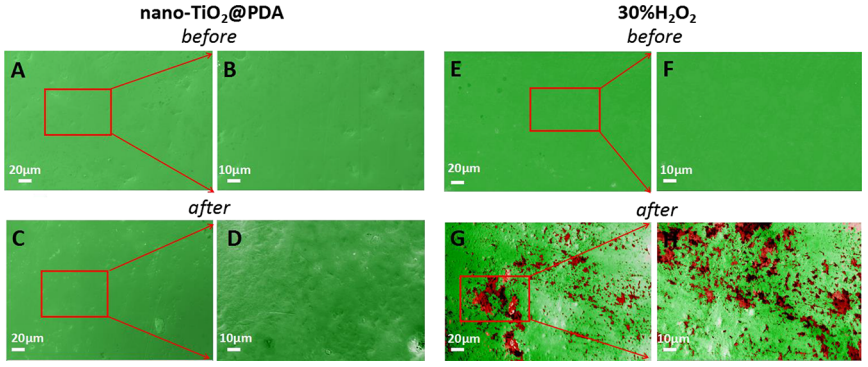

Figure 3. (A, B) SEM images of enamel before whitening. (C, D) SEM images of enamel surface after using nano-TiO_2@PDA under blue light irradiation for 0.5 h. (E, F) SEM images of enamel before whitening. (G, H) SEM images of enamel surface after using 30% H_2O_2 under blue light irradiation for 0.5 h.

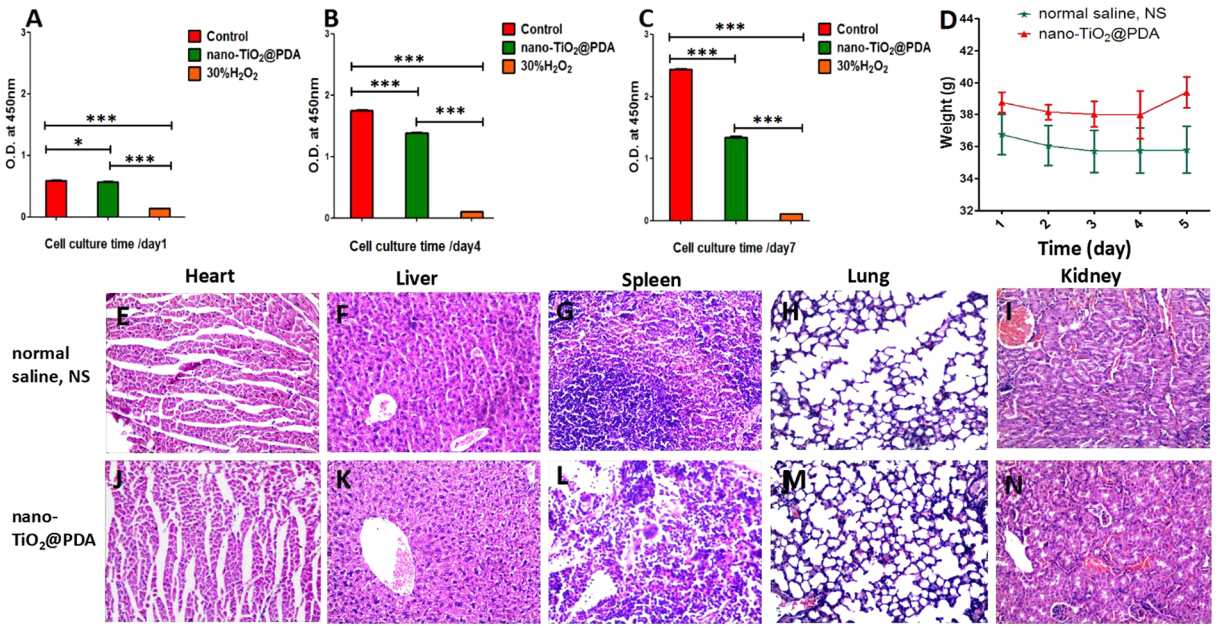

Figure 4. (A–C) Proliferation of human fibroblasts after coculture with nano-TiO_2@PDA or 30%H_2O_2 for 1, 4, and 7 days, respectively. (D) Weight change curve of mice on intragastric administration for 5 days. HE staining results of livers, kidneys, lungs, spleens, and hearts from the mice with (E–I) 5 successive days of feeding with nano-TiO_2@PDA or (J–N) normal saline as the control group.

configured 10% CCK8 culture medium, then, we added 1 mL of CCK8 into each hole and incubated them at 37 °C for 1 h, Next, we used the microplate reader to measure the absorbance at 450 nm, each sample was parallel test for three times.

7. Histopathologic. We prepared 8 male mice (about 30 g each) and divided them into test group and control group for 4 mice in each group. After 5 days acclimation, 8 mice were ethically treated during the procedure. The suspensions contained nano-TiO_2@PDA (333.33 mg/kg/day) were immediately exposed to the test group through oral gavage, the control group followed the same process by using normal saline (NS). Five days after administration, the mice were sacrificed and dissectted for histopathological examination. A small piece of liver, kidney, lung, spleen and heart were fixed by 4% paraformaldehyde. The sections were stained with hematoxylin–eosin. And then, we observed their histopathological characters by optical microscope.

8. Antibacterial Susceptibility. We selected 4 teeth and washed them. These teeth were disinfected by autoclaving and then cocultured with bacteria. One was brushed with only toothbrush for 3 min, the other three were brushed with nano-TiO_2@PDA, nano-TiO_2@PDA under blue light, and an on-sell antibacterial toothpaste for 3 min, respectively. After that, all the four teeth were washed by 5 mL of phosphate buffer solution (PBS, pH7.4) for two times, we observed the residual bacteria on the surface of these teeth by SEM. Afterward, we continued to cultivate these teeth for 2h after brushing and used plate colony-counting methods to evaluate its antibacterial property. Finally, we calculated and recorded their inhibition rate. The experiments were repeated for at least three times.

RESULTS AND DISCUSSION

In general, pure nano-TiO_2 is a kind of wide band gap semiconductor material with low availability rate under visible light.[19] To realize visible blue-light-activated properties, we modified the surface of nano-TiO_2 with PDA.[20] The corresponding preparation scheme was shown as Figure 1A. The subsequent TEM images demonstrated that the as prepared nano-TiO_2@PDA had core–shell structure. The average particle size of nano-TiO_2 was about 40 nm and the thickness of organics on the surface of nano-TiO_2 was about 2 nm (Figure 1B–D). To verify that the film on the nano-TiO_2 surface was PDA, we used different ratios between DA and nano-TiO_2 to prepare different composites, and the results demonstrated that with increasing DA, the thickness on the surface of the nano-TiO_2 also increased (Figure S2). EDS (X-ray energy-dispersive spectroscopy) and XRD (X-ray Dif-

DOI: 10.1021/acsbiomaterials.8b00548
ACS Biomater. Sci. Eng. 2018, 4, 3072–3077

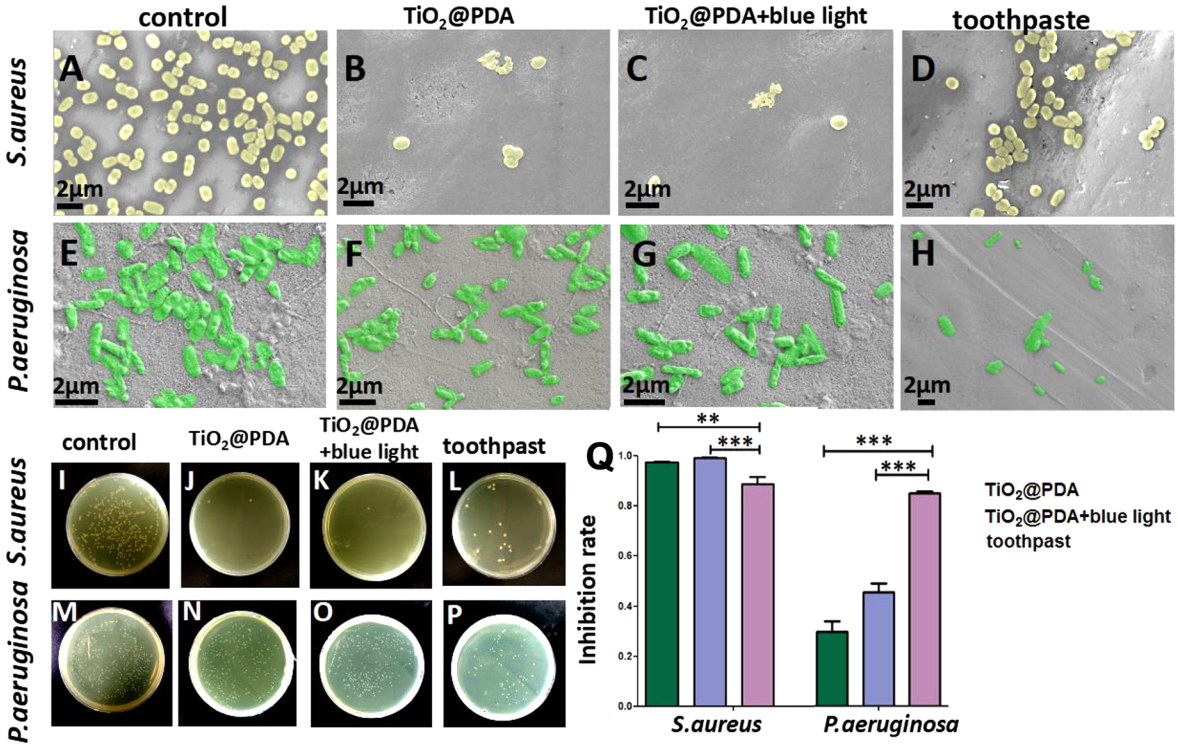

Figure 5. (A–H) SEM observation of the residual bacteria on the surface of teeth with different treatment. (I–P) Relative results from plate counting methods, (Q) and the corresponding quantitative inhibition rates.

fraction) diagrams (amplified, Figure S4) also proved that PDA was successfully coated on the surface of nano-TiO_2 (Figure 1E, F). Nano-TiO_2@PDA1, nano-TiO_2@PDA2 and nano-TiO_2@PDA3 were the composites with multiplied amount of DA, ultraviolet absorption spectra showed that the increasing of PDA can let the adsorption spectra shift to visible light area (Figure 1G). This phenomenon suggested that the composite can be inspired by visible light, which provided a reliable basis for its subsequent studies on blue-light-activated tooth whitening.

The prepared nano-TiO_2@PDA particles (wet, 494.10g/L, pH 7.72 ± 0.18) were coated on the surface of enamel evenly (Figure S1E, F). A blue-light-emitting diode (LED) was then used to irradiate this tooth (Figure S1G). Dental professional color card was then applied to contrast the change of color after 0.5, 1, 1.5, 2, 3, and 4 h on irradiation respectively (Figure 2A–F, left). For the ease of comparison, we set up a control tooth (Figure 2A–F, right) during the entire process. According to the dental professional color card (Figure 2G), we found that after 0.5 h of whitening, the levels of the tooth color were improved from A3 to B3. After 4 h of treatment, a ten-level whitening change could be achieved, which was similar to the effect of H_2O_2-based whitening agents in clinic (Figure S5).[21] Therefore, nano-TiO_2@PDA has an ideal effect as a tooth-whitening agent.

After the above-mentioned nano-TiO_2@PDA treatment, the integrity of enamel was then evaluated by SEM. As a result, it was intriguingly to discover that no significant enamel damage (Figure 3A–D) was found on the surface of tooth. In comparison, after treated with 30% H_2O_2, the surface of tooth enamel showed obvious demineralization and presented honeycomb structure (Figure 3E–H). The use of nano-TiO_2@PDA activated with blue light thus was more appropriate for real nondestructive tooth whitening.

To confirm the biological safety of nano-TiO_2@PDA, we chose human fibroblasts (oral mucosa is mainly fibroblast) to detect its cytotoxicity by CCK8.[22] Compared to 30% H_2O_2, the cell proliferative ability of group nano-TiO_2@PDA was close to control group after 1 day coculture with nano-TiO_2@PDA. After 4 and 7 days coculture with human fibroblasts, nano-TiO_2@PDA showed a certain degree of cytotoxicity, but far less than 30%H_2O_2 (Figure 4A–C). In practical usage, we could achieve satisfactory whitening effect by using nano-TiO_2@PDA for less than 4 h. In addition, we carried out a simple animal experiment to evaluate the toxic effect of nano-TiO_2@PDA on important organs and tissues of mice.[23−25] The results suggested that the weight of these mice did not have obvious decreasing in nano-TiO_2@PDA group (Figure 4D). The mental state of these mice were also normal, and no vomiting appeared. The staining results demonstrated that the hearts, spleens, lungs, spleens and kidneys of these mice after nano-TiO_2@PDA treatment were all normal (Figure 4E–N). From the pathological analysis, nano-TiO_2@PDA did not show obvious tissue toxicity. Actually, only tiny amount of the tooth whitening material will enter the stomach through mouth during the practical usage. According to the above results, the safety of nano-TiO_2@PDA is much more reliable than 30% H_2O_2.

Further, we evaluated antibacterial properties of nano-TiO_2@PDA. The teeth were cocultured with bacterial medium before being treated by nano-TiO_2@PDA or nano-TiO_2@PDA under blue light. An on-sale antibacterial toothpaste was also used as a comparison. Afterward, we observed the residual bacteria on the surface of these teeth. SEM images showed that nano-TiO_2@PDA exhibited an excellent antibacterial activity against Gram-positive bacteria (G+)--*Staphylococcus aureus (S.a)*, even better than the on-sell antibacterial toothpaste. However, the antibacterial activity of pure nano-TiO_2@PDA

DOI: 10.1021/acsbiomaterials.8b00548
ACS Biomater. Sci. Eng. 2018, 4, 3072−3077

against Gram-negative bacteria (G-)--*Pseudomonas aeruginosa (P.a)* was not so obvious (Figure 5A–H). Afterward, we used plate colony-counting methods to quantitatively evaluate its antibacterial properties. Similar conclusion was drawn (Figure 5I–Q). To further confirm this result, we repeated this experiment with another Gram-negative bacteria (G−)—*Escherichia coli (E. coli),* and got the same result as *Pseudomonas aeruginosa* (Figure S6A–E). Referring to some related literatures, the surface modification of nano-TiO_2 can decrease its antibacterial activity on Gram-negative bacteria.[26] The results also suggested that the antibacterial effect was much better under blue light, which was similar to the results in literatures.[27,28] Through SEM observation, some cracked bacteria (Figure S6F–H) were found on the surface of the teeth treated with nano-TiO_2@PDA under blue light. Collectively, nano-TiO_2@PDA has certain antibacterial activity on the surface of teeth, and the antibacterial activity will be increased when irradiated by blue light.

CONCLUSION

Tooth whitening material is actually one of the most frequently used biomedical materials. Effective and nondestructive tooth whitening is a long-term aim for most dental related researchers. In the present study, PDA membrane was modified on the surface of nano-TiO_2 particles. Under visible blue light, the as-prepared nano-TiO_2@PDA composite could energize electrons to release reactive oxygen species (ROS), which provided us a reliable basis for its application in the field of tooth whitening. Further experiments showed that blue light activated nano-TiO_2@PDA not only had ideal whitening effect, but, more importantly, exhibited no obvious damage on enamel surface, which made it possible for the essentially high effective and nondestructive tooth whitening, According to the subsequent investigation, this nanocompostie also had good biocompatibility and certain antibacterial function. The present study not only discovered a potential global used oral biomaterial, but also demonstrated a new mild but efficient manner to generate ROS for biomedical purpose. The ongoing research will be focused on two topics: the long-term biosafety of nano-TiO_2@PDA; and the extension of its usage to other biomedical areas, such as precise wound surface sterilization.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsbiomaterials.8b00548.

Supporting Experimental Section and Figures S1–S12 (PDF)

AUTHOR INFORMATION

Corresponding Authors

*E-mail: liaolan5106@163.com.
*E-mail: wangxiaolei@ncu.edu.cn.

ORCID

Xiaolei Wang: 0000-0003-3403-1174

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported by the National Natural Science Foundation of China (21461015 to X.W.); Science Foundation of JiangXi Provincial Department of Education (20165BCB19002, KJLD14010201530BCB23035 and 20161ACB21002 to X.W.); National Natural Science Foundation of China (81660444 to L.L.), Natural Science Foundation of Jiangxi Province (20171BAB205050 to L.L.), Key Development Plan of Jiangxi Province (20161BBG70149 to L.L.), Foundation of Jiangxi Provincial Department of Health and Family Planning Commission (20161082, 20175296 to L.L.) and Science Foundation of Jiangxi Provincial Department of Education (GJJ150281 to L.L.). All experiments were performed in compliance with the relevant laws and approved by the Institutional Animal Care and Use Committee at Institute of Translational Medicine, Nanchang University.

REFERENCES

(1) Alqahtani, M. Q. Tooth-bleaching procedures and their controversial effects: A literature review. *Saudi Dent. J.* **2014**, *26*, 33–46.
(2) Abdelkader, N. N. Modified Technique for Nonvital Tooth Bleaching: A Case Report. *Electron Physician* **2015**, *7*, 1423–1426.
(3) Mondelli, R. F. L.; Azevedo, J. F. D. e. G.; Francisconi, A. C.; Almeida, C. M.; Ishikiriama, S. Y. Comparative clinical study of the effectiveness of different dental bleaching methods - two year follow-up. *J. Appl. Oral Sci.* **2012**, *20* (4), 435–443.
(4) Kimyai, S.; Bahari, M.; Naser-Alavi, F. Effect of two different tooth bleaching techniques on microhardness of giomer. *J. Clin. Exp. Dent.* **2017**, *9* (2), e249–e253.
(5) Al-Tarakemah, Y.; Darvell, B. W. On the permanence of tooth bleaching. *Dent. Mater.* **2016**, *32*, 1281–1288.
(6) Dudek, M.; Roubickova, A.; Comba, L.; Housova, D.; Bradna, P. Effect of Postoperative Peroxide Bleaching on the Stability of Composite to Enamel and Dentin Bonds. *Operative Dentistry.* **2013**, *38*, 394–407.
(7) Bizhang, M.; Domin, J.; Danesh, G.; Zimmer, S. Effectiveness of a new non-hydrogen peroxide bleaching agent after single use - a double-blind placebocontrolled short-term study. *J. Appl. Oral Sci.* **2017**, *25*, 575–584.
(8) de Arruda, A. M.; dos Santos, P. H.; Sundfeld, R. H.; Berger, S. B.; Briso, A. L. F. Effect of Hydrogen Peroxide at 35% on the Morphology of Enamel and Interference in the De-remineralization Process: An In Situ Study. *Operative Dentistry.* **2012**, *37*, 518–525.
(9) Abouassi, T.; Wolkewitz, M.; Hahn, P. Effect of carbamide peroxide and hydrogen peroxide on enamel surface: an in vitro study. *Clin. Oral Investig.* **2011**, *15*, 673–680.
(10) China, A. L. P.; Souza, N. M.; Gomes, Y. d. S. B. d. L.; Alexandrino, L. D.; Silva, C. M. Effect of Fluoride Gels on Microhardness and Surface Roughness of Bleached Enamel. *Open Dent. J.* **2014**, *8*, 188–193.
(11) Prajatelistia, E.; Ju, S. W.; Sanandiya, N. D.; Jun, S.-H.; Ahn, J-S.; Hwang, D.-S. Tunicate-Inspired Gallic Acid/Metal Ion Complex for Instant and Efficient Treatment of Dentin Hypersensitivity. *Adv. Healthcare Mater.* **2016**, *5*, 919–927.
(12) Carey, C. M. Tooth Whitening: What We Now Know. *J. Evid. Based Dent. Pract.* **2014**, *14* (Suppl, 70–76), 70.
(13) Ito, Y.; MOMOI, Y. Bleaching using 30% hydrogen peroxide and sodium hydrogen carbonate. *Dent. Mater. J.* **2011**, *30* (2), 193–198.
(14) De Moor, R. J. G.; Verheyen, J.; Verheyen, P.; Diachuk, A.; Meire, M. A.; De Coster, P. J.; De Bruyne, M.; Keulemans, F. Laser Teeth Bleaching: Evaluation of Eventual Side Effects on Enamel and the Pulp and the Efficiency In Vitro and In Vivo. *Sci. World J.* **2015**, *2015*, 835405.

DOI: 10.1021/acsbiomaterials.8b00548
ACS Biomater. Sci. Eng. 2018, 4, 3072–3077

(15) Qu, T.; Liu, X. Nano-Structured Gelatin/Bioactive Glass Hybrid Scaffolds for the Enhancement of Odontogenic Differentiation of Human Dental Pulp Stem Cells. *J. Mater. Chem. B* **2013**, *1*, 4764−4772.
(16) Vaz, M. M.; Lopes, L. G.; Cardoso, P. C.; de Souza, J. B.; Batista, A. C.; Costa, N. L.; Torres, E. M.; Estrela, C. Inflammatory response of human dental pulp to at-home and in-office tooth bleaching. *J. Appl. Oral Sci.* **2016**, *24*, 509−517.
(17) Xu, Q.; He, C.; Ren, K.; Xiao, C.; Chen, X. Thermosensitive Polypeptide Hydrogels as a Platform for ROS-Triggered Cargo Release with Innate Cytoprotective Ability under Oxidative Stress. *Adv. Healthcare Mater.* **2016**, *5*, 1979−1990.
(18) Saita, M.; Kobatashi, K.; Yoshino, F.; Hase, H.; Nonami, T.; Kimoto, K.; Lee, M.-C. ESR investigation of ROS generated by H2O2 bleaching with TiO2 coated HAp. *Dent. Mater. J.* **2012**, *31* (3), 458−464.
(19) Ren, W.; Yan, Y.; Zeng, L.; Shi, Z.; Gong, A.; Schaaf, P.; Wang, D.; Zhao, J.; Zou, B.; Yu, H.; Chen, G.; Brown, E. M. B.; Wu, A. A Near Infrared Light Triggered Hydrogenated Black TiO2 for Cancer Photothermal Therapy. *Adv. Healthcare Mater.* **2015**, *4*, 1526−1536.
(20) Mao, W.-X.; Lin, X.-J.; Zhang, W.; Chi, Z-.X.; Lyu, R.-W.; Cao, A.-M.; Wan, L-J. Core−shell structured TiO2@polydopamine for highly active visible-light photocatalysis. *Chem. Commun.* **2016**, *52*, 7122−7125.
(21) Dionysopoulos, D.; Strakas, D.; Koliniotou-Koumpia, E.; Koumpia, E. Effect of Er, Cr:YSGG laser irradiation on bovine enamel surface during in-office tooth bleaching ex vivo. *Odontology* **2017**, *105*, 320−328.
(22) Tsuji, M.; Ueda, T.; Sawaki, K.; Kawaguchi, M.; Sakurai, K. Biocompatibility of a titanium dioxide-coating method for denture base acrylic resin. *Gerodontology* **2016**, *33*, 539−544.
(23) Esmaeillou, M.; Moharamnejad, M.; Hsankhani, R.; Tehrani, A. A.; Maadi, H. Toxicity of ZnO nanoparticles in healthy adult mice. *Environ. Toxicol. Pharmacol.* **2013**, *35*, 67−71.
(24) Zhou, J.; Horev, B.; Hwang, G.; Klein, M. I.; Koo, H.; Benoit, D. S. W. Characterization and optimization of pH-responsive polymer nanoparticles for drug delivery to oral biofilms. *J. Mater. Chem. B* **2016**, *4* (18), 3075−3085.
(25) Zhang, J.; Song, W.; Guo, J.; Zhang, J.; Sun, Z.; Ding, F.; Gao, M. Toxic effect of different ZnO particles on mouse alveolar macrophages. *J. Hazard. Mater.* **2012**, *219−220*, 148−155.
(26) Gupta, K.; Singh, R. P.; Pandey, A.; Pandey, A. Photocatalytic antibacterial performance of TiO2 and Ag-doped TiO2 against S. aureus. P. aeruginosa and E. coli. *Beilstein J. Nanotechnol.* **2013**, *4*, 345−351.
(27) Petrini, M.; Trentini, P.; Tripodi, D.; Spoto, G.; D'Ercole, S. In vitro antimicrobial activity of LED irradiation on Pseudomonas aeruginosa. Journal of Photochemistry & Photobiology. *J. Photochem. Photobiol., B* **2017**, *168*, 25−29.
(28) Bumah, V. V.; Aboualizadeh, E.; Masson-Meyers, D. S.; Eells, J. T.; Enwemeka, C. S.; Hirschmugl, C. J. Spectrally resolved infrared microscopy and chemometric tools to reveal the interaction between blue light (470 nm) and methicillin-resistant Staphylococcus aureus. *J. Photochem. Photobiol., B* **2017**, *167*, 150−157.

DOI: 10.1021/acsbiomaterials.8b00548
ACS Biomater. Sci. Eng. 2018, 4, 3072−3077