

Research Article

Biodegradable Polymer/TiO₂ Nanotubes Loaded Roxithromycin as Nanoarray Capsules for Long-Lasting Antibacterial Properties of Titanium Implant

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Bacterial infection is one of the main reasons for the clinical failure of oral titanium restorations. In this study, biodegradable polymer/TiO₂ nanotube nanoarray capsules were constructed on a titanium substrate surface to locally deliver drugs for long-lasting antibacterial properties. Anodization was applied to prepreparation TiO₂ nanotube array film on titanium substrate, and then, the upward opening TiO₂ nanotubes were sealed with biodegradable polymer (chitosan and polyethylene glycol) through electrochemical deposition. Scanning electron microscope (SEM) and X-ray photoelectron spectroscopy (XPS) were used to analyze the characterization of this system. The drug release characteristics and the antibacterial activity demonstrated that the polymer coating significantly reduced burst release and enhanced lasting antibacterial properties. The nanoarray capsules still preserved integrity with a little degradation after 2 days. The strategy described herein provides a versatile route for designing targeted drug delivery systems in orthopaedical and other biomedical fields.

1. Introduction

Numbers of dental procedures, which commonly used titanium- (Ti-) based implants, are the reliable treatment for tooth loss [1]. However, although Ti and its alloys possess favorable physicochemical properties such as appropriate mechanical strength with low modulus, good biocompatibility, excellent corrosion resistance, and degradation resistance [2–4], Ti and its alloys are still bioinertness. They cannot directly bond with bone tissue and cause complications or implant failure for the possibility of persistent infections [5] and local inflammation [6]. The usual treatments of these problems involve oral medicine and intravenous drug administration, though these treatments will lead to distributing drugs throughout the body and cause systemic side effects. Localized drug delivery is an appealing way to reduce systemic side effects and improve drug delivery efficacy.

With the emergence of nanotechnology, its application in medicine which caused an enormous interest is recognized as a potential area with great prospects for developing local drug delivery [7]. And nanotechnology is commonly being used to create as well as control the nanostructure of materials. Lately, considerable research has been focused on constructing nanostructure of TiO2 nanotubes (TNT) on Ti implant surface through anodization technique [8], which not only enhance osteoblast adhesion and bone formation [9-11] but also become superior nanostructure for local drug delivery [8, 12, 13]. Because TNT have attractive features, for example, high surface-to-volume ratio, controllable dimensions of tubular diameters and thickness, and no side effects on drug release rate with stability [12, 14], they are designed and advanced drug release performances themselves to approach the zero-order or first/zero type release for specific drugs. However, according to the diffusion mechanism of

drug molecules, it is inevitable for TNT drug delivery that may lead to a burst release at the preliminary stage [12, 15]. The burst release will release a high-dose drug in a short time to shorten the long-term sustained release of the drug loaded on TNT and influence the drug efficacy and even cause inevitable side effects. Thus, the fabrication and modification of TNT with reduced burst release and extended drug efficacy are crucial.

Drug delivery from nanotubes can be expounded by the diffusion-mediated process, which is driven by the diffusion of drug molecules to release from the nanotubes. Moreover, this diffusion process is seriously influenced by drug molecular size, diameters and thickness of nanotubes, morphology, and surface chemistry of the Ti implant [16-18]. Hence, despite the molecular size of the selective drugs, focusing on modification, the Ti implant is more convenient and effective. Several methods were studied for further controlling the release time and prolonging the drug efficacy from TNT. Hu et al. [19] fabricated multiple layers of gelatin and chitosan via a spin-assisted layer-by-layer assembly technique on the surface of drug-loaded TNT for prolonged drug release. Faria and de Queiroz [20] constructed TiO₂/ZnS nanotubes by solgel template synthesis and micelle-template inducing reaction, which showed a desirable release kinetics and controllable drug release time in cancer therapy. Gulati et al. [21] coated thin biocompatible polymer layers with the polymer of chitosan or poly(lactic-co-glycolic acid) to reduce burst release (from 77% to <20%), extend overall release (from 4 days to more than 30 days), and enhance osteoblast adhesion. Kazemzadeh-Narbat et al. [3] constructed a TiO₂ nanotube/mesoporous calcium silicate composite, which used a template method to deposit mesoporous calcium silicate (MCS) on the top of the nanotubes. The results showed that the MCS particles could reduce the exposure of surface area of a loaded drug so that the drug becomes difficult to diffuse to the solvent and thus accompanied by controllable drug release. Simovic et al. [22] used plasma polymerization to deposit allylamine layer with controlled thickness on the top of the titania nanotubes, which reduced the tube diameter from 80-90 nm to <20 nm and hence controlled the rate of drug release.

Compared with other methods, electrochemical deposition is a simple, rapid, and scalable functionalization technique, which is commonly used in sensor and electroplated fields [23–25] and also suitable for complex patterned surfaces [26]. Furthermore, electrochemical deposition is also controllable that the thickness and chemical composition can be changed by adjusting the electrodeposition conditions [27, 28]. According to these advantages, recent researches applied electrochemical deposition into the fields of hydrogels and dental and orthopaedical implants [29–31]. But there were few previous researches concentrating on the application in drug delivery system with electrodeposition, especially in localized drug delivery of TNT.

In the present study, the aim was to utilize these proven advantages of TNT and electrochemical deposition to prolong drug release and optimize drug delivery. Thus, we fabricated biodegradable polymer coating (chitosan or PEG) on a drug-loaded TNT surface (TNTDP). Roxithromycin, one of the macrolide antibiotics derived from erythromycin, shows significant antibacterial activity in gram-positive and anaerobic bacteria via inhibiting the synthesis of bacterial protein and is used to examine the modified effect of TNTDP. The SEM and XPS were used to analyze the surface characterization of TNTDP and to do so with drug-loaded TNT (TNTD) and TiO₂ nanotubes disc (TNT). The drug release characteristics and antibacterial activity with several bacterial species (*Staphylococcus aureus* (*S. aureus*), *Streptococcus sanguinis* (*S. sanguinis*), and *Streptococcus mutans* (*S. mutans*)) were also tested. We hypothesized that this study can provide a new approach to effectively reduce burst release and extend drug efficacy, and thus enabling the application of a wide range of therapeutic agents from implants locally in dental, orthopaedical, and other biomedical areas.

2. Materials and Methods

The fabrication of the biodegradable polymer/TiO₂ nanotubes loaded with roxithromycin as nanoarray capsules was carried out by a three-step process: anodization for synthesizing the TiO₂ nanotube array film, chemistry bathing deposition (CBD) of roxithromycin onto the TiO₂ nanotubes arrays, and building a biodegradable polymer coating by the electrochemical deposition process. The illustration of the typical fabrication of the nanoarray capsule film process is shown in Scheme 1.

2.1. Fabrication of TiO₂ Nanotubes on Ti Disc. Titanium foils (TA2) with a thickness of 0.2 mm, purchased from Shenle Hui Technology Co., Ltd. (Shenzhen, China), were cut into pieces of TNT discs (8 mm × 10 mm) after anodization. These discs were marked TNT samples. Briefly, the Ti foil was mechanically polished using sandpapers of P80 to P1200 sequentially and sonicated in absolute ethanol for 5 min to degrease. Then, the foils were rinsed with deionized water thrice and chemically polished with a 5 vt% hydrofluoric acid solution to dissolve the native oxide layer. After sonicating in deionized water for 2 min, the foils were applied as the anode and the cathode using a titanium plate, immersed in a 0.5 vt% hydrofluoric acid solution, and supplied with a voltage of 20 V by a regulated DC power supply (KXN-2005D, Zhaoxin Electronic Instrument Equipment Co., Ltd., Shenzhen, China) under magnetic stirring for 1 h to construct TiO₂ nanotube layers. When the experiment ended, the TNT foils were rinsed with deionized water and dried at 37°C.

2.2. Drug Loading and Electrodepositing Polymer Coating on Drug-Loaded TNT. Prior to drug loading, TNT discs were immersed into 75 vt% ethanol for 30 min, then dried in air and sterilized under UV light for 30 min. The roxithromycin drug solution was made in absolute ethanol with a concentration of 2 mg/ml. Then, $20 \,\mu$ l of drug solution was exactly pipetted onto each TNT discs and dried under vacuum at room temperature. After repeated 20 times, the TNT discs were cleaned by a small amount of phosphate-buffered saline (PBS, Macklin Biochemical Co., Ltd., Shanghai, China) to remove residual drug on the surface of TNT discs



SCHEME 1: The procedure of constructed TiO_2 nanotubes (TNT), drug-loaded TiO_2 nanotubes (TNTD), and electrodeposited polymer coating on the surface of drug-loaded TiO_2 nanotubes (TNTDP).

and dried at 37 $^{\circ}\text{C}.$ These drug-loaded TNT discs were termed TNTD samples.

A 0.5 wt% polymer solution of chitosan (with deacetylation degree of 90% and viscosity average molecular weight of 40 KDa) was prepared by dissolving chitosan into acetic acid (0.6 vt%, dissolved in deionized water). Then, the pH of the chitosan solution was adjusted to 5.0 using 2 mol/l NaOH before electrochemical deposition. The electrochemical deposition was worked by an electrochemical workstation (CHI-660E, CHI Instruments, Inc., Austin, TX, USA) with constant voltage mode, while the TNTD samples were anchored onto platinum cathodes and the platinum net was used as counter-electrode. The deposition was carried out in a 37°C water bath with a supplying voltage of +3 V for 0.5-5 min. After slowly rinsed with deionized water, the samples were dried at 37°C. The procedure of PEG coating was similar to the chitosan coating mentioned above with little difference. The concentration of electrolyte was 0.5 wt% PEG (with molecule of 4000) in deionized water which contained 0.5 wt% MgCl₂ and adjusted pH using 0.1 mol/l HCl. The supplied voltage was -1 V for depositing 0.5-1.5 min. These further handled samples were denoted by TNTDP-CS and TNTDP-PEG.

2.3. Surface Characterization

2.3.1. Surface Topographies of Each Sample. Mounting the samples on a platform through a double-sided conductive tape and platinum spraying, the surface topographies of the prepared samples before and after polymer coating were observed using field-emission scanning electron microscope (FE-SEM), Hitachi SU70 (Hitachi, Ltd., Tokyo, Japan).

2.3.2. X-Ray Photoelectron Spectroscopy (XPS) for Surface Chemistry Analysis. The surface chemistry of the prepared samples after drug loading and drug-loaded polymer coating compared to TNT was analyzed using XPS (Thermo Scientific ESCALAB 250Xi, Waltham, MA, USA). 2.4. The Characteristics of Drug Release In Vitro. The amount of roxithromycin released from TNTD and TNTDP samples was assessed by immersing in 1 ml of PBS with pH7.2 at 37° C. Before the examination, the drug-released solution (roxithromycin released into PBS) was transferred to a centrifuge tube and stored at 4°C. Then, ultraviolet-visible (UV-Vis) spectroscopy was used to examine the amount of roxithromycin at 483 nm [31] after the drug-released solution which reacted with concentrated H₂SO₄ for 30 min. And the TNT was also used as blank samples. A standard calibration curve of standard roxithromycin drug (purchased from National Institute for Food and Drug Control, Beijing, China) followed the same procedures.

2.5. Antibacterial Activity before and after Drug Releasing. The antibacterial activity of the prepared samples against S. aureus (CMCC(B) 26003), S. sanguinis (ATCC 10556), and S. mutans (ATCC 25175) were determined by the agar dilution method. The positive control samples used standard roxithromycin drug, and TNT was used as the blank samples, while the test samples used TNTD and TNTDP samples. Briefly, S. aureus, S. sanguinis, and S. mutans were seeded over soyabean-casein digest (SCD) and brain heart infusion (BHI) agar plates, respectively. The samples were randomly divided into three groups containing standard roxithromycin drug, TNT, TNTD, TNTDP-PEG, and TNTDP-CS. Then, the prepared samples were placed on the agar plates. After incubation for 24 h at 37°C in an aerobic environment (for S. aureus) and an anaerobic environment (for S. sanguinis and S. mutans), respectively, the inhibition zone of these kinds of bacteria was obtained to evaluate the antibacterial activity of roxithromycin.

2.6. Statistical Analysis. All the results were displayed as the mean \pm standard deviation (SD), which conducted three independent experiments unless otherwise specified. Data analysis was performed using IBM SPSS Statistics 19.0



FIGURE 1: The nanostructure of surface topography of samples showed in SEM images: (a) Ti foil with the treatment of mechanically polishing, (b) TNT samples without drug loading, (c) PEG layer coated on the TNT surface, (d) chitosan layer coated on the TNT surface, (e) cross-sectional image of PEG layer coated on the TNT surface, (f) cross-section of chitosan coating.

(IBM SPSS Software, USA) with p < 0.05 regarded as statistical significance.

3. Results

3.1. Surface Characterization. The surface topographies of the samples with different treatments are shown in Figure 1. After mechanically polished by silicon carbide papers, some grooves were presented on the surface of Ti foil with remaining a few silicon carbide particles (Figure 1(a)). For the TNT sample in Figure 1(b), we could observe the orderly regular TiO₂ nanotubes on the surface of the titanium substrate, which possessed 50-70 nm of the nanotubes in diameter. The walls of nanotubes were thin with a dimension of 5-9 nm, while the thickness of the TiO₂ nanotube layer was about 300 nm (Figure 1(f)). Observing the crosssectional images of the two polymer coatings (Figures 1(e) and 1(f)), the thickness of chitosan coating was similar, about 80-300 nm; the PEG coating was just about dozens of nanometers. This was attributed to the deposition time; thus, the chitosan coating would become thicker with a thickness of $3-5 \mu$ m after depositing for 5 min. Figures 1(c) and 1(d) were the SEM images of TiO₂ nanotubes coated with polymer through electrochemical deposition. It can be observed that the polymers (chitosan and PEG) were uniformly deposited on the top of nanotubes, though the polymer coatings still existed undulation because of the electrodeposition mechanism of chitosan and PEG. Moreover, in the PEG coating image, we also observed some particles, which inferred that they were the deposition of Mg particles.

The XPS analysis was used to examine the chemical state of the prepared sample surfaces, presented in Figure 2. The peaks at 459.08 eV, 464.88 eV, and 530.48 eV in Figure 2(a) represented Ti $2p_{3/2}$, Ti $2p_{1/2}$, and O 1 s, respectively, which

Survey 1 Scan, 40.8 s, 500 $\mu \rm{m},$ CAE 100.0, 1.00 eV



FIGURE 2: Continued.



FIGURE 2: XPS spectra of different samples: (a) TNT samples, (b) PEG layer coated on the TNT surface, (c) chitosan layer coated on the TNT surface.



FIGURE 3: The XPS spectra of O 1s and C 1s of different samples: (a) O 1s spectrum; (b)–(d) C 1s spectrum of TNT samples (b), PEG layer coated on the TNT surface (c), and chitosan layer coated on the TNT surface (d).



FIGURE 4: The images of roxithromycin reacted with concentrated H_2SO_4 in different samples after 48 h release and the drug release profile of antibacterial drug (roxithromycin) from the samples with or without polymer coatings: (a) TNTD samples. (b) TNTDP-PEG samples, (c) TNTDP-CS samples, and (d) the drug release profile.

meant there was a presence of Ti^{4+} and O^{2-} as well as forming Ti-O lattices. As a result of Atomic% calculated from the XPS data, the ratio of Ti and O was 1:2.18, which indicated that the main chemical state of the Ti foil surface after anodization was TiO_2 . For the samples coated with the polymer layer, there were not observed Ti 2p peaks because the thickness of polymer layers exceeded the detection depth of XPS. And some new peaks in Figure 2(b) and Figure 2(c) were observed while neither of the two peaks occurred in TNT samples (Figure 2(a)).

Furthermore, except for the new peaks, the C 1s and O 1s spectra of the polymer coating samples had been changed, as shown in Figure 3. Because of the differences of surface chemistry of different samples, the peak at 530.48 eV, 530.98 eV, and 531.08 eV in O 1s spectrum (Figure 3(a)) can be assigned to Ti-O (TNT sample) and C-O bonds (PEG and chitosan layers), even the C=O bond at 532.58 eV can be observed in the O 1s spectrum of the chitosan layer. In the C 1s spectrum (Figures 3(b), 3(c), and 3(d)), we only observed one peak at 284.98 eV for C-C in TNT sample, whereas some new peaks such as 286.18 eV for C-O, 289.88 eV for Mg-O-C in the PEG layer, 286.08 eV for C-N, and 287.68 eV for C=O in chitosan layer occurred. These results effectively demonstrated that PEG and chitosan layer successfully coated on the TNT surface.

3.2. Drug Release Characterization. As the derivation of erythromycin, roxithromycin can also react with concentrated H₂SO₄ so to exhibit a color change from colorlessness to yellow (shown in Figures 4(a)-4(c))[32]. This phenomenon can also be the evidence to prove the roxithromycin successfully loaded into the TiO₂ nanotubes. The shade of the color could indirectly reflect the release amount of roxithromycin and follow the sequence TNTD > TNTDP-CS > TNTDP-PEG, which was consistent with the drug release profile. The drug release profiles of roxithromycin loaded into TNT before and after coated a polymer layer (chitosan and PEG) are presented in Figure 4. A significant initial drug burst release during 12h in TNTD samples, in which the roxithromycin release amount reached $242.14 \pm 29.96 \,\mu\text{g}/$ ml. Although TNTDP-CS samples still occurred in the drug burst release which was similar to the TNTD samples, there was a significant reduction of burst release observed in the release profile (189.90 \pm 11.89 μ g/ml). Furthermore, up to the release time at 48 h, TNTDP-CS samples just released roxithromycin about $252.92 \pm 29.09 \,\mu$ g/ml (47.95%), much lower than that of the TNTD samples $(423.58 \pm 26.99 \,\mu\text{g/ml})$, 80.30%), which showed the overall release would be over 2 days with a slower rate of drug release (compared to the rate of burst release) so that the drug efficacy was extended. Contrarily, the TNTDP-PEG samples did not observe drug burst



FIGURE 5: The SEM images of surface topography of samples after immersing in PBS for 2 d, (a), (b) TNTDP-PEG samples and (c), (d) TNTDP-CS samples at different magnifications.

release instead of observing a slow and smooth linear release profile. The amount of drug released from sample to PBS was only $36.31 \pm 28.69 \,\mu$ g/ml during $48 \,h$, which inferred that the PEG layer with Mg particles deposited on TiO₂ nanotube surface would effectively hinder the diffusion of the drug from the nanotube structures (Figures 5(a) and 5(b)).

Figure 5 shows the nanostructures of TNTDP-PEG and TNTDP-CS after drug release for 48 h. We could significantly observe that the PEG coating was bitty and many Mg particles are deposited on TiO_2 nanotube surface (Figures 5(a) and 5(b)) because of the quickly biodegradable property of PEG. Unlike the TNTDP-PEG sample, the chitosan coating of the TNTDP-CS sample still preserved integrity with a little degradation (Figure 5(c)). But the adhesion of the coating to TiO_2 nanotube surface became weaker (Figure 5(d)) after 48 h of immersion so that may easily cause the exposure of drug-loaded nanotubes to PBS solution.

3.3. Antibacterial Activity of Roxithromycin Efficacy. To evaluate the extended roxithromycin efficacy, an experiment of the agar dilution method was adopted to examine by qualitative analysis directly. Figure 6 presented the evolution of the inhibition zone for TNT, TNTD, TNTDP-CS, and TNTDP-PEG samples during a time range of 24 hours on the agar plates. It was evident that the inhibition zone of TNTD was larger than that of TNTDP-CS, TNTDP-PEG, and TNT (without drug). The largest inhibition zone for TNTD was related to the drug fast release in the initial stage, and the inhibition zone will gradually shrink as the drug concentration gradually decreases around the sample; in other words, the concentration of the drug increased sharply within the first several hours and became almost asymptotic after 12 h, akin to the "burst" phenomena for drug delivery systems. After 12 hours, there was no significant variation in the inhibition zone for TNTDP-PEG because the drug-release equilibrium was attained and showed a steady consumption of the drug.

Obviously, it took a longer time for the TNTDP-CS sample to reach the drug-release equilibrium than the TNTDP-PEG sample. ccc evolution trend could be obtained for the TNTDP-CS sample anticipated. In addition, the slow drug releasing might be attributed to the degradation rate of polymer "capsule cap," which could restrict the transfer of the drug through the polymeric layer, thereby suppressing the drug leaching from the nanotubes to the immersion medium. The results were consistent with the previous examination of drug release, which demonstrated that electrodeposition of polymer coating on drug-loaded TiO₂ nanotubes would extend the drug efficacy.

4. Discussion

In this study, we constructed a biodegradable polymer layer coated on the drug-loaded TNT surface via electrochemical deposition, which no previous research had been reported. According to the SEM images in Figure 1, two kinds of uniform polymer layers (chitosan and PEG) were successfully coated on the TNT surface. Differed from other materials' mechanism of electrochemical deposition, chitosan was deposited on the cathode by the change of pH to form a layer [33, 34]. With continuous consumption of the chitosan around the cathode, the layer would occur undulation.



FIGURE 6: Photographs of the inhibition zone by the disk dilution assay.

Unlike the chitosan layer, undulation on the PEG layer was caused by Mg particles. The mechanism of electrodeposited PEG was accessed to the weak negative charge of ether bond on PEG molecular surface, which led to the result that it could not uniformly deposit on the cathode under pure PEG electrolyte (data not shown). When the PEG electrolyte extra added Mg^{2+} to increase the concentration of electrolytic ions, the mobility of ions was enhanced [35] and thus improved the deposition effect accompanied with Mg particles.

Moreover, the evidences in XPS (as shown in Figures 2 and 3) could directly prove the formation of polymer layers and their mechanism. The peak at 399.08 eV for N 1s in Figure 2(c), the C=O bond both in O 1s and C 1s spectra and the C-N bond at 286.08 eV in C 1s spectrum (Figures 3(a) and 3(d)) were the characteristic peaks on the main chain of chitosan without any change in functional groups of the backbone due to the deposition mechanism of chitosan. The supplied voltage, deposition time, and concentration of chitosan electrolyte were the factors that influenced the formation and thickness of chitosan coating. Also, compared with the TNT sample in Figure 3(b), the C 1s spectrum of the PEG layer coated on TNT (Figure 3(c)) was significantly changed, which inferred that due to the strong electronegativity of oxygen, Mg²⁺ would primarily react with the oxygen of the ether bond on PEG [36] chain to form a magnesium carbonate-like structure Mg-O-C that lead to the occurrence of the peak at 289.88 eV, then electrodeposited on the TNT surface with PEG. Additionally, different from chitosan coating, the major factors that influenced the formation and thickness of PEG coating were the concentration of PEG and Mg^{2+} electrolyte, which speculated that the higher concentration of Mg^{2+} in PEG electrolyte, the less roxithromycin release from the nanotubes (more Mg particles deposited on TiO₂ nanotubes surface, shown in Figure 5(b)).

As mentioned above, TiO₂ nanotubes as drug delivery system would lead to initial burst release; several techniques have been developed to prolong drug release from TNT, such as changed wettability of TiO₂ nanotubes surface to control the release rate for the hydrophobic drug [37, 38], constructed polymer coatings to close the pore of nanotubes [21, 39-41], and stimulated drug release by external factors [42-45]. Based on these previous researches, we hypothesized the electrochemical deposition of polymer layers could effectively reduce burst release and extend drug efficacy. The electrochemical deposition is a quick procedure finished within 5 min as well as the supplied voltage is very low (below 3 V), so we believe the voltage and the drug diffusion are negligible to affect the drug release. The drug release profile exhibited a first/zero release pattern (shown in Figure 4) and the initial roxithromycin release almost approached 50% in the TNTD samples. As a result of coating polymer layers, the significant changes of reduced burst release in the release profile (TNTDP-CS and TNTDP-PEG) were observed, which can be explained by the less exposure of drug-loaded nanotubes to PBS solution and slower drug diffusion during the degradation of polymers. Different degradation of polymers caused different drug release profiles, which was partially consistent with previous reports [21]. On the one hand, although the chitosan coating adhesion becomes weak accompanied by the coating degradation

(Figure 5(d)), it could still effectively cover TiO_2 nanotubes to prevent the roxithromycin release. On the other hand, though the PEG degraded quickly (Figure 5(a)), Mg particles embedded into PEG coating would become the obstacles on the pore of nanotubes to hinder the release of roxithromycin, and thus extend the drug release and efficacy. In general, coating polymer layers on TNTD can effectively reduce drug burst release and extend drug efficacy.

5. Conclusion

Nanoarray capsules, biodegradable polymer/TiO₂ nanotubes loaded with roxithromycin, were constructed via anodization and electrochemical deposition method on titanium foil. The SEM images after immersion in PBS for 48 h showed that the existence of Mg particles and slow the degradation rate of chitosan could effectively cover TiO₂ nanotubes to prevent the drug release. Furthermore, the polymer layers on the surface of drug-loaded TiO₂ nanotubes were able to significantly reduce the initial drug burst release, and the overall release would be over 2 days with a slower rate of drug release. Those results are widely applicable to various drugs and contribute to its application in dental, orthopaedical, and other biomedical areas.

Data Availability

The data used to support the findings of this study are included within the article.

Conflicts of Interest

The authors declare no conflict of interest with each other.

Authors' Contributions

Jianglin Ouyang and Haochao Huang contributed equally to this work.

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