

TiO₂ Nanotube Arrays Modified With Zinc and Loaded with Hydrophilic and Hydrophobic Drugs

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Abstract. TiO₂ nanotube arrays were prepared by anodization of Ti plat, then modified by hydrothermal method in Zn(NO₃)₂ solution and finally loaded alendronate or ibuprofen drugs by vacuum drying. The experimental results show that the amount of two drugs loaded on the modified TiO₂ nanotube array is increased. The release behavior of the modified nanotubes including burst release and sustained release. high hours before release. The modified TiO₂ nanotube arrays were more slowly released during the sustained release than unmodified nanotubes, indicating that the Zn²⁺ modified nanotubes have certain sustained-release effect.

1. Introduction

Bone disease, such as fracture, osteoporosis and bone cancer, can suffer people from some serious and chronic disease[1], in the field of oral surgery and orthopedic surgery, experts have made a lot of efforts and attempts, in order to make bone healing and bone growth rapidly at the period of osteogenesis component and bone model reconstruction[2-4]. During the bone metabolism, trace elements play an important role in the in vitro evaluation, which can accelerate bone regeneration. Zinc is one of essential trace elements, which has been proven to have direct effects on bone mineralization, especially in nucleation and the growth of minerals, in addition, by stimulating the assessment of the proliferation and mineralization of bone cells, the zinc in bone metabolism had demonstrated good assimilation effect[5-8]. so it plays an important role in skeletal development. Based on the important role of zinc ions in bone formation, a kind of zinc modified implant has been developed, for the zinc ions will released from the surface of the implant, which made it have special functions.

TiO₂ nanotube arrays have the regular hollow structure, so it has been used in the field of drug loading. In this paper, TiO₂ nanotube arrays were hydrothermal modified in zinc nitrate solution, and then loaded with hydrophilic drugs and hydrophobic drugs, the release behavior of TiO₂ nanotube array drug loading system in phosphate buffer solution (PBS) was investigated.

2. Materials and Method

2.1. Preparation of TiO₂ nanotube arrays

Titanium foils were cut into 1cm*10cm and successively polished by 280#, 320#, 400#, 600# abrasive paper until Ti surface was smooth and flat. TiO₂ nanotube arrays can be synthesized by anodic oxidation in the electrolyte contains 0.50 wt% NH₄F, glycerol and 10vol% H₂O at 60V and



30°C. After this, titania nanotube surfaces were rinsed with deionized water and then dried for subsequent use.

2.2. Hydrothermal treatment

Titanium sheet after anodic oxidation should be placed in 70 ml zinc nitrate solution, and be treated at 200°C for a certain time. After this process, the hydrothermal reactor should be cooled down at room temperature for 2h, then the titanium foils should be taken out, cleaned by deionized water and dried in 50°C. The next step was to change the hydrothermal treatment time (0.5h, 1.5h, 2h), in order to research and discuss the influence of different processing time on the drug loading amount. The surface morphology of the samples were studied by scanning electron microscopy (JSM-7500F).

2.3. Drug Loading and release

Add 10μL the alendronate and ibuprofen-ethanol solution respectively onto the surface of modified TiO₂ nanotube arrays, then dry these samples in a vacuum drying oven for 1 hour at room temperature (25°C). To make sure that an amount of drug was loaded into the nanotube, the loading and drying steps were repeated over 5 times.

Modified TiO₂ nanotube arrays loaded with drugs were put in 10ml PBS solution in a sample bottle. Then put the sample bottle in a constant-temperature water bath oscillator at 37.0°C at the speed of 100r/min. After a certain time interval, 0.5ml solution was removed to test the drug contents by UT1900 type double beam UV spectrophotometer.

3. Results and discussions

3.1. Morphology of TiO₂ nanotube arrays containing zinc titanate

Figure 1a shows the surface topography of the pure TiO₂ nanotube arrays prepared by anodic oxidation method. Figure 1b is the surface morphology of the above samples hydrothermal treated by zinc nitrate solution at 200°C. Compared with the figure 1, it can be found that the tube structure of TiO₂ nanotube array after the hydrothermal treatment can be seen clearly and almost unchanged, but the nanotube wall became obviously thicker. Figure 1d is the bottom of the TiO₂ nanotube arrays prepared in the above system, by contrast, figure 1c is the TiO₂ nanotube array after hydrothermal treatment. The results show that the whole interior of the nanotube had been successfully modified. The demonstration process is as follows: titanium and its oxide will form HTiO₃·nH₂O in alkaline solution (TiO₂+OH⁻+nH₂O → HTiO₃·nH₂O), under the condition of high temperature and high pressure, the reaction between the formation of titanic acid molecules and the precipitation molecules of Zn²⁺ around the feet can generate ZnTiO₃. Therefore, the collision reaction has no relation to the form of Zn²⁺ precipitation, the various forms of precipitation of Zn²⁺ can react with the titanic acid to produce zinc titanate, due to the large occupied space, the tube wall became thicker and the tube diameter became smaller.

In order to study the influence of hydrothermal time on the surface of TiO₂ nanotube arrays, TiO₂ nanotube arrays were hydrothermal treated in 0.01M zinc nitrate solution at 200°C respectively 0.5 h, 1.5 h, 2h. The surface morphology of the prepared samples is shown in figure 2. With the increase of hydrothermal time, the diameter of TiO₂ nanotube arrays were changed smaller and smaller, and it is almost impossible to see the TiO₂ nanotube arrays (figure 2c) when the hydrothermal time reaches 2h. The reason is probably because along with the prolonging of hydrothermal time, ZnTiO₃ are formed with the reaction of Zn²⁺ and TiO₂ nanotube arrays. Finally, a large number of ZnTiO₃ accumulated at outside tube with the continuous formation of ZnTiO₃, out of the pipe piles ZnTiO₃. Based on the above analysis, it is found that the hydrothermal time has a significant influence on the formation of ZnTiO₃ in the TiO₂ nanotube arrays.

In order to study the influence of hydrothermal temperature on the morphology of TiO₂ nanotube arrays. TiO₂ nanotube array were hydrothermal treated at 100 °C, 150°C and 200°C, as shown in figure. 3. With the increase of hydrothermal temperature, the diameter of TiO₂ nanotube arrays is more and

more small, and even some pipe is blocked, especially when the water temperature reaches 150°C. The reason may be that with the increase of hydrothermal temperature, more ZnTiO_3 are formed with the reaction of Zn^{2+} and TiO_2 nanotube. The higher the temperature, the faster the reaction, resulting in a large amount of ZnTiO_3 outside the tube.

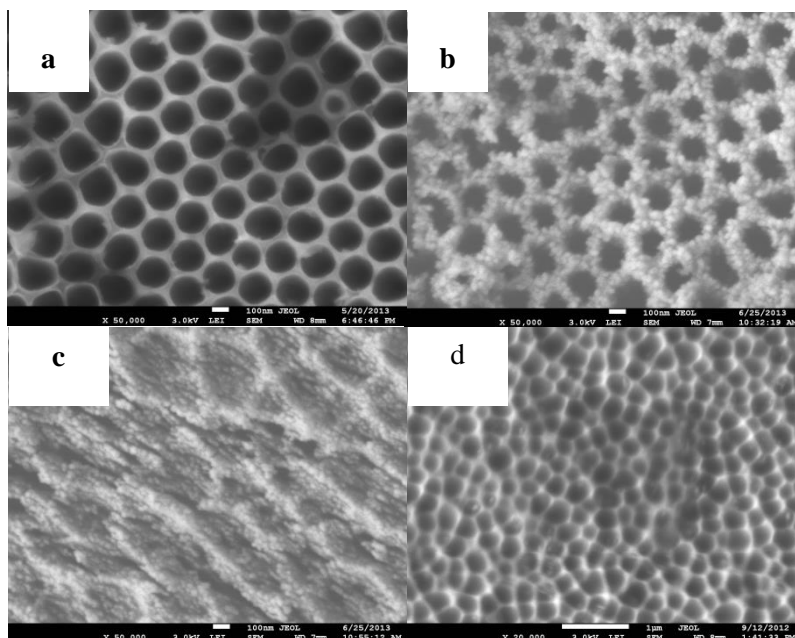


Figure 1. SEM images of modified and unmodified TNTs ,(a)(c)0.01M $\text{Zn}(\text{NO}_3)_2$ modified TNTs at 200°C with 0.5h; (b) (d) unmodified TNTs.

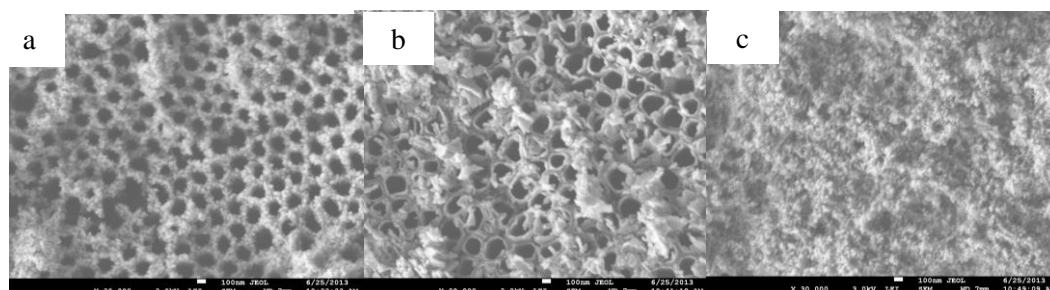


Figure 2. SEM images of modified TNTs hydrothermal at 200°C for 0.5h(a), 1.5h(b) and 2h(c)

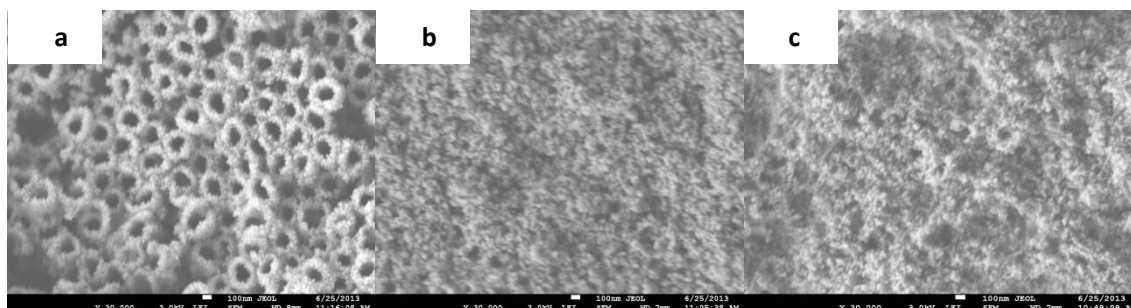


Figure 3. SEM images of modified TNTs hydrothermal at 100°C(a), 150°C(b) and 200°C (c) for 2h

3.2. Elemental analysis of TiO₂ nanotube arrays.

Figure 4 is EDS of TiO₂ nanotube arrays after 200°C hydrothermal treatment of 0.01M zinc nitrate solution at 0.5h. Analysis showed that the zinc(3.05%) had appeared in the amorphous TiO₂ nanotubes after hydrothermal treatment of zinc nitrate solution, which meant that the particles formed in the nanotube walls had already contained zinc element after the hydrothermal process. So it can be speculated that zinc had already been doped successfully into nanotubes.

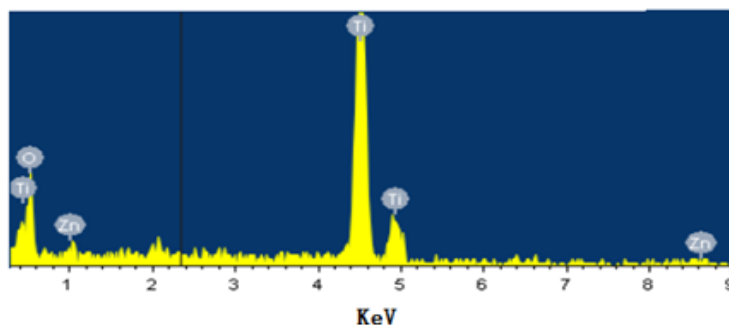


Figure 4. Energy spectrum analysis of TiO₂ nanotube array

3.3. Drug release process.

The alendronate and ibuprofen drug release curve of the zinc modified TiO₂ nanotube arrays and unmodified TiO₂ nanotube arrays were shown in Figure 5. Also, According to the two graphs, the release curves of the two loading systems are similar, and the drug release of the TiO₂ nanotube arrays modified with zinc titanate have the two stages: the early rapid release stage and the later slow release stage. The main reason of rapid release stage is that some of the drugs in the final vacuum drying failed to enter the nanotube interior, which had stacked on the nanotube nozzle and nanotube array surface, resulting in a sudden release. While the reason of the slow release is mainly from nanotube inside and drugs adsorbed in the tube wall. However, the slow release of the unmodified TiO₂ nanotubes was very poor, the drug was released completely at almost 24h. The reason is that the zinc titanate formed on the inner surface of the TiO₂ nanotube makes the inner part of the nanotube rough, and the drug was loaded inside the nanotube.

As for the ibuprofen drug release, there was a slow release after 150h, and the total amount of the drug had increased constantly. The reason may be that the diameter of the tube becomes smaller, the inside of the nanotube becomes rough, and the rough inner wall will make a positive obstruction in the drug release. All of these factors make it difficult to release ibuprofen particles inside the nanotube.

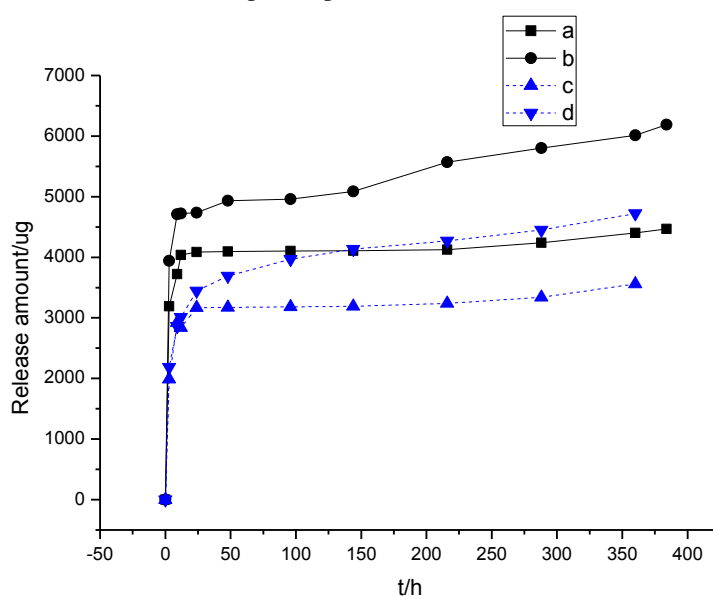


Figure 5. Comparative release of ibuprofen from modified TNTs (a) and unmodified TNTs(b), ibuprofen released from modified TNTs (c) and unmodified TNTs(d)

4. Summary

Modified TiO₂ nanotube arrays with zinc titanate were prepared by hydrothermal treatment, which can be loaded with hydrophilic and hydrophobic drugs via vacuum drying method, then the adsorption and release situation of hydrophilic alendronate and hydrophobic ibuprofen in modified TiO₂ nanotube arrays and unmodified TiO₂ nanotube arrays were compared. The sustained release effect of hydrophilic alendronate and hydrophobic ibuprofen in PBS solution were more obvious in TiO₂ nanotube arrays modified with zinc titanate, and had increased about 30%.

5. References

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Acknowledgments

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