Gentamicin-Loaded Borate Bioactive Glass Eradicates Osteomyelitis Due to *Escherichia coli* in a Rabbit Model

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The treatment of osteomyelitis induced by Gram-negative bacilli is rarely reported in the literature. This study established a rabbit tibia model of osteomyelitis induced by the Gram-negative bacillus *Escherichia coli*. Using this model, pellets composed of a chitosan-bonded mixture of borate bioactive glass and gentamicin were evaluated *in vitro* and *in vivo* for the treatment of osteomyelitis induced by *Escherichia coli*. Our results showed that the pellets in phosphate-buffered saline released gentamicin continuously over 26 days. Without the simultaneous use of a systemic antibiotic, the implantation of the gentamicin-loaded pellets into the osteomyelitis region of the tibia resulted in the eradication of 81.82% of infections, as determined by microbiological, histological and radiographic evaluation, and supported the ingrowth of new bone into the tibia defects after 6 weeks of implantation. The results indicate that the gentamicin-loaded borate bioactive glass implant, combining sustained drug release with the ability to support new bone formation, could provide a method for treating osteomyelitis induced by Gram-negative bacilli.

Osteomyelitis requires prolonged administration of systemic antibiotics, multiple surgical procedures, and long-term hospitalization in China. While the prognosis is uncertain and relapse rates are high, the huge therapeutic cost remains a challenge to the orthopedic surgeon. Theoretically, a local antibiotic delivery system is a reasonable solution, since it can provide a high dosage to the infected region without systemic toxicity and aid in the management of the dead space (1, 2). The first product on the market for local treatment of infected bone was polymethylmethacrylate (PMMA) antibiotic beads (such as Septopal). However, with this material, more than 90% of the trapped drug remains inside the cement beads. Furthermore, bone cement has to be removed by a second surgical procedure (3). Biodegradable polymers, such as polylactide-polyglycolide (PLGA), chitosan, or collagen, were also used as antibiotic-loaded systems. However, these systems cannot support osteoconductive bone ingrowth into the void and cannot maintain a constant release of antibiotics to cure the infection (3). To overcome these major limitations, antibiotics were added to osteoconductive bone fillers, such as calcium sulfate hemihydrate pellets (4) and tricalcium phosphate (TCP) (5). A limitation of TCP is that it degrades too slowly to match the bone regeneration rate (6). Calcium sulfate also has disadvantages, such as a transient cytotoxic effect, leading to inflammatory reactions, insufficient ability to stimulate bone regeneration, a high resorption rate, quick elution *in vitro*, friability, and low mechanical strength (7).

Borate glass was developed by replacing large amounts of silicon dioxide (SiO₂) in 45S5 bioactive glass with boric oxide (B₂O₃) and was found to have controlled and complete degradation properties, fair biocompatibility and bioactivity, and the ability to support the growth and differentiation of human mesenchymal stem cells (8–13). Our previous studies have shown that borate glass as a carrier of vancomycin or teicoplanin is successful at eradicating osteomyelitis induced by methicillin-resistant *Staphylococcus aureus* (MRSA) in a rabbit model, showing excellent biocompatibility and compressive strength, supporting full osteointegration with direct apposition of the newly formed bone, and stimulating bone regeneration as it degrades (7, 13).

*Staphylococcus aureus* remains the most common causative pathogen for osteomyelitis; however, Gram-negative bacilli are more common in adults with chronic or nosocomially acquired infections (14–17). In view of the fact that vancomycin and teicoplanin are not active against Gram-negative bacteria, the purpose of this study was to establish a model of osteomyelitis induced by *Escherichia coli* and to further evaluate the effects of borate glass as a gentamicin carrier on the treatment of osteomyelitis induced by Gram-negative bacteria in rabbits.

**MATERIALS AND METHODS**

Fabrication of gentamicin-loaded borate bioactive glass (GBBG) pellets. Borate bioactive glass (composition [mol%], 6 Na₂O, 8 K₂O, 8 MgO, 22 CaO, 54 B₂O₃, 2 P₂O₅) was prepared by mixing the required amounts of Na₂CO₃, K₂CO₃, MgCO₃, CaCO₃, H₂BO₃, and NaH₂PO₄ (analytical grade; Sinopharm Chemical Reagent Co., Ltd., China) and melting the mixture in a platinum crucible for ~2 h at 1,200°C. After the melting was quenched between cold steel plates, the glass was crushed, ground, and sieved to yield a particle size of <50 μm.

Preparation of drug-loaded pellets. Gentamicin powder (Hualuan Ltd. of North China Pharmaceutical Group Corporation [NCPC], China), glass particles, and chitosan solution (98% deacetylated), citric acid, and glucose (Sinopharm Chemical Reagent Co., Ltd., China) were mixed. The amounts of gentamicin powder, glass particles, and chitosan solution in the mixture were in the ratio of 11/23/48 (different concentrations of gentamicin):500:200 by weight; the amounts of chitosan, citric acid, and glucose were sufficient as determined by microbiological evaluation. The amounts of chitosan powder, glass particles, and chitosan solution were calculated to provide a constant antibiotic concentration of 5 mg/g for the different concentrations of gentamicin (500, 200 mg/g) as determined by microbiological, histological and radiographic evaluation, and supported the ingrowth of new bone into the tibia defects after 6 weeks of implantation. The results indicate that the gentamicin-loaded borate bioactive glass implant, combining sustained drug release with the ability to support new bone formation, could provide a method for treating osteomyelitis induced by Gram-negative bacilli.

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acid, and glucose in the solution were 1:10:20 by weight. The mixture was placed in a polyethylene mold, allowed to harden for 30 min, and dried for 24 h. Three kinds of pellets, containing 16, 32, and 64 mg/g gentamicin, respectively, were obtained. All pellets were prepared under sterile conditions. The gentamicin-loaded pellets were designated GBBG.

**In vitro elution study.** The three kinds of pellets were weighed, and the amounts of gentamicin were calculated theoretically before elution. Each size pellet was placed in 20 ml phosphate-buffered saline (PBS) (pH 7.4; 37°C), which was collected and replaced every 48 h until 26 days. Each collection of PBS eluate was stored at −20°C, and the concentration of gentamicin diffused from the pellets was measured from the PBS eluate within 7 days after collection. Each elution series was replicated three times.

The concentrations of antibiotic in the PBS eluate were determined from the assay standard curves for gentamicin by high-performance liquid chromatography (HPLC). The lower limit of detection was 0.1 μg/ml of gentamicin. The HPLC analyses were conducted on a Waters 600 multisilvent delivery system (Agilent Technologies, Palo Alto, CA, USA). The recovery rates were obtained by dividing the theoretical amount by the amount released.

**Bacterial preparation.** A standard strain of *E. coli* (ATCC 25922) (Department of Microbiology Laboratory of Shanghai Sixth People’s Hospital), which was sensitive to gentamicin, was used. The bacteria were stored on nutrient agar slopes (Oxoid, Basingstoke, Hampshire, United Kingdom) at 4°C. The inocula were prepared by subculturing the bacteria in 10 ml of nutrient broth (Oxoid) overnight at 37°C the day before inoculation. Each broth culture was then diluted in sterile PBS. The density of the inoculum was 10^8 CFU/ml of saline.

**Antibacterial activity.** The MIC of gentamicin for *E. coli* was determined by using an antibiotic 2-fold tube dilution method yielding drug concentrations of 0.05, 0.1, 0.2, 0.4, 0.8, 1.6, 3.2, 6.4, 12.8, and 25.6 μg/ml in two sets (unprocessed gentamicin and gentamicin released from pellets) of 10 tubes with 2 ml of sterile cation-supplemented Mueller-Hinton broth (Oxoid). One tube with no gentamicin (2 ml PBS) served as a control. The tubes were inoculated with *E. coli* prepared as described above at a density of 10^6 CFU/ml. The MIC was the lowest concentration of antibiotic that prevented turbidity after 24 h of incubation at 37°C.

**Animal model.** Thirty-five male New Zealand White specific-pathogen-free rabbits (age, 8 months; body mass, 2.34 to 3.4 kg [average, 2.8 kg]) were used. The study protocol was approved by the Animal Care Committee of Shanghai Sixth People’s Hospital, Shanghai Jiaotong University, Shanghai, China. All experiments were carried out in accordance with the guidelines of the local Animal Welfare Committee. During the study, animals were kept in individual cages under standard conditions (room temperature, 20 ± 0.5°C; relative humidity, 55% ± 5%; illumination, a photoperiod of 12 h of light and 12 h of darkness) and were allowed to be fully active. The rabbits were fed a routine diet.

Under intramuscular anesthetization (0.5 ml of ketamine [42.8 mg/ml] and 0.5 ml of xylazine [10 mg/ml] per kg of body weight), the right hind leg of each rabbit was shaved from the knee to the ankle, cleaned with povidone-iodine, and draped with sterile sheets. An 18-gauge needle was inserted percutaneously through the lateral aspect of the proximal tibial metaphysis into the medullary cavity. After the extraction of 0.3 ml bone marrow, 0.1 ml 5% sodium morrhuate (Eli Lilly, Japan K.K.), 0.1 ml *E. coli* (1 × 10^6 CFU/ml) in PBS, and 0.1 ml sterile PBS were injected sequentially.

The animals were physically examined weekly. Infectious symptoms and signs, such as weakness, loss of appetite, decreased mobility, degeneration of the operated limb, or flexion contracture of the affected knee joint, were observed and recorded. The infection was allowed to progress for 3 weeks, at which time the severity of osteomyelitis was determined radiographically.

**Treatment groups.** Four rabbits died due to septic complications after the induction of osteomyelitis and were excluded from any further study. The remaining 31 animals were randomly divided into three groups. Animals in group 1 (*n* = 11) were treated by debridement and implantation of GBBG beads (32 mg/g). Animals in group 2 (*n* = 10) were treated by debridement and implantation of pure borate glass pellets and 10 mg of gentamicin powder. Animals in group 3 (*n* = 10) were treated by debridement only. Each group was sacrificed 9 weeks after infection.

**Debridement and device implantation.** All animals were anesthetized again. The right hind leg was shaved, cleaned with povidone-iodine skin cleanser, and draped with sterile sheets again. A longitudinal incision of 2 cm was made at the proximal tibial metaphysis. A cortical bone window 1.5 cm long and 1 cm wide was created. Necrotic tissue was debrided through the window and the surrounding soft tissue until bleeding was observed. Purulent marrow was flushed out with sterile normal saline by using a 16-gauge catheter attached to a 10-ml syringe, inserted distally and proximally into the intramedullary canal. A sample of the debrided tissues was placed in a sterile tube for bacterial examination. If the entire bone was infected, another window was opened in the distal tibial metaphysis for debridement. After the surgical site was completely irrigated, the dead spaces were filled with different implants (−10 pellets) as described previously in the treatment group. The muscle flaps were realigned, and the deep fascia and skin were sutured in layers.

**Monitoring of rabbits.** Anteroposterior and lateral radiographs of the right tibia were taken immediately after the operation. All rabbits were examined clinically at 48-h intervals for the first week after the operation and weekly thereafter for as long as 6 weeks, with particular attention given to wound healing, limb mobility, signs of infection, and the rabbit’s ability to thrive. One rabbit from group 2 died due to an unknown cause at the first week after debridement and was excluded from any further examination. One rabbit from group 2 and two from group 3 died due to septic complications from the 4th to the 5th week after debridement and were included in further analysis, because the data could be obtained and had an influence on the effects of the last treatment. At the end of the study, the rabbits were sacrificed by intravenous injection of 2.5 ml of sodium pentobarbitone (200 mg/ml; Euthatal). The tibia was harvested for further evaluation.

**Microbiological evaluation.** Specimens were collected postmortem from the bone, marrow, and, if any, necrotic tissue at the site of infection. The specimens were placed in tubes and were sent to the laboratory, where they were incubated on blood agar for at least 48 h at 37°C. The plates were evaluated by a microbiologist for colony growth at 24 and 72 h. The isolates were analyzed by means of a Siemens MicroScan WalkAway 40S1 NC 31 automatic identification system (Siemens, Germany). The lower limit of detection was 1 CFU/g of *E. coli* for the infected tissue.

**Radiographic and histopathologic evaluation.** Anteroposterior and lateral radiographs of the right tibia were taken before the operation, after debridement, and before tibia harvest. One investigator (W. T. Jia), blind to the results, independently evaluated the radiographs to confirm the presence of osteomyelitis by using criteria described by Norden et al. (18). A numerical score was assigned to each variable. All scores were added to create a composite radiological score with a maximum of 6, representing radiographic severity.

The harvested tibia was fixed in 10% formal calcium for 7 days and in 4% Paraform for 3 days. Bone blocks were coded and were then cut from each tibia. The bone blocks were routinely treated and embedded. Sections (5 μm thick) in the longitudinal direction of the tibia were stained with hematoxylin and eosin (HE). All sections were examined and scored under conventional light microscopy by one pathologist, who was blind to the implantations and the results of the bacterial cultures. By using the criteria described by Smeltzer et al. (19), a numerical score was assigned to each variable, and all scores were added to create a composite histopathologic score with a maximum of 16, representing histopathologic severity. The degradation of implants and bone regeneration were also examined.

**Methods of data analysis.** Statistical analysis was performed by using SAS6.12 software (SAS Institute Inc., Cary, NC). Fisher’s exact test was used to compare the posttreatment positive rates of *E. coli* with each of the
three groups. One-way analysis of variance (ANOVA) was used to compare body weights, radiographic scores, and histopathologic scores of the three groups. If any significant difference was observed, the least-significant difference (LSD) test was applied to compare each of the three groups. The paired t test was applied to compare body weights and radiographic score changes, after treatment among each group. Data are reported at a significance level ($P$) of $<0.05$.

**RESULTS**

**In vitro study.** After gentamicin was incorporated into borate glass, the MIC for *E. coli* was 0.4 $\mu$g/ml, the same as that of unprocessed gentamicin. Gentamicin in borate glass powder was gradually released into the surrounding medium at concentrations sufficient to inhibit bacterial growth over 26 days (Fig. 1). The amounts of drug recovered at day 2, relative to the total amounts recovered over 26 days, were 39.6%, 87.03%, and 90.12% (wt/wt), respectively, for 16-, 32-, and 64-mg/g pellets. The cumulative percentages of antibiotic release were 46.56%, 55.59%, and 85.3%, respectively, for 16-, 32-, and 64-mg/g pellets. The burst effect was more intense with greater amounts of gentamicin in the pellets. The cumulative percentages of antibiotic release increased markedly as the amounts of gentamicin in the pellets increased (Table 1). Over all 26 days, the pellets kept their original shape but became more porous as the immersion time increased.

**In vivo study.** *E. coli* ATCC 25922 was detected in all 31 animals remaining at the third week after injection. The body weights of the rabbits at the times of infection, debridement, and sacrifice showed no significant differences between the three groups ($P$ = 0.864, 0.367, and 0.070, respectively, by one-way ANOVA) (Fig. 2). Average body weights decreased in all three groups at week 3 after infection, but increased by 0.37, 0.01, and 0.24 kg, respectively, for groups 1, 2, and 3 at week 6, at which time only the average body weight for group 1 exceeded that before infection. There were no significant differences in body weight changes within group 1 and group 3 ($P$, 0.077 and 0.068, respectively, by one-way ANOVA). Significant differences were observed within group 2 between body weights before infection and 3 weeks after infection and between body weights before infection and 6 weeks after treatment ($P$, 0.037 and 0.041, respectively, by the paired $t$ test).

Table 2 shows the results of microbiological examination following gentamicin treatment. Significant differences were observed between group 1 and group 2 and between group 1 and group 3 ($P$, 0.040 and 0.012, respectively, by Fisher’s exact test). GBBG cured 81.82% of the osteomyelitis in group 1.

Table 3 shows average radiographic and histopathologic scores. There were no significant differences among the radiographic scores of the three groups before treatment, but significant differences were observed after treatment ($P$, 0.000 by one-way ANOVA). By LSD multiple comparisons, significant differences were observed between group 1 and group 2 and between group 1 and group 3 ($P$, 0.001, and 0.003, respectively). Group 1 had the best radiographic scores after treatment among the three groups. A significant improvement in the radiographic scores of group 1 was observed after treatment ($P$, 0.000 by the paired $t$ test). The radiographic scores of groups 2 and 3 worsened after treatment, but there were no significant differences. Significant differences were observed among histopathologic scores between groups 1 and 2 and between groups 1 and group 3 ($P$, 0.014 and 0.004, respectively, by the LSD test). The average histopathologic score of group 1 was 3.82 ± 2.75, showing a treatment result better than those for group 2 and group 3.

Typical radiographs for the three groups are shown in Fig. 3.

**TABLE 1** Release of antibiotic from three kinds of pellets in vitro

<table>
<thead>
<tr>
<th>Concn of gentamicin in the pellet (mg/g)</th>
<th>Rate of recovery (%) on the 2nd day</th>
<th>Cumulative % of antibiotic released</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>39.6</td>
<td>46.56</td>
</tr>
<tr>
<td>32</td>
<td>87.03</td>
<td>55.59</td>
</tr>
<tr>
<td>64</td>
<td>90.12</td>
<td>85.3</td>
</tr>
</tbody>
</table>

**TABLE 2** Results of *E. coli* examination after treatment$^a$

<table>
<thead>
<tr>
<th>No. of animals</th>
<th>Group</th>
<th>Negative</th>
<th>Positive</th>
<th>Total</th>
<th>Clearance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>9</td>
<td>2</td>
<td>11</td>
<td>81.82</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>3</td>
<td>6</td>
<td>9</td>
<td>33.33</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>2</td>
<td>7</td>
<td>9</td>
<td>22.22</td>
</tr>
</tbody>
</table>

$^a$ Significant differences were observed between groups 1 and 2 and between groups 1 and 3 after treatment ($P$, 0.040 and 0.012, respectively, by Fisher’s exact test).
TABLE 3 Average radiographic and histopathologic scores of the three groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Radiographic score</th>
<th>Histopathologic score after treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>4.23 ± 0.96</td>
<td>1.82 ± 0.72</td>
</tr>
<tr>
<td>2</td>
<td>3.94 ± 0.95</td>
<td>4.28 ± 1.52</td>
</tr>
<tr>
<td>3</td>
<td>3.89 ± 1.24</td>
<td>4.11 ± 1.75</td>
</tr>
</tbody>
</table>

* Significant differences were observed between groups 1 and 2 and between groups 1 and 3 (P = 0.014 and 0.004, respectively, by the LSD test).

** Significant differences were observed by one-way ANOVA (P = 0.000). By LSD multiple comparisons, significant differences were observed between groups 1 and 2 and between groups 1 and 3 (P = 0.001 and 0.003; respectively).

Three weeks after the injection of *E. coli* into the tibia cavity, radiographic images showed the presence of osteomyelitis in all animals, along with bone destruction, new periosteal bone formation, and sequestrum formation. Six weeks after treatment, most of the implants in group 1 had been reabsorbed and replaced by new bone formation, and the infections were cured. Few implants in group 2 had been absorbed, and some were rejected due to worsening of the infection and poor blood supply. Inflammation and bone destruction obviously worsened for both groups 2 and 3.

Typical histological findings are shown in Fig. 4. For most of the rabbits in group 1, the treated tibia did not show macroscopic enlargement, and the histopathologic findings consisted of resorption of implanted pellets and new bone formation around and inside the implanted pellets. Osteogenic activity characterized by the presence of newly formed trabecular bone with a continuous coating of osteoblasts was clearly observed. There were also some macrophages surrounding the implants, indicating a kind of foreign-body reaction. Histopathologic findings for groups 2 and 3 consisted of marked infiltration of polymorphonuclear leukocytes, fibrosis with many proliferative lymphocytes and some plasma cells, fat necrosis, necrotic debris with pus cells in the center, sequestrum formation, destruction of bone, and subperiosteal new-bone formation, showing obvious osteomyelitis.

**DISCUSSION**

Although *Staphylococcus aureus* is still the main pathogen causing osteomyelitis, Gram-negative organisms also commonly cause such infections. Meyers et al. reported that osteomyelitis due to Gram-negative bacteria represented 28% of all cases of osteomyelitis (20). In one study of 55 patients, 32 had chronic osteomyelitis induced by Gram-positive and/or Gram-negative organisms (14). But there are very few experimental models of osteomyelitis induced by Gram-negative organisms. In this study, we have developed a rabbit model of *E. coli* osteomyelitis with pathophysiological, clinical, radiographic, and histological characteristics similar to those of human disease. By use of our model, osteomyelitis was developed in all 35 rabbits, with a low mortality rate (11.43%) and a high rate of recovery of the infecting organism (100%). In addition, we have further evaluated the efficacy of borate glass as an antibiotic vehicle in our model.

Gentamicin was selected as the antibiotic because it has strong antibacterial activity against all Gram-negative organisms and most Gram-positive organisms, especially against enterobacteria, and can maintain its activity over 6 months at room temperature (21). It also has joint action with teicoplanin and simultaneously compensates for the deficiency of teicoplanin and vancomycin, which are not active against all Gram-negative bacteria. Accordingly, in the treatment of combined bone infections caused by Gram-negative and Gram-positive organisms, especially infections with MRSA, two kinds of pellets, loaded with teicoplanin and gentamicin, respectively, could be used.

As an antibiotic carrier, the borate bioactive glass offers advantages. It can convert rapidly and completely into a hydroxyapatite (HA)-type material when immersed in PBS or simulated body fluid (SBF). This HA-type material has a porous structure that is an important requirement for scaffolds capable of supporting the transport of nutrients and new bone ingrowth. After being loaded with drug, the borate bioactive glass therefore served as a multifunctional device, initially providing a local drug release function and later serving as a scaffold for bone repair. At the same time, it can maintain its high compressive strength after immersion in SBF, as proved by our previous investigations (7, 13). It could also be used at a location where load bearing is required.

The MIC of the released gentamicin for the standard *E. coli* strain was identical to that of unprocessed gentamicin, indicating
that the antibacterial activity of the gentamicin was not altered following incorporation into the bioactive borate glass. In an attempt to decrease the burst effect of drug release, chitosan was used to bond the mixture of borate bioactive glass particles and gentamicin powder. In vitro, the released gentamicin maintained a concentration sufficient to inhibit bacterial growth during the whole study period. But on the second day, the burst effect of drug release seemed more intense as the amount of gentamicin loaded increased. This may be due to the simultaneous control of the drug release mechanism by diffusion and matrix degradation. After 26 days of immersion, 53.44%, 44.41% and 14.7% of the drug, respectively, was still trapped in the 16-, 32-, and 64-mg/g pellets. To balance the burst effect and the cumulative amounts of drug released, the 32-mg/g pellets were chosen in this study.

Six weeks after GBBG implantation, 2 out of 11 rabbits were positive for E. coli by culture, with poor radiographic and histopathologic scores. For the remaining 9 rabbits, all radiographic and histopathologic images and microbiological investigations showed that osteomyelitis was cured. In contrast, 1 out of 9 infections was cured for each of groups 2 and 3. Implantation of pure borate glass pellets and gentamicin powder (group 2) led to the same poor treatment result as debridement alone (group 3). This proved that GBBG also had a good delayed-release effect in vivo for gentamicin and that local implantation of gentamicin powder had no efficacy in osteomyelitis treatment. The fact that treatment with GBBG pellets alone yields an 81.82% cure rate in this study suggests that better results may be obtained if a systemic antibiotic is used together with GBBG pellets in a future study.

Radiographic and histopathologic images showed that the GBBG pellets were reabsorbed and replaced by new bone formation, findings consistent with those of our previous studies (7, 13). However, some foreign-body reaction around the material was also observed (Fig. 4), a finding inconsistent with our previous studies (7). The foreign-body reaction may be due to the addition of chitosan, an organic material degraded through phagocytosis by macrophages, being different from the conversion of borate glass to a HA-type material in the body fluids. In contrast, the area of implants and surrounding tissue in group 2 shows deteriorated bone infection and abscess formation but no sign of new bone formation. Our results demonstrate that the GBBG pellets first cured the infection by releasing the gentamicin loaded into them and then repaired the bone defect through new bone formation, promoted by the degradation of the borate glass.

In conclusion, the chitosan-bonded gentamicin and borate glass pellets cured the bone infection induced by E. coli and repaired the bone defects within 6 weeks of implantation in a rabbit tibia osteomyelitis model. This study demonstrates that borate bioactive glass can be used as a carrier of gentamicin not only to eradicate the osteomyelitis caused by Gram-negative bacteria but also, through the degradation of the borate glass, to repair the bone defect caused by infection.

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