Encapsulating PLGA Antibiotic Loaded Hip Prosthesis for Long Term Infection Prevention

1Lai, G A; 2Chen, K H; 2Chen M Y; 2Chen, S D; 1Hsu, C C; 2Yeh, M L
1National Cheng Kung University Hospital, Tainan, Taiwan, +2National Cheng Kung University, Tainan, Taiwan
mlyeh@mail.ncku.edu.tw

ABSTRACT INTRODUCTION:
Deep infection after artificial joint arthroplasty is considered one of the most devastating complications in orthopedics. Patients with deep infection may suffer multiple surgeries and long period of hospitalization. Some surgeons prefer cementless hip arthroplasty, so the infection prevention ability from current antibiotic loaded cement cannot be used in this approach. It is necessary to develop the prosthesis with auto anti-infection capacity. Ideally, the period of anti infection had better last up to 6 weeks.

Several biodegradable materials have been approved by FDA and used in clinic. Poly(lactic-co-glycolic acid) (PLGA) is the most popular and reliable polymer for this purpose so far. By controlling the molecular weight and concentration of PLGA, the degradation rate of PLGA can be controlled. The purpose of this study is using PLGA encapsulating antibiotic loaded sand blasted titanium disk to quantify the antibiotic release time by elution test.

MATERIALS AND METHODS:
Antibiotics, vancomycin and cefuroxime, were used in this study. 12 mg/ml antibiotic solution was directly dropped on the sand blasted titanium alloy discs. After water been evaporated, immersed discs into designed PLGA acetone solution for PLGA encapsulation. In order to prolong the antibiotic release period, double layer encapsulations were also prepared. The antibiotic used and PLGA encapsulation parameters were listed in Table 1.

Phosphate buffer solution (PBS) was used for elution test. The samples were immersed in 2 ml PBS and shaked continuously. The PBS was replaced with fresh PBS in 1, 6, 12, 24 h and everyday till end of the experiment. The extracted PBS was examined by spectrophotometer with wavelength set at 292 and 442 nm for antibiotic concentration of cefuroxime and vancomycin [1, 2]. The weight loss from PLGA degradation was observed by metallographic microscope.

The previous described minimum inhibition concentrations (MIC) of both antibiotics used in this study were verified by agar test. Antibiotics, vancomycin and cefuroxime, were used in this study. 12 mg/ml antibiotic solution was directly dropped on the sand blasted titanium alloy discs. After water been evaporated, immersed discs into designed PLGA acetone solution for PLGA encapsulation. In order to prolong the antibiotic release period, double layer encapsulations were also prepared. The antibiotic used and PLGA encapsulation parameters were listed in Table 1.

RESULTS SECTION:
The antibiotic release concentration reached the maximum at the first 6 hour for group B and C. However, group A and D showed smoother early antibiotic release curve. (Fig.1) The prescribed MIC for vancomycin and cefurixime were 2 and 8 μg/ml respectively and displayed obvious inhibition circle in our agar test. The effective anti-infection duration, eluted antibiotic concentration higher than MIC, for 4 hours. The PLGA degradation ratio showed group C had the highest degraded ratio. (Fig.2) However, group D with higher PLGA concentration of 2nd layer encapsulation displayed slower PLGA degradation rate. The microscopy images of discs after 5-day elution test showed the surface morphology after partial PLGA degradation. (Fig.3) Group C showed the highest pore formation on the surface.

DISCUSSION:
The results shows PLGA encapsulation actually extend antibiotic release period. Double layer encapsulation can even prolong the antibiotic release time up to 17 days. Because group D exhibited low degradation rate, it did not display obvious burst antibiotic release at early time. In group C, the same PLGA concentration for 2nd layer encapsulation with the 1st layer could dissolve the 1st layer degradation, so the early burst effect and shorter inhibition time occurred for this group. Although the proper antibiotic release period for anti-infection application on arthroplasty is 6 week, this multiple layer PLGA encapsulation may become an effective approach in long term antibiotic release. In conclusion, this study quantified the antibiotic release of the novel double layers PLGA encapsulating antibiotic loaded titanium disc up to 17 days. It could have potential to prevent orthopa stimulate invasion in the future.

Table1 Different encapsulating parameters of 4 groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Antibiotic Loading</th>
<th>1st PLGA Encapsulate</th>
<th>Antibiotic Loading</th>
<th>2nd PLGA Encapsulate</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Vancomycin 15%</td>
<td>15% mg/ml, 5 min</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>B</td>
<td>Cefuroxime 15%</td>
<td>15% mg/ml, 5 min</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>C</td>
<td>Cefuroxime 15%</td>
<td>15% mg/ml, 5 min</td>
<td>Cefuroxime 15%</td>
<td>15% mg/ml, 30 sec</td>
</tr>
<tr>
<td>D</td>
<td>Cefuroxime 15%</td>
<td>15% mg/ml, 5 min</td>
<td>Cefuroxime 30%</td>
<td>30 sec</td>
</tr>
</tbody>
</table>

REFERENCES: