In Vitro and In Vivo Evaluation of Gatifloxacin Biodegradable Implant for Treatment of Experimental Osteomyelitis

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Introduction

- Osteomyelitis (OM) is an inflammatory bone disease caused by pyogenic bacteria.
- In the treatment of chronic OM, antibiotic therapy alone has not always yielded satisfactory results.
- Therapeutically effective antibiotic concentration is not always achieved at the site of infection because bones are moderately perfused organs.

Objective

To design an implantable delivery system based on biodegradable polymer (polycaprolactone, PCL) for delivery of gatifloxacin (Gat) to treat OM experimentally induced in a rabbit model by methicillin resistant Staphylococcus aureus (MRSA).

Methodology

1. Preparation of implant: Solvent casting method.
2. Differential Scanning Calorimetry (DSC): 25-300°C.
3. Tensile strength: Tensile tester analyzer.
4. Organism: MRSA ATCC 33591
6. In vitro release: Concentration of drug released from implant in PBS was determined by disc diffusion assay.
7. In vitro inhibition: 5x10⁶ cfu of MRSA were inoculated into Mueller Hinton broth with and without implant. Bacterial inhibition by drug was calculated versus control.
8. Induction of osteomyelitis:
   - New Zealand white female rabbits were used.
   - Under anaesthesia, 18-gauge needle was inserted in the left tibial intramedullary cavity.
   - Sodium morrhuate, MRSA (1x10⁶ cfu), and sterile saline were injected sequentially.
   - A sterile stainless steel needle was inserted and left in the intramedullary cavity.
   - 2 weeks were given for development of OM.
9. Counts of MRSA in tibia: Bone homogenate was spotted onto blood and MSA plates in triplicates. Bacterial count was calculated per gram bone.
10. Bone debridement and insertion of implants:

   1. Cut was made in the cutaneous skin layer.
   2. An incision was made through the fascia.
   3. A gauze dissection was performed to separate the muscles and expose the tibia.
   4. Using two spatulae, the tibia was displayed.
   5. A bone flap was removed using a saw. The prepared implant was inserted.

11. In vivo release study: A disc diffusion bioassay using Bacillus subtilis (ATCC 6633) was used to measure gatifloxacin concentration 2 weeks after insertion of implant in bones.

Results

- The release showed a profile characterized by an initial burst followed by a second stage of gradual delivery over 27 days.
- Antibiotic concentrations achieved during the first 3 weeks after implantation, exceeded the MIC of Gat against MRSA.
- The infection was completely eradicated in all treated rabbits as indicated by the decrease in bacterial count.

Conclusion

Gatifloxacin-polycaprolactone implant may be a promising delivery system for treatment of osteomyelitis caused by MRSA.

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