

Oral presentation

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Rifampicin-loaded silicone: a new approach to tuning release rate with self assembled monolayers and cast molding

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Background

Treatment of CSF shunts with antimicrobial agents has shown great potential for preventing shunt infections. Providing a longer period of sustained antibiotic release is an important challenge to the development of clinical shunts for long-term implantation. This study aimed to evaluate the long-term *in vitro* drug release performance of cast-molded catheters with self-assembled silane monolayer coatings to provide a tuneable release rate.

Materials and methods

A cast molding approach was used to load rifampicin into the silicone precursor prior to curing. Self-assembled perfluorodecyltrichlorosilane (FAS) and octadecyltrichlorosilane (OTS) monolayers and FAS multilayers were deposited on the drug-loaded silicone surface by chemical vapor deposition and molecular vapor deposition, respectively. The morphology of adhered bacteria was observed by scanning electron microscopy and atomic force microscopy. The antibiotic release rate was determined by UV spectrometry. The efficacy of the rifampicin was determined by measurement of *S. epidermidis* adhesion on treated and untreated silicone surfaces using a colony counting method.

Results

The cast molding approach avoided the microstructural changes and minimized the initial "burst effect" compared with the diffusion-controlled technique. Compacted multilayered structures and sparsely-dispersed, single-layered structures of *S. epidermidis* colonization were observed on untreated silicone surfaces and rifampicin-loaded silicone surfaces, respectively. Deformation of the *Staphylococcus epidermidis* cells was observed. Sustained *in vitro* release from rifampicin-loaded silicone for at least 110 days at a level of approximately 2–4 µg/cm²-day was achieved. The rifampicin-loaded silicone decreased bacterial adherence by 99.8% on fresh 8.3% rifampicin-loaded silicone and by 94.8% on rifampicin-loaded eluted silicone. Additionally, FAS multilayers were effective in moderating the burst effect and achieving a longer-term delivery compared with FAS and OTS monolayers.

Conclusion

Incorporation of antibiotics into shunt catheters has been accomplished by others. However, the surfactant used in Cook Spectrum catheters to bind minocycline is toxic to nervous tissue, and drug release from Bactiseal™ catheters is reported to be only 28 days. Combining molecular vapor deposition of FAS or OTS with cast molding impregnation of rifampicin into silicone, we have pro-

longed drug release well beyond this time. Moreover, it was demonstrated that the FAS coatings are effective in controlling and tuning the drug release rate. Cast molding can be adapted to a host of pharmacologically active ingredients or combinations as desired and be applied to a variety of shunt-based drug release treatments. This novel coating approach can also create different designs for surface coatings to customize and tailor the delivery rates for specific patients.

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