151b Development of a Long-Lasting Silicone Catheter Impregnated with Rifamipicin

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Cerebrospinal fluid (CSF) diversion, or shunting, through a silicone catheter is the most common treatment for hydrocephalus and infection is one of the major complications of shunt treatment. Coating with antimicrobial agents on the device surface provides an alternate approach to minimize bacterial cell adherence. Two challenges to the development of clinical shunts for long term implantation are maintaining the structural integrity of the catheter materials and providing a long period of sustained antibiotic release. A cast molding approach was developed to load rifampicin into the silicone precursor before it was cured. It was found that this approach avoided the microstructural changes observed in samples prepared by the conventional diffusion-controlled technique and minimized the initial "burst effect" of drug release. Figure 1 illustrates the antibiotic release rate for two samples with 0.5% drug concentration prepared using the diffusion-controlled and the cast molding methods. Orders of magnitude higher release amounts were observed in the first 24 hours for the diffusion-controlled samples, which could be attributed to the greater quantities of drug crystals on or near the surfaces. Moreover, the burst effect could be tuned by introducing a self-assembly monolayer or multilayer of fluroalkylsilane (FAS). Drug release studies showed that the rifampicin loaded silicone can provide sustained release for least 90 days, which is considerably longer than reported for a commercial product. Quantitative comparisons of Staphylococcus epidermidis adhesion on untreated and rifampicin-loaded silicone surfaces have been evaluated in vitro. Microscopic techniques demonstrated that the morphology and growth of Staphylococcus epidermidis colonization was inhibited under the influence of the rifampicin. The rifampicin-loaded silicone prepared by this casting mold approach is suitable for future clinical applications and to minimize the catheter infections.

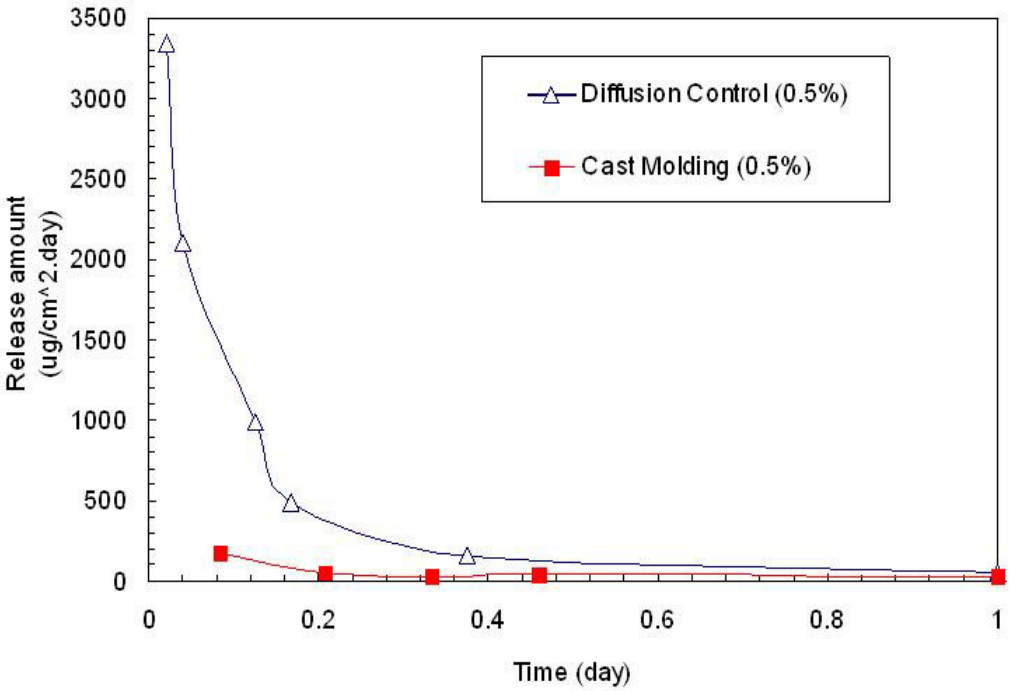

Figure 1. Burst effect behaviors of two rifampicin-loaded samples prepared by diffusion-controlled process (empty triangle) and cast molding (square) approaches. The burst effect of drug release was decreased dramatically by using the cast molding process