Tube – shaped Devices with Controlled Geometry for Programmed Drug Delivery

Min Park [1], Chun Gwon Park[1], SeungHo Lee[2], Eunbit Cho[2], Ji Eun Lee[2], Young Bin Choy[1, 2, 3, *]

[1]Interdisciplinary Program in Bioengineering, College of Engineering, Seoul National University, Seoul, 152-742, Republic of Korea

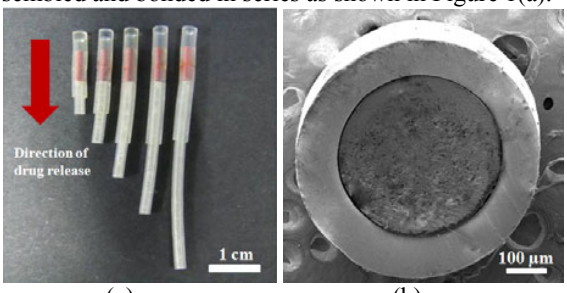
[2]Department of Biomedical Engineering, College of Medicine, Seoul National University, Korea, Seoul, 110-799, Republic of Korea

[3]Institute of Medical and Biological Engineering, Medical Research Center, Seoul National University, Seoul, 110-799, Republic of Korea

[*]ybchoy@snu.ac.kr

Statement of Purpose: Recently, a growing attention has been paid to drug delivery systems, most of which mainly focused on sustained drug release over a prolonged period of time. Indeed, the drugs, such as anti-inflammatory or anti-angina drugs, benefit from such delivery systems enabled with long-term drug release, hence enhanced drug bioavailability. However, this strategy does not always guarantee successful therapy as a drug regimen varies for each type of the drugs. For example, pulsatile drug delivery may offer more benefits for bioactive agents such as hormones or vaccines [1]. In this sense, a drug delivery device, which could be easily customized for accurately programmed drug delivery, should be advantageous due to many different types of the drugs. To achieve this goal, we developed tube-shaped drug delivery devices in this work. Two different tubes, each filled with a drug or a biocompatible polymer, polyethylene oxide (PEO), respectively, were assembled in series, where the former served as a drug reservoir (i.e., the drug tube) and the latter as a drug diffusion barrier (i.e., the PEO tube). The lengths of the PEO tubes were varied to control drug release from each of the assembled tubes. We were also to obtain a variety of drug release profiles (e.g., continuous and pulsatile drug release) by simply combining multiple assembled tubes.

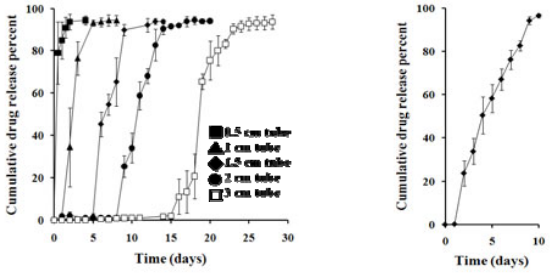
Methods: Each silicone tube (inner diameter = 1 mm and outer diameter = 1.5 mm) was filled with either a model drug (sodium fluorescein) or PEO (MW = 600,000). The drug tube was cut by 0.5 cm and employed as a drug reservoir. The PEO tube was cut by 0.5, 1, 1.5, 2 or 3 cm, respectively. Then, the drug tube and the PEO tube were assembled and bonded in series as shown in Figure 1(a).



(a) (b)

Figure 1. Images of the device and the PEO tube.

Results: As shown in Figure 1(b), the PEO could be densely and seamlessly packed in a tube. When the assembled tubes were immersed in the release media, the water reached the drug after a delayed period since the water penetrated via the PEO tube first. This delay was caused by slow dissolution of PEO and thus, the period of the delay depended on the length of the PEO tube. When the water eventually reached the drug, the drug dissolved and diffused out to the release media through the opposite direction of the water penetration into the assembled tube. Therefore, the period of drug release was also influenced by the length of the PEO tube. As shown in Figure 2(a), the onset time of drug release increased as the length of the PEO tube increased. The drug release started after 0.5, 1, 5, 8 and 15 days with the PEO tubes of 0.5, 1, 1.5, 2 and 3 cm, respectively. Therefore, by properly combining multiple distinct tubes together, we envisioned that pulsatile drug release should be possible. The periods of drug release could also be moderated by the length of the PEO tubes. After the delay, the drug was released in a sustained manner for 2, 4, 5, 7 and 10 days with the PEO tubes of 0.5, 1, 1.5, 2 and 3 cm, respectively (Fig. 2(a)). Therefore, we were again to combine multiple distinct tubes to obtain a continuous drug release profile. In this specific case, we employed the assembled tubes containing the PEO tubes possessing the lengths of a small difference to properly match the onset time of drug release from the longer PEO tube with the end time of drug release from the shorter PEO tube. As shown in Figure 2(b), we could achieve continuous drug release for about 9 days after 1 day delay with a combination of two assembled tubes, each containing the 1 cm and 1.5 cm PEO tubes, respectively.



(a) (b)

Figure 2. In vitro drug release profiles.

Conclusions: We have developed that the onset time and the period of drug release can be accurately tailored by controlling the length of the PEO tubes. A simple combination of multiple assembled tubes, each equipped with the PEO tube of different length, can achieve not only pulsatile but also continuous drug release. Therefore, we conclude that tube-shaped devices suggested in this work can be easily customized according to drug regimen, hence a wide applicability to many different types of the drugs.

References: M. F. Powell. Pharm. Res. 1996;13:1777-1785.