RELEASE OF ANTIBACTERIAL DRUG FROM SEGMENTED POLYURETHANE

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Abstract

The incorporation of antibiotic rifampicin into segmented polyurethanes and drug release has been described. Antibiotic-loaded polyurethane shows a high initial release rate and the matrix-controlled release for more 20 days. The release data depends on drug loading and polyurethane structure. The antibiotic-loaded polyurethane systems might be useful for prevent foreign body infection.

Key words: segmented polyurethanes, rifampicin, drug release.

Introduction

One of major problems in prosthetic medicine is the biomaterial-related infection. In most cases the antibacterial therapy alone can not cure the infection and the post-surgical removal of infected device or implant material becomes necessary. One of approaches to prevent foreign body infection is the incorporation of antibacterial agents into polymer. They might either inhibit the bacterial adhesion or kill adherent bacteria due to the continuous release of drug resulting in high local antibiotic concentration in the vicinity of the polymeric device or implant.

Segmented polyurethanes (SPU) are an important class of polymers that have found many applications as biomaterials due to excellent mechanical properties and relatively good biocompatibility. Many biomedical devices are made from SPU such as vascular prosthesis, catheters, blood pumps, heart valves and insulation for pacemakers [1]. However, like many synthetic polymers, polyurethane devices are susceptible to foreign body associated infection.

The purpose of the present study is development of polyurethane-based biomaterials with infection resistant properties. The incorporation of antibacterial drug rifampicin into SPU by solvent cast technique is described.. The drug release characteristics of such systems were also discussed.

Material and methods

Segmented polyurethane was obtained by two-step polymerization method using polypropylene glycol, toluene-2,4-diisocyanate and 1,4-butanediol as chain extender. Solutions of diisocyanate was placed in four-necked flask equipped with stirrer, nitrogen inlet, an outlet and thermometer and then the polyether diol solution containing 0,5 wt.% of catalyst was added slowly. The molar ratio of polyol and diisocyanate was 1:2,2. The reaction was carried out at 110-115^{o}C for

2 h in the nitrogen flow. Then the reaction mixture was cooled to room temperature and the chain extender was added slowly. The overall NCO:OH ratio was 1:1. The reaction mixture was placed in Teflon dish and dried under vacuum under at 50^{o}C. By varying the ratio of components SPU containing different hard and soft segment contents were synthesised. SPU was dissolved in an appropriated solvent and various amounts of antibiotic added to the solution. After careful evaporation of the solvent at 50°C, the drug-loaded films were furthermore evaporated for 24 h at reduced pressure to remove solvent completely.

The release behaviour of drugs from polyurethanes was examined by means of immersing the disc-shaped samples of 0,3-0,5 mm thickness and 10,0 mm diameter in a Ringer-Lock solution at 37°C. The amount of drug released was determined by UV-spectrometry by measuring the absorption maximum. UV spectra were recorded on a Jasco UV/VIS-7850 (Japan) spectrophotometer.

Results and Discussion

Segmented polyurethanes with different content of hard and soft segments were synthesised by two-step polymerization. The polyether diols were first reacted with two equivalents of the diisocyanate. Subsequent chain extension was obtained by reaction with an equivalent amount of a butanediol. Antibacterial drug rifampicin was incorporated as solution into the polymeric matrix. The obtained SPU films were contained homogeneously dissolved antibiotics.

The revenant parameters of the drug contained SPU were following: average molecular weight 160,000-210,000; content of hard segments 14.2-46.4 %. Polymeric mechanical properties were changed progressively with increasing of drug loading. Previously, we reported drug release from polyurethane materials in which different drugs were incorporated into polymeric matrix in a dispersed form [2, 3]. In this study the antibiotic release behaviour from SPU monolithic matrix into modelling biological media was analysed. The typical example of rifampicin release is presented at figure.

All the release data show the typical pattern for a matrix controlled mechanism. The cumulative amount of drug released from the polyurethane was linearly related to the square root of the time and the release rate decreased with time. The process is controlled by the dissolution of drug and diffusion through the polymer in accordance with Fick law. The total amount of rifampicin is released in 18-20 days.

Conclusion

The incorporation of antibiotics rifampicin into segmented polyurethanes to obtain drug delivery devices was described. Antibiotic-loaded polyurethane films show a high initial release

rate and the matrix-controlled release for more 20 days. The release data depends on drug loading and polyurethane macrodomain structure. The antibiotic-loaded polyurethane systems might be useful for prevent foreign body infection.

References

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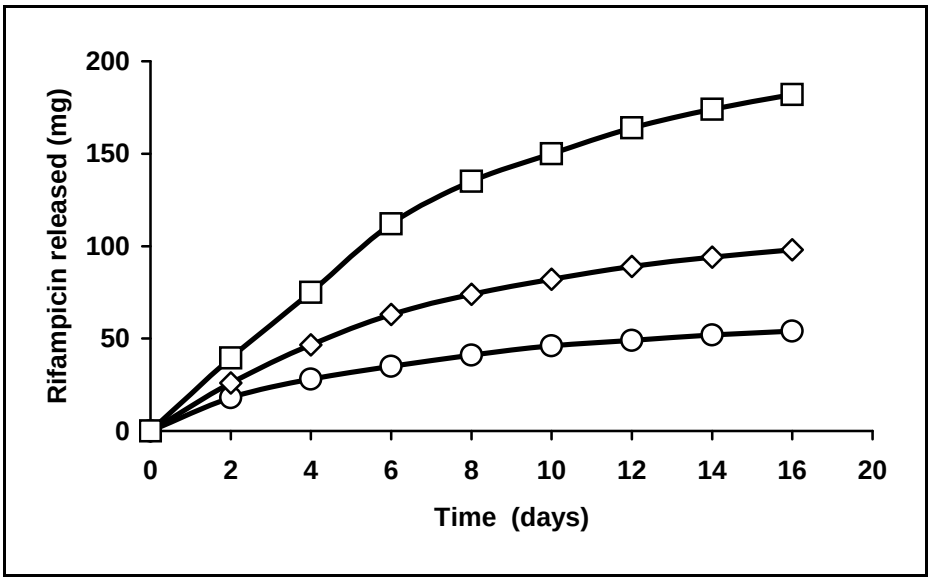

Figure. Release of rifampicin from SPU into Ringer-Lock solution at 37^{o}C.
Drug loadings (mg/g SPU): 100(O), 200(Δ), 300(□)