Drug Eluting Device References

Lubrizol LifeSciences’ thermoplastic polyurethanes (TPUs) are gaining momentum as a safe and reliable option for novel drug-delivery systems. Below is a partial list of publicly available papers, patents, and posters discussing TPUs’ benefits for use in vaginal, subcutaneous and oral drug delivery systems.

Review of Polyurethanes

Review of the variety of polyurethanes that are commercially available with a focus on those designed for the biomedical and pharmaceutical fields. A great variety of building blocks may be used to tailor the physical properties. The review focuses on biocompatibility and biodegradation and the use of PUs for the controlled release of drugs and biotherapeutics.

Vaginal Ring Design

“Intravaginal ring for the simultaneous delivery of an HIV-1 maturation inhibitor and reverse-transcriptase inhibitor for prophylaxis of HIV transmission”.

Intravaginal rings (IVRs) have emerged as cost effective way to deliver sustained release of drugs as compared to vaginal gels. Hydrophobic polyether polyurethane Intravaginal rings (IVRs) were investigated to deliver antiretroviral (ARV) drug in combination with a HIV reverse transcriptase inhibitor. The ARV used was N-[2-(3,4,5-trinemethoxybenzoylthio)benzoyl]-alaninamide (SAMT-10) and the HIV-1 reverse-transcriptase inhibitor used was pyrimidinedinone IQP-0528. SAMT’s are generally known to be hydrolytically unstable due to the thioester bond which poses a challenge to the design of the delivery system being used. Incorporation of the SAMT-10 and the IQP-0528 into the IVR by extrusion resulted in a matrix design. The drug loaded IVR’s when subjected to accelerated stability conditions of 40ºC/75%RH showed no degradation of the hydrolytically labile SAMT-10. The polyurethane matrix protects and prevents the degradation of SAMT-10. Further toxicological evaluations of these IVR’s indicated no evidence of formulation toxicity. SAMT-10 and IQP-0528 had different solubility in the polyurethane matrix, SAMT-10 had lower solubility. Presence of IQP-0528 increased the overall diffusivity of SAMT-10, whereas, the release of IQP-0528 was inhibited by the limited solubility of SAMT-10 in the matrix. Physical properties such as compression force of the IVR with the combination drugs was similar to the well accepted NuvaRing®. The study concluded that a sustained release of ARV in combination with a dual-acting entry inhibitor, IQP-0528, can be obtained through a polyurethane IVR.


Hydrophilic polyurethanes were explored as IVR materials to deliver hydroxychloroquine (HCQ, anti-HIV drug) for achieving sustained delivery (>14 days). The segmented structure of polyurethanes was found to be beneficial in obtaining a sustained release. HCQ release through both a matrix as well as a reservoir type IVR was evaluated and was found to be strongly dependent on the water swellability of the hydrophilic polyurethane. An initial burst release of HCQ in case of matrix design was controlled by coating it with either polyvinylpyrrolidone (PVP) or polyvinyl alcohol (PVA). A thin coating was effective in reducing the initial burst release of HCQ within the first 24 hrs. Reservoir type IVR’s were also fabricated from polyurethanes with different hydrophillicitics. Near zero-order release was obtained from a low-water-swellable polyurethane. Further, stability and toxicity of these IVR’s were tested and evaluated to be satisfactory warranting in vivo studies.
Physicochemical properties, mainly hydrophilicity. IVRs using polyurethanes for effective drug release. The versatility of polyurethanes was exploited to deliver drugs with varying the polyurethanes indicated that the IVR's were well tolerated in the vaginal cavity. This study successfully developed a new platform polyurethane. Toxicological evaluations to determine safety and efficacy of the drug dose released and the overall biocompatibility of also tested and found to have zero order release of TFV in vitro was obtained for 90 days through a reservoir IVR of a hydrophilic design was effective in delivering the 2 drugs in vitro at concentrations expected to be effective against HIV. A reservoir design was hydrophilic polyurethane segment provided greater TFV flux than conventional hydrophobic materials. The multi-segmented IVR hydrophilic polyurethane for controlled release of hydrophobic and hydrophilic drugs" Front. Chem. Sci. Eng., 8(4): 498-510. DOI: 10.1007/s11705-014-1451-9.

The versatility of segmented polyurethanes is demonstrated and the tailorability of those segments is emphasized as a key engineering tool to control drug release. Biocompatible and biodegradable polyurethanes were designed and release rates of model hydrophobic and hydrophilic drugs through then was determined. The release rates were determined in the presence and absence of enzymes to factor in the degradability of the polymer. A strong dependence of the polyurethane structure, hydrophobicity & degradability was observed on the degree of interaction with the drugs leading to differences in the release rates. The segmental structure and bi-phasic nature of the polyurethane allows for localization of the drugs depending on its size and hydrophilicity.


The HIV/AIDS pandemic and its impact on women prompt the investigation of prevention strategies to interrupt sexual transmission of HIV. Long-acting drug-delivery systems that simultaneously protect women from sexual transmission of HIV and unwanted pregnancy could be important tools in combating the pandemic. The article describes the design, in silico, in vitro and in vivo evaluation of a dual-reservoir intravaginal ring that delivers the HIV-1 reverse transcriptase inhibitor tenofovir and the contraceptive levonorgestrel for 90 days. Two polyether urethanes with two different hard segment volume fractions were used to make coaxial extruded reservoir segments with a 100mm-thick rate-controlling membrane and a diameter of 5.5 mm that contain 1.3 wt% levonorgestrel. A new mechanical diffusion model accurately described the levonorgestrel burst release in early time points and pseudo-steady state behavior at later time points. Tenofovir was formulated as a glycerol paste and filled into a hydrophilic polyurethane, hollow-tube reservoir that was melted-sealed by induction welding. These tenofovir- eluting segments and 2cm-long coaxially extruded levonorgestrel-eluting segments were joined by induction welding to form rings that released an average of 7.5 mg tenofovir and 21 mg levonorgestrel per day in vitro for 90 days. Levonorgestrel segments placed intravaginally in rabbits resulted in sustained, dose-dependent levels of levonorgestrel in plasma and cervical tissue for 90 days. Polyurethane caps placed between segments successfully prevented diffusion of levonorgestrel into the tenofovir-releasing segment during storage. Hydrated rings endured between 152 N and 354 N tensile loads before failure during uniaxial extension testing. In summary, this system represents a significant advance in vaginal drug-delivery technology, and is the first in a new class of long-acting multipurpose prevention drug delivery systems.


“Development and pharmacokinetics of a 90-day intravaginal ring for sustained co-delivery of the microbicide Tenofovir and contraceptive Levonorgestrel” Research Poster.

Segmented polyurethane intravaginal rings (IVRs) were investigated for the simultaneous release of a microbicide (Tenofovir, TFV) and a contraceptive (Levonorgestrel, LNG) for 90 days. A relatively hydrophobic polyurethane was used to form the LNG segment via hot melt extrusion and a hydrophilic polyurethane (~35% aqueous swelling) was used to form the TFV segment. The TFV polyurethane segments were hollow tube in which the TFV paste was filled and then the 2 segments were joined by induction welding. Near zero order release of TFV and LNG were obtained in vitro. In vivo studies in sheep also exhibited steady PK of both drugs which were comparable to IVR’s with TFV-only. The segmented IVR design showed remarkable mechanical integrity and also mechanical and chemical stability for a period of 5 months under accelerated conditions.


Prevention of sexually transmitted diseases such as HIV in poor countries has been an area of focus for decades. Intravaginal rings (IVRs) have been designed to empower women with the ability to control and prevent contraction of sexually transmitted diseases. Limitations in conventional IVR technology were identified and a new platform of IVR materials was developed to deliver antiretrovirals with diverse physicochemical properties and dosing requirements. The new platform of IVR technology was developed based on polyurethanes. Study suggested that parameters such as hard/soft segment ratio, chemical composition and degree of hydrophilicity were key in modulating drug release rates. Both matrix and reservoir type IVRs were designed and tested for drug release kinetics. A multi-segmented polyurethane IVR was designed to deliver dapivirine and tenofovir (TFV) due to their contrasting hydrophilicity. A hydrophilic polyurethane segment provided greater TFV flux than conventional hydrophobic materials. The multi-segmented IVR design was effective in delivering the 2 drugs in vitro at concentrations expected to be effective against HIV. A reservoir design was also tested and found to have zero order release of TFV in vitro was obtained for 90 days through a reservoir IVR of a hydrophilic polyurethane. Toxicological evaluations to determine safety and efficacy of the drug dose released and the overall biocompatibility of the polyurethanes indicated that the IVR's were well tolerated in the vaginal cavity. This study successfully developed a new platform IVRs using polyurethanes for effective drug release. The versatility of polyurethanes was exploited to deliver drugs with varying physicochemical properties, mainly hydrophilicity.
Intravaginal rings (IVRs) are promising devices for preventing sexual transmission of human immunodeficiency virus (HIV). A polyether urethane (PEU) elastomer IVR was prepared for the sustained delivery of UC781, a highly potent nonnucleoside reverse transcriptase inhibitor of HIV-1. A matrix rod of UC781 and PEU were hot-melt-extruded and show load-dependent diffusion-limited kinetics. The in vivo release in rabbits to the in vitro methods diffusion controlled method. A surface coating of PVP/glycerol helped prevent surface crystallization of UC781 during long-term storage. There was moderate stiffening upon storage. In vitro safety data showed good cell viability, tissue integrity and barrier function of EpiVaginal tissue culture. UC781 was formulated in a stable PU IVR and provided controlled release of UC781 both in vitro and in vivo.


A novel reservoir TFV intravaginal ring (IVR) was designed to maintain effective cervicovaginal concentrations. End-sealed controlled hydrophilicity polyetherurethane (PEU) tubing filled with a high-density TFV/glycerol/water semisolid paste IVRs were tested in vitro and an in vivo sheep model. In vitro, PEU with 35 wt% water-swelling showed approximately 10 mg/day release for 90 days and mechanical stiffness similar to that of the commercial NuvaRing. Two 90-day in vivo sheep studies demonstrated TFV pharmacokinetics against a TVF gel and safety. TFV vaginal tissue, vaginal fluid, and plasma levels were relatively time-independent over the 90-day duration at approximately 10(4) ng/g, 10(6) ng/g, and 10(1) ng/ml, respectively near or exceeding the highest observed concentrations in a TFV 1% gel control group. TFV vaginal fluid concentrations were approximately 1,000-fold greater than levels shown to provide significant protection in women using the TFV 1% gel. There were no toxicological findings following placebo and TFV IVR treatment for 28 or 90 days. Slight to moderate increases in inflammatory infiltrates in the vaginal epithelia were observed compared to naive animals. The controlled release of TFV from a PEU reservoir IVR demonstrated elevated sheep vaginal concentrations for 90 days and merits further evaluation as an HIV prophylactic.


Segmented polyether urethane (PEU) matrix intravaginal rings (IVRs) were fabricated to enable sustained release of two antiretroviral agents, dapivirine and tenofovir, to prevent the sexual transmission of the human immunodeficiency virus (HIV). The two drugs, hydrophobic dapivirine and hydrophilic tenofovir, were separately formulated into polymers with matching hydrophilicity via solvent casting and hot melt extrusion. The drug-loaded rods were joined together to form dual-segment IVRs. Compression testing of the PEU IVRs revealed that they are mechanically comparable to the widely accepted EVA-based NuvaRing IVR. Physical characterization of the individual IVR segments using wide-angle X-ray scattering and differential scanning calorimetry determined that dapivirine is amorphous and tenofovir crystalline within their polymeric segments. In vitro release of tenofovir from was sustained over 30 days while dapivirine exhibited linear release over the time period. A 90-day accelerated stability study confirmed that dapivirine and tenofovir are stable in the PEU matrix. Altogether, these results suggest that multisegment polyurethane IVRs are an attractive formulation for the sustained vaginal delivery of drugs with contrasting hydrophilicity such as dapivirine and tenofovir.

Subcutaneous Implants


Several aliphatic polyether polyurethanes are examined for their ability to control the rate of release (elution rate) of oxybutynin hydrochloride, USP, from subcutaneous implants.


The early development of a nonbiodegradable subcutaneous implant that uses select aliphatic polyether polyurethanes as semi-permeable membranes for the controlled pseudo-zero order release of risperidone, USP in both in-vitro and in-vivo models.
Body Compatibility Improvement


Polyether polyurethane (PEU) Tecoflex™ was surface-modified with the nonionic surfactant Tween80® PEU/T80 or the cell adhesive PLL-RGD peptide by an entrapment technique. Samples were implanted in the peritoneal cavity of Wistar rats for 30 days. Implants were retrieved and examined. It was observed that the peptide modified followed by the bare PEU surface exhibited severe inflammatory and fibrotic response with an average mean thickness of 19 μm and 12 μm, respectively. In contrast, PEU/T80 surface showed only a cellular monolayer of 2 μm–3 μm in thickness, with a mild inflammatory response and no fibrotic encapsulation. The peptide-modified substrate promoted an enhanced rate of macrophage cell fusion to form foreign body giant cell (FBGCs), whereas FBGCs were rarely observed on Tween80®-modified substrate. The expression levels of proinflammatory cytokines (TNF-a and IL-1ß) were upregulated on peptide surface followed by bare PU, whereas the cytokine expressions were significantly suppressed on PEU/T80 surface.

Oral Solid Dosage


“The production of hot melt extruded high drug load formulations with polyurethanes and dicarboxylic acids” A Master’s thesis dissertation, 2014, Ghent University, Department of Pharmaceutics.

Matrix type formulations were prepared using thermoplastic polyurethanes as excipients and incorporating high loading of drug via hot melt extrusion or injection molding. The objective of the study was to examine capabilities of polyurethanes for controlled drug release. The high drug loading would also enable reduction in the size of the formulation. Current excipient polymers are not capable of delivering controlled release with high drug loadings. Two polyurethanes were tested, a mid-durometer 100 shore A and a higher durometer 72 shore D. The 100A polyurethane was able to hold 65wt% drug and the 72D polyurethane was able to hold 75 wt% drug. Dyphylline was chosen as the model drug for this study. In order to obtained complete release of Dyphylline in 24 hrs, it was determined that the presence of a release modifier such as an acid was essential. Different dicarboxylic acids were investigated and their ability to control the release rate was attributed to the interactions between the Dyphylline and the acid, primarily hydrogen bonding. The study suggests full characterization be done on the drug-excipient interaction between the API and the dicarboxylic acid to rule out any long-term stability issues which might lead to toxicological concerns.


A polyether polyurethane (PEU), Tecoflex™, was evaluated as a microsphere matrix for the controlled release of theophylline. PEU microspheres containing theophylline were prepared by solvent evaporation from a dichloromethane solution of the polymer and drug. The dispersion medium was a dilute solution of poly (vinyl alcohol). Thirty-five percent theophylline microspheres with good spherical geometry were prepared. Drug release from the microspheres in simulated gastric gave a burst profile. Release from simulated intestinal fluids at 37ºC showed close to zero-order release. Attempts were made to modulate the release by incorporating poly(ethylene glycol) in the matrix and coating the spheres with paraffin wax. Preliminary data indicate that polyurethanes could be interesting matrices for controlled drug delivery.