Sustained Delivery Of Large Protein Immunoglobulin (IgG) Through Biodegradable Poly(Orthoester) Solid Implant

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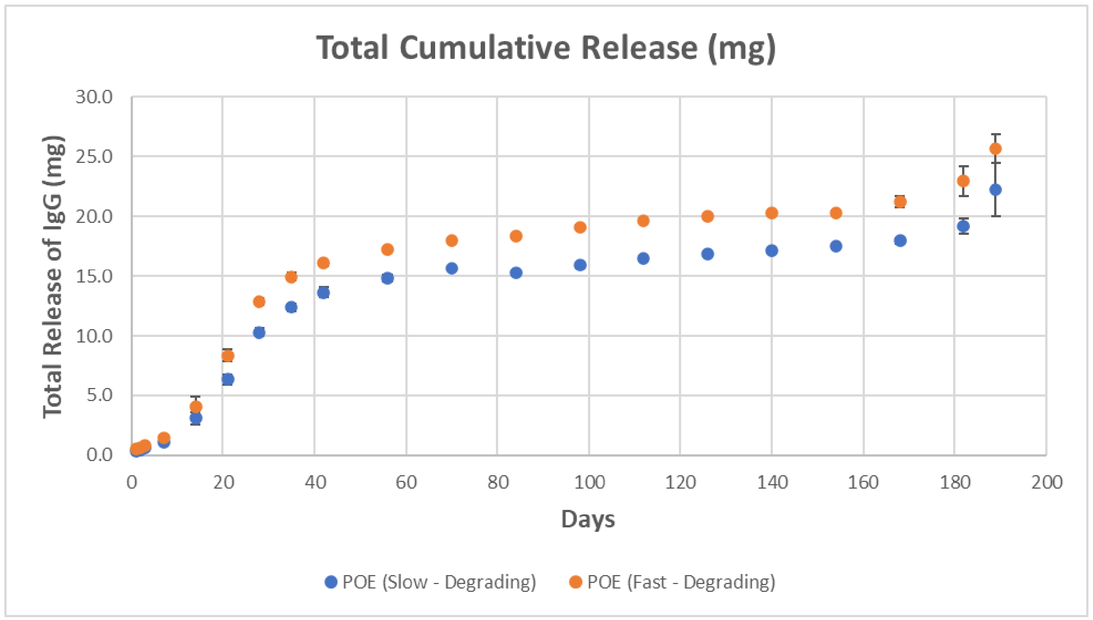
INTRODUCTION

Certain chronic diseases require long-term infusion treatments or frequent bolus injections of large proteins such as monoclonal antibodies. High treatment frequency often leads to compliance issues and increased patient treatment burden. To address these issues, a drug delivery system is needed that can provide sustained delivery of large proteins for over six months. Drug eluting solid implants are a promising method for long-term drug delivery, as they offer less frequent dosing. This contribution explores the development and processing of polyorthoester (POE) biodegradable polymer-based drug eluting implants for the release of immunoglobulin (IgG) for six months.

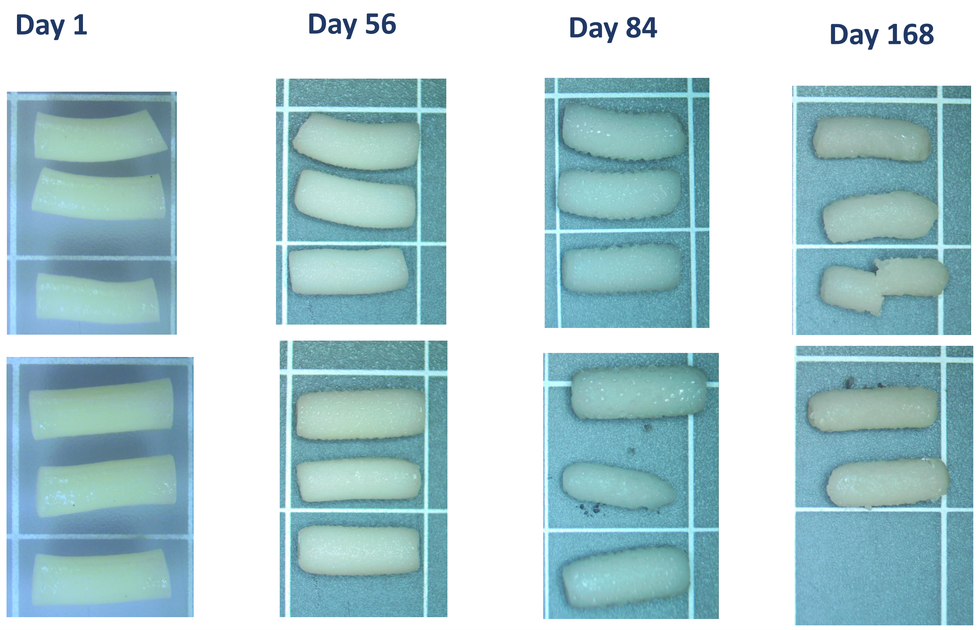
IMMUNOGLOBULIN RELEASE FROM POE (26 WEEKS)



BIODEGRADABLE POLY(ORTHOESTER) SOLID IMPLANT

POE Formulation Slow Degrading

POE Formulation Fast Degrading



RESULTS

Sustained release of IgG was demonstrated for six months. The slow-degrading POE formulation shows slower release by cumulatively releasing approximately 19.2 mg of the IgG over 6 months. However, the fast-degrading formulation shows faster release by cumulatively releasing approximately 23.1 mg of the IgG over 6 months. Both slow and fast degrading POE polymers have demonstrated degradation via changes in surface topography. At the end of the six months, the slow degrading POE showed 48% of total drug release while the fast-degrading POE showed 55% of total drug release.

METHODS

Two POE polymers (one slow-degrading formulation and one fast-degrading formulation) were used to achieve different release kinetics. 45% by weight-loaded IgG implants (N=6) were made from each polymer formulation via hot melt extrusion. The implants were made into cylindrical shapes measuring 3.5 mm in diameter and 1cm in length. The implants were weighed and placed into Eppendorf tubes with buffer solution (pH =7.4). The tubes were placed into incubators at 37°C and 100 rpm, and periodically sampled over the course of six months. HPLC–UV was performed to quantify IgG release. Light microscopy techniques were utilized to understand the degradation behavior of the polymers.

CONCLUSION

A solid POE implant with IgG (45 wt%) was successfully produced via hot melt extrusion. The release data indicated that a POE implant can provide long-term delivery of IgG. The degradation rate of the polymer will impact the release kinetics. This polymeric drug delivery system can be applied to a wide range of therapeutic areas to create long-acting implants for monoclonal antibody drug delivery.

PRESENTER BIOGRAPHY

Dr. Harsh Patel is team leader and senior formulation scientist developing materials and technologies for long-acting drug delivery. His areas of interest include long-acting dosage forms for oncology, ophthalmology, and women's health applications.

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