Development of Chitosan Based Methotrexate (MTX) Micro-implants to Treat Intraocular Lymphoma

S. Manna, J. J. Augsburger, Z. M. Correa, J. A. Landero, P. Kodali, R. K. Banerjee
University of Cincinnati

Purpose

Intraocular Lymphoma (IOL) is a rare form of lymphoma which is encountered in ocular oncology practice. In recent years, the most preferred treatment has been intravitreal MTX injection, which often results in undesired systemic toxicity. A sustained release device to administer therapeutic levels of MTX is required to avoid the complications encountered in the intravitreal injections. The *scientific objective* of this research is to develop a biodegradable MTX micro-implant and assess its toxicity, safety and drug efficacy by implanting it in the vitreous section of the eye. Chitosan (CS) would be used as the polymer matrix for the implant because of its biocompatible and biodegradable nature. Also, the numerous studies done involving CS with MTX prove the mutual compatibility of the two key constituents of the micro-implant.

Methods

MTX is mixed with low molecular weight chitosan (LMCS) in dilute HCl to make different mixtures of drug loading (Table 1). These mixtures are then injected into sterilized Tygon tubing (1/16 in I.D). The tubes containing the mixture are lyophilized to obtain LMCS-MTX fibers. The fibers extracted from the Tygon tubing are cut into desired implant lengths. The LMCS-MTX fibers are then dip coated in Polylactic Acid (PLA; MW 150,000) for a hydrophobic surface coating.

Results

Dimensions. The dimensions of the implants are obtained using optical microscopy. The diameter of the cross section of the uncoated implant B is 0.70 ±0.03 mm and that of the PLA coated implant A is 0.90 ±0.04 mm (Figure 1).

Release Rate. The in-vitro drug release rate profile is studied using UV-Visible Spectrophotometer (MTX characteristic peaks-258, 302, 372 nm). Initial release rate data obtained from implant C (1.14 ± 0.05 mm) have shown a therapeutic drug release rate (0.2-2.0 µg/ day) for a period of 50 days (Figure 2).

Conclusion

This implant is unique considering its shape and constituents. The development of biodegradable micro-implants for sustained release of hydrophilic drugs over 50 days is important for treating a wide spectrum of intraocular diseases like IOL.

Table 1. Summary of implant drug loading and dimensions

Implant (n=3)	MTX Drug loading (w/w %)	PLA coating	Dimensions (mm)	
			Length	Cross section (Mean ± SD)
A	25	Coated	4.2	0.90 ± 0.04
B	25	Uncoated	4.0	0.07 ± 0.03
C	10	Coated	4.4	1.14 ± 0.05

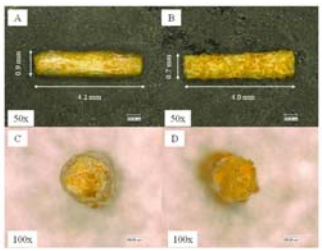

Figure 1. A. Top View of Coated Implant A; B. Top View of Uncoated Implant B; C. Cross section of coated Implant A showing PLA coating on the edge; D. Cross section of uncoated implant B.

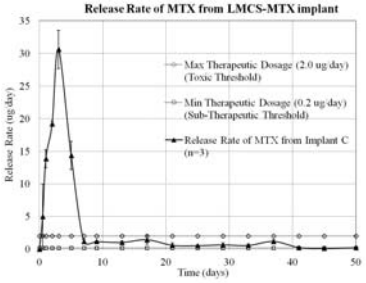

Figure 2. MTX release rate profile from Implant C