Ethoxyethyl Methacrylate Based Copolymers: A Novel Platform for Drug-Eluting Stent Coatings

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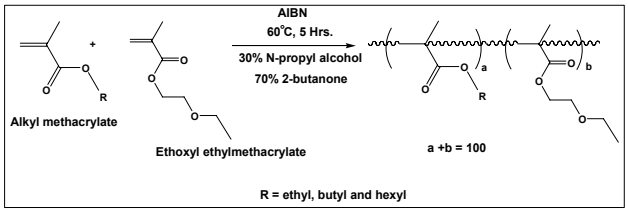
INTRODUCTION

Drug eluting stent (DES) therapy in coronary intervention has made a significant difference in lowering restenosis rates from ~30% for the bare metal stents to the present single digits[1]. Local drug delivery is achieved through biostable or bioabsorbable polymer coatings[2]. Polymer composition plays an important role in determining drug release kinetics and biocompatibility. Designing a polymer becomes a challenge since we have to accommodate hydrophobic anti-proliferative and anti-inflammatory drugs and at the same time build a hydrophilic character to obtain biocompatibility. Here we describe a series of copolymers composed of hydrophobic alkyl methacrylates and hydrophilic ethoxyethyl methacrylate (EOEMA) for Rapamycin eluting stent coatings..

MATERIALS AND METHODS

Copolymer Synthesis and Characterization:

EOEMA/alkylmethacrylate copolymers were synthesized using free radical polymerization in solution (Scheme 1). The alkyl group in the methacrylates and the monomer ratios were varied.



Scheme 1.Synthetic procedure for the EOEMA-copolymers

GPC was used for molecular weight measurement and NMR was used for structure and composition determination. DSC was used to determine the glass transition temperature (Tg). Properties of the copolymers are summarized in Table 1.

Stent Coating Process and Coated Stent Evaluation:

Primed Medtronic Driver stents were spray-coated using copolymer solutions in tetrahydrofuran comprising 30 wt.% Rapamycin. Coating durability was evaluated using internal Medtronic protocols. Rapamycin elution from EtO-sterilized stents was determined *in vitro* in a buffer at 37°C using HPLC

RESULTS AND DISCUSSION

A blend of polar and non-polar solvents to match the imbalance of monomer polarities was helpful in maintaining homogeneity during polymerization. NMR indicated that the compositions of the EOEMA/alkylmethacrylate copolymers prepared were in close correspondence with the monomer feed composition. GPC showed that all copolymers had relatively high molecular weights with narrow molecular weight distributions. Tg's of the copolymers were in line with their compositions. With increasing EOEMA-content, the Tg's decreased, as indicated in Table 1. Presence of Rapamycin increased Tg of all EOEMA-copolymers, indicating good compatibility between Rapamycin and the copolymers. Rapamycin release from the EOEMA-homopolymer C96, was fast whereas presence of alkylmethacrylate units in the copolymers significantly slowed the release. This effect was caused by the increase of Tg due to the presence of the alkylmethacrylate units.

Table 1. Properties of the EOEMA-copolymers

Polymer	EOEMA	Alkylmethacrylate		Tg C
	Molar %	R =	Molar %	
C96	100	N/A		-6
C124	N/A	Hexyl	100	-10
C91	28		72	-9
C82	52		48	-8
C92	76		24	-3
C123	N/A	Butyl	100	25
C93	27		73	11
C94	48		52	7
C95	73		27	2
C122	N/A	Ethyl	100	64
C97	20		80	45
C98	40		60	30
C99	70		30	11

CONCLUSIONS

The objective of the present study was to explore whether EOEMA-based copolymers would offer good potential in terms of elution control and durability, in order to be used as a coating in a DES system. The EOEMA-based copolymers met all requirements set for DES coatings with respect to drug elution and durability. The easy synthesis of these copolymers make them particularly suitable for future generation coatings, since these copolymers allow for precise control of drug elution rates.

REFERENCES

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