

AB₂ Miktoarm Star Polymers [PLGA-(MPEG)₂] as Nanocarriers for Drug Delivery

Ing Hong Ooi^{*}, Yie Kie Chong

International Medical University
126, Jln Jalil Perkasa 19, Bukit Jalil, 59000 Kuala Lumpur, Malaysia.
*inghong_ooi@imu.edu.my; chong.yiekie@student.imu.edu.my

Ismail Zainol

Universiti Pendidikan Sultan Idris, Department of Chemistry
Faculty of Science and Mathematics, 35900 Tanjong Malim, Perak, Malaysia
ismail.zainol@fsmt.upsi.edu.my

Extended Abstract

Among many biodegradable and biocompatible polymers, poly(Lactide-co-glycolide) (PLGA) copolymers are most widely investigated for various biomedical applications such as vaccination, drug and gene delivery, and tissue engineering (Danhier et al., 2012). Several innovative products of these polymers are in clinical use today. The biodegradability and biocompatibility of these polymers and, thus, bioresorption of degradation products remains as the primary attraction for further exploration. However, due to its high hydrophobicity, PLGA has some limitation in practical release formulation. Research focus over the last two decades has since been directed towards various approaches to overcome the disadvantages of these polymers. One important strategy is to conjugate PLGA with Poly(ethylene glycol) (PEG) through copolymerization, producing PLGA/PEG based AB diblock (Beletsi et al., 1999), ABA (Kissel et al., 2002) or BAB triblock (Jeong et al., 2000), multi-block (Huh and Beae, 1999 and Bae et al., 2000), branched block (Hrkach et al., 1997), star-shaped block (Breitenbach et al., 2000) and graft block (Jeong et al., 2000) copolymers, which has enabled a broader application in drug delivery and tissue engineering. This novel improvement in PLGA material performance is attributed to PEG having good hydrophilicity, antiphagocytosis against macrophages, resistance to immunological recognition, non-combination with proteins, chain flexibility, in addition to being biocompatible and biodegradable. Research has also shown that PLGA-PEG block copolymers are able to self-assemble into nanomicelle, with PLGA as its hydrophobic core and PEG as its hydrophilic corona shell. The PLGA core of the micelles can be loaded with poorly water soluble drugs, while the PEG shell provides colloidal stability *in vitro* and *in vivo*. In fact, the prospective utility of polymeric micelles as nanocarriers for drug and gene delivery has been largely demonstrated through preclinical and clinical trials (Nishiyama and Kataoka, 2006).

Miktoarm (mixed-arm) star polymers are of interest due to their intriguing properties which can be tailored by varying their polymer arms (Khanna et al., 2010). The AB₂ miktoarm star polymers composed of one arm of the polymer A and two arms of the polymer B. The synthesis of AB₂ star-branched polymers is reported in the literature, which involved a combination of different polymerization techniques (Khanna et al., 2010 and Lapienis, 2009). Synthetic strategy of AB₂ type miktoarm star polymers can be accomplished by using “core first” method which involves a polymerization using a multifunctional initiator or “arm first” method through which linear polymer arms are coupled to a multifunctional linking agent.

Recent study has shown that the water soluble anticancer drug doxorubicin (DOX) hydrochloride was successfully encapsulated into nano-sized miktoarm PEG-*b*-(PLLA)₂ star copolymer and had sustained *in vitro* release (Yin et al., 2009). In a most recent study, it was reported that monomethoxy poly(ethylene glycol)-*b*-poly(L-lactide-co-glycolide)₂ was shown to have good *in vitro* release behavior

that could be adjusted by the content of hydrophobic PLGA and pH of the release medium. In vitro cell experiments showed that the intracellular DOX release could be adjusted by content of PLGA (Li et al., 2012). The aim of this study is to synthesise and characterise AB₂ type miktoarm star polymers, i.e., PLGA-b-(MPEG)₂ having MPEG (monomethoxy Poly(ethylene glycol)) and PLGA blocks of different molecular weights. Preliminary results on the synthesis and characterisation, its ability to form nanoparticles will be discussed. Critical features of the polymeric nanoparticles as drug carriers including particle size and zeta potential, micelle stability, encapsulation efficiency, loading capacity and release kinetics of drugs will be discussed.

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