A NOVEL POLY (ETHYLENE GLYCOL) METHYL ETHER-BLOCK-POLYESTER COPOLYMER DISPERSANT FOR MAGNETIC CORE-SHELL NANOPARTICLES

SUPACHAI MEKKAPAT

A Thesis Submitted to the Graduate School of Naresuan University
in Partial Fulfillment of the Requirements
for the Master of Sciences Degree in Industrial Chemistry
May 2011

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This thesis entitled "A novel poly(ethylene glycol)methyl ether-block-polyester copolymer dispersant for magnetic core-shell nanoparticles" submitted by Supachai Mekkapat in partial fulfillment of the requirements for the Master of Science Degree in Industrial Chemistry is hereby approved.

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Supachai Mekkapat

Title	A NOVEL POLY (ETHYLENE GLYCOL) METHYL ETHER-BLOCK-POLYESTER COPOLYMER DISPERSANT FOR MAGNETIC CORE-SHELL NANOPARTICLES
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ABSTRACT

We here report the synthesis of magnetite (Fe_3O_4) nanoparticles coated with methoxy poly(ethylene glycol) (mPEG)-polyester amphiphilic block copolymers to obtain hydrophobic inner layer of polyester and hydrophilic corona of mPEG for efficient entrapment of an indomethacin model drug. The copolymer dispersants were prepared *via* a direct condensation between diacid and diol compounds and mPEG oligomer to obtain hydrophobic polyester block and hydrophilic mPEG block. Diacid compounds (malonic acid or maleic acid), diol compounds (ethylene glycol, 1,6-hexanediol or 1,12-dodecanediol) were used to investigate the influence of the polyester compositions on the stability of the particles. In addition, two different molecular weights of mPEG (2,000 and 5,000 g/mol) were used to study the effect of the hydrophilic block length on dispersibility of the particles in water. It was found that the copolymers prepared from 1,6-hexanediol can effectively stabilize the nanoparticles in water regardless of the types of diacid and $\overline{M}_n$ of mPEG used. The nanoparticles were about 10 nm in diameter and exhibited superparamagnetic behavior at room temperature with saturation magnetization about 40 emu/g magnetite. Thermogravimetric analysis (TGA) revealed the existence of less than 37% Fe_3O_4 and about 50% of the copolymer in the complexes.

The suitable compositions of mPEG-polyester copolymer were selected from the above studies for the synthesis of three types of the copolymer-magnetite complexes for entrapment of indomethacin; the particles coated with saturated,

aqueous dispersions. Vibrating sample magnetometry (VSM) signified the superparamagnetism of the complexes and TGA indicated the high percentage of the copolymer (53-61%) in the complexes. Entrapment (%EE) and loading (%DLE) efficiencies of indomethacin in the particle coated with saturated polyester (%EE 82%, %DLE 97%) were significantly higher than those of the particles coated with unsaturated polyester (%EE 48%, %DLE 61%). Crosslinking the unsaturated polyester inner layer resulted in the increase in both entrapment and loading efficiencies of the drug (%EE 59%, %DLE 77%). In addition, Percent drug release of the particles coated with the copolymers containing saturated and unsaturated polyesters reached their equilibriums within 3 h of dialysis, whereas those coated with the copolymer containing crosslinked polyesters was about 8 h of dialysis, indicating the sustainability of the drug released from the complexes by crosslinking reaction. This novel magnetic nanocomplex might be suitable for use as an efficient drug delivery vehicle with tunable drug-released properties.

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ABBREVIATIONS

Fe_3O_4	=	Magnetite nanoparticle
mPEG	=	Poly(ethylene glycol) methyl ether
Ma	=	Malonic acid
Me	=	Maleic acid
He	=	1,6-hexanediol,
Et	=	Ethylene glycol
M_s	=	Saturation magnetization
$SnOct_2$	=	tin (II) octoate, or stannous octoate
$FeCl_3$	=	iron (III) chloride anhydrous
$FeCl_2.4H_2O$	=	iron (II) chloride tetrahydrate
$\overline{M}_n$	=	Number Average Molecular Weight
g/mol	=	gram/mole
%EE	=	Percent entrapment efficiency
%DLE	=	Perçent drug loading efficiency
NMR	=	Nuclear Manetic Resonance spectroscopy
FT-IR	=	Fourier Transform Infrared Spectrometry
GPC	=	Gel Permeation Chromatography
AAS	=	Atomic Absorption Spectroscopy
TGA	=	Thermogravimetric Analysis
VSM	=	Vibrating Sample Magnetometry
TEM	=	Transmission Electron Microscopy
RT	=	Room Temperature