Teaser Memorandum

SUNGKYUNKWAN UNIVERSITY
Foundation for Corporate Collaboration

Title (Name of Technology):

PH SENSITIVE BLOCK COPOLYMER
AND POLYMERIC MICELLE USING THE SAME

Executive Summary

Doo-sung LEE, a professor of Sungkyunkwan University, has developed novel pH sensitive block copolymer that is obtained by copolymerization of: (a) a polyethylene glycol compound (A); and (b) at least one poly(amino acid) compound selected from the group consisting of a poly (β-amino ester) and poly(amido amine) or a copolymer thereof (B).

Sungkyunkwan University Foundation for Cooperate Collaboration, a Technology Licensing Organization in Sungkyunkwan University, intends to enter into a technology transfer or licensing transaction with regard to the agents. Terms of the transaction are not set, and interested parties may further discuss the details if they wish to enter into an agreement.

Industry Sector: Academic/Research (Diagnostic)

Therapeutic Target:

Development phase: early stage

Type of business relationship sought (including licensing availability): development collaboration, or non-exclusive or exclusive licensing agreement

Key Technology Highlight

□ Controlled biodegradation rate in the body

This technology is characterized in that a pH-sensitive poly (amino acid) compound, for example, a poly(β-amino ester), poly(amido amine) or a copolymer thereof is copolymerized with a hydrophilic polyethylene glycol compound to provide a block copolymer, which is sensitive to pH variations in the body, forms micelle structures at a specific pH range and has a controlled biodegradation rate in the body.

□ Stable micelle structure at a specific pH range

The pH-sensitive micelle maintains a stable micelle structure at a specific pH range, for example, pH 7.2~7.4 (i.e., pH range of normal cells in the body). However, the pH-sensitive micelle structure collapses in a pH of 7.2 or lower as can be found in abnormal cells such as cancer cells. Therefore, the pH-sensitive micelle can be used as carrier for target-directed drug delivery to cancer cells.

□ Use of delivery of genes and drugs

The block copolymer capable of forming the above-described pH-sensitive micelles can deliver a diagnostic substance to abnormal cells, and thus can also be applied to the filed of diagnosis including diagnostic imaging.

■ IP Owner Summary

□ Doo-sung LEE,
a professor of
Sungkyunkwan University

■ Personal Description of Researcher

□ Name
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□ Present Position
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Technology Overview

Technology Platform

The core technology of Wasol co,. ltd is to provide a pH-sensitive block copolymer obtained by copolymerization of: (a) a polyethylene glycol compound (A); and (b) at least one poly (amino acid) compound selected from the group consisting of a poly (β-amino ester) and poly(amido amine) or a copolymer thereof (B). There is also provided a method for preparing polymer micelles using the same block copolymer.

The pH-sensitive block copolymer is obtained by polymerization of a hydrophilic polyethylene glycol compound with a pH-sensitive biodegradable poly(amino acid) compound. Therefore, the pH-sensitive block copolymer can form a micelle structure due to its amphiphilicity and ionization characteristics depending on pH variations, and thus can be used as drug carrier for target-directed drug delivery depending on pH variations in the body.

Background and unmet needs:

In general, micelle is referred to as thermally stable and uniform spherical structure formed of amphiphilic low-molecular weight materials (for example, low-molecular weight materials having hydrophilic groups as well as hydrophobic groups). When a water insoluble drug is dissolved and introduced into a compound having such a micelle structure, the drug is present inside the micelle, and the micelle formed thereby is reactive to variations in temperature or pH in the body and thus can accomplish target-directed drug delivery. Therefore, such micelle type compounds have high applicability as carriers for drug delivery.

Korean Patent Application No. 2001-0035265 discloses a method for preparing micelles using polyethylene glycol and a biodegradable polymer. Both materials used in the above method are advantageous in that they have biodegradability and bioaffinity. However, because they are not sensitive to variations in a certain factor such as pH, they have difficulty in drug delivery to the desired site.

Meanwhile, pH in the human body ranges from 7.2 to 7.4. However, it is known that pH in the vicinity of abnormal cells such as cancer cells is a weak acidic pH ranging from 6.0 to 7.2. Accordingly, many attempts are made recently to accomplish drug delivery specific to cancer cells by developing a technical means for carrying out drug delivery at a pH of 7.2 or lower.

Discovery and Achievements:

We have recognized that when a poly(β-amino ester) or poly(amido amine) compound, which is a kind of poly(amino acid), is used alone, it shows pH- dependency but cannot form micelles through the self-assembly mechanism. Under the above recognition, we have found that when a poly(β-amino ester) compound or its mixture with a poly(amido amine) compound is copolymerized with a hydrophilic polyethylene glycol compound to form a block copolymer, the resultant block copolymer can form micelle structures capable of drug delivery at a specific pH range and thus can be applied as carrier with a controlled biodegradation rate for use in release-controlled drug delivery. This technology is based on this finding.

Additionally, in order to solve the problem of the high biodegradation rate of a poly (β-amino ester) compound interrupting the action of the block copolymer as drug carrier, we made intensive research into a method for controlling the biodegradation rate of the block copolymer. Finally, we succeeded in controlling the biodegradation rate and maintaining a desired biodegradation rate by copolymerization with a poly(amido amine) (which is a kind of poly (β-amino acid)) having an amide group instead of an ester group in its backbone and thus showing a relatively slow biodegradation rate.

FIG 1. formation of micelles through the self-assembly mechanism

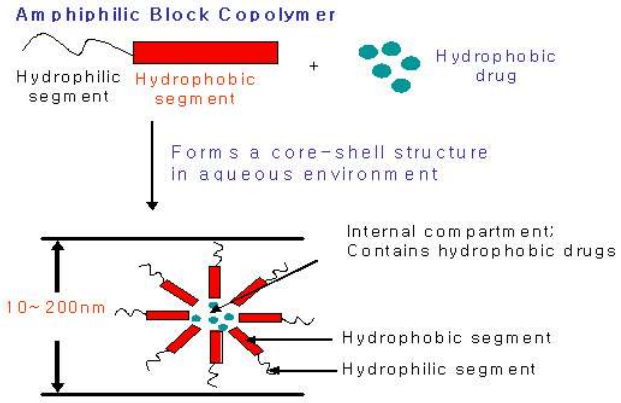
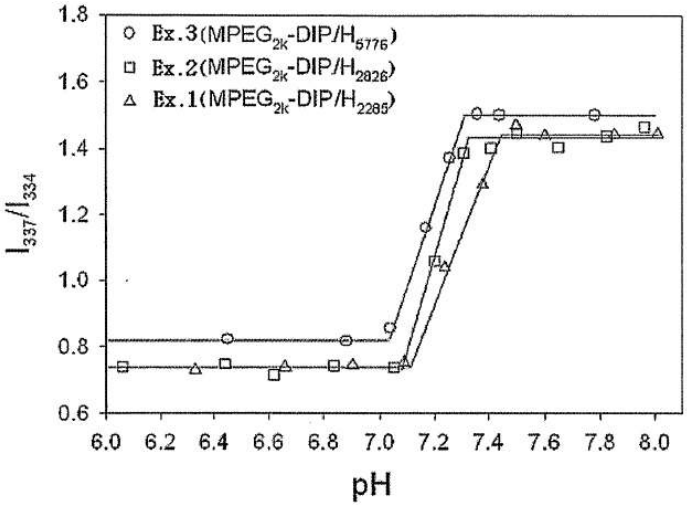


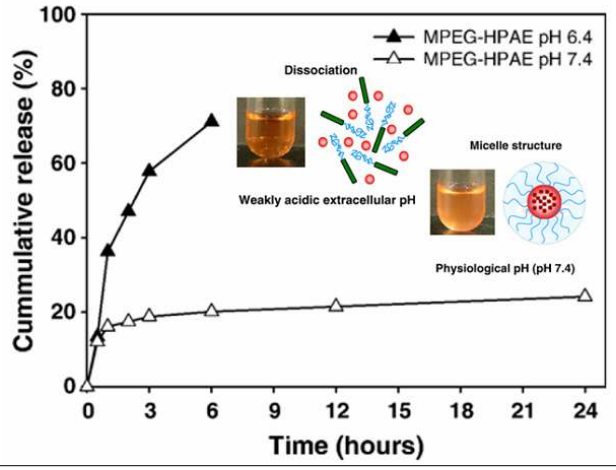
FIG 2. behavior of micelles of the block copolymers depending on pH variations

This is a graph showing the behavior of micelles of the block copolymers according to Examples 1-3, depending on pH variations



This indicates that such a change in molar ratio of the hydrophobic poly(β-amino ester) block and hydrophilic polyethylene glycol block in the final block copolymer causes a slight variation in ionization degree depending on pH variations, resulting in a change in micelles behaviors.

FIG 3. release behavior of doxorubicin according to pH variations



In Industrial Applicability, the pH-sensitive block copolymer has excellent pH sensitivity and can form polymer micelles reversibly through the self-assembly mechanism, and thus can be used as drug carrier for target-directed drug delivery depending on pH variations in the body and as diagnostic material.

Patents and Publications

Doo-sung LEE, a professor of Sungkyunkwan University have patents issued or filed for application in many contries such as U.S., Japan, Europe, China and Korea with regard to the pH-sensitive block copolymer.

TABLE. List of Patents for Novel pH Sensitive Block Copolyer and Polymeric Micelle

Country	Status	Application/Publish No.
KR	Resisterd	10-2005-0129615
PCT	Application/Published	PCT/KR2007/ 0039524
PCT	Application/Published	PCT/KR2005/004566
US	Published	US2007218120A1
JP	Published	JPT2008520798
DE	Published	DE112005003334