

学校编码: 10384
学号: 19320051301924

分类号 _____ 密级 _____
UDC _____

厦 门 大 学

硕 士 学 位 论 文

与壳聚糖相关的自组装纳米粒子的研究

Studies on Self-Assemble Nanoparticles Related with Chitosan

杨雪慧

指导教师姓名: 曾 尔 曼 副 教 授
董 炎 明 教 授

专 业 名 称: 高 分 子 化 学 与 物 理

论 文 提 交 日 期: 2 0 0 8 年 0 5 月

论 文 答 辩 时 间: 2 0 0 8 年 0 6 月

学 位 授 予 日 期: 2 0 0 8 年 月

答 辩 委 员 会 主 席: _____

评 阅 人: _____

2008 年 5 月

Studies on Self-Assemble Nanoparticles Related with Chitosan



A Thesis Presented for Master of Science
in Xiamen University

by

Yang Xuehui

Advisor: Associate Prof. Zeng Erman

Prof. Dong Yanmin

Department of Materials Science and Engineering

Xiamen University, Xiamen, 361005

2008

厦门大学学位论文原创性声明

本人呈交的学位论文是本人在导师指导下,独立完成的研究成果。本人在论文写作中参考其他个人或集体已经发表的研究成果,均在文中以适当方式明确标明,并符合法律规范和《厦门大学研究生学术活动规范(试行)》。

另外,该学位论文为(董炎明)课题(组)的研究成果,获得(董炎明)课题(组)经费或实验室的资助,在(董炎明)实验室完成。(请在以上括号内填写课题或课题组负责人或实验室名称,未有此项声明内容的,可以不作特别声明。)

声明人(签名): 杨雪慧

年 月 日

厦门大学学位论文著作权使用声明

本人同意厦门大学根据《中华人民共和国学位条例暂行实施办法》等规定保留和使用此学位论文，并向主管部门或其指定机构送交学位论文（包括纸质版和电子版），允许学位论文进入厦门大学图书馆及其数据库被查阅、借阅。本人同意厦门大学将学位论文加入全国博士、硕士学位论文共建单位数据库进行检索，将学位论文的标题和摘要汇编出版，采用影印、缩印或者其它方式合理复制学位论文。

本学位论文属于：

1. 经厦门大学保密委员会审查核定的保密学位论文，
于 年 月 日解密，解密后适用上述授权。

2. 不保密，适用上述授权。

（请在以上相应括号内打“√”或填上相应内容。保密学位论文应是已经厦门大学保密委员会审定过的学位论文，未经厦门大学保密委员会审定的学位论文均为公开学位论文。此声明栏不填写的，默认为公开学位论文，均适用上述授权。）

声明人（签名）：杨雪慧

年 月 日

目录

中文摘要	i
ABSTRACT	iii
第一章 绪论	1
1.1 自组装体系的研究	1
1.1.1 自组装的基本概念	1
1.1.2 大分子自组装的研究	2
1.1.3 高分子在溶液中的自组装	5
1.1.4 高分子混合物体系在溶液中的自组装	7
1.2 壳聚糖的研究进展	9
1.2.1 天然大分子——甲壳素、壳聚糖、壳寡糖	9
1.2.2 壳聚糖的化学改性	11
1.2.3 壳聚糖及其衍生物在生物医用领域的应用	12
1.3 本论文工作的提出	13
参考文献	14
第二章 苯甲酰化壳聚糖和氨基酸体系纳米粒子的制备和表征	21
2.1 引言	21
2.2 实验部分	21
2.2.1 材料和试剂	21
2.2.2 苯甲酰化壳聚糖的合成	22
2.2.3 苯甲酰化壳聚糖-氨基酸纳米粒子的制备	23
2.2.4 苯甲酰化壳聚糖-氨基酸纳米粒子的表征	24
2.3 结果与讨论	26
2.3.1 红外光谱法研究苯甲酰化壳聚糖-氨基酸纳米粒子的结构	26
2.3.2 浊度法研究苯甲酰化壳聚糖-氨基酸纳米粒子的形成过程	27
2.3.3 苯甲酰化壳聚糖-氨基酸纳米粒子的粒径测试及影响因素	28
2.3.4 苯甲酰化壳聚糖-氨基酸纳米粒子的形貌观察	32
2.4 本章小结	34

参考文献	35
第三章 邻苯二甲酰化壳聚糖和 DOVOB 体系纳米粒子的制备和表征	36
3.1 引言	36
3.2 实验部分	37
3.2.1 材料与试剂	37
3.2.2 合成邻苯二甲酰化壳聚糖 (PHCS)	37
3.2.3 合成 3,4,5-三{[3-(甲氧基)-4-(十二烷氧基)]苄氧基}苯甲酸 (DOVOB)	39
3.2.4 邻苯二甲酰化壳聚糖-DOVOB 纳米粒子的制备	44
3.2.5 邻苯二甲酰化壳聚糖-DOVOB 纳米粒子的表征	44
3.3 结果与讨论	45
3.3.1 红外光谱法研究邻苯二甲酰化壳聚糖-DOVOB 纳米粒子的结 构	46
3.3.2 浊度法研究邻苯二甲酰化壳聚糖-DOVOB 纳米粒子的形成过 程	47
3.3.3 邻苯二甲酰化壳聚糖-DOVOB 纳米粒子的粒径测试	48
3.3.4 相对浓度比例对自组装粒子粒径的影响	49
3.3.5 邻苯二甲酰化壳聚糖-DOVOB 纳米粒子的形貌观察	50
3.4 本章小结	51
参考文献	52
第四章 壳寡糖和聚丙烯酸体系纳米粒子的制备和表征	53
4.1 引言	53
4.2 实验部分	54
4.2.1 材料与试剂	54
4.2.2 聚丙烯酸 (PAA) 的合成	54
4.2.3 壳寡糖-聚丙烯酸纳米粒子的制备	54
4.2.4 壳寡糖-聚丙烯酸纳米粒子的表征	55

4.3 结果与讨论	55
4.3.1 浊度法研究壳寡糖-聚丙烯酸纳米粒子的形成过程	55
4.3.2 壳寡糖-聚丙烯酸正、反体系纳米粒子的结构	57
4.3.3 壳寡糖-聚丙烯酸纳米粒子的粒径测试	58
4.3.4 相对浓度比例对自组装粒子粒径的影响	59
4.3.5 壳寡糖-聚丙烯酸纳米粒子的形貌观察	60
4.4 本章小结	61
参考文献	61
第五章 药物吸附和释放的初步探索	63
5.1 引言	63
5.2 实验部分	64
5.2.1 药品和测试仪器	64
5.2.2 负载药物的壳寡糖-聚丙烯酸纳米粒子的制备	64
5.2.3 负载药物的体外释放	65
5.3 结果与讨论	65
5.3.1 维生素 C 的药物吸附-释放测试	66
5.3.2 维生素 B12 的药物吸附-释放测试	69
5.4 本章小结	76
参考文献	76
结论	78
硕士期间发表论文	80
致 谢	81

厦门大学博硕士论文摘要库

CONTENTS

Abstract in Chinese	i
Abstract in English	iii
1 Introduction	1
1. 1 Studies on self-assembly	1
1. 1. 1 Basic concept of self-assembly	1
1. 1. 2 Studies on macromolecular self-assembly	2
1. 1. 3 Self-assembly of polymers in solution	5
1. 1. 4 Self-assembly of polymer blends in solution	7
1. 2 Research progress of chitosan	9
1. 2. 1 Natural macromolecules——chitin、chitosan、chitooligosaccharide	9
1. 2. 2 Chemical modification of chitosan	11
1. 2. 3 Applications of chitosan and its derivatives in the biomedical materials field.....	12
1. 3 Plans and originalities of this work	13
References	14
2 Preparation and characterization of benzoyl chitosan—amino acid self-assemble nanoparticles	21
2. 1 Introduction	21
2. 2 Experiment part	21
2. 2. 1 Materials and reagents	21
2. 2. 2 Synthesis of benzoyl chitosan (DBC)	22
2. 2. 3 Preparation of benzoyl chitosan - amino acid nanoparticles	23
2. 2. 4 Characterization of benzoyl chitosan - amino acid nanoparticles.....	24
2. 3 Result and discussion	26
2. 3. 1 Research on the structure of benzoyl chitosan - amino acid nanoparticles by infrared spectroscopy.....	26

2. 3. 2 Research on the formation process of benzoyl chitosan - amino acid nanoparticles by turbidimetric assay.....	27
2. 3. 3 Research on the size of benzoyl chitosan - amino acid nanoparticles by dynamic laser scattering and research on its influencing factors.....	28
2. 3. 4 Topographic observation of benzoyl chitosan - amino acid nanoparticles	32
2. 4 Conclusion	34
References.....	35
3 Preparation and characterization of phthaloyl chitosan—DOVOB self-assemble nanoparticles.....	36
3. 1 Introduction.....	36
3. 2 Experiment part	37
3. 2. 1 Materials and reagents	37
3. 2. 2 Synthesis of phthaloyl chitosan (PHCS)	37
3. 2. 3 Synthesis of {3,4,5 -Tris [p- (n- dodecyloxy)- m- methoxybenzyl] benzoic acid} (DOVOB)	39
3. 2. 4 Preparation of phthaloyl chitosan - DOVOB nanoparticles	44
3. 2. 5 Characterization of phthaloyl chitosan - DOVOB nanoparticles.....	44
3. 3 Result and discussion.....	45
3. 3. 1 Research on the structure of phthaloyl chitosan - DOVOB nanoparticles by infrared Spectroscopy	46
3. 3. 2 Research on the formation process of phthaloyl chitosan - DOVOB nanoparticles by turbidimetric assay.....	47
3. 3. 3 Research on the size of phthaloyl chitosan - DOVOB nanoparticles by dynamic laser scattering	48
3. 3. 4 The influence of relative concentration proportion on the size of the self-assemble particles.....	49
3. 3. 5 Topographic observation of phthaloyl chitosan - DOVOB nanoparticles by scanning electron microscope.....	50

3. 4 Conclusion	51
References	52
4 Preparation and characterization of chitooligosaccharide-PAA self-assemble nanoparticles.....	53
4. 1 Introduction.....	53
4. 2 Experiment part.....	54
4. 2. 1 Materials and reagents	54
4. 2. 2 Synthesis of PAA	54
4. 2. 3 Preparation of chitooligosaccharide-PAA nanoparticles	54
4. 2. 4 Characterization of chitooligosaccharide-PAA nanoparticles.....	55
4. 3 Result and discussion.....	55
4. 3. 1 Research on the formation process of chitooligosaccharide-PAA nanoparticles by turbidimetric assay	55
4. 3. 2 The positive and reverse structures of chitooligosaccharide-PAA nanoparticles	57
4. 3. 3 Research on the size of chitooligosaccharide-PAA nanoparticles by Dynamic laser scattering	58
4. 3. 4 The influence of relative concentration proportion on the size of the self-assemble particles.....	59
4. 3. 5 Topographic observation of chitooligosaccharide-PAA nanoparticles by scanning electron microscope.....	60
4.4 Conclusion	61
References.....	61
5 Preliminary Exploration of Drug Delivery.....	63
5.1 Introduction.....	63
5.2 Experiment part.....	64
5. 2. 1 Materials and analysis methods	64
5. 2. 2 Preparation of chitooligosaccharide-PAA nanoparticles as a drug delivery system.....	64

5. 2. 3 Drug release in vitro	65
5.3 Result and discussion	65
5. 3. 1 The sorption and release of vitamin C	66
5. 3. 2 The sorption and release of vitamin B12.....	69
5.4 Conclusion	76
References.....	76
Conclusion.....	78
Published papers during learning terms.....	80
Acknowledgements	81

厦门大学博硕士学位论文摘要

中文摘要

具有许多新性能的核-壳型高分子纳米粒子，有着良好的应用前景。因而，国内外许多课题组一直致力于追求一种能够低环境负荷、低能耗、低成本地制造高度功能化纳米粒子的方法。自组装法能够很好地满足这些需求。通过自组装原理所获得的新型功能性纳米材料，在高技术领域的应用已经凸现出光明的前景。

传统的自组装方法是利用两亲性嵌段聚合物或接枝聚合物基于亲水-疏水平衡自组装，但两亲性嵌段聚合物或接枝聚合物的制备难度较大，很难推广应用。如果在两种不同的分子链中分别引入具有特殊相互作用的基团，就可以使本不相容的高分子共混体系实现相容。

本论文正是基于这些新趋势对实验工作进行设计。利用特殊相互作用——氢键作用和静电作用，进一步研究分子间的自组装行为。本论文的创新之处在于，选择具有生物相容性且来源广泛的天然多糖高分子壳聚糖的衍生物、壳寡糖和小分子或其他聚合物进行自组装，得到以其中一种物质为壳、另一种物质为核的自组装纳米粒子或亚微米粒子。根据所选物质的特点，通过改变 pH、物质品种等条件，制备一系列具有环境响应特性的纳米粒子。

本文的研究内容主要包括以下几方面：

1. 合成苯甲酰化壳聚糖 DBC 和邻苯二甲酰化壳聚糖 PHCS，合成一代树状分子 3,4,5-三[[3-(甲氧基)-4-(十二烷氧基)]苄氧基]苯甲酸 DOVOB，并用红外光谱、核磁共振对产物进行表征。

2. 研究苯甲酰化壳聚糖和天然分子氨基酸在选择性溶剂中基于大分子间氢键相互作用自组装形成粒子的行为。

3. 研究邻苯二甲酰化壳聚糖和树状分子酸在选择性溶剂中基于氢键的相互作用自组装形成纳米粒子的行为。

4. 研究壳寡糖和聚丙烯酸 PAA 在共溶剂中的基于静电力作用的自组装行为。

5. 以维生素 C 作为模型药物，以维生素 B12 作为实践药物，初步研究壳寡糖和聚丙烯酸体系对药物的吸附和缓释，测试制备的自组装粒子对药物的吸附以及体外释放行为。

关键词： 纳米粒子； 自组装； 壳聚糖

厦门大学博硕士论文摘要库

ABSTRACT

Core-Shell polymeric nanoparticles which have many advantages may lead to a wide range of applications. Therefore, scientists all around the world are pursuing a method, by which highly functionalized nanoparticles could be developed with low environmental load, low energy consumption and low cost. The approach of self-assembly can well fulfil all of these requirements. Novel functional nano-scale materials through self-assembly have brightened the prospect in high-tech areas.

Self-assembly of amphiphilic block copolymers or grafted polymers has been widely used to prepare the nano-sized particles where the hydrophobic blocks form the core and the hydrophilic ones form the shell. However, the preparation of amphiphilic block copolymers or grafted polymers is difficult, furthermore it is not always possible or practical of those polymers. Introducing specific functional groups into different chains, immiscible blends can be turned into miscible ones.

In this thesis, we designed our work on self-assembly of polymers by taking these new trends account as much as possible. We devoted to obtaining regular assemblies due to the inter-polymer complexation by hydrogen-bond or electrostatic. And this thesis further developed and deepened the studies on intermolecular regular assembly. The innovation of this paper is as follow: Chitosan's derivatives and chitooligosaccharide which are natural biopolymers with rich resource, low cost and biocompatibility are selected to self-assemble with small molecule substances or other macromolecules. Nanoparticles or submicron-particles which is core-shell structure can be obtained. This is one of the innovations of this work. Based on the selected substances' characteristics, with changing the pH of medium or the kind of substances, a series of nanoparticles which have environmental response factors can be obtained.

The follows are the main study contents.

1. Synthesis of benzoyl chitosan (DBC), phthaloyl chitosan (PHCS) and {3,4,5-tris [p- (n- dodecyloxy)- m- methoxybenzyl] benzoic acid} DOVOB, and the characterization of products by using FTIR & ¹H-NMR.

2. Studies on the self-assembly of benzoyl chitosan and amino acids in their selective solvents. The self-assemble behavior is induced by hydrogen bonding.

3. Studies on the self-assembly of phthaloyl chitosan and DOVOB in their selective solvents, which is induced by hydrogen bonding.

4. Studies on the self-assembly behavior of chitooligosaccharide and polyacrylate which is driven by electrostatic.

5. Vitamine C as model drug and vitamine B12 as applicable drug were used to study the drug-loaded content and drug release behavior of the system of chitooligosaccharide and polyacrylate. And test the sorption rate and release behavior in vitro of self-assembly nanoparticles.

Keyword: nanoparticles; self-assembly; chitosan

Degree papers are in the "[Xiamen University Electronic Theses and Dissertations Database](#)". Full texts are available in the following ways:

1. If your library is a CALIS member libraries, please log on <http://etd.calis.edu.cn/> and submit requests online, or consult the interlibrary loan department in your library.
2. For users of non-CALIS member libraries, please mail to etd@xmu.edu.cn for delivery details.

厦门大学博硕士论文摘要库