Design, Synthesis and Characterization of Cyclodextrin based pH-Responsive Polymeric Systems

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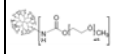
Introduction

The design of polyrotoxanes is one of the most vigorously investigated fields of supramolecular inclusion complexation. To date, a diverse number of polymeric inclusion complexation (PIC) structures have been formed making use of host guest system between CDs and various polymeric systems. The four most important driving forces for the formation of those ICs include hydrophobic interactions, between host (CD) and guest molecules; Van Der Waals forces, geometrical compatibility between the host and guest and hydrogen bonding between the hydroxyl groups of CD and the guest molecule. Understanding the properties of those forces will significantly contribute to the various applications of those PIC particularly in material stability and controlled drug release.

Research Objectives

- Investigate the binding between α-Cyclodextrin and pH-responsive polymers
- Establish the thermodynamic and physicochemical properties of the binding process
- Utilize laser light scattering to study the morphology and size of the designed polymers and their complexes.
- Examine the application of these systems in controlled drug release and pharmaceutical formulations

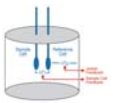
Materials

Polymer used	MW	Properties	Application
Polyethylenimine (PEI) 	5-10K	1) pH responsive at pH < 3 as amine group will be protonated 2) pH-triggered supramolecular architectures with (α-CD)	Controlled Drug delivery, Tissue Engineering, artificial gene delivery carrier
PEGylated-PAMAM dendrimers: 	PEG:~2K PAMAM:~7K	1)G3 Poly(amido amine) dendrimer : protonated and unprotonated at pH ~ 2 and ~ 10 respectively, and partially protonated at pH range of 7 to 8. 2)Poly(ethylene glycol): Forms inclusion complexation with (α-CD).	Drug Delivery, Gene carriers, antiviral agents, contrast agents, nanocatalysts

Instrumentation

Our main method for physical characterization:
Isothermal Titration Calorimetry (ITC)
Laser Light Scattering (LLS) (Dynamic /Static Light scattering)

ITC



DLS

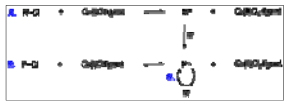
Stokes-Einstein eqn:

$$R_h = \frac{kTq^2}{6\pi\eta\Gamma}$$

http://www.retsch-technology.com/fr/applications/technical-basics/static-laser-light-scattering

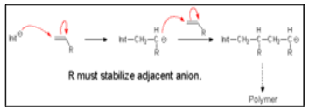
Methods

Atom Transfer Radical Polymerization



- Controlled / Living growth
- Low polydispersity factors
- No moisture sensitivity

Anionic Polymerization

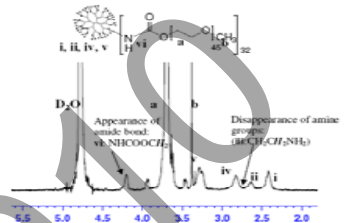


- Controlled / Living growth
- All chains grow under identical conditions
- Very Narrow polydispersity
- MW is predictable (Unlike other polymerizations)

Results and Discussion

^{1}H NMR (PEGylated-PAMAM)

Lim Ai Hwa,Interactions of amphiphilic molecules with dendrimers, Master of Engineering thesis, Nanyang Technological University (2009).

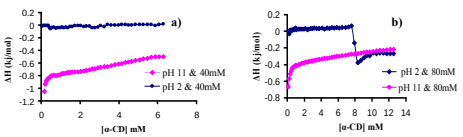


Corresponding chemical structure of PAMAM dendrimer	Number of chemical structure in one molecule of PAMAM	No. of MPEG grafted to PAMAM (mol/mol)	
		In feed (Amine groups)	Calculated MPEG attached
i	60	64	33
ii	30	64	30
iv	60	64	32
v	60	64	35
		Average mol ratio of MPEG to PAMAM:	32

1. Effect of Concentration

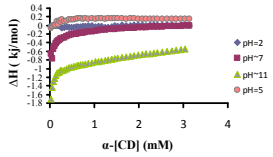
Binding enthalpy obtained from ITC

a) [α-CD] =40 mM and b) [α-CD] =80 mM



2. Effect of pH

Titrating [α-CD] =20 mM

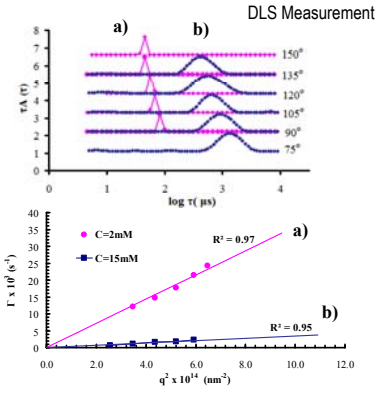


At pH < 2 No binding took place between α-CD and PEG at α-CD concentration< 9mM because of electrostatic repulsion from protonated amine groups present on the of PAMAM dendrimer.

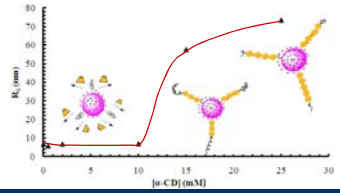
The binding enthalpy decreases as we lower the pH since the hydrophobic properties on the polymer diminishes with the increasing electrostatic forces, resulting in "minimal to no" threading of α-CD on PEG at low pH values.

3. Sizing and Mechanism

DLS Measurement



a) [α-CD] =2mM => $R_h \approx 6.7$ nm b) [α-CD] =15mM => $R_h \approx 53.5$ nm



Conclusions and Future Plans

- In the literature several pH responsive/α-CD supramolecular structures have been designed, synthesized and characterized.
- The interest in pH responsive systems comes from their potential application in many fields such as drug delivery, gene carriers and material/polymer stability.
- α-CD binding to PEGylated dendrimers (PAMAM) was studied using ITC and DLS instruments. Factors such as concentration, pH and ionic strength play vital role in the initiation of the binding process of those pH responsive polymers, and are currently being further investigated in our lab.