Research Communications

Poly(amidoamine) Dendrimers: A New Class of High Capacity Chelating Agents for Cu(II) Ions

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This communication describes preliminary results of an experimental investigation of the binding of Cu(II) ions to poly-(amidoamine) (PAMAM) dendrimers in aqueous solutions. Dendrimers are highly branched polymers with controlled composition and architecture consisting of three structural components: a *core*, *interior branch cells*, and *terminal branch cells*. PAMAM dendrimers possess functional nitrogen and amide groups arranged in regular "branched upon branched" patterns which are displayed in geometrically progressive numbers as a function of generation level. Terminal groups of PAMAM dendrimers may be any organic substituent such as primary amines, carboxylic groups, etc. In aqueous solutions, PAMAM dendrimers can serve as high capacity nanoscale containers for toxic metal ions such as Cu(II). Compared to traditional chelating agents (e.g., triethylene tetramine) and macrocyles (e.g., cyclams) with nitrogen donors, which can typically bind only one Cu-(II) ion per molecule, *a generation eight (G8) PAMAM dendrimer can bind up 153 ± 20 Cu(II) ions per molecule*. This clearly illustrates a distinct advantage of dendrimers over traditional chelating agents and macrocycles; that is the covalent attachment of nitrogen ligands to conformationally flexible PAMAM chains enclosed within a nanoscopic structure results in a substantial increase in binding capacity.

Introduction

Water contamination by toxic metal ions has become a major problem throughout the world (*1*). Polymer supported ultrafiltration (PSUF) is emerging as a promising process for the treatment of water contaminated by toxic metals (*2*). Two key physicochemical processes that control the efficiency of PSUF include (i) pollutant binding to polymers and (ii) polymer sorption onto utrafiltration membranes (*2*). Consequently, the utilization of polymers with (i) large binding capacities and (ii) weak sorption tendencies is critical to development of cost-effective PSUF processes.

Recent advances in nanoscopic chemistry such as the invention of dendrimers (*3*) are providing new opportunities to develop more efficient and cost-effective functional materials for PSUF. Dendrimers are highly branched polymers with controlled composition and architecture consisting of three structural components: a *core*, *interior branch cells*, and *terminal branch cells*. Modification of these main components provide a variety of means for controlling critical macromolecular parameters such as internal and external rigidity, hydrophilicity and hydrophobicity, degrees of void and excluded volumes, and response to stimuli such as changes in solvent polarity and temperature (*4*). Dendrimer technology has been defined that leads to either conical, spherical, or rod shaped nanostructures that are monodisperse with sizes in the range of 2−12 nm (*4−7*). These nanostructures can be designed to encapsulate metal ions and zerovalent metals with surface groups that make them soluble in appropriate media or bind onto appropriate surfaces (*8, 9*). The ability to synthesize water soluble dendrimers with (i) metal ion chelating functional groups and (ii) surface groups with weak binding affinity toward ultrafiltration membranes provides new and unprecedented opportunities for developing efficient, cost-effective and environmentally sound functional materials for PSUF.

This communication describes preliminary results of an experimental investigation of the binding of Cu(II) ions to poly(amidoamine) (PAMAM) dendrimers in aqueous solutions. These macromolecules were first synthesized by Tomalia and co-workers (*10*) via a two-step iterative process which presently provides a commercial route to PAMAM dendrimers. This synthesis proceeds via a series of successive building stages commonly referred to as generations. Figure 1 illustrates the structures of PAMAM dendrimers [EDA core and NH_2 terminal groups] evaluated in this study. As shown in Figure 1, PAMAM dendrimers possess functional nitrogen and amide groups arranged in regular "branched upon branched" patterns which are displayed in geometrically progressive numbers as a function of generation level. This high density of nitrogen ligands enclosed within a nanoscopic container makes PAMAM dendrimers especially attractive as high capacity chelating agents.

Experimental Section

Reagent grade copper chloride (99.999% pure $CuCl_2$) from Aldrich was used as source of Cu(II) ions. PAMAM dendrimers (EDA core with NH_2 terminal groups) of generation G3, G4, G5, G6, G7, and G8 were provided by the Army Research Laboratory (ARL)/Michigan Molecular Institute (MMI) Dendritic Polymers Center of Excellence. All dendrimer samples used in this study were supplied as stock solutions in methanol and used as received. Selected physicochemical properties of the PAMAM dendrimers evaluated in this study are given in Figure 1.

For each aqueous PAMAM dendrimer solution, experiments were carried out to determine the extent of binding (EOB) for Cu(II) ions as a function of metal ion/dendrimer

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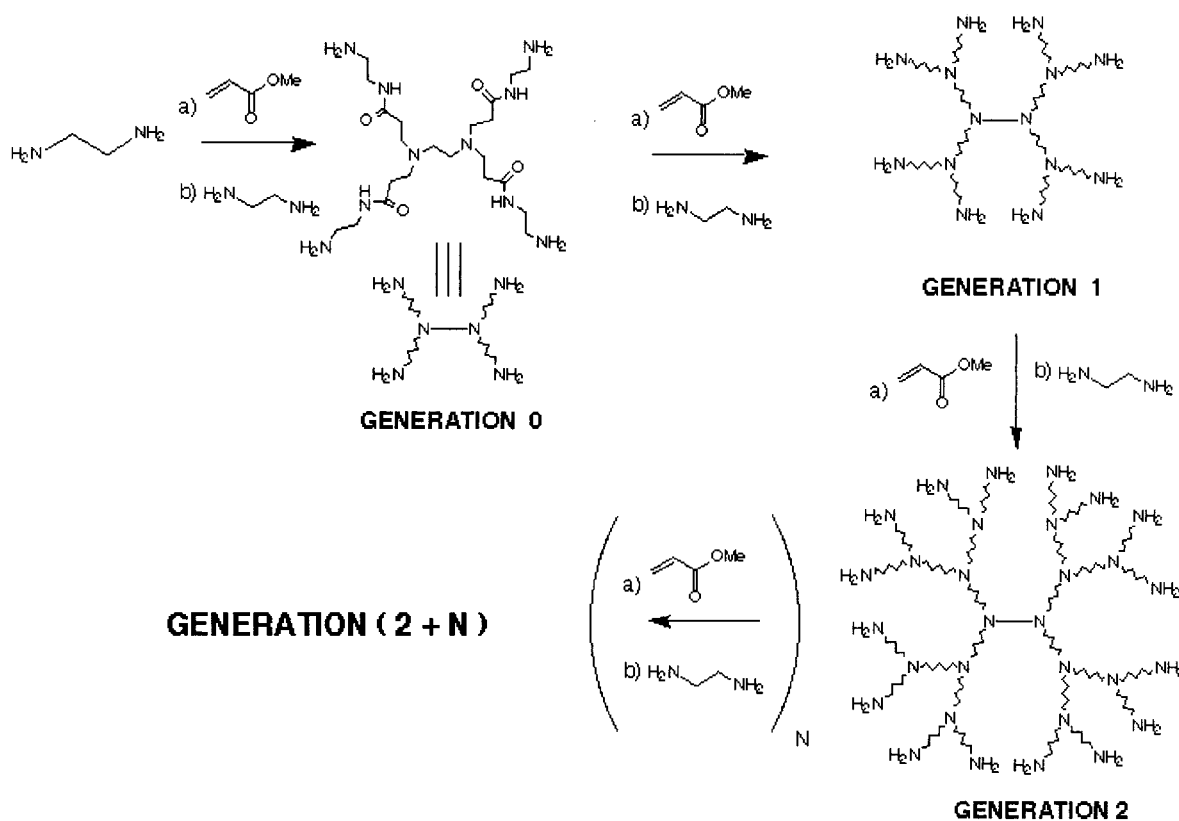† California Institute of Technology.
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FIGURE 1. Structures and selected properties of PAMAM dendrimers evaluated in this study.

Generation	[a]Molar Mass (Daltons)	[b]Number of Primary Amino Groups	[c]Number of Tertiary Nitrogens	[d]Number of Nitrogen Ligands	[e]Hydrodynamic Diameter (A)
3	6, 909	32	30	62	36
4	14, 214	64	62	126	45
5	28, 826	128	126	254	54
6	58, 048	256	254	510	67
7	116, 493	512	510	1022	81
8	233, 383	1024	1022	2046	97

[a]Theoretical molar mass. Data are taken from reference 13
[b]Number of primary amino groups. Data are taken from reference 13
[c]Number of tertiary nitrogen = Number of primary amino groups - 2
[d]Number of Nitrogen Ligands = Number of primary amino groups + number of tertiary nitrogens
[e]Measured Hydrodynamic Diameter. Data are taken from reference 13

loading [i.e., the molar ratio of Cu(II) ions to dendrimer in solution]. The binding assay procedure consisted of (i) mixing and equilibrating aqueous solutions of Cu(II) ions and PAMAM dendrimers, (ii) separating the copper laden dendrimers from the aqueous solutions by ultrafiltration using a Millipore disposable filter with a nominal molecular weight cutoff of 5000 daltons, and (iii) measuring the copper concentration in the equilibrated solutions (Cu_0) and aqueous phase (Cu_a) by atomic absorption spectrophotometry. A Perkin-Elmer Model 3030 atomic absorption spectrophotometer was used to measure the copper concentration. A certified Fisher copper standard was used to prepare the calibration standards. The pH of the equilibrated copper-dendrimer solutions were measured using an Orion Model 720 A pH meter with an Orion model 9863BN electrode. Three certified Fisher buffer solutions (pH = 4, 7, and 10) were used to calibrate the pH meter.

The concentration of copper bound to a dendrimer (Cu_b) was expressed as

$$Cu_b = Cu_0 - Cu_a \qquad (1)$$

The extent of binding (EOB), number of mol of Cu(II) bound per mol of dendrimer, was expressed as

$$EOB = \frac{Cu_b}{C_d} \qquad (2)$$

where C_d is the total concentration of dendrimer in the aqueous solution in mol/L.
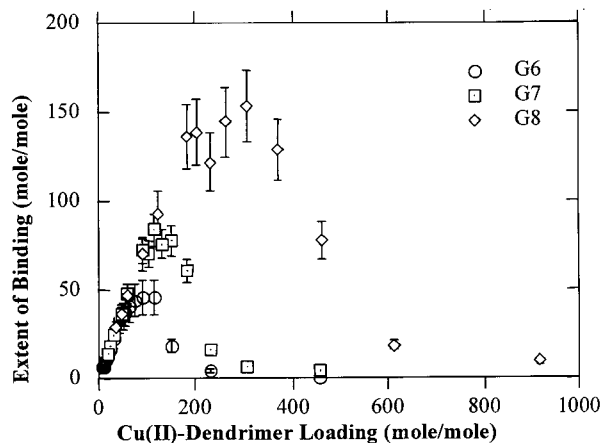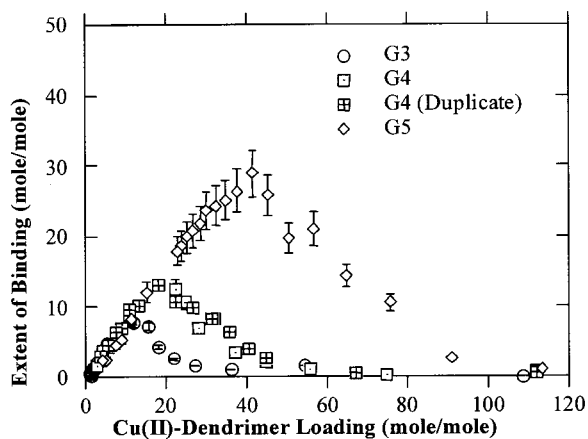
FIGURE 2. Extent of binding for Cu(II) ions in aqueous solutions of PAMAM dendrimers at room temperature as a function of Cu(II)-dendrimer loading.

The average of the relative differences between the measured and target values of the initial copper concentration in solution (Cu_0 and Cu_{0t}) was taken as a measure of experimental accuracy (ϵ_a)

$$\epsilon_a = \frac{\sum_{i=1}^{N_m} \dfrac{|Cu_{0i} - Cu_{0t}|}{Cu_{0t}}}{N_m} \qquad (3)$$

where N_m (usually ≥ 10) is the total measurements of Cu_0 performed during any given set experiments and Cu_{0t} (usually $= 10$ ppm) is the target value of the initial copper concentration in solution. Duplicate experiments of Cu(II) binding to PAMAM dendrimer G4 were also carried out to assess the precision of the EOB measurements. Figure 2 shows that, for PAMAM dendrimer G4, the EOB data are reproducible. Consequently, the estimated experimental accuracy (ϵ_a) was taken as a measure of the experimental error for all EOB data reported in this Communication.

Results and Discussion

The effect of the Cu(II)/dendrimer loading on the extent of binding (EOB) of Cu(II) ions in aqueous solutions of generation G3, G4, G5, G6, G7, and G8 PAMAM dendrimers at room temperature is shown in Figure 2. The symbols represent measured values of EOB along with the estimated measurement accuracy (ϵ_a). Figure 2 shows that the EOB for Cu(II) ions in aqueous solutions of PAMAM dendrimers goes through a maximum as the Cu(II)/dendrimer loading increases. For PAMAM dendrimers G3, G4, and G5, maximum EOB of 8 ± 1, 13 ± 1, and 29 ± 3 Cu(II) ions per dendrimer molecule are observed at metal/dendrimer loadings of 11, 18, and 41 Cu(II) ions per dendrimer molecule, respectively. For PAMAM dendrimers G6, G7, and G8, maximum EOB of 46 ± 9, 83 ± 9, and 153 ± 20 Cu(II) ions per dendrimer molecule are observed at metal/dendrimer loadings of 91, 114, and 306 Cu(II) ions per dendrimer molecule, respectively. These binding capacities are significantly larger that those of traditional chelating agents (e.g., triethylene tetramine) and macrocycles (e.g., cyclams) with nitrogen ligands, which can typically bind only one Cu(II) ion per molecule. These results clearly demonstrate a distinct advantage of PAMAM dendrimers over traditional chelating agents and macrocycles; that is the covalent attachment of nitrogen ligands to conformationally flexible PAMAM chains enclosed within a nanoscopic structure results in a substantial increase in binding capacity.

To gain insight into the relationship between EOB, Cu-(II)-dendrimer loading, and ligand protonation, the pH of each equilibrated copper-dendrimer aqueous solution was also measured. Tomalia et al. (*10*) have estimated the neutralization of the terminal primary amino groups and internal tertiary nitrogens of PAMAM dendrimers in aqueous solutions to occur at pH of 6.85 and 3.86, respectively. Figure 3 shows that the EOB for Cu(II) ions also goes through a maximum as solution pH increases. Maximum EOB is observed at pH of 5.9–6.1 as the nitrogen binding sites become protonated by H^+ ions released during the uptake of Cu(II) ions. When all the nitrogens are protonated, no binding of Cu(II) ions is observed. These results clearly illustrate the effect of metal ion-dendrimer loading on EOB. As this loading increases, the number of Cu(II) ions available for binding increase. However, the number of nitrogen binding sites decrease as they become protonated. The net result of these two opposing effects is that the EOB of Cu(II) ions goes to a maximum in aqueous solutions of PAMAM dendrimers as copper-dendrimer loading increases (Figure 2).

To assess the respective role of the primary amino groups and tertiary nitrogens in the uptake of Cu(II) ions by aqueous solutions of PAMAM dendrimers, the relationship between maximum EOB for Cu(II) ions and number of NH_2 terminal groups is plotted in Figure 4. The symbols represent measured values with error bars and estimated EOB values assuming two commonly observed coordination environments for Cu-(II) ions: bidendate [i.e., 1 Cu(II)/2 NH_2] and tetradentate coordination [i.e, 1 Cu(II)/4NH_2] (*11*). Figure 4 suggests that the EOB data can be adequately described by a tetradentate coordination model for PAMAM dendrimers G3, G4, G5, and G6. This result is consistent with measurements showing that Cu(II) ions tend to form square planar tetradentate complexes with a variety of nitrogen bearing chelating agents and macrocycles (*11*). However, for the higher generation PAMAM dendrimers (G7 and G8), Figure 4 indicates that neither the bidendate model nor the tetradentate coordination model fit the experimental data. This may be related to a "crowding" of the dendrimer surfaces associated with the geometric increase of the number of NH_2 terminal groups with generation level shown in Figure 1. Such a crowding could result in the formations of "more tightly packed" structures that (i) hinder the ability of the terminal primary amino groups to form tetradendate complexes with Cu(II) ions and (ii) enhance the ability of Cu(II) ions to interact with the tertiary nitrogen sites as suggested by Ottaviani et al. (*12*). We in fact think that both the primary amino groups
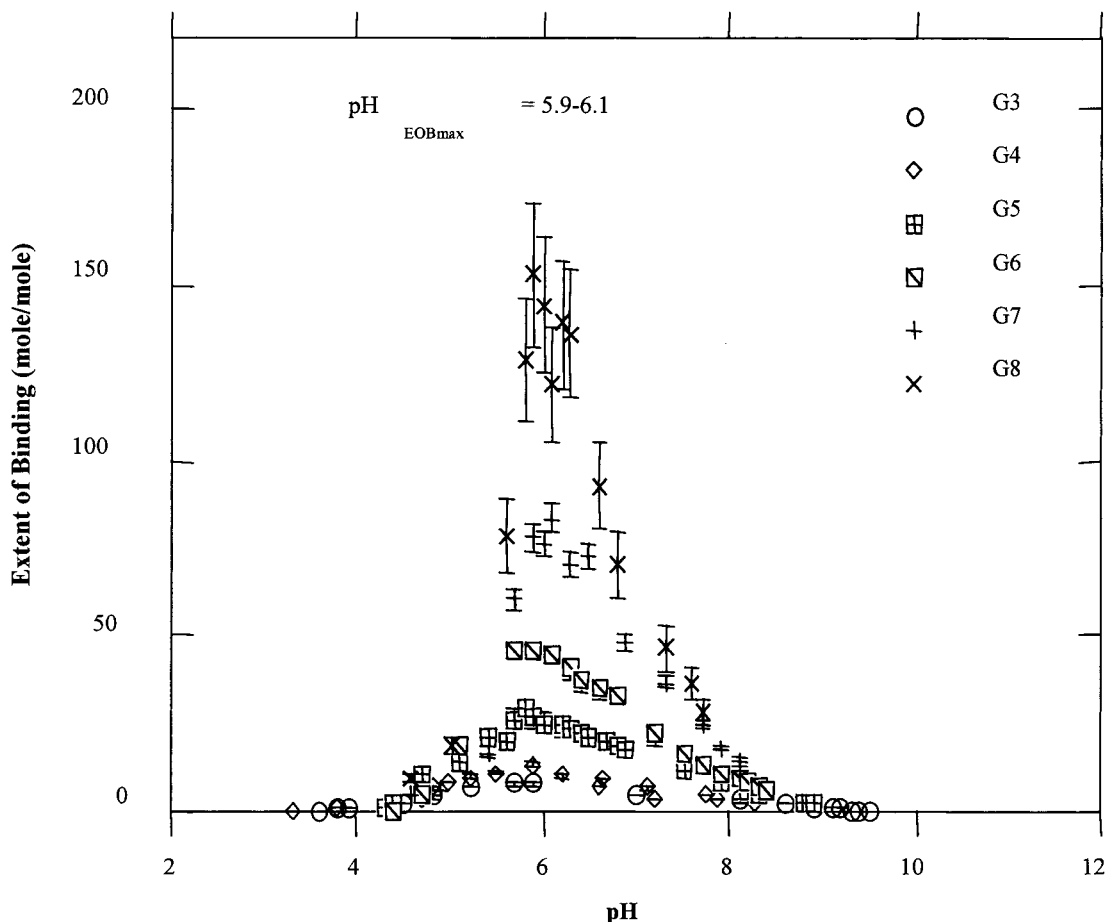
FIGURE 3. Extent of binding for Cu(II) ions in aqueous solutions of PAMAM dendrimers at room temperature as a function of solution pH.
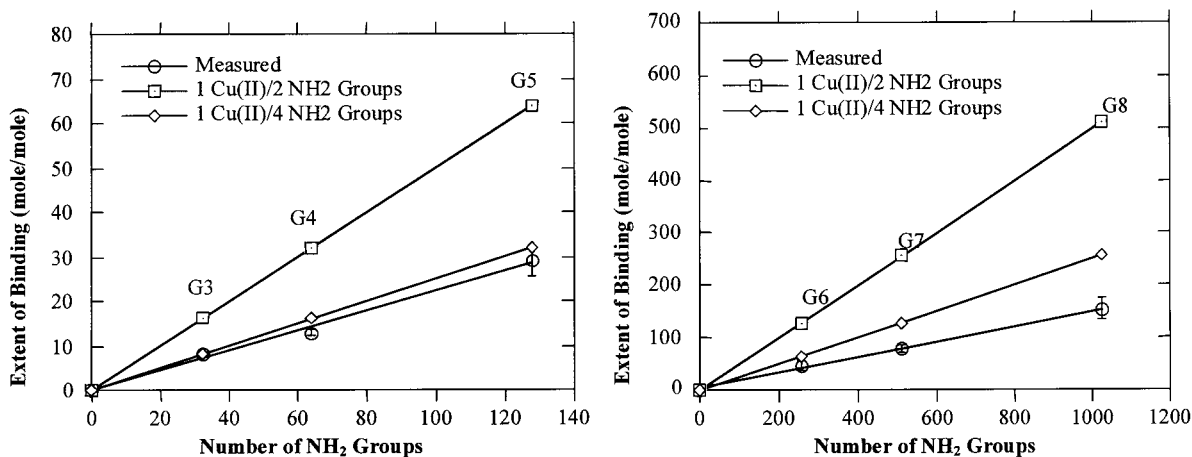

FIGURE 4. Maximum extent of binding for Cu(II) ions in aqueous solutions of PAMAM dendrimers at room temperature as a function of number of terminal NH_2 groups.

and tertiary nitrogens are involved in the binding of Cu(II) metal ions to PAMAM dendrimers in aqueous solutions. We anticipate their relative role to depend primarily on Cu(II)-dendrimer loading, dendrimer generation/surface chemistry, and solution pH.

Environmental Implications

The foregoing results clearly demonstrate that in aqueous solutions PAMAM dendrimers can serve as high capacity nanoscale containers for toxic metal ions such as Cu(II).

Separation of metal laden dendrimers from solutions can simply be achieved by ultrafiltration. The metal laden dendrimers can also be regenerated by protonating the ligands as suggested by the data shown in Figure 3. Consequently, we believe that dendrimers such as PAMAMs have great potential as efficient and cost-effective functional materials for PSUF treatment of water contaminated by toxic metals. We are currently investigating the effects of metal ion-dendrimer loading, dendrimer generation, and surface chemistry and solution pH and ionic strength on the EOB for Cu(II) and other metal ions.

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