## Lecture 13. Physicochemical properties of specific nanoparticles

**The purpose of the lecture:** to familiarize students with physicochemical properties of specific nanoparticles.

**Expected results:** students getting information about physicochemical properties of specific nanoparticles.

Dendrimers

Dendrimers are hyperbranched synthetic polymers that can be engineered into well-defined structures for various biological and pharmacological functions. Dendrimers contain a core group (C), branching generations (G1 to G4), and end groups that can be functionalized with functional groups such as an antibody (Ab) or another dendrimer containing a fluorescing group. During synthesis, as dendrimers grow in size, different generations begin to show distinct features that are amplified with increasing generations.

These unique features (i) make dendrimers suitable for a wide range of biomedical applications and (ii) may be implicated in their toxicity.

Intrinsic Viscosity (h)

Intrinsic viscosity characterizes the frictional contribution of polymers in dilute solutions and facilitates determination of molecular weight, size, and topology of linear polymers, dendrimers, or biological molecules such as proteins and polysaccharides. The h values for linear polymers increase as their size increases. Conversely, dendrimers exhibited a biphasic response: the values increased as the dendrimer size increased from G0 to G4; then, a further increase in the dendrimer size decreased the h values. The hydrodynamic radius of the dendrimers increased linearly as their size increased. Although mechanisms for the anomalous h values of dendrimers of different generations are not fully understood, this may be related to the discontinuous nature of steric hindrance that increases as the size increases from G0 to G4 and then decreases as the size increases further.

The Dendrite Box Concept

The branched structure of dendrimers contains empty and defined sized spaces surrounded by either hydrophilic or hydrophobic environments. These spaces can accept and store guest particles. The hydrophobic particles accumulate in the sites surrounded by a hydrophobic surface (black particles), while hydrophilic particles accumulate in sites surrounded by the hydrophilic environment (brown particles). Once entrapped, the particles are protected from the external environment. The entrapment space is known as the dendrimer box. The very high number of functionalities located on the surface and the outer shell allows the dendrimers to participate in hosteguest interactions and onsite release of the loaded particles.

Biomimicry

One of the outstanding properties of dendrimers is their ability to mimic biological particles, especially globular proteins. Studies have shown the close resemblance of higher order dendrimers to many proteins, such as insulin (3G), cytochrome (4G), and hemoglobin (5G). Dendrimers also mimic histone clusters; thus, they make stable complexes with the DNA and enhance gene expression.

Like proteins, dendrimers may respond to many external stimuli (solvent, pH, temperature, ionic strength) and adapt a tightly packed (resembling native proteins) or extended (resembling denatured proteins) conformation. However, there are some key differences between proteins and dendrimers.

1. Dendrimers normally have lower molecular density than comparable size proteins. Thus, they are less compact compared to the proteins.

2. The globular structure of proteins is due to the folding of the linear polypeptide chain into secondary and tertiary structures via intramolecular bonding (H-bonding, van der Waals interactions, ion pairing, and disulfide bonding), resulting in their compaction. In comparison, dendrimers acquire a globular shape by taking up smaller hydrodynamic volume.

3. Dendrimers incorporate a high degree of covalent bonding, which results in a less flexible structure than what is found in proteins.

Solvent and pH-Dependent Folding of Dendrimers

In 1983, De Gennes and Hervet showed that as the PAMAM dendrimers grow in size, the branching becomes increasingly crowded at the periphery, while remaining low density at the core. This gave an impression that dendrimers are rigid structures that, unlike proteins, are not capable of achieving multiple conformations. However, later studies have shown the dendrimers to be relatively less rigid because of the high mobility of the surface atoms, which lack interaction between the surface and the core atoms.

Therefore, the surface bonds can fold inward (resulting in a dense core) or outward (the opening of the dendrimers), depending upon the intermolecular charges as well as the van der Waals interactions.

Liu et al (2009), using G4 dendrimers, have shown the effects of pH on conformational changes (by measuring the density at various radii from the core) in the PAMAM dendrimer. At higher pH, dendrimers contained mostly nonionized, hydrophobic nitrogen moieties that facilitated low-energy van der Waals interactions between the surface and the core atoms, resulting in an inward folding of the surface atoms, thus increasing the core density (the highest density occurred at 1 nm). At neutral or lower pH, the nitrogen moieties were ionized, resulting in intermolecular repulsing and an ensuing opening of the dendrimers with dense outer shell (highest density occurred at 1.5e3 nm). This demonstrates an outward movement of dendrimer branches at acidic pH. In an earlier study, Jansen et al. (1994) constructed a dense-shell dendrimer by boc-modification of the surface groups that enhances formation of H-bonds between the surface groups.

Maiti et al. (2005) have investigated the effects of pH and solvents on dendrimer conformation by assessing the solvent-accessible areas, representing empty areas in the dendrimers. At high pH, the dendrimers exhibited only small, but restricted, areas and cavities. At neutral and low pH, the dendrimers open up, resulting in an increase in the empty surfaces. They also computed the void distribution of the inner cavities using alpha-shape and discrete flow methods. At a low pH, a single big cavity percolating the whole dendrimer structure and connecting the outer surface existed. At this pH, therefore, small molecules can diffuse in and out of the dendrimer interior.