

Dendritic polymers are widely used as multifunctional materials with specific properties (dendritic effect of surface groups and globular shape) for potential (bio-)medical and pharmaceutical applications such as e.g. DNA and drug carrier systems. The fundamental interest to understand the role of carbohydrates/oligosaccharides in various biological processes is steadily growing up besides the prerequisite to improve the behaviour and the biological properties of dendritic polymers towards biological molecules and systems. *In this context, one research interest of us is to focus on the fundamental understanding of the interaction, complexation and encapsulation properties of dendritic polymers with various oligosaccharide architectures to contribute to the development of potential diagnostic and therapeutic agents.*

Thus, the exploration of biological processes in nature requires the use of simple synthetic approach to receive water-soluble polymers with (oligo-)saccharide surface groups. Chemically attached (oligo-)saccharides on polymer surfaces preferably act as non-ionic components in water and under physiological conditions. The (oligo-)saccharides unify different properties/functions as the combination of water-solubility with (a) the inhibition or activation of proteins, enzymes and viruses and (b) the reduction of immune reaction in biological processes. Therefore, the realization of water-soluble dendritic polymer (PPI dendrimers and hyperbranched PEI) with oligosaccharide units as surface groups, shown in Figure 1, was strongly developed, based on the use of reductive amination as one-pot approach, during the last two years.

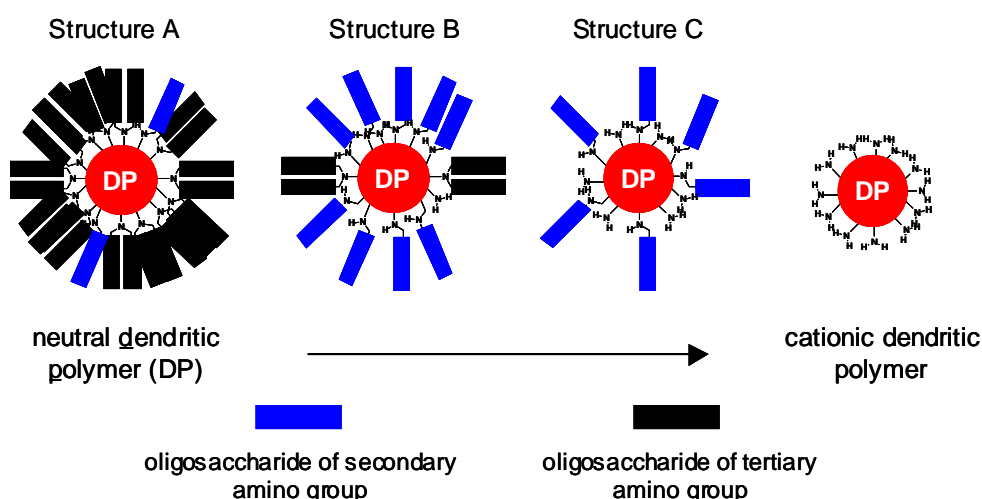


Figure 1. Realization of dendritic polymers with various oligosaccharide architectures. This includes the modification of PPI dendrimers and hyperbranched PEI.

Therefore, it was possible to vary the charge of the dendritic polymers in dependence on the oligosaccharide architectures, including the exhibition of neutral PPI dendrimers (structure A in Figure 1).

This was the starting point for us to undergo systematically studies to understand the interaction towards peptides, proteins, DNA, and RNA, including their complexation and encapsulation behaviour. Further trials were also initiated towards larger biological systems. Here, two topics of our studies are presented:

- Previous and present studies use positively and negatively charged dendritic polymers for biological studies governed by electrostatic interactions or by the formation of polyelectrolyte complexation (Figure 2). Further, the tailoring of biological processes or the inhibition or activation of biomolecules (e.g. proteins, enzymes and viruses) are initiated by dendritic polymers with mono- and oligosaccharide units as surface groups (Figure 2).

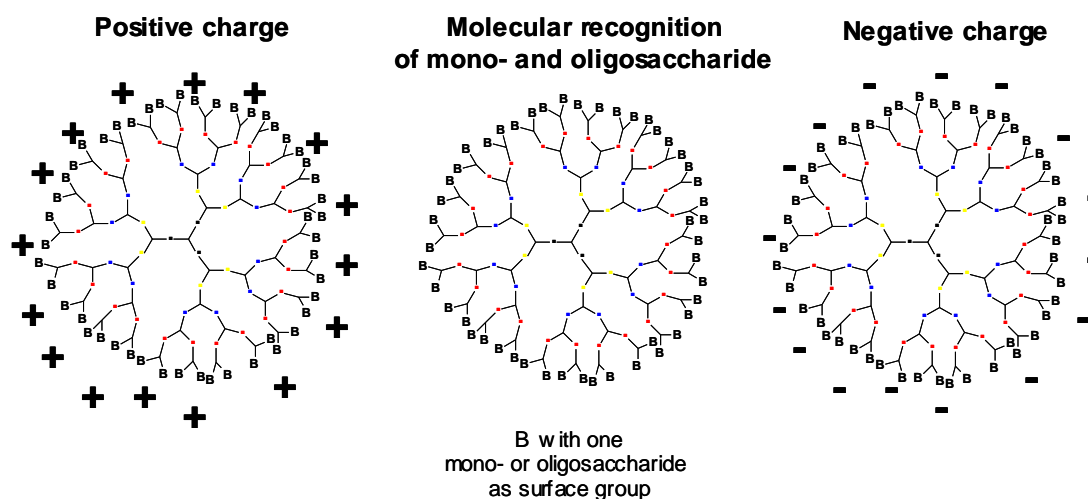


Figure 2. Present use of positively and negatively charged dendrimers and mono-/oligosaccharide-modified dendrimers for various bio-interactions.

Our research activities focus on the substitution of the biological effects of cationic dendritic polymers by preferred H-bonding driven interactions using densely-organized oligosaccharide shells on dendrimer surfaces (structure A in Figure 1). A comparison study of parent and modified PPI dendrimers revealed that similarly

strong interactions exhibited towards the human serum albumin (HSA) protein, but with different kind of interaction (electrostatic forces for cationic PPI dendrimer/HSA interaction and H-bonding forces for maltosed-modified PPI dendrimer/HSA interaction) as a first working model to explain this surprising result (Figure 3).

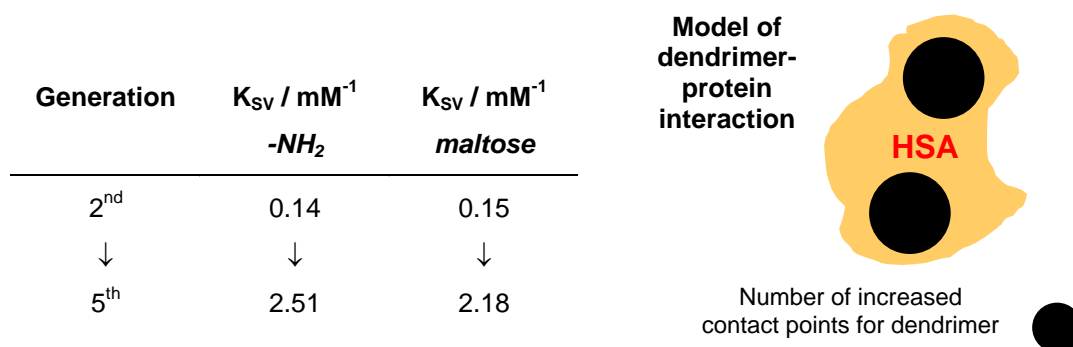


Figure 3. Comparison of Stern-Vollmer constants for the interaction of parent and modified PPI dendrimers with HSA protein submitted for publication – cooperation with Dr. Klajnert and Prof. Bryszewska / University of Lodz.

- One other point of interest is to investigate the influence of surface groups on the complexation behaviour of dendritic polymers towards bio-active molecules or metal ions for the development of carrier molecules with oligosaccharide substituents. Latest results outlined that there is no influence of the oligosaccharide (OS) surface groups on the complexation/interaction of ATP molecules towards hyperbranched PEI determined by isothermal titration calorimetry (Figure 4). Similar ATP/PEI ratios of about 25 were received (Figure 4). One assumption can be extracted from this study that the complexation of the ATP is governed by the dendritic PEI. In this context, Cu(II) complexation with maltose-modified PPI dendrimers were carried out and compared with parent PPI dendrimers (Figure 5). Complexation study of the parent PPI dendrimers in aqueous solution was not possible due to precipitation of the Cu(II)-PPI dendrimer complexes in water. Therefore, literature data were used for the comparison. Also in this case, a generation-dependent Cu(II) complexation was observed similar to the parent dendrimer. This means that the maltose surface groups have obviously no direct influence on the complexation properties of the dendritic PPI scaffold.

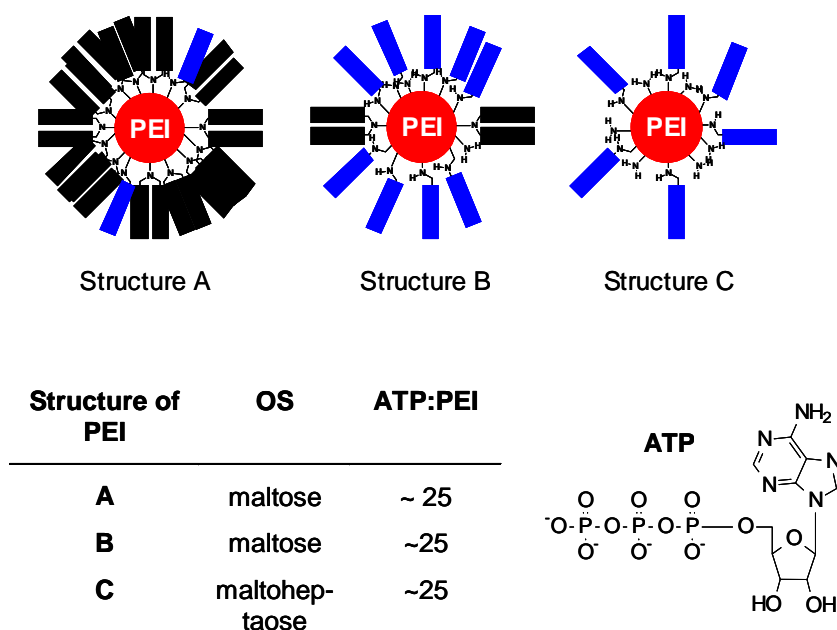


Figure 4. Complexation of oligosaccharide-modified hyperbranched PEI with ATP determined by isothermal titration calorimetry – cooperation with Prof. Haag / Free University of Berlin.

Generation	Surface groups	
	$-NH_2^a$	<i>maltose</i>
2 nd	4	3 ^b
↓	↓	↓
5 th	32	34 ^c

Cu(II) complexation in aqueous solution

^a In MeOH; Chem. Ber. **1997**, 130, 725. ^b MBS **2007**, 7, 373. ^c unpublished results for 3rd – 5th generation.

Figure 5. Comparison of Cu(II) complexation of maltose-modified PPI dendrimer towards parent PPI dendrimers.

Further, deeper studies are done to better understand our previous results, how oligosaccharide architectures can influence the interactions towards biomolecules and bio-systems. Future investigations are also directed to the introduction of bio-functions, especially the coupling of various receptors for the establishment of receptor-mediated biological processes.

Following cooperation partners, few selected, are supporting our research activities:

Dr. B. Klajnert and Prof. Bryszewska – University of Lodz:

Interaction of dendrimers with various biomolecules

Prof. Haag – Freie Universität Berlin:

Interaction with bio-active molecules by isothermal titration calorimetry

Dr. Seidel – TU Bergakademie Freiberg:

General interactions determined by isothermal titration calorimetry

Prof. Brutschy – Johann-Wolfgang-Goethe Universität Frankfurt:

Determination of M_w by LILBID-MS

Dr. Aigner – Philipps-Universität Marburg:

Hyperbranched PEI as carrier systems for si-RNA for in vitro and in vivo application

Dr. Fahmi – University of Nottingham:

Preparation of Au particles stabilized by PPI dendrimer and their adsorption behaviour on surfaces

Prof. Pompe – TU Dresden:

Application of fluorescent Au clusters stabilized by PPI dendrimers and their bio-distribution in various cell lines