Review Article

Star Polymers: An Overview

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ABSTRACT

This review article describes the synthesis, properties and some applications of star-shaped polymers. The arms constituted of homo- or co-polymers of different polymers are also reviewed. Methods of synthesis of various types of star-shaped polymers, including "arm first" and "core first" procedures, is given as an introduction along with some details. Then, the synthesis of star polymers (including miktoarm stars) with strictly defined as well as with varying number of arms and having cores formed from small and/or large molecules: branched, cross-linked, etc., is described.

Interest in star-shaped and branched systems based on poly (ethylene oxide) (PEO) is mainly motivated by their potential applications in the biomedical and pharmaceutical areas. The properties and applications of PEO stars are also reported, such as drug carriers, surface modifiers, hydrogels, components of membranes, and also have some biomedical applications. Their potential applications as components of different types of complexes, hydrogels, networks, and ultrathin coatings are indicated.

KEYWORDS: Star polymers; miktoarm star polymers; poly (ethylene oxide) stars; core first; arm first; drug carrier; interpenetrating polymeric networks.

Introduction

Polymers are a very important class of materials. Polymers occur naturally in the form of proteins, cellulose (plants), starch (food) and natural rubber. Engineering polymers, however, are usually synthetic polymers. The field of synthetic polymers or plastics is currently one of the fastest growing materials industries. Also, the macromolecular structure of synthetic polymers provides good biocompatibility and allows them to perform many biomimetic tasks that cannot be performed by other synthetic materials, which include drug delivery, use as grafts for arteries and veins, and use in artificial tendons, ligaments and joints. A polymer is a material whose molecules contain a very large number of atoms linked by covalent bonds, which makes polymers macromolecules.

Polymers consist mainly of identical or similar units joined together. The unit forming the repetitive pattern is called a "mer" or "monomer". Usually the biggest differences in polymer properties result from how the atoms and chains are linked together in space. Chemically, polymers are long-chain molecules of a very high molecular weight, often measured in the hundreds of thousands. For this reason, the term "macromolecules" is frequently used when referring to polymeric materials. The earlier polymers used were natural products especially cotton, starch, proteins, and wool. Beginning early in the twentieth century, synthetic polymers were made. The first polymers of importance, Bakelite and nylon, showed the tremendous possibilities of the new materials. However, the scientists of that day realized that they did not understand many of the relationships between the chemical structures and the physical properties that resulted. The research that ensued forms the basis for physical polymer science. Polymers are amorphous, often because their chains are too irregular to permit regular packing.

Special Types of Branched Polymers

Graft Polymers

A graft polymer molecule is a branched polymer molecule in which one or more side chains are structurally or configurationally different from the main chain – a polymer comprising of molecules in which the backbone is attached at various points to side chains containing atoms or groups differing from those in the main chain. The main chain may be a co-polymer or may be derived from a single monomer as shown in Figure 1.
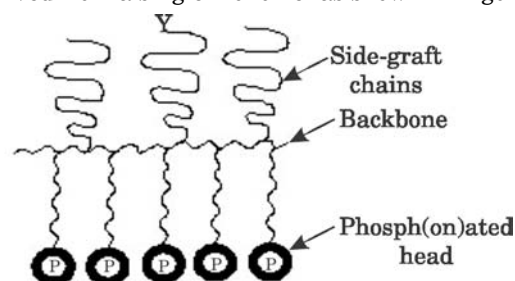

Fig. 1. Graft Polymer

Comb Polymers

A comb polymer molecule consists of a main chain with two or more three-way branch points and linear side chains. If the arms are identical, the comb polymer molecule is said to be regular (Figure 2).
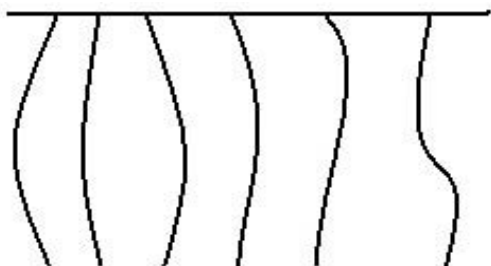

Fig.2. Comb Polymer.

Brush Polymers

A brush polymer molecule consists of a main chain with linear, unbranched side chains where one or more of the branch points has at least a four-way functionality. A polymer brush (Figure 3) consists of end-tethered (grafted, anchored) polymer chains stretched away from the substrate due to the volume-excluded effect. In mixed brushes, two or more different polymers grafted to the same substrate constitute the brush. Unlike unmixed brush polymer, different polymers in the mixed brush segregate into nanoscopic phases. The phase segregation is a lateral segregation process in a nonselective solvent in which different polymers form spherical or elongated clusters. Both the polymers are exposed on the top of the brush. In selective solvents, the mixed brush structure may be seen as a combination of lateral and layered segregation mechanisms. In the latter case, one polymer preferentially segregates to the top of the brush, while another polymer forms clusters segregated onto the grafting surface. The most important difference of the mixed brush compared to the homopolymer brush is that not only the height and density profile but also the composition profile depends on the solvent quality. In other words, the surface composition of the brush is switched by a change in its environment.
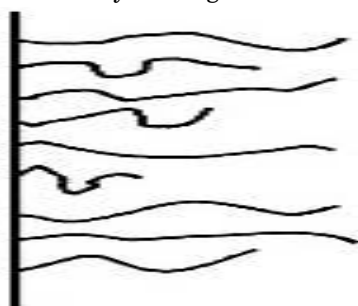

Fig.3. Brush Polymer.

Polymer Networks

A polymer network is a network in which all polymer chains are interconnected to form a single macroscopic entity by many crosslinks. An interpenetrating polymer network (IPN) is a polymer comprising two or more networks which are at least partially interplaced on a polymer scale but not covalently bonded to each other. The network cannot be separated unless chemical bonds are broken. The two or more networks can be envisioned to be entangled in such a way that they are concatenated and cannot be pulled apart, but not bonded to each other by any chemical bond. Simply mixing two or more polymers does not create an interpenetrating polymer network (polymer blend), nor does create a polymer network out of more than one kind of monomers which are bonded to each other to form one network (heteropolymer or copolymer). There are semi-interpenetrating polymer networks (SIPN) and pseudo-interpenetrating polymer networks also.

Star Polymers

A star polymer molecule is a branched polymer molecule in which a single branch point gives rise to multiple linear chains or arms. If the arms are identical the star polymer molecule is said to be regular. If adjacent arms are composed of different repeating subunits, the star polymer molecule is said to be variegated. Star polymers are gaining interest because of their characteristic rheological and dilute solution properties. The interest for branched polymers arises from their compactness and enhanced segmental density as compared to their linear counterparts of the same molecular weight. Therefore star shaped polymers resemble more closely the hard sphere model rather than linear polymers, especially when the numbers of arms in the star polymer increases. Besides the high segmental density star shaped polymers and linear polymers differ in shapes. The hard sphere character of star polymer is directly correlated to the degree of dynamic entanglement. By increasing number of arms degree of dynamic entanglement decreases for star shaped polymers and is substantially lower than linear polymers. This causes lower intrinsic viscosity of star polymers as compared to linear polymers of same molecular weight (van Aert et al., 1996). Star-shaped polymers consist of at least three linear polymeric chains of comparable lengths radiating from one single multifunctional branched point, usually called the core or the central nodule, and which can itself be polymeric. In a star-shaped polymer the core radius should be much smaller than the dimension, e.g., the root-mean square end-to-end distance of the arm. If the core size is much larger, such an entity can be considered as a "nanoparticle" since its property will be dominated by the cross-linked nanometer-sized core. If the nanoparticles are approximately spherical in shape, they are referred to as "nanospheres". The main feature of star-shaped polymers, differentiating them from the linear analogues of identical molar masses (Mn), is their compact structure (smaller hydrodynamic volume and radius of gyration, and therefore lower viscosity) and the multiple functionality that is useful in some of their applications. Star-shaped polymers are called homostars when all arms have the same chemical structure. Arms may be built of homo-, co-, or even ter-polymers, therefore the

final properties of the resulting star-shaped polymers (e.g., star-block and heterostar copolymers) may be adjusted by choosing the respective chemical structure of an arm and core, depending on the required application. Thus, star-block copolymers have each arm constituted of two homopolymeric blocks of different chemical nature, whereas heterostar copolymers have equal numbers of arms of two kinds, differing in chemical nature as well as average length, attached to the core. Based on the chemical compositions of the arm species, star polymers can be classified into two categories: homo-arm (or regular) star polymers or miktoarm (or heteroarm) star copolymers. Homoarm star polymers consist of a symmetrical structure comprising radiating arms with identical chemical composition and similar molecular weight. In contrast, a miktoarm star molecule contains two or more arm species with different chemical compositions and/or molecular weights and/or different peripheral functionality (Figure 4).
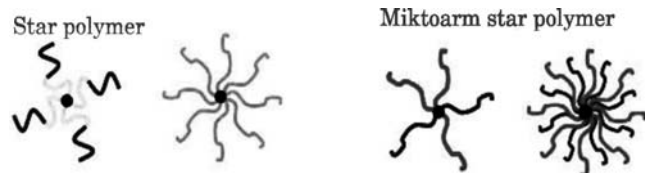

Fig. 4. Star Polymers.

Methods of Preparation

There are three methods for the preparation of star polymers namely,

1. Core first approach
2. Arm first approach
3. Coupling onto process

The "core-first" approach where the controlled polymerization is conducted from either a well defined initiator with a known number of initiating groups or a less well defined multifunctional macromolecule. An approach that until recently had not received as much attention is the "coupling onto" approach where a tele-functional linear molecule is reacted with a preformed core molecule containing complementary functionality. In order to improve the coupling efficiency, a highly efficient organic coupling reaction such as the click reaction is required. There are two approaches to the "arm-first" synthesis of star polymers. One is where a linear "living" copolymer chain, or added macro initiator, is linked by continuing the copolymerization of the mono-functional macro initiator with a divinyl monomer forming a crosslinked core. The other, is the direct copolymerization of a macromonomer with a divinyl monomer in the presence of a low molecular weight initiator. A combination of "arm-first" and "core-first" methods is particularly useful for synthesis of miktoarm star copolymers. One employs the retained initiating functionality in the formed "arm first" core to initiate the

polymerization of a second monomer in a "grafting out" or a "grafting from" copolymerization.

Core First

The following section on nano-composites formed by grafting from the surface of a functionalized particle is an evolution of the "core first" approach to synthesize star macromolecules. Initially a low molecular weight multi-functional molecule was used in a "grafting from" reaction to form star macromolecules with a well defined number of arms. Use of hexakis (chloromethyl) benzene as a well defined multifunctional initiator for the polymerization of styrene provided the first multiarm polymer prepared using atom transfer radical polymerization (ATRP). The composition of the core and arms were quickly expanded as shown in Figure 5. Since the tethered chains in a grafting from the reaction retain their terminal functionality they could be chain extended to form star block copolymers and/or the radically transferable atoms on the chain ends (X) could be converted to other functional groups (F) suitable for post-polymerization fictionalization reactions (Angot et al., 1998). Less well-defined multiarm star structures were prepared by grafting from a soluble multifunctional hyper branched core. The core was prepared by polymerizing a molecule containing both a reactive group suitable to initiate a controlled radical polymerization (CRP) and a polymerizable double bond, an initiator/monomer or an inimer. Self-condensing vinyl polymerization using ATRP has been applied to inimers, i.e. monomers that also contain activated halogen atoms, such as α-bromoesters and benzyl halides. For example, when 2-bromopropionyloxyethyl acrylate was polymerized in the presence of a copper catalyst with 4,4'-dinonyl-2,2'-bipyridine ligands, a hyper branched polymer with degree of branching ~0.5 and DP = 78 was obtained. Each soluble hyper branched polymer contained on average 78 active bromopropionyloxy groups which were used to initiate the polymerization of methyl acrylate forming a star with 78 arms (Figure 6).

A simple sequential polymerization of a cross linker followed by polymerization of a monomer provides a broadly applicable approach to star copolymers. This novel method, termed "star from in situ generated core", belongs to the broader category of "core first" methodology and presents an alternative strategy for synthesis when compared to the traditional "arm-first" method, in which monomer is polymerized first followed by formation of the core by co-polymerization of a cross-linker (Figure 7).
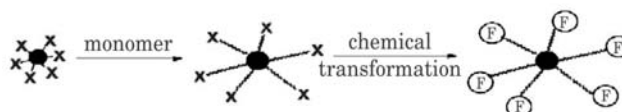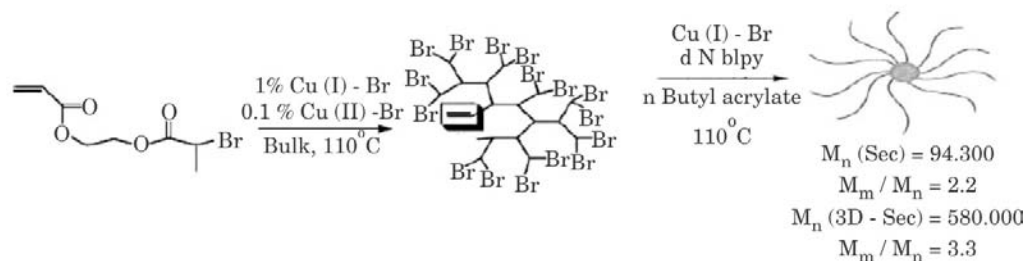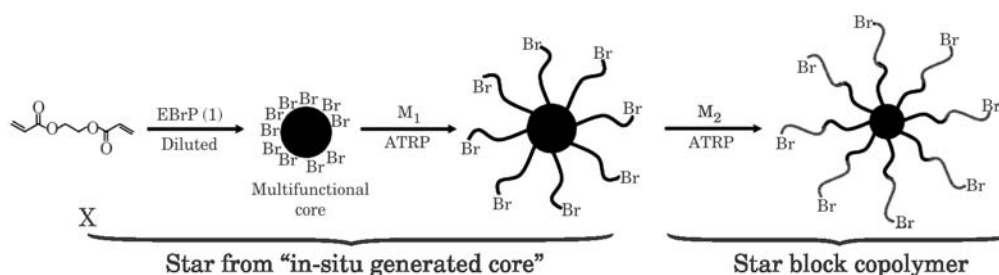

Fig.5. Core First Approach.

Fig.6. Synthesis of Polya-crylate Star Polymer.

M_n (Sec) = 94.300

M_m / M_n = 2.2

M_n (3D - Sec) = 580.000

M_m / M_n = 3.3

Star from "in-situ generated core"   Star block copolymer

Fig. 7. Star Block Copolymer.

To illustrate this new concept for the synthesis of star polymers using controlled radical polymerization techniques, ATRP was applied to the homopolymerization of a crosslinker, ethylene glycol diacrylate (EGDA) to generate a multifunctional crosslinked core (nanogel). Monovinyl monomers were added to the reaction mixture at a high conversion of the cross linker and were polymerized from the poly-EGDA nanogel macroinitiator (MI) to form the star arms. A spectrum of different acrylate monomers were polymerized from the first formed core providing star polymers with different compositions for the arms. Several parameters affected the structure of the star, such as the initial concentration of the crosslinker, the molar ratio of crosslinker to initiator, and the moment of addition of the monovinyl monomer to the ongoing polymerization reaction; affect the structure of star polymer. The star polymers preserved the initiating sites at the chain ends, and were further used as star MIs for arm extension by polymerization of a second monovinyl monomer to form a star block copolymer.

Arm First

Macroinitiator Approach

The "arm first" approach forms the core of the star macromolecule by coupling monofunctional "living" polymeric chains with a difunctional reagent and was first applied to living anionic polymerization (Figure 8). A similar approach was also successful using ATRP. Initially the simple chain extension of a linear macroinitiator with a crosslinker provided star macromolecules with a broad polydispersity as a result of star-star coupling reactions (Yen and Merril, 1997). There are several parameters in an ATRP that should be carefully controlled in order to maximize the yield of stars and prevent/reduce star-star coupling reactions.

Some detailed studies have been carried out on the coupling of monofunctional polystyrenes and polyacrylates with divinylbenzene (DVB) and di(meth)acrylates to prepare star polymers and the following guidelines were developed:

- The ratio of di-functional reagent to growing chains should be in the range of 10-20.

- Monomer conversion (or reaction time) has to be carefully controlled and stopped before star-star coupling occurs. It seems that ~5% of arms cannot be incorporated into the star macromolecules under typical one step conditions.

- Higher yields of stars can be observed for polyacrylates than for polystyrenes. This may be attributed to a higher proportion of terminated chains (due to slower propagation and higher concentration of radicals) in styrene polymerization under "standard" ATRP conditions. The choice of the difunctional reagent is important and reactivity should be similar to or lower than that of the arm-building monomers.

- Halogen exchange slightly improves the efficiency of star formation. Under typical conditions, ~50 arms are coupled into star structures. Apparent molecular weights, measured by gel permeation chromatography (GPC), show a 10-20-fold increase in molecular weight (from M_n = 10,000 to M_n ~ 150,000) but light scattering indicates that the stars have a much higher molecular weight (M_n ~500,000). Ranges of initiators, monomers and cross linkers were examined for the preparation of star molecules with peripheral functionality and cores of differing phobicity. Another approach to forming star polymers in high yield was via cross-linking self organized amphiphilic macro initiators by AGET ATRP in aqueous dispersed media. Linear

poly (ethylene oxide)-b-polystyrene (PEO-PS-Cl) block copolymers were the arm precursors. The amphiphilic block copolymers with halogen chain-end functionality formed divinyl cross-linker swollen micelles in water and then were cross-linked by the cross-linkers when polymerization was initiated. Due to the formation of micelles before the polymerization was initiated, star-star or star-linear chain reactions were not required for the star formation. This suppressed star-star coupling reactions and resulted in the formation of star polymers with low PDI (Mw/Mn < 1.1) but still high molecular weight (over 1000 kg/mol) is depicted in Figure 9.
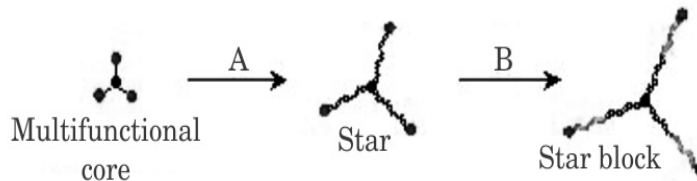
Macromonomer Approach

Another approach to arm first star copolymers, with an available core containing initiating functionality, is the CRP (controlled radical polymerization). This consists of higher molecular weight macro monomers in a pure homo-polymerization initiated with a small molecule initiator. This usually leads to a "brush molecule" with a degree of polymerization of 10-25 which, from a topological standpoint, can be considered a star (Figure 10).

The sequential addition of additional initiator and cross-linker to the reaction increases the number of macromonomer units incorporated into each star.
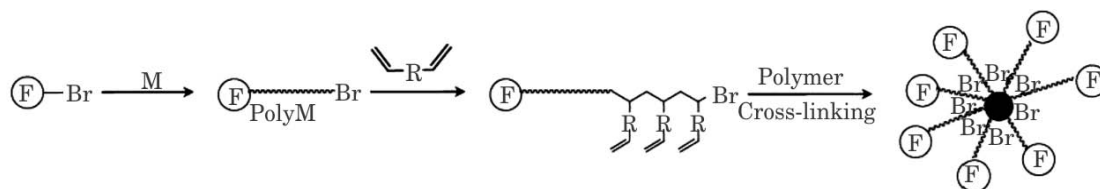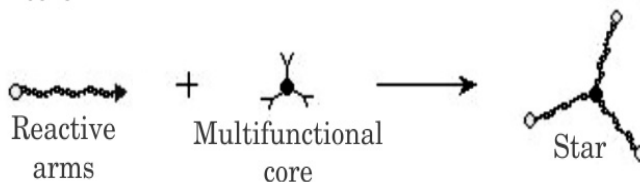

Fig.8. Synthesis of Star Shaped Polymers Using Arm First Approach.
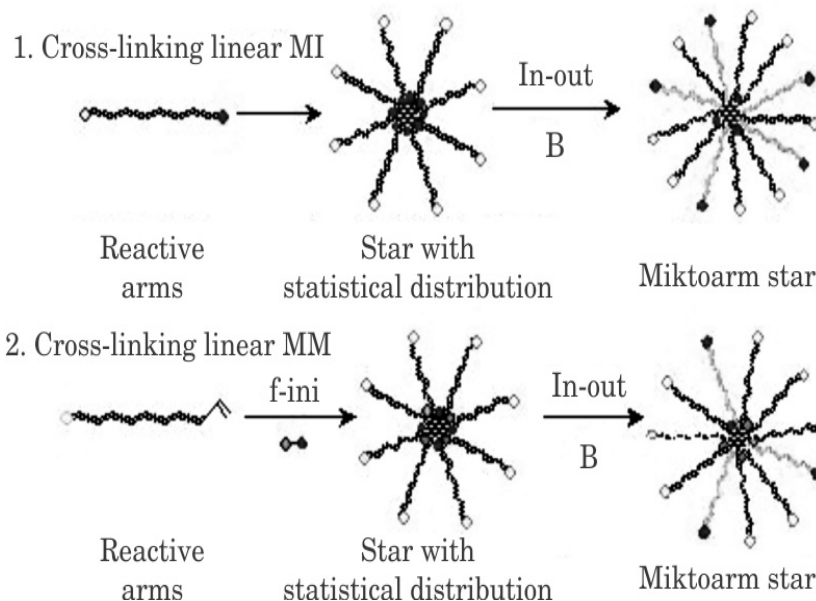

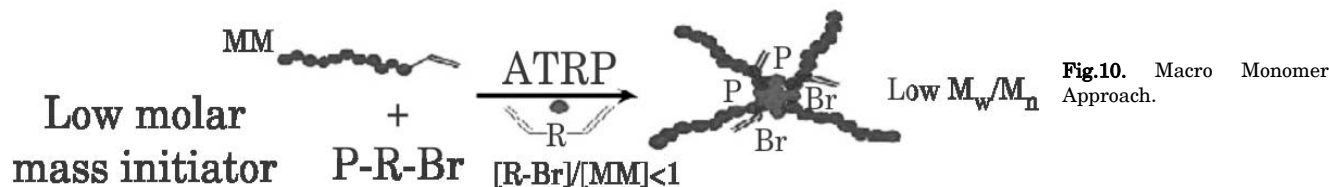**Fig.9.** Synthesis of Star Polymers By Different Methods.

Fig.10. Macro Monomer Approach.

Miktoarm Star Copolymers

In-Out Method

Both approaches to form star molecules using the arm first approach retain the initiating functionality within the core of the star and therefore provide a simple approach to form mikto-arm stars by conducting a controlled polymerization of a second monomer from the accessible initiator functionality in the core. As noted above, one arm-first procedure involves the synthesis of a linear mono-functional polymer chain polyA, which is used as a macroinitiator (MI) in a subsequent cross-linking reaction. It is used along with a divinyl compound to produce a (polyA)$_n$-polyX star polymer, where polyX represents the core of the star polymer and n is the number of polyA arms. The initiating sites are preserved within the core of the star polymer (i.e., alkyl halide groups in ATRP) and the (polyA)$_n$-polyX star polymer can be used as a multifunctional star initiator in a chain extension reaction with a different monomer, B, to yield a miktoarm star copolymer, (polyA)$_n$-polyX-(polyB)$_m$. This combination method for synthesizing miktoarm star co-polymers was termed the "in-out" method (Figure 11). The efficiency of initiation of the second set of arms is dependent on the compactness of the first formed core with less densely crosslinked cores providing more efficient initiation, i.e. a greater fraction of the encapsulated initiator sites for grafting out polymerization. Normally, one seeks to or has to form a chemically stable core. However, it is possible to select a cross-linking agent with a degradable link between the two functional cross-linking groups and prepare a material with a degradable core. This was accomplished by linking the first formed arms with a dimethacrylate crosslinker containing a disulfide link between the methacrylate units. As shown in the above scheme the mikto-arm star copolymer could be degraded in a reducing environment to form a mixture of an AB block copolymer and some residual A-homopolymer. The ratio between the block copolymer and homopolymer gave a direct measurement of the initiating efficiency of the constrained core initiating units; in this example it was only ~20%. Recently reported a new strategy has been reported for synthesis of miktoarm star copolymers using a simple and general "arm-first" method, i.e., one-pot ATRP cross-linking a mixture of different linear MIs and/or MMs with a divinyl cross-linker in order to synthesize miktoarm star copolymers with potentially any desired molar ratio and composition of the arms (Figure 12). Miktoarm star copolymers containing five

kinds of arms were synthesized for the first time by copolymerizing a mixture of five linear MIs with different chemical composition. When linear MMs were partially or completely used as arm precursors instead of MIs, miktoarm star copolymers with a high star yield and low polydispersity were successfully synthesized.
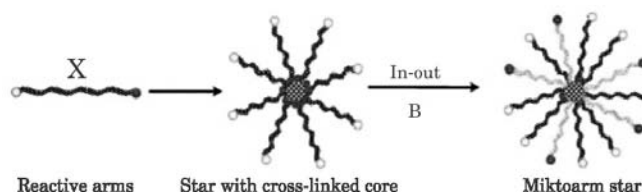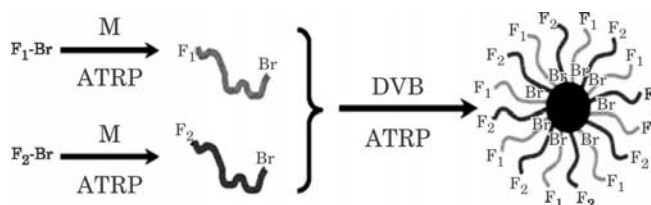

Fig. 11. In Out Method

Fig. 12. Miktoarm Star Synthesis.

Analysis of Star-Shaped Polymers

The structure of star polymers is usually evaluated by ^{1}H NMR spectroscopy and their molar masses are determined by size exclusion chromatography (SEC). Much of the published data is approximate because Mn and/or Mw are often calculated using a calibration based on linear standards, e.g., polystyrene. Only SEC with triple detection gives reliable values (Lapienis G and Penczek S, 2004). Stars obtained by methods arm first, core first, and the in out method have broad distribution of the number of arms (f), because of the influence of the reaction conditions. Several methods are used for determination of the number of arms (f), which are as explained below.

(1) By comparison of Mn (molar masses) determined for star polymer and the arm precursor, according to the formula: (Held D and Müller AHE, 2000)

$$fn = \frac{Mn_{(star)}(1 - W_{core})}{MN_{(arm)}} \qquad .....(1)$$

Where,

W_{core} - Denotes the weight fraction of a core.

fn - Number of arms

$Mn_{(star)}$ - Molar masses of star

$Mn_{(arm)}$ - Molar masses of arms

This method can only be used for star-shaped polymers with the first generation of arms (i.e., for the "first stars") from branching indices (g) equal to the ratio of radii of gyration (Rg) of star and linear polymers having the same molar masses (M) and determined independently.

$$g = \frac{(Rg)^2 star}{(Rg)^2 in}$$

Where,

Rg – Radii of gyration

(E.g. by SEC with triple detection). Then, the number of arms can be calculated according to the equations given by Stockmayer (Zimm and Stockmayer, 1949) Bywater (Bywater, 1979) and Burchard (Knischka, 2000) for regular and/or random stars.

Star-Shaped PEO Polymers with Different Structure of Arms (Miktoarm Stars)

According to Hadjichristidis "the term miktoarm stars was adopted for stars with chemical asymmetry." Thus, miktoarm stars are molecules having chemically different arms (A, B, C or D), linked to the branched point. Their structures, as shown in Figure 13, are described as follows: A2B, AB3, ABC, A2B2, and ABCD. Hadjichristidis developed methods for the synthesis of miktoarm polymers, and has published reviews describing various star structures and discussed their properties. Summarized here is the data of the synthesis and the structure of miktoarm star polymers, namely AB2, A2B, A2B2, A3B, ABC, ABCD, and A2B4, where at least one arm is built of homo- and/or co-polymer of PEO. Some arms are formed from commercially available MPEG. In the case of miktoarm PEO polymers having different structures of arms, various methods of synthesis have been applied. Some are as given below:

1. The selective step-by-step substitution of the chlorine atoms in chlorosilanes with anionic living polymer chains to form the star co-polymer (Roovers, 1999). Thus, living polystyrene (PS) chains reacted with $SiCl_4$ in a molar ratio 2:1 forming the structure $(PS)_2SiCl_2$. The addition of living PEO chains gave the final A2B2 miktoarm stars: $(PS)_2Si(PEO)_2$. Because of a steric hindrance, formation of stars with higher content of PS chains

(three or four arms) could be avoided. A2B stars were obtained when CH_3SiCl_3 was used instead of $SiCl_4$ (Figure 13).

2. A method based on a macromonomer technique in which non homopolymerizable macromonomers bearing a naphthalene or 1,1-diphenylethylene (DPE) group at one chain end are incorporated at the block junction of a diblock co-polymer. This strategy, based on the use of a core molecule bearing a protected anionic initiating function, was applied, e.g., for the synthesis of ABC terpolymers of styrene (A), ethy-lene oxide (B), and methacrylic acid, l-lactide (l-LA) or caprolactone (CL) as C. First, a diblock co-polymer of A and B containing a core molecule in its center, was prepared. After deprotection and several purification steps of the diblock co-polymer, the central function was activated to initiate the anionic polymerization of the third monomer (C).

3. A method based on two successive initiation steps on a "bifunctional macroinitiator", bearing two chemically different functional groups, is able to independently initiate two polymerizations. This method was also used for the synthesis of ABC star co-polymers.

4. Formation of difunctionalized macroinitiator, being able to initiate polymerization of the second monomer by introduction of a bifunctional molecule into the end of a living macromolecule. This method was usually applied to the synthesis of AB2 co-polymers.

5. Using two successive anionic polymerization steps and one polymer-polymer coupling reaction.

6. Recently the application of a "click" chemistry method has been reported (Grzegorz Lapienis, 2009) (Figure 14).

Characterization of Star Polymers

Characterization of star polymers is done using size exclusion chromatography, gel permeation chromatography, vapour phase osmometry, gas chromatography and by nuclear magnetic resonance spectroscopy.
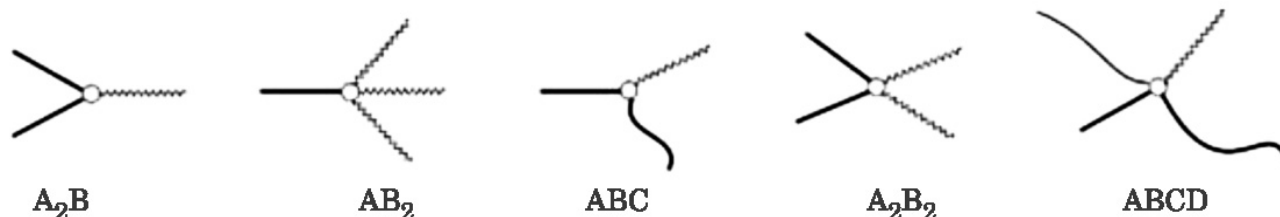

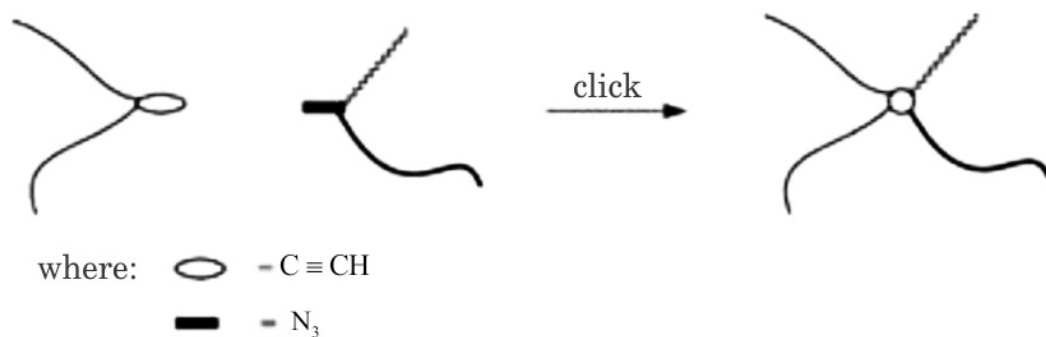**Fig.13.** Miktoarm Stars Are Molecules Having Chemically Different Arms.

Fig.14. Click Reaction.

Properties of Star-Shaped Polymers

Various properties of star-shaped polymers containing PEO arms have been investigated, e.g., thermal, crystallization and solution properties, ability for micellization, formation of complexes with salts, and ionic conductivity in the solid state polymers. It has been found that apart from the chemical structure of the stars, the length of arms also had considerable influence on their properties. Some of selected properties of star-shaped PEO polymers, available in the literature, are as discussed below (Kojima, 2000).

Thermal Properties of Star-Shaped Polymers

The thermal properties and the crystallization behavior of PEO stars, namely melting (Tm) and crystallization (Tc) temperatures and the degree of crystallinity (Xc), have been studied in many papers. Thermal and crystallization data were reported for heteroarm star co-polymers PS-DVB-PEO dendrimers with PCL-*b*-PEO arms   stars with hyperbranched or cubic silsesquioxane cores, dendrimer-like co-polymers (PS)₃-(PEG-P*t*BA)₃, star-shaped polymers having 3, 4, 7, 8, and 12 arms being PEO, PEO-PCL, or PEO-PLA block co-polymers, miktoarm AB2 (PEO(PS)₂), and ABC (PS-PEO-PCLstars, and others) . Star-shaped polymers have lower Tm and Tc temperatures and degrees of crystallinity (Xc), depending on the length and number of PEO arms, than their linear analogs with comparable molar masses. It is well known from literature that the increase of the number of arms usually lowers Tm and Xc of stars.

Formation of Complexes

Star-shaped polymers containing PEO arms form complexes with various molecules. In a few papers the formation of complexes of multiblock PEG-PEI molecules with DNA and crystalline inclusion complexes of multiarm hyperbranched polyether stars with various cyclodextrins has been reported.

Solution and Solvation Properties of Star-Shaped Polymers

The amphiphilic star-shaped polymers could change their conformation with solvent polarity because their hydrophilic segments extend in more polar solvents and hydrophobic segments in less polar media. The high ability of the PEO chains to solvate metal ions was noticed, especially when several chains were located in close vicinity to each other. Thus, star-shaped PEO polymers act as solubilizing agents for inorganic salts in organic media. Additionally, dendrimer-like co-polymers with short PEG arms (n = 3–5) solubilized lithium triflate salts in chloroform or Cu^{2+} ions in the organic solvents. The large polyfunctionality in the case of PEO stars may be advantageous because it leads to a good water solubility and biocompatibility (Grzegorz Lapienis, 2009).

Applications of Star Shaped Polymers

The exploitation of star-shaped and hyper branched biocompatible and biodegradable polymers is receiving considerable attention. Biocompatible segments of the star-shaped block copolymers are of particular interest to biomedical applications. PEG and its conjugates are used in wide areas of small molecule encapsulation, drug formulation, modification of proteins and pharmaceutical molecules, cosmetics, biomedical coatings, and other surface modifications. Their potential applications as components of different types of complexes, hydrogels, networks, and ultrathin coatings, etc. are indicated here (Harris and Zaplisky, 1997; Miao, 2005; Steege, 2007).

Hydrogels

Functional PEO star polymers are regarded as a particularly interesting class of materials since they represent versatile building blocks for structured polymer hydrogels (Keys, 1998; Knischka, 2001; Lutolf, 2003; Dalton, 2008). The arms' length and functionalities influence the network properties, the swelling, and the elasticity of the resulting gels (Sukumar and Lopina, 2002). Each macromonomer had four end groups able to react only with the groups on the other macromonomer, not only in the laboratory but also *in vivo.* Cross-linked PEO star gels obtained by electron beam irradiation or by irradiation with cobalt (Co⁶⁰) are interesting because of a high concentration of terminal hydroxyl groups which could be functionalized with drugs or other moieties (Keys, 1998). Stars with photo-cross-linkable groups formed gels possessing sufficient tissue adhesive properties to seal corneal lacerations (Carnahan, 2009).

Membranes

Membranes from star-shaped PEO polymers were used for selective gas permeation of propane/propylene, ethane/ethylene and $CO_2/N_2(H_2)$ (Yin et al., 2004). Star-shaped polymers, having a core derived from diepoxides units, with phosphate groups placed on the core and/or at the end of PEO arms, have already been successfully applied as the effective macroionophores in liquid membranes for the separation of Zn^{2+} or Cu^{2+} ions from a multi-cation mixture, which contain alkali, alkaline earth, and transient metal cations. The selectivity of these macroionophores is governed both by the properties and its placement in the star-shaped macromolecules of ionizable groups and the molar mass of the attached polyether arms (Wódzki, 2002; Lapienis, 2009).

Modification of Surfaces

PEO star macromolecules immobilized onto surfaces are more effective in preventing protein adsorption, due to their compact structure, high segment density, and many reactive end groups, than linear poly (ethylene oxide) (Yen and Merrill,1997). Grafting of PEG is a common strategy for reducing nonspecific interactions of surfaces with proteins (Groll, 2005). The surfaces were also modified for these purposes with star PEO molecules. Surfaces have been modified with layers prepared from homostar or star-block copolymers of PEO. Stable surface films were also formed by dendrimer-like polymers. Star-shaped biopolymers are also widely exploited as scaffolds for tissue engineering (Merrill, 1993). Drug release from star-block co-polymers with polylactide and polyglycolide blocks is generally controlled by both drug diffusion and polymer erosion. Therefore, after degradation of the polyester blocks PEO stars could be completely excreted due to their small hydrodynamic radius (Jie and Venkatraman, 2005).

Biomedical Applications

As mentioned above, PEO (PEG) exhibits specific properties such as chemical stability under basic or neutral conditions, water solubility, non-toxicity, ion-transporting ability, and the presence of functional group(s) for attaching biologically active molecules. Therefore, high functionality, good water solubility and biocompatibility are the main advantages of PEO stars that can be exploited in biomedical applications. Star-shaped biopolymers are also widely exploited as scaffolds for tissue engineering. Ultrathin coatings formed from reactive six-arm star-shaped PEG prepolymers, modified with peptides enabled cell adhesion of fibroblast and human mesenchymal stem cells in contrast to unmodified star-shaped PEG ultrathin films. Recently, a bioactive-functionalized electrospun matrix based on four-arm star-shaped PEG, functionalized with low-molar mass heparin, useful for applications in wound dressing and tissue engineering, has been reported. Dendrimers are large and usually hydrophobic molecules. Thus, the introduction of PEO arms causes their solubility as well as the solubility of capped biologically active molecules (e.g., drugs having usually

hydrophobic properties host-guest system). When the PEG is coupled to a dendrimer, the efficiency of drug encapsulation depends on PEG arm length and the arm number at the surface. It was proposed that the arms not only help to stabilize the entrapped molecules, but also to solubilize some hydrophobic molecules within PEG layers. PEGylated poly (amido) amino (PAMAM) dendrimers enhance the solubility of drugs, e.g., 5-fluorouracil, methotrexate, adriamycin, indomethacin, and pyrene (model of pharmaceuticals). Drug release from star-block co-polymers with polylactide and polyglycolide blocks is generally controlled by both drug diffusion and polymer erosion. Therefore, after degradation of the polyester blocks PEO stars could be completely excreted due to their small hydrodynamic radius. Stars with a hyperbranched polyester core were used for the encapsulation of paclitaxel and PEGylated poly (ethylene imine) (PEI) was studied as a potential gene delivery system (Grzegorz Lapienis, 2009).

High Performance Gene Delivery Polymeric Vector: Nano-Structured Cationic Star Polymers

The cationic polymers, which can generate nanoparticles by formation of polyion complexes 'polyplexes' with DNA, irrespective of its size and kind, are highly expected as one of the major materials for non-viral vectors. However, the primary obstacle toward implementing an effective gene therapy using the cationic polymers remains their relatively inefficient gene transfection *in vivo* than virus vectors. To achieve an enhancement of gene transfection using cationic polymers, numerous studies have been performed by various approaches: the chemical synthetic engineering approach in which the kind and composition of the polymers are modified; biochemical approach with targeting ligands such as galactose, mannose, transferrins, or antibodies into the polymers; functional molecular engineering approach in which stimulus-responsive polymers with light and thermal reactivity are designed as high performance vectors; and physical engineering approach in which physical stimulation with electroporation, gene gun, ultrasound and hydrodynamic pressure are provided at the transfection. However, few studies in the molecular structure of cationic polymers, which are usually synthesized by conventional radical polymerization, have been reported, except for the effects of changes in the polymer chain length and composition of polymers and complex multi-branching polymers, of which structural analysis is impossible. Since precise molecular design, including the molecular weight and three dimensional structures, by conventional radical polymerization was quite difficult in general, the systematic structure-dependency of cationic polymers in gene transfection has not been established.

Other Applications

Star-block three-arm double hydrophilic copolymers composed of poly (ethylene oxide) (PEO) and poly (acrylic acid) (PAA) blocks have been used for the stabilization of $CaCO_3$ particles. The adsorption layer of the star

copolymer protects the liquid precursor of amorphous calcium carbonate from coalescence and/or coagulation (Grzegorz Lapienis, 2009).

Conclusions

Due to an increasing interest in the exploitation of star shaped polymers, some of their properties and applications as drug carriers, surface modifiers and elements of membranes as well as hydrogels have been discussed this article. This article also gives ideas regarding the synthesis of star polymers and their properties with the ability to choose to attach the required functional moiety at its arms. Star polymers could prove to be an important tool for the delivery of multiple drugs having different functional groups and properties to the body in the years to come.

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