We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,300

Open access books available

172,000

International authors and editors

190M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Polymer Properties: Functionalization and Surface Modified Nanoparticles

*Chander Amgoth, Chiuyen Phan, Murali Banavoth,
Santosh Rompivalasa and Guping Tang*

Abstract

Herein, the various polymer properties and the underlying mechanism for the functionalization and surface modification of polymer nanoparticles have been discussed. There are numerous polymer particles designed and developed for various applications. The synthesis and characterization of different types of polymers followed by the engineering of nanoparticles and capsules depend on various factors. There are too many polymerization methods approached for the development of nanoparticles with desired surface properties. The ring-opening polymerization (ROP), emulsion polymerization (EP), atom transfer radical polymerization (ATRP), and free radical micro initiation are the significant approaches for the polymerization reactions. The polymer nanoparticle functionalization and modification of their surfaces based on requirements is an essential task. The solvent concentration, pH, temperature, and sonication have played a vital role to tune the morphology of polymer nanoparticles and capsules. Different characterizations such as FTIR, NMR (^1H and ^{13}C), HRMS, and MALDI-TOF are used for preliminary structural and confirmations. Further, SEM, FE-SEM, TEM, AFM, BET, XRD, Raman, EDAX, TGA-DSC, DLS, and zeta potential were used for morphological and thermal properties.

Keywords: polymers, properties, functionalization, surface modification, nanoparticles

1. Introduction

Across the globe, there is a great interest in the field of polymers and polymer-based nanoparticles followed by their nanotechnology-based applications. However, polymeric nanoparticles (PNPs) are under a wide range of utilization in various fields. Especially researchers and scientists are trying to design various nanoparticles (NPs) and capsules with surface modifiable character features [1]. The polymer nanoparticles do obey and endorse the aforementioned sentence with existing literature which shows numerous nanoparticles with modifiable size, shape, and their surface properties. For example, quantum dots (QDs) carbon nanotubes (CNTs), cellulose NPs and fibers [2] iron oxide nanoparticles (FeONPs), gold nanoparticles (AuNPs), silver nanoparticles (AgNPs), cobalt nanoparticles (CNPs), zinc oxide nanoparticles (ZnONPs), SnO_2 nanoparticles, protein-based nanoparticles, amino acid-based nanoparticles, silica (SiO_2) nanoparticles,

graphene nanosheets, titanium-based nanoparticles, core-shell nanoparticles, hollow core-shell (hCS) nanoparticles, hollow polymer-polymer nanoparticles (HPPNPs), polymer-metal nanoparticles (PMNPs), polymer-metal blends (PBs), polymer-silica nanocomposites (PSiNCs), polymeric micelles (PMs), solid-lipid nanocapsules (SLPNCs), liposomal nanoparticles, albumin-based nanoparticles, chitosan-based nanoparticles, platinum-based nanoparticles (PtNPs), ceramic nanoparticles, carbohydrate nanoparticles, etc. are reported and corroborated in the literature [2–5]. Furthermore, a significant interest in the synthesis and characterization of polymers followed by the design and development of polymeric nanoparticles (PNPs) with surface tunable properties has become an essential due to the various applications. For example, the amino acid-based polymer is much more suitable for the preparation of nanoparticles because of its biosafety and nontoxic and biodegradable nature. Similarly, thermosensitive polymer, for example, poly-N-isopropyl acrylamide (PNIPAM), shows lower critical solution temperature (LCST) at $\sim 32^{\circ}\text{C}$, and it is much more useful to prepare the nanoparticles or capsules with thermally tunable morphology and other futuristic characteristic properties [6]. However, the main advantage to polymer scientists is they can easily synthesize the polymer to engineer the nanoparticles followed by the significant functionalization and surface modifications by changing the solvents, concentration, and stirring methods or by changing the functional groups which are present in the synthesized polymer complex. Similarly, the ionic (cationic and anionic) polymers referred to as polaxomers can help to modify the surface of the particles. Polymeric nanoparticles are under a wide range of utilization in the field of biomedical, nanobiotechnology, nanobiopharma, and other pharmaceutical domains. For example, they are very much used in the field of drug delivery systems (DDSs), gene delivery systems (GDSs), protein delivery systems (PDSs), cell delivery systems (CDSs), and tissue engineering followed by plastic surgery, etc. [7, 8]. However, polymers have numerous industrial applications as well, such as cell phone manufacturing companies, soft drink and water bottle industries, electronics and electrical engineering departments, automobile industries, and many other industrial usages based on the requirements. Interestingly, polymeric nanoparticles with porosity have multidirectional usages such as drug or nanomedicine loading and its target specific release. The nanoparticles with ~ 200 nm (in diameter) are the ideal size for the biomedical applications. The pore size with ~ 100 nm in the polymer nanoparticles or capsules is much more suitable for drug delivery and cancer therapeutics. According to International Union of Pure and Applied Chemistry (IUPAC) definition, the microparticle size should be < 2 nm, (in diameter) and meso-particles or mesoporous particle and capsule size *ca.* 2–50 nm, and nanoparticles (particle size 50–200 nm) have been referred for various applications [6–8]. The effective and potential working capacity of nanoparticles has been defined by their size, shape, morphology, porosity, and other thermal properties. However, the qualitative quantification of use of polymer-based nanoparticles and their potential applications completely depends on the characteristic features like surface modification, size, and shape tenability. For example, many properties like color and atomic orientation are differing from the sizes of bulk to nanoscale [9, 10].

2. Classification of polymers

The word polymer derived from Greek has been split into two meaningful words: (1) poly means many, and (2) meros or mers means units or parts. More specifically monomer is the smallest repeating unit for the development of polymer. Simply polymers are made up of monomers. The word monomer is also derived

from the Greek. Mono means one or single and mer means part/s. As reported in **Table 1**, there are varieties of polymers classified based on their biodegradability, biocompatibility, thermal stability, pH-responsive nature, environmental responsive nature, etc. Based on occurrence these are again categorized into three types: (1) natural polymers, for example, starch, chitin, cellulose, etc., (2) synthetic polymers, for example, polystyrene (PS), polyurethane (PU), polyvinyl chloride (PVC), and (3) semisynthetic polymers, for example, cellulose nitrate, guncotton, cellulose acetate, etc. Absorbable synthetic polymers include polyvinyl alcohol (PVA), polylactic acid (PLA), polycaprolactone (PCL), and polyglycolic acid (PGA), and these are homopolymers. The heteropolymers include polytrimethylene carbonate (PTMC), polyetherimide (PEI), polydioxanone (PDO), polylactide-co-glycolide (PLGA), and the combination of block copolymers like and poly-glycolide-co-trimethylene carbonate (PGTMC) which are best examples for heterogeneous polymers. Apart from these polymers, there are pH-sensitive polymers like poly-L-lysine which is positively charged at lower pH conditions [22, 23]. Liposome and poly-histidine are the systems with pH sensitivity, and this can be easily interacted with negatively charged particles or membranes to promote fusogenic properties. Furthermore, some hydrogel-based nanoparticles show unique characteristics toward various biomedical as well as industrial applications. Liposomal and hydrogel based systems has tendency towards pH-sensitivity and it is a characteristic property to tune-up their morphology for many therapeutic applications. For example, PLGA, MeO-PEG-NH₂, and PAMAM-based nanoparticles show pH-dependent destabilization and thus are used for cytoplasmic experiments because of its ease of permeability through the membrane to deliver nanomedicines and nanoparticles [9, 10, 22, 23]. The NIPAM/pNIPAM (N-isopropyl acrylamide/ (poly-N-isopropyl acrylamide)) is the best example for the thermal sensitive polymer which shows lower critical solution temperature (LCST) or cloud point at ~32°C **Table 1**. Because of the thermal behavior, it is termed as magic or smart polymer and used for various medical and industrial usages. However, these polymers are mainly prepared based on two polymerizations reactions such as (1) addition polymerization and (2) condensation polymerization methods [24, 25].

S. no.	Name of the polymer	Monomer formula	Polymer formula	Polymer structure	Ref.
1	PVC (polyvinyl chloride)	C ₂ H ₃ Cl	(C ₂ H ₃ Cl) _n	Figure 1a	[11, 12]
2	PVA (polyvinyl alcohol)	C ₂ H ₄ O	(C ₂ H ₄ O) _n	Figure 1b	[12, 13]
3	PE (polyethylene)	C ₂ H ₄	(C ₂ H ₄) _n	Figure 1c	[12, 14]
4	PS (polystyrene)	C ₈ H ₈	(C ₈ H ₈) _n	Figure 1d	[14, 15]
5	PP (polypropylene)	C ₃ H ₆	(C ₃ H ₆) _n	Figure 1e	[15, 16]
6	NIPAM (isopropylacrylamide)	C ₆ H ₁₁ NO	(C ₆ H ₁₁ NO) _n	Figure 1f	[16, 17]
7	PTFE (Teflon)	C ₂ F ₄	(C ₂ F ₄) _n	Figure 1g	[17, 18]
8	PCL (polycaprolactone)	C ₆ H ₁₀ O ₂	(C ₆ H ₁₀ O ₂) _n	Figure 1h	[18, 19]
9	PEI (polyetherimide)	C ₃₇ H ₂₄ O ₆ N ₂	(C ₃₇ H ₂₄ O ₆ N ₂) _n	Figure 1i	[19, 20]
10	PSU (polysulfone)	C ₂₇ H ₂₂ O ₄ S	(C ₂₇ H ₂₂ O ₄ S) _n	Figure 1j	[20, 21]

Here, “n” represents the number of monomer units involved in the synthesis of the polymers.

Table 1.
Show the different types of polymers with their monomer units and their chemical formula followed by the structures in **Figure 1a–j**.

Figure 1.

Some of the polymers with their chemical structure, name, and active functional groups which are involved in functionalization and polymerization reactions.

Hence, polymers are prepared by the abovementioned two versatile polymerization methods, and there are several modified methods and approaches that can be followed for the preparation and synthesis of polymers such as ring-opening polymerization (R-O-P), emulsion polymerization, precipitation polymerization, diffusion polymerization, macroinitiator polymerization, macroinitiator polymerization, and atom transfer radical polymerization (ATRP) methods. As per the literature, first in the 1970s, lactic acid (LA)-based nanoparticles and capsules are

used for biomedical and other pharmaceutical applications, and later it has been extended for various fields [26]. Polymers when considered for biomedical applications, it needs to refer self-assembly nature and functionality followed by the formation of spherical and sphere-shaped nanocapsules and particles particularly for drug delivery systems. Based on degradability, thermosensitivity, and pH-responsive nature, these are again categorized into various classes and reported in **Figure 2** with some examples. However, biodegradable polymers which show a tendency to degrade in biological systems such as polylactic acid (PLA), polyglycolic acid (PGA) and poly terephthalic acid (PTA), polycaprolactone (PCL), and amino acid (AA)-based polymers are potential materials to engineer nanoparticles and capsules for nanotechnology and nanobiotechnology applications. The polymers which do not degrade in the biological systems are termed as non-biodegradable polymers such as carboxymethyl, ethyl cellulose, and acetates of cellulose. The poly anhydrides like poly sebacic acid (PSA), poly adipic acid (PAA), and other environmental-responsive polymers also enlisted in the non-biodegradable polymers. Thermo-responsive (temperature-sensitive) polymers show a significant change in the size and shape of nanoparticles to tune up based on requirements [27]. The thermosensitive behavior of PNIPAM and pH-responsive nature of L-glutamic acid gamma benzyl ester (L-GluA-5-BE), L-aspartic acid beta benzyl ester (L-AspA-4-BE), polyethylene glycol (PEG), poly L-glycolic acid (PLGA), and PAMAM allow changing the morphology of nanoparticles as well surface profile of the NPs and capsules (**Figure 1**). Apart from these polymers, electrical-responsive polymers show piezoelectric effects which are a characteristic property to mold the nanoparticles based on requirements. The supramolecular interactions between the atoms and molecules lead to compression or elongation and stretching of bonds, and it can play a vital role to change the properties of final compounds. However, polyvinylidene fluoride (PVDF) polymer has been considered as one of the magic polymers which allow structural and morphological modifications through the appropriate synthesis and preparation methodologies [28].

The chemically responsive polymers allow internal changes through the formation of anionic and cationic and amphiphilic nature through the oxidation, reduction, and redox (both oxidation and reduction) reactions and lead to surface modification based on smooth and rough surface. As per the literature, the increase in the size of the particles depends on an increase in monomer units or polymer units. Sometimes branching and hyper-branching nature also lead to the formation of larger nanoparticles and capsules. Polymers prepared with the

Figure 2.
Some of the polymers categorized based on their characteristic properties.

combination of a large number of high molecular mass polymers give micron-sized nanoparticles, and they can be used for bulk phenomenal approaches such as absorption, chemisorption, etc. There is a class of polymers named as block copolymers, and these are again categorized into several such as (a) random block copolymers (BCPs), (b) star block copolymers, (c) grafted block copolymers, and (d) alternating block copolymers, and these are classified based on their synthesis approaches and final structural confirmations, and these are low-density polymers (**Figure 2**) [20, 21, 26–29].

3. Polymer properties

There are some important physical and chemical properties needed to be considered before selecting polymers for synthesis followed by the design and development of nanoparticles such as (1) structural integrity, (2) low immunogenic nature, (3) biocompatibility (for biomedical applications), (4) biologically active nature, and (5) structural versatility (which can easily allow topographic changes internally as well externally). Polymers with physicochemical properties such as hydrophilic (solvent loving), hydrophobic (solvent repelling), and amphiphilic (affinity to absorb and repel the solvent) nature, surface energy, viscosity, lubricity, density, surface tension, pH sensitivity, smoothness, swelling nature, solubility, amorphous and crystalline nature, polymer dissolution, bioadhesive and sticky nature, polymer-solvent interaction, polymer erosion, flexibility, chain formatting nature, chemical composition, microstructural design, and other surface properties need to be examined carefully for the design of nanoparticles and capsules. By considering these properties, nanoparticle preparation methods can also be modified for the polymerization reactions (**Figure 3**). For example, (1) natural polymers like (a) chitin, (b) cellulose, and (c) starch can be widely used for nanoparticle development through the modified chemical synthesis methods [29, 30]. Further, (2) semisynthetic polymers like (a) cellulose nitrate, (b) rubber, (c) rayon and (d) silk and fiber-based materials, and (e) guncotton are synthesized based on their flexibility and other stresses and strain rate for various applications, and these are very much suitable to design the ribbon type of fibrils for textile industry-based usages. However, (3) synthetic polymers such as (a) polymethyl methacrylate amide (PMMA); (b) nylon, nylon-6, and nylon-6,6; and (c) polystyrene (PS) are very much useful for plastic industries to manufacture polyvinyl chloride (PVC)-based pipes, tubes, cables, and other plasticwares. The polymer tetrafluoroethylene (Teflon or PTFE) with monomer chemical formula ($-C_2F_4-$) is under wide range utilization in the name of Teflon tape as a sealant for pipe linkages and insulation tape. The natural rubbers isoprene and neoprene can be used to develop various products industrially [31, 32].

The natural rubber, vulcanized rubber, or sulfur has been used in tire industries. Similarly, formaldehyde and benzophenol combination is used to develop combs and other plasticwares, and its trade name is Bakelite. The polymer polyethylene (PE) is used for polyethylene covers/carriage bags and much more houseware and industrial manufacturing. The polymer PE is again categorized into two types based on its density for the manufacturing of plastic materials such as low-density polyethylene (LDPE) and high-density polyethylene (HDPE) based on applications [33]. The following properties of polymers are essential to develop potential nanoparticles for drug delivery systems (DDSs), gene delivery systems (GDSs), cell delivery systems (CDSs), tissue engineering (TE), and other nanobiotechnology applications such as molecular weight, self-assembly nature, density, network

Figure 3.
Schematic shows the characteristic properties of polymers needed to be considered for the design and development of nanoparticles.

forming capacity, and interlocking nature of functional groups followed by the self-assembly. Based on applications (biomedical or industrial), polymeric nanoparticles should possess the following characteristics such as biocompatibility and biodegradability with good cell survival rate, and they should obey the properties as mentioned in earlier sections [34]. However, every nanoparticle system has their limitations for their use in medical biotechnology and nanotechnology applications. By changing reaction methods, solvent concentration, temperature conditions, pH levels, its surface profile and another size, shape, and morphology can be modified [35]. Design and development of surfactant-free nanoparticles without using any harmful solvents and catalyst is a novel approach for green synthesis and technology. The term green synthesis, green technology, green nanoparticles, and green reactions define the methods and approaches followed by engineer nanoparticles and materials without any side effects, toxicity, and harm to mankind applications. The nanoparticles and capsules developed based on amino acid-based block copolymers, and plant extracts are termed as green nanoparticles as they show good biocompatibility for human beings [36].

4. Classification of nanoparticles

Based on core synthesis materials, nanoparticles are categorized into various types such as (a) protein nanoparticles (PrNPs), (b) polymeric nanoparticles (PNPs), (c) organic nanoparticles (ONPs), (d) inorganic nanoparticles (INPs),

(e) metal nanoparticles (MNPs), (f) metal oxide nanoparticles (MONPs), (g) amino acid-based nanoparticles (AANPs), (h) ceramic nanoparticles (CNPs), (i) hydrogel nanoparticles (HNPs), (j) solid-lipid nanoparticles (SLNPs), etc. [37–40].

However, these polymer-based nanoparticles and capsules are again classified into several categories as follows: (a) polymer-polymer nanostructures, (b) polymer-metal NPs, (c) polymer-nonmetal NPs, (d) polymer-inorganic NPs, and (e) polymer-organic (proteins, amino acids) NPs. However, polymer-polymer nanoparticles, polymer-silica NPs, amino acid-based polymers, and polymer-zinc oxide NPs have unique characteristic properties for various biomedical applications such as drug delivery systems (DDSs). Based on cytotoxicity, side effects and biocompatibility issue the quantum dots (QDs), and carbon nanotubes (CNTs) are avoided for the usage in the field of biomedical and pharmaceuticals. Aforementioned, there are various polymer-based nanoparticles which are already developed, but they all have their limitations, and for amino acid-based polymer nanoparticles and nanocapsules (NCs) like dendrimers, core-shell nanoparticles (CSNPs), the block copolymer (BCP), and mesoporous SiO_2 NPs, it is easy to change their surface and other properties [41]. However, **Figures 4** and **5** illustrate the classification of polymer and polymer nanoparticles and non-polymeric nanoparticles. The concept self-assembly has an obligatory role to rearrange and orient the active functional groups present in the monomers and polymers through the esthetic structural integrity throughout the surface of the nanoparticles and capsules. The concept self-assembly as well amorphous and crystalline nature of polymer are also one of the key factors which influence the arrangement and organization between functional groups like hydroxyl ($-\text{OH}$), amine ($-\text{NH}_2$), amide ($-\text{NH}$), keto ($-\text{C}=\text{O}$), ester ($\text{R}-\text{COO}-\text{R}$), acid ($-\text{COOH}$), aldehyde ($-\text{CHO}$), and saturated and unsaturated hydrocarbons as discussed in earlier sections [38–43]. The formation of porous spheroid-shaped nanoparticles and capsules depends on intra- and intermolecular interactions between functional groups. The molecular imprinting of hydrophilic nanoparticles with denser hydrophobic particles can lead to the formation and creation of pores within the particles and throughout the surface of the particles and capsules [41–44].

Figure 4. Shows the classification of various nanoparticles and their morphology acquired through the different microscopic characterizations.

Figure 5.
 Schematic illustration shows the classification of different types of nanoparticles and their synthesis approach methods.

Nanotechnologically there are two important approaches to prepare the nanoparticles such as top-down approach and bottom-up approach. However, top-down approach can be termed as breakdown approach, and it is the core method to prepare nanoparticles. For example, bulk gold cube to gold nanoparticles (AuNPs) can be achieved through the top-down approach, and simply particle segregation takes place during this approach [42–45]. Sonication, ultra-sonication, ball milling, and stirring are the best examples for the top-down approach to preparing nanoparticles. Similarly, bottom-up can be referred to as the buildup approach and in this approach nano to macro and macro to bulk materials can be achieved. This bottom-up approach is like aggregation of nanoparticles which leads to the formation of bulk materials. However, monomer to polymer formation is the best example for the bottom-up approach. Sometimes based on potential applications, these nanoparticles are called smart materials or smart nanoparticles (**Figure 5**) [43–46].

5. Advantages with polymer nanoparticle

These polymer-based nanoparticles are developed in principle to protect the guest particles or molecules from degradation and its functional activity, for example, porous polymer nanoparticles or nanocapsules loaded with anticancer drugs or nanomedicines [47]. Because of the soft nature of polymer NPs and nanocapsules, it is very easy to modify the surface of the particles and their mono-dispersion based on its applications. The enhanced absorption and modification of the drug distribution throughout the surface of the particles or capsules lead to the target-specific or tissue- or cell- or organ-specific pharmacokinetics and dynamics in various biomedical and pharmaceutical usages. Polymer-based nanoparticles and capsules allow easy surface functionalization and modification to tune up them with desirous properties. Sometimes smooth surface of the polymer thin films can become rough due to the internalization and incorporation of metal and other inorganic nanoparticles such as FeONPs, ZnONPs, AlNPs, AgNPs, AuNPs, SiO₂NPs, etc. The surface properties like particle smoothness and roughness or porous nature of particles in composite can give better results, but its surface and size may not fit for

the usage of biomedical applications [48]. In such cases the composite of polymer thin film embedded or doped with some other metal nanoparticles or organic and inorganic materials needs to be molded without changing its original activity or characteristic properties. However, the functional groups such as amide ($-NH$), amine ($-NH_2$), acid ($-COOH$), aldehyde ($-CHO$), keto ($-C=O$), ester ($R-COO-R$), anhydride ($R-CO-O-CO-R$), acid halides, hydrogen halides, salts, and solvents (organic, inorganic) can also influence the surface properties for the nanoparticles or nanocapsules. Based on the requirement, it can be chosen to modify the particles surface and size, shape, etc. The concentration of the solvent also affects the pattern of the nanoparticles and nanocapsules. Sometimes additives like precursors and surfactants can also show an adverse effect on the morphology of polymer nanoparticles [49]. The activity (bioactive nature) of polymer nanoparticles and nanocapsules can disturb the body metabolism. The active functional groups with their potential resonance capabilities can also interact with body fluids and interfere to shore-up the mutations. Apart from the solvent, there are several factors which can affect the patterning of the surface of the nanoparticles such as pH, thermal stability, rubbery nature, solid (amorphous and crystalline) nature, environmental conditions, etc. The stability, biocompatibility, and route or synthesis methodology are also playing a vital role to tune up the surface properties of the polymeric nanoparticles and capsules. For example, (a) protein nanoparticles have stability issues during storage. If the storage conditions are not followed properly, they may get contaminated and become toxic [50]. But these protein-based NPs are very much compatible with their unique characteristic features such as nontoxic nature and nonantigenic nature. As per the existing literature, it is known that bulk protein in plasma can easily bind to a variety of drug molecules through its trajectory while carrying them to deliver target specifically. And these are very much flexible to ease scale-up manufacturing and other nanobiotechnological applications; (b) albumin-based nanoparticles are very much suitable for the morphological modifications and to tune the surface properties. These are biocompatible and biodegradable without any detrimental activities upon mankind usages. Sometimes these albumin-based nanoparticles are used for drug delivery and other biomedical applications. However, protein albumin contains a huge number of charged amino acid residues, and it binds water-soluble drugs through charge interactions, and it leads to surface modifications and morphological changes [51].

6. Preparation of polymer nanoparticles

There are several approaches to prepare and synthesize the polymeric nanoparticles such as (a) desolvation, (b) emulsification, (c) esterification, (d) thermal gelation, (e) nanospray drying, (f) self-assembly, etc. Apart from these approaches, there are mainly two polymerization methods widely followed for the preparation of polymer nanoparticles such as (1) addition polymerization and (2) condensation polymerization. The preparation of polymer nanoparticles is not an easy task. The size and shape of the particle are a very important concern while preparing the polymer-based nanoparticles. As the number of monomers or polymer units increases, the size of the nanoparticle or capsule also increases. It is easy to prepare and reproduce the polymeric nanoparticles with the porous matrix for loading the drug molecules, but its size and shape cannot be formulated easily. Amino and carboxyl functional groups permit functionalization and surface modifications, but patterning them in a fruitful design is a challenging task, and it can overcome through the detailed study of their properties [52]. However, albumin is phase separated due to reduced water solubility followed by the formation of the tiny particles

Figure 6. Pictorial representation of different types of polymer nanoparticles. Image (a) core-shell nanoparticle, (b) liposomal nanoparticle, (c) star-shaped NPs, (d) dendritic nanoparticles, (e) coral reef-type nanoparticle, and (f) symmetric pattern of nanoparticles [46–51, 53].

such as coacervates which has a tendency to dissolve again and again with universal solvent. Albumin functional groups are cross-linked by agents like glutaraldehyde, and this cross-linking is achieved through the lysine and arginine amino groups which are present in the so-called amino acids. The stability of these cross-linked nanoparticles also affects the surface properties of the nanoparticles. Furthermore, separation methods, stirring methods, time, temperature, ultrasound, magnetic effect, sonication time, and bath temperature also show an adverse effect on the surface morphology of albumin nanoparticles.

There are significant advantages with the aforementioned approaches to prepare the polymer nanoparticles, emulsification technique requires removal of organic solvents and surfactants, thermal stabilization method is applicable to heat-stable molecules, chemical stabilization is needed to remove the toxicity of cross-linkers and uncontrolled linking, desolvation leads to the substitution for the emulsification and reproducibility with safe and suitable properties for the preparation of polymeric nanoparticles, and **Figure 6a–f** shows the morphology of different types of nanoparticles designed for pictorial representation [54, 55].

7. Characterizations of nanoparticles

Variety of techniques used to find out the chemical formula and structural confirmations of polymers after synthesis, for example, nuclear magnetic resonance (NMR) followed by the ^1H and ^{13}C for functional groups, chemical formula, and structure of the synthesized compound. Spectrophotometer fourier transform infrared (FTIR) for functional groups identification and it has been acquired through the absorption spectra followed by the analysis of peak positions, high-resolution mass spectrometer (HRMS), and low-resolution mass spectrometer to measure the molecular weight of samples, and this technique give very much

accurate mass of the synthesized compounds, matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) to measure the molecular mass of heavier compounds such as polymer macromolecules, mass of genetic materials such as deoxyribonucleic acid (DNA), ribonucleic acid (RNA) and other biomolecules, carbon, hydrogen, nitrogen, sulfur (CHNS) analyzer. Once the synthesized molecules are confirmed, then it needs microscopic characterizations for the morphology of polymeric nanoparticles. Morphology of polymer nanoparticles has been characterized by using scanning electron microscope (SEM), field emission scanning electron microscope (FESEM), transmission electron microscopy (TEM), high-resolution transmission electron microscopy (HRTEM) for morphology of nanoparticles, X-ray diffraction (XRD) to know the solid state and nature of materials such as amorphous, crystalline and partially crystalline nature of synthesized nanoparticles, energy dispersive spectroscopy (EDAX) for the presence of elements and elemental composition in the final compound, Brunauer–Emmett–Teller (BET) to measure the BET surface area, porosity, pore width, pore thickness, specific surface area, Langmuir surface area through the nitrogen (N_2) gas adsorption and desorption hysteresis curve analysis, Atomic force microscope (AFM) for surface properties like smooth/hard/rough surface of the polymer and non-polymer nanoparticles followed by the pore profile such as pore depth and width in case of porous capsules or particles, apart from this characterization Optical profilometer can also use to evaluate the surface properties of nanoparticles and thin films. To examine the thermal properties and degradation behavior of nanoparticles, the following characterization techniques are used such as differential scanning calorimetry (DSC) for heat flow measurements such as endo- and exothermic nature of particles. Endothermic has been defined as the system which absorbs heat from surrounding and exothermic the system which releases heat to surroundings, thermogravimetric analysis (TGA) for weight loss and degradation temperature of various nanoparticles, Raman to measure the band gap, dynamic light scattering (DLS) for particle size analysis, zeta potential to measure the charge of the polymeric and non-polymeric nanoparticles.

8. Preparation and functionalization of polymer nanoparticles

However, polymer nanoparticles can be prepared through various approaches through the monomer to polymer formation trajectory which is scientifically called as polymerization reactions followed by the development of nanoparticles. Interestingly, the group transfer polymerization (GTP), ring-opening polymerization (ROP), radical polymerization (RP), polymer re-precipitation (PRP), emulsion, micro radical polymerization (MRP), macro polymer initiation reactions (MPIR), addition polymerization reactions (APR), emulsion polymerization (EP), atom transfer radical polymerization (ATRP), addition polymerizations (AP), condensation polymerization (CP), oxidation polymerization (OP), and reduction polymerization (RDP) followed by the redox reactions and self-assembly approach of polymer materials are used to design and develop nanoparticles from the synthesized polymers. The hydrophobic and hydrophilic nature of polymers followed by the amphiphilic character has been considered while performing the polymerization reactions to develop nanoparticles [52–56]. After synthesis of the polymer by using any of the abovementioned polymerization reactions, the final compound can be used for morphological characterizations. Sometimes solid powder form of the sample can be used directly for SEM and TEM characterizations. But for polymeric samples, it needs to be dispersed in the suitable solvent before going

for morphological characterizations. Dispersion followed by the sonication, stirring, ultra-sonication, shaking, etc. based on particle aggregation and segregation tendency dispersion methods needs to be chosen. During the dispersion followed by the sonication, there are certain precautions needed to be taken care of such as sonication time, bath temperature, etc. Bath temperature and sonication time have to be optimized; otherwise structural disintegration or polymer particles may get collapsed or disrupted with over sonication and temperature conditions. Apart from the abovementioned methods, there are several modified chemical synthesis routes to approach to elucidate the nanoparticle design and development based on their applications. Nanoparticle formulation and functionalization depends on the synthesis methods and desired characteristic features of the polymers chosen [57]. Charged nanoparticles may have the tendency to attract or repel with other nanomaterials. In general, the size of nanoparticles increases upon blending with some other nanomaterials, and it leads to form bulk materials. For example, polystyrene (PS) nanoparticles followed by the sulfonation lead to increase the composite size. The swelling and dispersion and diffusion nature of nanoparticles lead to enhance the size of nanoparticles, and this is because of the additional functionalization. The monodispersion approach helps to get the uniform-sized nanoparticles with desired surface properties [58]. The synthesis approaches, nanoformulations, and functionalization of nanocarrier capsules and particles are very important in the drug delivery systems. And this can be achieved through the synthesis methods like ring-opening polymerization, polymer precipitation, self-assembly of polymer materials, etc. Polymers are having the capability to form the network-like structures due to its functional group entanglement and orientation to get the stability in its structure internally. The chain cross-linking and branching nature hyper-branching also lead to the functionalization of polymer nanoparticles. The synthesis of nanocarriers like nanocapsules, nanospheres, and nanoparticles with the characteristic features such as with the mesoscale porosity (pore diameter is 2–50 nm), nanoporous (pore diameter ~100 nm), microporous (pore diameter ~2 nm) and cavities, voids, and core-shell concept is important to absorb or encapsulate and entrap the drug molecules [59].

9. Morphology and surface patterning of nanoparticles

Scientists already developed different advanced techniques to examine the meso-, nano-, and micro-, and macroscale porosity within the polymer nanoparticles, and this porous surface patterning depends on the self-assembly of chosen materials. Polymer nanoparticles' preparation is fairly easy, and they show good control over the size and shape with longer clearance time. The extensive use of polymer nanoparticles has led to study the surface properties based on its pharmaceutical and industrial applications [57–61]. For example, PVA and PLA nanoparticles show unique characteristic properties to modify their surface with greater control of size. However, double emulsion techniques can be applied to stabilize the PVA nanoparticles. The protein containing nanoparticles has limitations on the increase of nanoparticle size upon functionalization with other nanomaterials. The protein bovine serum albumin (BSA) containing PLGA nanoparticles has good control on its size and shape while functionalizing through the solid-in-oil and oil-in-oil microsphere development method with suspended droplet hardening using impeller atomization followed by the droplet shearing in a spinning oil film approach. As shown in **Figures 7 and 8**, the gold nanoparticles have good interactions with polymer micelles and formed a new nanomaterial which is

the combination of polymer micelle and gold nanoparticles with functionalized features. Similarly, iron and iron oxide containing a core of magnetite had a primary coat of a polymer of dextrans to get microspheres for bio applications [62].

However, liposomes have a spherical vesicular structure formed by the combination of hydrophilic head part and hydrophobic tail or hydrocarbon (fatty acid) chain which are called phospholipid bilayers. The hydrophilic and hydrophobic parts of the phospholipids are the main cause to form the liposome and for its structural integrity. The images in **Figure 7** corroborate the monodispersed silica (SiO_2) nanoparticles prepared by using modified Stober's sol-gel method. The formation of spherical-shaped SiO_2 nanoparticles depends on the stirring methods, the solvent used for the preparation, rotations per minute (RPM), purity of chemicals used for the synthesis of SiO_2 nanoparticles, surfactants, and equipment used for the experiments [66]. **Figure 7** shows sharp uniform-sized monodispersed silica nanoparticles are penetrating the boundary of polymer thin film and sitting inside the film. Scientifically, it's a composite of polymer-silica, but specifically, here, in this case, polymer thin film has been inserted with the mesoporous silica nanoparticles. Nucleic acids are another class of biopolymers which are called as polysaccharides, and they can also be involved in the development of nanocarrier capsules or particles for biomedical applications. The chemical linkage between nucleic acid monomers is phosphodiester, and it also helps in the development of nanoparticles through the self-assembly manner. The synthesized PP-based nanoparticles have precise control

Figure 7. Transmission electron microscopic images. (a, b) Silica nanoparticle internalization into polymer thin film, (c) bare silica nanoparticles and separate polymer thin film interactions, (d) pure silica nanoparticles showing mesoscale porosity at the center and uniform size of particles at higher magnifications [62, 63].

Figure 8. Transmission electron microscopic images. (a, b) Gold nanoparticles functionalized with polymer micelle, image (c) dense polymer micelle, (d) gold nanoparticles arranged in a core-shell morphology with the eternal polymer micelles, (e) bare gold nanoparticles, and (f) shows lattice parameters of AuNPs [64, 65].

over size and shape, and it can be controlled through the crystal sequestering of atoms and molecules [67]. Distribution of the guest particles and molecules inside the host matrix can be optimized through the agitation methods like sonication time, temperature, stirring (RPM), incubation time, and encapsulation and entrapment. However, numerous possible applications in the biomedical field arise due to the presence of long-range order in the spatial distribution of nanocarriers. Block copolymers show unique and novel characteristic features to the pattern surface of capsules and nanoparticles with porosity. The self-assembly nature between functional groups of polymers is highly dependent on solvent interactions (**Figure 8**). Surface and morphology of particles can be tuned based on using selective solvents. Surface patterning is an ideal as lithography templates to the spontaneous self-assembly in nanometer (nm) to micrometer (μm) size topography. The surface patterned by self-assembly of block copolymers thereby reduces the number of process steps involved in the formation of such desired structures [68].

Sometimes pore size and shape throughout the surface of the capsules and nanoparticles may appear irregular and inconsistent because of interatomic and molecular orientations and imprinting methods. However, intermolecular attractions also show the effect on the morphology of particles. There are highly inconsistent pores with smooth and rough surfaces because of the solvent effect and sonication methods. From **Figure 9**, AFM images of the surface profile for zinc oxide nanoparticles have been measured, and it shows the surface characters. From the image (a), the arrangement of ZnONPs can be seen, and the line scan profile gives a channel type of surface morphology for zinc oxide nanoparticles, whereas wet chemical methods and sample preparation procedures also play a vital role to exhibit a considerable change in shape and surface morphology of polymer NPs. A non-contact mode AFM operation has been carried out to acquire the topography of the ZnONPs. However, tip size and magnification play a crucial role to acquire the topography of the NPs. Furthermore, for the uniform pores and consistent particle size, the shape can be optimized based on several factors such as sonication,

Figure 9. Atomic force microscopic images acquired for the ZnO nanoparticles. The image (a) corresponds to phase(s), and it shows the surface properties of ZnO NPs, image (b) elucidates the three-dimensional view of ZnONPs and their morphology, the image (c) illustrates the surface properties of ZnONPs arranged on the substrate, and these are acquired from the line scanning mode AFM operation as represented in the image (a) phase [64, 65, 69, 70].

Figure 10. Schematic shows the factors which cause the surface modification and functionalization in polymer nanoparticles.

solvent, pH, and concentration of the system (**Figure 10**). The nanoscale clustering and complexation of the peripheral of nanoparticles and capsules have been done through the modification of active functional groups as potential substrates for subsequent functionalization and surface modifications. The post-insertion method is used for the preparation of dendrimer nanoparticles and lipid nanocapsules (LNCs) with the chemically reactive surface. Ideally, this method has been designed for the grafting of ligands to the polymer compounds, and later it has been

extended to another particle development also. During the preparation of polymer nanoparticles or dendrimers, one can be focused on the experimental conditions such as the ratio between both reactants, quantity of solvent, external stimuli factors such as stirring methods, sonication, magnetic field, electric field applications, pH, temperature, viscosity, density, and molecular weight of reactants [69].

The reaction conditions such as slow, fast, and moderate reactions can be tuned or controlled based on literature. The polymers, i.e., PCL, PLGA, PNIPAM, PS, and PEG, are advantageous to design the nanocapsules because they have the capability to form network structure which helps to load the drug molecules efficiently, and these properties help to sustain release of the medicines. The rigid morphology and close compacted structure of nanoparticles or nanocapsules with covalent bonding cannot allow us to modify its surface even at rigorous conditions also [71]. The loosely bound functional groups allow modifying the surface of the nanoparticles based on our applications. The homogeneous mixture of ingredients present in the polymer nanoparticles leads to form a close-compacted and smooth surface of the particles.

However, development of a vinyl ether-functionalized poly phosphoester as a template for multiple post-polymerization conjugation core-shell type degradable polymeric nanoparticles was appended in the various publications, and those help to design and develop polymer NPs with surface-modifiable properties [72]. The confirmation and confinement of two reactants followed by the formation nanoparticles at the interface have a unique advantage to tune their surface properties based on its phase transitions and thermal stability, and this can help to improve and to know the reaction kinetics, higher yields, and selectivity of NPs. However, the presence of a liquid interface can accelerate the reaction through the phase-transfer catalyst which is employed to draw the reaction for the development of NPs based on phase transfer phenomena. Interestingly, the use of immiscible systems in emulsions offers an easy phase separation and formulation of desired nanoparticles. However, a brief overview on low molecular weight and low-density polymer complexes show the significant proximity of the interface in emulsions, and this strategy can be used for the efficient production of nano- and microparticles for various applications [65, 69–72]. However, several mechanisms were proposed for the formation of nanoscale pores within the nanoparticles because of the removal of some of the BCP fragments from the network of the PCL. The size of the BCP-based polymer nanoparticles reduced as blocks were removed from the parent blocks. As PCL is hydrophobic in nature, therefore BCP spheroids may be dissolved out from the PCL network structure and create the pores of the equivalent size of BCP spheroids. Moreover, as per factors appended in **Figure 10**, temperature change affects a lot on the pore size and morphology of nanoparticles [65, 73–78].

10. Conclusions

Herein, polymer synthesis, design, and development of nanoparticles and their functionalization have been discussed in detail. The various polymerization methods and different types of nanoparticles and capsules were reported in this chapter. The nanoparticle/capsule classification and surface functionalization followed by size, shape, and morphological changes based on industrial and biomedical applications have been corroborated. The polymer properties play a key role in the development of NPs with desired features, and such influencing factors were reported and elaborated in the respective sections. Nanoparticles and capsules with significant changeable surface and with a more specific surface area have potential applications in various fields. The porosity on the surface of nanoparticles and capsules is an important concern to prepare the NPs for both industrial and pharmaceutical applications.

IntechOpen

Author details

Chander Amgoth^{1*}, Chiuyen Phan², Murali Banavoth³, Santosh Rompivalasa³
and Guping Tang²

1 Department of Sciences and Humanities, MLR Institute of Technology,
Hyderabad, TS, India

2 School of Chemistry, Zhejiang University, Hangzhou, China

3 School of Chemistry, University of Hyderabad, Hyderabad, TS, India

*Address all correspondence to: chander@uohyd.ac.in

IntechOpen

© 2019 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

References

- [1] Villanova JC, Ayres E, Carvalho SM, Patricio PS, Pereira FV, Orefice RL. Pharmaceutical acrylic beads obtained by suspension polymerization containing cellulose nano-whiskers as an excipient for drug delivery. *European Journal of Pharmaceutical Sciences*. 2011;**42**:406-415. DOI: 10.1016/j.ejps.2011.01.005
- [2] Sczech R, Riegler H. Molecularly smooth cellulose surfaces for adhesion studies. *Journal of Colloid and Interface Science*. 2006;**301**:376-385. DOI: 10.1016/j.jcis.2006.05.021
- [3] Wang Y, Grayson SM. Approaches for the preparation of non-linear amphiphilic polymers and their applications to drug delivery. *Advanced Drug Delivery Reviews*. 2012;**64**:852-865. DOI: 10.1016/j.addr.2012.03.011
- [4] Yaping Z, Minsheng H, Wei W, Wei J. Synthesis of the cotton cellulose-based Fe (III)-loaded adsorbent for arsenic (V) removal from drinking water. *Desalination*. 2009;**249**:1006-1011. DOI: 10.1016/j.desal.2009.09.015
- [5] Guo X, Du Y, Chen F, Park HS, Xie Y. Mechanism of removal of arsenic by bead cellulose loaded with iron oxyhydroxide (β -FeOOH): EXAFS study. *Journal of Colloid and Interface Science*. 2007;**314**:427-433. DOI: 10.1016/j.jcis.2007.05.071
- [6] Jeong B, Bae YH, Lee DS, Kim SW. Biodegradable block copolymers as injectable drug-delivery systems. *Letters to Nature*. 1997;**388**:860-862. DOI: 10.1038/42218
- [7] Winzenburg G, Schmidt C, Fuchs S, Kissel T. Biodegradable polymers and their potential use in parenteral veterinary drug delivery systems. *Advanced Drug Delivery Reviews*. 2004;**56**:1453-1466. DOI: 10.1016/j.addr.2004.02.008
- [8] Tan Z, Xu J, Zhu T, Wang AY, Sun Q, Li Y, et al. Bright and color-saturated quantum dot light-emitting diodes, a new star for next-generation displays and solid-state lighting. *Proceedings of SPIE*; **7518**:751803. DOI: 10.1117/12.843089
- [9] Chen S, Zou Y, Yan Z, Shen W, Shi S, Zhang X, et al. Carboxymethylated-bacterial cellulose for copper and lead ion removal. *Journal of Hazardous Materials*. 2009;**161**:1355-1359. DOI: 10.1016/j.jhazmat.2008.04.098
- [10] Zhou D, Zhang L, Zhou J, Guo S. Cellulose/chitin beads for adsorption of heavy metals in aqueous solution. *Water Research*. 2004;**38**:2643-2650. DOI: 10.1016/j.watres.2004.03.026
- [11] Bayramoglu G, Arica MY. Kinetics of mercury ions removal from synthetic aqueous solutions using by novel magnetic p (GMA-MMA-EGDMA) beads. *Journal of Hazardous Materials*. 2007;**144**:449-457. DOI: 10.1016/j.jhazmat.2006.10.058
- [12] Jin L, Bai R. Mechanisms of Lead adsorption on chitosan/PVA hydrogel beads. *Langmuir*. 2002;**18**:9765-9770
- [13] Miyajima M, Koshika A, Okada J, Ikeda M. Mechanism of drug release from a poly (L-lactic acid) matrix containing acidic or neutral drugs. *Journal of Controlled Release*. 1999;**60**:199-209
- [14] Nam K, Nam HY, Kim PH, Kim SW. Paclitaxel-conjugated PEG and Arginine-grafted bio-reducible poly (disulfide amine) micelles for co-delivery of drug and gene. *Biomaterials*. 2012;**33**:8122-8130. DOI: 10.1016/j.biomaterials.2012.07.031
- [15] Lu Y, Chen SC. Micro and nano-fabrication of biodegradable polymers for drug delivery. *Advanced Drug*

Delivery Reviews. 2004;**56**:1621-1633. DOI: 10.1016/j.addr.2004.05.002

[16] Yan H, Tsujii K. Potential application of poly (N-isopropylacrylamide) gel containing polymeric micelles to drug delivery systems. *Colloids and Surfaces. B, Biointerfaces*. 2005;**46**:142-146. DOI: 10.1016/j.colsurfb.2005.10.007

[17] Knop K, Hoogenboom R, Fischer D, Schubert US. Poly (ethylene glycol) in drug delivery: Pros and cons as well as potential alternatives. *Angewandte Chemie, International Edition*. 2010;**49**:6288-6308. DOI: 10.1002/anie.200902672

[18] Gupta S, Tyagi R, Parmar VS, Sharma SK, Haag R. Polyether-based amphiphiles for delivery of active components. *Polymer*. 2012;**53**:3053-3078. DOI: 10.1016/j.polymer.2012.04.047

[19] Yang XZ, Dou S, Wang YC, Long HY, Xiong MH, Mao CQ, et al. Single-step assembly of cationic lipid polymer hybrid nanoparticles for systemic delivery of siRNA. *ACS Nano*. 2012;**6**:4955-4965. DOI: 10.1021/nn300500u

[20] Zhang Q, Xie G, Yan H. Compatibility of block copolymers on blends of polysulfone and semiaromatic polyester crystalline polymer. *Polymer - Plastics Technology and Engineering*. 2003;**42**:311-326. DOI: 10.1081/PPT-120017936

[21] Twu Y-K, Huang HI, Ying CS, Wang SL. Preparation and sorption activity of chitosan/cellulose blend beads. *Carbohydrate Polymers*. 2003;**54**:425-430. DOI: 10.1016/j.carbpol.2003.03.001

[22] Ragnarok LH, Davidson R, Nystrom C, Ragnarsson G. Pore swelling in beads made of cellulose fibers and fiber fragments. *International Journal of Pharmaceutics*. 1995;**122**:49-56

[23] Butun S, GullInce F, Erdugan H, Sahiner N. One-step fabrication of biocompatible particles carboxymethyl cellulose polymeric for drug delivery systems. *Carbohydrate Polymers*. 2011;**86**:636-643. DOI: 10.1016/j.carbpol.2011.05.001

[24] Xia HF, Lin DQ, Yao SJ. Preparation and characterization of macroporous cellulose-tungsten carbide composite beads for expanded bed applications. *Journal of Chromatography. A*. 2007;**1175**:55-62. DOI: 10.1016/j.chroma.2007.10.004

[25] O'Connell DW, Birkinshaw C, O'Dwyer TF. Heavy metal adsorbents prepared from the modification of cellulose: A review. *Bioresource Technology*. 2008;**99**:6709-6724. DOI: 10.1016/j.biortech.2008.01.036

[26] Li P, Wang Y, Peng Z, She F, Kong L. Development of chitosan nanoparticles as drug delivery systems for 5-fluorouracil and leucovorin blends. *Carbohydrate Polymers*. 2011;**85**:698-704. DOI: 10.1016/j.carbpol.2011.03.045

[27] Takegawa A, Murakami M, Kaneko Y, Kadokawa J. Preparation of chitin/cellulose composite gels and films with ionic liquids. *Carbohydrate Polymers*. 2010;**79**:85-90. DOI: 10.1016/j.carbpol.2009.07.030

[28] Wolff B, Schmitz W, Schneider H. Composites of bead cellulose and hydrophilic solubilizers. *International Journal of Pharmaceutics*. 1996;**139**:87-94

[29] Bai YX, Li YF. Preparation and characterization of crosslinked porous cellulose beads. *Carbohydrate Polymers*. 2006;**64**:402-407. DOI: 10.1016/j.carbpol.2005.12.009

[30] Gurgel LV, Junior OK, Gil RP, Gil LF. Adsorption of Cu(II), Cd(II), and Pb(II) from aqueous single metal solutions by cellulose and mercerized

cellulose chemically modified with succinic anhydride. *Bioresource Technology*. 2008;**99**:3077-3083. DOI: 10.1016/j.biortech.2007.05.072

[31] Wong AD, DeWit MA, Gillies ER. Amplified release through the stimulus-triggered degradation of self-immolation oligomers, dendrimers, and linear polymers. *Advanced Drug Delivery Reviews*. 2012;**64**:1031-1045. DOI: 10.1016/j.addr.2011.09.012

[32] Patri AK, Majoros IJ, Junior JRB. Dendritic polymer macromolecular carriers for drug delivery. *Current Opinion in Chemical Biology*. 2002;**6**:466-471. DOI: 10.1016/S1367-5931(02)00347-2

[33] Jeong B, Bae YH, Kim SW. Drug release from biodegradable injectable thermosensitive. *Journal of Controlled Release*. 2000;**63**:155-163

[34] Svirskis D, Sejdic JT, Rodgers A, Garg S. Electrochemically controlled drug delivery based on intrinsically conducting polymers—Review. *Journal of Controlled Release*. 2010;**146**:6-15

[35] Liu T, Qi X, Huang S, Jiang L, Li J, Tang C, et al. Exploiting hydrophobic borohydride-rich ionic liquids as faster-igniting rocket fuels. *Chemical Communications*. 2016;**52**:2031-2034. DOI: 10.1039/c5cc09737a

[36] Tyrrell ZL, Shen Y, Radosz M. Fabrication of micellar nanoparticles for drug delivery through the self-assembly of block copolymers. *Progress in Polymer Science*. 2010;**35**:1128-1143. DOI: 10.1016/j.progpolymsci.2010.06.003

[37] Wolf B. Bead cellulose products with @lm formers and solubilizers for controlled drug release. *International Journal of Pharmaceutics*. 1997;**156**:97-107

[38] Kim H, Kim Y, Guk K, Yoo D, Lim H, Kang G, et al. Fully

biodegradable and cationic poly (amino oxalate) particles for the treatment of acetaminophen-induced acute liver failure. *International Journal of Pharmaceutics*. 2012;**434**:243-250. DOI: 10.1016/j.ijpharm.2012.05.067

[39] Tencomnao T, Chaleawlerlert-upon S, Apijaraskul A, Rakkhithawatthana V, Pimpa N, Sajomsang W, et al. Gold/cationic polymer nano-scaffolds mediated transfection for non-viral gene delivery system. *Carbohydrate Polymers*. 2011;**84**:216-222. DOI: 10.1016/j.carbpol.2010.12.063

[40] Liu C, Bai R. Preparation of chitosan/cellulose acetate blends hollow fibers for adsorptive performance. *Journal of Membrane Science*. 2005;**267**:68-77. DOI: 10.1016/j.memsci.2005.06.001

[41] Siepmann J, Peppas NA. Modeling of drug release from delivery systems based on hydroxypropyl methylcellulose (HPMC). *Advanced Drug Delivery Reviews*. 2001;**48**:139-157

[42] Chang C, Duan B, Cai J, Zhang L. Superabsorbent hydrogels based on cellulose for smart swelling and controllable delivery. *European Polymer Journal*. 2010;**46**:92-100. DOI: 10.1016/j.eurpolymj.2009.04.033

[43] Ramakrishna P, Mallikarjuna B, Chandra Babu A, Sudhakar P, Rao KC, Subha MCS. Interpenetrating polymer network of crosslinked blend microspheres for controlled release of Acebutolol HCl. *Journal of Applied Pharmaceutical Science*. 2011;**1**:212-219

[44] Liang S, Zhang L, Xu J. Morphology and permeability of cellulose/chitin blend membranes. *Journal of Membrane Science*. 2007;**287**:19-28. DOI: 10.1016/j.memsci.2006.10.002

[45] Wang Y, Zhao Q, Han N, Bai L, Li J, Liu J, et al. Mesoporous silica nanoparticles in drug delivery and

- biomedical applications. *Nanomedicine: Nanotechnology, Biology, and Medicine*. 2015;**11**:313-327. DOI: 10.1016/j.nano.2014.09.014
- [46] Hussein GA, Pitt WG. Micelles and nanoparticles for ultrasonic drug and gene delivery. *Advanced Drug Delivery Reviews*. 2008;**60**:1137-1152. DOI: 10.1016/j.addr.2008.03.008
- [47] Lukyanov AN, Torchilin VP. Micelles from lipid derivatives of water-soluble polymers as delivery systems for poorly soluble drugs. *Advanced Drug Delivery Reviews*. 2004;**56**:1273-1289. DOI: 10.1016/j.addr.2003.12.004
- [48] Cunliffe D, Kirby A, Alexander C. Molecularly imprinted drug delivery systems. *Advanced Drug Delivery Reviews*. 2005;**57**:1836-1853. DOI: 10.1016/j.addr.2005.07.015
- [49] Efentakis M, Politis S. Comparative evaluation of various structures in polymer-controlled drug delivery systems and the effect of their morphology and characteristics on drug release. *European Polymer Journal*. 2006;**42**:1183-1195. DOI: 10.1016/j.eurpolymj.2005.11.009
- [50] Wang T, Li M, Gao H, Wu Y. Nanoparticle carriers based on copolymers of poly (ε-caprolactone) and hyperbranched polymers for drug delivery. *Journal of Colloid and Interface Science*. 2011;**353**:107-115. DOI: 10.1016/j.jcis.2010.09.053
- [51] Yan W, Hsiao VKS, Zheng YB, Shariff YM, Gao T, Huang TJ. Towards nanoporous polymer thin film-based drug delivery systems. *Thin Solid Films*. 2009;**517**:1794-1798. DOI: 10.1016/j.tsf.2008.09.080
- [52] Vashist A, Gupta YK, Ahmad S. Interpenetrating biopolymer network-based hydrogels for an effective drug delivery system. *Carbohydrate Polymers*. 2012;**87**:1433-1439. DOI: 10.1016/j.carbpol.2011.09.030
- [53] Malafaya PB, Silva GA, Reis RL. Natural-origin polymers as carriers and scaffolds for biomolecules and cell delivery in tissue engineering applications. *Advanced Drug Delivery Reviews*. 2007;**59**:207-233. DOI: 10.1016/j.addr.2007.03.012
- [54] Giavaresi G, Tschon M, Borsari V, Daly JH, Liggat JJ, Fini M, et al. New polymers for drug delivery systems in orthopedics: in vivo biocompatibility evaluation. *Biomedicine & Pharmacotherapy*. 2004;**58**:411-417. DOI: 10.1016/j.biopha.2004.08.001
- [55] Cypes SH, Saltzman WM, Giannelis EP. Organosilicate-polymer drug delivery systems: Controlled release and enhanced mechanical properties. *Journal of Controlled Release*. 2003;**90**:163-169. DOI: 10.1016/S0168-3659(03)00133-0
- [56] Sadekar S, Ghandehari H. Transepithelial transport and toxicity of PAMAM dendrimers: Implications for oral drug delivery. *Advanced Drug Delivery Reviews*. 2012;**64**:571-588. DOI: 10.1016/j.addr.2011.09.010
- [57] Rackstraw BJ, Stolnik S, Davis SS, Bignotti F, Garnett MC. Development of multicomponent DNA delivery systems based upon poly (amidoamine)-PEG copolymers. *Biochimica et Biophysica Acta*. 2002;**1576**:269-286
- [58] Nakamura K, Nara E, Akiyama Y. Development of an oral sustained release drug delivery system utilizing pH-dependent swelling of a carboxyvinyl polymer. *Journal of Controlled Release*. 2006;**111**:309-315. DOI: 10.1016/j.jconrel.2005.12.018
- [59] Crowley MM, Schroeder B, Talarico M, Fredersdorf A, Obara S, Kucera S, et al. Physicochemical

properties and mechanism of drug release from ethyl cellulose matrix tablets prepared by direct compression and hot-melt extrusion. *International Journal of Pharmaceutics*. 2004;**269**:509-522. DOI: 10.1016/j.ijpharm.2003.09.037

[60] Kabanov AV, Batrakova EV, Alakhov VY. Pluronic block copolymers as novel polymer therapeutics for drug and gene delivery. *Journal of Controlled Release*. 2002;**82**:189-212

[61] Li G, Liu J, Pang Y, Wang R, Mao L, Yan D, et al. Polymeric micelles with water-insoluble drug as hydrophobic moiety for drug delivery. *Biomacromolecules*. 2011;**12**:2016-2026. DOI: 10.1021/bm200372s

[62] Gong J, Chen M, Zheng Y, Wang S, Wang Y. Polymeric micelles drug delivery system in oncology. *Journal of Controlled Release*. 2012;**159**:312-323. DOI: 10.1016/j.jconrel.2011.12.012

[63] Amgoth C, Suman J. Thermosensitive block copolymer [(PNIPAM)-b-(glycine)] thin film as a protective layer for drug-loaded mesoporous silica nanoparticles. *Materials Research Express*. 2017;**4**:105306. DOI: 10.1088/2053-1591/aa91eb

[64] Amgoth C, Dharmapuri G, Kalle AM, Paik P. Nanoporous capsules of block copolymers of [(MeO-PEG-NH)-b-(L-GluA)]-PCL for the controlled release of anticancer drugs for therapeutic applications. *Nanotechnology*. 2016;**27**:125101. DOI: 10.1088/0957-4484/27/12/125101

[65] Amgoth C, Suman Joshi DSD, Dharmapuri G, Mohan Lakavathu M. Self-assembled block copolymer [(BenzA)-b-(PCL)] micelles to orient randomly distributed AuNPs into hollow core-shell morphology and its role as payload for nanomedicines. *Materials Science and Engineering: C*.

2018;**92**:790-799. DOI: 10.1016/j.msec.2018.07.033

[66] Prakash S, Malhotra M, Shao W, Duchesneau CT, Abbasi S. Polymeric nanohybrids and functionalized carbon nanotubes as drug delivery carriers for cancer therapy. *Advanced Drug Delivery Reviews*. 2011;**63**:1340-1351. DOI: 10.1016/j.addr.2011.06.013

[67] Patel T, Zhou J, Piepmeyer JM, Saltzman WM. Polymeric nanoparticles for drug delivery to the central nervous system. *Advanced Drug Delivery Reviews*. 2012;**64**:701-705. DOI: 10.1016/j.addr.2011.12.006

[68] Agarwal RC, Kant S, Singh PN, Maiti P, Pandit JK. Polymeric nanoparticulate system: A potential approach for ocular drug delivery. *Journal of Controlled Release*. 2009;**136**:2-13. DOI: 10.1016/j.jconrel.2008.12.018

[69] Oster J, Parker J, Brassard L. Polyvinyl-alcohol-based magnetic beads for rapid and efficient separation of specific or unspecific nucleic acid sequences. *Journal of Magnetism and Magnetic Materials*. 2001;**225**:145-150

[70] Sarparanta MP, Bimbo LM, Makila EM, Salonen JJ, Laaksonen PH, Helariutta AMK, et al. The mucoadhesive and gastro-retentive properties of hydrophobin-coated porous silicon nanoparticle oral drug delivery systems. *Biomaterials*. 2012;**33**:3353-3362. DOI: 10.1016/j.biomaterials.2012.01.029

[71] Whittlesey KJ, Shea LD. Delivery systems for small molecule drugs, proteins, and DNA: The neuroscience/biomaterial interface. *Experimental Neurology*. 2004;**190**:1-16. DOI: 10.1016/j.expneurol.2004.06.020

[72] Yun J, I'm JS, Lee YS, Kim HI. Electro-responsive transdermal drug delivery behavior of PVA/PAA/

MWCNT nanofibers. European Polymer Journal. 2011;47:1893-1902. DOI: 10.1016/j.eurpolymj.2011.07.024

[73] Muhlen AZ, Schwarz C, Mehnert W. Solid lipid nanoparticles (SLN) for controlled drug delivery Drug release and release mechanism. European Journal of Pharmaceutics and Biopharmaceutics. 1998;45:149-155

[74] Ramesh G, Dharmapuri G, Suman Joshi D, Amgoth C. Composite BME-AuNPs: Chemopreventive effect on skin carcinoma and inhibition on leukemia blood cancer cells. Advanced Materials Letters. 2017;8:1057-1064. DOI: 10.5185/amlett.2017.1733

[75] Amgoth C, Dharmapuri G. Synthesis and characterization of polymeric nanoparticles and capsules as payload for anticancer drugs and nanomedicines. Materials Today: Proceedings. 2016;3:3833-3837

[76] Paik P, Manda R, Amgoth C, Santhosh KK. Polyaniline nanotubes with rectangular-hollow-core and its self-assembled surface decoration: High conductivity and dielectric properties. RSC Advances. 2014;4:12342. DOI: 10.1039/c3ra47155a

[77] Doddapaneni SJDS, Amgoth C, Kalle AM, Suryadevara SN, Alapati KS. Antimicrobial and anticancer activity of AgNPs coated with *Alphonsea sclerocarpa* extract. 3 Biotech. 2018;8:156. DOI: 10.1007/s13205-018-1155-9

[78] Liang Y, Deng L, Chen C, Zhang J, Zhou R, Li X, et al. Preparation and properties of thermoreversible hydrogels based on methoxy poly (ethylene glycol)-grafted chitosan nanoparticles for drug delivery systems. Carbohydrate Polymers. 2011;83:1828-1833. DOI: 10.1016/j.carbpol.2010.10.048