Nanotechnology in the Life Sciences

Hemen Sarma · Sonam Gupta · Mahesh Narayan · Ram Prasad · Anand Krishnan *Editors*

Engineered Nanomaterials for Innovative Therapies and Biomedicine

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Nanotechnology in the Life Sciences

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Nano and biotechnology are two of the 21st century's most promising technologies. Nanotechnology is demarcated as the design, development, and application of materials and devices whose least functional make up is on a nanometer scale (1 to 100 nm). Meanwhile, biotechnology deals with metabolic and other physiological developments of biological subjects including microorganisms. These microbial processes have opened up new opportunities to explore novel applications, for example, the biosynthesis of metal nanomaterials, with the implication that these two technologies (i.e., thus nanobiotechnology) can play a vital role in developing and executing many valuable tools in the study of life. Nanotechnology is very diverse, ranging from extensions of conventional device physics to completely new approaches based upon molecular self-assembly, from developing new materials with dimensions on the nanoscale, to investigating whether we can directly control matters on/in the atomic scale level. This idea entails its application to diverse fields of science such as plant biology, organic chemistry, agriculture, the food industry, and more.

Nanobiotechnology offers a wide range of uses in medicine, agriculture, and the environment. Many diseases that do not have cures today may be cured by nanotechnology in the future. Use of nanotechnology in medical therapeutics needs adequate evaluation of its risk and safety factors. Scientists who are against the use of nanotechnology also agree that advancement in nanotechnology should continue because this field promises great benefits, but testing should be carried out to ensure its safety in people. It is possible that nanomedicine in the future will play a crucial role in the treatment of human and plant diseases, and also in the enhancement of normal human physiology and plant systems, respectively. If everything proceeds as expected, nanobiotechnology will, one day, become an inevitable part of our everyday life and will help save many lives.

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Preface

This book aims to shed new light on the role of engineered nanomaterials in innovative therapies and biomedicine. Engineered nanomaterials have a wide range of application in advanced medical technology, including soft-tissue engineering, dermatology and cosmetics, neural tissue engineering, cancer diagnosis, forensic science, human pathologies, and drug delivery.

Thus, by demonstrating the efficacy of such engineered nanomaterials, this book may provide new insights into these fast-developing fields. These engineered nanomaterials are extremely useful and will most likely become the next-generation nano-size factories with numerous applications in advanced medical technology. Engineered nanomaterials represent a sustainable approach in diverse areas of medicine, and we have, in this book, attempted to bring together the most recent scientific research data on engineered nanomaterials in biomedical fields that have the potential for a sustainable future. The chapters in this book comprise the contribution of eminent experts in the field and incorporate the most recent studies in each area. We hope that this book will be of great advantage to researchers and add a new dimension to the sustainable use of engineered nanomaterials.

The book contains 17 chapters written by 88 authors from leading nanotechnology research groups in Brazil, India, Iran, Saudi Arabia, South Africa, Sweden, and the USA. The introductory chapter critically evaluates the application of engineered nanomaterials in drug delivery for innovative therapies and biomedicine. Other chapters highlight natural polymer-based electrospun nanomaterials for soft-tissue engineering; metal nanoparticles for dermatology and cosmetics; L-asparaginase; nanomaterials, neural stem cells, and neural tissue engineering; treating vital dimorphic fungal infections in women; the development of nanomaterials based on graphene for biomedical purposes; quantum dots; nanostructured materials for cancer diagnosis; green synthesized nanoparticles and their potential antibacterial properties; the application of nanotechnology in forensic science; engineered clay nanomaterials; nanomedicine; emerging nanomaterials; polyurethane nanocomposites for bone tissue engineering; homeopathy as a nanomedicine; and the mycosynthesis of nanoparticles and their potential application in pharmaceutical bioprocessing.

We are confident that research scholars, bioengineers and biomedical scholars, graduate and graduate students in nanotechnology, nanobiotechnology, health, clinical, and pharmaceutical sciences will find this book extremely useful.

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Bengaluru, Karnataka, India — Sonam Gupta
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Chapter 1
Engineered Nanomaterials as Drug Delivery Systems and Biomedicines

Sajjad Ghahari, Saeid Ghahari, Somayeh Ghahari, Ghorban Ali Nematzadeh, Arabinda Baruah, Jyoti Ahlawat, Mahesh Narayan, and Hemen Sarma

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Abbreviations

5-FU	5-Fluorouracil
AChE	Acetylcholinesterase
AD	Alzheimer's disease
Ag	Silver
Au	Gold
BBB	Blood–brain barrier
bEnd.3	Cerebral endothelial cells
BEO	Barije essential oil
BRN	Bromelain
C225	Epidermal growth factor receptor cetuximab
CAP	Cold atmospheric plasma
Cas	CRISPR-associated nucleases
CNTs	Carbon nanotubes
CTH	Collagen triple helix
DDSs	Drug delivery systems
Dementia	Memory loss
DLC	Drug loading capacity
DNPs	Deoxycholic acid-modified nanoparticles
DOX	Doxorubicin
FET	Field-effect transistor
FF	Diphenylalanine
G3	L-arginine
GSH	Glutathione
HD	Huntington's disease
HDFs	Human dermal fibroblasts
HepG2	Human liver hepatocellular carcinoma cells
HT-29	Human Leukemia Cell Line
HTCC	Ammonium chloride *N*-(2-hydroxy) propyl-3-trimethyl ammonium chitosan chloride
LDL	Low-density lipoprotein
LL37	Antimicrobial peptides
LSPR	Localized surface plasmon resonance
LvN	Levofloxacin

MCF7	Human breast cell
MCF-7	Model breast cancer cells
MG	Malachite green
miRNA	MicroRNAs
MNPs	Metal nanoparticles
MNS	Magnetic nanoparticulate system
MNs	Microneedles
MOLT	Human colon cell
MRI	Magnetic resonance imaging
MTX	Methotrexate
NBs	Nanobiomaterials
NCEs	Nasopharyngeal carcinoma cells
NCs	Nanocarriers
NDs	Neurodegenerative disorders
NIPAm-AA	Nisopropylacrylamide derivative
NIR	Near-infrared
NLC	Nanostructured lipid carrier
NMs	Nanomaterials
NPs	Nanoparticles
NSAIDs	Non-steroidal anti-inflammatory drugs
OX26 mAb	Anti-transferrin receptor monoclonal antibody
PAs	Peptide amphiphiles
PD	Parkinson's disease
PEG	Polyethylene glycol
PLGA	Polyglycolide
PTX	Paclitaxel
QDs	Inorganic quantum specks
RNP	Ribonucleoprotein
Se	Selenium
SLNPs	Solid Lipid nanoparticles
SPIO	Superparamagnetic iron oxide
SPs	Shuttle peptides

1.1 Engineered Nanomaterials for Drug Delivery

Drugs are active pharmaceutical products that are used to treat diseases and improve a person's health and quality of life by improving bodily functions. Medicines enter the body via various routes, including intravenous, oral, intrathecal, subcutaneous, intramuscular, sublingual, rectal, nasal, ocular, transdermal, and cutaneous administration (Maurya et al. 2020). The medicine must reach its target site within a person's body to mediate its effect. The method of transporting the drug molecules to the desired location inside the body is called drug delivery, and numerous drug delivery systems have been developed to achieve this function efficiently. Such targeted delivery is essential for the drug to show its therapeutic effect. If a drug is not properly transported to the desired site of action, it may get attached to a collateral site and exhibit adverse side effects. Hence, it is a matter of utmost significance that the drug shows its effects only at the desired location (Maurya et al. 2020). Moreover, the material and method of synthesis of nanomaterial affect drug molecule efficacy (Bhagwat and Vaidhya 2013). Therefore, it is essential to choose the material and method for synthesizing the nanomaterial intelligently such that the drug of your choice is delivered to the desired location with minimal side-effects (Tiwari et al. 2012). Finalizing material and method for the synthesis of drug delivery system has always been a highly challenging task for researchers as the choice of candidate depends on several factors such as interaction with the drug molecule of interest, solubility under physiological conditions, toxicity profile of the nanomaterial, ability to achieve controlled and sustained release, to name a few. Therefore, this chapter focuses on various nanomaterial systems that can be used for drug delivery applications.

1.1.1 Nanoengineering

Design and development of materials that have at least one dimension in the nano meter range is termed as "nanoengineering." Nanoengineering is mainly synonymous with nanotechnology but instead emphasizes on the engineering aspects of the field rather than pure on science. In biomedical research, nanoengineering has been widely used. Nanoengineering is also used to develop systems for drug delivery. Moreover, engineering at the nanoscale allows enhancement of the drug delivery system's physical, biological and chemical properties (Maurya et al. 2020).

1.1.2 Biomaterials for Drug Delivery

The substances that are obtained from biological sources and have biomedical applications are termed biomaterials. Owing to their potential therapeutic and diagnostic applications, biomaterials constitute a highly promising class of engineered materials. The following characteristics must be present in a biomaterial that can be used as a drug carrier:

(a) Ability to deliver the drug molecules at the desired site.
(b) Controlled drug release at the target site.
(c) The carrier must remain intact after entering the body.
(d) The encapsulated drug must be protected from enzymatic degradation.
(e) Enhanced half-life of the drug inside the carrier.
(f) Biodegradation of the nanocarrier after the successful drug release.

Nanoengineering is used to modify the biomaterials in order to achieve the properties mentioned above. Some of the examples of nanoscaled biomaterials include polymer micelles, ferritins, organic dendrimers, and liposomes (Rajabi et al. 2016).

1.2 Application of Polymers in Drug Delivery

Many pharmaceutically active combinations have been developed due to advances in drug discovery methods, but some of them are ineffective in achieving their goals due to a lack of appropriate drug carrier candidates (Agrawal 2014). Thus, in search of effective drug delivery techniques, various materials have been explored and studied, and polymers are one of the most successful candidates with massive potential in this domain. Polymers have long-chain structures consisting of repeating monomeric units (Priya et al. 2016). They are frequently employed for targeted as well as controlled delivery of pharmaceutical drugs. Polymers have several advantages that make them an excellent candidate for drug delivery applications (Liechty et al. 2010). Since polymers are chemically inert, they can act as excellent drug carriers, increasing their bioavailability by improving the pharmacokinetics and pharmacodynamics of the drug. Polymers can also assist in achieving reduced immunogenicity, increasing solubility and stability of drugs, and achieving targeted drug delivery (Priya et al. 2016; Prasad et al. 2017). Additionally, polymeric nanocarriers can extend drug accessibility and distribution at the desired location (Maurya et al. 2020). Therefore, polymer-based drug carriers have been widely used against ailments such as cancer, diabetes, hepatitis B and C, and rheumatoid arthritis (Agrawal 2014).

1.3 Drug Delivery Systems Based on Protein and Peptides

1.3.1 Peptide-Based Systems for Drug Delivery

Various synthetic and natural peptides are available for designing drug delivery systems (DDSs) (Yazdia et al. 2020). Nanostructured peptides have been widely used for this purpose (Liberato et al. 2016). For instance, Li and his co- workers (2016a) reported a diphenylalanine (FF)-based nanosphere encasing gold nanoparticles for the delivery of a hydrophobic anticancer medication (Camptothecin). These stimuli-responsive nanocarriers respond to differences in glutathione (GSH) levels and pH in the tumor microenvironment compared to healthy tissues. These nanocarriers showed enhanced cellular uptake compared to free drugs. These nanocarriers also displayed significant cytotoxicity on A549 cancer cells compared to free drug. In a different study, a metallo-short peptide-based DDS for doxorubicin (DOX) delivery as an anticancer system was reported (Das et al. 2018). This DDS was developed using two tripeptides that were conjugated through Cu(II). It allowed controlled and sustained release of the drug. Stimuli-responsive DOX delivery was achieved by the displacement of histidine residue at the site (Das et al. 2018). The size of tumor was reduced to 4.1 and 0.78 for free DOX and drug loaded nanocarrier after 15 days of treatment in MCF-7/ADR tumor-bearing mice (Chen et al. 2017). In various studies, stimuli-responsive peptides have been utilized to create targeted DDSs (Shah et al. 2018).

In another report, Guan et al. (2019) showed that targeted DOX delivery to the brain could be achieved using a short peptide ligand by changing the surface of liposomes with D8 peptide. In this process, enhanced circulation half-life, immuno-com-patibility, as well as biosafety, was observed (Guan et al. 2019). In a simi-larstudy, peptide-based supramolecular hydrogels (i.e., peptide conjugates and short peptides) were used in drug delivery (Li et al. 2016b). Non-steroidal anti-inflammatory drugs (NSAIDs), which can have negative gastrointestinal and renal consequences, were encapsulated in hydrogel peptides and delivered locally (Li et al. 2013). DDSs could also be made using cyclic peptides in addition to linear peptides. For instance, Wang and his co-workers developed nanocarriers for DOX delivery by allowing cyclic octapeptides to selfassemble to form nanotubes which could further self-aggregate giving a micron-scale assembly (Wang et al. 2014). On CF-7/ADR cells, drugs encapsulated in these nanocarriers showed more significant effect and cellular uptake compared to the free drugs (Wang et al. 2014). Another very interesting class of peptides is amphiphilic peptides or peptide amphiphiles (PAs) that has been utilized for the co-delivery of microRNAs (miRNA) and DOX to accomplish synergistic impact for prostate cancer treatment (Yao et al. 2016). A portion of the new peptide-based drug delivery systems are summed up in Table 1.1.

Table 1.1 Advanced drug delivery systems based on peptides

Nanocarrier type	Payload	Results	Ref.
Short peptide-based composite hydrogels	Malachite green (MG), PEGylated $NbSe_2$ nanosheets	Shear-thinning and thermo-responsive injectable hydrogel; on-demand release of MG triggered by NIR irradiation	Wu et al. (2019)
Shuttle peptides (SPs)	Recombinant proteins, CRISPR-associated nucleases (Cas)	No poisonousness; SPs efficiently deliver protein and Cas RNP[a] to airway epithelia	Krishnamurthy et al. (2019)
Peptide nanoparticles	Pirarubicin	Efficient tumor targeting; multisensitivity of nanocarriers toward reducing agents, pH, and particular enzymes; peptide NPs efficiently suppress tumor growing in mice sample	Jiang et al. (2019)
Peptide-based hydrogel (DMSO-H_2O mixtures (G1) and L-arginine (G3) aqueous solutions)	DOX[b], PTX[c]	Extremely biocompatibility; great DLC[d] of both PTX (hydrophobic) and DOX (hydrophilic) in G1; G3 encapsulate only DOX; considerably greater DOX release in pH 6 in comparison with 7.4	Xu et al. (2020)

[a]Ribonucleoprotein
[b]Doxorubicin
[c]Paclitaxel
[d]Drug loading capacity

1.3.2 Protein-Based Drug Delivery Systems

Proteins are an essential class of biomaterials that have been used as delivery vehicles to deliver medicines to the desired location (Yazdia et al. 2020). They can be derived from plants and animals via cost-effective techniques and further converted into nanosized drug delivery systems (DDSs) using various synthesis methods (Tarhini et al. 2017).

Silk fibroin, collagen, keratin, elastin, and resilin are some of the most commonly used animal-derived proteins in tissue engineering and drug delivery (DeFrates et al. 2018; Pandey et al. 2020). Plant-derived proteins such as gliadin, zein, vicilin, and legumin are also promising candidates for manufacturing various delivery systems (Malekzad et al. 2018). For instance, a protein based DDS for intracellular transport of antibodies has been reported by Lim et al. (2017), which were found to have greater and quicker cytosolic delivery. A chemical and photothermal technique of cancer therapy has been reported by Liu et al. (2020) utilizes a pH/NIR-sensitive theranostic nanocarrier. Figure 1.1 shows various proteins used in synthesis of nanoparticles as delivery systems.

The efficiency of drug release by a carrier can be improved by controlling the molecular mass of the proteins and also by altering the morphology as well as the porosity of the DDS (Jao et al. 2017). The significant benefits of DDS derived from protein-based polymers include biodegradation, biocompatibility, monodispersity, and low cost of production. Numerous DDSs have been developed from various protein-based polymers, such as silk-like, elastin-like, and other recombinant polymers (Frandsen and Ghandehari 2012). Some of the DDSs derived from proteins are summarized in Table 1.2.

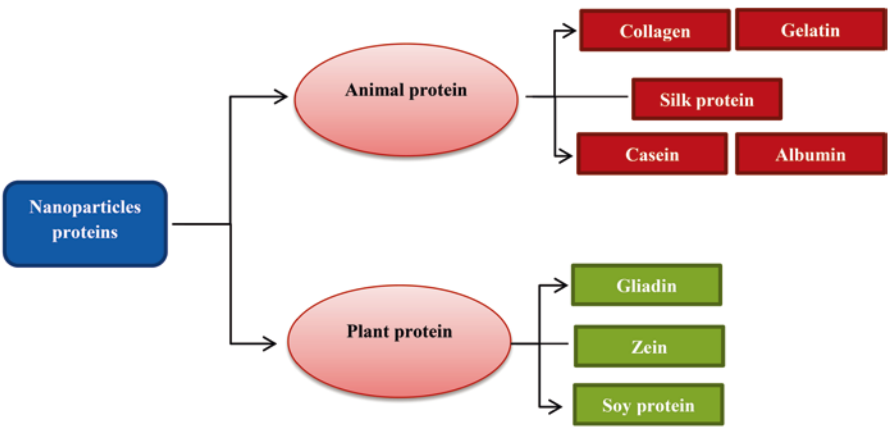

Fig. 1.1 Various proteins used in manufacturing nanoparticles as delivery systems

Table 1.2 DDSs based on proteins

Nanocarrier type	Base protein	Drug	Results	Ref.
Electrospun nanofibers	Zein	Barije essential oil (BEO)	Uniform nanofibers; great drug encapsulation effectiveness, prevent α-amylase and α-glucosidase activity, the first-order release of BEO in simulated stomach media	Heydari-Majd et al. (2019)
Fibers (~90 μm)	Collagen	Ciprofloxacin	Aromatic π–π interactions among drug and collagen triple helix (CTH) prevent premature release, without an initial burst	Arafat et al. (2019)
Hydrogel	Casein	Insulin	Slow insulin release in acidic pH, accelerated release under neutral or alkaline conditions, preserved insulin structure after release, a good candidate for oral administration of insulin	Khodaverdi et al. (2019)
Microsphere	Gelatin	Paclitaxel	Prolonged drug release from genipin cross-linked gelatin, high anticancer efficiency, improved survival time, reduced carcinomatosis	De Clercq et al. (2019)
NPs	Silk fibroin	α-Mangostin	More excellent drug loading capability utilizing cross-linkers, sustained drug release in 3 days, decreased hematotoxicity, more significant cytotoxicity in comparison with free drug versus Caco-2 and MCF-7 cancer cells	Pham et al. (2019)
NPs	Albumin	Citicoline	Permeable to the blood–brain barrier (BBB), it efficiently encapsulates negatively charged therapeutics via electrostatic interactions, pH-dependent release behavior	Pradhan et al. (2019)
Selenium NPs	Protein corona	DOX	Cationic Se NPs increase corona, greater release at low pH values, no burst release, reduced cell viability of cancer cells	Chakraborty et al. (2019)

1.4 Lipid Vesicles in Drug Delivery

The vesicular systems have gained enormous attention worldwide in the last few years (Pattnaik et al. 2020). When amphiphilic building blocks are exposed to water, they form highly organized assemblies of one or more concentric lipid bilayers known as lipid vesicles. Lipid vesicle-based drug delivery systems have several biopharmaceutical benefits making them an ideal vehicle for efficient drug delivery (Varghese et al. 2018). Lipid vesicles are endowed with several advantageous features as drug carriers. They can effectively encapsulate

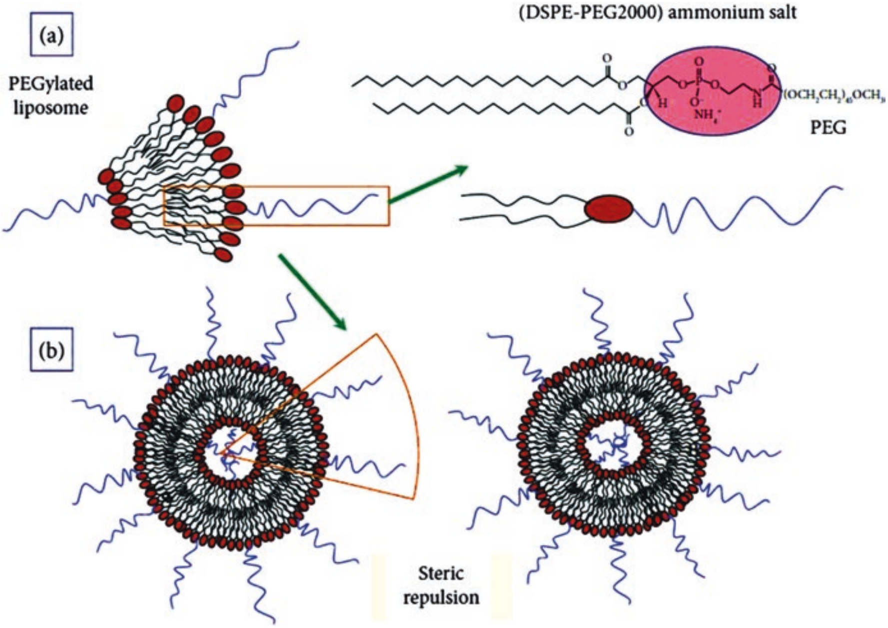

Fig. 1.2 (**a**) PEGylated nanocarrier made up of DSPE-PEG2000 ammonium salt (**b**) Sterically stabilized lipid bilayer nanocarrier (Lombardo et al. 2019)

lipophilic and hydrophilic drug molecules. They further enhance the bioavailability of the loaded drugs and reduce side effects of some drugs. Lipid vesicles increase the circulation time, allowing targeted delivery. Emulsomes, liposomes, transfersomes, ethosomes, enzymosomes, cubosomes, pharmacosomes, sphingosomes, ufasomes, and virosomes are some examples of the vesicular systems. Figure 1.2a demonstrates a PEGylated nanocarrier made up of phospholipid-1,2-distearoylsn-glycero-3-phosphoethanolamine-N-[methoxy(polyethylenegly col)-2000]or (DSPE-PEG2000) ammonium salt. Sterically stabilized lipid bilayer nanocarrier is shown in Fig. 1.2b.

1.5 Drug Delivery Using Metal Nanoparticles (MNPs)

The size of MNPs, which is comparable to that of cell organelles, is one of their most intriguing characteristics (Ahmad et al. 2020). Owing to their exceptionally small size, they can permeate through the biological membranes, which is not possible for the macromolecules. MNPs have been utilized in DDS for over 30 years (Ahmad et al. 2017). Also, they allow surface modifications to achieve desired pharmacological activity (Jiang et al. 2007). For example, coating MNPs with polyethylene glycol (PEG) increases the circulation time of the nanocarrier inside the body,

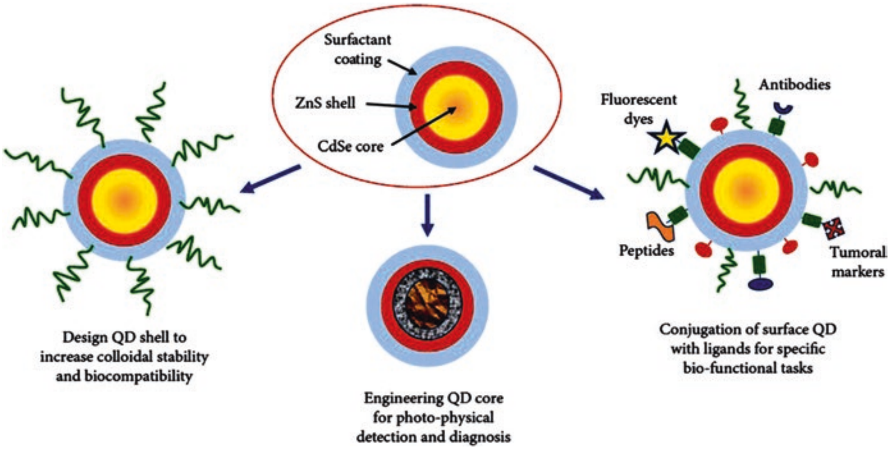

Fig. 1.3 Schematic representation of engineered QD nanocarriers for drug delivery and diagnostic applications (Lombardo et al. 2019)

and alleviates chances of clearance by the mononuclear phagocyte system (Ahmad et al. 2015). Furthermore, MNPs' surface chemistry permits binding of desired ligands, such as peptides, antibodies, or nucleic acid sequences, to their surface, allowing targeted delivery (Akhter et al. 2011). Figure 1.3 shows a schematic representation of engineered QD nanocarriers for drug delivery and diagnosticapplication. Following the ingestion of surface-modified nanoparticles by the cells, the drug delivery at the intended site is increased (Tan et al. 2012), resulting in improved therapeutic efficiency and patient compliance (Delcassian et al. 2019).

1.5.1 Gold Nanoparticles Based DDSs

Targeted drug delivery is superior to conventional passive drug delivery. Targeted endocellular disease therapy relies heavily on Au NPs conjugated with drug molecules (Kong et al. 2017). Au NPs in conjugation with antibiotics and different drug moieties can be used for targeted drug delivery. Several drugs, such as streptomycin, ampicillin, and kanamycin, have been reported in conjugation with gold nanoparticles to design efficient DDSs (Saha et al. 2007). Wang et al. (2018a) used gold nanoparticles grafted with antimicrobial peptides (LL37) for the treatment of diabetic ulcers. In a different study, Bagga et al. (2016) developed bromelain - capped Au NPs to enhance the efficiency of levofloxacin (LvN). The Au-BRN-LvN NPs showed greater antibacterial activity than. Similarly, Rad et al. (2018) found that AuNPs coated with amikacin and gentamicin had enhanced antibacterial activity against *A. baumannii*. Amoli-Diva et al. (2017) used AuNP-grafted light-responsive hydrogel to create an intriguing switchable on/off drug release system for the delivery of ofloxacin. The surface plasmon resonance (SPR) characteristics of AuNPs (scale, shape, and size) indicate that they are one of the most baffling nano-vectors for cancer treatment. AuNPs conjugated with specific antibodies against a receptor expressed on cancer cells were used for targeted delivery to cancerous cells (Fernandes et al. 2017). Apart from conjugation with a specific ligand, the surface of AuNPs could be coated with polyethylene glycol and lined with anticancer medications (Akhter et al. 2011). Similarly, when AuNPs are combined with methotrexate (MTX), they increase cellular uptake and cause cytotoxicity against various tumor cell lines (Chen et al. 2007). In addition, when 5-fluorouracil (5-FU) is lined with AuNPs, its efficacy against skin cancer improves while the side effects are reduced (Safwat et al. 2018). Mottas et al. (2019), for the first time, demonstrated the efficacy of AuNPs coated with a combination of 1-octanethiol and 11-mercaptoundecanesulfonic acid in delivering an immunostimulatory TLR7 ligand to tumor lymph nodes. After subcutaneous injection into tumor-bearing mice, functionalized NPs were rapidly transported to tumor-draining lymph nodes. They promote the activation of tumor-specific cytotoxic T-cells as well as local immune activation. Payne et al. (2018) developed dihydrochalcone-functionalized AuNPs for antineoplastic activity. When the cytotoxic efficiency of the functionalized AuNPs against HeLa cells was tested, significant toxicity against cancerous cells was discovered (Payne et al. 2018).

1.5.2 Use of Silver Nanoparticles in Drug Delivery

Silver (Ag) is an oligodynamic antimicrobial agent, which means it can significantly reduce the number of viable microbes. The clinical utility of AgNPs as an antimicrobial agent in healing wounds has boosted AgNPs research in nanomedicine (Aziz et al. 2014, 2015, 2016, 2019). Salvioni et al. (2017) produced AgNPs with significant antimicrobial activity and low toxicity that can be used in pharmaceutical formulations for humans and/or animals as needed. Chowdhury et al. (2016) also developed AgNPs using green synthesis route with significant antimicrobial activity against clinically relevant pathogens such as *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus epidermidis*, and *Staphylococcus aureus*. Furthermore, these green AgNPs have been shown to be nontoxic to human dermal fibroblasts (HDFs). AgNPs derived from *Camellia sinensis* were tested on human breast cell (MCF7), human colon cell (MOLT), and human leukemia cell line (HT-29) tumors, and confirmed their ability to inhibit tumor growth (Yadav and Mendhulkar 2018). On three human cancer cell lines, these biobased AgNPs demonstrated remarkable anticancer activity (Yadav and Mendhulkar 2018). AgNPs are highly cytotoxic to A549 cells (Fard et al. 2018). Zhao et al. (2012) developed a multifunctional magnetic/Ag theranostic nanocomposite conjugated to the epidermal growth factor receptor cetuximab (C225) for the treatment of cells from the nasopharyngeal carcinoma cells (NCEs).

1.5.3 Drug Delivery Using Magnetic Nanoparticulate System (MNS)

Magnetically controlled delivery involves attaching drug molecules to biocompatible microneedles (MNs) and administering them to patients intravenously. When the drug/MNs combination reaches a specific site, the medications become available as a result of a change in physiological conditions such as temperature, pH, or enzymatic activity (Alexiou et al. 2003). Methotrexate (MTX), doxorubicin (Dox), and paclitaxel (PTX) are just a few of the potent drugs for treating advanced solid carcinomas that have recently been loaded with MNs for cancer-targeted drug delivery. Liang et al. (2016) designed functionalized superparamagnetic iron oxide (SPIO) nanoparticles conjugated to doxorubicin (Dox) (SPIO-Dox) for chemotherapy and magnetic resonance imaging (MRI). SPIO-Dox accumulated more efficiently at the site of the tumor, even in small tumors, and patients experienced less cardio- and hepatotoxicity. Mosafer et al. (2017) examined the SPIONs-Dox loaded theranostic NPs against the C26 colon carcinoma cell line in mice. Higher cellular absorption of SPIONs-Dox was observed, which was accompanied by significantly improved antitumor activity and helped mice survive longer. Yu et al. (2018) demonstrated a dual cancer treatment strategy for A549 cells by combining cold atmospheric plasma (CAP) with PTX-loaded MNs. An in vitro analysis revealed that CAP and PTX have a synergistic impact on A549 cell growth inhibition (Yu et al. 2018). Wang et al. (2018b) assessed the antitumor effect of PTX-loaded MNs in the human brain (GBM) U251 cells. Farjadian et al. (2016) demonstrated that hydroxyl-modified MN is an effective carrier for the anticancer agent MTX. They investigated the anticancer properties of MNs conjugated with MTX in MCF-7 cells and discovered an increase in cellular toxicity. Wu et al. (2017) investigated the magnetic nanocomposite MTX delivery system in conjunction with the cancer cell lines MCF-7 and HepG2. Additionally, in vitro research has demonstrated that nanocomposites are effective against cancer cells while being relatively safe for normal cells. In vitro cytotoxicity of MTX-conjugated MNs against MCF-7 breast cancer cell line was investigated by Nosrati et al. (2018a, b). The prepared MTX-MNS had a significant anticancer effect on the MCF-7 cell line.

1.6 Nanoengineered Biomaterials for Neurodegenerative Disorders

The term "neurodegenerative disorders (NDs)"refers to a broad category of neurological disorders characterized by significant clinical and pathological manifestations centered on neuronal damage (Balasubramanian et al. 2020). They are severe, incurable diseases that currently have no known etiology and a rapid progression. Despite the lack of a clear connection between NDs and a rise in mortality, they are still a significant source of concern because of their potential to damage body function. Over 100 NDs have been identified, however, Parkinson's disease (PD), Alzheimer's disease (AD), and