Chapter 3
The Role of Nanomedicine in the Treatment of Neurodegenerative Disorders

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Abstract Neurodegenerative disorders are responsible for malfunctioning of brain and peripheral nervous system. The therapeutic drugs that are commonly utilized for the treatment of these disorders are not able to pass through the blood–brain barrier (BBB) as it permits passage of specific nutrients which are helpful for growth. Thus, nanotechnology (NT) can be very much valuable in solving this problem as there are different forms of nanomaterials that can act as efficient drug delivery systems and help in crossing the BBB and providing effective treatment for neurodegenerative disorders like Alzheimer's disease, Parkinson's disease, and many more. Thus, in this chapter, we tried to conglomerate all the recent developments related to neurodegenerative disorders and also provide a brief overview about the importance of nanotechnology in varied biomedical applications.

Keywords Neurodegenerative disease · Nanoparticles · Blood–brain barrier · Nanotechnology

3.1 Introduction

3.1.1 Neurodegenerative Diseases

Neurodegenerative diseases (ND) are heterogeneous type of disorders that are caused due to malfunctioning of brain or peripheral nervous system. They are caused due to malfunctioning of brain or peripheral nervous system. The term ND explains a varied range of conditions that majorly affect the neurons in human brain.

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Neurons are said to be considered as building blocks of the nervous system including the brain and spinal cord. Neurons do not have the capacity to reproduce or replace themselves. Age factor also plays a major role in neurodegenerative disorders. Alzheimer's disease (AD) and Parkinson's disease (PD) are most frequently caused disorders of this heinous type of disease. The combinational reaction of gene with the surroundings also leads to these disorders according to recent scientific reports.

There are many environmental factors, such as pesticides, metals, chemicals, and biological factors such as endotoxins, which cause ND.

3.1.2 Nanoscience

Nanoscience is a rapidly growing field of science which involves the study of structures and materials in the nanometer scale. Thus, nanoscience involves manipulation of atoms and molecules at supramolecular scale. Specialized methodologies are used to manufacture objects in nanoscale. There are various type of nanosubstances fabricated, such as nanofibres, nanocrystals, and quantum dots. Nanoelectromechanical systems (NEMS) are those devices which are used to carry out tasks which are too small for humans to do by themselves. High-powered microscopes are used to magnify nanoparticles. Scanning electron microscopes, nanoindenters, electrospinning equipment, optical profilers, and atomic force microscopes are generally used for the characterization of nanoparticles. There are varied types of metallic and biosynthesized nanoparticles (NPs) which are prepared through physical, chemical, and biological methods.

3.1.3 Nanobiomaterials

Biomaterials are biological substances which are introduced into the body as part of a medical device which replaces an organ or body function. According to their bioactivity, biomaterials can be classified into bioinert, alumina dental implant, bioactive hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$] which are coated on a metallic dental implant, surface active bioglass, and bioresorbable tricalcium phosphate [$(Ca_3(PO_4)_2$] implant. Bioinert biomolecules have very less interaction with the surrounding tissue, whereas bioactive biomolecules undergo greater interaction with surrounding tissues including the softer ones. There is a lot of scope of manufacturing nanoparticles from biomaterials. Thus, according to a study done by Han et al. (2006), silver nanoparticles can be produced by following green synthesis in which reduction of silver nitrate occurs in the presence of water-soluble polymer such as poly-L-lysine. This study brings water-soluble polymers into limelight as an effective biomaterial in the production of varied type of nanoparticles. With the help of nanoparticles, we can also test the efficiency of varied biomaterials. The study by Attia et al. (2005)

supports the above statement, in which hyaluronic acid (HA) was produced by adding amino acid, which are said to be bioadditives, and was also prepared in the presence of magnetic nanoparticles, and the results were compared. In the presence of bioadditives, it showed highest dry weight of HA by adding glutamic acid (GA), whereas the preparation done in the presence of magnetic NPs showed highest dry weight of HA after addition of Fe_3O_4NPs which helped in evaluating the efficiency of NPs in the preparation of HA.

3.1.4 Polymeric Micelles and Other Nanoparticles

Polymeric micelles ("micellar nanocontainers") were developed as carriers of drugs and diagnostic imaging agents. They were formed spontaneously in aqueous solutions of amphiphilic block of copolymers and had a core-shell architecture along with a core of hydrophobic polymer blocks (e.g., poly(propylene glycol) (PPG), poly (D,L-lactide), poly (caprolactone)) and a shell of hydrophilic polymer blocks (often PEG). The size of polymeric micelles usually varies from ca. 10 to 100 nm. Their core can be incorporated into considerable amounts (up to 20–30% wt) of water-insoluble drugs which prevented premature drug release and degradation.

The shell stabilized various micelles in dispersion and masked the drug from interactions with serum proteins and untargeted cells. After they reach the target cells, drug was released from the micelle via diffusion. Several clinical trials were completed or underway, which were used to evaluate polymeric micelles for delivering anticancer drugs. One of the early studies used micelles of Pluronic® block copolymers (PEG-b-PPG-b-PEG) as carriers for CNS drug delivery (Duncan 2003).

These micelles were conjugated with either polyclonal antibodies against brain α2-glycoprotein or insulin as targeting moieties. Both antibody- and insulin-vectorized micelles were shown to deliver a drug or a fluorescent probe to brain in vivo. Furthermore, there was a considerable increase in neuroleptic activity of a drug (haloperidol) which was solubilized in the targeted micelles compared to a free drug. Subsequent studies demonstrated that the insulin-modified micelles undergo receptor-mediated transcytosis in BMVEC from luminal (blood) to abluminal (brain) side (Woods 2003).

Polymer NPs are said to be a better type of nanocarriers as they have greater biocompatibility and biodegradability than others. These NPs are synthesized from a wide range of polymers which involve both natural and synthetic substances that are made up of poly (lactide-co-glycolide), poly(lactic acid), and many more. With respect to the delivery of drugs to various specific cells in the body, the composition of GNPs varies from one drug delivery system to other. These types of nanocarriers are also very cheap and economical when compared with those of other types of NPs. Gold NPs (GNPs) are said to be the most extensively studied NPs and applied most importantly in Cancer Biology and Medicine. Gold NPs have varied biomedical applications, such as genomics, immunoassays, microorganism detection and control, photothermolysis of cancer cells, targeted drug delivery, optical imaging,

and monitoring of biological cells and tissues by resonance scattering. Au nanospheres were the first GNPs to be discovered, which were followed by various forms, such as nanorods, nanoshells, and nanocages (Schrag et al. 2006).

Protein NPs are considered to be most efficient colloidal drug carrier systems which primarily affect the drug targeting system with the help of modified protein NPs by reducing drug toxicity. Prevention of enzymatic degradation by these NPs was considered to be a vital merit for these NPs. These types of NPs are already being extensively used as pharmaceutical carriers in various cancer therapies. Parenteral, peroral, and ocular types of administration are conducted using protein NPs in order to deliver large and small biological molecules.

Lipid NP systems are also extensively being used in cancer therapy in the form of solid NPs (SLNPs) and nanostructured lipid carriers (NLCs). SLNPs were formed from a single purified lipid which forms a crystalline lattice structure which was helpful for the incorporation of small molecular drugs. They are said to have a unique size-dependent properties which made them to have varied biomedical applications. Quantum dots are also known as fluorescent semiconducting nanocrystals, which have several biomedical applications, such as biolabels, sensors, light emitting diodes, and medicine (Schrag et al. 2006).

The most frequently used nanocarriers in recent times have varied types of nanogels as they have gained much importance in recent times due to their excellent medical applications and properties such as biocompatibility, which is vital for clinical treatment of many types of cancers. Due to their high porosity, nanogels are widely utilized as reaction vectors in preparation of hybrid NPs, which are helpful in capturing metal NPs like Fe_3O_4NPs (Schrag et al. 2006).

Nanomaterials can be classified into four types, that is, zero dimensional (e.g., NPs, QD), one dimensional (e.g., nanotubes, nanowires), two dimensional (e.g., ultrathin films), and three dimensional (e.g., nanocrystal grains and clusters). There are various applications of nanomaterials which are illustrated in Fig. 3.1, such as biosensors, wound healing, and target imaging (Langer 2001).

3.1.5 Disease Therapy

The main role of utilizing autoimmune disease therapy is to block pathological infection without disturbing the immunity of our body toward varied infections. Various studies have been performed, which gave a clarification about the role of nanoparticles in autoimmune disease therapy (Agarwal 2006). Shyam et al. (2013) briefed the importance of carbon nanotubes and graphenes in biomedical applications which minimized drug loss and drug degradation. This study also proved the uniqueness of NPs as they were functionalized with specific biomolecules. Serra and Santamaria (2018) stated that NPs act as vehicles for immune modulators and also for antigen delivery to APCs. This study also revealed that NPs act as direct T-cell targeting compounds. Several studies have shown the importance of certain

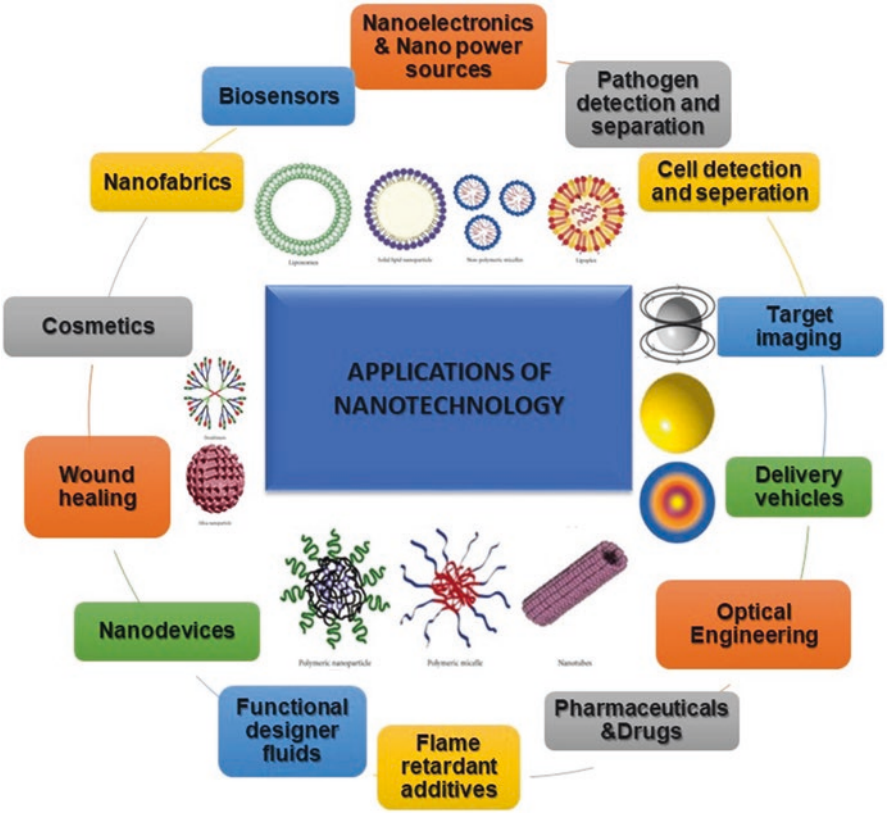

Fig. 3.1 Applications of nanotechnology

types of nanoparticles as effective carriers of therapeutic drugs to the target cells of the body.

3.2 Recent Developments in the Treatment of ND Using Nanomaterials

Neurodegenerative disorders are mainly caused due to poor delivery of therapeutic drugs into the brain. Blood–brain barrier is considered to be a functional barrier which permits only selective essential nutrients to the brain, which made us to know the importance of designing an effective route of administration of drugs to treat neurodegenerative diseases. Akinc and Battaglia (2013) briefed about the importance of intranasal drug delivery system of lipid NPs to treat neurodegenerative disorders, such as Parkinson's disease and Alzheimer's disease, as it was said to be a noninvasive type of drug delivery system and directly provides drug to the brain

through intra- and extraneuronal pathways. This study has also proved that most of the therapeutic drugs have failed to cure neurodegenerative diseases. Intranasal drug delivery with the help of lipid NPs was said to be the most effective and simplest methodology of drug administration as utilization of lipid NPs helps by enhancing bioadhesion to nasal mucosa and providing protection to the encapsulated drug.

Amanzadeh et al. stated that drug delivery into brain to treat temporal epilepsy can be increased by preparing PEGylated PLGA nanoparticles of epigallocatechin 3-gallate with the help of double emulsion method, and along with this immune histochemistry, cytotoxicity and behavioral tests were carried out in order to know the efficiency of drug delivery of these types of nanoparticles (NPs). The results of these studies depicted that monodisperse NPs with average size of about 169 nm and encapsulation efficiency of 95% were nontoxic. Neurotoxicity studies were also carried out, which showed decrease in neuronal death and neuroinflammation. Thus, this study proved that epigallocatechin 3-gallate PEGylated PLGA NPs were found to be the best alternative for therapeutic drugs, such as phenytoin and carbamazepine, which are being used to treat temporal epilepsy.

Another study by Sonvico et al. (2018) briefed about intranasal delivery of insulin using NPs would help in the treatment of Alzheimer's disease as it showed promising results in clinical trials. The biocompatibility and stability of these NPs proved to be helpful for the design of an effective intranasal drug delivery system.

3.3 Cell-Mediated Delivery of Nanocarriers to the Brain

A distinct case of the vehicle-mediated CNS drug delivery employs specific cell carriers that can incorporate micro- and nanocontainers loaded with drugs and act as perfect Trojan horses by migrating across the BBB and carrying drugs to the site of action. It is documented that AD, PD, stroke, ALS, and HAD have in common an inflammatory component. The process of inflammation is characterized by extensive leukocytes (neutrophils and monocytes) recruitment. Our knowledge of the function of MP has evolved considerably since Ilya Mechnikov, over a century ago, discovered an inflammatory cell type in starfish larvae capable of engulfing foreign objects (Kim 2007). The past century has realized that a great deal of progress in understanding the role MP plays in immunity and most notably in the CNS. Macrophages orchestrate intracellular killing of pathogenic microbes, antigen presentation, and secretion of biologically active factors, as well as mediation of pathological processes (Teleanu et al. 2019). Underlying such cellular functions is inflammation; the same response often proves detrimental in localized and systemic diseases, including those operative in neurodegenerative disorders. Inflammatory processes are engaged in attempts to eliminate the invader along with clearance of damaged tissue.

With regard to the nervous system neuroinflammation, perpetrated through activation of brain MP along with other glial elements, including astrocytes and endothelial cells, may act through paracrine pathways to accelerate neuronal injury in

highly divergent diseases, such as AD, PD, stroke, ALS, HAD, and spongiform encephalopathies or prion-mediated neurodegeneration. The biological processes causing inflammatory responses into a neurotoxic state, thus, are common links to many other neurodegenerative diseases (Robichaud 2006). As the role of the immune system is clarified, new opportunities for amelioration of the neurodegeneration from neurotoxins produced by the immune system will become critical for early treatment. In neurodegenerative diseases, CNS inflammatory infiltrates are complex and multifaceted. The initial responders or the MP cell elements of innate immunity set up a cascade, which later involve the activation and recruitment of the adaptive immune system and ultimately tissue destruction. MP and T cells possess the unique property of migrating toward the site of inflammation through the processes known as diapedesis and chemataxis. Their combat arsenal consists of uptake of the foreign particle, producing toxic compounds, and liberation of substances stored in intracellular vesicles via exocytosis. Therefore, these cells can be used for cell-mediated CNS drug delivery when loaded with a drug and administered into the blood stream (Tyler and Federoff 2006).

There have been many findings by various researchers all over the world about the importance of NPs in varied biomedical applications. When it comes to treatment for neurodegenerative diseases, there is an alarming need to know the combinational effects of neurotoxicology and nanotoxicology. Thus, Bencsik et al. (2005) stated the importance of evaluating both neuro- and nanotoxicity, as NPs may affect the human brain health due to large amount of industrial production. This study also briefs about the essential need for innovating specialized tools to carry out an effective evaluation of both neuro- and nanotoxicology.

There are certain types of cytokines that help in preventing neurodegenerative diseases from attacking our body. The study by Davis et al. (2005) helped in evaluating biological activity of NPs which contained leukemia inhibitory factor (LIF). Initially, packaging of LIF was done in nanoparticles which comprise poly (ethylene glycol)-poly(lactic acid) (PEG-PLA), which lead to the formation of LIF-loaded NPs which were also known as NanoLIF. In order to increase the cytokine delivery to inflammatory macrophages, the surface of NanoLIF was made to undergo changes with the help of CD11b antibody, which targets the activated peripheral macrophages. ELISA was used to evaluate the release of cytokine from NanoLIF. M1 murine leukemia cell proliferation assay was helpful in measuring the biological activity of NanoLIF. The results from this study showed that the average diameter of NanoLIF was found to be 30 nm and had a neutral surface charge. This study also proved that NanoLIF could release LIF at rapid rate at about 0–6 h after incubation at 370°C initially and slows down within 72 h. This study was very much helpful in proving that NanoLIF and CD11b-NanoLIF were responsible for minimizing M1 cell proliferation in a larger amount and thereby blocking neurodegenerative diseases from attacking our body.

In one of the studies, various in silico techniques were employed to make the therapeutic drugs which are commonly employed in the treatment of neurodegenerative disorders to cross the blood–brain barrier (BBB) using nanotechnology (Smith and Gumbleton 2006). There is a vital need in designing a methodology that

would exploit the BBB cells at molecular level without disturbing the normal functioning of the barrier. Receptor and adsorptive-mediated transcytosis were considered to be one of the most valuable mechanisms which would help in transport of nanomaterials from the blood to the brain by passing through BBB. Electrostatic interaction of a ligand including the charges expressing at the luminal surface of endothelial cells is said to be completely dependent on adsorptive-mediated transcytosis (Smith and Gumbleton 2006).

There have been many studies in which combination of various drugs with nanomaterials has helped in treating various neurodegenerative disorders. The study by Gobbi et al. (2005) proved that nanoliposomes (NL) when functionalized with phosphatidic or with cardiolipin was found to be helpful in the treatment of Alzheimer's disease (AD). Along with the use in treatment for AD, NPs can also be used in protecting neuronal cells against oxidative stress. Due to toxic effects, metal chelators are not being employed in recent times to prevent oxidation damage, and as NPs are free from toxicity, these can be used as a best alternative to metal chelators.

Nanotechnology has also produced in vitro diagnostic tools for varied neurodegenerative diseases like AD by measuring known pathogenic markers, such as tau proteins and ADDLs of human cerebral spinal fluid (CSF). In one of the studies, Georganopoulou et al. (2005) used bio-barcode of GNPs in determination of ADDL concentration in order to diagnose the disease early. A study introduced another in vitro technique in which quantum dots were conjugated with streptavidin which lead to easy recognition of APP, which was found to be highly sensible when compared with that fluoroimmunoassay (Flachenecker 2006).

Parkinson's disease [PD] is said to be a progressive neurological disorder generally affecting old age people. Nanotechnology plays a major role in release of dopamine from brain, which is helpful in treating PD. Trapani et al. (2005) prepared chitosan NPs along with which DA was adsorbed on to the external surface. Then, they were administered intraperitoneally into the mice whose results showed less cytotoxicity when they were compared with that of only DA-administered mice. There are in vivo diagnostic techniques for early detection and diagnosis of PD with the help of nanotechnology. Neumann (2006) designed a highly sensitive immunosensor for early PD detection with the help of Au doped–TiO_2 nanotubes arrays.

CNS injuries are commonly caused during neurodegenerative disorders, which are generally followed by accumulation of reactive oxygen species. Thus, in order to minimize these levels, fullerenes were utilized, which would act as radical sponges which have the capacity to incorporate multiple radicals in a single molecule, which thereby leads to removal of superoxide oxygen radicals by dismutation catalytic mechanism. One of the main reasons excluding BBB for the poor treatment for neurodegenerative disorders is that the therapeutic drugs which are being used for treatment are only symptomatic as they do not reduce the progressive pathological condition of the patient (Pardridge 2005). Tosi et al. (2008) in a review study stated that nanomedicine for every CNS disorder does not exist, which clearly shows that, however, nanomedicine is useful for treatment and early diagnosis of neurodegenerative disorders. Thus, there is an alarming need to try to produce new

nanomedicines that could be metallic, polymer, or biosynthesized, which would be helpful in treating these kinds of heinous disorders.

The transport mechanisms that are involved in BBB could be manipulated which were proved by various studies, which were related to kinetic flux that disclosed unidirectional, concentration dependent movements of compounds across the BBB. Various studies have reported that polymeric NPs (PNPs) have the capability of delivering varied CNS drugs, such as Doxrubicin, which proves that PNPs could play a vital role in the treatment of different CNS disorders in near future (Gaillard et al. 2005).

In a recent study by Huang et al. (2006), lactoferrin was initially made to modify NPs which were then injected into rats suffering with PD, which resulted in showing increased locomotor activity and enhanced DA levels in rats suffering with PD. Vinogradov et al. (2012) tried to create a new combination with NPs by encapsulating oligonucleotides in nanogels, which led to absorption of oligonucleotides into brain through BBB by reducing the amount of absorption of oligonucleotides in liver and spleen.

Nanosuspensions were considered to be excellent nanocarriers because of their effective properties, which were evaluated in various studies done till date on simplicity, high drug loading capacity, and application to various number of CNS drugs. Electrical stimulation is another type of methodology which is being adopted in recent times to treat CNS disorders (Lehericy 2007). In a recent study, carbon nanotubes were used to enhance chronic electrical stimulation of CNS, which would be helpful in treating neurodegenerative disorders (Kingsley 2006).

There have been various studies which were adopted to modify the concept of electrical stimulation in CNS with an aim to prevent these diseases, and by doing these studies, they could identify that nanofibers would also be helpful in treating neurodegenerative diseases. Silva (2006) reported that carbon nanofiber-based electrode arrays had the capability to provide both physical substrate and molecular signals when they were injected at the degenerative sites of brain.

Polymeric nanomicelles have also been one of the promising type of nanomaterials which can be utilized for treatment in CNS disorders in near future as some of the studies have proved that nanomicelles can transport DNA to the CNS by performing both in vitro and in vivo studies, but there is still a lot of scope to exploit this type of nanomaterial which has the capability to produce several biomedical applications (Wang et al. 2008).

A study has reported that N-butylcyanoacrylate (PBCA) NP combined with clioquinol (CQ), which is said to be a quinoline derivative, was injected into a transgenic mice, and the results showed that this type of NPs which were used to deliver clioquinol to the brain helped in solubilization of beta-amyloid plaques which were responsible for the cause of AD, and thus, it led to inhibition of these structures, which further caused prevention of AD. Similarly, there have been many studies which are helpful in proving that PBCA NPs help in transporting varied number of drugs to the CNS in an effective manner (Banks 2002).

There have been several studies which reported that accumulation of more number of metal ions which actually gets increased with age was said to be responsible

for causing AD or enhancing their effects in patients suffering with AD. Thus, in order to prevent this, Cui et al. (2005) reported that when Cu (I) chelator d-penicillamine was conjugated with NPs, it leads to reversing of metal-induced precipitation of B-amyloid protein, which finally lead to the prevention of AD.

The study by Kogan et al. (2006) reported that GNPs can also be useful in destruction of B-amyloid plaques by incorporating them into B-amyloid fibrils and then exposing them to weak microwave fields, which resulted in producing energy which was six times lower than that of energy produced from cell phones and proved that it was safer to use in the presence of healthy cells.

Ritchie et al. (2015) reported that Thioflavin-T NPs (ThT) was helpful in detection of AD by identifying B-amyloid in senile plaques of AD. The above study was followed by another study by Härtig et al. (2017) who tried to induce ThT NPs comprising of PBCA into the brains of transgenic mice, and the results showed that photoconversion of ThT occurred from the fixed tissues, and transmission electron microscopy proved the presence of nanocapsules in microglia and neurons of mice. The delivery of ThT from nanocapsules was observed with the help of confocal microscopy.

Several studies have shown that varied number of peptides and proteins which are emerging as nanobiomaterials have the capability of self-assembling themselves into various nanostructures such as nanotubes, nanovesicles, helical ribbons, and three-dimensional scaffolds (Tamai and Tsuji 2000). Stupp et al. (2014) injected a nanobiomaterial into a lab mice which was suffering with a spinal cord injury, and the results showed that the mice which was initially made to get paralyzed was able to walk after injecting with the nanomaterial by regenerating the damaged neurons. This was only possible because of self-assembling property of these nanobiomaterials.

In any nanomaterial, self-assembling property plays a key role in preventing AD-like disorders. Thus, there have been several studies made on GNA, which is a derivative of DNA that possessed the self-assembling property along with some additional properties which were lacking in DNA, such as antiamyloid activity and formation of mirror image structures, which were helpful in synthesis of various therapeutic proteins that are useful in vivo gene delivery of AD treatments (Saltzman 1999).

3.4 Nanogels

Nanogels are considered as nanosized networks of cross-linked polymers that often combine both ionic and nonionic chains, such as polyethyleneimine (PEI) and PEG or poly (acrylic acid) and Pluronic®. Such networks swell in water and can be incorporated through ionic interactions of oppositely charged molecules, such as oligonucleotides, siRNA, DNA, proteins, and low molecular mass drugs (Broadwell and Sofroniew 1993).

Transport of oligonucleotides incorporated in nanogel particles across an in vitro model of the BBB was recently reported (Weissig 2006). Notably, nanogels decreased the amount of degradation at oligonucleotides during their transport in BMVEC. To further enhance delivery across the BBB, the surface of nanogels was further modified by either transferrin or insulin.

In vivo studies suggested that nanogel increased brain uptake of oligonucleotides while decreasing its uptake in liver and spleen. Overall, nanogels are promising carriers for CNS drug delivery, although they are in relatively early stages of development (Bocti 2006).

3.5 Other Nanomaterials

Carbon nanotubes attracted attention in nanomedicine although there were serious concerns regarding their safety. Continuous electrospun nanofibers are also unique as they depict nanostructures in two dimensions and macroscopic structures in another dimension. They are safer to be manufactured than carbon nanotubes and possess less risk of air pollution. Electrospun nanofibers of a degradable polymer, PLGA, loaded with dexamethasone have been used for neural prosthetic applications (Dhib-Jalbut 2006).

A conducting polymer, poly(3,4-ethylenedioxythiophene), was deposited to the nanofiber surface, and the coated nanofibers were then mounted on the microfabricated neural microelectrodes, which were implanted into brain. The drug was released by electrical stimulation that induced a local dilation of the coat and increased permeability (Khachaturian 2006). Simpkins and Bodor (2014) proved that redox-based drug delivery nanosystems were successful in delivering and targeting release of DA into the brain through BBB, which generally blocks DA from entering the parenchymal layer of brain, and thus, these types of nanosystems are helpful in treatment for patients suffering with PD.

Gene therapy with help of nonviral vectors has proved to be effective in the treatment of PD, but various studies in recent times have also proved that NP-based gene therapy can also be developed for treating PD patients in a more safer and economical way. Wang et al. (2006) reported that NP-based gene therapy demonstrated lesser side effects than other types of gene therapy. This study also proved that this type of gene therapy resulted in showing enhanced clinical symptoms and abnormal metabolism from baseline when measured with the help of tomography. Ramanathan et al. (2018) conducted an experiment on animal model by condensing DNA plasmids into NPs which would help in repairing defective genes and thus finally prevent neurodegeneration in those animals by showing improved symptoms in them which proved that NP-based gene therapy effectively cures neurodegenerative disorders like PD.

3.6 Nanorobots

Nanorobots are biomachines which can algorithmically respond to stimulation and also have the capability of actuation, sensing, signaling information, processing, and intelligence. In a recent study, Prinster (2006) reported that stem cell therapy is useful in preventing the attack of PD by conducting experiments on rats into which they implanted stem cells directly into brain which lead to regeneration of striatal neurons and partial recovery of motor deficit which are actually related to deficiency of PD.

3.7 Conclusion

Nanotechnology is very much useful as it possesses many biomedical applications in drug delivery, separation technology, nanoelectronics, catalysis, and most importantly for treatment of neurodegenerative disorders. Polymer and protein NPs are said to be very much useful as an excellent nanocarriers to treat various CNS disorders. Several studies have proved that quantum dots had varied biomedical applications as biolabels, sensors, light-emitting diodes, and medicine. One study has proven that NP-based gene therapy can also be developed for treating PD patients in a safer and economical way. In another study, it was proved that lipid NPs when given by intranasal drug delivery system were helpful in treatment for various neurodegenerative disorders such as AD and PD. Some of the studies also proved that NPs act as vehicles for immunomodulators and also for antigen delivery to APCs. One of the studies stated that silver nanoparticles can be produced by following green synthesis in which reduction of silver nitrate occurs in the presence of water-soluble polymer such as poly-L-lysine. Thus, by this review, we can clearly understand the importance of nanotechnology in preventing NDs from attacking our body, and there is still a lot of scope to analyze and find more new biosynthesized NPs which have the capability to cure neurodegenerative disorders in near future.

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