P Prabhakar et al /J. Pharm. Sci. & Res. Vol. 12(4), 2020, 492-498

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Nanotechnology in Drug Delivery System: Challenges and Opportunities

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Abstract

In recent decade drug development and delivery becomes one of the high growing, demanding and manufacturing sector with high capital investment. This process a time consuming and expensive process, facing the problem of low bioavailability, toxicity, low efficacy, biocompatibility, side effects, fast excretion and degradability. Biocompatible nanomaterials having exceptional properties of high invasion rate, slow, controlled and targeted drug release, easily accessible to receptors overcome all these problems and are advantageous over traditional form of drug. Inspite of all the significance, toxicity of various nanoparticles used as drug delivery system is one of the major concern associated with it. In this review problem associated with convention drug and significance of nanoparticles in drug delivery and its toxic effect is discussed.

Keywords: Drugs, enzymes, drug target, nanomaterials, drug delivery systems, toxicity

1. INTRODUCTION

Drug is a molecular entity that has chemical as well as physiological effect on the living cells, tissues, organ or the whole organism. They may also kill pathogens like bacteria, virus or fungi. This is a general concept behind all drugs. The chemical substance present in the drug that causes the physiological effect is called the active ingredient of the drug [1]. A drug comprises of both active and inactive ingredient in which active ingredient are present in minute amount and inactive ingredient are used as excipients, filler, binder or lubricant having no physiological effect on the body[2]. In most cases, drugs acts by binding to specific receptors or enzymes and inhibiting or otherwise modulating their activities. An effective drug must survive within the body and must not modulate the properties of biomolecules other than target molecules[3]. Drugs were obtained primarily from plants and present time they are synthesized artificially. They are used to cure almost all the disease and abnormalities and helped mankind to fight against infectious diseases and epidemics[4]. Inspite of all these significance modern drug dosage forms are facing the problem of its efficacy, bioavailability, toxicity, biocompatibility, side-effects, inactivity are which hinders the drug development and delivery process[5]. In recent decades, highly sophisticated engineered nanomaterials have been exploited to overcome these problems. In this review we have discussed wide application of nanomaterials in drug delivery systems and behavior of nanoparticles inside the living body when incorporated with drug molecules with its future scope.

2. DRUG DEVELOPMENT AND DELIVERY

In convention or traditional drug development and delivery system process includes oral ingestion or intravascular injection. The systemic blood circulation is responsible for distribution of drug inside the body. Thus, only a small portion of active drug ingredients reaches the organs[6]. Sometimes drug also affects non-target organs which results in adverse effect[7]. Also, the development of new drug molecule is high expensive and time consuming process. The current problems and challenges associated with a drug development and delivery which pharmaceutical companies are facing:

2.1 Low Solubility- Low aqueous solubility is the major problems encountered while the development of a specific formulation of the drug. Poor solubility affects the bioavailability of the dug[8][9]. Hence, it is the major challenge for new chemical entity discovered by the scientists and industries.

2.2 Low bioavailability- Bioavailability is the fraction of drug dose available for systemic circulation. It is one of the major pharmacokinetic properties of the drug. A drug has 100% bioavailability when administered intravenously, while its bioavailability decreases when it is administered through other routes (such as orally) due to incomplete absorption. Hence, bioavailability must be considered while administrating the drug other than intravenous [10].

2.3 Low efficacy- Efficacy is the maximum response achieved from an applied dose of drug. In order to be high efficient drug, the drug must have high affinity results in tight binding with the target. This is known as affinity of the drug molecule[11]. The maximum response will be reduced if the affinity of the drug for target molecule is low. Low efficacy is the one of the major problem associated with drug molecule that leads to time taking in treatment of severe diseases[12].

2.4 Fast Excretion- Excretion or elimination is the removal of drug from the body by excretory organs like kidneys. Fast excretion of drug molecule makes the drug very less effective as desired amount of drug molecule is not reached to the target organs [13].

2.5 Fraction of drug required zone is not persists- In some part of the organ there is a need of accumulation of drug in a specific amount such as in tumor cells concentration of drug need to be high as relative to normal cells for proper optimum treatment. Lack of optimum accumulation of drug is associated with chemotherapeutic agents for cancer treatment[14].

3. DRUG DELIVERY SYSTEM (DDS):

To overcome these issues and problem related with a drug formulation concept of drug delivery system was introduced. The formulation methodology and system for delivering a pharmaceutical compound in the body as needed to safely achieve its desired therapeutic effect are known as drug delivery system. It is a method of delivering medication to a patient in a manner that increases the concentration of the medication in some parts of the body relative to others[15].

3. Nanotechnology in Drug Delivery System

Nanotechnology is the science and technology of developing materials specially engineered materials at nanoscale. It is manipulation of materials at nanoscale. The word "nano" is a Greek which means dwarf. One nanometer is equal to one billionth (10^{-9}) of a meter. One nano meter is also equal to the combined diameter of three atoms. The Most considerable nanotechnology to be technology at sub-micron scale: 100's of nanometers[16]. Nanotechnology as defined by size is naturally very broad, including fields of science as diverse as surface science, organic chemistry, molecular biology, semiconductor physics, micro fabrication, etc[17][18]. Nanotechnology has been exploited by researchers in the development of novel nanocarriers/nano drug delivery systems for the successful delivery drug molecules to the site of action[14]. This system is based on a method that delivers a certain amount of a therapeutic agent for a prolonged period of time to a targeted diseased area within the body. This helps maintain the required plasma and tissue drug levels in the body therefore, avoiding any damage to the healthy tissue via the drug. This nano drug delivery system is highly integrated and requires various disciplines, such as chemists, biologist and engineers, to join forces to optimize this system[19]. Current efforts in the area of drug delivery include the development of targeted delivery in which the drug is only active in the target area of the body (for example, in cancerous tissues) and sustained release formulations in which the drug is released over a period of time in a controlled manner from a formulation[20]. For an efficient targeted delivery, drug carrier must bypass the host's defense mechanisms and reached to its intended site of action[21]. In this method drug is medicated to a high concentration in some parts of the body relative to others. The goal of a targeted drug delivery system is to prolong, localize, target and have a protected drug interaction with the diseased tissue. The conventional drug delivery system is the absorption of the drug across a biological membrane, whereas the targeted release system is when the drug is released in a dosage form[22]. The advantages to the targeted release system is the reduction in the frequency of the dosages taken by the patient, having a more uniform effect of the drug, reduction of drug side effects Targeted delivery is believed to improve efficacy while reducing side effects. Here the objective is to develop such a system to deliver the drug to much sophisticated organs without any side effects[23]. Recent years researchers have focused on targeted drug delivery systems in curing chronic diseases like diabetes and cardiovascular ailments. Such targeted drug delivery systems are highly significant in treatment of cancer. Considering nature of the drug, its side effects, route of administration, its site of action, a targeted delivery system is optimized. There is a concept of optimum concentration range under which significant therapeutic effect is derived. Drug concentration above or below this range is can be toxic or no therapeutic effects. There is a very little progress in efficacy of the drug during therapeutic action on the cells due to low bioavailability, suggesting a multidisciplinary approach to deliver the therapeutics at the targeted site[24]. This reveals new ideas which are an interface of controlling the pharmacokinetics, pharmacodynamics, immunogenicity, non-specific toxicity, bio-recognition and efficacy of the drugs[15]. Such new strategy is a beautiful combination of molecular biology, polymer science, pharmacy, bio-conjugate chemistry and nanotechnology. Such cutting edge techniques are significant in minimizing degradation and loss of drug, prevention from side effects, increase in bioavailability and drug concentration accumulated in required sites. In recent decades scientists and researchers have developed several drug delivery systems and some of them are currently under development[25]. Soluble polymers, micro particles, microcapsules, cells, cells ghosts, lipoproteins, liposomes, micelles, dendrimers, hydrogels and carbon nanotubes are widely recognized as modern drug delivery systems. These carriers have specificity to slow degradability and sensitive to pH or temperature and targeted by conjugating them with specific antibodies for particular area of interests. Drug targeting falls under two categories: (i) passive and, (ii) active targeting. Passive targeting leads to preferential accumulation of drug at the target site while active targeting involves surface functionalization of drug carriers with ligands which are selectively identified by receptors on cell surface. As ligand-receptor interactions can be highly selective so, more accuracy is observed in targeting the site of interest[26].

3.2 Action Mechanism of Nano Drug Delivery Systems:

When designed to avoid the body's defense mechanisms nanoparticles have beneficial properties that can be used to improve drug delivery. Various nanoparticle formulations have been disseminated in drug development in an attempt to increase efficacy, safety and tolerability of incorporated drugs. Nanoparticle based formulations have shown high solubility, control release, improved pharmacokinetic and pharmacodynamic properties. Particle size, surface charge and shape play important roles in creating effective nanoparticle delivery systems that function through a variety of mechanisms[27].

3.2.1 Particle size- Particle size and size distribution are the most important characteristics because these determine the chemical and physical properties of nanomaterials. The hydrodynamic size and size distribution determine the in vivo distribution, biological fate, toxicity, and targeting ability of these nanomaterials for drug delivery system. They can manipulate drug loading, its release and stability. It has been reported that nanomaterials are advantageous over micro scale particles and due to small size and high

mobility that make them capable of higher cellular uptake suitable for wider range of cellular and intracellular targets[28] [29].

3.2.2 Surface Charge- Surface charge is usually expressed and measured in terms of the nanomaterials zeta potential which reflects the electrical potential of particles that is influenced by its composition and the medium in which it is dispersed. Zeta potential having a value of ± 30 mV have been reported to be stable in suspension leads to preventing aggregation of particles[30]. Surface charge of nanomaterials is crucial to drug loading. Drugs can be loaded via a number of processes such as covalent conjugation, hydrophobic interaction, charge-charge interaction or encapsulation. Loading of molecules depends upon nature of the drug as well as nature of target molecule, also alters the surface charge. By changing zeta potential attachment or adsorption of charged molecule can be determined on the surface of nanoparticle[31].

3.2.3 Drug Loading

Incorporation of a drug on or in nanomaterials is referred to as drug loading. An ideal nanoparticles drug delivery system should have a high drug-loading capacity without aggregation. High drug loading capacity can minimize administration or the number of doses[32]. Dispersibility is needed for smooth and efficient delivery of the drugs. Drug loading can be accomplished in several ways; however, drug loading and entrapment efficiency depend on drug solubility in the nanoparticles, dispersion medium, nanomaterials size and composition, drug molecular weight (MW) and solubility, drug-nanomaterials interaction, and/or the presence of surface functional groups (i.e. carboxyl, amine, ester, etc.) on either the drugs or on the nanomaterials[14][33].

3.2.4 Drug Targeting

Targeting of tumor leads to improving chemotherapy by nanomaterials provide a highly specific and versatile platform for cancer treatment. Enhanced permeability and retention enables selective localization in tumor spontaneously due to fenestrated blood vessels as in case of drug loaded liposome (doxorubicin-liposome complex). It has been shown to effectively improve selective localization in human tumors in vivo of small-molecule drugs such as doxorubicin as demonstrated by nanosize liposomes target tumors spontaneously because of the fenestrated blood vessels. This is due to enhanced permeability and subsequent drug retention[34]. Targeting of nanomaterials as drug delivery vehicles or nanocarriers for site-specific delivery has a number of advantages over targeting ligand-drug conjugates. Efficient drug loading of high concentrations of drug within the nanocarriers can be delivered specifically to the target cell or tissue when a ligand interacts with its receptor which results in the delivery of large payloads of therapeutic agent relative to number of ligand-binding sites. This is very advantageous in imaging tumor through the increase in tumor signal to background ratio[35]. The nanocarriers are attached to the ligand and the drug is loaded independent of the coupling of ligands. This also bypasses drug activity that may be due to formation of ligand-drug complex conjugate or inactivated by potentially aggressive coupling reaction. A large number of ligand molecules can be attached to the nanocarriers depending upon the size of the nanomaterials and the size of the drug to increase the probability of binding to target cells especially for those with low binding affinities[36][37]. Active targeting enables efficient distribution of the carriers in the tumor, thereby reducing the return of drug back to the circulation that may be caused by high intratumoral pressure and, when ligand is only attached to the carrier due to the small size of the conjugate, it can only extravagate at the disease site but not in normal vasculature, and as such, the ligand cannot interact with the target epitopes of normal tissues avoiding side effects[38].

3.2.5 Binding to the receptor sites

Conventional drug carriers lead to modification of the drug distribution profile as it is delivered to the MPS (Mono Phagocytic System) such as liver, spleen, lungs, and bone marrow. However, nanoparticles as drug carriers can be recognized by the host immune system when intravenous administered causing them to be cleared by phagocytes from the circulation[39]. The size of the nanoparticles, surface hydrophobicity, and surface coating functionalities determine the level of blood components (e.g. opsonins) that bind to its surface influencing the in vivo fate of nanoparticles[40]. To enhance the chances of success in drug targeting, it is important to prevent the opsonization while prolonging the circulation of nanoparticles in vivo. The nanoparticles can achieve this by pre-coating with hydrophilic polymers and/or surfactants or by using nanoparticles with biodegradable hydrophilic copolymers such as PEG (Polyethylene Glycol)[41]. Nanoparticles undergo extravasation during entry into tumor tissues which occurs by means of the enhanced permeability and retention (EPR) effect. Thus, drugs carried by nanoparticles for delivery or nano-enabled drugs at the lower size range are preferable to the upper submicron and micron sizes to achieve longer circulation half-lives through the reduced macrophage mononuclear uptake and more efficient cellular uptake[42]. It has been reported that the vascular pore size of majority of solid tumors ranges between 380nm-780nm. Depending upon type of tumor, growth rate, and microenvironment, organization of vasculature may differ. Hence, to reach at tumor sites size of the nanocarriers must be smaller than cutoff pore diameter. Usually, size of a normal vasculature is greater than few nm which is impermeable to drug loaded nanocarriers as compared to free and unassociated drug molecule. Such size range of nanocarriers increases drug concentration at targeted sites and simultaneously reduces distribution of drug and toxicity to normal healthy tissues[43].

3.2.6 Release of Drug

The process of diffusing or dissolution drug in the body, which is loaded into nanoparticle, is known as drug release while biodegradation refers to collapsing the drug delivery system inside the body. Both drug release and biodegradation are important to consider when developing a nanoparticle drug delivery system. Besides active components, solubility, diffusion and particle size also determines the effectiveness of the drug. High surface-to-

volume ratio is leads to faster drug release at the surface due to small size of particles. In contrast, larger particles have large cores, which allow more drugs to be encapsulated per particle and give slower release. Thus, manipulation of particle size provides a trigger to tuning drug release rates [44]. The interaction of nanomaterials with cells provides an advantage to cross through the blood brain barrier. The blood brain barrier consists of a tightly packed layer of endothelial cells surrounding the brain that prevents high-molecular weight molecules from passing through it. The ability of nanoparticles to pass through the blood brain barrier is an important advantage for drug delivery systems for effective treatments[45]. However, the efficacy of nanoparticles toward the treatment of neurological disorders, like brain tumor, stroke, and Alzheimer's disease, have been largely constrained in spite of the advances and breakthroughs in nanotechnology-based medical approaches. Targeting of drugs to the central nervous system remains for the future success and development of nanotechnology-based diagnostics and therapeutics in neurology[5].

4. TOXICITY OF NANOMATERIALS USED AS DRUG DELIVERY SYSTEMS

Due to high surface-to-volume ratio and quantum size effect nanomaterials exhibit unique properties as compared to bulk materials. They have shown toxicity which is unusual and not seen with bulk materials. Even gold which remains inert at bulk is highly active at nanometric scale[18]. However, there is a limited data available on the fate of nanomaterials inside the living cells and their toxic effect. Many studies have been made in the past decade and suggested that nanoparticles have different toxicity profiles when compared with their bulk particles because of their smaller size and higher reactivity. Nanoparticles are usually smaller in size, comparable to large biological molecules such as enzymes, receptors, of a size about 100 to 10,000 times smaller than human cells[46]. These nanoparticles can offer unparalleled interactions with biomolecules both on the surface and inside the body cells. It may seem that NPs do not have toxic effects. However, the greater surface area to volume ratio of these particles causes their higher chemical reactivity and results in increased production of reactive oxygen species (ROS). Reactive Oxygen Species (ROS) formation is one of the mechanisms of nanoparticles toxicity which could cause oxidative stress, inflammation and consequent damages to the proteins, cell membrane and DNA. Dealing with cytotoxicity, invitro analysis is the first choice for most of nanomaterials[25][39]. Many research work have been reported the cytotoxicity of a number of nanoparticles like silver nanoparticles, quantum dots, carbon nanotubes, zinc oxide nanoparticles, titanium oxide nanoparticles, gold nanoparticles which are used as an ideal biocompatible drug delivery systems[47]. They have shown highly efficacy toward abnormal cells. Some advanced ceramic material materials like glass ceramic has shown toxicity to the abnormal cells like cancer cells. Nanoparticles are making significant contributions to the development of new approaches of drug delivery in cancer and can provide a platform for combined therapeutics with subsequent monitoring of response. Increasing evidence suggests that the special physicochemical properties of nanomaterials pose potential risks to human health. Therefore it is necessary to understand how cells respond to nanomaterials and through what mechanisms[48].

Table 1. Toxicity of few nanoparticles

Nanoparticles	Test Organ/Species	Toxic Effect	References
ZnO nanoparticles	Human pulmonary adenocarcinoma cell line LTEP-a-2	*Cytotoxicity on human pulmonary adenocarcinoma cell line LTEP-a-2*	[49][50][51]
TiO_2 nanoparticles	Human peripheral blood mononuclear cells	*Suppressed IDO activity and IFN-c production*	[52][53]
Silver nanoparticles	Human colon carcinoma cells	*Oxidative stress and cytotoxicity*	[54][55][56]
Nickel oxide nanoparticles	Human pulmonary epithelial cell lines: BEAS-2B and A549	*Inflammation and genotoxic effect in lung epithelial cells*	[57]
Fullerenol nanoparticles	Cultured human lung fibroblasts	*Cytotoxicity and genotoxicity*	[58][59]
ZnO nanoparticles	Human polymorph nuclear neutrophil (pmns)	*Delay in human neutrophil apoptosis*	[60]
Silver nanoparticles	Human umbilical vein endothelial cells (huvecs)	*Endothelial cell injury and dysfunction*	[61]
Bare titanium dioxide, zinc oxide, magnesium oxide, silver, gold nanoparticles and their triglyceride-coated form	Suspensions of Balb/c skin cells	*Cytotoxicity*	[62]
Metal oxide NPs (ZnO, CeO_2, TiO_2, and Al2O3)	Human peripheral blood lymphocytes (pbls)	*Induced changes in the expression levels of adhesion molecules and the c-x-c chemokine receptor type 4 (cxcr4) in these cells, T-cell proliferation upon cell exposure to TiO_2 and Al_2O_3 nanoparticles*	[63]
Titanium dioxide nanoparticles	Human gastric epithelial cells	*Oxidative stress, DNA damage*	[63]

4.1 Interaction of nanoparticles with cells

Inhalation, ingestion or dermal invasions are the route through which nanoparticles can enter into the human body. After entering into the living body it interacts with a number of biomolecules such as sugars, proteins and lipids. They are dissolved in the body fluids like interstitial fluid between cells, lymph or blood. There is immediate coating of nanoparticles takes place and thus the newly formed structure is called "protein corona" that determines the biological fate of nanoparticles. Its composition is dynamic and depends on the relative concentrations of the individual components and on their affinities toward the nanoparticle surface. In fact, nanoparticles have to be viewed as evolving systems that adapt to varying concentrations of the biomolecules present in the fluid[64][65]. It has been suggested that the final corona reflects its own prior history. The size of nanoparticles has a strong effect on their interactions with living cells, influencing uptake efficiency, internalization pathway selection, intracellular localization and cytotoxicity[64][66]. Still, we believe that there are a few general trends that can be trusted; (a) For an efficient endocytosis there must be an optimal size of nanoparticles which is independent of particle composition, (b) Such a small size can alter with surface properties and type of the cell, (c) There is a higher probability of internalization by passive uptake than bigger one[64][67]. Receptor mediated endocytosis is initiated by membrane wrapping process as nanoparticles interacts with cell membrane. It requires the concerted formation of multiple NP receptor interactions. There is a less receptors are available for small nanoparticles as compared to larger one. Several small nanoparticles needed to be interacting with receptors simultaneously to trigger membrane wrapping. While an individual, large nanoparticle can act as a crosslinking agent to cluster receptors and induce uptake. But as per mathematical modeling analysis receptor mediated endocytosis is optimal due to no unavailability of ligand on nanoparticles and no shortage of ligand on the surface of the cell[68]. As the size matters, a 50-60 nm nanoparticle is highly efficient in capable for activating enough receptors to initiate successful internalization in respect of thermodynamics. Cellular responses can be modified by protein corona which is controlled by the ligand present on the surface on the nanoparticles. Two factors, size and coating have own influence on the distribution of internalized nanoparticles[69]. The positively charged 5.2nm CdTe QDs (Quantum Dots) nanoparticles were distributed throughout the cytoplasm of N9 cells but did not enter the nucleus, whereas positively charged 2.2nm QDs were localized predominantly in the nuclear compartment[70]. In contrast, intracellular distribution was not influenced by the size of QDs which was functionalized by with thiols, amines or mercaptopropionic acid. The ultimate intracellular destination of Au nanoparticles coated with cell penetrating peptide was controlled by its diameter. Smallest one with a size of 2.4 nm Au nanoparticles was capable to localize nucleus while nanoparticles with a size of 5.5 nm and 8.2 nm remain sequestered in endolysosomal zone[34]. Accordingly, understanding the underlying mechanism of cellular uptake is an important step toward understanding the biological fate of nanoparticles, both the favorable and adverse aspects. Physico-chemical features of nanoparticles/cell interactions are influential factors in determining the particle-cell interactions and consequently influence behavior of the cell. It has been reported that preferential cellular uptake of positively charged nanoparticles over negatively charged nanoparticles due to electrostatic interactions seems simplistic and reductive and considers only surface potential despite of involvement of many other parameters in the equation[71].

4.2 Interaction of nanoparticles with living cells and Key role of the protein corona

When nanoparticles enter into the biological system it comes under the influence of a number of biomolecules, rapidly absorbs at its surface and covers it entirely. This so called "protein corona" that manipulates the properties of nanoparticles and thus a new 'biological identity' is introduced. Such a new biological identity creates an additional complexity in respect of complex formation[72]. The protein corona formation is a dynamic process consists of competitive molecular binding at the surface of the nanoparticle. Protein which is highly abundant absorbed on the surface and their replacement is followed by high affinity proteins. Because of high complexity as well as its dynamic nature, the existence of protein corona is always a doubtful[73]. Also, it has been recognized that it induces the change I hydrodynamic diameter and zeta potential of nanoparticle. Even if it is true that the initial charge of the nanoparticle actually influences the nature of the proteins that adsorb and consequently has an indirect impact on nanoparticle/cell interactions[74].

4.3 Mechanism of Toxicity caused by Nanoparticles

Physicochemical reactivity of nanoparticles lead to the formation of free radicals or ROS including superoxide radical anions and hydroxyl radicals direct or indirect through activation of oxidative enzymatic pathways result in oxidative stress[74]. In general, there are several sources for oxidative stress: (a.) Oxidant-generating properties of particles themselves as well as their ability to stimulate generation of ROS as a part of cellular response to nanoparticles, (b.) Transition metal-based nanoparticles or transition metal contaminants used as catalysts during the production of non-metal nanoparticles, (c) Relatively stable free radical intermediates present on reactive surfaces of particles, (d) Redox active groups resulting from functionalization of nanoparticles, (e) Small NPs have a higher probability to be internalized by passive uptake than large ones, (f) Under otherwise identical conditions, small NPs are more likely to cause toxic cellular responses[75].

5. DISCUSSION

The Drug delivery system is one the most important part of pharmacology as it introduces the drug into living body physically. They are the engineered technologies for targeted delivery or controlled release of therapeutic

agents. Administering drugs locally rather than systemically (affecting the whole body) is a common way to decrease side effects and drug toxicity while maximizing a treatment's impact. But now days the drug delivery system are facing the problem of bioavailability, bio-compatibility, toxicity, efficacy and control release. To overcome all these challenges nanomaterials are exploited for their exceptional biological properties. Their biocompatible, biodegradable, stealth, controlled and targeted drug release mechanism have proven their wide application as drug carriers. But together withi nanomaterials are not safe at all. Thus, Identification and determination of toxic properties of the nanomaterials can lead to the manipulate the properties of some novel formulation based on highly biodegradable and much efficient drug delivery system considering of human and environmental health risk. So far, in this review we have discussed the problem and challenges in modern drug development and role of nanomaterials to overcome all these problems Thus, knowledge of these molecules and the pathways in which they participate is crucial to drug development. Due to such a small size nanomaterials can easily entered into the biological system and can affect the normal functions of the cells. Application of nanomaterials in developing delivery system is promising area to overcome these issue and recent research have focused on exploitation of the novel properties of nanomaterials.

6. CONCLUSION

Drug discovery and delivery is one of the most important interfaces of biochemistry and medicine. In this review we have discussed the advantages and problems that current drug delivery systems are facing and role of nanotechnology to overcome all these shortcomings. Due to biodegradable, biocompatible nature, targeted and sustain release drug profile, nanomaterials are always preferred as an ideal drug delivery vehicles. But such nanomaterials are not completely safe thus possess toxic effect on healthy cells. Therefore, assessment of nanoparticles toxicity is necessary in biomedical applications specially in novel drug delivery systems as well as gene delivery and therapeutic applications.

Conflict of research interests

Authors declare no conflict of research interests.

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