Nanomedicines: A Focus on Nanomaterials as Drug Delivery System with Current Trends and Future Advancement

Authors
Jaya Pandey[1], Ragini Dubey[1], Aditya Kate[2], Bhairav Prasad[3], Arzoo Sinha[2], Mohit S Mishra[2]

Affiliations
1 Amity School of Applied Sciences Lucknow, Amity University Uttar Pradesh, Lucknow Campus, India
2 Amity Institute of Biotechnology, Amity University, Chhattisgarh, India
3 Department of Biotechnology, Chandigarh College of Technology, Landran, Mohali, India

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70469 Stuttgart, Germany

Corresponding
Dr. Mohit S Mishra
Amity University Chhattisgarh Raipur India
Amity Institute of Biotechnology
State Highway 9 Baloda-Bazar Road
Raipur
India
Mobile No. +91-8177926933
msmishra@rpr.amity.edu

ABSTRACT

The rapid advancement of nanomedicine presents novel alternatives that have the potential to transform health care. Targeted drug delivery as well as the synthesis of nanocarriers is a growing discipline that has been intensively researched to reduce the complexity of present medicines in a variety of diseases and to develop new treatment and diagnostic techniques. There are several designed nanomaterials used as a delivery system such as liposomes, micelles, dendrimers, polymers, carbon-based materials, and many other substances, which deliver the drug moiety directly into its targeted body area reducing toxic effect of conventional drug delivery, thus reducing the amount of drug required for therapeutic efficacy and offering many more advantages. Currently, these are used in many applications, including cancer treatment, imaging contrast agents, and biomarker detection and so on. This review provides a comprehensive update in the field of targeted nano-based drug delivery systems, by conducting a thorough examination of the drug synthesis, types, targets, and application of nanomedicines in improving the therapeutic efficiency.

Introduction

Nanoparticles as drug delivery structures are being increasingly used to improve therapeutic efficacy and patient response to medication by turning them into advanced systems of therapeutic and diagnostic drugs by manipulating their size, surface properties, dosage, and reduced side effects. Linking the idea of a drug working as a "magic bullet" by Paul Ehrlich proposed centuries ago, tremendous progression have been made in this arena to widen the scope for targeted delivery of drugs since then, that could selectively eliminate diseased cells without damaging the neighbouring normal cells [1–3]. Targeted nano drug delivery using nanocarriers is one such concept that can transfer drugs at the location because of their altered features with enhanced capability to transmit beneficial molecules of drugs at the desired location more effectively. The nano-carrier and the drug molecule organized together with each other encapsulating or adsorbing the drug on its surface, and then binding to a cell surface-specific receptor thereby achieving targeted delivery of drugs in a cell- or tissue-specific manner is an effective way of drug development medicinal chemistry today. The review centres on the integration, appropriate features for effective minute particulate assisted drug administration and their forms as well and the different uses in which these nano-particu-

late structure have shown possibility. To sum up, we have discussed the tremendous possibilities of rising novel particle approach in field of pharmaceutical sector.

Target nanocarrier molecules offer the benefits like shielding the molecule from untimely metabolic breakdown, increase infiltration of the drug into the cell, regulate pharmacokinetic, pharmacodynamic properties, drug distribution and augment absorption of the drug molecule in the targeted organ etc. They upsurge bioavailability, shield and alleviate more subtle agents, curtail side effects, and offer resources for active targeting. It enables delivery less water-soluble drugs and can provide means of bypassing the liver, thereby preventing the first pass metabolism. The hydrophobic drugs may also be encapsulated inside the central space of the nanocarriers and delivered at the site effectively. They offer to regulate physicochemical properties of the drug molecule and can control the rate at which a drug is made available in the body where it is released by increasing the properties like stability, water solubility of drugs, prolong the cycle time, increase the uptake rate of target cells or tissues, and reduce enzyme degradation, expand impact and effectiveness of drugs [4, 5].

The drug delivery system not only has an objective of delivery therapeutics to the target diseased part of body in controlled manner but also to maintain the drug level in the body. Recently, nano level technique has found its means of revolutionizing science and has a range of applications in biomolecular detection and diagnostics, therapeutics, catalysis, thermionics, genetic analysis, oculus, electro optical, medicaments, light, and scavengers and many more. Nanotechnology applications in drug delivery is a key research area for the pharmaceutical and biotechnology industries in the future, due to its unique ability to tackle the shortcomings and downsides of conventional medications [6].

Nanomaterials are being used as drug delivery systems as they are supramolecular structures made up of polymers with exceptionally small size varying from 10 nm to < 1000 nm and greater surface area to volume proportion and highly stable too, there are various categories of nanomaterials as shown in ▶ **Table 1**. They are pH- labile chemically steady structures that can be constructed with different biochemical way that are eco-friendly and economical [7, 8]. These are significantly utilized in remedial and diagnostic treatment along with the development of drug delivery playing an essential field in the nanotechnology.

The dimension of the nano-carrier plays significant role in drug delivery systems. Suitable appropriate size and large surface area of the nanoparticles shows rise in solubility. Hence, enhances the ability of nano-carrier to cross the blood brain barrier (BBB) and get absorbed through the solid junction of endothelial cells of the skin after entering the pulmonary system [9]. Traditional drugs which are taken orally or via injection are not always produced as the most favourable formulation for each product. A product needs more advance and novel approach like targeted drug delivery to enhance the efficacy. The basic functions of the nanoparticles are to have enough concentration of drug in targeted sites and to decrease the side effects by controlling the pharmacokinetics of the drug. These have gained popularity because they offer controlled drug release at a single dose. In addition, with help of adaptation, the nanosystem could inhibit the endogenous enzymes from degrading the compound [10].

Basics of Nanotechnology based techniques in designing nanomaterial

Nanotechnology is the science that forms the basis of utilization of nanomedicines in prevention and curing different diseases by means of suitable nanoparticles and nanobots which are utilized in a wide range of applications including diagnosis, drug delivery, and activating targets in a living system [11–13]. The past decade studies interpreted that the biological response and nano interaction significantly plays an important role in designing the nanoparticles for effective drug delivery. Poorly soluble drugs have different biopharmaceutical concerns such as less diffusion capacity, enough for intravenous intake, and adverse effects. The limitations of such drugs can be overcome by developing nano-materials in drug delivery systems [14, 15].

The designing of nanoparticles for drug delivery has been widely studied to possess several advantages like drug solubility, drug release, diffusivity, and eliciting immune response [16]. It can also lead to the enhancement and advancement of efficient directive routes, decrease virulence factor, less side effects, proper targeted drug delivery with better distribution and increased biotransformation of drug as shown in the ▶ **Fig 1**. The designed drug delivery mechanisms are targeted to the specific receptor sites or carry the moderate release of the therapeutic compounds to the specific sites [17]. This requires the ability to overcome the resistance such as opsonisation by the macrophage system. Two approaches by which nanoparticles transports drugs are passive and self-delivery. In passive delivery the incorporation of the drugs into hollow space

▶ **Table 1** Different Types of Nanomaterials used in drug delivery [7].

S. No.	Types	Examples
1	Inorganic-based nanomaterials	Different metal and metal oxide nanomaterials like silver (Ag), gold (Au), aluminum (Al), cadmium (Cd), copper (Cu), iron (Fe), zinc (Zn), and lead (Pb) nanomaterials, whereas examples of metal oxide-based inorganic nanomaterials are zinc oxide (ZnO), copper oxide (CuO), magnesium aluminum oxide ($MgAl_2O_4$), titanium dioxide (TiO_2), cerium oxide (CeO_2), iron oxide (Fe_2O_3), silica (SiO_2), and iron oxide (Fe_3O_4), etc.
2	Organic based nanomaterials	Organic-based nanomaterials are formed from organic materials excluding carbon materials like dendrimers, cyclodextrin, liposome, and micelle.
3	Carbon-based nanomaterials	Graphene, fullerene, single-walled carbon nanotube, multiwalled carbon nanotube, carbon fiber, an activated carbon, and carbon black,
4	Composite-based nanomaterials	Combination of metal-based, metal oxide-based, carbon-based, and/or organic-based nanomaterials, and these nanomaterials have complicated structures like a metal-organic framework like Chitosan nHA and nano-silver particles (nAg), Alginate Nano-silica ($nSiO_2$)

▶ **Fig. 1** Several parameters for the consideration for designing the nanostructures.

of the nanostructure by means of water-resistant effect which further plays an important role in drug release to target sites due to the low consistency of medicament present in hydrophobic region. Similarly, self -delivery shows that delivery of the drug imported on the nanocarrier to target location. The duration of drug release plays critical role as the drug can dissociate anytime from carrier leading to inappropriate site. So, nano-based drug delivery mechanism leads to the significant approach in treatment of cancer in recent times [18–21].

Synthesis of nanomaterials

Nanomaterial is synthesised mainly by two approaches classified as constructive and destructive techniques. As seen in ▶ **Fig 2** [22, 23], Constructive technique is also known as the bottom-up approaches that depicts the formation of nanomaterials from atom and crystals in sequential manner. Several examples of bottom-up techniques for production of nanomaterials are depolymerisation, chemical solution deposition, and biosynthesis [22]. Destructive technique is known as top-down approaches, defines the decrease in particle size of a mass substance to nano-scale. Examples include mechanical machining, electroplating, nanolithography, thermal decomposition, along with physical vapour deposition are techniques involved in synthesis of nanoparticles [23–25].

Characteristics of nanoparticles

The potential and applications of nanoparticles is greatly influenced by the characteristics they possess. Nanoparticle characterization is determined by various measurement techniques:

Particle size

The novel improvements in the formulation of existing drugs by pharmaceutical companies are driven by an innovative approach of drug delivery to cure diseases. These new formulations will be valuable to patients, and they will also create an influential market force to drive the development of even more upgraded delivery methods. The dimension and distribution of the nanoparticles are mostly calculated with the help of electron microscopy [26]. The toxicity, distribution, and targeting delivery are mostly dependent on particle size. The particle size is inversely proportional to the ratio of surface area and volume of an entity. The closeness of the drug to the surface of the nanoparticles will determine the proximity of drug release to the target site [27]. The evaluation of particulates and units is done by examining the pictures of scanning electron microscopy (SEM) and transmission electron microscopy (TEM), although the bulk samples in fixed stages are estimated with the support of laser diffraction methods. In the fluid phase, small pieces are assessed using photon spectroscopy and centrifugation. In the same manner, the minute pieces in the gaseous phase are measured by scanning mobility particle size (SMPS), which provides exact through rapid value compared to other methods.

External charge of nanoparticles

The surface charge on the nanocarrier determines its ability to interact to the drug of interest. The surface charge along with the distribution stability in mixture were measured a zeta potentiometer, whereas differential mobility analyser (DMA), were utilized to determine the surface charge of nanocarrier in gaseous [28].

Surface area

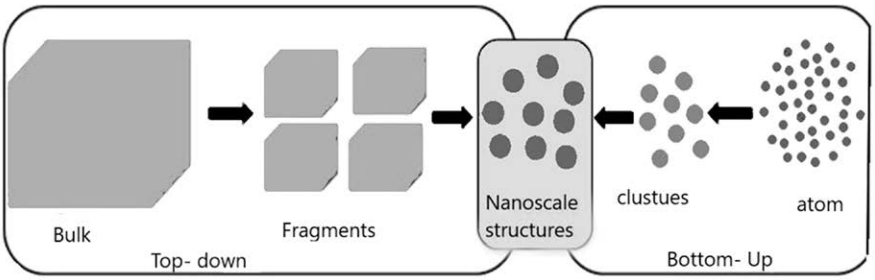
The surface area of the nanoparticles is an important factor as it directly determines the performance of the carrier. It has different shapes like sphere-shaped, plane, cylindrical, narrowed, and irregular forms with crystalline or amorphous surfaces that helps importantly in determining the properties of nanoparticles [29]. Brunauer Emmett–Teller (**BET)** analysis determines the measurement of solid surface area whereas, nuclear magnetic resonance (NMR) spectroscopy and differential mobility analyzer (DMA) are utilized to measure the exterior area of nanocarrier in liquid and the gaseous phase respectively [30].

Constitution

Normally synthetic mixture in the nanoparticles regulates its purity and proper functioning. The presence of undesired elements in nanoparticles may lead to the secondary reactions, reducing their efficiency. The measurement of the composition is usually carried out with the help of electron spectroscopy for chemical analysis (ESCA). There are several techniques that involve atomic emission spectroscopy, ion chromatography and mass spectrometry, are involved in chemical metabolism of the carriers along with wet chemical analysis [31].

Drug Liberation

The drug is liberated from the nanoparticles by depending on various components such as temperature, drug desorption, drug distribution, pH, nanoparticles matrix swelling and erosion [32]. Va-



▶ **Fig. 2** Top-down and Bottom approach for the synthesis of the nanomaterial.

riety of nanoparticles determines the drug liberation process. There are two types of polymeric nanomaterials: nanocapsules and nanospheres. The chemical compound is physically dispersed and released from the nanoparticles by eroding of the template in nanospheres. Nanospheres are a uniform system in which the polymer chains are arranged in uniformity to surfactants in micelle formation [33]. There is a rapid burst of drug release due to the weak interaction to the large surface area of the nanoparticles followed by a sustained release. On the other hand, nanocapsules are a heterogeneous system in which the drug is located inside a reservoir composed of the polymer. In nanocapsules, the diffusion of drug through the polymer is the determining factor of drug delivery due to the release controlled by drug diffusion through the polymeric layer [34]. The ionic interaction between the drug and polymer complexes which inhibit the release of drug from the capsules is avoided by simply adding other auxiliary agents such as polyethylene oxide-propylene oxide. This lowers the interaction resulting into the greater efficiency of the drug- release to target tissues [12, 35].

Targeted drug delivery

The purpose of nanoparticles medicament administration is to bind and administer its constituents to group of cells and reduce drug triggered poisonous effect to healthy tissues. Therefore, to coat specific ligands such as antibodies, peptides, designed proteins or nucleic acid on the surface of the nanoparticles for its delivery to the targeted sites is significant [36]. The small molecules are the most prominent targeting agents due to their advantages such as ease of preparation, solidity, and chemical phenomenon [37]. However, nano-particulates can enter the human body via nebulizing, parental and direct administered intake. Furthermore, lymphatic system distributes and eliminates the particles due to the uptake from the blood stream vein [38]. As fluid regains, many foreign materials and chemicals from the tissues are also picked up and as the fluid is filtered back into the blood, the lymph nodes detect foreign matter passing through and macrophages engulf and clear it from the body [39, 40].

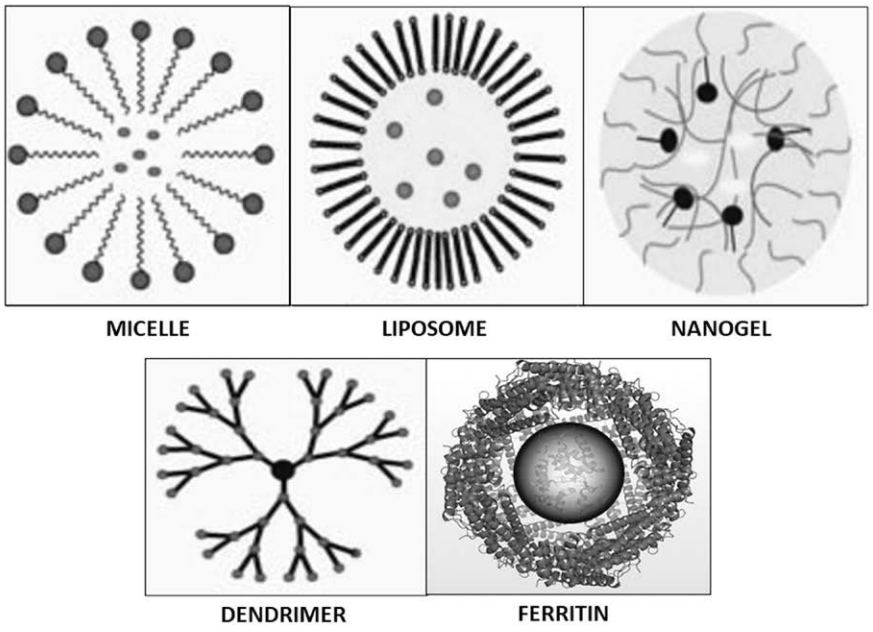
Types of nanostructures used for drug delivery

Organic Nanoparticles

Information of several natural compounds face concerns associated with the clinical trial phases as the use of large-sized materials in drug delivery possesses key challenges of in-vivo instability, poor absorption, solubility, bioavailability, toxic effect of drug and lack of target-specific delivery. Therefore, using a new method of drug delivery with target specificity is an important approach for solving the critical problems faced by natural compounds. The nanoparticles like dendrimers, micelles, liposomes, and ferritin are polymers used in drug delivery system. These types of nanoparticles are biodegradable and non-toxic which makes them suitable for drug delivery without side effects [21, 41]. Some of the organic nanoparticles possess void core known to be as nanocapsules as represented in ▶ **Fig. 3** [42]. The nanoparticles such as micelles and liposomes are sensitive towards electromagnetic emission. Their applications and competency are determined through their carrying capacity, stability and drug delivery system [43]. The organic nanoparticles are broadly used for drug deliverance because of their high efficiency [44].

Carbon based Nanoparticles

In 1991, Carbon based nanoparticles structures were discovered mainly constituted of carbon nanotubes and fullerenes [45]. A carbon nanotube comes with cylindrical framework and is distributed as single walled carbon nanotube (SWCNT) and multi walled carbon nanotube (MWCNT) [46]. A carbon nanotube has distinctive properties like thermal conductivity lengthwise and non-conductivity diagonally of the tube along with mechanical strength, optical properties and electrical conductivity which have biomedical application. Moreover, Carbon nanotubes could be customized chemically into specific groups, molecules, or polymers to justify the properties suited for biological application. For instance, carbon nanotubes are developed for drug application. However, cytotoxicity is an area which has showcased the interest of research because of its inadequacy [47, 48].



▶ **Fig. 3** Organic nanoparticles prominently used for drug delivery.

Fullerenes

Fullerenes are the carbon allotropes having a dimension of approximately 7 m in diameter with sixty carbon atoms structures of hollow cage called as shortened icosahedrons as shown in ▶ **Fig. 4**. Due to the various properties like high strength, heat resistance, electrical conductivity, structure, and electron affinity it has wide commercial applications [49].

Fullerenes are extensively studied nanoparticles because of its uses in medicinal field such as in binding particular antibodies to the system to point resistant bacteria. Few researchers have carried ample amount of study on fullerene toxicity that indicated carbon nanoparticles were most efficient to use for drug administration. Moreover, other carbon-based nanoparticles such as graphene, carbon nanofiber, carbon black, etc have unique properties like large breaking strength, soft, springy, temperature and power conductivity, resistance to UV degradation and due to the mechanical properties, they can be modified to use in delivery system [50].

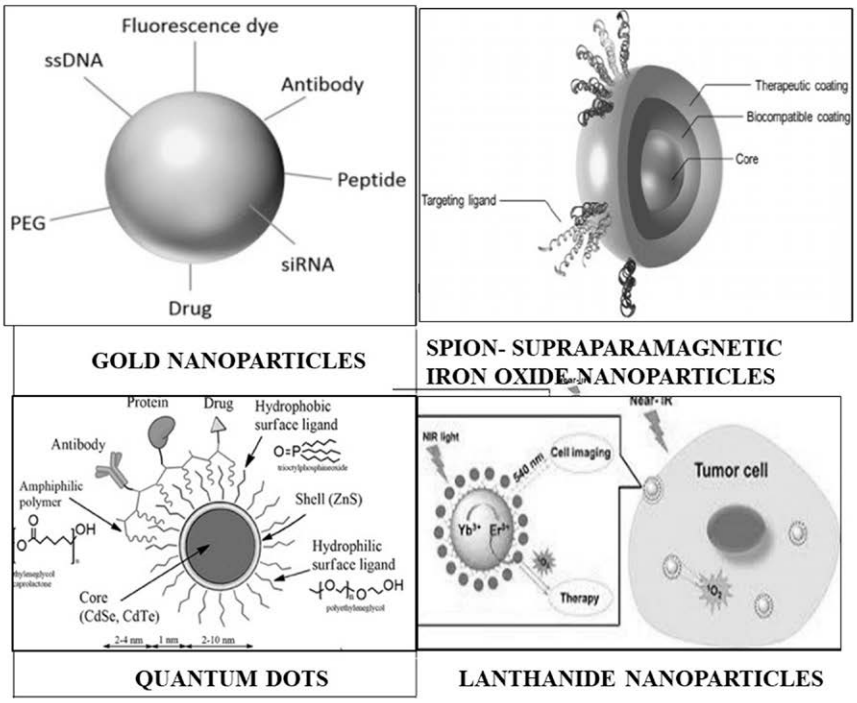
▶ **Fig. 4** Structural representation of Fullerene – an allotrope of carbon.

Inorganic Nanoparticles

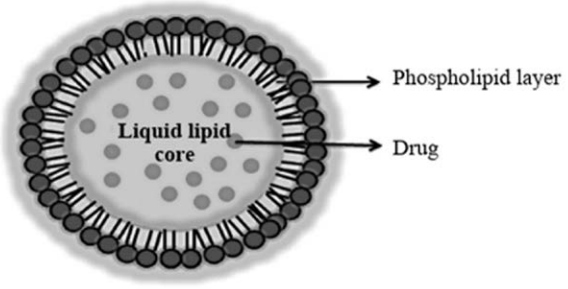
An inorganic nanoparticle includes metal and metal oxide-based nanoparticles. Metal-based nanoparticles consist of several metals like aluminium, cadmium, copper, gold, iron, lead, silver, zinc, etc. which are mostly employed for production of nanoparticles shown in ▶ **Fig 5** [51]. These are synthesized into nano-size particles with the help of either constructive or destructive methods. Moreover, all metals can be synthesized into nanoparticles [52]. They have unique properties like sizes as low as 10 – 100 nm, shapes like spherical and cylindrical, surface properties like surface charge, crystalline and amorphous structure, cross reactivity, and delicacy to environmental factors such as air, moisture, heat and sunlight etc [53]. Similarly, Metal oxides-based nanoparticles are type of nanoparticles which are produced to modify the properties such as increased reactivity and efficiency as compared to metal-based nanoparticles [54] ▶ **Fig. 6**.

Lipid based Nanoparticles

Lipid based nanoparticles consist of lipid and an array containing rigid fat-soluble molecules and similarly their outside core is stabilized by surfactants and emulsifier [55]. Fat containing molecule is normally spherical in shape with a diameter ranging from 10 – 100 nm. These nanoparticles have a wide range of applications es-



▶ **Fig. 5** Examples of Inorganic Nanoparticles.



▶ **Fig. 6** Lipid Nano-particle is used as drug delivery vehicles.

pecially in the biopharmaceutical field as drug carriers, delivery, and RNA release in tumour therapy. Hence, the field of nanotechnology is on verge of exponential growth [56].

Polymeric based Drug Delivery system

Polymeric materials have already revolutionized the world of biomaterials. An efficient amount of work has already been done to integrate polymeric nanomaterial with drug delivery systems due to the promising advantages. Polymeric materials are associated with several characteristics which make polymeric material ideal for biological purposes particularly in medicament administration. Some of the favourable properties of these materials include excellent biocompatibility and biometric behaviour, in addition to being relatively easy to design and prepare. When incorporated into drug delivery systems, polymers have demonstrated their unique capacity to release therapeutic agents to specified target bunch of cells effectively [57].

Quantum Dots

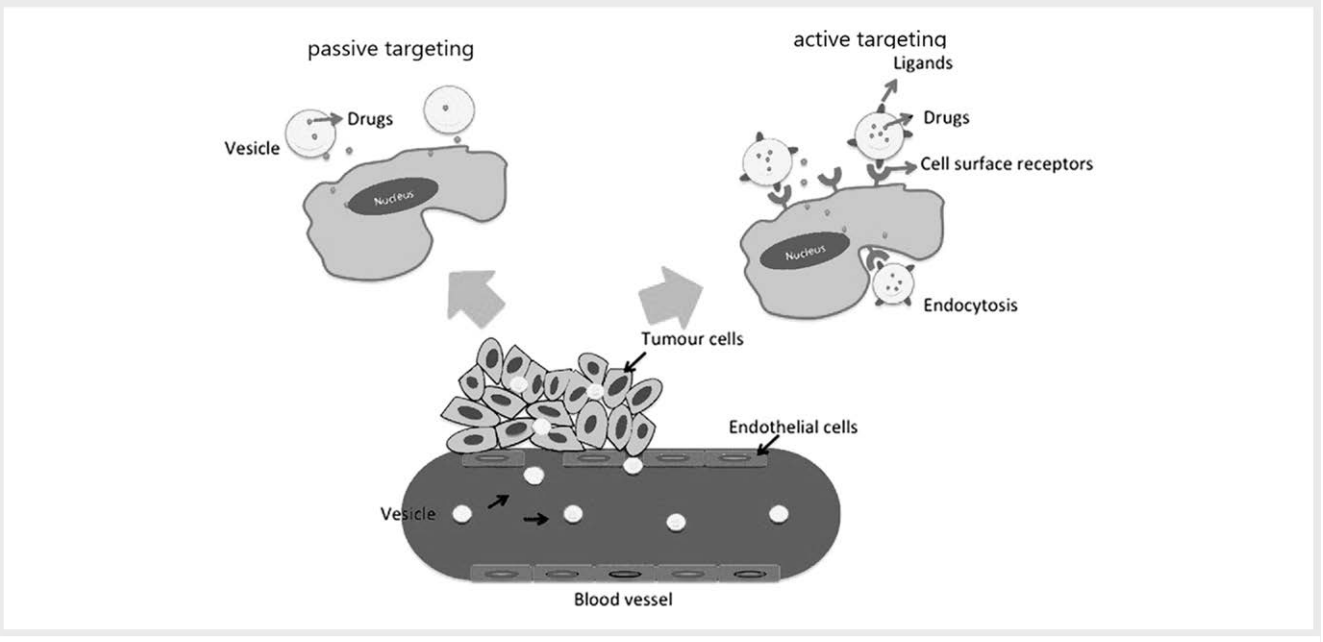
Semiconductors are promising nano-sized crystal with dimension of around 2–10 nm and are used as fluorescent labels [58]. It consists of inorganic core which indicates about the colour emitted and an aqueous organic coated covering to improve optical properties. The biomolecular junction of the quantum dots can be modified according to the targeted biomarkers [59]. Quantum dots centres are produced by cadmium selenide, or cadmium sulphide. Similarly, the outer core is produced on the middle with the highest bandwidth to impart power insulant protection of the florescence characteristics. Their physical size shows great deal of importance and owning to the narrow size, high photo-stability, broad UV excitation and high fluorescence, quantum dots are used for tracking intracellular process for longer duration, to invite bio-imaging and real time monitoring [60]. The applications of quantum dots are in wide areas such as immunoassay, diagnostic tools, DNA hybridisation, fluorescence imaging of tissue, Genetic therapy, marking of cells, remedial tools and as a carrier of agents [61]. Below ▶ **Table 2** represents different kind of nano carrier functional along with its characteristics, advantages, and applications in drug delivery system [62].

Drug Targeting Approaches

Drug targeting strategies are categorised into two approaches namely passive and active targeting as shown in the below ▶ **Fig 7** [63].

▶ **Table 2** Different kind of nano-carrier functional in drug delivery system [63].

Name of Nanoparticle	Characteristics	Advantages	Application	Reference
Liposomes	Biocompatible, offer easy entrapment, phospholipid vesicles	Offer active and passive delivery of various agents such as gene, protein, peptides etc.	Enhanced solubility, Controlled targeted drug delivery	[63]
Carbon nanotubes	Unique strength, electrical properties such as semiconducting conducting, insulating,	Cell specificity, reduced toxicity and increases drug efficacy.	Gene and DNA delivery.	[63]
Fullerenes	Composed of 60 Carbon atoms with dimension around 7 Å in diameter.	Free radical scavenger and stimulate host immune response and production of antibodies.	Diagnostic, Drug transport, Photosensitizer etc.	[63]
Dendrimers	Complex Branching	It has a size of >10 nm therefore can easily penetrate through cells carrying drugs.	Uniform size distribution and controlled drug delivery to the targeted tissues.	[63]
Polymeric nanoparticles	Biocompatible with drug protection and biodegradable.	Effortless design and different structures	Efficient carrier for controlled drug delivery.	[63]



▶ **Fig. 7** Active and Passive approach of drug delivery by nanoparticles to the targeted tumour cells.

Passive Targeting

In passive targeting, the nanocarrier carrying the drug compound doesn't release through body mechanisms such as excretion, phagocytosis, or opsonisation. One such highly used approach of nano-level techniques is nanomedicines which helps in diagnosing, treating, and preventing from further complications by increasing the localisation of drugs to target infected tissues by passive targeting mechanism called as Enhance Permeability and Retention (EPR) effect. The flow of the carrier remains continuous in the blood stream until it binds to the target receptor by properties like size, temperature, pH, or shape. Sudden gathering of the drug at specific areas with leaky vasculature commonly known as Enhanced Permeation and Retention (EPR) effect is based on passive targeting [64]. Nanomedicines should be large enough to resist the speedy blood flow but also small enough to get around easily from the capture by macrophages fixed in the reticule-endothelial system like liver and spleen. Moreover, the hydrophilic surface attained by coating the surface of nanoparticles with polyethylene glycol (PEG) also helps from capture by macrophages. Direct drug injection, catheterization and gathering of chemotherapeutic agents in solid tumor are few common examples of passive targeting [65]. Ligand receptor complex can be greatly selective in this type of targeting by giving the accurate way to targeted site delivery. Moreover, nanoparticles face numerous resistances such as mucosal barriers, non-specific drug accumulation and delivery due to uncontrolled drug release [66].

Active Targeting

In active targeting, ligands like small molecules, antibodies, aptamers and [67] interact with the drugs and delivery system to facilitate the targeting on the surface of the specific cell. Drug targeting via magnetic field and ultrasonic energy are also considered as

active targeting. This approach has significant and wider opportunities and alternatives for drug delivery [68]. The two general important attributes of nano-based drug delivery system are:

Target specificity by nanocarrier

Proper dimension and interaction of ligands provide efficient means of drug delivery along with concentrated non-specific toxicity [69]. The biological ligand present on the surface of nanoparticles interacts with receptors located on the diseased tissue. Association with antibodies will give suitable binding to the target sites and the endocytosis will be improved with properly adjusted binding affinities [70].

Drug released time

To avoid non-specific toxicity, the nanocarrier moving in the blood stream should not remove the drug encapsulated in it and remain attached until it reaches the target site for release. To overcome it, engineered nanocarrier with several layers is synthesized where every layer will have one drug and their release will be determined in conformity of suitable timing in sequential order for combination therapy [71].

Drug Targets in the Body

A target in the living organism to which the entity like ligand or a drug bind resulting into the change in function of body is an important aspect in drug delivery. The main targets in the living system are discussed as below:

Receptor

Receptors are generally located on cell membrane which allows specific drug carrier interaction with cells ingested by means of receptor mediated endocytosis (RME) [72]. The folate receptors in the cancer cells which are overly expressed are useful for drug delivery in cancer including malignancies in lung, brain, ovary, and breast [73]. Moreover, peptide receptor is expressed in high amount in some tumor cells which results into the conjugation of a peptide to drug carriers, thus allowing precise targeting of cytotoxic substance with decent interaction with the receptors [74].

Lipids

Lipids located on the cell membrane are emerging as novel approach as drug targets. Signal transduction mechanisms are affected inducing apoptosis due to the interaction of phospholipids with cell membrane results into altering the composition, membrane permeability and flexibility of the lipid components [75].

Proteins/Antigens

The proteins/antigens are located on cell surface and expression of various proteins/antigens on cell surface shows significance in biochemical activity of cells which can be interpreted by using monoclonal antibodies against these proteins/antigens [76]. In drug targeting, tumor specific antigen can be used on all cells located in the tumor and similarly on tumor cells itself [77]. The growth factor known as erythroblastic oncogene B (erbB2) is over expressed on tumor cell surface in 20–30 % human breast adenocarcinomas [78]. It is used for immunotherapy with liposomal doxorubicin formulation attached to anti-growth factor antibody. Moreover, the growth factor shows efficient accessibility, consistent distribution on the infected cell with low expression on healthy cells [79].

Applications

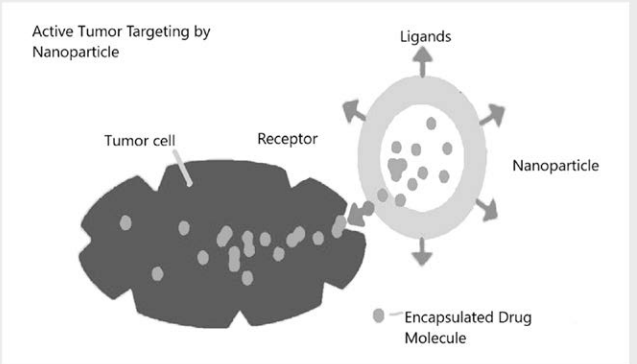
Cancer treatment

The most widely recommended therapies offered to cancer patients typically involve chemotherapy, radiation and/or surgery [80]. However, these options are associated with several limitations for example chemotherapeutic agents, while highly effective in their ability to kill rapidly dividing cancer cells, are associated with severe cytotoxic effects to normal cells. Due to these challenges, nanotechnology-based targeted drug delivery systems have been widely investigated for their potential to not only reduce the adverse effects associated with traditional antineoplastic drugs, but also provide enhanced therapeutic efficacy. The ▶ **Fig. 8** depicts the active targeted drug delivering by the nanoparticles to inhibit the effect of active tumor [81–83].

Among the various nanotechnology-based systems that have been investigated; polymeric nanocarrier have attracted a considerable amount of attention. Scientists have successfully manipulated the core-shell structure of polymeric nanocarrier to both encapsulate and conjugate drugs to this core [84]. As well as providing a protective barrier between healthy tissues and the encapsulated drug, polymeric nanocarrier have improved drug pharmacokinetics and enhanced the accumulation of encapsulated drugs directly into tumours [85].

CNS Disorders

The blood brain barrier (BBB) acts as a resistant which restrains and limits the passage of substances into the brain. While BBB serves to protect the brain against invading pathogens and potential neurotoxins, it also significantly limits the passage of therapeutic agents into the brain to treat Central Nervous System (CNS) conditions. Several kinds of nanoparticle carriers are investigated to conquer these challenges, some of which include metallic, polymeric, lipid and targeted nanoparticles carriers [86]. In comparison to metallic nanoparticles, polymeric nanoparticles are soft, more flexible, and less dense, allowing for these particles to be more malle-



▶ **Fig. 8** Active tumor targeting by Nanoparticle drug delivery.

able for therapeutic drug encapsulation [87]. Various properties of polymeric nanoparticles, such as their dimension, external charge with aspect ratio could be altered to meet the demand of broad spectrum of drugs [88]. Polymeric nanoparticles undergo a process called endocytosis, which involves the engulfment of the nanoparticles by the accepting cell's membrane to cross the blood brain barrier (BBB) [89]. Several studies have also investigated different methods, such as the addition of endogenous substances to functionalize the polymeric nanocarrier surface to further enhance the site-specific delivery of encapsulated drugs into the brain [90].

HIV and AIDs treatment

Nanoparticles which transport antiretroviral drugs to the targeted sites are emerging as promising tools in treatment [91]. Nanoparticulate could be augmented with vaccines to thwart HIV infections more effectively. To achieve it, a mixture of various drugs which is commonly called as Highly Active Antiretroviral Therapy (HAART) can be utilized [92]. Nano-biotechnology plays significant role in drug delivery to the targeted sites in the body and improves flexibility. Antiretroviral drugs, when taken orally, should traverse the epithelial resistance. Nanoparticles via endocytosis/phagocytosis efficiently traverse Blood Brain Barrier (BBB) and many studies have been reported depicting efficient release of anti HIV medication [93].

Future Prospects

Nanomedicines are a current fascinating field of exploration to detect harmful diseases along with providing the cure to it by following proper parameters. The design of Nano-based drug delivery system requires assistance from various fields of people like mathematicians, biologist, chemists, and medical scientists. In near future, detailed tracing and analysis is required in integrity, surface characteristics, bio-distribution, pharmacokinetics, and immunological effects. Advanced technologies are essential to explore the challenges more efficiently. Also, there should be evaluation framework to analysis the nano-based drug delivery system and animal-based representation should be recognized. The proper targeting, target examination, protection of patient and commercial role of nano-based drug delivery systems should be of beneficial guidance. Moreover, understanding the biological nature and heterogeneity of the target will provide efficient help for synthesis of nanoparticles for the treatment. Finally, more attention should be on the synthesis of a structurally simple and reproducible drug delivery mechanism as it possesses high potential to read the patients. However, regulatory mechanism and safety evaluation of nano-based medicines will be valuable study for the further improvement in the future. The nanomedicines research has now revolutionized the drug delivery approach in human body.

Conclusion

Nanotechnology is a fast-growing interdisciplinary field that has important application in health-based industry. Nano-based drug has prominent application in drug delivery and development of techniques which have formed novel approach and provided opportunities to customized and safe treatment options. Nanotechnology is utilized for drug delivery with the help of nano-carrier for therapy and handling of chronic disease such as cancer, hypertension, HIV, and diabetes. Drug loaded nanomaterials have become one of the most important aspects in medicine due to various advantages of nanoparticles in drug administration such as drug targeting, controlled drug release, protection of therapeutic payload and improved bioavailability. Development of new drug delivery systems is providing advantage for pharmaceutical sectors as well.

Credit authorship contribution statement

Aditya Kate: Conceptualization, Investigation, Review of literature, Editing, Correction and Writing – Original draft. Mohit Mishra: Review, Formal analysis, Proof reading, Editing and Supervision. Bhairav Prasad: Proof Reading. Jaya Pandey: Final Correction, Critical Revision and Editing. Ragini Dubey: Finishing and Editing Arzoo Sinha: Preparation of figures.

All authors approved the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

[1] Alsehli M. Polymeric nanocarriers as stimuli-responsive systems for targeted tumor (cancer) therapy: Recent advances in drug delivery. S Pharma J 2020; 28: 255–265. doi:10.1016/j.jsps.2020.01.004

[2] Badar A, Pachera S, Ansari AS, Lohiya NK. Nano Based Drug Delivery Systems: Present and Future Prospects. Nano Nanotech J 2019; 2: 19–121

[3] Manzari MT, Shamay Y, Kiguchi H et al., Targeted drug delivery strategies for precision medicines. Nat Rev Mater 2021; 6: 351–370. doi:10.1038/s41578-020-00269-6

[4] Ayub A, Wettig S. An Overview of Nanotechnologies for Drug Delivery to the Brain. Pharmaceutics 2022; 14: 224. doi:10.3390/pharmaceutics14020224

[5] Nakamura Y, Mochida A, Choyke PL, Kobayashi H. Nanodrug Delivery: Is the Enhanced Permeability and Retention Effect Sufficient for Curing Cancer ? Bioc. Chem 2016; 27: 2225–2238. doi:10.1021/acs.bioconjchem.6b00437

[6] Fang J. EPR Effect-Based Tumor Targeted Nanomedicine: A Promising Approach for Controlling Cancer. J Pers Med 2022; 12: 95. doi:10.3390/jpm12010095

[7] Majhi KC, Yadav M. Synthesis of inorganic nanomaterials using carbohydrates in Green Sustainable Process for Chemical and Environmental Engineering and Science 2021

[8] Nabipour H, Hu Y. Sustainable drug delivery systems through green nanotechnology. Nanoeng Biomat Adv. Drug Delivery 2020; 61–89. doi:10.1016/b978-0-08-102985-5.00004-8

[9] Bhattacharya T, Soares GAB, Chopra H, Rahman MM, Hasan Z, Swain SS, Cavalu S. Applications of Phyto-Nanotechnology for the Treatment of Neurodegenerative Disorders. Materials 2022; 15: 804. doi:10.3390/ma15030804

[10] Kate A, Sahu LK. Green Catalysis for Chemical Transformation: The Need for the Sustainable development. Cur Res Green Sust Chem 2021; 5: 100248. doi:10.1016/j.crgsc.2021

[11] Sharma PK, Sharma HP, Chakole CM, Pandey J, Chauhan MK. Application of Vitamin E TPGS in ocular therapeutics – Attributes beyond excipient. J Ind Chem Soc 2022; 99: 100387. doi:10.1016/j.jics.2022.100387

[12] Rizvi SAA, Saleh AM. Applications of nanoparticle systems in drug delivery technology. S Pharma J 2018; 26: 64–70. doi:10.1016/j.jsps.2017.10.012

[13] Chowdhury A, Kunjiappan S, Panneerselvam T, Somasundaram B, Bhattacharjee C. Nanotechnology and nanocarrier-based approaches on treatment of degenerative diseases. Int Nano Lett 2017; 7: 91–122. doi:10.1007/s40089-017-0208-0.

[14] Ma X, Williams RO. Polymeric nanomedicines for poorly soluble drugs in oral delivery systems: an update. J Pharma Investig 2018; 48: 61–75. doi:0.1007/s40005-017-0372-2

[15] Farshbaf M, Valizadeh H, Panahi Y, Fatahi Y *et al.* The impact of protein corona on the biological behavior of targeting nanomedicines. Int J Pharma 2022; 614. doi:10.1016/j.ijpharm.2022.121458

[16] Mitchell MJ, Billingsley MM, Haley RM *et al.* Engineering precision nanoparticles for drug delivery. Nat Rev Drug Discov 2021; 101–124. doi:10.1038/s41573-020-0090-8

[17] Salvati A, Poelstra K. Drug Targeting and Nanomedicine: Lessons Learned from Liver Targeting and Opportunities for Drug Innovation. Pharmaceutics 2022; 14: 217. doi:10.3390/pharmaceutics14010217

[18] Attia MF, Anton N, Wallyn J, Omran Z, Vandamme TF. An overview of active and passive targeting strategies to improve the nanocarriers efficiency to tumour sites. J Pharma Pharmaco 2019; 221–224. doi:10.1111/jphp.13098

[19] Blanco E, Shen H, Ferrari M. Principles of nanoparticle design for overcoming biological barriers to drug delivery. Nat Biotech 2015; 33: 941–951. doi:10.1038/nbt.3330

[20] Karimi M, Ghasemi A, Sahandi Z *et al.* Smart micro/nanoparticles in stimulus-responsive drug/gene delivery systems. Chem Soc Rev 2016; 45: 1457–1501. doi:10.1039/c5cs00798d

[21] Patra JK, Das G, Fraceto LF, Campos EVR, Rodriguez-Torres MDP, Acosta-Torres LS, Diaz-Torres LA, Grillo R, Swamy MK, Sharma S, Habtemariam S, Shin HS. Nano based drug delivery systems: recent developments and future prospects. J Nanobiotechnology 2018; 16: 71. doi:10.1186/s12951-018-0392-8.

[22] Abid N, Khan AM, Shujait S *et al.* Synthesis of nanomaterials using various top-down and bottom-up approaches, influencing factors, advantages, and disadvantages: A review. Adv Colloid Inter Sci 2022; 300. doi:10.1016/j.cis.2021.102597

[23] McCarron E, Chambers G. A review of suitable analytical technology for physio-chemical characterisation of nanomaterials in the customs laboratory. Talanta Open 2022; 4: 227. doi:10.1016/j.talo.2021.100069

[24] Behera A. Nanomaterials. Adv Mat 2021; 77–125. doi:10.1007/978-3-030-80359-9_3

[25] Scott SM, Ali Z. Fabrication Methods for Microfluidic Devices: An Overview. Micromachines 2021; 12: 319. doi:10.3390/mi12030319

[26] Ealias AM, Saravanakumar MP. A review on the classification, characterisation, synthesis of nanoparticles and their application. IOP Conference Series: Mat Sci Eng 2017; 263. doi:10.1088/1757-899X/263/3/032019

[27] Anik MI, Hossain MK, Hossain I, Mahfuz AMUB, Rahman MT, Ahmed I. Recent progress of magnetic nanoparticles in biomedical applications: A review. Nano Select 2021; 2: 1146–1186. doi:10.1002/nano.202000162

[28] Jain AK, Thareja S. In vitro and in vivo characterization of pharmaceutical nanocarriers used for drug delivery. Artificial Cells. Nanomed Biotech 2019; 47: 524–539. doi:10.1080/21691401.2018.1561457

[29] Jeevanandam J, Barhoum A, Chan YS, Dufresne A, Danquah MK. Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations. Beilstein, J Nanotech 2018; 9: 1050–1074. doi:10.3762/bjnano.9.98

[30] Raliya R, Chadha TS, Hadad K, Biswas P. Perspective on nanoparticle technology for biomedical use. Curr Pharma Des 2016; 22. doi:10.2174/1381612822666160307151409

[31] Mukherji S, Bharti S, Shukla G, Mukherji S. Synthesis and characterization of size- and shape-controlled silver nanoparticles. Phys Sci Rev 2018. doi:10.1515/psr-2017-0082

[32] Shelma R. Polymeric Nanoparticles for Drug Delivery, A Holistic and Integrated Approach to Lifestyle Diseases. CRC Press; 2022: 319–332

[33] Castro K, De C, Costa JM, Campos MGN. Drug-loaded polymeric nanoparticles: a review. Int J Poly Mat Poly Biomat 2022; 71: 1–13

[34] Rai S, Singh N, Bhattachary S. Concepts on smart nano-based drug delivery system. Recent pat nanotech 2021; 19: 321–330

[35] Bodratti A, Alexandridis P. Formulation of Poloxamers for Drug Delivery. J Funct Biomat 2018; 9: 11–17. doi:10.3390/jfb9010011

[36] Chen L, Hong W, Ren W et al. Recent progress in targeted delivery vectors based on biomimetic nanoparticles. Sig Transduct Target Ther 2021; 6: 225–229. doi:10.1038/s41392-021-00631-2

[37] Ibrahim MA, Abdellatif AA. Applications of nanopharmaceuticals in delivery and targeting. Nanopharmaceuticals: Prin Appl. Springer; Cham: 2021: 1: 73–114

[38] Zhang Z, Jianping YUQ, Wu W. An update on oral drug delivery via intestinal lymphatic transport. Acta Pharmaceutica Sinica 2021; 11: 2449–2468

[39] Senthilkumar N, Sharma PK, Sood N, Bhalla N. Designing magnetic nanoparticles for in vivo applications and understanding their fate inside human body. Coord Chem Rev 2021; 445. doi:10.1016/j.ccr.2021.214082

[40] McGuckin MB, Wang J, Ghanma R *et al.* Nanocrystals as a master key to deliver hydrophobic drugs via multiple administration routes. J Cont Release 2022; 521–525. doi:10.1016/j.jconrel.2022.03.012

[41] Farah D, Umer F, Nainan D. Applications of Nanoparticles in Treatment of Respiratory Disorders. Life and Sci 2022; 3: 8–11

[42] Itani R, Faraj A. siRNA Conjugated Nanoparticles – A Next Generation Strategy to Treat Lung Cancer. Int J Mol Sci 2019; 20: 6088. doi:10.3390/ijms20236088

[43] Yadav K, Pradhan M, Singh D, Singh MR. Targeting autoimmune disorders through metal nanoformulation in overcoming the fences of conventional treatment approaches. Int Trans Autoimmunity 2022; 361–393

[44] Hong S, Dong WC, Hong NK, Chun GP *et al.* Protein-based nanoparticles as drug delivery systems. Pharmaceutics 2020; 12: 604–607

[45] Khan ME. State-of-the-art developments in carbon-based metal nanocomposites as a catalyst: photocatalysis. Nano Adv 3 2021; 7: 1887–1900

[46] Fan Y, Hou Y, Wang M, Zheng J, Hou X. Bioinspired carbon nanotubes-based materials, Materials Advances 2022; 8: 773–779

[47] Simon J, Flahaut E, Golzio M. Overview of Carbon Nanotubes for Biomedical Applications. Materials 2019; 12: 624–628. doi:10.3390/ma12040624

[48] Rathinavel S, Priyadharshini K, Panda D. A review on carbon nanotube: An overview of synthesis, properties, functionalization, characterization, and the application. Mat Sci Eng: B 2021; 268: 664–667. doi:10.1016/j.mseb.2021.115095

[49] Chakole CM, Sahoo PK, Pandey J, Chauhan MK. A green chemistry approach towards synthesizing hydrogel for sustained ocular delivery of brinzolamide: In vitro and ex vivo evaluation. J Ind Chem Soc 2022; 99: 323–336. doi:10.1016/j.jics.2021.100323

[50] Mahender M, Pandey J, Reddy A. Stereoselective Synthesis for Potential Isomers of Ticagrelor Key Starting Material. J Hetero Chem 2019; 56: 2866–2872. doi:10.1002/jhet.3677

[51] Yaqoob AA, Ahmad H, Parveen T, Ahmad A, Oves M, Ismail I, Qari HA, Umar K, Mohamad MMN. Recent Advances in Metal Decorated Nanomaterials and Their Various Biological Applications: A Review. Front Chem 2020; 8: 341–344. doi:10.3389/fchem.2020.00341

[52] Jeyaraj M, Gurunathan S, Qasim M, Kang MH, Kim JH. A Comprehensive Review on the Synthesis, Characterization, and Biomedical Application of Platinum Nanoparticles. Nanomaterials 2019; 9: 1719–1723. doi:10.3390/nano9121719

[53] Irfan I, Ezaz G, Ammara N, Aysha N. Detail review on chemical, physical and green synthesis, classification, characterizations and applications of nanoparticles. Green Chem Lett Rev 2020; 13: 853–856. doi:10.1080/17518253.2020.1802517

[54] Nikolova MP, Chavali MS. Metal Oxide Nanoparticles as Biomedical Materials. Biomimetics 2020; 5: 27–31. doi:10.3390/biomimetics5020027

[55] Fernandes F, Dias-Teixeira M, Delerue-Matos C, Grosso C. Critical Review of Lipid-Based Nanoparticles as Carriers of Neuroprotective Drugs and Extracts. Nanomaterials 2021; 11: 563–566. doi:10.3390/nano11030563

[56] Din FU, Aman W, Ullah I, Qureshi OS *et al.* Effective use of nanocarriers as drug delivery systems for the treatment of selected tumors. Int J Nanomed 2017; 12: 7291–7309. doi:10.2147/IJN.S146315

[57] Singh N, Pandey J. Advances in Henry Reaction: A Versatile Method in Organic Synthesis. Mini Rev Org Chem 2019; 16: 1–12. doi:0.2174/1570193X16666190214150144

[58] Datta R, Jaitawat SS. Nanotechnology – The new frontier of medicine. Med J Armed Forces India 2016; 62: 263–268. doi:10.1016/S0377-1237(06)80016-X

[59] Pamidimarri SD, Velramar B, Madavi T, Pandey S, Ratre YK, Sharma PK, Chauhan S. Quantum Dots: Characteristics and Prospects from Diagnosis to Treatment. Eng Nanomat for Innov Thera Biomed 2022; 5: 175–204

[60] Wagner AM, Knipe JM, Orive G, Peppas NA. Quantum dots in biomedical applications. Acta Biomat 2019; 94: 44–63. doi:10.1016/j.actbio.2019.05.022

[61] Tandale P, Choudhary N, Singh J, Sharma A *et al.* Fluorescent quantum dots: An insight on synthesis and potential biological application as drug carrier in cancer. Biochem Biophys Rep 2021; 26: 230–233. doi:10.1016/j.bbrep.2021.100962

[62] Khanna K. Targeted Delivery of Nanomedicines. ISRN Pharma 2012; 1–9. doi:10.5402/2012/571394

[63] Pablo VV, Mosier NS, Irudayaraj J. Nanoscale Drug Delivery Systems: From Medicine to Agriculture. Front Bioeng Biotech 2020; 8: 79–81. doi:10.3389/fbioe.2020.00079

[64] Ahuja A, Narde GK, Wadi N, Meenakshi DU. Drug Targeting Approaches and Use of Drug Delivery Systems in Management of Cancer. Cur Pharma Des 2021; 27: 4593–4609

[65] Bhatia S. Natural polymer drug delivery systems: Nanoparticles. plants, and algae 2016. doi:10.1007/978-3-319-41129-3

[66] Forest V, Pourchez J. Nano-delivery to the lung-by inhalation or other routes and why nano when micro is largely sufficient? Adv Drug Del Rev 2022; 8: 114–173.

[67] Yoo J, Park C, Yi G, Lee D, Koo H. Active targeting strategies using biological ligands for nanoparticle drug delivery systems. Cancers 2021; 11: 345–349. doi:10.3390/cancers11050640

[68] Kheirkhah P, Denyer S, Bhimani AD et al. Magnetic Drug Targeting: A Novel Treatment for Intramedullary Spinal Cord Tumors. Sci Rep 2018; 8: 11417–11421. doi:10.1038/s41598-018-29736-5

[69] Sarwar H, Khalid M, Basher M, Mia M, Rahman M, Jalal Udhin M. Smart nanocarrier-based drug delivery systems for cancer therapy and toxicity studies: A review. J Adv Res 2019; 15: 1–18. doi:10.1016/j.jare.2018.06.005

[70] Kunjiappan S, Pavadai P, Vellaichamy S *et al.* Surface receptor-mediated targeted drug delivery systems for enhanced cancer treatment: A state-of-the-art review. Drug Devel Res 2021; 82: 309–340

[71] Glassman PM, Hood ED, Ferguson LT *et al.* Red blood cells: The metamorphosis of a neglected carrier into the natural mothership for artificial nanocarriers. Adv Drug Del Rev 2021; 178: 113992–113999

[72] Sahu T, Ratre YK, Chauhan S, Bhaskar LV, Nair MP, Verma HK. Nanotechnology based drug delivery system: Current strategies and emerging therapeutic potential for medical science. J Drug Del Sci Tech 2021; 63: 102487

[73] Pandian SRK, Theivendren P, Ravishankar V *et al.* Emerging Nanomaterials for Cancer Targeting and Drug Delivery, Eng Nanomat Innov Therap Biomed 2022; 7: 343–372

[74] Khan MI, Hossain MI, Hossain MK *et al.* Recent Progress in Nanostructured Smart Drug Delivery Systems for Cancer Therapy: A Review. ACS Appl Bio Mat 2022; 18: 132–151.

[75] Szlasa W, Zendran I et al. Lipid composition of cancer cells membrane. J. Bioeng. Biomemb 2020; 52: 321–342

[76] Yaman S, Chintapula U, Rodriguez E, Ramachandramoorthy H, Nguyen KT. Cell-mediated and cell membrane-coated nanoparticles for drug delivery and cancer therapy. Cancer Drug Resist 2020; 3: 879–911. doi:10.20517/cdr.2020.55

[77] Raj S, Khurana S, Choudhari R, Kesari KK, Kamal MA, Garg N, Kumar D. Specific targeting cancer cells with nanoparticles and drug delivery in cancer therapy. Seminars in cancer biology 2021; 69: 166–177

[78] Russo J. Defining Breast Cancer. The Future of Prevention and Treatment of Breast Cancer 2021; 1–31

[79] Farshad M, Mehdi B, Anvar S, Roghayyeh Vakili-G, Mahmoud Reza J, Mohammad S. A review on liposome-based therapeutic approaches against malignant melanoma. Int J Pharma 2021; 599: 120413–120417. doi:10.1016/j.ijpharm.2021.120413

[80] Krzyszczyk P. The growing role of precision and personalized medicine for cancer treatment. Technology 2018; 6: 79–100. doi:10.1142/S2339547818300020

[81] Ghosh S, Jayaram P, Kabekkodu SP, Satyamoorthy K. Targeted drug delivery in cervical cancer: Current perspectives. Europ J Pharma 2022; 174751–174755

[82] Yadav A, Singh S, Sohi H et al. Advances in Delivery of Chemotherapeutic Agents for Cancer Treatment. AAPA Pharma Sci Tech 2022; 23: 25–41

[83] Eunus A, Shazid S, Torequl M, Ishaq K, Subrata S, Atiqur R, Jamal Uddin S, Manik Chandra S, Shahnawaz R, Niranjan D, Saheem A, Jamil S, Swati T, Siddhartha M, Mubarak M. Targeting cancer cells with nanotherapeutics and nanodiagnostics: Current status and future perspectives. Seminars in Cancer Biology 2021; 69: 52–68. doi:10.1016/j.semcancer.2020.01.011

[84] Arora G, Shrivastava R, Kumar P, Krishnamurthy D, Matharu AS. Recent advances made in the synthesis of small drug molecules for clinical applications: An insight. Curr Res Green Sust Chemi 2021; 4: 120032–120038. doi:10.1016/j.crgsc.2021.100097

[85] Joseph X, Akhil V, Arathi A, Mohanan PV. Nanobiomaterials in support of drug delivery related issues. Mat Sci Eng: B 2022; 279: 115680–115688

[86] Zhang X, Zhou J, Gu Z, Zhang H, Gong Q, Luo K. Advances in nanomedicines for diagnosis of central nervous system disorders. Biomaterials 2021; 269: 120492–120500

[87] Navya PN, Kaphle A, Srinivas SP et al. Current trends and challenges in cancer management and therapy using designer nanomaterials. Nano Convo 2019; 6: 23–17

[88] Patel J, Patel A, Patel M, Vyas G. Introduction to Nanoparticulate Drug Delivery Systems. Pharma Pharmacodyn Nano Drug Del Syst 2022; 3–23

[89] Nelemans L, Leonid G. Drug Delivery with Polymeric Nanocarriers, Cellular Uptake Mechanisms. Materials 2020; 13: 366–370. doi:10.3390/ma13020366

[90] Gauro R, Nandave M, Jain VK et al. Advances in dendrimer- mediated targeted drug delivery to the brain. J Nanopart Res 2021; 23: 76–79

[91] Lembo D, Donalisio M, Civra A, Argenziano M, Cavalli R. Nanomedicine formulations for the delivery of antiviral drugs: a promising solution for the treatment of viral infections. Expert Opinion on Drug Delivery 2018; 15: 93–114

[92] Wei X, Gang Z, Ran D, Nishta K et al. T-Cell-Mimicking Nanoparticles Can Neutralize HIV Infectivity. Adv Mat 2018; 30: 1802233. doi:10.1002/adma.201802233

[93] Wang J, Ni Q, Wang Y, Zhang Y, He H, Gao D, Liang XJ. Nanoscale drug delivery systems for controllable drug behaviours by multi-stage barrier penetration. J Cont Release 2021; 331: 282–295