

A review on the emerging use of targeted therapy by Nanoparticles and Nano medicine

Noor-Ul-Ain¹, Haiqa Ahsan²

¹Department of pharmacy, The University of Faisalabad, Pakistan

²Department of chemistry, Government College University Faisalabad, Pakistan

Corresponding author at: Department of Pharmacy, The University of Faisalabad, Pakistan

Contact: +923367744654, **Email:** ananoorkhan105@gmail.com

Abstract

There are number of innovations have been made in the field of medicine to give the ill patient the best of the treatment. As such the use of nanoparticles has also become an increasing demand because of their remarkable actions on the edge of targeted drug therapy. There are number of disorders that must be treated by the way as a specific treatment for the diseases like cancer in which the main purpose of the formation of these particles is to protect the healthy cells from the harmful effects of the drugs. And this could be only possible by making the drugs as specific in their action so these can only target the cells of interest as the abnormal one. Nano medicines are small particles which when given to the patient cause an improvement in the abnormality by better absorption and better distribution to the cells like abnormal one. So it is need of hour to make such drugs which have remarkable effects on the diseased part of body.

Keywords: Nano medicine, target delivery, cancer, remarkable, abnormality

Introduction of nanoparticles:

A nanoparticle is a small particle that ranges between 1 to 100 nanometres in size. Undetectable by the human eye, nanoparticles can exhibit significantly different physical and chemical properties to their larger material counterparts.

Nanomaterials are particles that have their size in 1-100 nm range at least in one dimension. There are different sources of these particles. For example [1], we can get these particles as engineered particles, as incidental components and via natural sources. There are several forms of nanomaterials.

1. Nanomaterials – They have all their dimensions in 1-100 nm scale.
2. One dimensional nanostructure – one dimension has its size outside the nanoscale.
3. Two-dimensional nanostructures – two of the dimensions are not in nanoscale.
4. Bulk nanostructures – none of the dimensions is in the nanoscale (all are above 100 nm).

The table below shows the size of nanoparticles compared to other structures:

Particle Type	Diameter Size Range
Atoms and small molecules	0.1 nm
Nanoparticles	1 to 100 nm
Fine particles (also called particulate matter - PM _{2.5})	100 to 2,500 nm
Coarse particles (PM ₁₀ , or dust)	2500 to 10,000 nm
Thickness of paper	100,000 nm

The material properties change as their size approaches the atomic scale. This is due to the surface area to volume ratio increasing, resulting in the material's surface atoms dominating the material performance. Owing to their very small size, nanoparticles have a very large surface area to volume ratio when compared to bulk material, such as powders, plate and sheet. This feature enables nanoparticles to possess

unexpected optical, physical and chemical properties, as they are small enough to confine their electrons and produce quantum effects.

For example, copper is considered a soft material, with bulk copper bending when its atoms cluster at the 50nm scale. Consequently, copper nanoparticles smaller than 50nm are considered a very hard material, with drastically different malleability and ductility performance when compared to bulk copper [2]. The change in size can also affect the melting characteristics; gold nanoparticles melt at much lower temperatures (300 °C for 2.5 nm size) than bulk gold (1064 °C). Moreover, absorption of solar radiation is much higher in materials composed of nanoparticles than in thin films of continuous sheets of material.

Bulk Materials:

Bulk materials are particles that have their size above 100 nm in all dimensions. Most of the times, we use this term in order to name a substance that is granular or lumpy and exists in free-flowing form. We use the grain size and grain distribution in characterizing these materials. Moreover, we can explain their properties using the bulk density, moisture content, temperature, etc. There are two forms of these materials as follows:

1. Cohesionless, free-flowing bulk materials
2. Cohesive bulk materials

Bulk materials include the material we use in the construction field; plaster, sand, gravel, cement, etc. Moreover, it includes raw materials that we use for various industries such as ore, slag, salts, etc. In addition to that, this includes powdered materials such as pigments, fillers, granules, pellets, etc.

How to differentiate nanoparticles from matter:

- Nanomaterials are particles that have their size in 1-100 nm range at least in one dimension. We cannot see their particles through the naked eye. Moreover, examples of these materials include nanozymes, titanium dioxide nanoparticles, graphene, etc [2]. Bulk materials are particles that have their size above 100 nm in all dimensions. We can see their particles through the naked eye. The examples of these materials include plaster, sand, gravel, cement, ore, slag, salts, etc. The below infographic presents the difference between nanomaterials and bulk materials in tabular form.

- Nanomaterials are invisible to the naked eye. But the bulk materials, we can see their particles. The difference between nanomaterials and bulk materials is that nanomaterials have their size in 1-100 nm range at least in one dimension whereas bulk materials have their size above 100 nm in all dimensions [3].
- Nanoparticles are usually distinguished from microparticles (1-1000 μm), "fine particles" (sized between 100 and 2500 nm), and "coarse particles" (ranging from 2500 to 10,000 nm), because their smaller size drives very different physical or chemical properties, like colloidal properties and optical or electric properties.
- Being more subject to the brownian motion, they usually do not sediment, like colloidal particles that conversely are usually understood to range from 1 to 1000 nm.
- Being much smaller than the wavelengths of visible light (400-700 nm), nanoparticles cannot be seen with ordinary optical microscopes, requiring the use of electron microscopes or microscopes with laser. For the same reason, dispersions of nanoparticles in transparent media can be transparent, whereas suspensions of larger particles usually scatter some or all visible light incident on them. Nanoparticles also easily pass through common filters, such as common ceramic candles, so that [4] separation from liquids requires special nanofiltration techniques.
- The properties of nanoparticles often differ markedly from those of larger particles of the same substance. Since the typical diameter of an atom is between 0.15 and 0.6 nm, a large fraction of the nanoparticle's material lies within a few atomic diameters from its surface. Therefore, the properties of that surface layer may dominate over those of the bulk material. This effect is particularly strong for nanoparticles dispersed in a medium of different composition since the interactions between the two materials at their interface also becomes significant.

Nanomedicine innovation in medical science:

Nanomedicine is the use of nanotechnology in medicine. Nowadays Nano medicine is used for patients suffering from a wide range of disorders including kidney disease, chronic pain, fungal infection, and many others.

It is a rapidly increasing interdisciplinary field that seeks to develop new and improved methods for screening, diagnosis, and treatments [2]. Begin new and effective nanomedicines need an understanding of how basic building blocks arranged at the Nano scale causes unique and

different features that are not possible with bulk commodities these nanomaterial's are interrelated with biological structure at the scale of molecules, and thus have found wide use of biomedical research and applications. Many different tools exist to characterize and predict nanomaterial interaction with cells and molecules. For confirmation in vitro, nanomaterials are tested in vivo to better understand how their delivery and system contact behavior at the tissue scales. Eventually, researcher aims to use these nanomaterial's to improve the screening, diagnosis, and treatment of disorders, given that the nanomaterial's can be demonstrated to be both safe and effective in clinical trials

- Nanomaterial's can be used in Nano medicine for medical purposes in three different ways: Nano therapy, Nano diagnosis-controlled drug delivery, and regenerative medicine. A new way that combines diagnosis and therapy termed theranostics is emerging and is a promising approach that holds on in the same system both the diagnosis/ imaging agent and the medicine. A new way which combines diagnosis and therapy termed theranostics is emerging and is a promising change in clinical practice by the introduction of novel medicines of both diagnosis and therapy or care, having enabled to address unsatisfied medical wants [4], by combining effective molecules that otherwise could not be used because of their high noxious, increase efficacy and reduce the dose and noxious, exploiting different mechanisms of action.
- This is a result of the inborn properties of nanomaterials that have brought many advantages in the pharmaceuticals and other medical fields developments. Due to their small size, nanomaterials have a high particular area in connection to volume. Accordingly, the particle surface energy is increased, making the nanomaterial much more active. Nanomaterials tend to soak up biomolecules example, lipids proteins, and many others when connected with biological fluids. One of the most important interactions with the living matter reliefs on the serum biomolecule adsorption layer known as "covid" which forms on the top of colloidal nanoparticles. Its mixture depends on the portal of entry into the body and on the particular fluid that the nanoparticles come across. Further dynamic changes can influence the "covid" framework as the nanoparticles cross from one biological section to other.
- Moreover, optical magnetic and electrical properties can change and be accord through electron confinement in nanomaterials. In addition, nanomaterials can be made to have different sizes. Shape, dimensions, chemical mixtures, and surface [5] e, making them react with specific biological targets. A successful biological result can only be gain resorting to careful particle design. As such, a comprehension knowledge of how the nanomaterials interrelated with biological systems are required

- Thus, a piece of great knowledge about how the physicochemical properties of the bio interface influence the biological signaling pathways[12], kinetics, and transport will thus provide analytical rules to the design of nanomaterials.

Nanoparticles used as targeted drug delivery

- Nanoparticles used as drug delivery channels are generally less than 100nm in at least one dimension and made up of different biodegradable materials such as natural or synthetic polymers, metals, or lipids. Nanoparticles are taken up by cells more effectively than larger micro molecules and therefore, could be used as a channel and delivery system. For therapeutic applications, drugs can either be integrated into the matrix of the particles or attached to the particles or attached to the top of the particles. A drug targeting system should be able to control the destiny of a drug entering the biological environment [6]. Nanoparticles with different constitutions and biological properties have been extensively looked into drug and gene delivery applications. An effective approach for achieving systematic drug delivery would be to rationally develop Nano system based on the understanding of their interactivity with the biological environment, target cell population, target cell surface reporters, change in the cell that takes place with the progression of the disease, procedure, and site [11] of drug action, drug retention, multiple drug administration it is also important to understand to hurdles to the drug such as stability of therapeutic agents in the living cell habitat. Reduced drug effectiveness could be due to instability of drug inside the cell, unavailable due to multiple targeting or chemical properties of delivering molecules, alterations in the genetic makeup of cell's top receptors, overexpression of efflux pumps, changes in signaling pathways with the development of disease, or drug degradation [7]. A better understanding of the mechanism of absorption, intracellular trafficking retention, and protection from humilation inside a cell are required for enhancing the efficacy of the encapsulated therapeutic agent.

Future innovation of nanoparticles in the medical field:

In recent years nanoparticles have appears as important players in modern medicine, with application vary from variance agents in medical imaging to carriers for gene delivery into single cells. Nanoparticles have several properties that differentiate them from bulk materials simply by the integrity of their sizes, such as chemical reactivity, energy intake, and biological portability

The benefits of nanoparticles to modern medicine are many more. Indeed, there are some instances where nanoparticles enable analyses and therapies that simply cannot be carried out otherwise [8]. However, nanoparticles also take a unique environment with them and different social challenges, particularly regarding toxicity.

Nanoparticles can be provided notable improvements in traditional biological imaging of cells and tissues using a different microscope as well as in MRI of various body parts. Chemical composition differentiates the nanoparticles used in two different types of techniques. A summary of them is provided in the table [10].

Area	Nanoparticle type	Major in vivo applications	Significant characteristics
Imaging(optical)	Quantum dots	Site-specific imaging in-vivo	Imaging of lymph forks, lung blood artery, and tumors.
Magnetic resonance imaging	Super paramagnetic iron oxide (nanoparticles)	Cancer observation	Enhanced variance for imaging of liver, lymph nodes, and bone marrow.
Drug and heredity characters delivery	Polymer- and liposome-based (nanoparticles)	Cancer treatment	Targeted delivery by surface functionalism. Strategies for soluble water-insoluble drugs, (paclitaxel).
		Neurodegenerative disease treatment	Transport across blood–brain hurdles (egg, by PEG incorporation Therapies for diseases unresponsive to small

Area	Nanoparticle type	Major in vivo applications	Significant characteristics
			molecule drugs (gene treatment).
		HIV/AIDS treatment	Solubilizing water-insoluble drugs
		Ocular disease treatment	Ability to prolong drug residence times within ocular mucus coating or retina
		Respiratory disease treatment	Mitigation of provoking responses in respiratory tract.

Use of nanoparticles in medicine:

The use of engineered nanomaterials (nanoparticles) offers the ability to carry therapeutics to specific sites of a disease, thus reducing the off-target toxicity of many drugs. This is especially true in the use of chemotherapeutics where off-target reactions cause harmful side effects in cancer patients as mentioned above, one of the main uses of nanoparticles in the medical field has been the area of targeted drug delivery. It is a critical condition to deliver a drug to the desired target site in a controlled manner while not causing additional adverse health effects to the patient or cause any injury. We can control the absorption of the drug at the targeted side like cancer Nanoparticles has been present for improved systems in medical imaging for disease diagnosis. Much of the potential for nanomaterials as diagnostic agents comes from their ability to enhance the difference in spectroscopy. In particular, super paramagnetic [9] iron oxide has been shown to enhance magnetic resonance imaging and as an outcome, can aid in the detection of liver disease. Angiogenesis is a key hallmark of cancer and thus its observation would be of importance. Nanoparticles can be used for targeting sites of angiogenesis and variance diagnostic imaging. For example, cyanoacrylate micro bubbles can be conjugated to ligands specific to biomarkers, such as vascular endothelial growth factor receptor and $\alpha\beta 3$ integrin, which are more plentiful with increased angiogenesis. HLS conjugation allows for ultrasound observation of tumor phenotypes and quantification of these biomarkers, as well as, indicating responses to surgery.

References:

1. Guo D, Xie G, Luo J. Mechanical properties of nanoparticles: basics and applications. *Journal of physics D: applied physics*. 2013 Dec 3;47(1):013001.
2. Hajipour MJ, Fromm KM, Ashkarran AA, de Aberasturi DJ, de Larramendi IR, Rojo T, Serpooshan V, Parak WJ, Mahmoudi M. Antibacterial properties of nanoparticles. *Trends in biotechnology*. 2012 Oct 1;30(10):499-511.
3. Kolhatkar AG, Jamison AC, Litvinov D, Willson RC, Lee TR. Tuning the magnetic properties of nanoparticles. *International journal of molecular sciences*. 2013 Aug;14(8):15977-6009.
4. Rivera Gil P, Oberdörster G, Elder A, Puentes V, Parak WJ. Correlating physico-chemical with toxicological properties of nanoparticles: the present and the future. *ACS Nano*. 2010 Oct 26;4(10):5527-31.
5. Shameli K, Ahmad MB, Jazayeri SD, Shabanzadeh P, Sangpour P, Jahangirian H, Gharayebi Y. Investigation of antibacterial properties silver nanoparticles prepared via green method. *Chemistry Central Journal*. 2012 Dec;6(1):1-0.
6. Sun L, Chow LC, Frukhtbeyn SA, Bonevich JE. Preparation and properties of nanoparticles of calcium phosphates with various Ca/P ratios. *Journal of research of the National Institute of Standards and Technology*. 2010 Jul;115(4):243.
7. Li Z, Chai F, Yang L, Luo X, Yang C. Mechanical properties and nanoparticles precipitation behavior of multi-component ultra high strength steel. *Materials & Design*. 2020 Jun 1;191:108637.
8. Sabourian P, Yazdani G, Ashraf SS, Frounchi M, Mashayekhan S, Kiani S, Kakkar A. Effect of Physico-Chemical Properties of Nanoparticles on Their Intracellular Uptake. *International Journal of Molecular Sciences*. 2020 Jan;21(21):8019.
9. Liu Q, Guan J, Qin L, Zhang X, Mao S. Physicochemical properties affecting the fate of nanoparticles in pulmonary drug delivery. *Drug discovery today*. 2020 Jan 1;25(1):150-9.
10. Loza K, Heggen M, Epple M. Synthesis, structure, properties, and applications of bimetallic nanoparticles of noble metals. *Advanced functional materials*. 2020 May;30(21):1909260.
11. Jameel MS, Aziz AA, Dheyab MA. Comparative analysis of platinum nanoparticles synthesized using sonochemical-assisted and conventional green methods. *Nano-Structures & Nano-Objects*. 2020 Jul 1;23:100484.
12. Gharpure S, Akash A, Ankamwar B. A review on antimicrobial properties of metal nanoparticles. *Journal of nanoscience and nanotechnology*. 2020 Jun 1;20(6):3303-39.