

Applications of Nanotechnology In Diagnosis and Treatment of Disorders: A Review

Priyanka¹, Roopesh Sharma², Vancha Harish¹, Ruchi Sharma^{1*}

¹School of Pharmaceutical Sciences, Faculty of Applied Medical Sciences, Lovely Professional University, Phagwara – 144411, Punjab, India

²Faculty of Pharmaceutical Sciences, Pt. J.R.Government Polytechnic College, Hoshiarpur-146001, Punjab, India

***Corresponding Author**, Email: sharmamph.ruchi@gmail.com

Abstract

Nanotechnology in itself is a vast term covering the different aspects of science like biology, chemistry, physics etc. When it gets associated with the applications in the medical field, then it is commonly known as the Nanomedicine. The applications include; gene delivery, detection and diagnosis, probing of DNA structure and tissue engineering. For the interaction with cells and tissues, different types of devices are been designed, these crafted Nanomachinery can further helps to understand the cellular mechanisms in an improved manner in living organisms. There are many imperative applications of nanotechnology in the medicinal field with regards to the targeted drug delivery, improved bioavailability, and delivery of sustain released drugs. Therefore, presented review provides the role of nano science in formulation of drug delivery systems, detection and treatment of various disorders.

Introduction

Nanotechnology

Nanotechnology can be defined as a science that deals with the nanoparticles ranging from 1-100 nanometers. It has enormous potential to attain benefits for the diagnosis and treatment of various diseases, improvement of medication etc. It provides greater opportunities to the scientists, researchers and clinicians of national and international origin to share their ideas, notions as per their specializations in their respective fields. Although, nanotechnology is been implemented for its application in various fields, but it has been observed to emerge prominently for the diagnosis and treatment of various disorders in the field of healthcare[1].

This technique is finding its application worldwide with numerous advancements in design and development of smart drug delivery systems for the diagnosis and treatment of diverse health issues [2].

Applications of nanotechnology

It has been reported that generally the Nano-ranged drug delivery systems becomes the most efficient, when delivered through the intravenous route because of their small size. In the medical field, nanotechnology plays a vital role in diagnosis and treatment of diseases by been utilized in fluorescent markers for symptomatic and screening purposes [3]. Furthermore, Medical Imaging is another application of nanotechnology and can be defined as a technique used to create images of human body. For magnetic resonance imaging (MRI) some simple nanoparticles can act as contrast enhancement probes. The various medical imaging procedures includes-

- 1) Magnetic Resonance Imaging
- 2) Positron Emission Tomography
- 3) Computed Tomography

Nanomedicine: Advancements and applications

The extensive researches related to nanomedicine has brought greater health benefits and many advancements in the diagnostic field. The current knowledge of nanotechnology comes from the amalgam of different aspects of sciences like chemistry, biology, physics etc. Implementation of which includes applications such as the destruction of the lethal cancerous cells with high efficiency. The results depict affirmative approach to establish the therapy as an alternative to traditional cancer treatment, because of targeted drug delivery [4-5]. With the enormous applications related to the field of medicine, the emergence of nanoscience and nanotechnology has changed the landscape of pharmaceutical industry. Nanotechnology, implemented in formulating a variety of drug delivery systems such as nanosuspensions, nanoemulsions and nanomicelles are been already proven to enhance the therapeutic effects of the medication as compared to the traditional approach [6].

Nano delivery systems are the advanced systems involving diagnostic tools which act as a site specific targeted systems in a controlled manner. Nano- based formulations provides

a number of benefits for the treatment of certain chronic diseases by site targeting and further helps in precise delivery of medicines. Here, Nanomedicine is one of the emerging field as it provides the utilization of nanodimensional materials or tools such as nanorobots, naosensors that helps in early diagnosis, nanotools [6-7].

The following systems are profoundly been utilized for theranostic approaches:

- a) Gold nanoparticles
- b) Quantum dots
- c) Magnetic Nanoparticles (MNPs)

a) Gold nanoparticles

Gold nanoparticles (AuNPs) are defined as the gold particles having a range of diameter from 1-100 nm. Their use has been found for the prospective of diagnosis and for the therapeutic applications. Furthermore, because of their unique and versatile properties, they are employed in bionanotechnology as well [8]. Gold nanoparticles along with the biomolecular interactions show biomedical applications in diagnostics. They find exposure in biomedical field because of their unique properties like chemical stability, easy synthesis, good biocompatibility etc. AuNPs based system provides accurate and precise diagnosis of diseases like genetic disorders, pathogen infection etc. The diagnosis of various diseases is performed by a specialized personal in centralized laboratories [9].

Properties of gold nanoparticles [10]

Gold nanoparticles have a number of properties that is described below :

- The nanoparticles at a specific wavelength shows a phenomenon called surface Plasmon phenomenon that results in the strong scattering of light.
- As gold nanoparticles have unique optical properties, they are used for the techniques like bio-imaging and photonics.
- These are highly electrical and heat conductive.
- The particles are inert particles so are used in a number of techniques.
- These are non-toxic, biocompatible and show high dispersity

Applications of Gold Nanoparticles

The applications of gold nanoparticles are increasing on a rapid scale because of their unique properties and are explained below and presented in Table 1.

1. Diagnosis of cancer

AuNPs are used in diagnosis of cancer with the help of nanodevices that are capable of selective targeting (9). The diagnosis of cancer in beginning stages is of great importance because, the survival of cancer patients depends upon the early diagnosis. The gold nanoparticles are employed with different methods and techniques for the diagnosis of cancer eg. Molecular imaging, illumination microscopy, ELISA etc. Also the drug delivery with targeted nanoparticles is likely to provide safe and effective therapies for cancer. Nanomedicine is playing a major role in early detection and treatment of cancer cells. Furthermore, Gold is also being used to access biodistribution and cellular uptake of nanoparticles. The assessment of biodistribution helps in accessing suitable in-vivo and in-vitro toxicity of nanoparticles [11-12].

2. Electronics

Gold nanoparticles are used as conductors, as they have high conductivity which helps in improving the electrochemical sensors, with a clinical importance from DNA groupings and proteins. As gold nanoparticles are widely used in electrochemistry, its properties are controlled through size and molecule partition. Gold nanoparticles also help in the reversing of redox responses. Adding up, gold nanoparticles are also being used to expand the redox surface region due to which immobilization of biomolecules comes in consideration. Even, they are important component in the chip design. Gold nanoparticles at nanoscale are being used to connect resistors, conductors etc [9-10].

3. Photodynamic Therapy

Photodynamic therapy is a prominent therapy for the cancer treatment wherein through the specific wavelength of light the heat generation of nanoparticles and activation of photosensitizer drugs occurs. Due to the surface Plasmon resonance effect, AuNPs are considered for both photo thermal agents and photosensitizer carriers. Photo thermal therapy works with the commencement of photosensitizing agents for the treatment of cancer tumors. Photo thermal therapy has advantages over the conventional methods as it is having a property of deep penetration through the tissues as it helps in the effective treatment of tumors. For the deep penetration, photosensitizing agents should be highly soluble in biocompatible solutions, low toxicity levels and ease in functioning.

Photodynamic therapy has an antitumor activity depends upon the generation of radical oxygen species [11-12].

4. Diagnosis of HIV/AIDS

In spite of research and surveillance made for the cure of Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome, is ruining the mankind with no preventive cure till now. HIV is needed to be diagnosed at the early stage to save the humankind. As approximately 37.9 million people around the world were diagnosed with HIV/AIDS in 2018. From such a vast number, approximately 79% of population came to know their HIV status in the same year. As antiretroviral therapy is an access made globally to end HIV/AIDS, but only 23.3 million people were found have access to this therapy. Meanwhile, advances in the nanotechnology promoted the treatment of HIV/AIDS [13]. One of the advancement made with the help of gold nanoparticles is biobarcode enhancement examination (BCA), that detects HIV-1 p24 antigen at low levels. It gives fast and effective results for the treatment of HIV/AIDS [8-9].

5. Lateral Flow Assays (LFAs)

LFAs are used to quantify and detect the analytes in complex mixtures, where the sample has to be placed on a test device. LFAs are expanding on a large scale because of their low development cost and ease of production. LFAs are mainly used for the detection of antigens and antibodies so are used in hospitals, clinical laboratories etc. A number of samples can be tested by using LFAs for ex. urine, sweat, saliva, serum etc. LFAs are having long half life and their storage is quiet easy as they are adaptable [13-15].

Role of Gold Nanoparticles in Nanobiotechnology [12-16]

Gold is a metal that is used in conjugation with other metals because of its protection from discoloring. Gold nanoparticles are used for the treatment of a number of sicknesses, for example, skin ulcers, measles, smallpox. Presently, the prospective of utilization of gold nanoparticles has changed, as scientists have discovered a new approach in the use of gold nanoparticles that leads to the development of broad spectrum antiviral drugs. These broad spectrum antiviral drugs have a potential to develop a resistance against antimicrobial drugs and can also cure the viruses that are

currently untreatable. Gold nanoparticles are also having a possible range in the applications like diagnostic testing, clinical applications such as gene therapy, early stage tumor detection. The innovation made by the scientists of Switzerland is highly effective in the field of diagnostics i.e. at Sona Nanotech they produced a unique product of gold nanoparticles, synthesizing high quality rod shaped gold nanoparticles with high volumes without the utilization of a toxic chemical cetyltrimethylammonium bromide (CTAB). Gold Nano rods can be used inside the body as these are first to be created without CTAB in the world and are best suited for diagnostic testing.

Table.1 Current applications of AuNPs in cancer diagnosis and their advantages

AuNPs:Size and function	Type of cancer	Techniques/ methods	Advantages
25 nm	Precervical cancer	Illumination microscopy	Powerful tool for detecting cellular and molecular changes
PEG- modified form	Breast cancer	Molecular imaging	Detection of cancer
15 nm	Oral cancer	SERS	Detection of oral cancer
20 nm	Leukemia lymphoma	Spectroscopic method	Early and accurate detection of cancer
30 nm- 150.5 nm	Liver cells	Electrochemical based Immune sensor	Cancer biomarkers

But gold nanoparticles are found to be misused in the field of biomedical because of following reasons-

- They possess similar compound steadiness.
- They show good biocompatibility with other biomaterials.

Collagen gels are being also found to be effective for the treatment, as there is a cross linking of gold nanoparticles with the collagen gels in order to treat the damaged skin or ageing. Collagen gels are used to repair the damaged skin by acting as soft tissue fillers. So, in present time the applications of gold nanoparticles is increasing day by day in the health care as they are effective [14-16].

b) Quantum dots

Quantum dots (QDs) can be defined as man-made nanocrystals of cadmium selenide 200-10,000 that are covered with zinc sulfide. As long as these semiconducting nanoparticles come in contact with the UV light, they emit light of various colors. Quantum dots were first discovered in the early 1980s. These nano carrier possess a variety of properties depending upon their size, shape etc. For eg. as they have electronic properties so can be used as active material in single-electron transistors. Quantum dots are being used by the manufacturing technology for a wide range of applications such as catalysis, electronics, medical imaging, sensing etc. In contrast to imaging and spectroscopic applications the quantum dots are found to be uniform and reproducible. Also the colloidal quantum dots also found a wide range of applications in the field of bioanalytics and biolabelling [10, 17].

Application of quantum dots**Diagnostic applications**

As quantum dots are semiconductor nanocrystals ranging from 2 to 10 nm. The fluorescent properties of quantum dots help in medical imaging and disease focusing. The dots have the property of being aggregating at a specific site because of their porousness property. Semiconductor nanoparticles help in recognizing the oncogens with a precisely outlined arrangement. Even quantum dots help in collection of a number of DNA changes inside the cell and usually bypass the requirement of a biopsy. Hence, they are being used in a number of clinical applications. In contrast to the diagnostic applications of QDs, photo illumination of QDs labeled with DNA brings about the remarkable standardization identification. Even this innovation was used for developing a new method to identify some sub-atomic markers in solitary tissue. The QDs based methodologies are essential as they help in identification of numerous diseases. The detailing provided by the QDs is effective to such an extent that it kills the requirement of biopsy and moreover this is non-obtrusive [16-20].

c) Magnetic Nanoparticles

Nanotechnology is boon to the life sciences and healthcare system as it allows scientists, physicians etc. to work at the molecular levels. There are a number of advantages associated with the use of nanotechnology as it exhibits some unique physicochemical properties. There

is wide range of Nano scale materials being used in biomedical sciences, magnetic nanoparticles (MNPs) acquires a huge consideration because of unique attractive properties. It includes metallic, bimetallic and super paramagnetic iron oxide nanoparticles (SPIONs). SPIONs are preferred at room temperature for the biomedical use, in therapeutics and medical diagnosis requires the use of magnetic nanoparticles. They must have some characteristic properties for in- vivo biomedical work i.e. non- toxic and non- immunogenic. They must possess high magnetization so that their movement in the blood can be controlled by magnetic field. The synthesis of nanoparticles poses a great challenge as a number of factors come in consideration like particle size, shape, size distribution etc. MNPs of smaller size are being used as they have higher effective area but on the other hand utilization of such smaller size nanoparticles poses the problem in biomedical as it turn out to be little typical [21]. The MNPs are classified on the basis of their response to an externally applied magnetic field. There are five types of magnetism- diamagnetism, paramagnetism, ferromagnetism, antiferromagnetism and ferrimagnetism. These particles are being used for the medical imaging purposes, pathology research field, immunoassays etc. These particles exhibit in- vivo and in- vitro applications which attain utmost importance and give the beneficial results. In- vivo applications includes therapeutic applications and drug delivery applications whereas in- vitro applications includes diagnostic, catalysis and medical imaging applications. The most potential application of these magnetic nanoparticles is related to the treatment of tumor growth through and for the controlled transport of pharmaceuticals [21-22]. Inspite of their appropriate immune response, they are also used to mark the particular particles, cell populations, structures and several microorganisms.

Applications

Stimuli- responsive imaging

MNPs are used for the tumor analysis and stimuli responsive imaging helps in the early investigations of the tumor. Multifunctional theranostics integrated with concurrent diagnostics and therapeutics capabilities attracted a lot of attentions in the field of Nanomedicine providing a great opportunity towards the treatment of cancer. There is a boost responsive framework for specificity and exact control that is directly connected to the MR imaging of malignancies [21-23]. The advancements are made in boost responsive framework as it is directly related to the early detection and effective treatment of tumors.

pH responsive imaging

MNPs based drug delivery systems are designed mainly for cancer imaging and anti cancer therapy. To improve the bioavailability and to minimize the adverse effects, pH sensitive core shell magnetic nanoparticles are designed with controlled size and shape. For the better and effective detection of tumor, the MNPs are synthesized with the techniques like homogeneous precipitation, coprecipitation and microemulsion etc. The pH responsive magnetic NPs are widely used for the control release of cytostatic drugs into the tumor site because of their unique physicochemical and biological properties [22-24]. Even, there are some nanoparticles that react to unmistakable pH contrasts needs to put in the pH responsive framework for imaging and treatment of tumor. For progressed theranostics framework and results, MNP- based pH responsive imaging is performed with non- conventional malignancy therapeutics. So, pH- responsive theranostics helps in early detection of tumors and is helpful in safe tumor medication [24].

Enzyme-responsive imaging

In enzyme responsive imaging, catalysts play a significant role as they act as remedial elements for anti cancer medication discharge or acute imaging modalities. Enzyme responsive or catalyst responsive framework is designed by consolidating a specific peptide arrangement to detect or to identify the tumor related protein. This enzyme responsive framework is being used in the drug delivery and intracellular imaging [23-25]. Certain polymers can be designed for cleavage through enzymes for biocatalytic reactions eg. hydrolytic enzymes like lipases, proteases etc and oxidoreductases like peroxidases are being used for pro-drug delivery as they possess the cleavage property for various natural and synthetic polymers. But, many enzyme responsive polymers can be digested through associated enzymes, thus more accurate and precise framework needs to be designed.

Furthermore, Magnetic silica nanoparticles have been introduced in selective drug delivery and intracellular tumor imaging to prevail the multifunctional applications in enzyme-responsive imaging. Silica coated MNPs were covalently bound with drugs like doxorubicin [(Dox) conjugate enzyme- cleavable peptide precursor] which shows highly effective response towards cancer. It shows multiple beneficial applications towards intracellular tumor imaging and in selective drug delivery system but is cytotoxic to other cells [26].

Redox- responsive imaging

Redox- responsive NPs came into existence from the reductive tendency between the intracellular and extracellular cells and also the reductive moiety upregulation in the tumor cells. Actually, the redox properties between intracellular compartments and extracellular matrix are accordingly different. As an advancement redox-responsive NPs with aggregation-induced emission for fluorescence imaging are synthesized by encapsulation method with fluorophore. For an ordinary cell, the fluorescence property of redox- responsive NPs is being tested after reaction with glutathione (GSH). The encapsulation with fluorophore develops high efficiency of the diagnostic system due to increased fluorescence intensity of NPs [26-27].

Thermo- responsive imaging

Thermo- responsive NPs are being explored because of their easy conduct in the minor temperature conditions. There are certain different temperature conditions likewise, hyperthermic conditions in the tumors because of irregular blood stream is boost to thermo-responsive imaging. For an effective thermo-responsive framework, a maintained body temperature (37 degree Celsius) and hoisted temperature (40-42 degree Celsius) is required for tumor detection. As thermo- responsive polymer also plays a vital role in thermo-responsive imaging, polyisopropylacrylamide is being one of the most effective thermo-responsive conduct [26-28].

Diagnostic applications

MNPs are being so effective in the diagnosis of ailments, especially tumor. With the beginning of NMR technique, the clinical diagnosis for the ailments and tumor become easy and effective. It helps in the early detection of the tumor and arises the need for the new pharmaceuticals, magneto pharmaceuticals as shown in Table 2. These drugs are being administered to a patient in order to enhance the image contrast between the normal tissue and the diseased tissue and also to check the level of functioning of different organs and blood flow in the body [29].

Therapeutic applications

MNPs exhibit various therapeutic applications especially in hyperthermia. Superparamagnetic iron oxide flips the direction of magnetization between parallel and

antiparallel orientations. It is a property to destroy the pathological cells by increasing the temperature of tumor tissues. For these magnetic cationic liposomal NPs exhibits an effective temperature increase for the destruction of the pathological cells of tumor. This could be one of the most effective and beneficial advancement in the treatment of a cancer or for the successful cancer therapy. This property allows the heating to a specific area of a cancerous tissue without destroying the normal cells. MNPs also bring the improved delivery of bactericidal compounds and are further used for the treatment for the condition that requires therapeutic interventions to cross blood brain barrier [29-32].

Table.2 Example of molecular targeting strategies combined with Nanoparticles [30,32]

Name of the agent/drug	Target	Application
Tranferrin	Tranferrin receptor	Breast cancer imaging
Monoclonal antibody	Colorectal carcinoma	Colon cancer imaging
Folic acid methotrexate	Folate receptor	Breast cancer imaging
Rituxan (Rituximab)	CD20 antigen (Beta- cell non-Hodgkin lymphoma)	Lymphoma imaging
Annexin V	Phosphatidylserine	Apoptosis imaging
Chrolotoxin	MMP-2	Brain tumor imaging

Summary and Conclusion

Nanotechnology is a multidisciplinary field growing on a rapid scale that applies designing and assembling standards at a sub- atomic level. The innovation of this technology has empowered the advancement of nanoscale gadgets that can be conjugated with a few useful particles at the same time, anticancer medications and imaging tests. The NPs exhibits some unique characteristics due to which they introduce a new prospective. There is assemblance of different sorts of properties related to materials science like conductance of individual particles, ectronic, attractive and optical properties in these particles. A vital optical property of the NPs like AuNPs is the nearness of a confined surface Plasmon reverberation (LSPR), which can be defined as the aggregate swaying of the conductive electrons of the gold molecules that is activated through the connection with an occurrence of electromagnetic wave. AuNPs also exhibits properties to diagnose HIV/AIDS as it keeps on ruining the

humankind with no cure or immunization against it. Similarly, the quantum dots were first discovered to be unsteady and hard to use in arrangement however implanting the dots in the pores of a latex dot made them steadier. The novel properties of this system render these exceedingly luminescent quantum dots perfect fluorophore for wavelength-and-force multiplexing. Among the wide range of nanoscale materials being explored for biomedical utilize, Magnetic nanoparticles (MNPs) have picked up huge consideration because of their characteristic properties, which empower following through the radiology foundation, Magnetic Resonance (MR) imaging.

Inside the most recent two decades, the utilization of attractive smaller scale and nanoparticles in biomedical applications has turn out to be moderately typical. Thermo-responsive nanoparticles have been broadly explored as shrewd medication conveyance transports inferable from their easy stage progress conduct in light of minor temperature changes. The hyperthermic condition in tumors and different ailments coming about because of irregular blood stream and metabolic movement is a potential interior boost. An outside warmth vitality can likewise be exerted to empower thermo- responsiveness by prompting a bigger and more unexpected nearby temperature change. Additionally, the enzyme-responsive imaging also plays a vital role as it is useful in selective drug delivery and intracellular imaging.

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