Recent Advances in Nanoparticles for Enhanced Molecular Diagnostics and Therapeutics

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Abstract: ***For the last decades, a plethora of Nanoparticles (Nps) have been developed and evaluated for their potential application in molecular diagnostic and therapeutic agents. Nanotechnology is a field that is vast in making an impact in all fields of human life. Nanoparticles are microscopic particles that measure 1–100 nm in size, with various applications in the biomedical field. Advances in nanotechnology and medical science have spurred the development of engineered nanoparticles and nanomaterials with particular focus on their applications in molecular diagnosis. The aim of this review is to provide the state of the art of the applications of Nanoparticles (noble metal NPs, especially gold, silver NPs, magnetic NPs, fluorescent NPs, Carbon NPs especially quantum dots) as emerging molecular diagnostics that take advantage of the unique nanoscale properties of nanoparticles (NPs) to increase the sensitivity, detection capabilities of the disease.***

Keywords: Nanoparticles, Medical science, Magnetic NPs and sensitivity

1. Introduction

The word “nano” is used to indicate one billionth of a meter or 10 - 9 [1]. Nanoparticles are microscopic particles that measure 1–100 nm in size, with various shapes (Figure 1 and Figure 2) their applications in the biomedical field.

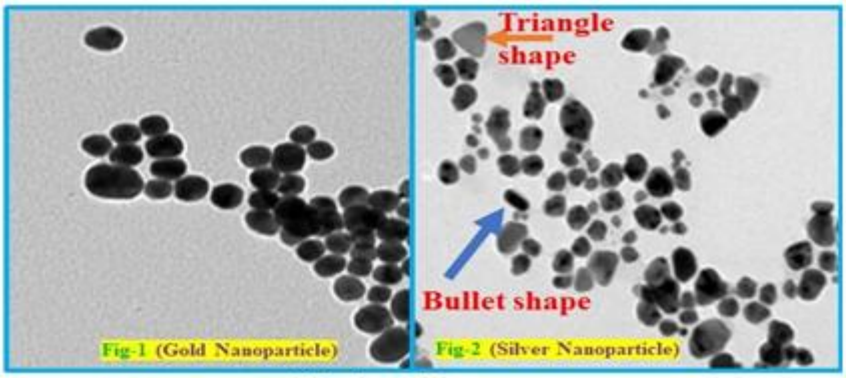

Fig 1 and 2
Gold and Silver nanoparticles with different size and shape

Advances in nanotechnology and medical science have spurred the development of engineered nanoparticles and nanomaterials with particular focus on their applications in molecular diagnosis. Recent advances in nanotechnology have led to the development of various nanoparticle formulations for diagnostics and therapeutic applications. Nanotechnology will improve the sensitivity and integration of analytical methods to yield a more coherent evaluation of life processes. NPs play a prominent role in optical molecular imaging. Nanoparticles possess very high surface to volume ratio. Zinc, Silver, Palladium, Aluminum, Gold, Carbon, Titanium, Copper s and Iron NPs have been routinely used for the synthesis since more than decade [2]. There are many kinds of Nps for the treatment of liver fibrosis [3].

2. Applications

Fluorescent NPs have great potential in targeted theranostics including imaging - guided surgery, immunoassay - based cells, cancer imaging, proteins and bacteria detections, and therapy. Nps shape, composition (chemical integrity), architecture, diverse size and surface properties of the NP systems contribute to their unique properties for the successful delivery of therapeutic precursor [4]. Full potential of nanotechnology as it pertains to disease diagnosis requires the ability to fabricate nanoscale devices and materials with a high degree of precision and accuracy.

Clinical application of molecular technologies to elucidate, diagnose and monitor human diseases is referred to as molecular diagnosis. Gold NPs, silver NPs as well as Cerium oxide NPs (CeO2NPs), are among the different inorganic NPs commonly used for liver fibrosis therapy [5]. Noble metal NPs, especially gold NPs, fluorescent NPs, especially quantum dots, and magnetic NPs, the three main players in the development of probes for biological sensing [6]. Throughout this review, we presented current knowledge on nanoparticles and their applications in molecular diagnosis. Nps - based technologies offer exciting new approaches to disease diagnostics [7]. Optical properties of AuNPs were revealed as early as the Middle Ages. (AuNPs) Gold nanoparticles also referred to as gold colloid, possess excellent physical and optical properties for enhanced capabilities in promising tools for medical applications, such as cost - effective, faster, sensitive, and simpler assays [8] and lack of acute toxicity [9]. Michael Faraday prepared a gold colloid using chemical synthesis method and demonstrated its extraordinary optical properties like initially appear red in the nanoscale and gradually change to dark blue as the particle size increases [10]. The synthesis of AuNPs can be easily reproducible and in common chemical laboratories and surface modification of AuNPs is usually based on the formation of Au–S bonds, which is provides diverse functionalization options and highly stable. Metal NPs show properties like surface plasmon resonance (SPR), which allows them to be used in near - infrared (NIR) - resonant biomedical imaging modalities such as magnetic resonance imaging (MRI), photoacoustic imaging (PAI), fluorescence imaging and X - ray scatter imaging. the plasmon resonance of AuNPs in the visible range can be employed to detect particle structures using dark - field microscopy. The past few years have witnessed a variety of AuNP - based IVD systems for SERS, fluorescent, electrochemical, and colorimetric assays of various analytes ranging from small organic molecules to complex proteins. Human health is under constant threat by various factors, most notably diseases. The AuNP dimers can provide enhanced detection sensitivity than individual AuNPs. AuNPs hold several advantages over other nanomaterials that make them particularly suitable for IVDs [11]. AuNPs are a perfect candidate for colorimetric assays because of their ultrahigh extinction coefficients [12]. *In Vitro Diagnostics (*IVD) s can make clinical diagnosis faster, easier, and less painful to patients. In - In home tests systems no specialist facilities or healthcare professionals are required for the tests and the subsequent data analysis. Tremendous progress has been made in the design of IVD tools using nanomaterials. The plasmon resonance of AuNPs in the visible range can be employed to detect particle structures using dark - field microscopy. Due to the lack of accurate and sensitive biosensors and molecular probes which recognise the distinct molecular features of these diseases.

Electrophoretic particle entrapment system is used to immobilize nanoparticles coated with biological reagents, has been used to develop a highly sensitive immunoassay for detection of single biological molecules at multiple sites with nanometer scale precision include POC [13]. POC involves analytical patient testing activities provided within the healthcare system but performed outside the physical facilities of the clinical laboratories. POC does not require permanent dedicated space but includes kits and instruments, which are either hand carried or transported to the vicinity of the patient for immediate testing at that site. The patients may even conduct the tests.

Recent developments in ‘lab on a chip’ and microfluidics systems with specifically designed nanoscale features enables a few complex diagnostic procedures to be combined into one simple device for point - of - care diagnosis (POC).

Diarrhea is a major cause of severe gastrointestinal illness in the infant especially in many developing countries. In one study characterized EPEC specific aptamers and applied it as an AuNP - based apt sensor for point of care (POC) diagnosis purpose [14].

Acanthamoeba keratitis is an aggressive and rapidly progressing ocular pathology whose main risk factor is the use of contact lenses. An early and differential diagnosis is considered the main factor to prevent the progression and improve the prognosis of the pathology and scientists developed a dual - mode colorimetric - based method for fast, visual, and accurate detection of *Acanthamoeba* using AuNPs [15].

SARS - CoV - 2 and COVID - 19 detection methods developed commercially for rapid and accurate [16]. Currently, cardiovascular, and cerebrovascular diseases are the leading causes of disability and mortality among older adults. Due to the lack of efficient diagnostic is a major challenge in the clinical management of vascular aging and related diseases [17]. Atherosclerosis is a chronic progressive disease, which may result in serious clinical outcomes, such as acute heart events or stroke with high mortality. With the recent developments in nanotechnology, various inorganic NPs with imaging enhancement and non - invasive therapy functions have been studied in the imaging and treatment of atherosclerosis [18].

QDs consist of a semiconductor core encapsulated by another semiconductor shell with a typical diameter of 2–10 nm. QDs (Quantom dots) are a type of semiconductor NPs that can emit fluorescence signals under ultraviolet light (UV) irradiation with a high quantum yield. QDs may be excited by a single excitation wavelength, and broad absorption spectra, allows for them to facilitate multiplexed diagnosis. Based on quantum confinement effects, the wavelength of the emitted light is determined by the size of the QDs. Due to many advantages, many research groups have developed lateral flow immunoassay systems using QDs. Potential applications of QDs in molecular diagnostics can be Cancer, Detection of pathogenic microorganisms, Multiplexed diagnostics, Genotyping Immunoassays and antibody tagging. QDs have been used as possible alternatives to the dyes for tagging viruses and cancer cells. QD probes in immunohistochemistry is considered one of the most important and clinically relevant applications. Measurement of the intensity of fluorescence produced by QDs provides a quantitative method for microbial detection. Bioconjugated QDs provide a new class of biological labels for evaluating biomarkers on intact cells and tissue specimens. Several advances have recently been made using QDs for live cell and in vivo imaging, in which QD - labeled molecules can be tracked and visualized in 3D. A multiplex immunoassay has been developed and used for the simultaneous and sensitive detection of cholera toxin, ricin, shiga - like toxin 1, and *Staphylococcal* enterotoxin B [19].

Carbon - based NPs, such as CNTs, fullerene, graphene, and carbon quantum dots (CQDs) have been widely explored for various applications like biosensing and bioimaging [20]. Carbon NPs are comparatively inexpensive probes that can be easily prepared. Carbon NPs display high contrast against the background, they are advantageous in achieving highly sensitive tests without an additional enhancement strategy [21]. Early and accurate diagnosis of Liver metastasis (LM) is of great importance. Iron oxide NPs, which belong to the ferrimagnetic class of magnetic materials, are used for a wide variety of biomedical and bioengineering application. Superparamagnetic iron oxide NPs (SPION) have been extensively used for diagnostic purposes. SPIONs used clinically for specific magnetic sorting, can be used as a magnetic cell label for *In vivo* cell visualization. The fact that SPIONs coated with different commercially available antibodies can bind to specific cell types opens extensive possibilities for cell tracking *In vivo.*

Due to their high liver uptake, iron oxide NPs have been employed relatively extensively for visualizing primary lesions in the liver, e. g. in case of hepatocellular carcinoma (HCC) as well as liver metastases [22, 23].

Hyaluronic acid - coated iron oxide nanoparticles (HIONPs) for highly sensitive diagnosis of LMs enhance the signal of MRI in tumor metastases [24]. MNP - based microfluidic devices, will help in developing decentralized or 'point of care' testing globally, contributing to affordable healthcare, particularly, for middle - and low - income developing countries [25].

Silver - based NPs have been used for cancer diagnosis and cancer treatments recently [26]. Ag exhibits higher thermal and electrical conductivities, and more efficient in the electron transfer than gold with sharper extinction bands. In the recent days applications of Ag NPs in the fields of biosensor and imaging are prominent [27].

Scientists established a SpyCatcher - modified ferritin NPs platform and these NPs are rapidly drained to lymph nodes and target dendritic cells, especially CD8α+ population., upon subcutaneous immunization [28]. The field of single NP plasmonics has grown enormously. Single nanoparticle plasmonic biosensors are efficient in label - free single - molecule detection, as well as in monitoring real - time binding events of even several biomolecules [29]. Anisotropic Janus nanoparticles (JNPs), have been widely investigated for cancer theranostics and due to asymmetric modification of JNPs allows the independent release of multiple drugs [30]. Peripheral arterial disease (PAD) is defined as a slow, progressive disorder and in the recent years' researchers are exploring the use of nanotheranostics for PAD detection and therapy [31].

Nanomaterials and nanotechnologies will greatly enhance the throughput and sensitivity of the identification and screening of potential biomarkers. Numerous diseases, and including cancer originate from mutations and alterations to normal cellular regulatory and metabolic pathways. The marriage of biology and nanofabrication has revolutionized biosensing by integration of biological recognition elements into devices [32]. Perfluorocarbon Nps with 200 nm used to label endothelial progenitor cells taken from human UCB enables their detection by MRI in vivo following administration [33].

Despite large numbers of preclinical studies using NPs as imaging probes, only a few have moved to clinical settings [34]. Detection of proteins is an important part of molecular diagnostics. Uses of protein nanobiochips and nano - barcode technology for detection of proteins. The use of metal nanoparticles as labels represents a promising approach. They exhibit a high stability in signal and new detection schemes that would allow for robustness and low - cost readout in biochips. Nanopore technology for analysis of nucleic acids converts strings of nucleotides directly into electronic signatures [35].

Detection of specific DNA sequences is central to modern molecular diagnostics and in an alternative approach, the transconductance membrane gene for cystic fibrosis was detected using a multiplexed 'amplification refractory mutational system' assay and silver Nps [36].

3. Conclusion

The use of nanoparticles (Nps) for bio - detection has become a new research direction for scientists. Throughout this review, we presented current knowledge on nanoparticles and their applications in molecular diagnosis. Due to the unique spectroscopic properties of NPs, more detection methods can be established to perform a variety of analytical experiments on a single biochip. The development of nanotechnology will bring infinite hope to the development of molecular detection and diagnosis as it can be used to investigate the activities of biomolecules in the body to investigate issues affecting human health.

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Conflict of interests
The authors declare that there is no conflict of interest regarding the publication of this article.

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