Nanotechnology Perceptions
ISSN 1660-6795
www.nano-ntp.com

Nanotechnology and Medical Diagnostics: A Systematic Review

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Nanotechnology has changed many sectors such as medicine and diagnostics by virtue of various properties it has and the numerous uses that they have for it. Thus, application of nanotechnology in medical diagnosis over the last few years demonstrated promising results in increasing the sensitivity, selectivity, and rate of detection of various diseases. This systematic review aims at focusing on the state of the art of nanotechnology for medical diagnostics and its use in various health care facilities. Owing to their small size, large surface area to volume ratio and distinctive physicochemical characteristics, nanoparticles are essential in medical diagnostics. AuNPs owing to their viewable properties, non-toxicity and capability to attach with a variety of specific molecules are extensively used in diagnosing disease indicators including cancer markers, viral proteins and mutations. The plasmonic properties help in the detection of the material through color changes, fluorescence or SERS signals. Quantum dots (QDs), semiconductor nanocrystals with size selectable fluorescence properties, have been developed as multiplex tags mainly because of their small size, their narrow emission bands, and high photostability. They allow for the analysis of multiple proteins or cells in a single run are used most commonly in immuno assays, DNA mapping and in cellular tagging. Catalysts employ magnetic nanoparticles for diagnostics purpose whereby the magnetic features are applied in MRI contrast agents, magnetic particle imaging, and magnetic biosensors. These nanoparticles applied in the early diagnosis of several diseases including cancer, infections, and cardiovascular diseases. Nanotechnology has significantly impacted cancer biomarker detection, autoimmune disorder diagnostics, and infectious disease management. Gold nanoparticles, quantum dots, and magnetic nanoparticles offer innovative solutions for detecting cancer biomarkers, enhancing sensitivity, specificity, and miniaturization. For autoimmune disorders, nanotechnology facilitates precise and accessible detection of autoantibodies, cytokines, and inflammatory markers, overcoming limitations in traditional methods. Thus, in diagnostics of infectious diseases, nanotechnology has changed rapid diagnostic tests for HIV, pulmonary tuberculosis, malaria, and influenza diagnosis with increased sensitiveness, specificity, and compactness. Nevertheless, the solutions have issues like stability, manufacturability, price, approval by health departments, and the ability to penetrate into the healthcare system. Thus, the applied nanotechnology in the field of diagnostics proved to be more sensitive, specific, and rapid for detecting diseases. Further investigations, innovations and partnership among the stakeholders are crucial to unlock the full potential of nanotechnology-based diagnostics in the healthcare delivery system.

Keywords: Nanotechnology, Medical Diagnostics, Nanoparticles, Cancer Biomarkers, Autoimmune Disorders, Infectious Diseases, Rapid Diagnostic Tests.

1. Introduction

A brief appraisal of nanomaterials indicates that this technology has invaded other areas such as medicine and diagnostics through features and uses. As more nanotechnology applications have entered the medical diagnostics arena in the previous several years, it has become possible to enhance the diagnostic parameters of the tests. Nanoparticles and other nanomaterial have been likewise applied for the development of methods and techniques for diagnostics of the various diseases. Thus, the goal of the present systematic review is to identify and analyse the novel developments in the field of nanotechnology-based medical diagnostics and their implementation in different fields of medicine.

Nanoparticles are widely used in the diagnosis of diseases because they are small with large surface area to volume ratio and are in most cases possess peculiar chemical and physical characteristics. The attributes described here allow nanoparticles to bind with biomolecules, work as signal enhancers and allow selective labelling of disease related biomarkers.

AuNPs are widely applied in diagnostic methods because of their optical characteristics, non-toxicity, and versatile terminal modification. This kind of gold nanoparticles can be incorporated with antibodies or nucleic acids to target certain disease biomolecules like tumour necrosis factor, viral coat proteins, and even a mutated gene. The gold nanoparticles are of great utility for detection due to its plasmonic characteristics that facilitates colorimetric or SERS signal.

Semiconductor nanocrystals termed as quantum dots that have tunable fluorescence properties by their size have been introduced in multiplexed bioanalysis in diagnoses.[2, 3] This approach can be made because the emission linewidths of quantum dot conjugates are typically very narrow and the photostability is very high. These properties make them ideal for uses that include immunoassays, DNA sequencing, and especially in cellular imaging.

Magnetic nanoparticles are being considered in medical diagnostics due to their magnetic characteristic uses in MRI contrast agents, magnetic particle imaging, and magnetic biosensors. Magnetic nanoparticles with functional groups can be guided towards the targeting cell or biomarkers of the disease, it means functionalized magnetic nanoparticles can identify diseases such as cancer, sickness causing agents, and cardiovascular diseases quickly and with high sensitivity.

2. Methodology:

A systematic review approach was followed to compile the existing evidence on the use of nanotechnology in medical diagnosis. Comprehensive search strategy was developed and used to identify relevant publications published in peer-reviewed journals. For instance, PubMed, Scopus and web of science were searched for articles using combinations of words related to nanotechnology, nanoparticles, medical diagnostics and disease detection.

The inclusion criteria defined studies that dealt with nanomaterials for diagnostic purposes in different healthcare settings. The search covered only English publications over a period of five years to include recent developments within the field. Data extraction and analysis were conducted for evaluating outcomes, methodologies of the included studies as well as their limitations.

Quality assessment tools such as PRISMA guidelines (figure1) were applied to ensure that this systematic review process is rigorous and transparent. The report provided a synthesis of findings from the studies and identified main themes that demonstrate where we are in terms of nanotechnology-based medical diagnostics right now.

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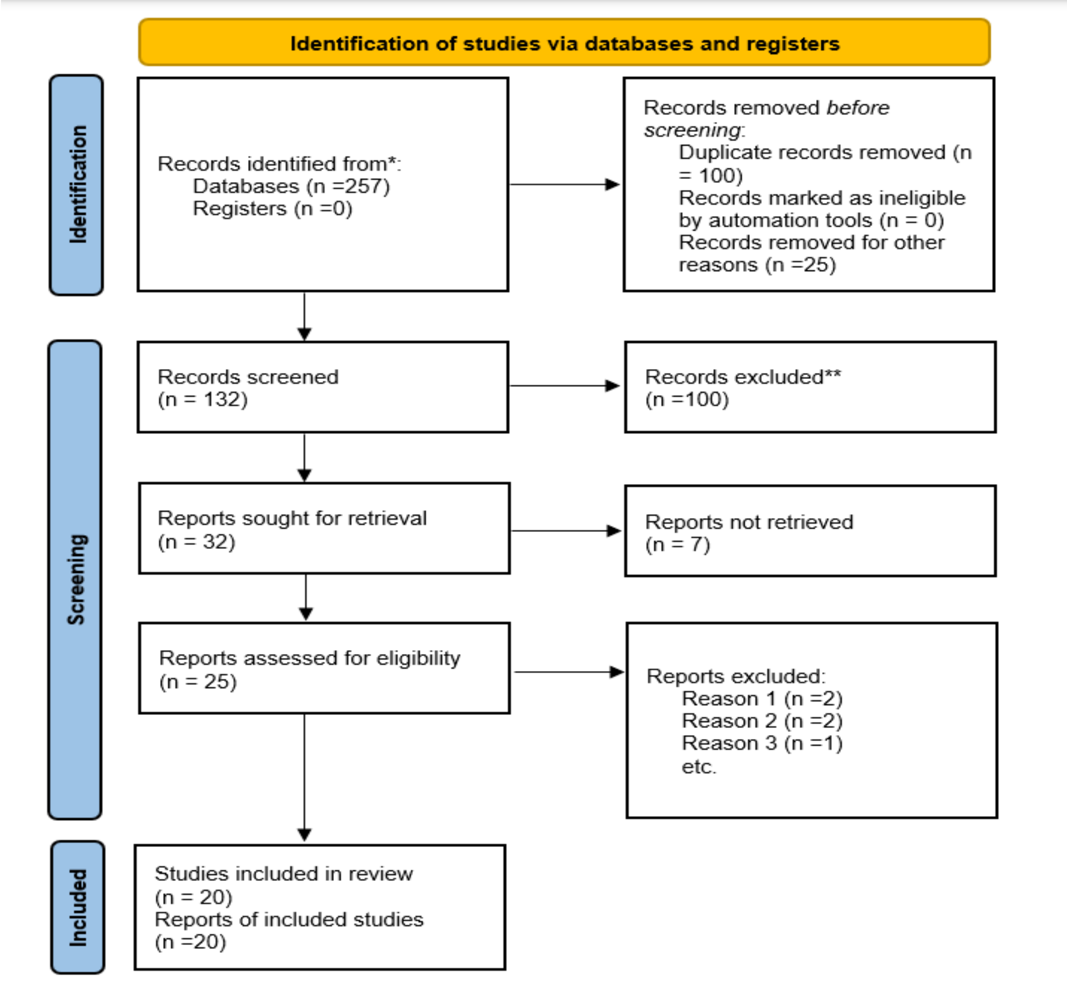

Figure 1 with PRISMA flow chart:

The thematic systematic review will be based on the following four headings:

Detection of Cancer biomarkers and nanotechnology:

Nanotechnology is seen as a game changer in the detection and diagnosis of cancer biomarkers at a very youthful pace. Incorporation of these nanomaterials into diagnostic methods offers a new flavour and future to oncology by improving the sensitivity, specificity and even the size of the devices to be used.

Cancer biomarkers are thus defined as measurable characteristics that allow for cancer identification, its advancement, or the efficiency of the applied treatment. In the past people used ELISA and PCR methods for detection of these biomarkers which suffer from low sensitivity and need help of well-equipped laboratory. These are the problems that nanotechnology provides solutions for.

Gold nanoparticles, quantum dots, and magnetic nanoparticles are some of the nanoparticles that can focus on cancer biomarkers depending on the modifications that are made to them. For instance, metallic gold nanoparticles have been used to design colorimetric probes that can be used in the assessment of the level of tumour markers in the body fluids of patients. These nanoparticles can be conjugated with antibodies or aptamers that will interact with the target biomolecules on cancer cells and this provokes a colour change on interaction with the target molecule. [4].

Another group of nanomaterials that can be used for the detection of biomolecules is quantum dots due to their potential in fluorescence-based detection approaches. Quantum dots are fluorophores or can be conjugated with biomolecules for instance antibodies that can enable the release of fluorescence when bound to cancer biomarkers and has high sensitivity allowing for multiple detection. What makes this multiplication a positive quality of the technology is that it is preferred in cancer detection where a range of biomarkers is usually measured to get a whole picture of cancer status.

Another is through the use of Magnetic nanoparticles which can facilitate the issue by allowing segregation, and enrichment of the biomarkers from the larger, interfering biological matrixes. Ligands can then be added to these nanoparticles that will stick to the target biomarkers. Afterward, an outside magnetic field can be added to select the biomarkers of interest which increases detection sensitivity and shortens sample preparation time [6].

The other emergent techniques constitute nano sensors, which include graphene-based sensors that take advantage of the electrical properties of nanomaterial to determine biomarkers with the lowest concentration. Graphene nano sensors have shown potential in targeting relative, label-free detection of cancer biomarkers making it a giant step towards point-of-care diagnosis.[7]

Nanotechnology and detection of autoimmune disorders

Autoimmune diseases are not simple diseases since the immune system attacks the body's tissues and cells by mistake. Many of these conditions are diagnosed and/or monitored by the identification of autoantibodies to specific intracellular proteins, cytokines, and other inflammatory modulators. Conventional methods of diagnosis present problems, which include reduced sensitivity and specificity and the requirement for large laboratory services. Nanotechnology-based assays can be effectively used as more specific and sensitive for biomarkers for the diagnosis of autoimmune diseases and to monitor disease progression.

Automatic antibodies which are bending towards self-antigen are common biomarkers of numerous autoimmune diseases, for instance, rheumatoid arthritis, systemic lupus erythematosus and type 1 diabetes. For example, gold nanoparticles (AuNPs) have been used in the synthesis of highly sensitive assays of rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPAs) in diagnosing people with RA. These nanoparticles have larger surface area for the conjugation of antibodies that in turn increases the efficiency of binding and the subsequent detection sensitivity as explained next [8]. In the same way, quantum dots (QDs) have been used in multiplex assays to measure multiple autoantibodies at the same time and provide a broad perspective on the patient's condition with high sensitivity and selectivity.[9]

Small proteins called cytokines that are involved in cell signalling also are important in the inflammatory events seen in autoimmune diseases. Nanotechnology has made it possible for assays to be developed that can be able to detect cytokines at very low levels. For instance, magnetic nanoparticles (MNPs) can be functionalized with cytokine-specific antibodies so that cytokines released into the boundary can be extracted. From the application of the external magnetic field, pursue the cause of target cytokines can be quickly and efficiently obtained, enhancing signal to noise ratio and increasing the detection sensitivity[10]. Moreover, graphene-based sensors have been developed due to their such advantages as the highest electrical conductivity as well as the highest surface to volume ratio. Such properties allow for using graphene nano sensors for the real-time determination of cytokines secreted by the patients' cells for a better understanding of the inflammation states in autoimmune diseases [11].

Other biomarkers associated with inflammation include C-reactive protein (CRP) and interleukin-6 (IL-6) which are helpful in the evaluation of the disease activity in Autoimmune Diseases. Molecular biosensors made using nanotechnology are used to measure these markers with proportional degrees of accuracy. For instance, silica nanoparticles conjugated with specific ligands will indicate CRP with higher sensitivity as compared to immunoassays. This also shows that the nanoparticle-based assay method is relatively stable and can be easily reproduced hence can be used in clinical diagnosis. [12].

Nanotechnology and diagnosis of infectious diseases:

The extremity of using nanotechnology-based RDTs in eradicating infectious diseases like HIV AIDS, TB, Malaria, and influenza cannot be overemphasized. The use of these innovations in diagnosis means that the early treatment of these diseases is possible as well as preventing the spread of these diseases among community members especially where the usual resources are limited. On the following, a critical assessment about the current state and difficulties of nanotechnology based RDTs for these diseases are presented.

HIV Diagnosis

Technological advancement in the form of nanotechnology generally has enhanced HIV diagnostic assays based on many factors such as the sensitivity, specificity, and the speed in which the results of these diagnostic assays could be produced. For example, gold nanoparticles (AuNPs) have applied in LFA for the identification of HIV antibodies with high sensitivity (13). These tests are easy to carry along and easily operated implying that they can be used conveniently in the countryside and can be used where there are inadequate resources. Nevertheless, several issues arise when it comes to standardization and repeatability of these assays mainly in different environmental conditions.

Tuberculosis Diagnosis

In terms of diagnostics, the TB diagnostics are still relativized due to the requirement of complex laboratory setting and longer duration. There are recent advancements in nanotechnology techniques to found Mycobacterium tuberculosis antigens with high sensitivity and almost rapid ways, for example using magnetic nanoparticles. Such approaches allow for the samples to be processed and tested quickly at the time of patient encounter, which is critical in breaking the chain of transmission of TB. However, to other tests, they can be too expensive to run and the implementation calls for technical help which is hard to come by in low-income areas.

Malaria Diagnosis

Diagnostics in malaria in particular and POC platforms in general have also been enhanced with nanotechnology; quantum dots and nanowire-based sensors. These technologies are used in identification of Plasmodium species with high sensitivity at low parasitic loads (15). One of the vital benefits of these nanotechnology-based RDTs is that they quantify results, which remain vital in the management and monitoring of diseases. However, the issue of production and selling of these tests is limited by legal frameworks as well as economic analysis of costs and returns.

Influenza Diagnosis

Diagnostics of influenza have also benefited from nanotechnology with the availability of assays that involves the use of carbon-nanotubes and gold-nanoparticles, for the identification of viral antigens and RNA segments respectively (16). They are high throughput as well as fast, which are essential characteristics in the diagnosis of flu and subsequent administration of antiviral therapy as well as preventing the spread of flu epidemics. However, there are some barriers that hamper the way to the wide use of nanotechnology-based influenza diagnostics, namely, scalability, cost, and implementation into the current healthcare systems.

Challenges and Future Directions

However, this and other promising works reveal several issues that need to be solved for the broader practical implementation of nanotechnology-based RDTs. Others are obtaining low cost of production, compliance to set legislation, and yielding uniform efficiency in various environments. Also, there is a necessity for further clinical testing and implementation of these technologies to improve their effectiveness.

Rapid diagnostic tests and possibilities in HIV, TB, malaria, influenza, and many other diseases using nanotechnology. These are distinct advantages with regard to sensitivity, specificity, and transportability, which can prove critical when it comes to treating the diseases quickly and efficaciously. Thus, some obstacles concerning the cost, approval, as well as application in working processes, are still essential to overcome in order to harness the advantages of these emergent diagnostics.

Nanotechnology and detection of viral antigens:

The use of nanotechnology in diagnosis involves the identification of viral antigens; this has been seen to provide great sensitivity, specificity and relatively shorter time for producing results. This technology appears to revolutionize the approaches for viral diagnostics especially in the context of infectious diseases such as HIV, influenza, and emerging novel coronavirus; SARS-CoV-2. Nevertheless, its use is not devoid of problems and there are certain questions of practical application that will have to be answered to widely implement it. The following is an evaluation of the existing state of nanotechnology associated with detection of viral antigens.

Advantages

Enhanced Sensitivity and Specificity: The selected nanomaterials are gold nanoparticles (AuNPs), quantum dots (QDs), and carbon nanotubes and they possess optical, electrical and magnetic characteristics. These properties allow one to detect a virus at an early stage and when the amount of antigens in blood is very low. Frequencies of gold nanoparticles can also be designed to be colour changing on binding with antigens and hence confirming the presence of virus by simple colour observations (17). Quantum dots are very fluorescent and can be employed for fluorescent based detection, thus multiplex detection technique can be used to detect multiple viral antigens at once. (18).

Nanotechnology based assays have fast turnaround time that are a fraction of the time needed for traditional methods such as polymerase chain reaction (PCR) and enzyme-linked immunosorbent assay (ELISA) which take days. Such quick detection is very important when there is an outbreak, helping to immediately isolate and treat infected persons hence reducing disease spread.

Portability and ease of use: Many nanotechnology-based diagnostic tools are made in portable designs that are simple to use making them suitable for point-of-care testing in resource-limited settings. In this respect, lateral flow assays (LFAs) incorporating nanoparticles function like pregnancy tests and require no special training to be used. (19).

Problems:
Stability and Shelf Life: Nanomaterials could be temperature- and humidity-sensitive, hence affecting their stability and shelf life. This, therefore, means that for the broad acceptance of these diagnostic tools in low-resource settings, in particular, the reliability of the device over time and under different storage conditions should be ensured.

Manufacturing and Scalability: Producing nanomaterial-based diagnostics to scale remains a challenge. Standardization and optimization of the manufacturing processes are warranted to ensure consistency and reproducibility. Moreover, the production cost has to be low enough so that, compared to conventional diagnostic techniques, it will be within reach for end users [21].

Regulatory and Validation Barriers: Before entering into clinical settings, new technologies for diagnosis have to go through a rather long and tedious process of acquiring regulatory approval. That basically means that, at the clinical level, precise validation has to be done in nanotechnology-based assays, proving reliability in results, sensitivity, and specificity. That could prove to be very resource-intensive, time-consuming, and thus delay the usability associated with such innovative tools. (22).

Integration into health-care systems: Nanotechnology-based diagnostics will mandate education of health personnel and updating of diagnostic workflows for successful integration into health-care systems. Nanotechnology requires investments in education and infrastructure, which involves additional investments that resource-limited health care systems cannot afford.

Basically, nanotechnology-based viral antigen detection has numerous benefits in terms of improved sensitivity, quick results, and user-friendliness; hence, it has huge potential to revolutionize viral diagnostics. Such technologies realize their full potential only when the problems associated with stability, manufacturing, scalability, regulatory approval, and integration into health care are solved. Hence, continuous research and development, coupled with desires from all stakeholders, is needed to make nanotechnology-based diagnostics one of the cornerstones in the fight against viral infections.

3. Conclusion

To conclude, it is observed that nanotechnology has essentially improved medical diagnostics in terms of sensitivity, specificity, and speed of detection. Applications take within the gamut of diseases like cancer, autoimmune disorders, and infectious diseases: HIV, TB, malaria, and influenza. Notwithstanding this promising development in the area, challenges such as stability, scalability of the manufacturing process, and regulatory issues still remain to be conquered. Much research, development, and stakeholder collaboration need to be done if this transformative power of diagnostics based on nanotechnology is to be taken to its full potential in healthcare.

All the authors have significantly contributed.

There is no external financial aid:

There is no conflict of interest.

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