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# A Review on Nanoparticles-Based Biosensors: Bridging Innovation, Medical, and Safety Challenges

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**Abstract**

One of the most revolutionary scientific disciplines of the twenty-first century is nanotechnology, which presents special chances for the creation of novel materials and nanoscale gadgets. Because of their remarkable physicochemical characteristics, nanoparticle-based biosensors mark a significant breakthrough in diagnostic, biomedical, food safety, and environmental applications. The main kinds of nanoparticles utilized in biosensing, such as metal and metal oxide nanoparticles, are highlighted in this study along with information on their production techniques and unique physicochemical characteristics. The fundamental processes of biosensing, including colorimetric, magnetic, and electrochemical methods, are also covered, with a focus on how they might enhance detection limits, stability, and selectivity. Applications include ambient toxin monitoring, glucose monitoring, pathogen detection in food safety, and early illness diagnosis, including Alzheimer's and cancer biomarkers. Notwithstanding their potential, problems with cytotoxicity, genotoxicity, inadequate biocompatibility, and the long-term buildup of nanomaterials in biological systems and the environment still exist. Prospects for the future demand the creation of more robust, biocompatible biomaterials, sophisticated testing techniques to forecast long-term impacts, a better comprehension of biological reactions, and more stringent regulations for the safety of nanotechnology. Overall, if safety and standardization concerns are methodically resolved, nanoparticle-enabled biosensors have the potential to be extremely important in precision medicine, food security, and sustainable environmental monitoring.

**Key words**: Nanotechnology; Nanoparticles; Biosensors; Medical diagnostics; Food safety; Toxicity; Nanomaterial safety.

## 1. Introduction

Nanotechnology is one of the most attractive XXI century technologies. It involves the ability to observe, quantify, manipulate, assemble, and create materials at the nanoscale level, which is frequently between 1 and 100 nm [1]. It allows the transformation or self-assembly of individual atoms, molecules, or molecular clusters into specific configurations to create materials with novel and notably distinct characteristics [2]. The applications of nanotechnology are among the most innovative and promising technology in wide industries including food packaging and safety, medicine, drug delivery, healthcare, cosmetics, chemical industries, energy science, environment management and optoelectronics; these uses are based on the special magnetic, chemical, optical and structural characteristics of nanosized particles that are not showed by bulk substance. [3]. Bulk materials are characterized as particles whose dimensions surpass 100 nm across all axes [4]. In contrast, nanomaterials are categorized as substances possessing at least one external dimension within the size range of approximately 1-100 nm [5]. In summary, the primary distinction between nanomaterials and bulk materials lies in the fact that the dominant thermal, mechanical, optical, electrical, and magnetic characteristics of the material exhibit significantly greater variation at the nanoscale compared to the bulk scale [6]. A biosensor is a device that can report the presence or activity of analytes using a biomolecular component providing specificity to the sensor by binding or interacting with the analyte and is able to cause a detectable change in mass, fluorescence, electric charge, or refractive index, and a transducer element, able to transform this interaction into a suitable electronic signal [7]. They are coupled together in one of the four possible ways, such as membrane entrapment, physical adsorption, and covalent bonding. Nanoparticles enhance sensor performance by increasing their high surface area to volume ratio, which allows for more interaction with the target analyte, thereby improving sensitivity. This large surface area also facilitates customization by enabling functionalization with biomolecules for greater selectivity. Their unique electrical and optical properties, along with their ability to enhance catalytic activity and improve electron transport, further boost sensitivity and selectivity [8]. Additionally, nanoparticles can increase the stability of sensors by providing stable electron transport pathways, acting as robust labeling agents for biomolecules, and forming stable composite structures with enhanced overall durability [9]. In the light of these data, this review highlights the major classes of nanoparticles used in biosensing, along with their synthesis methods and distinctive physicochemical properties and their application on medical and food field.

**2. Research Methodology**
This review gathered, examined, and summarized the literature on The nanotechnology and their applications in food and safety and medicine. A comprehensive search was conducted using prominent scientific databases, including ScienceDirect, PubMed, Web of Science, SpringerLink, Wiley Online, Scopus, Science and Google Scholar. Additionally, patent of_ice's such as WIPO, CIPO, and USPTO were consulted to gather all relevant published articles on the disease. The term biosensor ' is frequently used, either alone or in combination with the terms ' nanoparticles, food, diagnostic.' There were no language limitations. The titles, abstracts, and contents of the collected data were used to identify and manipulate them. The bibliographies of selected articles were further screened to uncover additional pertinent research.

**3. Types of Nanoparticles Used in Biosensing**

Only metal atoms make up metal nanoparticles, which have excellent electrical conductivity and surface plasmon resonance. Metal oxide nanoparticles, on the other hand, are complexes made of metal and oxygen atoms that exhibit unique visual phenomena, enhanced chemical stability, and uses in fields such as magnetic resonance imaging and photocatalysis [10]. The primary distinction between them is their composition: one is a metal-oxygen complex, while the other is a pure metal. [11].

3.1. Metal nanoparticles

Metal nanoparticles (NPs) are exclusively composed of metallic elements. These NPs possess unique electrical characteristics attributed to the well-documented phenomenon of localized surface plasmon resonance (LSPR) [12]. Copper (Cu), silver (Ag), and gold (Au) nanoparticles demonstrate a wide absorption spectrum within the visible range of the solar electromagnetic spectrum. The utilization of metal NPs spans various scientific disciplines, owing to their enhanced attributes such as the controlled synthesis of facets, dimensions, and morphologies of metal NPs [13]. Metal nanoparticles are very fascinating materials for a variety of practical applications due to their improved optical, optoelectrical, catalytic, antimicrobial/cancer/viral characteristics [14] with the most Applications in **:** Drug delivery, biomolecule sensing, DNA detection, and photothermal therapy [15].

3.2. Metal oxide nanoparticles

Nanoparticles (NPs), one of the currently used nanomaterials, have drawn a lot of attention because of their small size and large surface area [16]. These characteristics give researchers new approaches to diagnosing and treating diseases that were previously believed to be unachievable because of size restrictions. MONPs have developed into valuable materials for the drug and health-related industries because to their many benefits, including high stability, easy preparation techniques, superior engineering control over factors like size, shape, porosity, etc., and cellular penetration capabilities [17]. Furthermore, compared to their bulk counterparts, metal oxide nanoparticles can interact more deeply with a variety of cellular structures because of their smaller size. More significantly, though, because of their significantly enhanced biocompatibility, they do not induce systemic toxicity[18]. Many kinds of MONPs are currently employed in clinical settings as biosensors, anticancer, wound-healing, and image contrast agents. The most promising of these for use in biomedicine are magnesium oxide nanoparticles (MgO NPs), silver oxide nanoparticles (AgO NPs), and zinc oxide nanoparticles (ZnO NPs).the Applications of metal oxide nanoparticls is mostly in Biosensing, imaging, photocatalytic and antibacterial applications, and magnetic resonance imaging (MRI)[19].

## 4. General Method of Synthesis for Metal Oxide Nanoparticles

The synthesis of NPs can be accomplished through three primary methodologies: physical, chemical, and biological techniques (Figure 1). The physical approach has numerous limitations, including high expenses, energy demands, radiation exposure, substantial waste production, temperature and pressure requirements, reduced stability, high dilution, challenges in size and shape control, and modifications to the surface chemistry and physicochemical properties of NPs [20,21]. Additionally, most metal nanoparticles are produced through chemical processes, which can lead to unforeseen issues such as excessive energy consumption, environmental pollution, and potential health hazards [22]. Green synthesis is beneficial due to its rapid assembly for large-scale applications, cost-effectiveness, eco-friendliness, and avoidance of hazardous substances, high temperatures, and excessive energy consumption [23]. In physical methods, the production of nanomaterials follows a top-down approach, whereas biological and chemical techniques employ a bottom-up strategy. This green synthesis approach falls under the category of bottom-up methods, which involve biological processes. In a bottom-up system, atoms aggregate to form clusters, eventually leading to the creation of nanostructures [24].

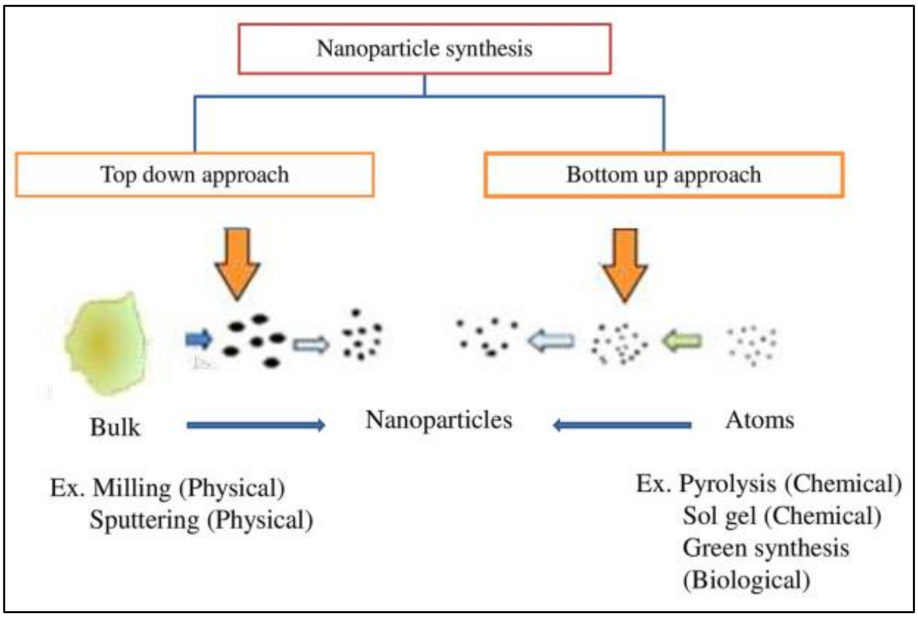


**Figure 1.** Various methods of metal oxide nanoparticles synthesis [25]

## 5. Properties of Nanoparticles

*High Surface Area to Volume Ratio*: This characteristic increases their reactivity, allowing more surface atoms to engage in chemical reactions. The large surface area is essential for applications like catalysis, drug delivery, and sensors, where surface interactions play a critical role [26].
*Enhanced Mechanical Properties*: Nanoparticles display improved mechanical properties, including greater strength and hardness, attributed to their small size and high surface energy. These qualities are advantageous in applications that require durable materials, such as coatings and composites [27].
*Electrical properties*: Nanoparticles often exhibit improved electrical conductivity compared to their bulk counterparts. This is due to the quantum effects that become prominent at such small scales, affecting electron movement and energy levels [28].
*Magnetic properties*: Nanoparticles can exhibit superparamagnetism, where they show magnetic behavior only in the presence of an external magnetic field. This property is particularly useful in applications like magnetic resonance imaging (MRI) and data storage [29].

## 6. Mechanisms of Nanoparticle-Based Biosensing

### 6.1. Electrochemical biosensors

Because of their distinct physicochemical characteristics, high surface-to-volume ratio, and capacity to enhance electron transmission, nanomaterials and nanostructures are essential for improving the performance of electrochemical biosensors. Their functionality enables customized designs for certain uses, such as the detection of viruses [30]. Several types of nanomaterials are used including Graphene quantum dots and gold nanoparticles provide biocompatibility, excellent conductivity, and a variety of synthesis techniques, including environmentally acceptable "green" production; High electrical conductivity, flexibility, and effective electron transport make carbon nanotubes, nanowires, and nanofibers ideal for signal amplification; By combining large surface area, reactivity, and customizable structures, graphene, MOFs, COFs, and transition metal dichalcogenides allow enable functionalization with biomolecules for targeted viral detection [31]. Hybrid nanostructures create sophisticated, multipurpose platforms for electrochemical biosensing by combining (figure 2). All things considered, these tailored nanomaterials greatly increase the sensitivity, selectivity, and stability of biosensors, creating new avenues for accurate and timely virus detection in biomedical applications [32].

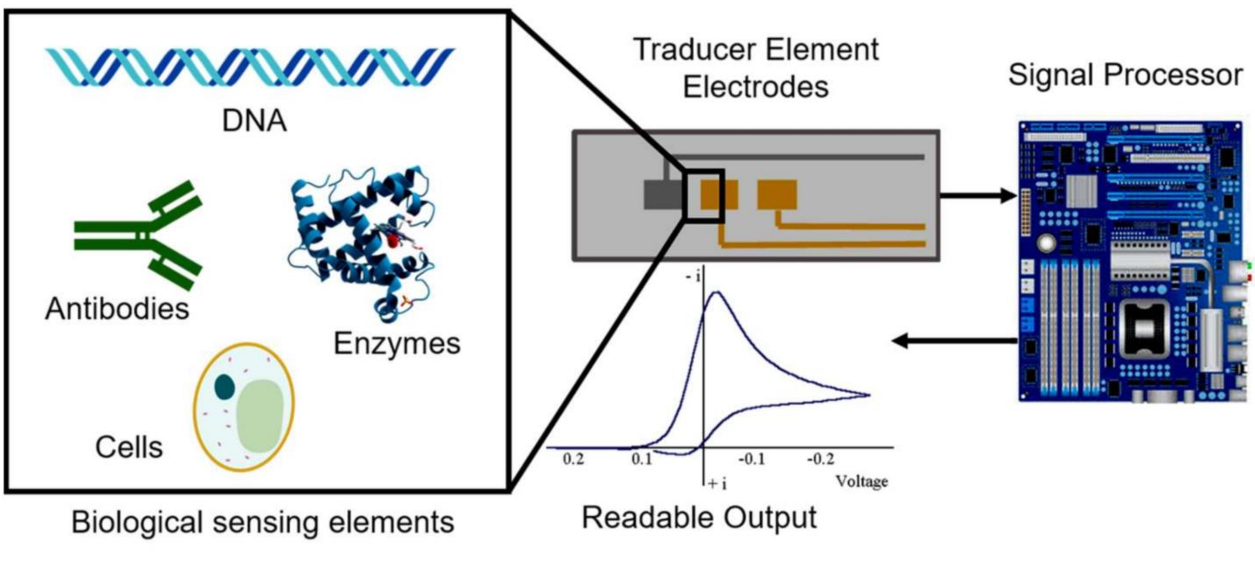


**Figure 2.** Electrochemical biosensor. Biological sensing elements are coupled to electrodes [33].

6.2. Colorimetric biosensors

The creation of colorimetric biosensors has been aided by nanomaterials, especially noble metals, 2D structures, and nanozymes, via processes including redox reactions and localized surface plasmon resonance (LSPR) [34]. The size and form of the Au and Ag nanoparticles used in LSPR-based biosensors impact their sensitivity. Ag nanoprisms for biothiols and AuNP-based sensors for Salmonella are two examples. Researchers created core–shell (Au@Ag@AgCl) and bimetallic nanoparticles (Ag–Au BUHNPs) to increase stability and signal brightness, which resulted in increased sensitivity for the detection of ammonia and harmful microorganisms(figure 3) [35].

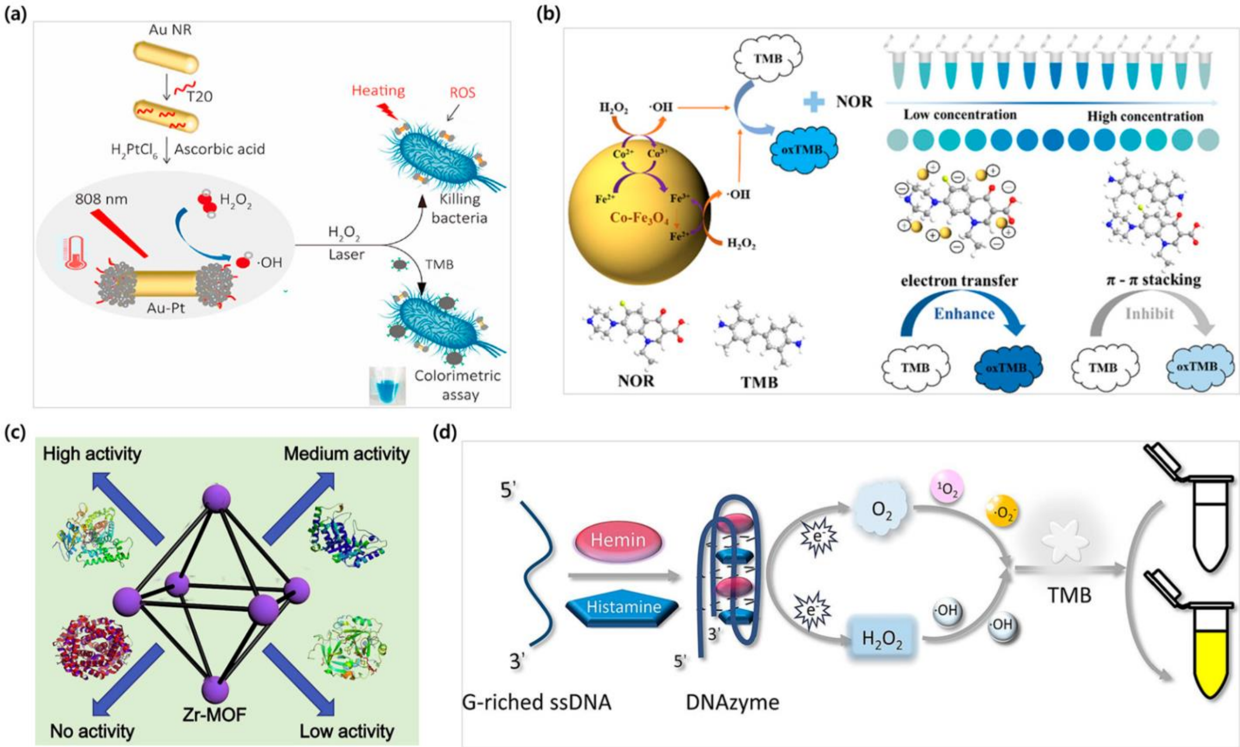


**Figure 3.** Enzyme-like nanomaterial-based colorimetric sensing [36]

The optical characteristics of Au/Ag are combined with graphene, $MnO_2$, and $MoO_3$ nanosheets to create noble metal–decorated 2D nanomaterials. These hybrids enhance the LSPR response, making it possible to detect environmental pollutants (Cu2+, sulfate-related chemicals) and biomolecules (dopamine, GSH, melamine, and exosomes) with greater sensitivity [37].
Colorimetric biosensors based on nanozymes replicate the activity of natural enzymes but are more stable and less expensive. Metal-organic frameworks (MOFs) for the selective detection of proteins and pathogens, Au-Pt nanoparticles for SARS-CoV-2, and $Fe\text{-}O_4$ and $Co\text{-}Fe\text{-}O_4$ nanozymes for biothiols and antibiotics are a few examples [38]. Heterostructures like CuS/ZnS and DNAzymes also increase adaptability. Because of their high surface area and conductivity (figure 4), 2D nanozyme systems (MXene, graphene oxide, $WS_2/WSe_2$, and $MnO_2$) significantly improve catalytic activity. [39]. They have been used to detect ochratoxin A, uric acid, nucleic acids, kanamycin, and mercury with remarkable sensitivity and versatility. For biomedical, food safety, and environmental monitoring applications, colorimetric biosensors based on nanomaterials and nanozymes offer straightforward, affordable, and extremely sensitive detection platforms [40] .

Furthermore, oxidation-reduction reactions, which are frequently mediated by natural enzymes (such as glucose oxidase and HRP) or nanozymes with enzyme-mimicking activity, are utilized by redox-based colorimetric biosensors. These systems enable for the quantitative detection of biomolecules, poisons, or genetic markers by producing color changes in substrates such as TMB or ABTS. In addition to LSPR and redox, other signal-generating processes include pH changes, hydrolysis events, and metal-ligand coordination [41].

The fundamentals of colorimetric biosensing, in general, integrate optical and chemical processes, with the characteristics of nanoparticles being crucial in boosting sensitivity, stability, and adaptability in biomedical, environmental, and diagnostic applications [42].

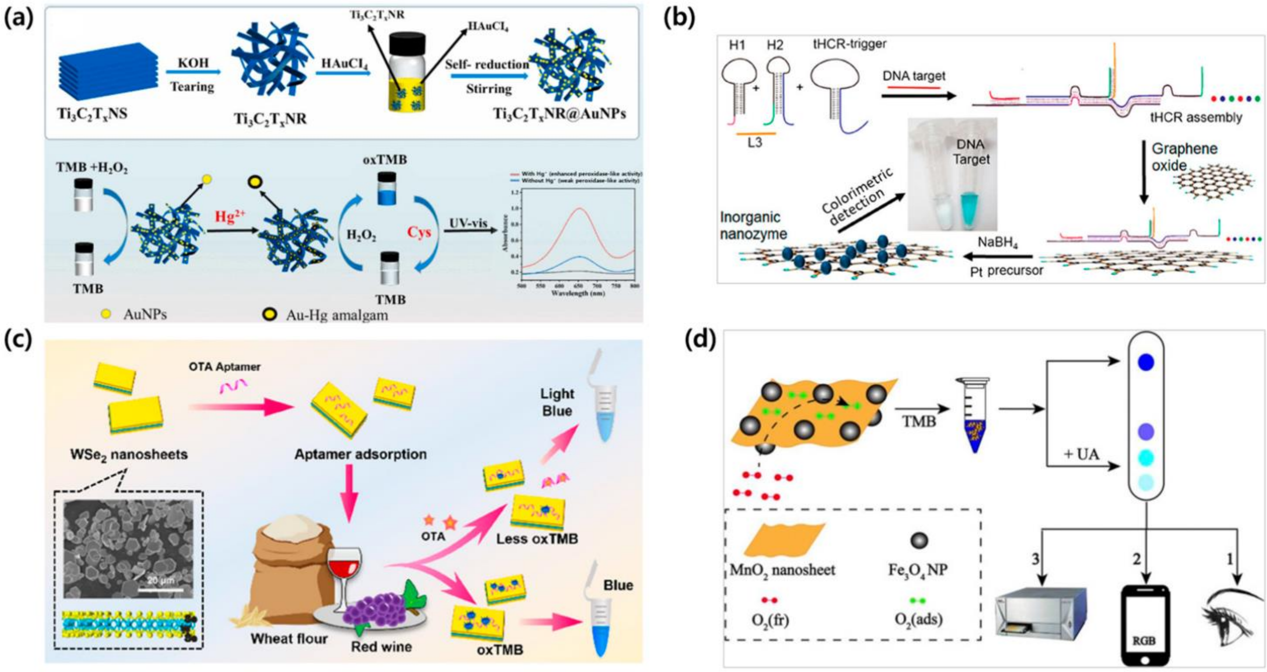


**Figure 4.** Enzyme-mimicking 2D nanomaterial-based colorimetric sensing [43]

6.3. Magnetic biosensors

Because of their nanoscale size, magnetic nanoparticles (MNPs) have special mechanical, chemical, and magnetic properties that make them useful in a variety of biological, environmental, and diagnostic domains [44]. They are highly effective in biomedicine at immobilizing and separating biomolecules (proteins, antibodies, enzymes, and DNA) from complex samples. The identification and extraction of microRNAs (miRNAs), which are tiny non-coding RNAs implicated in numerous physiological and pathological processes and have significant potential as diagnostic biomarkers, is a crucial application [45].The ability of MNPs to selectively bind, release, and concentrate nucleic acids makes downstream detection more dependable because miRNAs are difficult to extract from biological materials and exist in very low concentrations (figure 5). While qRT-PCR, microarrays, northern blot, and other conventional miRNA detection techniques are still in use, MNP-based biosensing technologies are becoming more and more potent substitutes. Functionalized MNPs greatly increase the sensitivity and specificity of miRNA detection by combining with electrochemical, optical, plasmonic, and fluorescent technologies [46].

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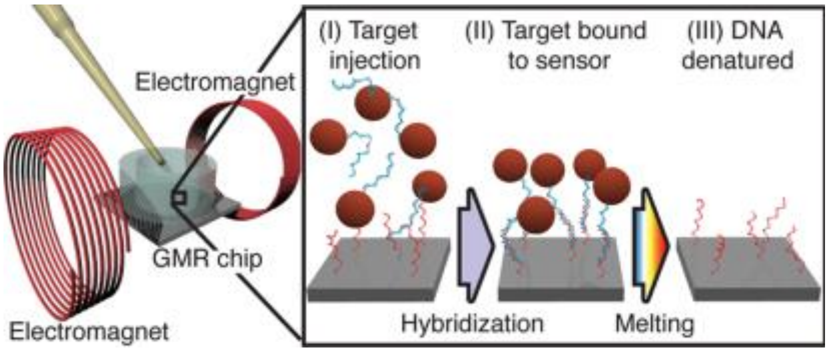


**Figure 5.** Magnetic biosensors [47]

## 7. Applications of Nanoparticle-Based Biosensors

### 7.1. Medical diagnostics

Early, precise, and real-time illness detection is made possible by nanoparticle-enabled biosensors, which are transforming medical diagnostics. They are used in the following areas: cardiovascular health (early biomarker detection), autoimmune and chronic disease monitoring, infectious illnesses (quick pathogen identification), and cancer diagnosis (figure 6) [48]. In neurology, they identify proteins such as tau and amyloid-β to diagnose Alzheimer's disease, and in diabetes, they facilitate ongoing glucose monitoring. Additionally, they provide theranostic treatments for periodontal disease, oral cancer, and implants [49].
They are particularly useful in healthcare settings with limited resources because of their high sensitivity and specificity, cost-effectiveness, early identification and continuous monitoring, portability for point-of-care testing, and support for tailored medication [50].

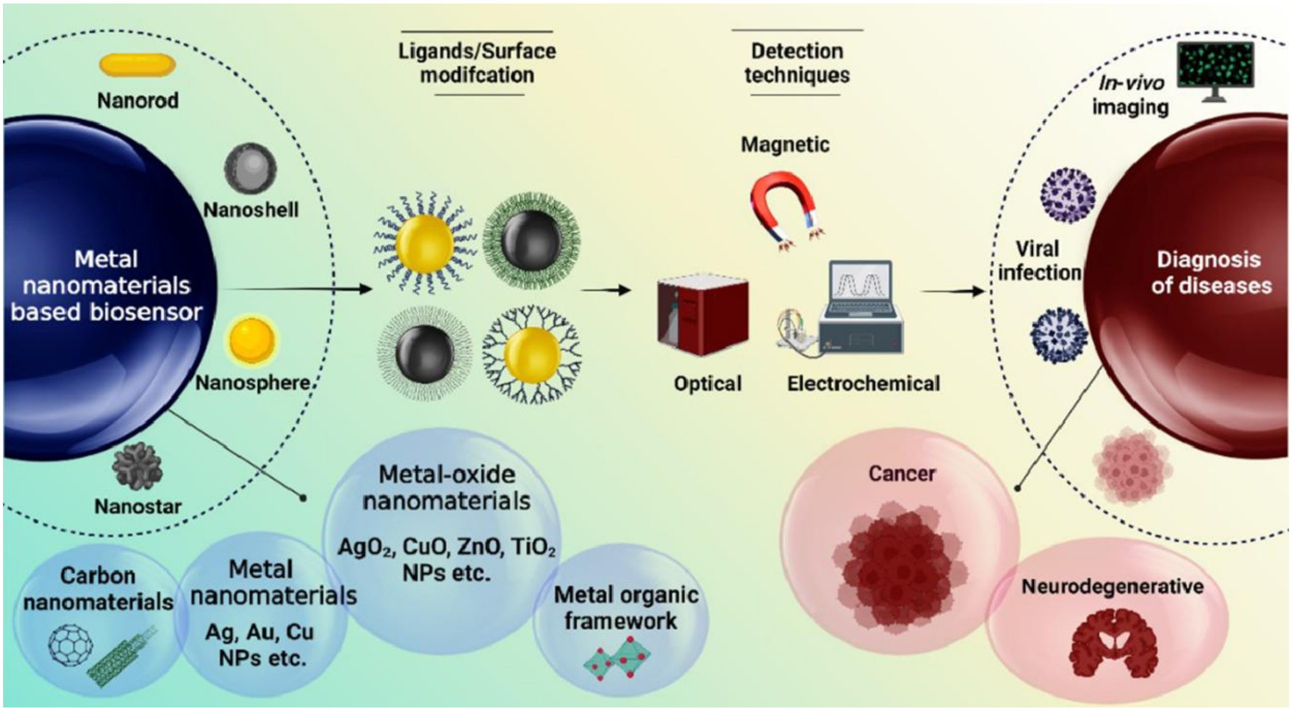


**Figure 6.** Metal nanoparticles-assisted early diagnosis of diseases [48]

7.2. Food safety

For the real-time monitoring of food pollutants such infections, toxins, heavy metals, pesticides, adulterants, and spoiling indicators (figure 7), nanoparticle-based biosensors are becoming increasingly potent instruments. They guarantee food quality, freshness, and safety across the supply chain when integrated into smart packaging or portable electronics [51].

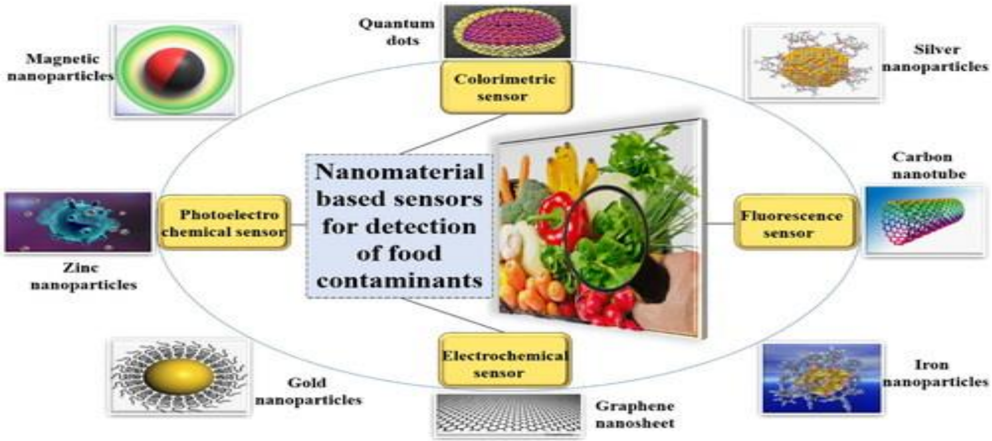


**Figure 7.** Nanomaterial based sensors for detection of food contaminants

Important uses consist of:

Aptasensors based on gold/silver nanoparticles are used to detect pathogens (such as Salmonella and E. Coli). Monitoring of toxins (pesticides, heavy metals, and mycotoxins). Identification of adulterants (unauthorized colors, additions). Using volatile organic compounds (VOCs) to check spoilage. Signs of freshness by monitoring temperature, oxygen content, and shelf life. Using packaging authentication to detect counterfeits. How they operate: Signal transduction and amplification are triggered by target-specific biorecognition (e.g., DNA, antibodies), resulting in quantifiable outputs like color change or electrical response [52].

Benefits: They are essential for contemporary food safety due to their high sensitivity and specificity, quick detection in comparison to conventional techniques, and real-time continuous monitoring [53].

**8. Advantages of Nanoparticle-Based Biosensors**

Because of the special optical, electrical, and catalytic qualities of nanomaterials, nanoparticle-based biosensors outperform conventional biosensors in terms of sensitivity, detection limits, response times, and signal amplification. These characteristics increase their utility in food safety, environmental monitoring, and diagnostics by enabling miniaturization, portability, and cost-effectiveness [54]. A Few Benefits:

- Increased Sensitivity & Lower Limits: Large surface-to-volume ratio allows efficient biomolecule immobilization and detection of ultra-low concentrations.
- Signal Amplification: Gold nanoparticles and quantum dots boost signal strength, improving accuracy.
- Rapid Response: Fast electron transfer and catalytic activity reduce detection time.
- Enhanced Biorecognition: Nanoparticles improve biomolecule binding, specificity, and biocompatibility [55].
- Miniaturization & Portability: Small size enables compact, user-friendly point-of-care devices.
- Multifunctionality: Nanomaterials can be engineered to pre-concentrate analytes or act as labels [56].

## 9. Challenges and Future Perspectives

A number of restrictions prevent the safe and efficient use of biomaterials in environmental and medicinal settings. Biomaterials have the potential to cause cytotoxicity, which is the killing of cells, genotoxicity, which is the damage of DNA, or sensitization and irritation, which can result in allergic reactions [57]. Biocompatibility Failure: Inadequate biocompatibility may result in thrombotic events (the formation of blood clots) or inflammation, which are acute immunological reactions [58]. Long-Term Effects: It is difficult to evaluate long-term safety since current testing methods are unable to adequately capture chronic and recurring harmful effects. Nanomaterial Concerns: There are specific dangers associated with nanomaterials, including as organ accumulation, persistent inflammation, and unknown long-term environmental effects [59].

Innovation in material designs, testing, and safety assessment must be the main emphasis of research in order to overcome these obstacles.

• Creation of New Biomaterials: Create cutting-edge biomaterials that are more biocompatible, have the ability to actively control immune responses, and promote tissue regeneration [60].
• Advanced Testing Techniques: Before clinical use, develop complex in vitro and in vivo models that more precisely forecast biocompatibility and long-term toxicity.
Comprehending Biological Reactions: Expand your understanding of the intricate biological relationships that exist between biomaterials and host systems, particularly at the nanoscale [61].
• Nanotechnology Safety: Create regulations that cover the hazards that nanomaterials pose to human health and the environment, guaranteeing their safe use over the course of their lifetime [62].

## 10. Conclusion

Because of their great sensitivity, quick reaction times, and numerous uses in environmental monitoring, food safety, and medicine, nanoparticle-based biosensors have completely changed sensing technology. Although they are preferable to traditional biosensors due to their distinct physicochemical characteristics, toxicity, low biocompatibility, and long-term environmental consequences continue to be significant obstacles. For these issues to be successfully translated into clinical and industrial practice, safer biomaterials, sophisticated predictive testing methods, and regulatory safety frameworks must be developed. Nanoparticle-enabled biosensors have enormous potential to influence the direction of diagnostics, individualized treatment, and sustainable global development with continued research.

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