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## Exploring the frontiers of emerging sensing of silver nanoprisms: recent progress and challenges

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In recent years, the development and use of nanomaterials have transformed numerous aspects of biomedical science. Nanomaterials have played a pivotal role in advancing disease diagnosis and treatment across a wide range of applications. Within this scope, silver nanoprisms (AgNPs) stand out due to their remarkable properties, such as extensive surface area, chemical robustness, and tunable electrical conductivity, making them excellent candidates for biomedical purposes. By tailoring these nanomaterials through functionalization or coating surface, their multifunctionality can be enhanced, unlocking new opportunities for their application in areas such as diagnosis, imaging, and therapeutic intervention. This review begins with an overview of AgNPs' synthesis techniques and their unique physicochemical characteristics. Recent advancements in analytical methods utilizing AgNPs, categorized by sensing mechanisms such as optical and electrochemical approaches, are highlighted in the context of diagnostics. Lastly, the challenges and future prospects of bringing AgNP-based technologies to commercialization and integrating them into disease diagnostics and medical treatment are explored. The integration of AgNPs in disease therapy holds promise for the development of advanced chemotherapy agents that effectively address the challenges of efficient cancer treatment looking ahead, the ongoing advancement of nanocarrier systems comprising AgNPs-based molecules holds great promise for improving the quality of life for patients worldwide.

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### 1. Introduction

Over the last few decades, advances in nanoscience and nanotechnology have fundamentally altered the treatment, detection, and prevention of different diseases. In this regard, palladium (Pd), platinum (Pt), silver (Ag), gold (Au), and cobalt (Co) have been widely used in biomedical applications.<sup>1,2</sup> Among the noble metal nanomaterials exploited in biomedical applications, different forms of Ag nanomaterials are among some of the more intriguing and significant due to their specific biological, chemical, and physical properties.<sup>3</sup> The various structures of Ag nanomaterials demonstrate diverse features, including conductivity, chemical stability, and catalytic and antibacterial activities. Silver nanoparticles (AgNPs),<sup>4</sup> AgNPs,<sup>5</sup> Ag nanocubes,<sup>6</sup> Ag nanowires,<sup>7</sup> Ag quantum dots,<sup>8</sup> Ag nanoshells,<sup>9</sup> and Ag nanoclusters<sup>10</sup> are significant forms of Ag nanomaterials. Interestingly, impressive attention was oriented

toward the biomedicine-related assessment of AgNPs, with sizes ranging from 1 nm to 100 nm, which are a class of zero-dimensional materials, which refer to materials confined in all three spatial dimensions, with distinctive morphologies.<sup>11</sup> For a long time, with limited information regarding the toxicity of this structure, it has been used as antibacterial agents in various fields such as food storage, the health industry, cosmetics, and textile coatings. Over the last few years, although several reviews have evaluated the special properties and applications of AgNPs in biomedical fields, but there is a massive gap in the review of AgNPs.<sup>12,13</sup> These types of Ag nanomaterials present more efficient and versatile alternative to traditional Ag forms (spherical structure) in biomedical applications owing to the high sensitivity, specific optical properties, and tunability. For example, AgNPs suffer from weak surface-enhanced Raman scattering (SERS), as powerful optical technique that amplify Raman scattering signal of molecules absorbed on the rough metal surfaces, signal due to the lack of sharp edges and the smooth surface of AgNPs. Furthermore, the adsorption of AgNPs is limited to the visible spectrum and the surface area of AgNPs is smaller than AgNPs, resulting in a reduction their efficiency and the performance of catalysis. Moreover, better photothermal conversion efficiency of AgNPs can be used for therapy.<sup>14-16</sup> However, specific structural properties of AgNPs (sharp tips of these nanoprisms) can cause

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stability limitation, especially as a spectrophotometric probe for anion detection. These structures are prone to etching in the presence of halide ions, polyelectrolytes or oxidizing agents in specific conditions.<sup>17,18</sup> This phenomenon degrades their original optical features and changes their stability. Addressing these issues is crucial for their practical applications. Indeed, functionalization and the combination of other materials can increase their stability, making them ideal for specific or selective recognition of different biomedical applications. In this regard, investigation the synthesis and identification and introduction of physical and chemical characteristics of AgNPs can massively assist researchers in developing high-performance approaches based on AgNPs.<sup>19</sup>

In summary, the evaluation of the performance of AgNPs in sensing, consisting of biomedical applications, food safety analysis, and environmental monitoring, is the main purpose of this review (Scheme 1). The investigation of thickness, edge length, and roundness of the Ag nanoprisms can broaden researchers' horizon about their performance.

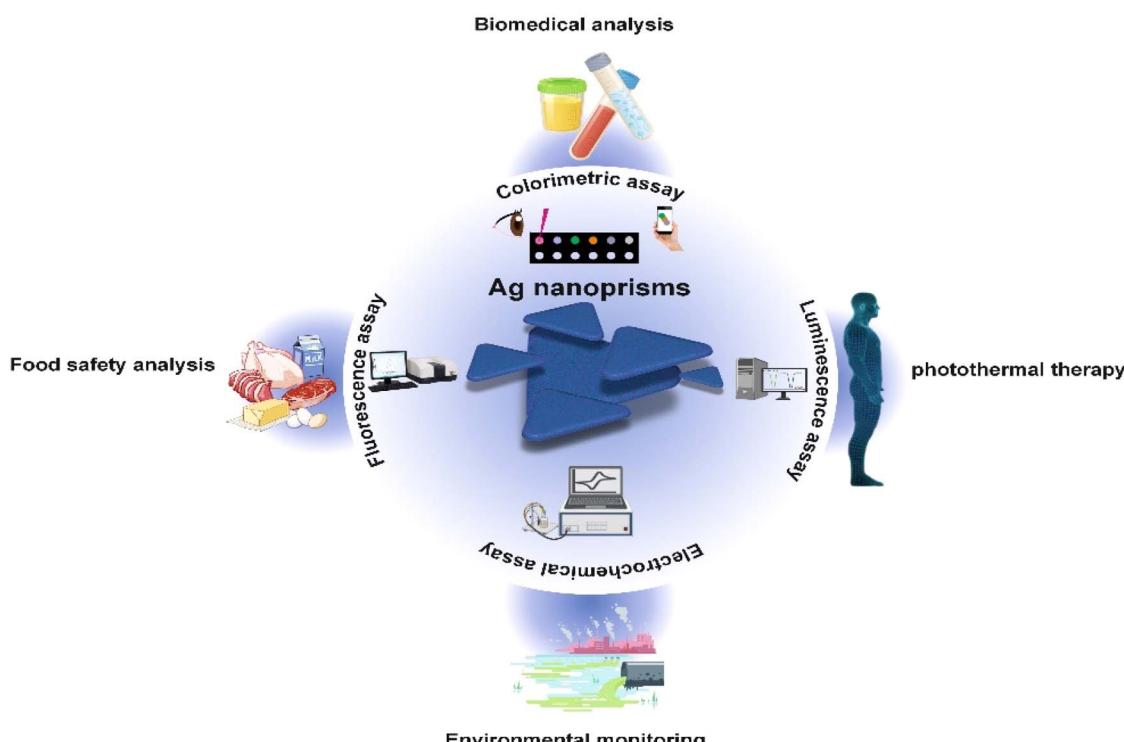
### 1.1. Road MAP

- Introduces the synthesis and physico-chemical properties of AgNPs.
- Recent research on different analytical methods based on AgNPs, including optical and electrochemical techniques, is summarized for diagnosis.
- Current and future challenges faced by the commercialized implementation of the AgNPs in the diagnosis of disease and biomedical therapy were discussed.

## 2. Physical and chemical properties of AgNPs

AgNPs, as one of the important members of Ag nanomaterials, are less than 100 nm in size and consist of approximately 20 to 15 000 silver atoms.<sup>20</sup> These nanoprisms have attracted considerable attention due to their triangular and prism-like shape. This specific shape and structure improve interaction of these materials with light and electrical for enhancing optical properties, such as absorption and light scattering. These nanomaterials reveal exceptional physical and chemical characteristics, making them high potential candidates in numerous fields including photonics, biomedical, catalysis, and sensing.<sup>21</sup> The physical properties of AgNPs consist of shape and morphology, surface area, localized surface plasmon resonance (LSPR), mechanical attributes, and optical properties. Moreover, excellent functionalization capability, redox activity, surface chemistry, high catalytic potential, and antibacterial properties are the most significant chemical features.<sup>22,23</sup>

Although the thickness and edge lengths of AgNPs vary, their flat surface and triangular structure of AgNPs introduce high surface area nanomaterials and increased edge effects.<sup>24</sup> These structures provide highly reactive and specific optical properties, in comparison to other structures of Ag nanomaterials, in catalytic and sensing applications. On the other hand, they are prone to degradation due to their high surface energy.<sup>25</sup> This makes them useful for temperature indicators in the specific chemical reactions that result in color change due



Scheme 1 Utilization of AgNPs in research area.



to temperature variations. LSPR, as important optical feature of AgNPs, operates based on the oscillation of conduction electrodes when excited by incident light. The shape and size of these nanoprisms, as well as surrounding environment can be tuned LSPR.<sup>26</sup> Moreover, the LSPR of AgNPs was changed by reduction and oxidation. The colorimetric change of AgNPs, typically showing yellow to purple colors, primarily relies on this plasmonic property which provides color change upon exposure to certain chemicals and aggregation.<sup>27,28</sup> In addition, their excellent enhanced Raman scattering features present high-performance candidate for SERS probe.<sup>29</sup>

In terms of chemical properties, AgNPs demonstrate excellent chemical reactivity due to the high surface activity and reactive sites at the vertices and edges. In detail, these nanomaterials can be useful in photocatalytic systems owing to their high ability to react with light (plasmon-induced catalysis).<sup>30</sup> Furthermore, the redox reaction based on AgNPs can be operated by donating electrons of silver atoms in different chemical processes.<sup>31</sup> Additionally, the releasing silver ions ( $\text{Ag}^+$ ) can act as antibacterial materials regarding their ability to disrupt bacterial cell walls and inference function of bacterial enzymes.<sup>32</sup> The various reactive sites of AgNPs able them to modify with biomolecules and polymers in order to improve chemical properties.<sup>33,34</sup> The comparison of the advantages of AgNPs with other Ag nanomaterials highlights the efficiency of these nanoprisms. For instance, AgNPs demonstrate multi peaks, in contrast to the single plasmon resonance peak of AgNPs. In addition, AgNPs exhibit better tunability compared to silver nano-cubes (AgNCs) due to their specific shape. Moreover, the comparison of AgNPs with other nanomaterials demonstrated that AgNPs are ideal candidate for sensing due to its specific properties. The general comparison of AgNPs with common employed nanomaterials, including carbon-based nanostructures and noble nanomaterials is summarized in Table 1. In this regard, the versatility of AgNPs based on physical and chemical properties for biomedical application are reviewed in the next section.

### 3. Sensors and biosensors based on AgNPs for biomedical application, environmental monitoring, and food safety analysis

Over the last decades, AgNPs have received significant attention in the different methods due to their specific physical and

chemical properties. Electronic and optical features of these Ag nanomaterials have been exploited in numerous studies for introducing sensitive and selective colorimetric, SERS, luminescence, fluorescence, and electrochemical platforms for detection of a wide range of targets. Recently, the synthesis of AgNPs with well-controlled morphology and physicochemical properties for various sensing applications. In many bio(sensors), the AgNPs is used to achieve highly accurate identification methods.

#### 3.1. Colorimetric probes based on AgNPs

Colorimetric sensors based on AgNPs, as powerful sensing devices, have been widely exploited in different fields due to their specific optical properties. Indeed, the implementation of AgNPs in colorimetric approaches, which demonstrate strong adsorption and scattering in the visible range, make them suitable for clinical diagnostics, environmental monitoring, and food safety. The principle of detection in these sensing approaches relies on the production color based on LSPR.<sup>35,36</sup> These types of colorimetric sensors were successfully employed to detect various targets, such as selenium  $\text{Se}^{4+}$ , fumonisins, homocysteine (Hcy), dopamine (DA), hydrogen peroxide ( $\text{H}_2\text{O}_2$ ), histamine (HIS), ethylenediamine (EDA), arsenic ion ( $\text{As}^{3+}$ ), 6-thioguanine (6-TG), glucose, cysteine (Cys), glutathione (GSH), and acetaldehyde, with low detection limits and good linearity.

The complexity of human serum, containing salts, proteins, and other biomolecules, makes AgNPs unstable in this environment. The proteins of serum have a preference to adsorb on the surface of AgNPs and this idea has been used in several studies for biomedical application. This phenomenon is not limited to biomedical and it can be used for environmental monitoring. Recently, various platforms have been developed based on the etching and etching protection of AgNPs. These nanoprisms are etched by  $\text{H}_2\text{O}_2$ ,<sup>37</sup> heat,<sup>38</sup> UV light,<sup>39</sup> and inorganic anions.<sup>40-42</sup> For instance, Amjadi *et al.*,<sup>43</sup> exploited etching effect of  $\text{Se}^{4+}$  on AgNPs for colorimetric detection of  $\text{Se}^{4+}$ . In the presence of the target, the morphological transformation of AgNPs to nanodiscs led to a change color of the solution from light blue to violet. In the reported sensor, the colorimetric response provided a visual quantification in linear range and limit of detection (LOD) of 2.5 to 100  $\mu\text{g L}^{-1}$  and 1.2  $\mu\text{g L}^{-1}$ , respectively. In addition, the method possesses an excellent selectivity for analysis of the target in food and water samples. Similarly, Chen and colleagues,<sup>44</sup> utilized passivation and apical activation of unmodified triangular AgNPs for presenting a novel colorimetric strategy of  $\text{Hg}^{2+}$  detection. Thiosulfate

Table 1 The general comparison of AgNPs with other nanomaterials

Materials	Performance	Cost	Scalability	Best use cases
AgNPs	Tunable LSPR for sensitive optical detection, sharp	Low-cost	Moderate	Highly sensitive optical sensors
Carbon-based nanostructures	Electrical conductivity and optical properties	Low-cost	Scalable production technique	Affordable electrochemical sensors
Noble nanomaterials	Stability and easy functionalization	High-cost	Scalable production technique	Highly stable sensors



anions ( $S_2O_3^{2-}$ ) were used to etched the triangular AgNPs into round nanodisks, resulting changed color from blue to yellow. When the target was added to the system, the precipitation interaction of  $S_2O_3^{2-}$  and  $Hg^{2+}$  prevented the color and shape of the AgNPs. Under optimal conditions, the spectroscopic changes in the LSPR wavelength of AgNPs were measured as the analytical signals for label-free detection of  $Hg^{2+}$  with a LOD of 0.2 nM and a linear range of 5.0 nM to 10.0  $\mu$ M. In addition, this method has been successfully applied to the measurement of  $Hg^{2+}$  in wastewater samples with an excellent relative standard deviation (RSD, 4.81%). Most recently, Amjadi and colleagues,<sup>45</sup> designed another colorimetric assay using a 6-TG anti-attaching iodide-induced etching reaction of AgNPs in terms of determination of 6-TG in human plasma samples. When the target was added to the system, the blue color of solution remains unchanged. In the reported colorimetric approach, the relationship of color intensity and concentration of 6-TG provided a linear range and LOD of 2.5 to 500  $\mu$ g L<sup>-1</sup> and 0.95  $\mu$ g L<sup>-1</sup>, respectively. Recently, researchers,<sup>46</sup> reported a simple colorimetric probe based on anti-etching of  $Hg^{2+}$  on AgNPs for detection of  $Hg^{2+}$ . For this purpose, the difference of morphology and color of AgNPs was the principle of this work. In the absence of  $Hg^{2+}$ , the morphology of AgNPs was changed to nanodisks by etching iodide (I<sup>-</sup>) ions, resulting in color change from blue to red. However, in the presence of  $Hg^{2+}$ , the redox reaction between  $Ag^0$  and  $Hg^{2+}$  leads to the formation of Ag-Hg nanoalloy, protecting the corners and edges of AgNPs from I-etching and keeping the morphology frozen. The prepared sensor could successfully detect  $Hg^{2+}$  with a LOD of 3 nM and which is lower than the mercury toxic level defined by the United States Environmental Protection Agency. In addition, due to the acceptable sensitivity of the approach, it can be considered high potential colorimetric detection method of  $Hg^{2+}$  to challenging environmental samples.

Although several etching and anti-etching effects on AgNPs were successfully used in colorimetric sensors, dual function matter has improved the colorimetric sensors based on AgNPs. One of the excellent examples of this concept in colorimetric sensors for detection of biothiols (Hcy, Cys, and GSH) in human serum was developed by Li *et al.*<sup>47</sup> The principle of detection was based on both anti-etching and aggregating agents of biothiols on the surface of AgNPs. In this study, color change mechanism operated with/without interaction of biothiols with AgNPs. In the presence of the targets, their Ag-S covalent interactions with AgNPs protected AgNPs from chloride ions etching in human serum, maintaining blue/purple color of AgNPs. In the absence of biothiols, the color of AgNPs turned yellow due to their etching. Therefore, the constructed strategy can open new prospects for developing other practical applications by adjusting pH. They showed that AgNPs were etched by Cl<sup>-</sup> in human serum, which contained non-sulfur-containing amino acids, resulting turned a colorimetric signal to yellow color.

In addition to the importance of improving sensitivity of sensing platforms, recently there have been several attempts to introduce portable and miniaturization sensing platforms. Interestingly, application of the microfluidic paper-based

colorimetric devices ( $\mu$ PCD) as substrate of sensing can consider a new way to achieve portable analysis devices.<sup>48</sup> Recently, Baghban and co-workers,<sup>49</sup> used AgNPs on the paper for presenting a lab-on-paper technology which is colorimetric monitoring of DA in real human and urine samples. In this study, the etching effect of phosphate-buffered saline (PBS) buffer, as a great model of human serum, is blocked by DA. The redox reaction between DA and AgNPs was evaluated by color change at two pH values (5.35 and 6.14). The intensity of color change was captured by the camera of the smartphone on the surface  $\mu$ PCDs, with a limit of quantification 0.01  $\mu$ M. Moreover, UV-vis analysis, as a standard method, confirmed the obtained result of smartphone. Notably, designing several sensing zones on the developed paper-based colorimetric sensor can be considered a chance for simulation detection of various targets in the future. In 2024, this research group,<sup>50</sup> reported another  $\mu$ PCDs based on AgNPs for sensitive detection of dapoxetine (DPX) in human urine. For this purpose, similar to the previous, the etching effect was used to measure the difference of color with/without the target. Most recently, Saadati and colleagues,<sup>51</sup> presented a novel and low-cost microfluidics paper based on the using AgNPs detection strategy for rapid and accurate identification of biogenic amines in meat samples. In this protocol, the colorimetric platform implemented AgNPs, as sensing probes, on the surface of paper-based test strips which designed by 8 zones. This system introduced visual detection for HIS and EDA with a LLOQ of 0.1  $\mu$ M and 0.05  $\mu$ M, respectively. This group fabricated another platform on the surface of paper-based microfluidics, which consists of 8 sensing zones for rapid and sensitive colorimetric detection of As<sup>3+</sup>. In order to improve the performance of AgNPs, Cys and methionine were coppered in the structure of AgNPs. When the target was added to the system, the changing morphology and color of sensing zones, which decorated with AgNPs were proportional to the concentration of As<sup>3+</sup>.<sup>52</sup> In 2023, Ahmadi *et al.*,<sup>53</sup> used similar approach based on AgNPs on the surface of sensing zones for synthetic dyes, including Tartrazine (Tar) and Sunset Yellow (Sun), detection in fruit juices. The constructed chemosensor revealed good analytical performance in measuring tartrazine and sunset yellow in different types of orange juice. The linear range of developed chemosensor for tartrazine and sunset yellow was 0.07–0.3 mM and 0.05–0.2 mM, respectively. Furthermore, UV-vis spectrophotometric method verified the results of colorimetric detection. The concept of using AgNPs on the surface of paper-based microfluidics was used for quantification of ractopamine (RAC).<sup>54</sup> Similar to previous studies, etching effect on the AgNPs, which was used on the surface of the sensing zones, was principle of colorimetric detection. In this work, the integration of smartphone for photography and analysis of color intensity provided an accurate and reliable detection approach. The idea of a combination of smartphone and these microfluidics paper-based analytical devices for portable determination of hydrazine (Hyd) was developed by Ghaseminasab and co-workers.<sup>55</sup> Smartphone-assisted capture the changing color intensity of AgNPs in the various concentrations of Hyd. The proposed method revealed a linear range from 0.02 to 5 M for AgNPs.



Along with portability, the application of chromogenic substrate and enzymes in the structure of colorimetric sensors based on the AgNPs has attracted considerable attention for improving selectivity. Recently, Farshchi and coworkers,<sup>56</sup> utilized 3,3,5,5-tetramethylbenzidine (TMB), as a chromogenic substrate, in  $\mu$ PCDs for the rapid and sensitive quantification of acetaldehyde. The redox reaction between AgNPs, TMB solution, and acetaldehyde caused color change to the naked eye within 15 min. Although the oxidation mechanism of TMB by  $\text{H}_2\text{O}_2$  produce color, the use of combination TMB and AgNPs in  $\mu$ PCDs introduced sensitive, affordable, and portable colorimetric sensing device on the paper. In the fabricated approach the performance of other Ag nanomaterials, such as AgNPs and AgNPs-citrate was evaluated by AgNPs. Using AgNPs-citrate as an optical probe can significantly improve the performance of this study. Most recently, Avenido exploited AgNPs-citrate as colorimetric probe of  $\text{H}_2\text{O}_2$ .<sup>57</sup> The functionalized AgNPs with citrate changed optical properties and this, in turn, increased the in-plane dipole plasmon resonance (IPDPR) band. Furthermore, the production of distinct color (purple, blue, orange, red, and yellow) is another consequence of structural change. In 2023, Avenido and colleagues,<sup>58</sup> improved the performance of AgNPs-citrate with silver nanospheres (AgNSs) for determination of  $\text{H}_2\text{O}_2$ . In this protocol, dual-shaped silver nanostructures (AgNSs and AgNPs-citrate) increased optical features, stability, and more importantly introduced a synergistic redox mechanism. In the presence of target, a range of colors was produced by transformation of AgNSs to AgNPs-citrate. This phenomenon led to growth AgNSs on the edge of AgNPs-citrate and increasing LSPR. In the designed sensing platform, the ratiometric approach was used to measure the difference in absorbance values.

In addition to enzyme-free sensing platforms, enzyme-based colorimetric biosensors based on AgNPs have attracted great attention for biomedical applications due to their role in controlling reaction, reducing the effect of serum components, and increasing plasmonic signal. Enzymes like glucose oxidase (GOx) can increase the selectivity of AgNPs. In these platforms, enzymes produce detectable signal and AgNPs act as plasmonic reporters. One of the brilliant examples of enzyme application in biosensors-based on AgNPs for fumonisins detection was operated by GOx-triggered etching of AgNPs.<sup>59</sup> For this purpose, the competitive strategy used GOx-FB1 conjugation as competitive antigens to compete with fumonisins for binding with decoration monoclonal antibodies on the surface of microplate wells. The oxidation of glucose by GOx produced  $\text{H}_2\text{O}_2$  which etched AgNPs into small nanomaterials, resulting in color change from light blue to violet.

Modification of AgNPs chromogenic substrate and enzymes presents a promising solution for addressing the instability of these nanomaterials in real samples. The application of enzymes can decrease non-specific interactions and increase sensitivity. In addition, functionalization can overcome protein corona formation and oxidation. In this regard, stabilization techniques can optimize the performance of these nanomaterials in complex biological media. The analytical performance of the developed colorimetric assay based on AgNPs are

completely discussed in Table 2. In conclusion, etching and aggregation are basic colorimetric approaches based on AgNPs for biosensing and sensing. The performance of this method was improved by using smart gadget, bioreceptors, and functionalization. In favor of the smart gadgets, although smartphone could increase the capturing color intensity, this field can be boosted by exploiting artificial intelligence (AI) in the future. In addition, the integration of other bioreceptors such as aptamers, antibodies, and peptides with AgNPs can improve the sensitivity and selectivity of colorimetric platforms.

### 3.2. Fluorescence probes based on AgNPs

Fluorescence sensing is a technique operated according to the excitation of electrons of various fluorophores such as dyes, nanomaterials, and biomolecules. The AgNPs have been widely used in the structure of fluorescence sensors for detection of various targets which can be used in biomedical analysis, environmental monitoring, and food safety analysis.<sup>73,74</sup> For instance, Yaiwong *et al.*,<sup>61</sup> constructed a fluorescence approach using AgNPs for quencher of gold quantum dots (AuQDs) in quantification of  $\text{H}_2\text{O}_2$ . In detail, the intensity of fluorescence signal of AuQDs has an indirect relationship with concentration of AgNPs on the surface of these nanomaterials due to their ability to facilitate energy transfer from AuQDs. When the  $\text{H}_2\text{O}_2$  was added to the platform, the fluorescence signal of AuQDs was recovered due to the reduced quenching effect caused by the interaction of AgNPs and AuQDs. This effect occurs when energy transfer happens from the AuQDs to the AgNPs, leading to a decrease in fluorescence. The designed sensing mechanism could detect  $\text{H}_2\text{O}_2$  with a linear range of 1 pM to 100 nM. Moreover, excellent selectivity of fluorescence probe was verified with using different interferences. Another significant role of AgNPs can attribute to their role in the inner filter effect (IEF) which overlaps between the absorption spectrum of a quencher and the excitation spectrum. Recently, different fluorescence sensors have used optical features, structural, and reactivity characteristics of AgNPs for quencher fluorescence signal by IEF. Most recently, [fluorescence quencher], Salari *et al.*,<sup>62</sup> developed a fluorescence sensor based on nitrogen and phosphorus doped carbon dots (N, P-CD) and AgNPs for detection of 6-mercaptopurine (6-MP) in human blood samples. In this work, quench fluorescence of N, P-CDs owing to an overlap between the absorption spectrum of the etched AgNPs and N, P-CDs emission spectrum. Under normal conditions, the reported sensing approach is able to fluorimetric detection of 6-MP of with a LOD of 10 nM. Similarly, this group exploited AgNPs and rhodamine B in another fluorescence sensor for nicotinamide adenine dinucleotide (NADH) determination in biological samples.<sup>63</sup> For this purpose, a fluorescence quencher (AgNPs/ $\text{H}_2\text{O}_2$ ) was used for rhodamine B quencher due to the spectral overlapping of their absorption and excitation of rhodamine B. When NADH was added to the system, the fluorescence quenching of rhodamine B, which was conducted in the presence of AgNPs/ $\text{H}_2\text{O}_2$  and the inner was restored. These aspects were used to design a fluorometric probe for detecting NADH in the range of 30 to 450 nM. Both of the developed



Table 2 Analytical figure of merit for various sensing approaches based on AgNPs for biomedical application

Method	Technique	Target	Sample	Detection range	LOD or LLOQ	Ref.
Optical	Colorimetric	Se <sup>4+</sup>	Water and food	2.5 to 100 $\mu\text{g L}^{-1}$	1.2 $\mu\text{g L}^{-1}$	43
		Hg <sup>2+</sup>	Wastewater	5.0 nM to 10.0 $\mu\text{M}$	0.2 nM	44
		6-TG	Human plasma	2.5 to 500 $\mu\text{g L}^{-1}$	0.95 $\mu\text{g L}^{-1}$	45
		Hg <sup>2+</sup>	Water	3.0 to 500 nM	30 nM	46
		Hcy, Cys, and GSH	Human serum	0 to 5 $\mu\text{M}$ and 0 to 4 $\mu\text{M}$	0.041 $\mu\text{M}$ , 0.079 $\mu\text{M}$ , and 0.086 $\mu\text{M}$	47
		DA	Human blood plasma and urine	0.01 $\mu\text{M}$ to 10 000 $\mu\text{M}$	0.01 $\mu\text{M}$	49
		DPX	Human urine	0.01 $\mu\text{M}$ to 1 mM	0.01 $\mu\text{M}$	50
		EDA and HIS	Raw chicken and beef	0.1 $\mu\text{M}$ to 0.01 mM and 0.05 to 1 $\mu\text{M}$	0.1 $\mu\text{M}$ and 0.05 $\mu\text{M}$	51
		As	Human urine	0.0005 to 1 ppm	0.0005 ppm	52
		Food dyes	Orange juice	0.07 to 0.3 mM and 0.05 to 0.2 mM	0.07 mM and 0.05 mM	53
	Fluorescence	Ractopamine	Chicken	0.1 to 10 000 $\mu\text{M}$	10 nM	54
		Hyd	Water	0.08 M to 6 M	200 $\mu\text{M}$	55
		Acetaldehyde	Human biofluids	10 <sup>-7</sup> to 10 M	10 <sup>-7</sup> M	56
		H <sub>2</sub> O <sub>2</sub>	Drinking water	10 to 800 mM	4.8 $\mu\text{M}$	57
		H <sub>2</sub> O <sub>2</sub>	Drinking water	0.2 to 800 $\times 10^{-3}$ M	0.2 to 10 $\times 10^{-3}$ M	58
		Fumonisins	Corn	0.1 to 500 ng mL <sup>-1</sup>	0.1 ng mL <sup>-1</sup>	59
		Malondialdehyde	Human urine	0.00012 to 1.192 mM	0.00012 mM	60
		H <sub>2</sub> O <sub>2</sub>	—	1 pM to 100 nM	1 pM	61
Electrochemical	Photoluminescence	6-MP	Human blood	30 to 500 nM	10 nM	62
		NADH	Human serum	30 to 450 nM	12 nM	63
		H <sub>2</sub> O <sub>2</sub> and glucose	Lake water	0 to 1000 $\mu\text{M}$	0.12 $\mu\text{M}$ and 0.6 $\mu\text{M}$	64
		LA	Human serum	0 to 60 $\mu\text{M}$	386 nM	65
		DA	Human serum	0.6 to 100 nM	0.22 nM	66
	Photoluminescence	H <sub>2</sub> O <sub>2</sub>	—	1 nM to 1 $\mu\text{M}$	1 nM	67
		Luminescence	Glucose	30 mM to 0.05 mM	0.038 mM	68
	Voltammetric	Cu <sup>2+</sup>	—	0 to 100 $\mu\text{M}$	5 nM	69
		miR-153	Human plasma	6.25 $\mu\text{M}$ to 50 $\mu\text{M}$	6.25 $\mu\text{M}$	70
		LYVE-1	Human plasma	20 to 320 pg mL <sup>-1</sup> and 0.625 to 10 pg mL <sup>-1</sup>	0.312 pg mL <sup>-1</sup>	71
	Voltammetric	TCAM	Drinking water	0.5 to 10 $\mu\text{M}$ and 10 to 80 $\mu\text{M}$	0.17 $\mu\text{M}$	72

fluorescence sensors by this group used AgNPs for increasing reactivity and sensitivity of platforms which operated based on the IEF for fluorescence quencher. In addition to quenching fluorescence *via* IEF, AgNPs can catalyze signal generation through chemical reactions. Most recently, Li *et al.*<sup>64</sup> a simple and highly sensitive proportional fluorescence sensor was developed incorporating blue-emitting CDs, AgNPs, and *o*-phenylenediamine (B-CDs–AgNPs–OPD) for H<sub>2</sub>O<sub>2</sub> and glucose detection. In this protocol, AgNPs were exploited as catalytic and signal amplification agents for facilitating fluorescence signal production. In terms of H<sub>2</sub>O<sub>2</sub>, the edges and tips of the AgNPs can be easily etched into Ag<sup>+</sup> ions by H<sub>2</sub>O<sub>2</sub>, enabling highly sensitive detection of H<sub>2</sub>O<sub>2</sub> in direct aspect and, indirect matter in glucose detection, it has a role in production 2,3-diaminophenazine (DAP) which quenching B-CDs based on IFE. IFE-based fluorescence modulation is another significant concept in this field. Most recently, Zhang *et al.*<sup>65</sup> developed a triple-emission fluorescence sensor to detect lactic acid (LA) by utilizing the IFE-based fluorescence modulation between the fluorescent probe and AgNPs. For this purpose, the produced

H<sub>2</sub>O<sub>2</sub> from oxidization of LA, by lactate oxidase (LOx), etched AgNPs. This change led to a shift in the absorption peak and used for detecting LA in the concentration range of 0 to 60  $\mu\text{M}$ , and the sensor recovery in human serum is 97.96–115.47% with an RSD of 0.61–1.16%. The experimental results show that the triple-emission fluorescence sensor in this method has the characteristics of a wide detection range, low detection limit, and excellent linear relationship, which provides a simple detection method for LA in serum and a new strategy for the early detection of cancer.

AgNPs with anisotropic features have played an important role in the enhancement of fluorescence effect due to their sharp vertices of triangular structure. This specific shape able them to demonstrate high electromagnetic field enhancement ability.<sup>75,76</sup> Recently, Shen *et al.*<sup>66</sup> reported a selective fluorescence sensor based on using AgNPs and acetate on terbium ions (Tb<sup>3+</sup>)–DA complexes for providing surface enhanced fluorescence (SEF) effect and appropriate distance of in detection of DA. The specific structure of AgNPs introduced an excellent substrate for binding Tb<sup>3+</sup>–DA complexes. Under



a specific wavelength of light emitting fluorescence signal of  $\text{Tb}^{3+}$  was amplified by using the synergistic enhancement effect of silver nanoprisms and acetate. The prepared method demonstrated sensitivity at subnanomolar levels and had strong anti-interference abilities.

The developed studies of AgNPs-based fluorescence sensors are limited and require attention in the future. According to the strong LSPR extinction band of AgNPs in the visible-light region, they have been used as powerful fluorescence quenchers through energy or electron-transfer processes. Furthermore, their incorporation with other nanomaterials such as metallic-based, polymer, and ions can introduce efficient strategies based on different effects. IFE is a central part of these sensors based on AgNPs for biomedical analysis, environmental monitoring, food safety. The versatility of AgNPs in IFE has led to use of them to quench fluorescence *via* IFE, catalyze signal generation, and modulate emission approaches for ratiometric quantification.

### 3.3. Luminescence probes based on AgNPs

The application of AgNPs in luminescence, as one of the important optical methods, sensors have attracted great attention due to the LSPR properties of these materials. In this regard, AgNPs as luminescence modulators have been integrated with different nanomaterials such as AuQDs, Au, metal organic framework (MOF), and CdSe quantum dots (QDs) in different sensing platforms for quenching or enhancing luminescence signal.<sup>77,78</sup> For example, Lertvachirapaiboon *et al.*<sup>67</sup> developed a photoluminescence sensor based on the plasmonic effect of AgNPs for quantification of  $\text{H}_2\text{O}_2$ . In this instance, the plasmonic quenching of AuQDs was induced by AgNPs and this was reversed in the presence of the target. In detail, the interaction of AgNPs with AuQDs was changed due to the oxidative etching of AgNPs with  $\text{H}_2\text{O}_2$ . Under normal conditions, this change was considered the basic principle of detection in this study. In another study, Huang and co-workers,<sup>68</sup> implemented Ag@Au nanoprisms-MOF for rapid, sensitive, single-use, and quantitative glucose in human serum and urine. For this purpose, Ag@Au nanoprisms increased phosphorescence intensity through metal-enhanced phosphorescence. The reported biosensor operated based on the dual functionality consisting of oxygen consumption for glucose determination and using an enhancement technique. In detail, the biosensing approach exhibited rapid response (0.5 s), a low detection limit (0.038 mM), and a wide linear range (30 mM to 0.05 mM). Similarly, Chan and colleagues,<sup>69</sup> used enhancing ability of AgNPs for increasing CdSe QDs photoluminescence *via* photobrightening in  $\text{Cu}^{2+}$  quantification. The enhanced photoluminescence intensity of CdSe QDs was selectively quenched in the presence of the target. This simple methodology offered a rapid and reliable detection of  $\text{Cu}^{2+}$  with a LOD of as low as 5 nM and a dynamic range of up to 100  $\mu\text{M}$ .

In conclusion, AgNPs have played a significant role in improving the performance of developed luminescence sensors by taking the plasmonic properties of AgNPs into account. According to the few numbers of luminescence sensors based

on AgNPs, there is a requirement of foundation attention for future developments in this field.

### 3.4. Electrochemical probes based on AgNPs

Electrochemical methods, as powerful analytical techniques, have attracted considerable attention in sensing. In general, these techniques operated based on converting chemical information of interaction into electrical signals. The implementation of AgNPs, as promising high-performance materials, on the sensing zone of electrochemical sensors improves the performance of sensing by increasing conductivity and surface area. Importantly, these nanomaterials demonstrate high potential for capturing various biomolecules.<sup>79,80</sup> This phenomenon can be used to immobilize different bioreceptors to improve selectivity of electrochemical sensors. One of the brilliant examples of using AgNPs in electrochemical biosensor for detection of microRNA-153 (miR-153), which is important biomarker for diagnosis of Parkinson's disease, in human plasma was reported by Darvish and co-workers.<sup>70</sup> The modification of glassy carbon electrode (GCE) with poly-chitosan (CS) and conductive matrix, containing AgNPs, graphene quantum dots (GQDs), and cysteamine A (Cys A), introduced an efficient substrate for immobilization of DNA. The conjugation of this bioreceptor with miR-153 changed the electrochemical signal which measured by differential pulse voltammetry (DPV) with a lower limit of quantification of 6.25  $\mu\text{M}$ . The integration of GQDs, with high functionalize and biocompatible properties, in the structure of AgNPs could improve attachment of DNA. This concept was developed in another paper-based electrochemical immunosensor for identification of lymphatic vessel endothelial hyaluronan receptor-1 (LYVE-1). This biomarker is a promising biomarker in various cancers including lung, gastric, liver, and breast cancers. The detection principle of this protocol relied on the construction of antigen-antibody complex on the surface of modification paper electrode with GQD-AgNPs conductive ink. The reported immunoassay showed two linear ranges including 20–320 pg  $\text{mL}^{-1}$  and 0.625–10 pg  $\text{mL}^{-1}$ .<sup>71</sup>

Recently, a sensitive and selective electrochemical sensor for trichloroacetamide (TCAM) detection in drinking water based on triangular AgNPs and  $\text{MoS}_2$  nanosheets was reported by Fang *et al.*<sup>72</sup> In this context, AgNPs and on the edge of  $\text{MoS}_2$  nanosheet catalyzed the dechlorination reaction of TCAM and absorbed  $\text{H}^+$ , respectively. In the presence of the target, AgNPs@ $\text{MoS}_2$  demonstrated a high degree of charge transfer rate, good stability, and high electrocatalytic activity.

In conclusion of this section, it is important to point out that, future research may focus on developing integrated systems that enable sample processing, and multiplexed analysis. Indeed, integration with emerging technologies such as AI and machine learning (ML) can enhance analytical capabilities and enable predictive modeling for personalized disease care. They play an important role in real-time monitoring, introducing user-friendly platforms, optimization of sensor design, signal enhancement, presenting predictive modeling, and data analysis. In favor of real-time monitoring, continuous data



analysis and anomaly detection can achieve based on immediate feedback, which can be analyzed by AI, and ML algorithms, respectively. Moreover, pattern recognition by AI algorithms and feature extraction by ML can improve data analysis.<sup>81,82</sup>

The review of developed sensing platforms based on AgNPs in Table 2 demonstrated that the vast majority of reported platforms operated by colorimetric assay. In this regard, smartphones have played an important role in these platforms. However, the shortage of electrochemical and other optical methods can be filled by integration of these methods with cutting-edge technology in sensing and biosensing. Indeed, the significance of microfluidics systems, Internet of Thing (IoT), and AI is undeniable. The application of these materials can be received more attention due to their stability in harsh environment. Interestingly, these materials can be used as carriers of bioreceptors. Hence, the application AgNPs is in the early stages and it can be boosted in the future.

## 4. Marketing evaluation

Although there has been a growing interest in AgNPs and their biomedical applications, the introduction of promising technology based on AgNPs in the global healthcare market encounters multiple obstacles. The market growth can be attributed to increased demand for the development of simple, sensitive, selective, portable, and semi-automatic analytical devices, which can provide direct quantification of biomarkers in biological samples without the need to sample preparation. With the continuous advancement of the field of application AgNPs in sensing, the incorporation of intelligent systems such as smartphones and AI can boost their performance.

## 5. Conclusions and future perspective

As discussed, AgNPs stand out due to their remarkable properties, such as extensive surface area, chemical robustness, and tunable electrical conductivity, making them excellent candidates for biomedical purposes. By tailoring these nanomaterials through strategic bulk functionalization or surface engineering, their multifunctionality can be enhanced, unlocking new opportunities for their application in areas such as diagnosis, imaging, and therapeutic interventions. In this review, recent advancements in analytical methods utilizing AgNPs, categorized by sensing mechanisms such as optical and electrochemical approaches, were highlighted in the context of diagnostics. The review then surveyed their application in various biomedical treatments, including photothermal therapy, radiation therapy, and immunotherapy, which demonstrate precision and targeted efficacy. Lastly, the challenges and future prospects of bringing AgNP-based technologies to commercialization and integrating them into disease diagnostics and medical treatment are explored. In summary, the application of AgNPs in sensors have introduced high potential analytical approaches due to their physical and

chemical properties. Although, in many cases, nanomaterials have been used for improving the performance of sensing platforms, AgNPs have presented a new class of progress due to their specific features. These materials have acted in different roles in sensors for various purposes including biomedical analysis, environmental monitoring, and food safety analysis. Most of the developed sensors based on AgNPs operated by colorimetric technique and there are few optical and electrochemical sensors based on AgNPs. There is a massive shortage in developing electrochemical and other types of optical sensors. Although colorimetric sensors enjoy affordability and simplicity, the low sensitivity is their most important limitation. In this light, developing electrochemical and other optical sensors can introduce highly sensitive, multiplex, and real-time sensing platforms. In addition, these analytical approaches have high potential for portability which can be used for point-of-care (POC) analysis devices. Along with specific physical and chemical properties of AgNPs, the stability of AgNPs is another key point which can be used for fabrication portable sensing devices that can be operated in harsh conditions. However, various environmental conditions, mechanical stability, chemical interferences, and biological factors can effect their stability and the performance. In order to mitigation these factors, materials engineering, which can coat the protective materials, robust sensor design, environmental control, and functionalization of surfaces are important strategies. Interestingly, the recognition of functionalized groups of these nanomaterials can open a new window for introducing new modification AgNPs and hybrid nanomaterials with better properties. These nanomaterials can be used for multiplex detection in both electrochemical and optical sensors. This concept can be achieved by applying different techniques including using selective bioreceptors/receptors in the structure of these materials, designing different sensing zones, using dual-mode and triple-mode arrays, and using advanced data analysis techniques. The development of enzyme-mimicking nanozymes based on AgNPs is another significant pathway can be attracted considerable attention in the future. Furthermore, biocompatibility or toxicity concerns associated with AgNPs in biomedical applications, particularly *in vivo* diagnostics or therapeutics are another significant matter must be taken into account in the future works. Accepting the fact that standardization, reproducibility, stability, scalability, specificity, and integration with analytical tools are addressed in an appropriate way, AgNPs will hold critical promise for commercial and clinical applications. In addition, regulatory challenges, such as lack of clear guideline, safety and toxicity challenges, and data requirements for approval, as well as cost-related challenges, including market competition and funding for development, are significant challenges in bringing AgNPs-based biosensors to the global healthcare market.

## Data availability

All relevant data supporting the findings of this study are available within the article. Access to some data is restricted due to privacy or ethical restrictions.



## Conflicts of interest

There are no conflicts to declare.

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