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REVIEW ARTICLE

Recent progress in optical nanosensors for antibiotics detection

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Abstract
Water covers more than two-thirds of the earth's surface, but only around 0.3% is suitable for human use. Water sources are highly polluted with various chemicals, heavy metals, and agricultural wastes. The quick and precise assessment of these contaminants in the water is one of the most important aspects of environmental monitoring. Antibiotics are one of the emerging groups of persistent organic pollutants in aquatic ecosystems due to their uncontrolled release and overuse. This review highlights important optical sensing techniques and analytical tools for onsite antibiotic monitoring in water samples that are simple to use and require minimal sample preparation. The integration of nanomaterials with these optical technologies has helped with exceptional detection capability and good stability due to their unique optical properties. In particular, this review summarizes surface plasmon resonance, colorimetry, fluorescence, surface-enhanced Raman spectroscopy-based detection, and their realization toward the chip and optical fiber-based sensors development. The characteristics and advantages of various nanomaterials for antibiotic detection, their mechanism of action, and future trends are discussed in detail. The insights of this review article will be informative and guide the researchers to develop advanced optical sensors for antibiotic detection.

Keywords Antibiotic detection · Optical sensor · Metal nanoparticle · Localized surface plasmon resonance · Fluorescence · Surface-enhanced Raman spectroscopy

Introduction

The use of antibiotics has significantly increased in recent decades, and hence, it has emerged as one of the major environmental pollutants (Liu and Wong 2013). Antibiotics are widely used in the pharmaceutical, aquaculture, cattle, and agricultural sectors. (Lipsitch et al. 2002; Dixit and Park 2014; Schar et al. 2020; Shao et al. 2021). As a result, the soil and surrounding water sources get contaminated. Antibiotic abuse is also prevalent in animal husbandry to promote growth and increase the performance of livestock. There is also a major concern regarding the presence of antibiotics residue at various levels in milk which gets transferred from lactating animals when they are administered with antibiotics. Antibiotics are neither completely metabolized nor absorbed by the human/animal body after administration; approximately 90% of the residues of each dose are defecated through urine, and 75% of the remainder is removed by feces (Sarmah et al. 2006; Zuccato et al. 2010). These unmetabolized compounds are disposed of in the hospital and domestic effluents, and some of them are discarded in sewage water treatment plants until they reach waterways, ponds, seas, rivers, and groundwater (Moldovan 2006; Lapworth et al. 2012). Aquaculture is another significant cause of environmental pollution by antibiotics, which contributes to the contamination of different layers of water such as surface and groundwater and sediment due to the utilization of antibiotics as fish food additives to increase growth and prevent disease (Hossain et al. 2017; Pham-duc et al. 2019). Pharmaceutical industries are also one of the major environmental contamination sources due

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to the disposal of effluents generated throughout the synthesis, processing, and filing of antibiotics or their residue (Santos et al. 2010). Antibiotics in all of these natural environments, even at ultra-low level, can affect the survival, reproduction, and metabolism of populations of organisms, as well as alter the structure of communities and ecological functions of ecosystems, and they can also cause alteration in important microbial processes for the ecosystems, such as nitrogen conversion, methanogenesis, sulfate reduction, nutrient cycle, and deterioration of organic matter (Martinez 2009; Comero et al. 2013; Bielen et al. 2017; Grenni et al. 2018; Martin-Laurent et al. 2019). Since the widespread and constant consumption of antibiotics has a direct relation to their occurrence in the environment, it has aroused a growing global concern demanding their precise detection.

According to a global survey reported in 2018, the use of antibiotics has increased by 39% in the entire world from 2000 to 2015, and it was predicted that the worldwide antibiotics usage in 2030 might be 200% higher than that in 2015 without effective policy control (Klein et al. 2018). Each year, more than 2.8 million antimicrobial-resistant infections occur in the USA alone, leading to more than 35,000 fatalities (CDC 2019). According to predictive statistical models, there were approximately 4.95 million deaths all over the world related to bacterial antimicrobial resistance in 2019, with 1.27 million of those deaths directly attributed to bacterial antimicrobial resistance.

The lack of knowledge, inappropriate usage, and misuse of antibiotics result in sustainable side effects and human health risks including disruption of gut microbiota. Further, antibiotic residues in the environment have the potential to generate antibiotic-resistant genes and antibiotic-resistant bacteria, which pose serious public health risks and threats by causing diseases (Dong et al. 2020; Lyu et al. 2020). Although antibiotic resistance might occur spontaneously due to microbial adaptability to their surroundings, it has been suggested that this resistance is growing as a result of excessive usage and improper disposal of antibiotics. According to the World Health Organization, the existence of antibiotic-resistant genes and antibiotic-resistant bacteria is acknowledged as one of the most concerning public health issues of the century (Zarei-Baygi et al. 2019). The condition might have worsened due to the substantial use of antibiotics during the current COVID-19 pandemic. The generic symptoms (such as fever and/or cough) of COVID-19 overlapping with those of malaria and tuberculosis (TB) have caused misdiagnosis and/or inappropriate prescribing of certain antibiotics, impacting the drug-resistant level of these pathogens causing the infectious diseases (Knight et al. 2021).

Numerous approaches are available for the detection of antibiotics including gas chromatography, high-performance liquid chromatography (Zhang et al. 2019), liquid chromatography/mass spectroscopy (Kawano et al. 2014), microbiological methods (Breton et al. 2007), electrochemical methods (Zhu et al. 2012), capillary electrophoresis (Fanali 1996) and enzyme-linked immunosorbent assays (Yu et al. 2017). A few of these have displayed the ability to perform simultaneous detection and quantification of antibiotics. However, these approaches usually require expensive/large apparatus, skilled operators, and time-consuming, laborious procedures. In addition, some of these techniques suffer from low selectivity, low sensitivity, lack of field deployability, and real-time monitoring potential.

Over the last two decades, optical strategies for antibiotic recognition have fascinated more attention owing to their fast response, high sensitivity, high specificity, easy miniaturization, cost-effectiveness, ability to couple with readout platforms, free from electrical interference, and ease of multiplexing. The integration of the nanomaterial has further improved detection sensitivity with high specificity due to their unique nanoscale properties such as size-shape tunable localized surface plasmon resonance (LSPR), high surface area-to-volume ratio, high extinction coefficient and photoelectric properties (Cao et al. 2014; Yadav et al. 2019; Yaghubi et al. 2020; Maan and Satija 2022). This review summarizes the current state of the art of nanomaterial-based optical detection of antibiotics in water. Different sensing approaches based on surface-enhanced Raman spectroscopy (SERS), colorimetry, and fluorescence phenomena along with their integration with fiber optic and microchips-based platforms have been discussed. The insights into the reaction mechanism for specific antibiotic detection and sensor performance are elaborated. Further, the main challenges and future research directions for antibiotic detection are discussed.

LSPR and SPR-based nanosensors

In recent years, LSPR-based colorimetric sensors have been extensively investigated to detect a wide range of analytes by employing plasmonic nanoparticles as the probe. The properties of nanoparticles, such as charge and interparticle distance, are affected by the oppositely charged antibiotics. The interaction of nanoparticles with these antibiotics results in a decrease in interparticle distance and/or neutralization of their surface charge leading to aggregation and prominent color change or LSPR wavelength as summarized in Table 1. Based on this principle, an aggregation-based strategy has been successfully developed for the detection of neomycin in water samples by employing citrate-capped, negatively charged gold nanoparticles (AuNPs) as the color indicator (Apyari et al. 2013). The reaction is based on the fact that electrostatic repulsion among the AuNPs decreases in the presence of some positively charged moieties and thereby

Table 1 Overview of the LSPR-based optical sensors for antibiotics detection

Nanoparticle	Antibiotic	Color change	Plasmonic wavelength change	LOD	References
AuNPs	Neomycin	Red to blue	520 to 700 nm	45.55 nM	Apyari et al. (2013)
AuNPs	Gentamicin	Red to blue	520 to 600 nm	12.45 nM	Gukowsky et al. (2018)
AgNPs	Amoxicillin	Yellow to red	No peak shift; peak broadening	4.46 µM	ul Ain et al. (2018)
AuNPs	Spiramycin	Colorless to multicolor	Appearance of new peaks at 520 to 560 nm	0.18 µM	Leng et al. (2019)
AgNPs	Gentamicin	Yellow to light pink	No peak shift; peak broadening	0.29 µM	Ul Ain et al. (2019)
AgNPs	Streptomycin	Yellow to orange/red	400 to 560 nm	36 pM	Ghodake et al. (2020)
AuNPs	Naproxen	Red to blue	520 to 650 nm	2.61 nM	Khodaveisi et al. (2017)
AuNPs	Ciprofloxacin	Red to blue to gray	No peak shift	36.2 nM	Springer et al. (2019)
AuNPs	Kanamycin	Pink to white	No peak shift	2.5 nM	Abedalwafa et al. (2020)
AuNPs	Kanamycin	Red to blue-purple	No peak shift	10 pM	Zou et al. (2021)

AuNPs gold nanoparticles, AgNPs silver nanoparticles

triggers the aggregation of the dispersed nanoparticles (Fig. 1). This leads to a change in the LSPR peak and color of the colloidal solution from ruby red to blue. Since neomycin is an aminoglycoside antibiotic with a positive charge, it triggers the aggregation of negatively charged citrate-capped AuNPs. This results in a shift in the LSPR peak from 520 to 700 nm, while the solution color turns from ruby red to blue. In order to reduce the interference from metal cations, the authors suggested the pre-treatment of the sample with ethylenediaminetetraacetic acid (EDTA) as a masking agent. This strategy could successfully detect the neomycin in ear drops and eye drop solutions with a detection limit of 28 ng/mL. In another similar approach, AuNPs aggregation-based assay has been realized to detect gentamicin with a detection limit of 12.45 nM (Gukowsky et al. 2018). Gentamicin has hydroxyl and aliphatic amine groups and thus has a strong hydrogen-bonding capacity. Upon exposure to cysteamine-capped AuNPs (amine–terminated), gentamicin exhibits a high affinity for AuNPs through hydrogen bonding interactions and thereby induces interparticle cross-linking. In addition, the electron-rich nitrogen-containing ligand of gentamicin directly coordinates with the surface of AuNPs and promotes the aggregation of AuNPs. As a result, the absorption peak of colloidal AuNPs shifts from 520 to 600 nm with a simultaneous color change from red to blue. By employing the same principle, an aggregation-based assay has been developed for ciprofloxacin detection by utilizing sucrose-capped negatively charged AuNPs (Springer et al. 2019).

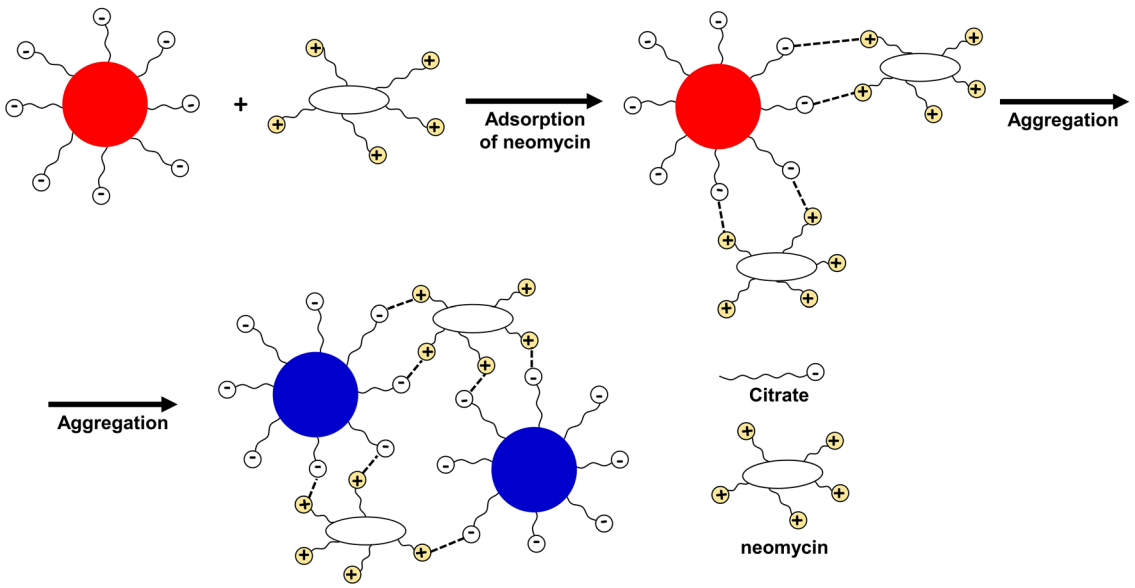

Fig. 1 Neomycin triggered aggregation of citrate-capped AuNPs. Reprinted from Ref. Apyari et al. (2013). Copyright (2013), with permission from Elsevier

In another approach, an aggregation-based assay was developed for the detection of amoxicillin by utilizing quercetagetin flavonoid-coated silver nanoparticles (Qt-AgNPs) (ul Ain et al. 2018). Since quercetagetin possesses six hydroxyl groups, upon interaction with amoxicillin, hydrogen bonds are formed between the hydroxyl group of Qt-AgNPs and the hydroxyl and amine groups of amoxicillin. This induces the aggregation of the nanoparticles, and the solution color changes from yellow to red with a prominent redshift. This approach could achieve the detection limit of 4.46 µM for amoxicillin. In the same way, methyl gallate-stabilized AgNPs (Ul Ain et al. 2019) and gallic acid-stabilized AgNPs (Ghodake et al. 2020) could be successfully utilized to detect gentamicin and streptomycin with a detection limit of 0.29 µM and 36 pM, respectively.

In an interesting approach, thiolated β-cyclodextrin (Tβ-CD) functionalized AuNPs (Tβ-CD-AuNPs) have been developed to selectively detect naproxen antibiotics (Khodaveisi et al. 2017). The sensing was based on the fact that Tβ-CD-AuNPs form aggregates in the presence of naproxen and Zn^{2+} ions. The Tβ-CD, present at the AuNP surface, acts as a lipophilic cavity and thus reacts with the hydrophobic end of naproxen to form the Tβ-CD-naproxen complex, while the carboxylic group of naproxen interacts with Zn^{2+} ions, yielding $(naproxen)_2Zn$ (Fig. 2). This eventually triggers the aggregation of functionalized AuNPs with a shift in the LSPR band from 520 to 650 nm as a function of naproxen concentration. A visible color change from red to blue helps in the visual detection of naproxen. This strategy could achieve the limit of detection (LOD) and quantification of 2.61 nM and 9.12 nM, respectively.

Recently, a functional array has been developed for colorimetric determination and discrimination among the different antibiotics, particularly, chlortetracycline, amoxicillin, erythromycin, neomycin, gentamicin, lincomycin, spiramycin, and thiamphenicol by utilizing the distinctive colors of AuNPs (Leng et al. 2019). This approach was based on the synthesis of multi-colored AuNPs via interlocking ring formation by virtue of the transfer of Au^+ ions from proteins to antibiotics. The rapid nucleation creates the multi-colored AuNPs in the rings which range in various sizes (Fig. 3). The "three color" (RGB) principle was utilized as the foundation of this detection technique where each antibiotic displayed distinct color response pattern that could be quantitatively distinguished using statistical methods. A LOD of 0.18 µM was achieved by this array for spiramycin detection.

Translational efforts have been made by developing colorimetric biosensor strips for kanamycin detection (Abedalwafa et al. 2020). Herein, kanamycin-selective aptamer-immobilized electrospun nanofiber membranes (Apt-NFMs)

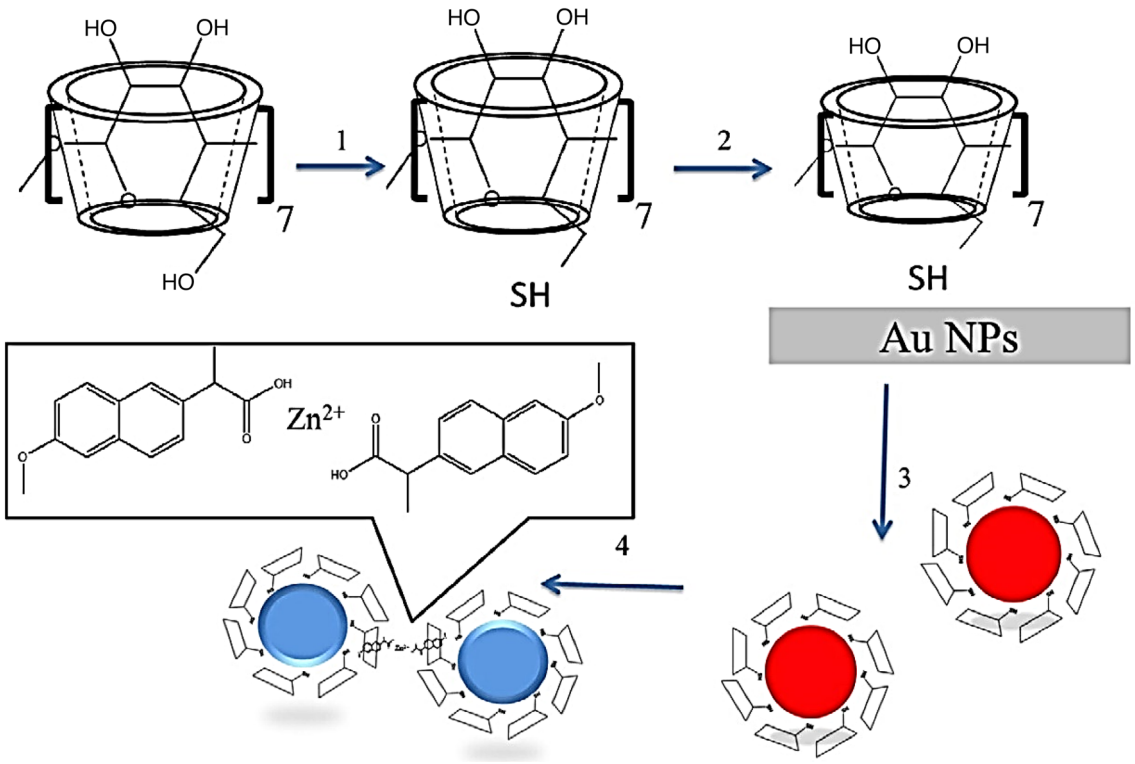

Fig. 2 Schematic diagram illustrating the aggregation of functionalized Au-NPs by naproxen in the presence of Tβ-CD and Zn^{2+} ions. (1) Thiolation of β-CD; (2) Mixing of thiolated β-CD and AuNPs; (3) Formation of thiolated β-CD capped AuNPs; (4) Aggregation of AuNPs. Reprinted from Ref. Khodaveisi et al. (2017). Copyright (2017), with permission from Elsevier

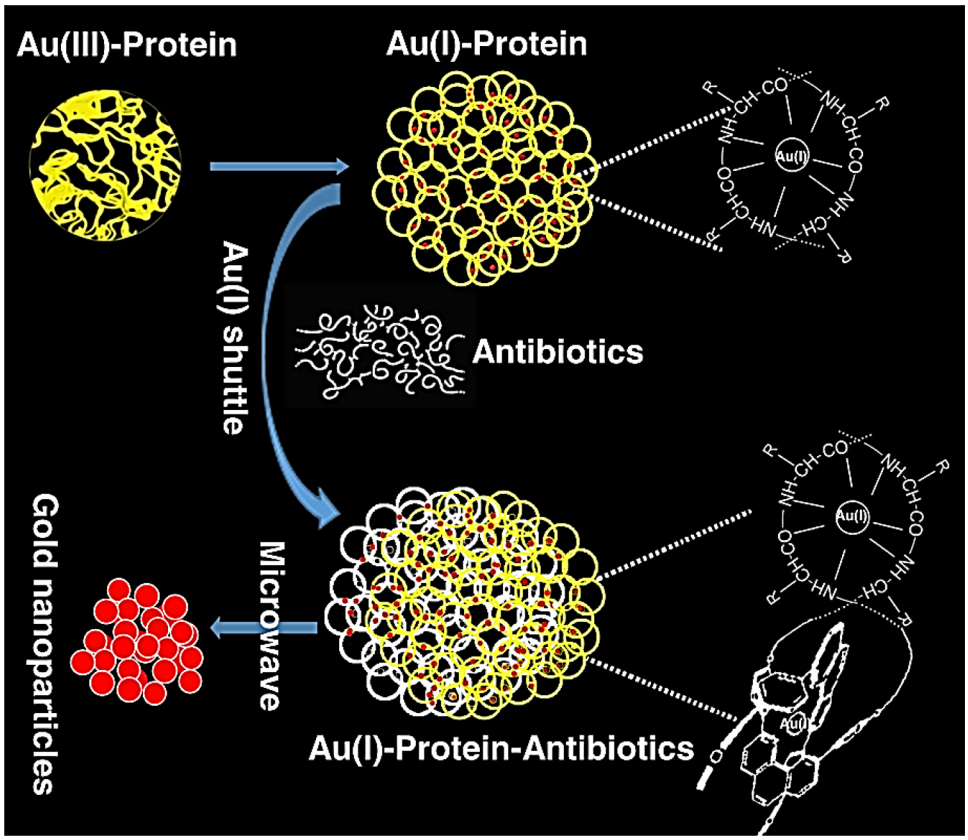

Fig. 3 Schematic representation of the synthesis of sub-10-nm AuNPs via the formation of interlocking rings in proteins and antibiotics. Reproduced with permission from Springer Nature (Leng et al. 2019), Copyright (2019)

were used as capture substrate while DNA-conjugated AuNPs (cDNA-AuNPs), which are complementary to the aptamer, served as a signal probe. In the presence of kanamycin, cDNA@Au dissembles from Apt-NFMs because the aptamer has a greater affinity for kanamycin than its corresponding cDNA-AuNPs, which causes kanamycin to displace cDNA@Au (Fig. 4). A color change from red to white with a spectral shift of LSPR helps in the quantification of

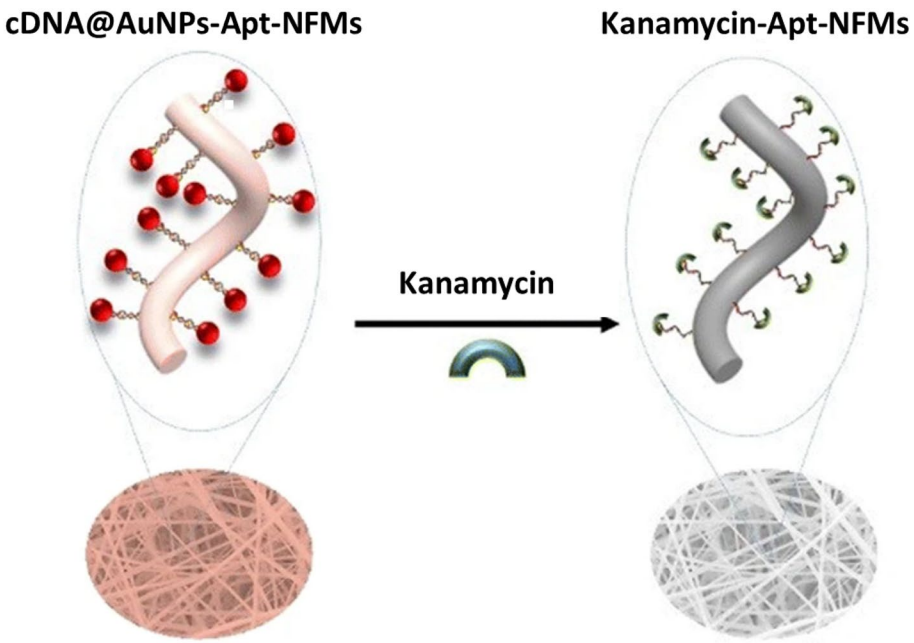

Fig. 4 Schematic illustration of kanamycin detection strategy using aptamer-immobilized electrospun nanofiber membranes. Reproduced with permission from Springer Nature (Abedalwafa et al. 2020), Copyright (2020)

kanamycin, and under the optimized condition, this membrane could achieve the 2.5 nM detection limit.

Similar to LSPR, various SPR-based sensors have also been reported to detect antibiotics (Table 2). For example, AuNP-enhanced surface plasmon resonance-based sensing approach has also been attempted to detect antibiotics (Frasconi et al. 2010). In this approach, first, AuNPs were functionalized with electropolymerizable thioaniline groups and (mercaptophenyl) boronic acid. Boronic acid offers ligation sites for the assemblage of several antibiotic substrates due to vicinal diol functionalities. Bisaniline cross-linked AuNPs composites are produced when the functionalized AuNPs are electropolymerized on the surfaces of Au film (SPR substrate) in the presence of neomycin, kanamycin, or streptomycin. An antibiotic-specific molecularly imprinted pattern was obtained after the removal of antibiotics (Fig. 5). The coupling between the localized plasmon of the nanoparticle and the surface plasmon wave connected to the Au surface enhances the SPR responses. The LOD for the developed sensor was found to be 2.00 ± 0.21 pM, 1.00 ± 0.10 pM, and 200 ± 30 fM for neomycin, kanamycin, and streptomycin, respectively. High-affinity nano-molecularly imprinted polymers (Nano-MIPs) selective for ciprofloxacin, moxifloxacin, and ofloxacin have also been employed to develop SPR-based optical sensors (Sullivan et al. 2022). The functionalized MIP-based SPR sensor has been reported to achieve a detection limit of 39.3 nM, 26.1 nM, and 42.7 nM for ciprofloxacin, moxifloxacin, and ofloxacin, respectively. Similarly, the SPR-based sensor has been developed by some other research groups for the detection of erythromycin (395.1 pM) (Sari et al. 2016), amoxicillin (73 pM) (Ayankojo et al. 2018), and ciprofloxacin (9.688 nM in ultrapure water and 21.428 nM in synthetic sewage water) (Sari et al. 2018).

To obtain detection in the attomolar range, a new sandwich assay for tetracycline detection has been developed by using a DNA aptamer and antibody with the aid of gold nanostars (AuNSs) enhanced SPR (Kim and Lee 2017). In this assay, an aptamer-functionalized Au chip is treated with a tetracycline spiked water sample followed by treatment with the antibody-AuNSs conjugate. In the presence of tetracycline, an aptamer-tetracycline-antibody-AuNSs complex forms that enhance the SPR response while quantifying the amount of tetracycline (Fig. 6). The detection limit of tetracycline was found to be 10 aM with good selectivity.

Fluorescence-based nanosensors

Unique optical properties of various nanomaterials have also been exploited to develop fluorescence or quenching-based sensors for trace-level detection of various antibiotics (Table 3) (Kailasa et al. 2022). For instance, fluorescent silicon nanoparticles (SiNPs) have been utilized for the successful detection of tetracycline (Lin and Wang 2015). The fluorescent property of SiNP is significantly influenced by the presence of the amino ($–NH_2$) group as the lone pair of electrons in the transitional state between the organic and inorganic phases would be responsible for the photoluminescence. When these SiNPs interact with tetracycline, the drug binds with the amino groups, resulting in quenching in the emission peak intensity (Fig. 7). This label-free SiNPs-mediated sensing approach could selectively detect tetracycline, oxytetracycline, and chlortetracycline down to 25.9 nM, 20.4 nM, and 28.3 nM, respectively. A similar strategy was reported by Xu et al. 2017 for the detection of oxytetracycline as the electronegative hydroxyl group of oxytetracycline strongly interacts with electropositive SiNPs (Xu et al. 2017). This causes the quenching in blue emission (436 nm) of SiNPs resulting in the switching of SiNPs fluorescence from blue emission (436 nm) to green emission (502 nm). The LOD of the developed sensor was determined to be 0.18 μM.

Table 2 Overview of the SPR-based optical sensors for antibiotics detection

Nanoparticle/Film	Antibiotic	LOD	References
AuNPs@Au	Neomycin Kanamycin Streptomycin	2.00 pM 1.00 pM 200 fM	Frasconi et al. (2010)
MIP@Au	Erythromycin	395.1 nM	Sari et al. (2016)
Nano-MIPs@Au	Amoxicillin	73 pM	Ayankojo et al. (2018)
Nano-MIPs@Au	Ciprofloxacin Moxifloxacin Ofloxacin	39.3 nM 26.1 nM 42.7 nM	Sullivan et al. (2022)
Nano-MIPs@Au	Ciprofloxacin	9.69 nM (water) 21.43 nM (SSW)	Sari et al. (2018)
AuNPs@Au	Tetracycline	10 aM	Kim and Lee (2017)

AuNPs gold nanoparticles, *Nano-MIPs* molecularly imprinted polymer nanoparticles, *SSW* synthetic sewage water

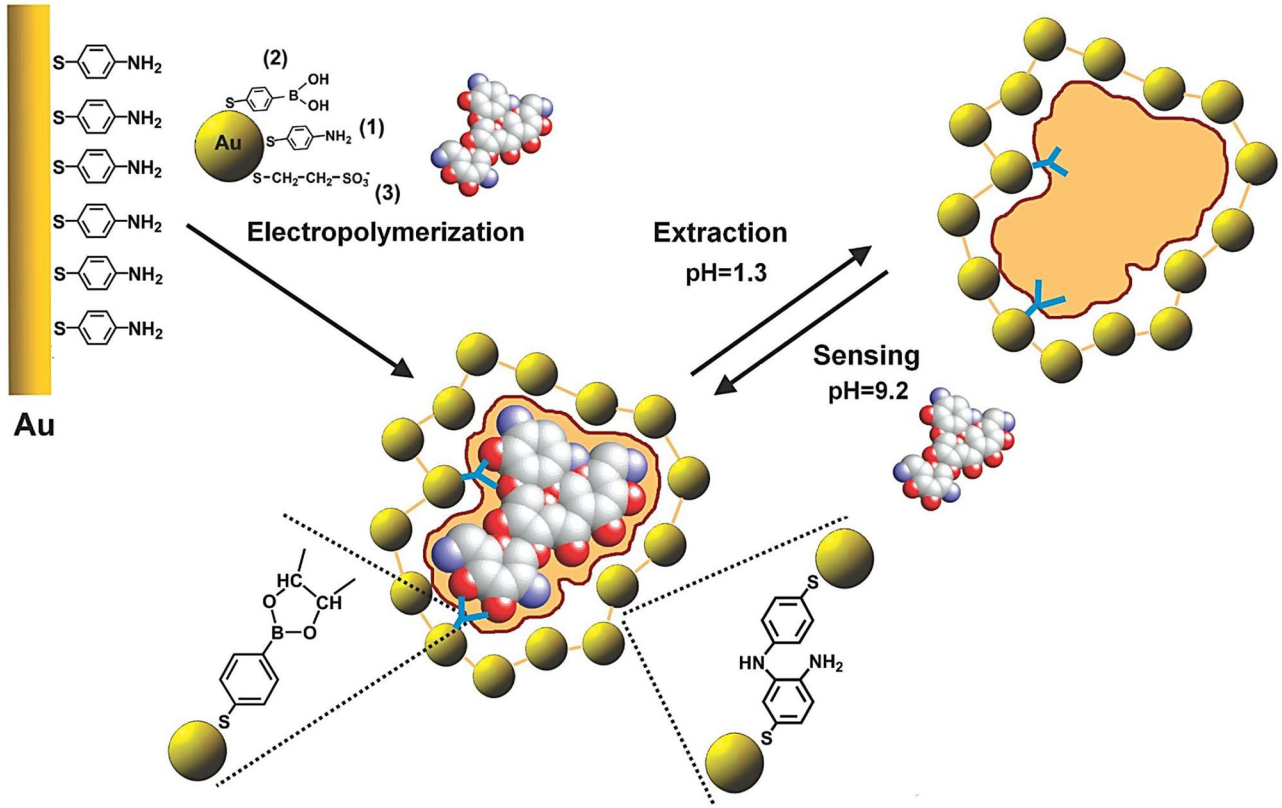

Fig. 5 Imprinting of molecular recognition sites for antibiotic substrates (for example, neomycin) through the electro-polymerization of a bisaniline cross-linked AuNP composite on an Au surface. Reproduced with permission from (Frasconi et al. 2010). Copyright (2010), American Chemical Society

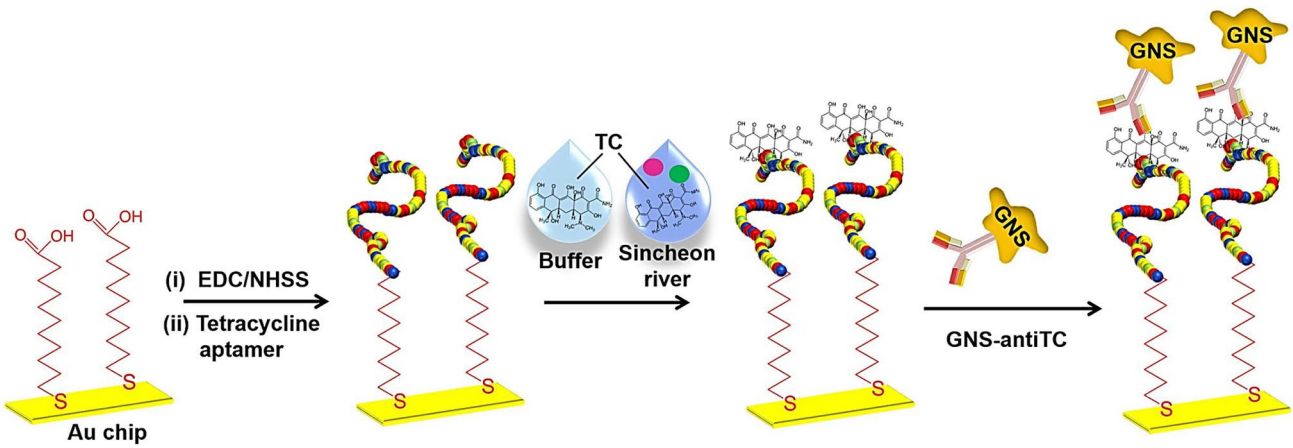

Fig. 6 Schematic overview of the strategy for tetracycline detection. The tetracycline aptamer was first immobilized on an SPR chip, followed by the covalent attachment of aptamer probes. The tetracycline sample was interacted at the sensor surface and followed by the binding of gold nanostar-antibody conjugate for further SPR signal amplification. Reproduced with permission from (Kim and Lee 2017). Copyright (2017), American Chemical Society

In another approach, a levofloxacin sensor has been developed using highly luminescent N- and S-co-doped carbon dots (NSCDs) as a ratiometric fluorescent probe (Li et al. 2018). The NSCDs have a narrow size distribution and exhibit strong blue fluorescence with excitation/emission peaks at 353 and 426 nm, respectively. The UV absorption

Table 3 Overview of the fluorescent nanosensors for antibiotic detection

Nanoparticle	Antibiotic	LOD	References
SiNPs	Tetracycline Oxytetracycline Chlortetracycline	25.9 nM 20.4 nm 28.3 nM	Lin and Wang (2015)
SiNPs	Oxytetracycline	0.18 µM	Xu et al. (2017)
NSCDs	Levofloxacin	14.11 nM	Li et al. (2018)
MIPs@SiO_2-FITC	Ciprofloxacin	4.04 nM	Wu et al. (2018)
N-CQDs	Tetracycline Terramycin Chlortetracycline	0.23 µM 0.37 µM 0.28 µM	Qi et al. (2019)
MOF	Tetracycline Doxycycline Oxytetracycline Chlortetracycline	2.7 nM 2.7 nM 2.6 nM 4.5 nM	Li et al. (2020a)
RAlNS	Tetracycline	0.12 nM	Bai et al. (2020)
Cd-MOF/Tb^{3+}	Cefixime	26.7 nM	Qin et al. (2021)
AuNPs	Carbendazim	2.33 nM	Su et al. (2020)
B-CQDs	Amoxicillin	0.82 µM	Zhang et al. (2020)
MRFNs	Tetracycline Chlortetracycline	0.58 µM 0.07 µM	Si et al. (2020)
AuNCs	Tetracycline	4 nM	Li et al. (2020b)
MIN-s@PEGDA	Ciprofloxacin	6.86 µM	Huang et al. (2021)
AuNPs	Sulfamethazine	2.95 nM	Wang et al. (2021)
AgNPs	Vancomycin	0.19 nM	Mohamed (2022)
MHNTs@FMIPs	Oxytetracycline	8.1 nM	Wang et al. (2022)

SiNPs silicon nanoparticles, *NSCDs* N- and S-co-doped carbon dots, *RAINS* rhombic like Al nanosupporter, *B-CQDs* boron doped carbon quantum dots, *MRFNs* Maillard reaction fluorescent nanoparticles, *AuNCs* gold nanocluster, *MIN-s@PEGDA* molecularly imprinted nanoparticles composite polyethyleneglycol diacrylate hydrogel, *MHNTs@FMIPs* molecularly imprinted magnetic halloysite nanotubes

band of levofloxacin and NSCDs have a similar wavelength; hence, the lowest empty molecular orbital of levofloxacin can accept an electron from the conduction band of NSCDs, this electron transfer results in the quenching of fluorescence of NSCDs. Further, levofloxacin exposure causes the emission maxima to shift to 499 nm and a visible fluorescence color change is observed from bright blue to green when kept under 365 nm UV light. The developed sensor could achieve the 5.1 µg/L detection limit.

Recently, a fluorescence resonance energy transfer-based label-free fluorescent aptasensor was developed for the quantitative detection of sulfamethazine using AuNPs and rhodamine B (Wang et al. 2021). The detection principle is based on the prevention of NaCl-mediated aggregation of the AuNPs by means of adhering of the sulfamethazine-specific aptamer (SMZ1S). As a result, AuNPs remain dispersed in the colloidal solution and efficiently quench the fluorescence of rhodamine B. In the presence of sulfamethazine antibiotic, it specifically binds with aptamer and thereby results in the NaCl-driven aggregation of the AuNPs in a concentration-dependent manner. As a result, the fluorescence quenching ability of the AuNPs is substantially reduced and a linear increase in the fluorescence intensity of rhodamine B is observed with the increase in sulfamethazine concentration. The proposed fluorescent aptasensor showed an excellent linear detection range of sulfamethazine from 4.49 nM (1.25 ng/mL) to 143.71 nM (40 ng/mL) with a limit of detection of 2.95 nM (~ 0.82 ng/mL).

Recently, boron-doped carbon quantum dots (B-CQDs)-based fluorescent sensor has been developed to detect amoxicillin (Zhang et al. 2020). The amoxicillin molecule has amine, hydroxyl, and carbonyl groups that strongly interact with the B-CQDs probe through intermolecular hydrogen bonds. The B-CQDs exhibit an intense blue fluorescence and the fluorescence signal intensity of the B-CQDs-amoxicillin system is linearly amplified as amoxicillin concentration increases. The enhancement in the fluorescence signal was ascribed to amoxicillin-mediated effective separation of B-CQDs that eventually diminishes their nonradioactive transition or amoxicillin serving as ligands in the B-CQD-amoxicillin system to improve the B-CQDs' fluorescence properties by reducing defects. The limit of detection of the sensing system was determined to be 0.825 µM. In another approach, green synthesized Maillard reaction fluorescent nanoparticles (MRFNs) were successfully employed for the quantitative detection of tetracycline and chlortetracycline (Si et al. 2020). The Maillard process, also known as the "non-enzymatic browning reaction", is when sugar reacts with amino acids, dipeptides, or tripeptides to form colored compounds. In aqueous solutions, MRFNs exhibit high intrinsic fluorescence. A linear rise in the chlortetracycline concentration led to a significant increase in the fluorescence intensity of MRFNs, however, the intensity of MRFNs drastically dropped linearly as the tetracycline concentration gradually increased. Authors suggested that the internal filtration effect or fluorescence resonance energy transfer is the possible cause of the tetracycline's fluorescence quenching impact on MRFNs. In contrast, chlortetracycline has one additional chlorine atom compared to tetracycline, which may be a suitable leaving group due to the simple fracture of C–Cl, which would allow chlortetracycline to readily establish covalent bonds with MRFNs and increase their fluorescence intensity. In addition, the energy loss caused by excited electrons returning to the ground state is decreased as the stiffness of the molecular structure increased. This sensing modality could achieve a limit of detection value of 0.579 µM and 0.076 µM for tetracycline and chlortetracycline, respectively.

A MIP-based fluorescent sensor was developed for the detection of ciprofloxacin in a water sample (Wu et al. 2018). Polyacrylamide-based MIP was conjugated on FITC

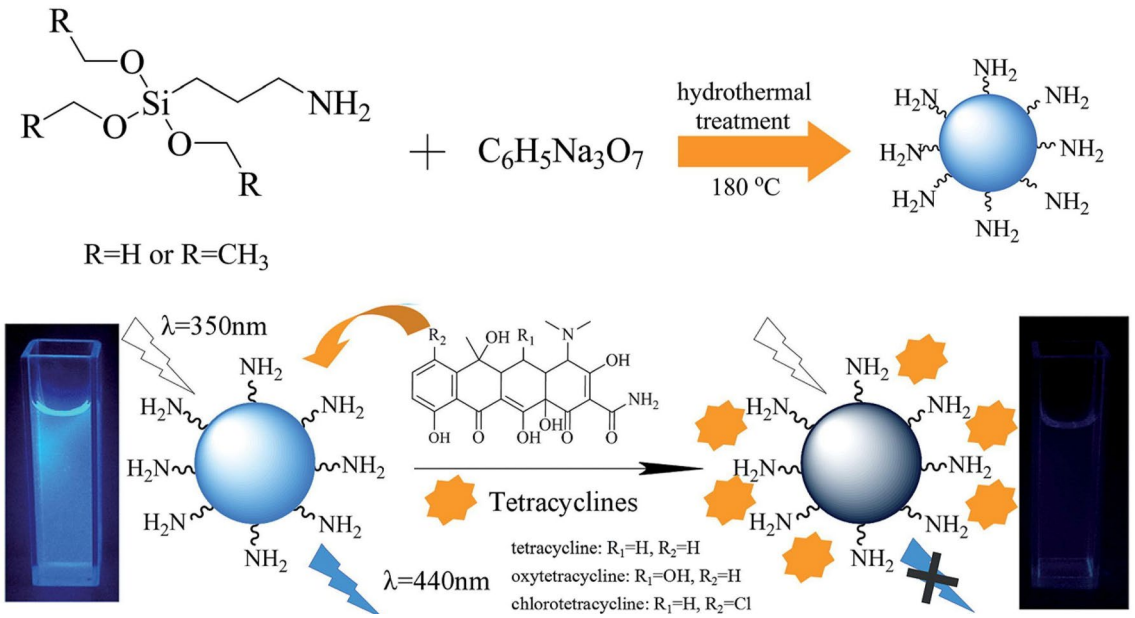

Fig. 7 Schematic representation of the synthesis of fluorescent silicon nanoparticles (SiNPs) and the mechanism of fluorescence quenching by tetracyclines. Photo: silicon nanoparticles in PBS solution (pH 7.4) excited by UV light at 365 nm without (left) and with (right) 10 mM of tetracycline. Reproduced from Ref. Lin and Wang (2015), with permission from The Royal Society of Chemistry

imprinted SiO_2 nanoparticles that serve not only as ciprofloxacin binding sites but also facilitate the interaction with the drug in the aqueous sample due to its hydrophilic nature. The binding of ciprofloxacin to these functional nanomaterials results in quenching of fluorescence that could detect the drug as low as 4.04 nM (Fig. 8). In a similar line, a fluorescent quenching-based approach has been utilized to develop an optical nanosensor for the detection of tetracycline (Qi et al. 2019). In this approach, nitrogen-doped carbon quantum dots (N-CQDs) were employed as a fluorescent probe that shows quenching upon interaction with tetracycline, terramycin, and chlortetracycline. Since the chemical

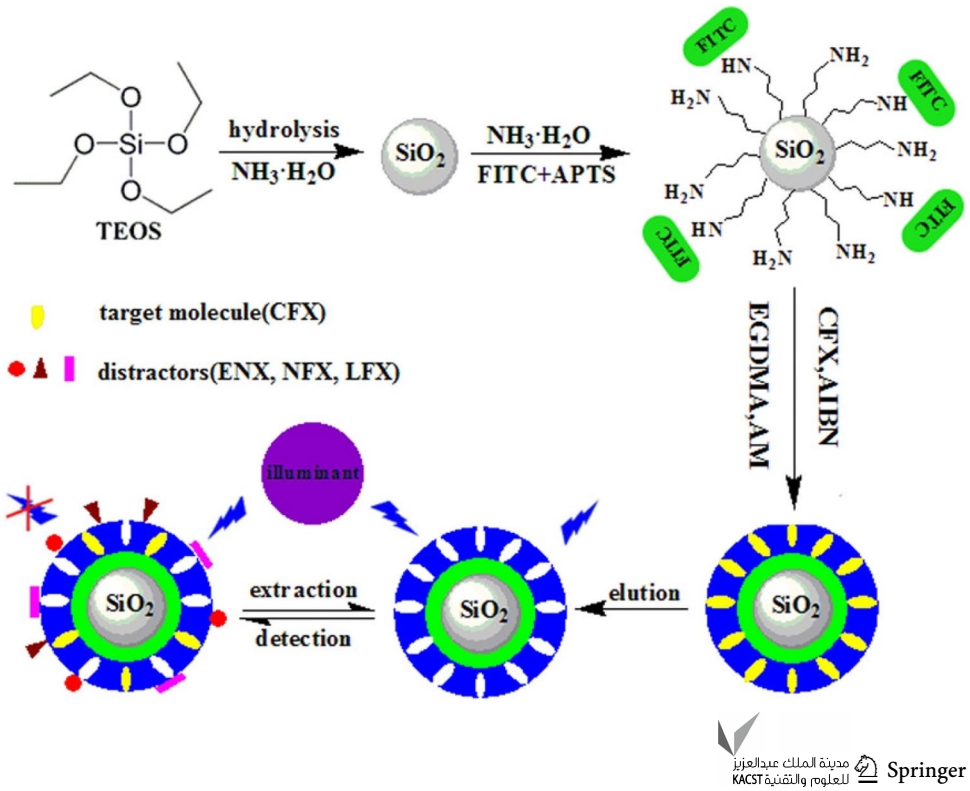

Fig. 8 Diagrammatic representation for the preparation of MIPs@SiO_2-FITC and fluorescence-based detection of ciprofloxacin. Reproduced with permission from John Wiley & Sons, Inc., from Ref. Wu et al. (2018)

structures of tetracycline, terramycin, and chlortetracycline are similar and thus access the same recognition sites resulting in quenching of the fluorescence of quantum dots. The antibiotic concentration was found to be inversely proportional to the fluorescent intensity and the LOD values for tetracycline, terramycin, and chlortetracycline were estimated to be 0.2367, 0.3739, and 0.2791 μM, respectively.

Fluorescence-based lateral flow immunoassay (FLFIA) has also been developed for the detection of tetracycline from aqueous samples by employing fluorescent rhombic-like Al nanosupporter (RAINS) (Bai et al. 2020). In this study, the lateral flow assay strip was designed by treating the sample pad and conjugating pad with a blocking buffer followed by functionalization of the test area with tetracycline and BSA and the control area with immunoglobulin G (IgG) antibody. For the analysis of tetracycline, the antibody-conjugated RAINS was incubated with the sample and then added to the sample pad which migrates to the test and control areas due to capillary action. If tetracycline is present in the sample, it binds with the antibody-RAINS conjugates and thereby prevents the binding of RAINS at the tetracycline-coated test region, but it binds at the IgG-coated control region; hence a fluorescent line appears on the control, which indicates the presence of tetracycline. If the sample is free of tetracycline, the free antibody-RAINS conjugate binds with the tetracycline in the test region and with the IgG in the control area, which results in the generation of a fluorescent signal in both the test region and the control region (Fig. 9). The developed RAlNS-FLFIA strip could achieve a 0.0516 ng/mL detectable limit.

Recently, cadmium-metal–organic frameworks/terbium ion (Cd-MOF/Tb^{3+}) fluorescent nanosheets have been developed for the specific detection of cefixime in the aqueous sample (Qin et al. 2021). The authors reported that the photo-induced electron transfer and inner filter effect due to the interaction of cefixime and Cd-MOF/Tb^{3+} nanosheets cause absorption of the excitation energy of Cd-MOF/Tb^{3+}, which eventually diminishes or quenches the fluorescence. The MOF-based fluorescent nanosheet could efficiently detect the cefixime as low as 26.7 nM within 20s. In another study, a fluorescent aptasensor has been developed that uses AuNPs and rhodamine B as indicators and a carbendazim-specific aptamer as the sensing probe to specifically detect the drug in the aqueous solution (Su et al. 2020). The carbendazim-specific aptamer wraps the AuNPs through van der Waals force and keeps them essentially dispersed in the NaCl solution. The excitation maxima of these well-dispersed AuNPs overlap with the emission spectra of fluorescent dye rhodamine B and thus act as an efficient quencher. In the presence of carbendazim, the aptamer forms a stable complex with the drug, leaving the AuNPs exposed to NaCl solution and thereby inducing agglomeration (Fig. 10). As a result, the aggregated form of AuNPs absorption peak shifts to a higher wavelength and loses its fluorescence quenching ability as a function of carbendazim concentration. By differentiating the fluorescence intensity, the concentration of carbendazim could be measured quantitatively in a linear range of 2.33–800 nM with a LOD of 2.33 nM.

In an interesting approach, a ratiometric fluorescent sensor has been developed for sensitive and selective detection of tetracycline (Li et al. 2020b). This sensor utilizes L-histidine-capped gold nanoclusters (AuNCs) and europium ions (Eu^{3+}) as fluorescence indicators. The L-histidine of AuNCs has carboxyl groups that combine with Eu^{3+} ions through electro-attractive interaction. The AuNCs-Eu^{3+} system exhibits robust fluorescence emission from the AuNCs at 475 nm and modest fluorescence from Eu^{3+} at 620 nm when excited at 375 nm. When this system interacts with tetracycline, the drug forms a stable complex with Eu^{3+} which results in quenching of the fluorescence of AuNCs, while enhancing the 620 nm emission peak of Eu^{3+}. This AuNCs and Eu^{3+}-based ratiometric fluorescent sensor could detect the tetracycline up to 4 nM.

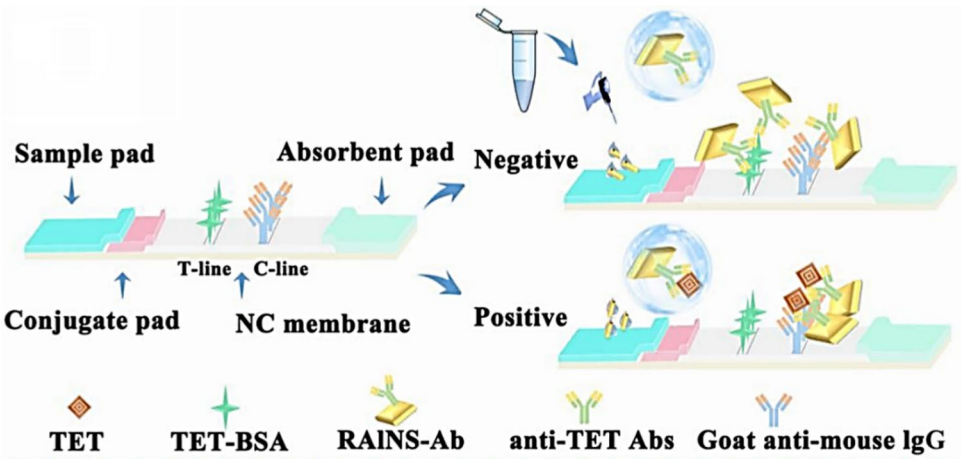

Fig. 9 Fluorescence-based lateral flow immunoassay for the rapid detection of tetracycline. *TET* tetracycline, *BSA* bovine serum albumin, *RAINS* rhombic-like Al nanosupporter, *NC* nitrocellulose). Reprinted from Ref. Bai et al. (2020). Copyright (2020), with permission from Elsevier

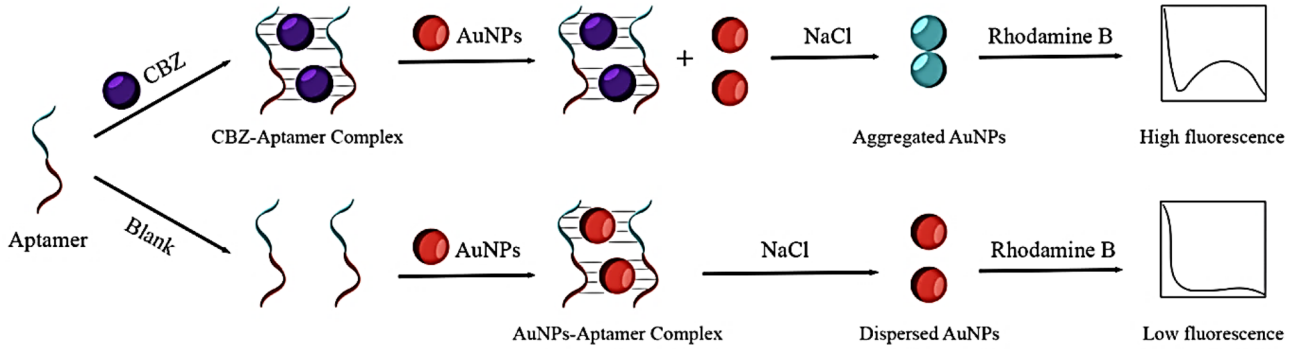

Fig. 10 Schematic of the fluorescence assay for carbendazim (CBZ) detection in aqueous solution based on gold nanoparticles (AuNPs)-mediated quenching of the fluorescence of rhodamine B. Reprinted from Ref. Su et al. (2020). Copyright (2020), with permission from Elsevier

Surface-enhanced Raman spectroscopy-based nanosensors

Nanomaterials-based SERS-substrates have also been extensively studied for the ultra-low level detection of various target molecules including antibiotics owing to their high sensitivity and characteristic fingerprinting structural information (Thu et al. 2022). A variety of SERS substrates have been developed by combining the noble metal nanoparticles of gold and silver with specific organic Raman reporter molecules (Table 4). For example, a SERS-based sensor has been reported for the qualitative detection of penicillin G in water samples (Pinheiro et al. 2017). For this, colloidal AuNPs were adsorbed onto cubic-shaped ferromagnetic nanoparticles resulting in the formation of a strong magnetic-plasmonic structure. The developed nanostructures showed prominent electromagnetic field enhancement (enhancement factor > 10^{10}) and thus could detect penicillin G. In another study, Yue Tian et al. reported the utilization of bimetallic Au@Ag core–shell nanorods for SERS-based detection of levofloxacin (Tian et al. 2018). For the Raman spectroscopic analysis, the antibiotic was incubated with Au@Ag core-shells nanorods followed by centrifugation and separation of antibiotic-interacted nanorods. The presence of bimetallic nanorods significantly enhanced the signals with amplification in the signal intensity observed at 1614 cm^{-1} when measured with an excitation of 633 nm. The developed sensing strategy could detect levofloxacin up to 1 pM.

To make SERS-based detection easy, Wang et al. (2019) proposed to combine the membrane separation technology and SERS phenomenon for the sensing of enrofloxacin hydrochloride in water. To demonstrate this, AgNP-based SERS imprinted membranes (ASIMs) were designed by employing AgNPs as SERS-substrate, poly(vinylidene fluoride) membranes as the support material, acrylamide and ethylene glycol dimethacrylate as functional monomer and cross-linker, respectively, to create MIP against enrofloxacin hydrochloride. This substrate could selectively bind with enrofloxacin hydrochloride and detect up to 100 nM. In a different approach, the use of slippery SERS substrates has

Table 4 Overview of the SERS-based nanosensors for antibiotic detection

Nanoparticles	Antibiotic	LOD	References
AuNRs, Au@AgNRs	Levofloxacin	1 pM	Tian et al. (2018)
AgNPs	Enrofloxacin	100 nM	Wang et al. (2019)
AuNRs	Ciprofloxacin Norfloxacin	30.18 nM 31.3 nM	Usman et al. (2019)
AuNPs	Tetracycline	1 nM	Alwan et al. (2020)
AgNPs/PDA/MS	Ciprofloxacin Enrofloxacin	1.05 nM 0.99 nM	Wang et al. (2020a, b)
AuNSs	Tetracycline	90 pM	Qian et al. (2020)
AgNPs, β-$AgVO_3$ NRs	Chloramphenicol	100 pM	Barveen et al. (2021)
AgNDs	Tetracycline	1 nM	Pagano et al. (2021)
AgNSs	Ciprofloxacin	0.69 nM	Thu et al. (2022)

AgNDs silver nanodisk, *AgNPs* spherical silver nanoparticles, *AuNPs* Spherical gold nanoparticles, *AuNRs* gold nanorod, *AuNSs* gold nanostar, *Au@Ag NRs* bimetallic Au@Ag core–shell nanorod, *β-$AgVO_3$ NRs* silver vanadate nanorods, *LOD* limit of detection

been suggested for the ultra-sensitive detection of ciprofloxacin and norfloxacin (Usman et al. 2019). A superhydrophobic slippery SERS substrate was formed on the glass slide by a coating of octadecyl trichlorosilane and Polydimethylsiloxane liquid followed by drop-casting of silicone oil and annealing at 150 ℃ for 90 min (Fig. 11). This was followed by drop casting of AuNRs which organize on the substrate as a superlattice array because of good hydrophobicity and low energy of the surface. For the quantification, norfloxacin and ciprofloxacin drug-containing sample is deposited on the AuNRs-deposited slippery substrate which displays the characteristic Raman signal of norfloxacin and ciprofloxacin at 1380 cm^{-1} and 1391 cm^{-1} which gradually increases with the concentration of the drug. Throughout the droplet's evaporation, the antibiotic molecules occupy space in the gaps of the AuNRs superlattice array forming a "hot spot" for Raman signal recognition, allowing for the detection of norfloxacin and ciprofloxacin at a concentration as low as 31. 3 nM and 30.18 nM, respectively.

Recently, an effective SERS substrate has been developed for the detection of tetracycline by depositing AuNPs on the macroporous silicon (macroPSi) surface (Alwan et al. 2020). The macroPSi, having a high density of dangling bonds (Si–H), were fabricated by photoelectrochemical etching at room temperature. This was followed by in situ AuNPs coating by immersing the macroPSi substrates in the aqueous solution of gold chloride and hydrofluoric acid which resulted in Au^{3+} ions reduction by the Si–H dangling bonds and their aggregate formation as potential hot-spots. These substrates could achieve the detection limit of 1 nM with a 2×10^8 enhancement factor.

Qian et al. (2020) developed a Raman immunochromatographic assay (ICA) strip for the SERS-based detection of tetracycline. In this approach, 4-aminothiophenol (ATP)-modified AuNSs conjugated with anti-tetracycline monoclonal antibody (ATP-AuNSs-anti-tetracycline-mAb) were used as nanotag. In the nitrocellulose strip membrane, the goat anti-mouse immunoglobulin G and tetracycline-cationic bovine serum albumin (tetracycline-cBSA) were discretely dispersed to form the control line and test line, respectively. In the absence of an antibiotic, the sample flows from the sample pad to the absorption pad, the ATP-AuNSs-anti-tetracycline-mAb conjugates with the tetracycline-cBSA in the test line, and a gray line appears due to the aggregation of AuNSs. In contrast, in the presence of the tetracycline, ATP-AuNSs-anti-tetracycline-mAb forms immunocomplex with tetracycline molecules and thus would not be able to interact with the tetracycline-cBSA in the T zone. Hence, the color intensity of the T line decreases as the concentration of tetracycline in the sample increases, while no gray line is observed in the T zone, after a certain level of antibiotic concentration. Since goat anti-mouse IgG is complementary to mouse IgG, and because of their affinity toward anti-tetracycline-mAb, the ATP-AuNSs-anti-tetracycline-mAb binds with the IgG coated on the control line. As a result, a gray line is developed on the control line both in the presence and absence of tetracycline (Fig. 12). The SERS signal

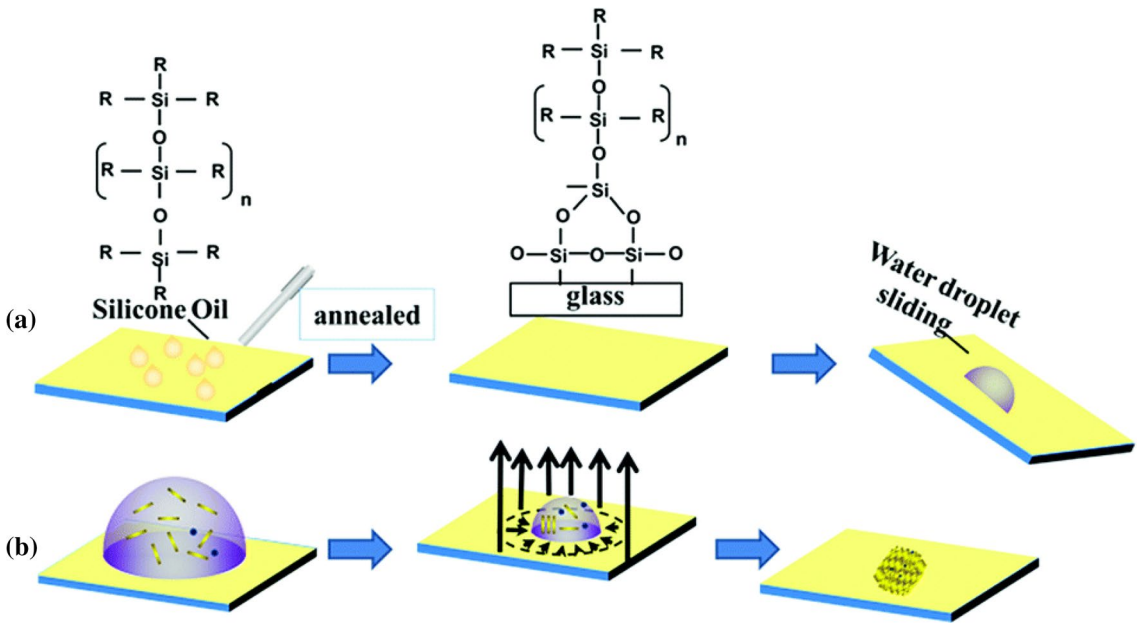

Fig. 11 Schematic of **a** the fabrication steps of slippery surface with the chemical structure of silicone oil and its bonding with the glass substrate and **b** the enrichment and concentration of Au nanorods and analyte molecules by an evaporation process. Reproduced from Ref. Usman et al. (2019), with permission from The Royal Society of Chemistry

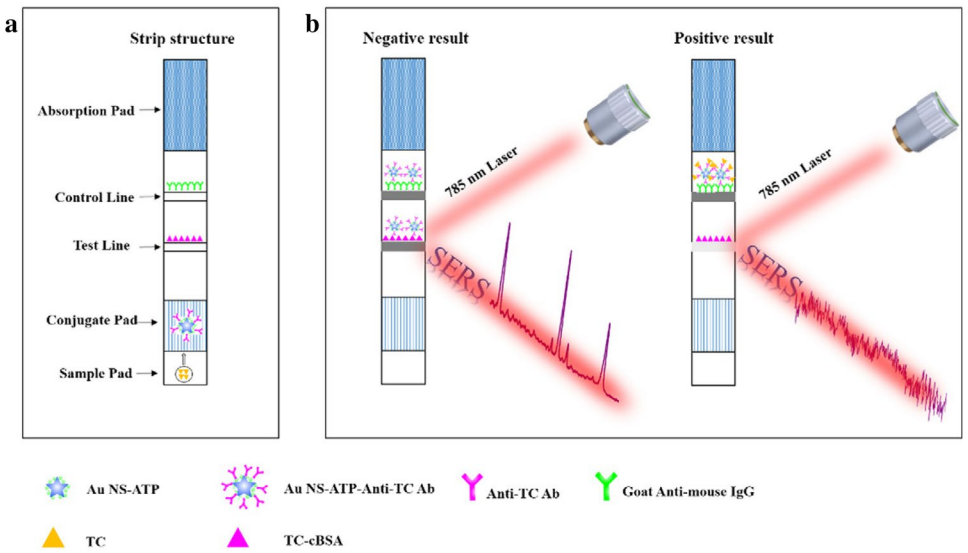

Fig. 12 Schematic illustration of AuNSs tag based SERS-immunochromatographic assay (ICA) sensing strip for tetracycline detection. (**a**) sensing strip structure and (**b**) tetracycline detection strategy. Reprinted from Ref. (Qian et al. 2020). Copyright (2020), with permission from Elsevier

measurement reveals a significant decrease in intensity with the increase in tetracycline concentration, and under optimized conditions, this approach could determine the LOD of 90 pM.

Recently, an innovative heterogeneous SERS substrate was developed for chloramphenicol antibiotic detection by employing AgNPs on silver vanadate nanorods (β-$AgVO_3$ NRs) (Barveen et al. 2021). The SERS substrate was fabricated in two steps: (i) immobilization of β-$AgVO_3$ NRs on the flat glass substrate and (ii) followed by a coating of AgNPs on these glass substrates via photo-induced in situ synthesis. This heterogeneous AgNPs and β-$AgVO_3$ NRs-based substrate significantly increased the Raman signal intensity toward the detection of chloramphenicol molecules with an analytical enhancement factor as high as 2.05×10^8 and a detection limit of 100 pM.

To improve the applicability of SERS-based antibiotic detection, functional SERS platforms have been developed using filter paper as a support material due to its high porosity, low-cost, flexible nature, and biodegradability along with an additional advantage of improved sampling efficiencies, direct in situ and on-site detection capability. Pagano et al. (2021) developed a filter paper-based SERS substrate was developed by using LSPR properties of silver nanodisks (AgNDs) for the sensing of tetracycline. The AgNDs-impregnated filter paper enabled the fast and easy analysis of tetracycline in water samples by simply drop casting and drying the sample on this support. The developed paper substrate allowed the tetracycline detection down to 1 nM concentration in an aqueous solution. Similarly, SERS-based detection of ciprofloxacin has been demonstrated by employing silver nanostars (AgNSs) coated on aluminum foil (AgNSs@Al-foil) with a detection limit of 0.694 nM and Raman enhancement factor up to 4×10^9. (Thu et al. 2022).

Chip-based optical nanosensors

The development of a field deployable portable sensor with high sensitivity and low turnaround time is the need of the hour for the detection of antibiotics in water. In recent years, lab-on-a-chip systems have been widely studied for biosensing, which results in shorter analysis time, low sample volumes, high throughput, and portability. The basic principle of chip-based optical nanosensors is to measure any refractive index changes occurring due to the specific binding events between immobilized bioreceptors on a thin metallic film-coated optical substrate and the target analyte. Significant efforts have been made toward the development of antibiotics detection chips in the past decade (Table 5). The first attempt to develop a microflow injection system using a chemiluminescence-based antibiotic detection was successfully demonstrated by Sierra et al. (Sierra-Rodero et al. 2012). In this study, aminoglycoside antibiotics like neomycin, streptomycin, and amikacin could specifically be detected in the water samples with dynamic detection limits of 0.3–3.3, 0.9–13.7, and 0.8–8.5 µM, respectively. The technique relies on the inhibitory action of antibiotics on the reaction of luminol and hydrogen peroxide catalyzed by Cu^{2+} ions. This microfluidic setup demonstrated improved detection limits as compared to conventional microflow injection systems.

The use of aptamers as bioreceptor molecules in sensors has been widespread owing to their specific binding ability to the analyte of interest, and stability in a wide range of temperatures and pH. Blidar et al. (2019) functionalized an Au chip using thiol-terminated aptamers as a biorecognition layer, followed by mercaptohexanol as a blocking agent through multipulse amperometry. The sensor was subjected to SPR tests which could detect even minor changes in

Table 5 Chip-based optical nanosensors for antibiotics detection

Antibiotics	Sensing materials	Sensing method	LOD	References
Neomycin Streptomycin Amikacin	Cu(II)-catalyzed Chemiluminescence	Chemiluminescence	0.09 µM 0.28 µM 0.24 µM	Sierra-Rodero et al. (2012)
Ampicillin	Gold nanofilm	SPR	1 µM	Blidar et al. (2019)
Gentamicin	Luminesce reporter protein (NanoLuc)	Luminescence	0.46 µM	Matsuura et al. (2019)
Streptomycin; Kanamycin	Enzyme-embedded metal–organic framework	Colorimetry	1.54 pM 0.7 pM	Wang et al. (2020b)
Sulfamethoxazole	poly(MAA-HEMA-EGDMA)	SPR	4.34 pM	Kurç and Türkmen (2022)

refractive index near the surface and demonstrated a wide detection range of 2.5–1000 µM with a LOD of 1 µM. This SPR-based aptasensor was successfully employed to detect ampicillin in river water and showed to be selective for ampicillin detection with minimal interference from other antibiotics and medications. In another study, MIP-based enhanced Au SPR chips were created for sulfamethoxazole detection (Kurç and Türkmen 2022). These synthetic receptors (MIPs) are extremely stable and have specific binding sites for their targets which is desirable for a sensor. In the presence of the analyte of interest, a change in mass due to the binding events causes a proportional increase in refractive index which induces SPR signals. The sensor response could be obtained from sulfamethoxazole spiked water for the concentration range of 0.025–253.2 µg/L with a LOD and limit of quantification of 0.0011 µg/L and 0.0034 µg/L, respectively. The study was further extended to detect sulfamethoxazole in real samples such as commercial milk, in the presence of antagonistic antibodies (amoxicillin and cephalexin).

The usage of paper-based sensors including a system of intricate biomolecular networks or synthetic gene circuits based on synthetic biology has been suggested recently. Hideyuki Matsuura et al. developed a one-pot paper-based bioassay using a luminesce reporter protein (NanoLuc) and a cell-free in vitro transcription/translation system which could detect aminoglycoside (Matsuura et al. 2019). Metal–organic frameworks are an emerging class of biocompatible polymers used for biomolecule encapsulation (for sensing, storage, catalysis, and drug delivery) and have shown promise for antibody conjugation and subsequent biomedical applications (Wang et al. 2017). In a study reported by Wang et al. (2020a, b), horseradish peroxidase (HRP) was used as a transduction material embedded into the porous structure of metal-azolate framework-7 (MAF-7) over which aptamers were uniformly coated as a recognition layer. 3,3′,5,5′-Tetramethylbenzidine (TMB) impregnated chip was attached to a tube cap as shown in (Fig. 13). Due to oxidation of colorless TMB to its blue-green oxidized form, oxTMB, a substantial color signal is obtained and quantified using colorimetry. Streptomycin and kanamycin could be detected using this MOF-based sensor with a LOD of 0.51 and 0.34 pg/mL, respectively. This colorimetric sensor also demonstrated a wide dynamic range of 0.005–6 ng/mL and 0.5–300 pg/mL for streptomycin and kanamycin, respectively.

Optical fiber-based nanosensors

In recent years, optical fibers have been widely used for the detection of a wide range of analytes in water and other samples. Optical fibers possess the advantages of miniaturization and flexibility toward structural modification for improved sensitivity and assay design. Huang et al. (2021) designed a Y-shaped fiber connected to a laser light source, spectrometer, and detector which could detect ciprofloxacin to a limit of 6.86 µM from environmental water samples. The sensor surface was modified with a molecularly imprinted nanoparticle (MIN) (produced using ciprofloxacin molecule as a template) and a hydrogel consisting of polyethyleneglycol diacrylate (PEGD) (Fig. 14). The ciprofloxacin molecules bound to the cavities of the MIN at the sensor surface emitted fluorescence signal when excited by a 400 nm laser light source. This fluorescent signal is transmitted back to the Y-type fiber and reaches the spectrometer through a filter which eliminates the interferences from the laser light source.

In another study by the same group, they developed a ratiometric fluorescent sensor using Y-type fibers to selectively detect ciprofloxacin (Yuan et al. 2022). The fluorescence quenching property of CdTe quantum dots coupled with glutathione and mercaptopropionic (GMPA@CdTe-QDs) in the presence of ciprofloxacin molecules was utilized. The detector region of the Y-type fiber was dipped in a quartz cuvette having solutions of GMPA@CdTe-QDs with different concentrations of ciprofloxacin and the fluorescent intensity at 440 nm and 710 nm were picked up through a spectrometer at other ends of the fiber. The LOD achieved for ciprofloxacin was 0.90 µM. This portable sensor has the advantage of on-field deployment for real water sample analysis of ciprofloxacin such as in aquaculture.

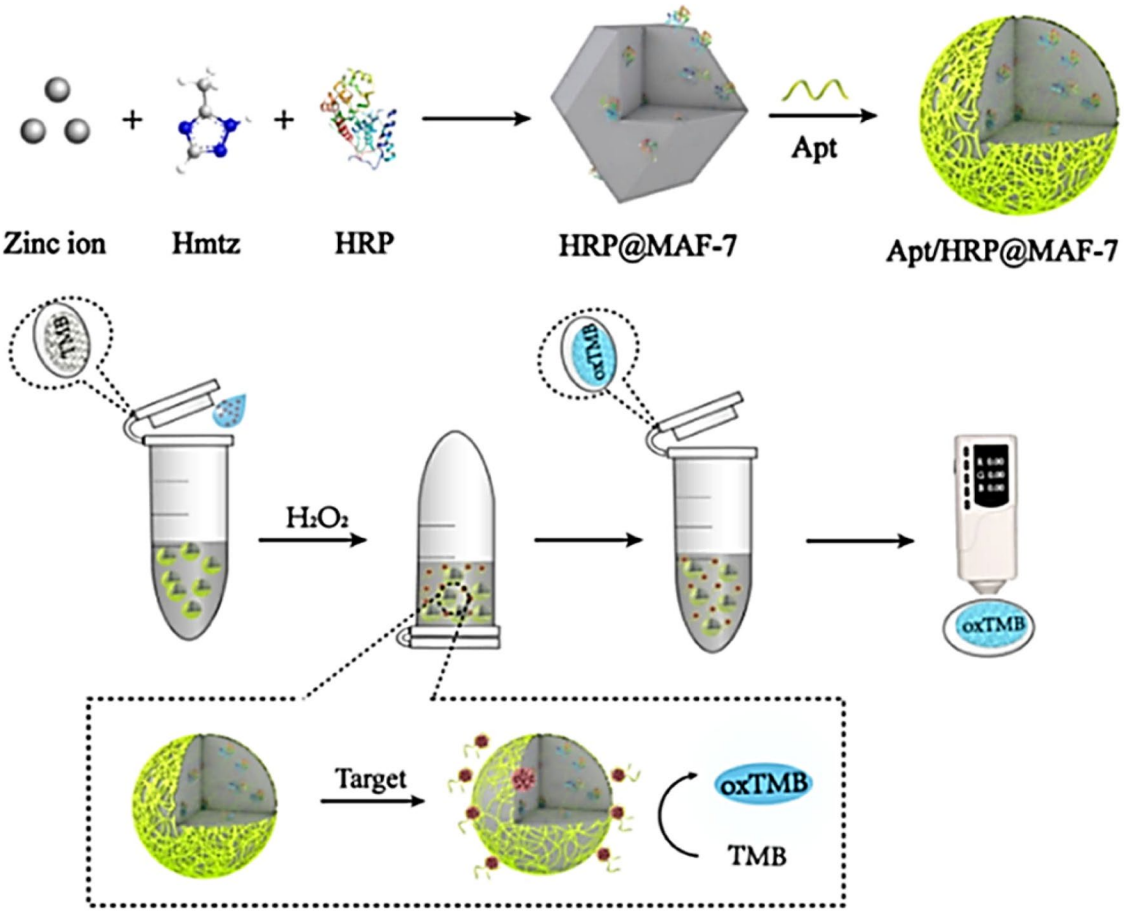

Fig. 13 Illustration of the MOF-based sensor fabrication along with the principle of the colorimetric sensor. Reproduced with permission from Wang et al. (2020a, b). Copyright (2020), American Chemical Society

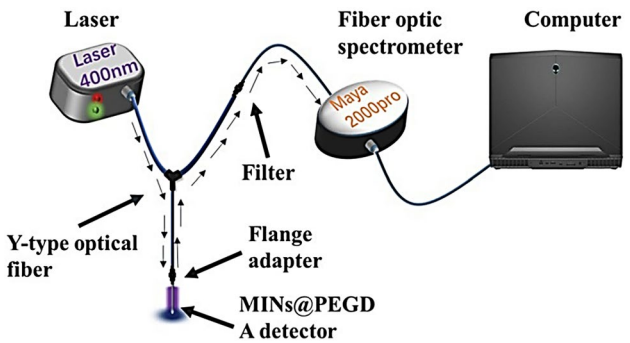

Fig. 14 Molecularly imprinted Y-shaped fluorescent optical sensor with detector modified with MINs@PEGD. Reprinted from Ref. Huang et al. (2021). Copyright (2021), with permission from Elsevier

Nanomaterials such as carbon nanotubes (CNT) can increase the sensitivity and improve the limit of detection by increasing the adsorption capacity of a particular antibiotic. Pathak et al. (2018) immobilized hydroxylated CNTs onto silver layer modified silica unclad optical fiber for the detection of sulfamethoxazole. Amine groups of sulfamethoxazole selectively bind with –OH terminated CNTs via π–π electron exchange mechanism which changes the refractive index around the optically active silver medium over the fiber surface. The sensor works in the dynamic range of 0–200 µM of sulfamethoxazole with a LOD of 0.892 µM. Recently, micro-structured hollow fiber (MHF) bundles with minimal light loss have been explored to enhance the Raman signal obtained from low concentration analyte (Hanf et al. 2014). In this direction, Teng et al. (2021) silanized the suspended core of an MHF fiber and immobilized AgNPs over the surface to realize the SERS effect (Fig. 15). Whenever a trace amount of analyte, ciprofloxacin, and norfloxacin, enters the microfluidic sensor, it interacts with the evanescent field caused due to SERS substrate on the suspended core. The Raman signal generated due to this interaction could be picked up and coupled back for detection into the suspended core. The LOD for these two antibiotics was found to be at the sub-nanomolar level which is substantially lower than the maximum residue limit prescribed by the European Union.

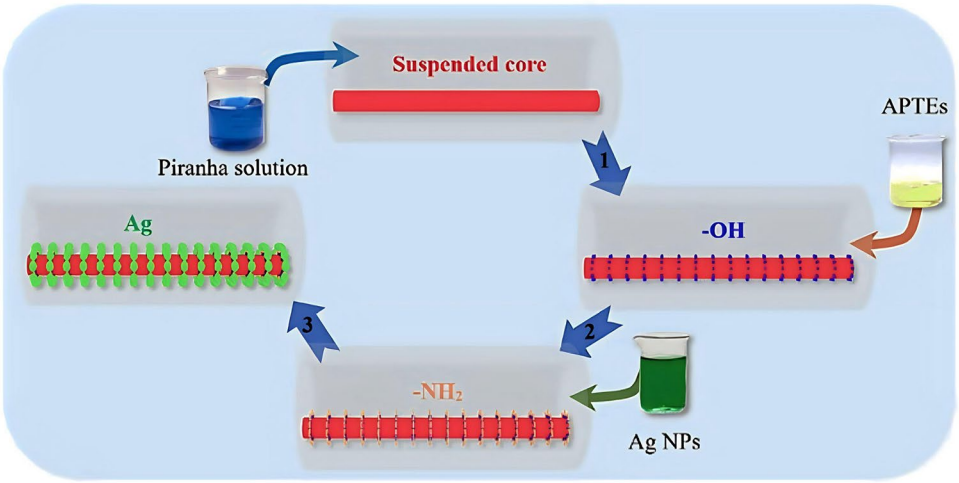

Fig. 15 Functionalized steps with AgNPs used in MHF-based sensors. Reproduced with permission from Teng et al. (2021)

The evanescent field around the optical fiber surface can be enhanced by modifying the geometry of the optical surface in a U-shape and the absorbance sensitivity of U-shaped fiber increases 10 times as compared to straight fiber since the depth of the evanescent field at the bent region increases (Sai et al. 2009). These U-bent fiber probes have been explored for the detection of β-lactam antibiotics from environmental water samples (Nag et al. 2021). To develop this sensor, the U-bent surface was first hydroxylated and then modified with polyaniline nanofibers (Fig. 16). Later, the β-lactamase enzyme was immobilized into polyaniline-coated probes. In the presence of β-lactam antibiotics, an enzymatic hydrolysis reaction occurs resulting in the release of a proton subsequently changing the pH of the surrounding medium which could be detected by the electroactive polymer coated on the surface. This causes a concentration-dependent change in absorbance response at 435 nm when the fiber ends are connected to a light source and a photodetector. The sensing method showed a detection limit of β-lactam antibiotics (ceftazidime) at 0.18 nM from stimulated tap water.

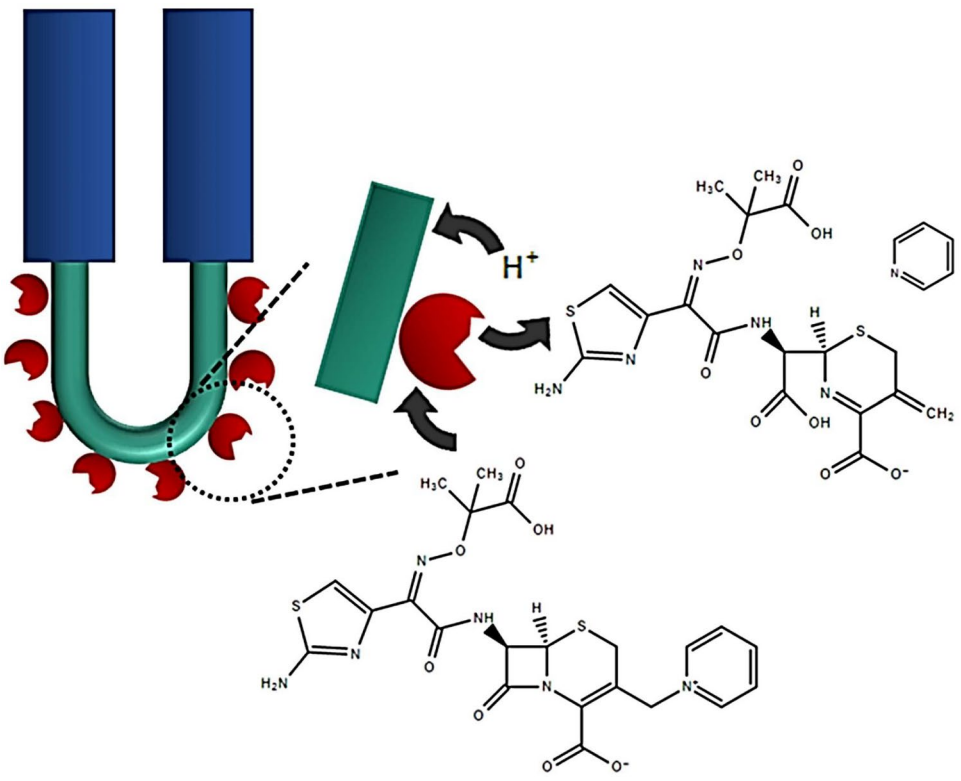

Fig. 16 Polyaniline-modified U-bent fiber optic sensor probe. Reproduced with permission from Nag et al. (2021). Copyright (2021), American Chemical Society

Table 6 Comparative analysis of different optical sensing techniques

Parameter	LSPR	SPR	SERS	Fluorescent
Label free	+++	+++	+++	+/−
Real-time analysis	+++	+++	+	+++
Sample size	+++	+++	+++	+++
Rapid detection	+++	++	+++	+++
Sensitivity	+++	+++	+++	+++
Field deployability	+++	+	+	+
Multiplexing	+++	+	+	+
Affordability	+++	+	+	++

Excellent (+++), Good (++), Fair (+), Poor (−)

Conclusion and future scope

Antimicrobial resistance is becoming a broader concern, and the demand for reliable antibiotic-sensing devices for environmental samples has increased tremendously. In this review, we have discussed various techniques utilizing nanomaterials and their properties to develop ultrasensitive sensors for the detection of antibiotics in water and aquatic environments. A considerable number of optical detection techniques including SPR, LSPR, fluorescence, SERS, and their integration with chip and optical fiber sensor platforms are discussed in detail. All these techniques have several advantages and limitations, and among these, LSPR-based sensing approach offers immense potential with added advantage of field applications by means of simple colorimetric detection (Table 6). So far, AuNPs, AgNPs, CNTs, QDs, MOFs, MIPs, etc. have been utilized to develop chemosensors and biosensors for a wide range of antibiotic detection with minimal or no pre-treatment. The excellent properties of the nanomaterials have enabled the on-site visual detection of antibiotics with a few paper and chip-based technologies along with excellent sensitivity and LOD. Moreover, a few technologies have shown the potential for multiplexed detection with good field deployability. The chemical makeup of antibiotics changes the physical, chemical, and ionic properties of these nanoparticles, causing them to aggregate, or display changes in fluorescence properties.

The detection and measurement of trace amounts of antibiotics are still challenging with a single signal strategy; thus, the development of a multi-readout technique in the future can improve the sensor's versatility. The development of robust field deployable point of care (PoC) devices for the detection of antibiotic residue along with multiplexed sensing will reduce the overall cost of analysis and turnaround time. Array fiber optic absorbance biosensor (ArFAB) is one such platform that might enable multiple analyte detection using U-bent fiber optic probes, (Kuzhandai Shamlee et al. 2022). Nanomaterials combined with advanced technology, such as microfluidics, 3D bioprinting, mobile phones, and smartwatches, can also be used to successfully build sensitive biosensors. Further theoretical research is needed in order to comprehend the physical and chemical properties of novel materials and utilize them for developing novel biosensors.

Declarations

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethical approval This article contains no studies with human and animal participants.

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