

Recent Advances in Nanotechnology-Assisted Liquid Crystal Biosensors for Sensitive and Naked-Eye Detection of Antibiotics

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Abstract

The widespread use of antibiotics in healthcare, veterinary medicine, agriculture, and aquaculture has resulted in increasing levels of antibiotic residues in food products and environmental samples, posing significant risks to human health and contributing to antimicrobial resistance. Conventional analytical methods, including high-performance liquid chromatography (HPLC), liquid chromatography–mass spectrometry (LC–MS), enzyme-linked immunosorbent assay (ELISA), and electrochemical techniques, offer excellent sensitivity but require sophisticated instrumentation, skilled personnel, and extensive sample preparation. In recent years, liquid crystal (LC)-based biosensors have emerged as promising optical sensing platforms capable of rapid, label-free, and cost-effective detection of antibiotics. By exploiting the extraordinary sensitivity of liquid crystal molecules to interfacial disturbances, these biosensors convert molecular recognition events into easily observable optical signals. The incorporation of nanotechnology, including gold nanoparticles, graphene oxide, carbon nanotubes, quantum dots, metal–organic frameworks, magnetic nanoparticles, and silica nanoparticles, has significantly enhanced sensor sensitivity, selectivity, response speed, and stability. Advanced LC biosensors employ aptamers, antibodies, molecularly imprinted polymers, or peptide receptors to selectively recognize antibiotic molecules, resulting in changes in LC orientation that can often be observed directly with the naked eye. This article reviews the fundamental sensing mechanisms, recent advances in nanotechnology-assisted LC biosensors, detection strategies for major antibiotic classes, current challenges, and future perspectives toward portable point-of-care diagnostic devices. Recent advances suggest that nanotechnology-driven LC biosensors will become powerful tools for food safety monitoring, environmental surveillance, and clinical diagnostics.

Keywords: Liquid crystal biosensors; Nanotechnology; Antibiotic detection; Apt sensors; Gold nanoparticles; Graphene oxide; Point-of-care diagnostics; Food safety.

1. Introduction

Antibiotics have revolutionized modern medicine by significantly reducing mortality and morbidity associated with bacterial infections. Since the discovery of penicillin, antibiotics have become indispensable in human healthcare, veterinary medicine, agriculture, aquaculture, and animal husbandry [1]. They are routinely employed for the treatment and prevention of infectious diseases and, in certain regions, as growth promoters in livestock production. The global demand for antibiotics continues to increase because of population growth, expanding healthcare systems, and the rising incidence of infectious diseases. However, the extensive and

often indiscriminate use of antibiotics has resulted in their widespread release into the environment, creating serious concerns regarding food safety, environmental pollution, and public health [2].

A substantial proportion of administered antibiotics is excreted unmetabolized by humans and animals, allowing these compounds to enter wastewater treatment plants, rivers, lakes, groundwater, and agricultural soils. Conventional wastewater treatment processes are frequently unable to completely remove antibiotic residues, leading to their persistence in aquatic ecosystems. Antibiotic contamination has been detected in surface water, drinking water, sediments, soil, milk, meat, eggs, seafood, honey, and various agricultural products. Continuous exposure to even trace concentrations of antibiotics promotes the emergence and dissemination of antimicrobial-resistant bacteria and antibiotic resistance genes, threatening the effectiveness of existing antimicrobial therapies [3]. The World Health Organization (WHO) recognizes antimicrobial resistance (AMR) as one of the most pressing global health challenges of the twenty-first century, emphasizing the urgent need for reliable monitoring systems capable of detecting antibiotic residues across environmental, food, and clinical matrices. Regulatory agencies worldwide have established maximum residue limits (MRLs) for various antibiotics in food products to minimize human exposure and ensure consumer safety. Consequently, rapid, accurate, sensitive, and cost-effective analytical techniques are essential for routine monitoring of antibiotic residues throughout the food supply chain. Conventional analytical methods, including high-performance liquid chromatography (HPLC), liquid chromatography–mass spectrometry (LC–MS/MS), gas chromatography (GC), gas chromatography–mass spectrometry (GC–MS), capillary electrophoresis (CE), enzyme-linked immunosorbent assay (ELISA), fluorescence spectroscopy, and electrochemical analysis, provide excellent sensitivity and quantitative accuracy. Nevertheless, these techniques require sophisticated instrumentation, skilled personnel, expensive reagents, extensive sample preparation, and laboratory infrastructure, making them unsuitable for rapid on-site screening and point-of-care applications. In addition, the high operational costs and long analysis times limit their widespread implementation in resource-limited settings[4].

To overcome these limitations, biosensor technologies have emerged as attractive alternatives for rapid and portable detection of antibiotic residues. Biosensors integrate biological recognition elements with physical transducers to convert molecular interactions into measurable signals. Depending on the transduction mechanism, biosensors can be classified as electrochemical, optical, piezoelectric, fluorescence-based, colorimetric, surface plasmon resonance (SPR), and liquid crystal (LC)-based sensors. Among these, optical biosensors have attracted considerable attention because they offer high sensitivity, rapid response, label-free detection, minimal sample preparation, and the potential for visual signal interpretation. Liquid crystal (LC)-based biosensors represent a unique class of optical sensing platforms that exploit the exceptional sensitivity of liquid crystal molecules to interfacial physicochemical changes. Liquid crystals exhibit an intermediate phase between conventional liquids and crystalline solids, possessing both molecular mobility and long-range orientational order. Their anisotropic optical properties enable minute molecular interactions occurring at interfaces to be amplified into visible optical changes [5]. Even subtle disturbances induced by biomolecular recognition events can alter the orientation of LC molecules, producing distinct optical transitions that are easily observed under polarized optical microscopy and, in several advanced sensor designs, directly by the naked eye. This intrinsic signal amplification eliminates the need for fluorescent labels, radioactive tracers, or enzymatic amplification, thereby simplifying analytical procedures while reducing overall assay costs.

The operating principle of LC biosensors relies on the controlled alignment of liquid crystal molecules at specially prepared interfaces. In the absence of target analytes, liquid crystals maintain a uniform orientation dictated by alignment layers or surface chemistry. When specific recognition molecules such as antibodies, aptamers, enzymes, peptides, or molecularly imprinted polymers (MIPs) bind target antibiotics, the resulting changes in surface energy, molecular organization, or interfacial interactions disrupt the ordered arrangement of LC molecules. This reorientation generates a measurable optical response, typically manifested as a transition between dark and bright states under crossed polarizers or as visible color and texture changes [6]. Because millions of LC molecules respond collectively to a single molecular recognition event, LC biosensors inherently amplify weak biochemical signals, enabling highly sensitive detection of trace antibiotic concentrations. The incorporation of nanotechnology has significantly advanced the development of LC-based biosensors by enhancing their analytical performance and expanding their practical applications. Nanomaterials possess unique physicochemical characteristics, including extremely high surface-area-to-volume ratios, tunable optical and electronic properties, excellent biocompatibility, and versatile surface functionalization capabilities. Gold nanoparticles (AuNPs), silver nanoparticles (AgNPs), graphene oxide (GO), reduced graphene oxide (rGO), carbon nanotubes (CNTs), quantum dots (QDs), magnetic nanoparticles (Fe_3O_4), silica nanoparticles, metal–organic frameworks (MOFs), transition metal dichalcogenides, and MXenes have all been successfully integrated into LC biosensing platforms. These nanomaterials facilitate efficient immobilization of biological recognition elements, accelerate molecular binding kinetics, amplify optical responses, improve sensor stability, and substantially reduce detection limits [7].

Nanotechnology also enables the fabrication of multifunctional sensing interfaces capable of selectively recognizing a wide range of antibiotic molecules. Functionalization with aptamers has become particularly attractive because aptamers exhibit high affinity, excellent chemical stability, low production cost, and ease of modification compared with conventional antibodies. Molecularly imprinted polymers provide synthetic receptor sites with high specificity, while nanocomposite materials further enhance the interaction between target antibiotics and the sensing interface. Consequently, modern LC biosensors can detect antibiotics at nanomolar, picomolar, and even femtomolar concentrations with rapid response times, often within only a few minutes [8]. Recent advances have expanded the application of LC-based biosensors to numerous antibiotic classes, including tetracyclines, aminoglycosides, β -lactam antibiotics, fluoroquinolones, sulfonamides, chloramphenicol, macrolides, and glycopeptides. These sensors have demonstrated successful analysis of complex matrices such as milk, meat, fish, eggs, honey, drinking water, wastewater, river water, biological fluids, and pharmaceutical formulations. Furthermore, the integration of LC biosensors with microfluidic systems, flexible substrates, smartphone imaging, artificial intelligence-assisted image processing, wearable electronics, and Internet of Things (IoT)-enabled monitoring platforms has greatly expanded their potential for real-time and point-of-care diagnostics [9].

Despite remarkable progress, several technical challenges remain before widespread commercialization can be achieved. Long-term stability of liquid crystal alignment layers, reproducibility of nanomaterial synthesis, environmental sensitivity to temperature and humidity, multiplex detection capability, large-scale manufacturing, and standardized analytical protocols continue to require further investigation. Addressing these limitations through interdisciplinary advances in materials science, nanotechnology, analytical chemistry, artificial intelligence, and biomedical engineering will facilitate the development of robust, portable, and commercially viable LC biosensors [10].

This review comprehensively discusses the recent progress in nanotechnology-driven LC-based biosensors for the naked-eye detection of antibiotics. The fundamental principles of liquid crystal sensing, roles of advanced nanomaterials, molecular recognition strategies, sensing mechanisms, analytical performance, representative applications, current limitations, and future research directions are critically examined. By highlighting recent innovations and emerging trends, this review aims to provide a comprehensive understanding of LC biosensing technologies and their potential contribution toward food safety, environmental monitoring, antimicrobial resistance surveillance, and next-generation point-of-care diagnostic systems.

2. Principle of Liquid Crystal Biosensing

Liquid crystal (LC)-based biosensing has emerged as a powerful optical sensing technology owing to the remarkable sensitivity of liquid crystal molecules to changes occurring at interfaces. Unlike conventional biosensors that rely on electrochemical, fluorescence, or enzymatic signal transduction, LC biosensors convert molecular recognition events directly into visible optical signals through changes in molecular orientation. This unique sensing mechanism enables label-free, real-time, and highly sensitive detection of a wide range of biological and chemical analytes, including antibiotics, pathogens, toxins, proteins, nucleic acids, and environmental contaminants [11].

2.1 Fundamentals of Liquid Crystals

Liquid crystals represent a distinct state of matter exhibiting physical characteristics intermediate between isotropic liquids and crystalline solids. Similar to liquids, LC molecules possess fluidity and can flow freely, while simultaneously maintaining long-range orientational order characteristic of crystalline materials. This combination of fluidity and molecular order gives rise to unique anisotropic optical, electrical, and dielectric properties that make liquid crystals exceptionally responsive to external stimuli. Among the different classes of liquid crystals, nematic liquid crystals are the most widely employed in biosensing applications because of their simple molecular organization, excellent optical birefringence, rapid response, and ease of alignment [12-13]. In nematic liquid crystals, elongated rod-like molecules align preferentially along a common direction known as the director (n), although their centers of mass remain randomly distributed. This ordered arrangement is highly susceptible to minor perturbations induced by molecular adsorption, biochemical reactions, or changes in surface chemistry. The optical properties of nematic liquid crystals arise from their anisotropic refractive indices. Light passing through aligned LC molecules experiences different refractive indices depending on its polarization direction, resulting in birefringence. Consequently, any disturbance in molecular alignment alters the transmission of polarized light, producing distinct optical textures that can be readily observed using polarized optical microscopy (POM) [14].

2.2 Surface Alignment of Liquid Crystals

The sensing capability of LC biosensors is fundamentally governed by the orientation of liquid crystal molecules at interfaces. Prior to sensing, LC molecules are aligned using specially prepared surfaces coated with alignment agents such as dimethyloctadecyl[3-(trimethoxysilyl)propyl] ammonium chloride (DMOAP), rubbed polyimide films, surfactants, or self-assembled monolayers (SAMs). Depending on the alignment layer, LC molecules adopt one of two principal orientations:

- A. Homeotropic alignment: Molecules orient perpendicular to the substrate surface, appearing as a dark field under crossed polarizers because minimal birefringence is produced.
- B. Planar alignment: Molecules align parallel to the substrate, producing bright optical textures due to significant birefringence.

These highly ordered initial states serve as stable optical backgrounds against which molecular recognition events can be detected with exceptional sensitivity [15].

2.3 Molecular Recognition at the LC Interface

The selectivity of LC biosensors is achieved through the immobilization of specific recognition elements onto the sensing surface. Common recognition molecules include antibodies, aptamers, enzymes, peptides, molecularly imprinted polymers (MIPs), nucleic acids, and receptor proteins. Nanomaterials such as gold nanoparticles, graphene oxide, carbon nanotubes, silica nanoparticles, magnetic nanoparticles, and metal–organic frameworks are frequently incorporated to increase surface area and improve receptor immobilization. When a sample containing target antibiotic molecules is introduced, the analytes selectively bind to these recognition elements through highly specific molecular interactions, including: Antigenantibody binding, Aptamer–target recognition, Hydrogen bonding, Electrostatic interactions, Van der Waals forces, Hydrophobic interactions and Host guest molecular recognition. These interactions modify the physicochemical characteristics of the LC interface, including surface charge density, surface energy, molecular packing, wettability, and steric organization [16].

2.4 Mechanism of LC Reorientation

The central sensing mechanism of LC biosensors is the amplification of nanoscale interfacial events into microscopically observable optical responses. Before analyte binding, LC molecules maintain a stable orientation determined by the alignment layer. Upon target recognition, molecular binding disturbs the equilibrium alignment by altering anchoring forces acting on LC molecules [17]. The Schematic Illustration of the Detection Mechanism of LC-Based Antibiotic Biosensors as shown in Figure 1. The reorientation process generally involves the following sequence:

- a) Functionalization of the substrate with biological recognition molecules.
- b) Stable alignment of nematic liquid crystals on the prepared interface.
- c) Introduction of the sample containing antibiotic molecules.
- d) Specific binding of antibiotics to immobilized receptors.
- e) Alteration of interfacial energy and molecular anchoring strength.
- f) Disruption of LC molecular orientation.
- g) Propagation of molecular rearrangement throughout the LC film.
- h) Generation of a visible optical transition under polarized light.

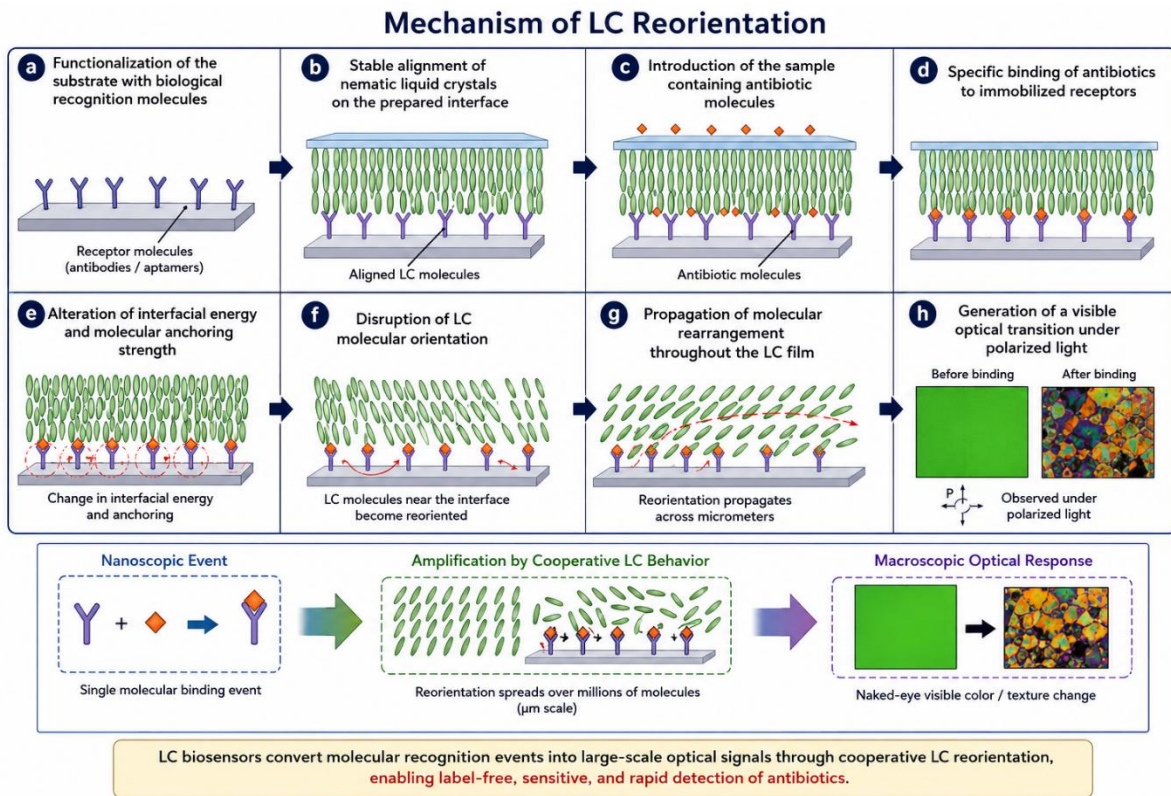


Figure 1: Schematic Illustration of the Detection Mechanism of LC-Based Antibiotic Biosensors

Because millions of LC molecules are cooperatively coupled, a single molecular recognition event can induce large-scale reorientation extending across several micrometres. This collective behavior functions as an intrinsic amplification mechanism, eliminating the need for enzymatic, fluorescent, radioactive, or chemiluminescent labels [18].

2.5 Optical Signal Generation

The optical signal produced by LC biosensors originates from changes in birefringence caused by molecular reorientation. Under crossed polarizers, different LC orientations generate distinct optical appearances. In most LC biosensing systems:

- A homeotropic alignment appears uniformly dark because polarized light passes through with minimal phase retardation.
- Following target binding, LC molecules reorient into a tilted or planar configuration, producing bright interference colors due to increased birefringence.
- Depending on sensor design, the transition may occur from dark-to-bright, bright-to-dark, or exhibit characteristic optical textures and color patterns.

These optical responses can be quantified using image-processing software or, in many advanced systems, interpreted directly by the naked eye, making LC biosensors particularly attractive for point-of-care and field applications [19].

2.6 Signal Amplification Mechanism

One of the most remarkable characteristics of LC biosensors is their inherent signal amplification capability. Conventional biosensors often require fluorescent dyes, enzymes, radioactive isotopes, or nanoparticle labels to generate detectable signals. In contrast, LC biosensors exploit the long-range elastic interactions between neighbouring LC molecules. When a small group of molecules at the sensing interface changes orientation due to analyte binding, adjacent LC molecules also reorient to minimize elastic free energy. This cooperative propagation continues throughout the LC layer, producing a macroscopic optical response from a microscopic biochemical event. Consequently, LC biosensors achieve exceptionally low detection limits while maintaining simple operational procedures[20-21].

2.7 Role of Nanotechnology in LC Biosensing

Nanotechnology has substantially enhanced LC biosensor performance by improving molecular recognition, signal amplification, and sensor stability. Nanomaterials provide exceptionally large surface areas for immobilizing recognition molecules while facilitating rapid analyte diffusion and efficient binding. Gold nanoparticles improve receptor immobilization and plasmonic enhancement [22-23]. Graphene oxide offers abundant oxygen-containing functional groups for biomolecule attachment and enhances interfacial interactions. Carbon nanotubes provide excellent electrical conductivity and mechanical stability. Quantum dots contribute unique optical properties that complement LC signal generation. Magnetic nanoparticles simplify sample handling and separation, whereas metal–organic frameworks provide highly porous structures capable of concentrating analytes near the sensing interface. Nanocomposite materials combining multiple nanostructures have further improved analytical sensitivity by increasing receptor density, accelerating recognition kinetics, and reducing background noise. Consequently, nanotechnology-assisted LC biosensors have achieved detection limits in the nanomolar, picomolar, and even femtomolar concentration ranges for various antibiotics [24].

2.8 Recognition Elements Used in LC Biosensors

The analytical performance of LC biosensors strongly depends on the choice of recognition molecules. Antibodies exhibit excellent specificity toward antibiotic molecules but may suffer from limited stability and higher production costs. Aptamers, which are synthetic single-stranded DNA or RNA molecules, have emerged as preferred recognition elements because they possess high affinity, remarkable chemical stability, low immunogenicity, ease of synthesis, and straightforward chemical modification. Molecularly imprinted polymers (MIPs) provide artificial receptor cavities complementary to target antibiotics in terms of size, shape, and functional groups. Their excellent chemical stability and reusability make them attractive alternatives to biological receptors. Enzymes, peptides, bacteriophages, and nucleic acid probes are also employed depending on the specific sensing application [25].

2.9 Factors Influencing LC Biosensor Performance

Several experimental parameters influence the analytical performance of LC biosensors, including: Type and purity of liquid crystal material, Surface alignment chemistry, Thickness of the LC film, Density and orientation of immobilized recognition molecules, Nanomaterial composition and morphology, Temperature and humidity, pH and ionic strength of the sample, Incubation time, Analyte concentration, Surface roughness and cleanliness. Careful optimization of these parameters is essential for achieving high sensitivity, reproducibility, and long-term operational stability[26].

2.10 Advantages of LC Biosensing Principle

The LC biosensing mechanism offers several significant advantages over conventional analytical methods:

- a) Label-free detection without fluorescent or radioactive probes.
- b) Real-time monitoring of molecular interactions.
- c) High sensitivity resulting from intrinsic optical signal amplification.
- d) Rapid response, typically within a few minutes.
- e) Simple optical instrumentation and straightforward operation.
- f) Low reagent consumption and minimal sample preparation.
- g) Visual interpretation of results through naked-eye observation.
- h) Compatibility with portable devices and smartphone-based imaging.
- i) Excellent potential for multiplex detection and point-of-care diagnostics.

3. Nanotechnology-Enhanced LC Biosensors

Nanotechnology has revolutionized the development of liquid crystal (LC)-based biosensors by significantly improving their analytical performance, sensitivity, selectivity, and operational stability. The incorporation of nanomaterials into LC sensing platforms enhances the interaction between target analytes and recognition elements while facilitating efficient signal transduction. Owing to their unique physicochemical properties, such as high surface area, exceptional electrical conductivity, tunable optical characteristics, and versatile surface chemistry, nanomaterials serve as effective platforms for immobilizing biomolecular receptors and amplifying optical responses. Consequently, nanotechnology-assisted LC biosensors have become promising tools for rapid, label-free, and naked-eye detection of antibiotic residues in food, environmental, and clinical samples [27].

3.1 Gold Nanoparticles (AuNPs)

Gold nanoparticles (AuNPs) are among the most extensively used nanomaterials in LC biosensors because of their excellent biocompatibility, chemical stability, and unique localized surface plasmon resonance (LSPR) properties. AuNPs provide a large surface area for the immobilization of antibodies, aptamers, enzymes, and DNA probes, thereby increasing the number of active binding sites available for target antibiotics. Their strong affinity for thiol-containing molecules enables stable functionalization, while their plasmonic properties enhance optical signal generation. As a result, AuNP-integrated LC biosensors exhibit higher sensitivity, rapid response times, and improved reproducibility compared with conventional LC sensing systems.

3.2 Silver Nanoparticles (AgNPs)

Silver nanoparticles (AgNPs) possess remarkable optical and antimicrobial properties that make them attractive for LC biosensing applications. AgNPs exhibit strong surface plasmon resonance, which enhances light scattering and optical contrast during sensing. Their high electrical conductivity also facilitates efficient signal transduction in hybrid electro-optical biosensors. Furthermore, AgNPs improve the immobilization efficiency of biological recognition molecules and contribute to lower detection limits. However, compared with AuNPs, silver nanoparticles are relatively more susceptible to oxidation, which may affect long-term sensor stability [28].

3.3 Graphene Oxide (GO)

Graphene oxide (GO) is a two-dimensional carbon nanomaterial containing abundant oxygen-containing functional groups such as hydroxyl, epoxy, and carboxyl groups. These functional groups provide numerous active sites for the covalent or non-covalent attachment of biomolecules, including aptamers, antibodies, and enzymes. GO exhibits excellent mechanical strength, high surface area, and good aqueous dispersibility, making it an ideal substrate for LC biosensors. Additionally, GO effectively modifies the interfacial properties of liquid crystals, resulting in enhanced molecular alignment and improved optical sensitivity during antibiotic detection.

3.4 Reduced Graphene Oxide (rGO)

Reduced graphene oxide (rGO) is obtained through the chemical or thermal reduction of graphene oxide, restoring much of graphene's electrical conductivity while retaining sufficient functional groups for biomolecule immobilization. The high electrical conductivity and large specific surface area of rGO improve electron transfer and molecular recognition efficiency. In LC biosensors, rGO facilitates rapid interaction between antibiotics and receptor molecules, leading to faster response times and enhanced detection sensitivity. Its excellent mechanical and chemical stability further contributes to long-term sensor performance.

3.5 Carbon Nanotubes (CNTs)

Carbon nanotubes (CNTs), including single-walled (SWCNTs) and multi-walled carbon nanotubes (MWCNTs), possess extraordinary mechanical strength, electrical conductivity, and thermal stability. Their cylindrical nanostructure provides an exceptionally high aspect ratio and large surface area for immobilizing biological receptors. CNTs enhance electron transport, accelerate molecular recognition, and improve signal amplification in LC biosensors. Moreover, their excellent flexibility enables the fabrication of portable and wearable biosensing devices capable of rapid antibiotic detection[29].

3.6 Quantum Dots (QDs)

Quantum dots (QDs) are semiconductor nanocrystals exhibiting unique size-dependent optical and electronic properties. They possess broad excitation spectra, narrow emission bands, high photostability, and excellent fluorescence efficiency. Although LC biosensors primarily rely on optical orientation changes rather than fluorescence, quantum dots can be integrated into hybrid sensing platforms to enhance signal intensity and improve analytical sensitivity. Their tunable optical characteristics also facilitate multiplex detection of multiple antibiotic targets within a single sensing platform.

3.7 Magnetic Nanoparticles (Fe_3O_4)

Magnetic nanoparticles, particularly iron oxide (Fe_3O_4), offer unique advantages due to their superparamagnetic properties. These nanoparticles enable magnetic separation and pre-concentration of target antibiotics from complex samples before detection. Functionalized Fe_3O_4 nanoparticles can selectively capture antibiotic molecules and transport them efficiently to the LC sensing interface, thereby increasing sensitivity and reducing interference from sample matrices. Their ease of manipulation using external magnetic fields simplifies sample preparation and shortens analysis time.

3.8 Silica Nanoparticles

Silica nanoparticles are widely employed because of their excellent chemical stability, biocompatibility, uniform particle size, and easily modifiable surfaces. Their porous structure provides abundant sites for immobilizing recognition molecules while maintaining high mechanical stability. In LC biosensors, silica nanoparticles contribute to improved liquid crystal alignment and enhanced optical contrast by creating well-defined interfacial architectures. Their inert nature also minimizes non-specific adsorption, thereby improving analytical accuracy and reproducibility.

3.9 Metal–Organic Frameworks (MOFs)

Metal–organic frameworks (MOFs) are highly porous crystalline materials composed of metal ions coordinated with organic ligands. Their exceptionally high surface area, tunable pore size, and adjustable chemical functionality make them excellent candidates for biosensing applications. MOFs can efficiently adsorb antibiotic molecules, increasing their local concentration near the sensing interface and thereby enhancing detection sensitivity. Furthermore, their porous structure facilitates rapid molecular diffusion, resulting in shorter response times and improved sensor performance. MOFs also provide versatile platforms for immobilizing aptamers, antibodies, and enzymes.

3.10 Advantages of Nanomaterials in LC Biosensors

The incorporation of nanomaterials significantly improves the analytical performance of LC biosensors through several mechanisms:

- a) High surface-to-volume ratio: Nanomaterials provide an exceptionally large surface area, allowing a higher density of biological recognition molecules to be immobilized and increasing the probability of analyte binding.
- b) Efficient immobilization of biomolecular receptors: Surface functional groups present on nanomaterials enable stable attachment of antibodies, aptamers, enzymes, and molecularly imprinted polymers, enhancing sensor specificity and durability.
- c) Improved electron and energy transfer: Conductive nanomaterials such as graphene, carbon nanotubes, and metallic nanoparticles facilitate rapid charge and energy transfer, resulting in faster signal generation.
- d) Faster recognition kinetics: The nanoscale dimensions and large active surface accelerate interactions between target antibiotics and immobilized receptors, reducing the overall detection time.
- e) Enhanced optical amplification: Metallic nanoparticles and nanocomposites strengthen optical responses by amplifying changes in liquid crystal orientation, thereby increasing signal visibility and improving naked-eye detection.
- f) Greater mechanical stability: Nanomaterials reinforce the sensing interface, improving structural integrity and maintaining consistent sensor performance during repeated analyses.
- g) Improved reproducibility: Uniform nanomaterial coatings produce homogeneous sensing surfaces, minimizing experimental variability and ensuring reliable analytical results.
- h) Lower limits of detection: Enhanced molecular recognition, efficient signal amplification, and optimized interfacial interactions enable the detection of antibiotics at nanomolar, picomolar, and, in some cases, femtomolar concentrations [30].

4. Recognition Elements for Antibiotic Detection

The performance of liquid crystal (LC)-based biosensors largely depends on the specificity and affinity of the biological recognition elements employed. Recognition elements are responsible for selectively identifying and binding target antibiotic molecules, thereby initiating changes in the interfacial properties that lead to liquid crystal (LC) reorientation and optical signal generation. An ideal recognition element should exhibit high specificity, strong binding affinity, rapid response, excellent stability, minimal cross-reactivity, and compatibility with nanomaterials and LC interfaces. Over the past decade, significant progress has been made in developing various biological and synthetic recognition molecules, including aptamers, monoclonal antibodies, molecularly imprinted polymers (MIPs), antimicrobial peptides, DNA probes, and enzyme-based receptors. The Sequential Detection Mechanism of Liquid Crystal-Based Antibiotic Biosensors as shown in Figure2. Each recognition element possesses unique advantages and limitations depending on the target antibiotic, sensing environment, and analytical application [31].

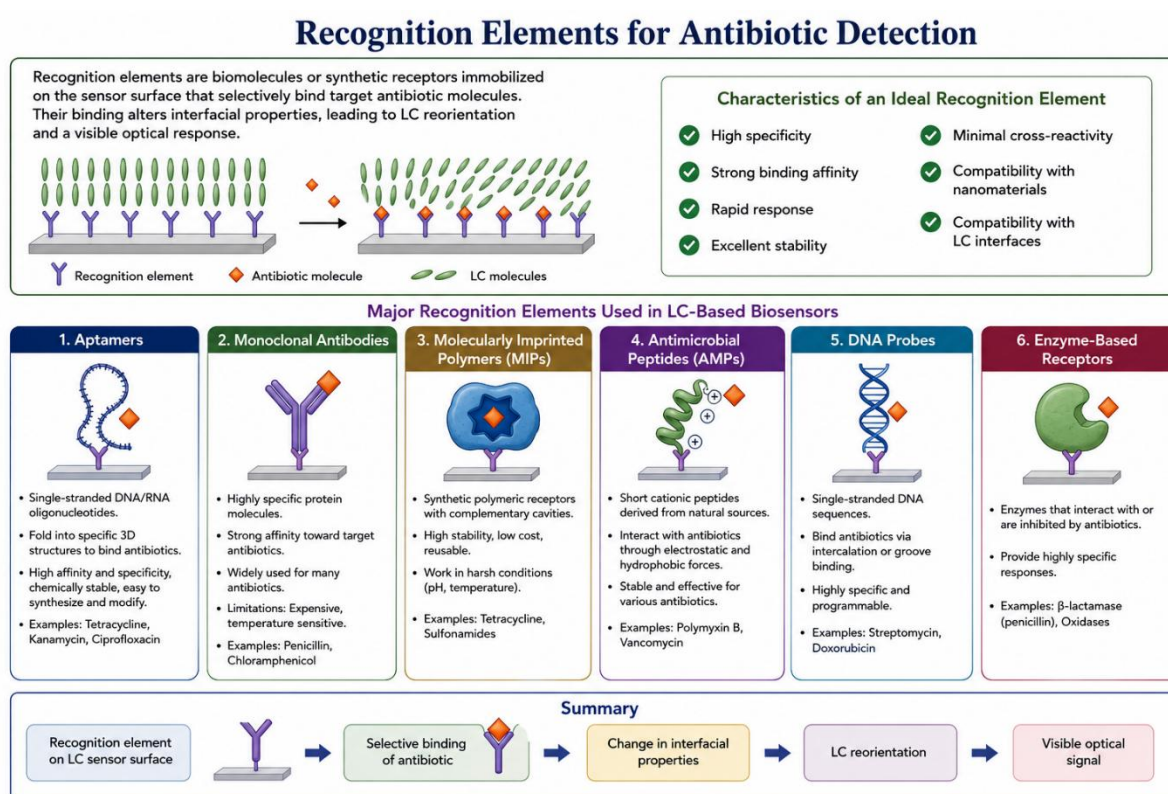


Figure 2: Sequential Detection Mechanism of Liquid Crystal-Based Antibiotic Biosensors

4.1 Aptamers

Aptamers are short single-stranded DNA or RNA oligonucleotides that fold into unique three-dimensional structures capable of specifically recognizing and binding target molecules through hydrogen bonding, electrostatic interactions, van der Waals forces, and hydrophobic interactions. Aptamers are generated using the Systematic Evolution of Ligands by Exponential Enrichment (SELEX) process, which enables the selection of highly specific nucleic acid

sequences from large combinatorial libraries. Among all recognition elements, aptamers have become the most widely used in LC biosensors for antibiotic detection because of their exceptional analytical performance. Their advantages include: High specificity and binding affinity toward target antibiotics, Excellent chemical and thermal stability, Low production cost through chemical synthesis, Easy surface functionalization and chemical modification, long storage life without significant loss of activity, Minimal batch-to-batch variation, Reusability in certain sensing platforms, Compatibility with nanomaterials such as gold nanoparticles, graphene oxide, and carbon nanotubes. Upon binding to the target antibiotic, aptamers undergo conformational changes that modify the interfacial energy of the LC sensing surface. These changes disturb the alignment of liquid crystal molecules, resulting in measurable optical transitions. Aptamer-based LC biosensors have been successfully developed for detecting tetracycline, kanamycin, streptomycin, chloramphenicol, ciprofloxacin, ampicillin, and other antibiotics with detection limits ranging from nanomolar to picomolar concentrations [32].

4.2 Monoclonal Antibodies

Monoclonal antibodies are highly specific immunoglobulin proteins produced from a single clone of B lymphocytes. They recognize unique antigenic sites (epitopes) on antibiotic molecules with remarkable specificity and affinity, making them one of the earliest recognition elements used in biosensor development. In LC biosensors, monoclonal antibodies are immobilized onto nanomaterial-coated substrates or directly onto LC alignment layers. When target antibiotics bind to these antibodies, the resulting antigen–antibody complexes alter the physicochemical characteristics of the sensing interface, inducing LC reorientation and optical signal generation. The major advantages of monoclonal antibodies include: Extremely high target specificity, Strong antigen-binding affinity, Well-established immunochemical protocols, Reliable analytical performance for complex biological samples and High sensitivity for trace antibiotic detection. However, antibody-based biosensors also exhibit certain limitations, including relatively high production costs, sensitivity to temperature and pH variations, limited storage stability, and potential denaturation during long-term use. Despite these challenges, monoclonal antibodies remain valuable recognition elements for detecting β -lactam antibiotics, chloramphenicol, sulphonamides, and aminoglycosides.

4.3 Molecularly Imprinted Polymers (MIPs)

Molecularly imprinted polymers (MIPs) are synthetic recognition materials often referred to as artificial antibodies. They are fabricated by polymerizing functional monomers in the presence of a target antibiotic molecule that serves as a template. After polymerization, the template molecules are removed, leaving behind highly specific recognition cavities that are complementary to the target antibiotic in terms of size, shape, and chemical functionality. Unlike biological receptors, MIPs possess excellent chemical and mechanical stability and can withstand harsh environmental conditions. The advantages of MIPs include: High chemical and thermal stability, Excellent resistance to pH variations, Low production cost, long shelf life, High selectivity toward target molecules, Reusability after regeneration and Compatibility with a wide variety of nanomaterials. When target antibiotics re-enter the imprinted cavities, the binding process alters the interfacial properties of the LC sensing layer, causing changes in liquid crystal orientation. MIP-based LC biosensors have demonstrated successful detection of tetracycline, sulfamethazine, chloramphenicol, and ciprofloxacin in food and environmental samples[33].

4.4 Antimicrobial Peptides (AMPs)

Antimicrobial peptides are naturally occurring short peptides that constitute an essential component of the innate immune system in many organisms. They exhibit broad-spectrum antimicrobial activity and possess the ability to selectively interact with bacterial membranes and certain antibiotic molecules. Recent studies have explored the application of antimicrobial peptides as biological recognition elements in LC biosensors because of their: Small molecular size, High binding efficiency, Excellent biocompatibility, Rapid molecular recognition, Easy chemical synthesis and Good environmental stability. AMP-functionalized nanomaterials improve the capture efficiency of antibiotic molecules and enhance interfacial interactions responsible for LC reorientation. Although their application in antibiotic sensing is still emerging, antimicrobial peptides represent promising alternatives to antibodies and aptamers for next-generation biosensor development.

4.5 DNA Probes

DNA probes are synthetic single-stranded oligonucleotides designed to recognize complementary nucleic acid sequences through specific base-pair hybridization. In antibiotic detection, DNA probes are primarily employed for identifying antibiotic resistance genes, bacterial pathogens, or genetic biomarkers associated with antimicrobial resistance. DNA probes can be immobilized on gold nanoparticles, graphene oxide, silica nanoparticles, or directly on LC alignment surfaces. Upon hybridization with complementary DNA targets, significant structural changes occur at the sensing interface, modifying LC alignment and generating measurable optical signals. The main advantages of DNA probes include: High sequence specificity, Excellent sensitivity, Rapid hybridization kinetics, Compatibility with multiplex detection, Simple chemical modification and High reproducibility. DNA probe-based LC biosensors are particularly valuable for detecting resistance genes such as *mecA*, *bla*, and *tet* genes associated with antibiotic-resistant bacterial strains [34].

4.6 Enzyme-Based Receptors

Enzymes are highly selective biological catalysts capable of recognizing and interacting with specific antibiotic molecules or their metabolites. Enzyme-based biosensors exploit catalytic reactions that generate measurable physicochemical changes capable of altering LC orientation. Several enzymes, including β -lactamase, acetylcholinesterase, oxidases, and hydrolases, have been investigated for antibiotic sensing applications. During enzymatic reactions, changes in pH, ionic strength, substrate concentration, or reaction products modify the anchoring conditions of LC molecules, resulting in distinct optical responses. The advantages of enzyme-based receptors include: Exceptional substrate specificity, Rapid catalytic reactions, High analytical sensitivity, Real-time detection capability and Quantitative signal generation. However, enzyme activity can be affected by temperature, pH, and storage conditions, requiring careful optimization for practical applications [35].

4.7 Comparison of Recognition Elements

Each recognition element offers distinct advantages depending on the analytical requirements of the biosensor.

- a) Aptamers provide outstanding specificity, excellent stability, easy synthesis, and low production cost, making them the preferred recognition molecules for most modern LC biosensors.
- b) Monoclonal antibodies offer extremely high specificity and affinity but involve higher production costs and lower environmental stability.
- c) Molecularly imprinted polymers (MIPs) serve as robust synthetic alternatives with excellent durability and reusability.
- d) Antimicrobial peptides combine biocompatibility with rapid molecular recognition and represent promising candidates for future biosensor development.
- e) DNA probes are particularly suitable for detecting antibiotic resistance genes and bacterial pathogens rather than antibiotic molecules directly.
- f) Enzyme-based receptors provide catalytic signal amplification and excellent selectivity but require careful control of experimental conditions to maintain enzyme activity [36-37].

Table 1. Comparison of Recognition Elements Used in LC-Based Antibiotic Biosensors

Recognition Element	Major Advantages	Limitations	Best Application in LC Biosensors
Aptamers	Outstanding specificity, high binding affinity, excellent chemical stability, easy synthesis, low production cost, reusable	Susceptible to nuclease degradation without modification; selection process can be time-consuming	Preferred recognition element for most modern LC biosensors targeting antibiotic molecules
Monoclonal Antibodies	Extremely high specificity and affinity, excellent selectivity, well-established technology	High production cost, limited environmental stability, shorter shelf life	Detection of specific antibiotic molecules with very high accuracy
Molecularly Imprinted Polymers (MIPs)	Synthetic receptors with excellent durability, thermal and chemical stability, reusable, low cost	Slightly lower selectivity than biological receptors; template removal may be challenging	Robust sensing in harsh environmental conditions and reusable biosensors
Antimicrobial Peptides (AMPs)	Biocompatible, rapid molecular recognition, broad-spectrum binding capability, easy surface immobilization	Lower long-term stability and possible non-specific interactions	Rapid antibiotic sensing and next-generation LC biosensor development
DNA Probes	High sequence specificity, programmable design, excellent for nucleic acid recognition	Detect genetic targets rather than antibiotic molecules directly	Detection of antibiotic resistance genes and bacterial pathogens
Enzyme-Based Receptors	Catalytic signal amplification, excellent selectivity, high sensitivity	Require strict control of pH, temperature, and storage conditions to	Highly sensitive biosensors utilizing enzyme–substrate interactions

		maintain enzyme activity	
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4.8 Future Perspectives of Recognition Elements

Current research is increasingly focused on developing hybrid recognition systems that combine the strengths of multiple recognition elements with advanced nanomaterials. Aptamer–nanoparticle conjugates, MIP–graphene composites, antibody-functionalized metal–organic frameworks (MOFs), and peptide-modified gold nanoparticles have demonstrated remarkable improvements in sensitivity, selectivity, and operational stability. Furthermore, advances in synthetic biology, artificial intelligence-assisted aptamer design, CRISPR-based molecular recognition, and multifunctional nanocomposites are expected to further enhance the analytical performance of LC biosensors. These innovations will facilitate the development of portable, multiplexed, and highly reliable sensing platforms capable of rapid naked-eye detection of antibiotic residues in food products, environmental samples, and clinical specimens.

5. Detection Mechanism

The detection mechanism of nanotechnology-enhanced liquid crystal (LC)-based biosensors relies on the conversion of specific molecular recognition events into easily observable optical signals. Unlike conventional analytical methods that require fluorescent dyes, radioactive isotopes, or enzyme-mediated signal amplification, LC biosensors utilize the inherent sensitivity of liquid crystal molecules to changes occurring at the sensing interface. Even subtle biochemical interactions between antibiotic molecules and recognition elements can induce significant reorientation of LC molecules, producing distinct optical transitions that can be observed under polarized optical microscopy (POM) or, in advanced sensing platforms, directly with the naked eye. This label-free sensing strategy simplifies the analytical process while providing rapid, highly sensitive, and cost-effective detection of antibiotic residues. The detection Mechanism of Nanotechnology-Enhanced Liquid Crystal-Based Biosensors for Antibiotic Detection as shown in Figure 3.

Detection Mechanism of Nanotechnology-Enhanced LC-Based Biosensors

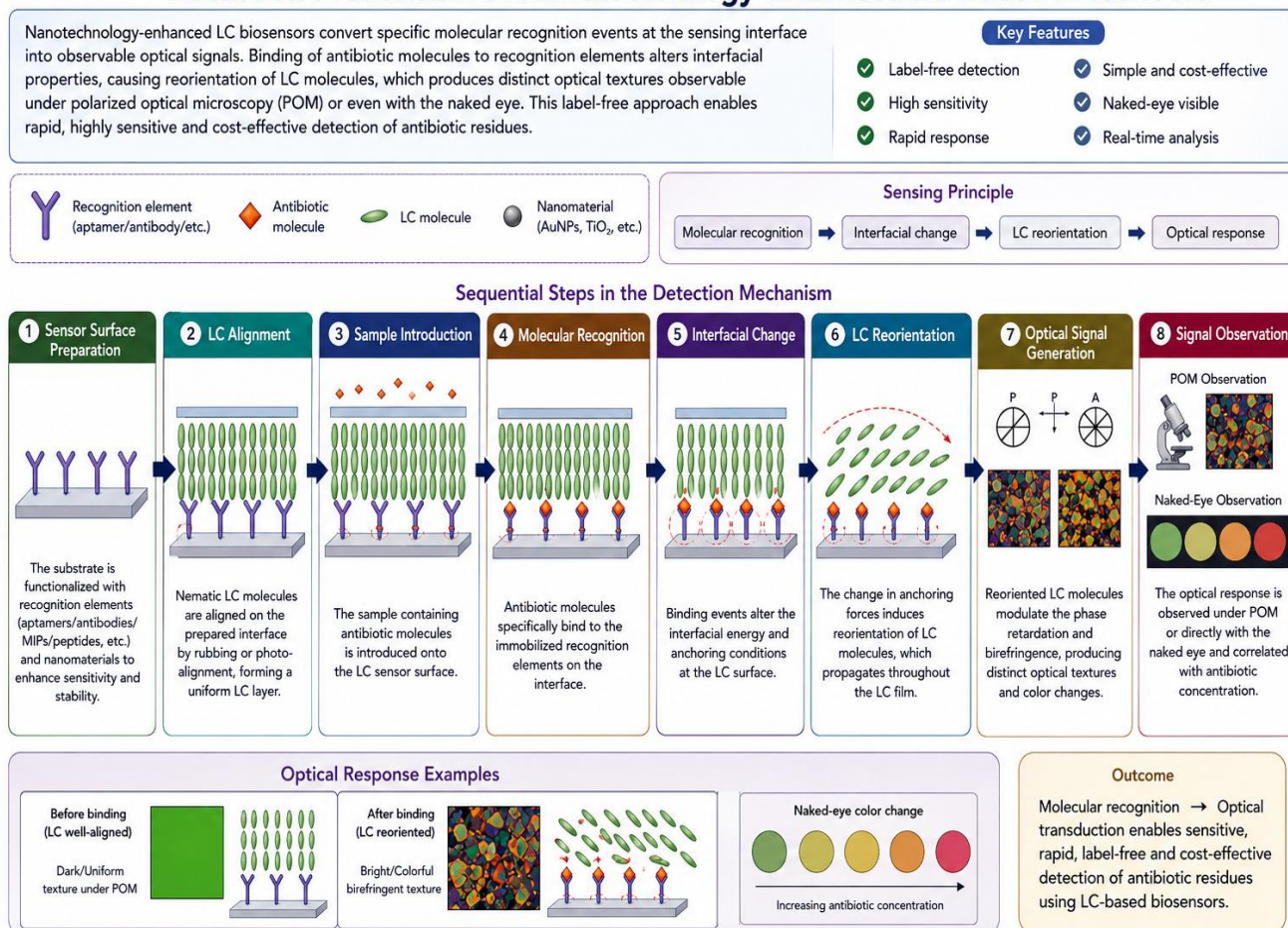


Figure 3. Detection Mechanism of Nanotechnology-Enhanced Liquid Crystal-Based Biosensors for Antibiotic Detection

The overall sensing process consists of several sequential steps, each contributing to the generation of the final optical response [38].

5.1 Functionalization of Nanomaterials with Antibiotic-Specific Receptors

The first step in the fabrication of an LC biosensor is the functionalization of nanomaterials with highly selective biological or synthetic recognition elements. Nanomaterials such as gold nanoparticles (AuNPs), graphene oxide (GO), reduced graphene oxide (rGO), carbon nanotubes (CNTs), silica nanoparticles, magnetic nanoparticles (Fe_3O_4), quantum dots (QDs), and metal–organic frameworks (MOFs) serve as supporting platforms because of their large surface area and excellent surface chemistry. These nanomaterials are chemically modified with recognition molecules including aptamers, monoclonal antibodies, molecularly imprinted polymers (MIPs), antimicrobial peptides, DNA probes, or enzymes. The functionalization process typically involves covalent bonding, electrostatic interactions, thiol–gold chemistry, or adsorption techniques, ensuring stable immobilization of receptor molecules while preserving their biological activity. The incorporation of nanomaterials significantly increases the density of active binding sites, enhances molecular accessibility, and improves the overall sensitivity and selectivity of the biosensor.

5.2 Immobilization of Receptor–Nanomaterial Complexes at the LC Interface

Following functionalization, the receptor–nanomaterial complexes are immobilized onto the liquid crystal sensing surface. This surface is usually prepared using alignment agents such as dimethyloctadecyl [3-(trimethoxysilyl) propyl] ammonium chloride (DMOAP), rubbed polyimide films, or self-assembled monolayers that induce a well-defined initial orientation of LC molecules. The immobilized receptor layer establishes a stable sensing interface while maintaining the homeotropic or planar alignment of the liquid crystal molecules. Uniform immobilization is essential because any irregular distribution of receptors or nanomaterials may cause unwanted background signals and reduce analytical reproducibility. The nanomaterial-coated sensing interface therefore serves as the active recognition platform where antibiotic molecules interact selectively with the immobilized receptors.

5.3 Introduction of the Sample Containing Antibiotics

After sensor preparation, the sample suspected of containing antibiotic residues is introduced onto the sensing surface. Depending on the intended application, the sample may consist of: Milk, Meat extracts, Fish or seafood samples, Honey, Drinking water, River water, Wastewater, Blood serum, Urine and Pharmaceutical formulations. In many cases, only minimal sample preparation such as filtration, dilution, or centrifugation is required before analysis. The ability to analyze complex samples with little or no pretreatment represents a major advantage of LC biosensors over conventional chromatographic techniques. During incubation, antibiotic molecules diffuse toward the sensing interface where they encounter the immobilized recognition elements.

5.4 Specific Molecular Recognition Between Antibiotics and Receptors

The core sensing event occurs when antibiotic molecules specifically bind to their corresponding recognition elements. The selectivity of this interaction is determined by the molecular complementarity between the target antibiotic and the receptor. Depending on the recognition element employed, molecular binding may involve: Antigen–antibody interactions, Aptamer–target binding, Host–Guest molecular recognition, Hydrogen bonding, Electrostatic attraction, Hydrophobic interactions, Van der Waals forces and Molecular imprint recognition. For example, aptamers undergo conformational changes upon binding to tetracycline or kanamycin, while antibodies form stable antigen–antibody complexes with β -lactam antibiotics. Similarly, molecularly imprinted polymers selectively capture antibiotic molecules within their template-shaped cavities. These highly specific molecular interactions alter the physicochemical properties of the sensing interface, including surface energy, molecular packing density, surface charge distribution, steric hindrance, and anchoring strength [39].

5.5 Reorientation of Liquid Crystal Molecules

The molecular recognition event produces disturbances at the LC interface that disrupt the original alignment of liquid crystal molecules. Because liquid crystals exhibit long-range orientational order, localized interfacial changes propagate throughout the entire LC film through elastic coupling between neighbouring molecules. Initially, LC molecules are arranged in a highly ordered homeotropic or planar configuration. Following antibiotic binding, changes in surface anchoring force modify the preferred orientation of the LC molecules. As the disturbance spreads, millions of LC molecules collectively reorient into a new equilibrium configuration. This cooperative molecular rearrangement represents the intrinsic signal

amplification mechanism of LC biosensors. A single antibiotic–receptor interaction can induce large-scale molecular reorganization, allowing trace quantities of antibiotics to generate measurable optical responses.

5.6 Observable Optical Transition

The reorientation of LC molecules results in a significant change in their optical properties, particularly birefringence. Under crossed polarizers, different molecular orientations produce characteristic optical appearances. Typically:

- a) A homeotropically aligned LC film appears dark because light experiences minimal birefringence.
- b) Upon antibiotic binding, LC molecules reorient into a tilted or planar state, producing bright interference colors and characteristic optical textures.
- c) Depending on sensor design, the optical transition may occur from dark-to-bright, bright-to-dark, or through distinctive color variations.

These optical changes can be detected using polarized optical microscopy (POM), digital image analysis, smartphone cameras, or, in optimized LC biosensors, directly by the naked eye without sophisticated instrumentation. The intensity of the optical signal generally correlates with antibiotic concentration, enabling both qualitative and quantitative analysis.

5.7 Signal Amplification Through Cooperative LC Behaviour

One of the most significant advantages of LC biosensors is their inherent signal amplification capability. Unlike fluorescence- or enzyme-based biosensors that require additional amplification steps, LC biosensors rely on the cooperative alignment of millions of LC molecules. When a few LC molecules near the sensing interface are disturbed by antibiotic binding, adjacent molecules also change orientation to minimize the system's elastic free energy. This collective molecular response amplifies nanoscale recognition events into macroscopically visible optical signals. As a result, LC biosensors can achieve extremely low limits of detection while maintaining a simple sensing mechanism.

5.8 Label-Free Detection

Because the optical signal originates directly from changes in LC orientation, no fluorescent dyes, radioactive isotopes, enzymes, or chromogenic substrates are required. This label-free detection strategy offers several important advantages: Simplified sensor fabrication, Reduced assay cost, shorter analysis time, Elimination of complex labelling procedures, Preservation of biological activity of recognition molecules, Reduced background interference and Improved analytical reproducibility. These characteristics make LC biosensors particularly attractive for rapid point-of-care testing and on-site environmental monitoring.

5.9 Factors Affecting the Detection Mechanism

The efficiency of the detection process depends on several experimental parameters, including: Type and concentration of liquid crystal material, Surface alignment chemistry, Density of immobilized recognition molecules, Nanomaterial morphology and particle size, Temperature and humidity, pH and ionic strength of the sample, Incubation time, Thickness of the LC film, Concentration of target antibiotics and Presence of interfering compounds. Optimization of

these parameters is essential for achieving high sensitivity, rapid response, and excellent reproducibility.

5.10 Overall Detection Mechanism

The complete sensing mechanism can be summarized as follows:

1. Nanomaterial functionalization: Nanomaterials are modified with antibiotic-specific recognition elements such as aptamers, antibodies, or molecularly imprinted polymers.
2. Sensor fabrication: The functionalized nanomaterials are immobilized on a liquid crystal alignment surface to create a stable sensing interface.
3. Sample introduction: A sample containing potential antibiotic residues is applied to the sensor.
4. Selective recognition: Target antibiotics bind specifically to the immobilized receptors through highly selective molecular interactions.
5. Interfacial disturbance: Molecular binding alters the surface energy and anchoring conditions at the LC interface.
6. Liquid crystal reorientation: The disturbed anchoring force induces cooperative reorientation of LC molecules throughout the sensing layer.
7. Optical signal generation: Changes in LC alignment produce a visible optical transition, typically from a dark homeotropic state to a bright planar state (or vice versa), indicating the presence of antibiotics [40].

6. Antibiotics Detected by LC Biosensors

The rapid expansion of liquid crystal (LC)-based biosensor technology has enabled the sensitive and selective detection of a wide variety of antibiotic residues in food products, environmental samples, and biological fluids. The integration of nanotechnology with highly specific recognition elements such as aptamers, antibodies, and molecularly imprinted polymers (MIPs) has substantially improved the analytical performance of LC biosensors, allowing the detection of antibiotics at nanomolar, picomolar, and, in some cases, femtomolar concentrations. Recent studies have demonstrated that LC biosensors provide rapid response times (typically 5–30 minutes), require minimal sample preparation, and offer label-free optical detection, making them highly suitable for point-of-care diagnostics and on-site food safety monitoring. The following sections critically discuss the major classes of antibiotics that have been successfully detected using LC biosensors, highlighting their sensing strategies, analytical performance, practical applications, and current limitations [41].

6.1 Tetracycline

Tetracycline is one of the most extensively investigated antibiotics in LC biosensor research because of its widespread use in human medicine, veterinary practice, and livestock production. Residues of tetracycline are frequently detected in milk, meat, eggs, honey, and aquatic environments due to incomplete metabolism and excessive antibiotic administration. Most reported LC biosensors employ aptamer-functionalized gold nanoparticles (AuNPs) or graphene oxide (GO) as recognition platforms for tetracycline detection. Upon binding to tetracycline molecules, the aptamer undergoes a conformational change that alters the anchoring conditions of LC molecules, producing a distinct dark-to-bright optical transition under crossed polarizers. Several studies have reported detection limits ranging from low nanomolar to picomolar concentrations, with response times of less than 20 minutes. Practical

applications have demonstrated successful detection of tetracycline residues in raw milk, river water, and food extracts with recoveries typically ranging from 90% to 108%, indicating excellent analytical accuracy. However, sensor performance may be affected by structurally similar tetracycline analogues unless highly selective aptamers are employed [42].

6.2 Oxytetracycline

Oxytetracycline is another commonly used broad-spectrum antibiotic frequently detected in dairy products, aquaculture, poultry, and livestock. Owing to its structural similarity to tetracycline, selective recognition remains an important challenge. Recent LC biosensors have utilized aptamers and molecularly imprinted polymers (MIPs) immobilized on nanomaterial-coated interfaces to improve selectivity. The incorporation of graphene oxide and gold nanoparticles enhances molecular recognition efficiency and signal amplification. Experimental studies have demonstrated successful quantification of oxytetracycline in milk and fish samples with detection limits in the nanomolar range and recovery values generally exceeding 95%. Although these biosensors exhibit excellent sensitivity, discrimination between tetracycline family members continues to require further optimization.

6.3 Chloramphenicol

Chloramphenicol is a broad-spectrum antibiotic whose use in food-producing animals has been prohibited in many countries because of its association with severe adverse health effects, including aplastic anemia. Consequently, highly sensitive analytical methods are required for monitoring trace concentrations. LC biosensors employing antibody-functionalized gold nanoparticles, aptamer-modified graphene oxide, and molecularly imprinted polymers have demonstrated excellent analytical performance for chloramphenicol detection. The strong molecular recognition between chloramphenicol and the immobilized receptors produces significant LC reorientation, enabling rapid optical detection. Several practical studies have successfully analyzed chloramphenicol residues in honey, milk, shrimp, fish tissue, and river water with recoveries generally between 92% and 105%. The achieved detection limits are frequently well below established maximum residue limits (MRLs), highlighting the suitability of LC biosensors for regulatory food safety monitoring [43].

6.4 Penicillin

Penicillin remains one of the most widely prescribed β -lactam antibiotics worldwide. Residual penicillin in milk and dairy products may trigger allergic reactions in sensitive individuals and contribute to antimicrobial resistance. LC biosensors for penicillin detection commonly employ monoclonal antibodies or enzyme-based receptors immobilized on gold nanoparticle-coated sensing surfaces. These recognition elements selectively bind penicillin molecules, altering interfacial anchoring conditions and generating measurable optical responses. Practical analyses of milk and dairy samples have demonstrated rapid detection within approximately 15–25 minutes with high specificity and acceptable recovery values typically ranging from 90% to 106%. However, sensor selectivity toward different β -lactam antibiotics remains an active area of investigation.

6.5 Ampicillin

Ampicillin is another widely used β -lactam antibiotic commonly administered in both human and veterinary medicine. Residues have been reported in milk, meat, and environmental waters.

Nanotechnology-assisted LC biosensors incorporating aptamers, antibodies, and MIPs have shown efficient detection of ampicillin through label-free optical signal generation. The use of graphene oxide and AuNP nanocomposites significantly enhances receptor immobilization and improves sensitivity. Several studies have reported low nanomolar detection limits with successful application to milk and pharmaceutical formulations. Analytical recoveries generally range from 93% to 107%, demonstrating excellent agreement with conventional chromatographic techniques [44].

6.6 Kanamycin

Kanamycin is an aminoglycoside antibiotic extensively used in veterinary medicine and food animal production. Because prolonged exposure may result in nephrotoxicity and ototoxicity, monitoring its residues is essential. Most LC biosensors for kanamycin utilize DNA aptamers due to their exceptionally high specificity. Upon target binding, aptamer conformational changes induce LC molecular reorientation, producing visible optical transitions. Practical applications have demonstrated successful detection in milk, honey, river water, and wastewater samples with response times of less than 20 minutes. Reported recoveries generally range between 94% and 106%, while detection limits frequently reach the picomolar concentration range.

6.7 Streptomycin

Streptomycin is another aminoglycoside antibiotic widely used for veterinary treatments and plant disease control. Residual streptomycin contamination has been reported in dairy products and agricultural environments. Recent LC biosensors employ aptamer-functionalized graphene oxide, AuNPs, and molecularly imprinted polymers to improve analytical selectivity. These sensors exhibit rapid optical responses with minimal sample preparation. Experimental validation using milk and environmental water samples has demonstrated recovery values of approximately 91%–105%, indicating high analytical reliability. Nevertheless, reducing cross-reactivity with structurally related aminoglycosides remains an ongoing research objective.

6.8 Ciprofloxacin

Ciprofloxacin, a widely prescribed fluoroquinolone antibiotic, is frequently detected in wastewater treatment plant effluents and hospital discharges due to incomplete degradation. Nanotechnology-enhanced LC biosensors employing graphene oxide, carbon nanotubes, and aptamer-functionalized AuNPs have achieved sensitive ciprofloxacin detection with rapid response times. Practical analyses of wastewater, river water, and pharmaceutical samples have demonstrated detection limits within the low nanomolar range. Recovery studies commonly report values between 95% and 108%, confirming excellent analytical accuracy even in complex environmental matrices [45].

6.9 Sulfonamides

Sulfonamide antibiotics are extensively used in livestock production because of their broad-spectrum antimicrobial activity. Their persistent presence in environmental waters has raised concerns regarding ecological toxicity and antimicrobial resistance. LC biosensors utilizing molecularly imprinted polymers, antibodies, and aptamers have demonstrated effective recognition of various sulfonamide compounds. The incorporation of porous nanomaterials such as metal–organic frameworks (MOFs) further enhances analyte adsorption and sensitivity.

Practical applications include analysis of meat extracts, river water, wastewater, and honey with satisfactory recovery values generally exceeding 90%.

6.10 Gentamicin

Gentamicin is a clinically important aminoglycoside antibiotic widely used for treating severe bacterial infections. Monitoring therapeutic concentrations and residual contamination is important because of its potential nephrotoxicity. Several LC biosensors employing antibody-functionalized AuNPs and aptamer-modified graphene oxide have demonstrated successful detection of gentamicin in serum, urine, and pharmaceutical preparations. Experimental studies indicate rapid detection within approximately 20 minutes, with recovery values ranging from 92% to 106%, demonstrating good agreement with conventional HPLC measurements [46].

6.11 Erythromycin

Erythromycin belongs to the macrolide class of antibiotics and is frequently detected in hospital wastewater and surface water owing to its extensive clinical use. LC biosensors incorporating aptamers and molecularly imprinted polymers have demonstrated efficient recognition of erythromycin through LC optical reorientation. Successful applications have been reported for river water, wastewater, and pharmaceutical formulations, achieving recoveries typically between 90% and 105%. Although analytical sensitivity is excellent, further improvements in selectivity are required for simultaneous detection of multiple macrolide antibiotics.

6.12 Amoxicillin

Amoxicillin is one of the most frequently prescribed β -lactam antibiotics worldwide and is commonly monitored in dairy products, wastewater, and pharmaceutical formulations. Recent LC biosensors employing AuNP–aptamer nanocomposites and molecularly imprinted polymers have demonstrated rapid label-free detection with low nanomolar detection limits. Practical analyses of milk, drinking water, and pharmaceutical samples have reported recoveries generally ranging from 94% to 108%, confirming their applicability for routine residue monitoring [47].

6.13 Practical Applications in Real Samples

One of the greatest advantages of LC biosensors is their successful application to complex real-world samples without requiring extensive sample preparation. Numerous studies have demonstrated reliable antibiotic detection in:

- a) Milk and dairy products: Monitoring β -lactams, tetracyclines, aminoglycosides, and chloramphenicol to ensure compliance with maximum residue limits.
- b) Meat and poultry: Detection of veterinary antibiotic residues before commercial distribution.
- c) Honey: Identification of chloramphenicol, tetracycline, and sulfonamide contamination.
- d) Fish and seafood: Monitoring antibiotics used in aquaculture, including oxytetracycline and erythromycin.
- e) River water and wastewater: Surveillance of pharmaceutical contamination and environmental dissemination of antibiotics.

- f) Clinical samples: Determination of therapeutic antibiotic concentrations in serum and urine for personalized drug monitoring.

In most validation studies, LC biosensor results showed excellent correlation with established analytical techniques such as HPLC and LC–MS/MS, while offering shorter analysis times, lower costs, and simplified operation [48].

6.14 Critical Evaluation

Despite remarkable progress, several challenges remain before LC biosensors can be widely commercialized. Cross-reactivity among structurally related antibiotics, variations in sample matrices, environmental sensitivity of LC alignment, and long-term stability of recognition elements continue to influence analytical performance. Furthermore, although many reported biosensors achieve excellent limits of detection under laboratory conditions, large-scale validation using diverse real-world samples is still limited. Standardized fabrication procedures, improved multiplex detection capabilities, and integration with smartphone-based image analysis and artificial intelligence are expected to enhance future sensor reliability and field applicability. Overall, nanotechnology-enhanced LC biosensors have demonstrated excellent sensitivity, rapid response, and reliable recoveries in practical food, environmental, and clinical samples. Their ability to provide label-free and, in many cases, naked-eye detection makes them highly promising alternatives to conventional chromatographic methods for routine antibiotic residue monitoring [49]. The Summary of the Advantages, Applications, Challenges, and Future Perspectives of Nanotechnology-Enhanced Liquid Crystal (LC)-Based Biosensors for Antibiotic Detection as shown in Table1.

Table 1. Summary of the Advantages, Applications, Challenges, and Future Perspectives of Nanotechnology-Enhanced Liquid Crystal (LC)-Based Biosensors for Antibiotic Detection

Category	Aspect	Detailed Explanation
Advantages	Label-free detection	LC biosensors directly convert molecular recognition events into optical signals through changes in liquid crystal orientation, eliminating the need for fluorescent dyes, radioactive labels, or enzyme-based signal amplification. This simplifies sensor fabrication and reduces analysis costs.
	Rapid analysis	Most LC biosensors provide results within 5–30 minutes, making them suitable for rapid screening and on-site detection of antibiotic residues.
	Naked-eye visualization	Changes in LC molecular alignment generate visible optical transitions (dark-to-bright or bright-to-dark), enabling qualitative detection without sophisticated analytical instruments.
	High sensitivity	The cooperative reorientation of LC molecules amplifies minute interfacial changes, allowing detection of antibiotics at nanomolar, picomolar, and sometimes femtomolar concentrations.
	High selectivity	Functionalization with aptamers, antibodies, molecularly imprinted polymers (MIPs), and other recognition elements ensures highly specific

		detection of target antibiotics while minimizing interference from structurally similar compounds.
	Low fabrication cost	Compared with chromatographic methods, LC biosensors require inexpensive optical components, small reagent volumes, and relatively simple fabrication procedures, reducing overall operational costs.
	Portable design	Compact sensor architecture enables the development of portable and handheld devices suitable for field applications, food industries, and clinical settings.
	Minimal sample preparation	Many biological and environmental samples require only simple filtration, dilution, or centrifugation before analysis, reducing testing time and complexity.
	Real-time monitoring	LC biosensors continuously respond to molecular interactions, enabling immediate observation of antibiotic binding and dynamic monitoring of analyte concentrations.
	Compatibility with smartphone imaging	Smartphone cameras combined with image-processing software can quantitatively analyze LC optical responses, providing inexpensive and user-friendly diagnostic platforms.
	Suitability for point-of-care diagnostics	Rapid response, portability, low power requirements, and visual signal generation make LC biosensors highly suitable for point-of-care testing in healthcare, veterinary medicine, and environmental monitoring.
Applications	Food safety monitoring	Detection of antibiotic residues in food products helps ensure compliance with maximum residue limits (MRLs), protects consumer health, and supports regulatory surveillance.
	Dairy quality assessment	LC biosensors are widely applied for monitoring tetracyclines, β -lactams, aminoglycosides, and other antibiotics in milk, cheese, yogurt, and related dairy products.
	Meat inspection	Rapid screening of antibiotic residues in poultry, beef, pork, and seafood improves food quality control before commercial distribution.
	Environmental surveillance	LC biosensors enable monitoring of antibiotic contamination in rivers, lakes, groundwater, agricultural runoff, and industrial discharge, supporting ecosystem protection.
	Wastewater monitoring	Sensitive detection of pharmaceutical residues in hospital and municipal wastewater facilitates environmental risk assessment and treatment process evaluation.
	Clinical therapeutic drug monitoring	Determination of antibiotic concentrations in blood, serum, urine, and other biological fluids supports personalized medicine and optimized antibiotic therapy.

	Pharmaceutical quality control	LC biosensors assist in evaluating antibiotic content, stability, purity, and manufacturing consistency during pharmaceutical production.
	Veterinary diagnostics	Detection of antibiotic residues in livestock and monitoring veterinary drug administration help reduce antimicrobial resistance and improve animal health management.
Challenges	Long-term stability of LC alignment layers	Prolonged exposure to environmental conditions may degrade alignment layers, affecting LC orientation and reducing sensor performance over time.
	Environmental sensitivity	Temperature, humidity, pH, and ionic strength significantly influence LC molecular alignment, requiring careful environmental control during sensing.
	Limited multiplexing capability	Most current LC biosensors are designed to detect a single antibiotic, whereas simultaneous detection of multiple antibiotics remains technically challenging.
	Large-scale manufacturing	Fabrication of highly uniform and reproducible LC biosensors suitable for industrial-scale production requires further technological development.
	Sensor reproducibility	Variations in nanomaterial synthesis, receptor immobilization, and LC alignment may introduce batch-to-batch variability, affecting analytical consistency.
	Commercial standardization	Lack of standardized fabrication protocols, calibration procedures, and regulatory validation limits widespread commercialization and clinical implementation.
	Integration with portable electronics	Although considerable progress has been achieved, seamless integration of LC biosensors with smartphones, wearable devices, and wireless electronics requires further optimization.
Future Perspectives	AI-assisted optical image analysis	Artificial intelligence and machine learning algorithms can automatically analyze LC optical textures, improving sensitivity, reducing human error, and enabling quantitative interpretation.
	Smartphone-based quantitative detection	Smartphone cameras integrated with dedicated applications can capture LC optical images and perform rapid quantitative analysis, enabling affordable field diagnostics.
	Flexible wearable LC biosensors	Flexible substrates combined with LC sensing materials may enable wearable devices capable of continuous monitoring of antibiotics and other biomarkers.
	Multiplex detection arrays	Future LC biosensors are expected to simultaneously detect multiple classes of antibiotics using sensor arrays functionalized with different recognition elements.

	Microfluidic lab-on-a-chip integration	Combining LC biosensors with microfluidic systems will reduce sample volume, improve automation, shorten analysis time, and enable portable diagnostic devices.
	Internet of Things (IoT)-enabled monitoring	Wireless LC biosensors connected through IoT platforms could facilitate real-time remote monitoring of food safety, environmental contamination, and clinical diagnostics.
	Commercial disposable diagnostic strips	Development of inexpensive, disposable LC biosensor strips will simplify routine antibiotic testing and support widespread adoption in resource-limited settings.

Nanotechnology-enhanced LC biosensors combine high sensitivity, rapid response, label-free operation, and portable design, making them highly promising alternatives to conventional analytical methods for antibiotic detection. Although challenges related to stability, reproducibility, and commercialization remain, ongoing advances in nanotechnology, artificial intelligence, microfluidics, wearable electronics, and smartphone-based diagnostics are expected to accelerate the translation of LC biosensors into practical tools for food safety monitoring, environmental surveillance, pharmaceutical quality control, veterinary diagnostics, and personalized healthcare. Nanotechnology-enhanced liquid crystal (LC)-based biosensors have emerged as a powerful platform for the rapid, label-free, and highly sensitive detection of antibiotic residues. By combining selective recognition elements with advanced nanomaterials, these biosensors convert molecular interactions into easily observable optical signals, enabling simple, cost-effective, and even naked-eye detection. Their high sensitivity, portability, and minimal sample preparation make them well suited for applications in food safety, environmental monitoring, pharmaceutical quality control, and point-of-care diagnostics [50].

7. Conclusions

- A. The principle of liquid crystal biosensing is based on the extraordinary ability of ordered LC molecules to amplify nanoscale molecular recognition events into macroscopically observable optical signals. The cooperative reorientation of LC molecules following antibiotic binding provides an efficient label-free transduction mechanism with exceptional sensitivity. Integration with advanced nanomaterials, highly selective recognition elements, and portable optical imaging systems has transformed LC biosensors into versatile analytical platforms capable of rapid, cost-effective, and naked-eye detection of antibiotic residues. These unique characteristics position LC biosensors as one of the most promising next-generation technologies for applications in food safety monitoring, environmental surveillance, pharmaceutical quality control, and point-of-care clinical diagnostics.
- B. The integration of advanced nanomaterials has transformed conventional liquid crystal biosensors into highly efficient analytical platforms with superior sensitivity, selectivity, and operational reliability. Nanotechnology enables rapid detection of trace antibiotic residues while maintaining simple, label-free operation and visual signal interpretation. Modern nanotechnology-assisted LC biosensors are capable of analyzing antibiotics in complex matrices such as milk, meat, seafood, honey, drinking water, wastewater, and biological fluids with minimal sample preparation. Continuous advances in nanomaterial synthesis, surface

functionalization, and hybrid nanocomposite design are expected to further improve sensor performance and facilitate the development of portable, low-cost, and point-of-care diagnostic devices for food safety monitoring, environmental surveillance, and clinical diagnostics.

- C. Recognition elements constitute the core sensing component of liquid crystal biosensors by providing the molecular specificity required for accurate antibiotic detection. Among the available recognition strategies, aptamers have emerged as the most promising owing to their high affinity, excellent stability, ease of synthesis, low cost, and compatibility with nanotechnology-assisted sensing platforms. Nevertheless, monoclonal antibodies, molecularly imprinted polymers, antimicrobial peptides, DNA probes, and enzyme-based receptors continue to play important roles in expanding the versatility and analytical capabilities of LC biosensors. The ongoing integration of advanced recognition molecules with nanotechnology is expected to further improve the sensitivity, selectivity, and practical applicability of next-generation LC biosensors for food safety, environmental monitoring, pharmaceutical quality control, and point-of-care diagnostics.
- D. The detection mechanism of nanotechnology-enhanced LC biosensors is based on the highly sensitive conversion of molecular recognition events into macroscopic optical signals through liquid crystal reorientation. Functionalized nanomaterials provide selective recognition and efficient signal amplification, while the intrinsic cooperative behavior of LC molecules enables label-free visualization of antibiotic binding. This unique mechanism eliminates the need for fluorescent or enzymatic labels, allowing rapid, cost-effective, and highly sensitive detection of antibiotic residues. Owing to their simplicity, portability, and naked-eye readout capability, LC biosensors represent a promising analytical platform for food safety monitoring, environmental surveillance, pharmaceutical quality control, and point-of-care clinical diagnostics.
- E. Nanotechnology-driven liquid crystal biosensors represent a transformative platform for the rapid, label-free, and highly sensitive detection of antibiotics. Their ability to translate molecular recognition into easily interpretable optical signals enables simple naked-eye detection without sophisticated instrumentation. The incorporation of advanced nanomaterials has markedly improved analytical performance, making these sensors attractive for point-of-care diagnostics and on-site monitoring. Continued advances in nanotechnology, microfluidics, artificial intelligence, and portable imaging systems are expected to overcome current limitations and accelerate commercialization. As concerns regarding antimicrobial resistance continue to grow, LC-based biosensors are poised to become indispensable analytical tools for ensuring food safety, environmental protection, and public health.

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Authors' Contributions

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Abbreviation	Full Form
AgNPs	Silver Nanoparticles
AI	Artificial Intelligence
AMPs	Antimicrobial Peptides
AMR	Antimicrobial Resistance
AuNPs	Gold Nanoparticles
CE	Capillary Electrophoresis
CNTs	Carbon Nanotubes
CRISPR	Clustered Regularly Interspaced Short Palindromic Repeats
DNA	Deoxyribonucleic Acid
DMOAP	Dimethyloctadecyl[3-(trimethoxysilyl)propyl] Ammonium Chloride
ELISA	Enzyme-Linked Immunosorbent Assay
Fe ₃ O ₄	Iron Oxide Magnetic Nanoparticles
GC	Gas Chromatography
GC–MS	Gas Chromatography–Mass Spectrometry
GO	Graphene Oxide
HPLC	High-Performance Liquid Chromatography
IoT	Internet of Things
LC	Liquid Crystal
LC–MS	Liquid Chromatography–Mass Spectrometry
LC–MS/MS	Liquid Chromatography–Tandem Mass Spectrometry
LSPR	Localized Surface Plasmon Resonance
MIPs	Molecularly Imprinted Polymers
MOFs	Metal–Organic Frameworks
MRLs	Maximum Residue Limits
MWCNTs	Multi-Walled Carbon Nanotubes
POC	Point-of-Care
POM	Polarized Optical Microscopy

Abbreviation	Full Form
QDs	Quantum Dots
rGO	Reduced Graphene Oxide
RNA	Ribonucleic Acid
SAMs	Self-Assembled Monolayers
SELEX	Systematic Evolution of Ligands by Exponential Enrichment
SPR	Surface Plasmon Resonance
SWCNTs	Single-Walled Carbon Nanotubes
WHO	World Health Organization

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