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Next-Generation Biosensors for Pharmaceutical Analysis: Advances in Point-Of-Care Drug Detection and Monitoring

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Abstract: The rapid evolution of biosensor technologies has transformed pharmaceutical analysis by enabling highly sensitive, selective, and rapid drug detection platforms suitable for point-of-care and real-time therapeutic monitoring. Conventional analytical approaches such as high-performance liquid chromatography, liquid chromatography–mass spectrometry, and immunoassays remain gold standards for pharmaceutical quantification; however, their dependency on centralized laboratories, expensive instrumentation, skilled personnel, and time-intensive workflows has accelerated the demand for portable biosensing alternatives. Recent advances in nanotechnology, microfluidics, artificial intelligence, wearable electronics, and molecular biorecognition systems have significantly expanded the capabilities of next-generation biosensors in pharmaceutical applications. Electrochemical, optical, piezoelectric, fluorescence-based, and field-effect transistor biosensors are increasingly being integrated with aptamers, antibodies, enzymes, molecularly imprinted polymers, and CRISPR systems for highly accurate therapeutic drug monitoring and decentralized healthcare delivery. Point-of-care biosensors have demonstrated substantial utility in antibiotic monitoring, anticancer drug analysis, immunosuppressant quantification, overdose detection, and personalized pharmacotherapy. Simultaneously, wearable and implantable biosensors are facilitating continuous monitoring using sweat, saliva, tears, and interstitial fluid. Despite remarkable progress, challenges associated with biofouling, calibration drift, reproducibility, regulatory approval, and large-scale commercialization continue to limit widespread clinical implementation. Artificial intelligence-assisted biosensor analytics, smartphone integration, and cloud-based therapeutic management systems are expected to accelerate the transition toward intelligent decentralized pharmaceutical care. This review comprehensively discusses recent developments in biosensor technologies for pharmaceutical analysis, emphasizing point-of-care drug detection, therapeutic monitoring, wearable systems, analytical validation, clinical applications, translational challenges, and future prospects.

Keywords: Biosensors, Pharmaceutical analysis, Point-of-care testing, Therapeutic drug monitoring, Wearable biosensors.

1. INTRODUCTION

1.1. Evolution of Pharmaceutical Analysis from Conventional Laboratory Methods to Biosensor-Based Platforms

Pharmaceutical analysis has historically relied on laboratory-centered analytical technologies such as high-performance liquid chromatography (HPLC), ultra-high-performance liquid chromatography (UHPLC), gas chromatography, capillary electrophoresis, spectrophotometry, and liquid chromatography–mass spectrometry (LC-MS/MS). These analytical platforms provide exceptional sensitivity and selectivity for the quantification of active pharmaceutical ingredients, metabolites, degradation products, and impurities. However, such techniques require sophisticated instrumentation, extensive sample preparation, trained personnel, controlled laboratory environments, and prolonged analytical timelines, thereby limiting their utility in decentralized and emergency healthcare settings [1, 2].

The emergence of biosensor technology has fundamentally changed the landscape of pharmaceutical analysis by enabling rapid, portable, low-volume, and real-time analytical systems. Biosensors integrate biological recognition elements with physicochemical transducers to convert biological interactions into measurable analytical signals. Early biosensor systems were primarily enzyme-based glucose sensors developed for diabetes monitoring, but recent advances have enabled multiplexed drug detection, pharmacokinetic monitoring, biomarker profiling, and continuous therapeutic assessment [3, 4].

The convergence of nanotechnology, flexible electronics, microfluidics, and artificial intelligence has accelerated the development of next-generation biosensors with enhanced sensitivity, miniaturization, and connectivity. Modern biosensors can detect pharmaceutical compounds at nanomolar or picomolar concentrations while operating in complex biological matrices such as blood, sweat, saliva, tears, and interstitial fluid [5]. These developments have shifted biosensors from simple diagnostic tools toward integrated digital therapeutic monitoring systems capable of supporting precision medicine.

In recent years, pharmaceutical industries and healthcare systems have increasingly explored biosensor technologies for applications including therapeutic drug monitoring, counterfeit drug detection, process analytical technology, pharmacokinetic analysis, and bedside monitoring [6]. The COVID-19 pandemic further highlighted the importance of decentralized diagnostic and monitoring systems, accelerating investments in portable biosensor platforms suitable for remote healthcare and community-based pharmaceutical management [7].

1.2. Need for Point-of-Care Drug Detection and Real-Time Therapeutic Monitoring

Therapeutic drug monitoring (TDM) plays a critical role in optimizing pharmacotherapy, particularly for drugs characterized by narrow therapeutic indices, high interpatient variability, nonlinear pharmacokinetics, or significant toxicity profiles. Conventional TDM workflows involve centralized laboratory analysis, which may delay dose adjustment and clinical decision-making [8]. Delayed drug concentration reporting is especially problematic in critically ill patients, oncology settings, transplant medicine, and emergency toxicology.

Point-of-care (POC) biosensors address these limitations by enabling rapid bedside drug analysis and near real-time therapeutic assessment. The ability to perform immediate drug quantification can improve clinical responsiveness, reduce hospitalization duration, and minimize adverse drug reactions [9]. For example, rapid monitoring of antibiotics such as vancomycin or aminoglycosides can prevent nephrotoxicity and optimize antimicrobial stewardship programs.

The increasing prevalence of personalized medicine has also intensified the need for individualized therapeutic monitoring systems. Genetic polymorphisms, age, organ dysfunction, drug–drug interactions, and disease-specific factors substantially influence drug metabolism and pharmacodynamics [10]. Biosensor-based monitoring platforms facilitate dynamic dose optimization by providing continuous pharmacokinetic data directly at the patient interface.

Another major driver for POC biosensors is the global expansion of decentralized healthcare services. Rural healthcare systems, resource-limited regions, emergency departments, home-based care settings, and telemedicine platforms require analytical technologies that are portable, low-cost, and easy to operate [11]. Smartphone-integrated biosensors and wearable analytical systems are increasingly fulfilling these requirements while simultaneously enabling digital healthcare connectivity.

Real-time therapeutic monitoring is particularly valuable in chronic disease management. Continuous biosensing technologies can support longitudinal monitoring of antiepileptic drugs, immunosuppressants, psychiatric medications, and cardiovascular therapeutics. Such systems may improve medication adherence, reduce adverse events, and support adaptive dosing strategies [12].

1.3. Scope and Objectives of the Review

The growing complexity of pharmaceutical therapy and the rising demand for personalized healthcare have positioned biosensor technologies at the forefront of modern pharmaceutical analysis. Although several reviews have discussed diagnostic biosensors and biomedical sensing systems, there remains a need for a comprehensive review specifically focused on next-generation biosensors in pharmaceutical analysis and therapeutic drug monitoring.

This review aims to critically evaluate recent advances in biosensor technologies for pharmaceutical applications, with particular emphasis on point-of-care drug detection and monitoring. The manuscript discusses biosensor fundamentals, recognition elements, transduction mechanisms, nanomaterial integration, wearable systems, artificial intelligence-assisted analytics, and regulatory considerations. Applications in therapeutic drug monitoring, pharmaceutical quality control, overdose detection, and decentralized healthcare are also comprehensively examined.

Special attention is given to electrochemical biosensors, aptamer-based sensing systems, paper-based platforms, lab-on-a-chip technologies, smartphone-integrated biosensors, wearable biosensors, and implantable analytical systems. The review additionally compares biosensor technologies with conventional analytical approaches including HPLC, LC-MS/MS, spectrophotometry, and immunoassays.

The translational potential of biosensors for clinical implementation, personalized medicine, and decentralized pharmaceutical care is discussed alongside existing technological and regulatory barriers. Emerging directions such as AI-assisted closed-loop therapeutic systems, self-powered wearable biosensors, and multiplexed analytical platforms are also explored.

2. FUNDAMENTALS OF BIOSENSORS IN PHARMACEUTICAL ANALYSIS

2.1. Basic Architecture of Biosensors: Bioreceptor, Transducer, Signal Processor, and Output System

A biosensor is an integrated analytical device capable of detecting target analytes through biological recognition coupled with signal conversion mechanisms. The classical biosensor architecture consists of four major components: the bioreceptor, transducer, signal processor, and output system [13]. The bioreceptor represents the biologically active component responsible for selective analyte recognition. Bioreceptors may include enzymes, antibodies, aptamers, nucleic acids, receptors, molecularly imprinted polymers, or living cells. The specificity of the biosensor largely depends on the molecular affinity and selectivity of the recognition element [14].

The transducer converts biochemical interactions into quantifiable electrical, optical, thermal, or mechanical signals. Electrochemical transducers are the most widely utilized in pharmaceutical biosensing because of their low cost, miniaturization potential, and excellent analytical sensitivity. Optical and piezoelectric transducers are also increasingly employed for high-resolution drug monitoring applications [15].

Signal processing systems amplify and interpret the generated signals while minimizing background noise and matrix interference. Advances in digital electronics, machine learning algorithms, and embedded computing have significantly improved signal interpretation accuracy in portable biosensor devices [16]. Modern biosensors often incorporate wireless communication modules for smartphone or cloud-based integration.

The output system provides analytical results in user-accessible formats such as digital displays, smartphone applications, wireless dashboards, or automated therapeutic adjustment systems. Recent developments in user-interface engineering have enhanced the practicality of biosensors for bedside and home-based healthcare applications [17].

2.2. Classification of Biosensors Based on Recognition Elements

Biosensors are commonly classified according to the biological recognition element employed for analyte detection. Enzyme-based biosensors constitute one of the oldest and most commercially successful categories. These systems utilize catalytic enzymatic reactions to generate measurable analytical signals proportional to analyte concentration [18]. Immunosensors employ antibodies or antibody fragments for highly selective antigen recognition. Such biosensors are extensively utilized in therapeutic drug monitoring, biomarker analysis, and pharmaceutical impurity detection. Monoclonal antibodies improve specificity, whereas recombinant antibody technologies enhance stability and scalability [19].

Aptamer-based biosensors have emerged as promising alternatives to antibody-based platforms. Aptamers are short oligonucleotide sequences capable of binding specific targets with high affinity. Compared with antibodies, aptamers offer superior thermal stability, synthetic reproducibility, lower production costs, and easier surface modification [20]. Molecularly imprinted polymer (MIP)-based biosensors utilize synthetic recognition cavities generated through template-directed polymerization. These systems exhibit excellent chemical stability and resistance to harsh environmental conditions, making them suitable for long-term pharmaceutical sensing applications [21].

Cell-based biosensors incorporate living cells to detect pharmacological or toxicological responses. Such systems are particularly valuable for evaluating drug bioactivity, cytotoxicity, and pharmacodynamic effects [22]. Whole-cell biosensors also provide insights into cellular signaling pathways influenced by pharmaceutical compounds.

2.3. Classification of Biosensors Based on Transduction Mechanisms

Transduction mechanisms determine how biochemical interactions are converted into measurable analytical signals. Electrochemical biosensors dominate pharmaceutical applications because of their sensitivity, affordability, and compatibility with miniaturized electronics [23]. These sensors include amperometric, potentiometric, conductometric, and impedimetric platforms. Optical biosensors detect analyte-induced changes in absorbance, fluorescence, luminescence, refractive index, or surface plasmon resonance. Optical approaches provide exceptionally low detection limits and high multiplexing capability [24].

Piezoelectric biosensors measure mass-induced resonance frequency changes on crystal surfaces. Quartz crystal microbalance systems are increasingly employed for real-time drug-binding studies and pharmaceutical interaction analysis [25]. Thermal biosensors detect temperature variations generated during biochemical reactions, whereas magnetic biosensors exploit magnetic nanoparticles for analyte capture and signal enhancement. Nanoelectronic biosensors including field-effect transistor (FET)-based systems represent a rapidly growing category characterized by ultrahigh sensitivity and real-time signal acquisition [26].

2.4. Analytical Performance Parameters: Sensitivity, Selectivity, Accuracy, Precision, Limit of Detection, and Response Time

The analytical performance of biosensors is critically influenced by multiple validation parameters. Sensitivity refers to the ability of the sensor to generate measurable signal changes in response to analyte concentration variations [27]. Nanomaterials, signal amplification strategies, and surface engineering significantly enhance biosensor sensitivity. Selectivity represents the capability to discriminate target analytes from interfering compounds present within complex biological matrices. High selectivity is essential in pharmaceutical analysis because structurally related metabolites, proteins, salts, and endogenous biomolecules may generate analytical interference [28].

Accuracy and precision determine the reliability and reproducibility of biosensor measurements. Accuracy reflects closeness to the true analyte concentration, whereas precision describes measurement consistency across repeated analyses. Clinical implementation requires rigorous reproducibility validation under variable environmental and biological conditions [29]. The limit of detection (LOD) represents the lowest analyte concentration distinguishable from background noise. Advanced nanobiosensors can achieve femtomolar-level detection for certain therapeutic agents and biomarkers [30]. Response time is equally important for point-of-care applications because rapid therapeutic decisions depend on immediate analytical feedback.

Environmental stability, shelf-life, operational robustness, and resistance to biofouling also influence practical biosensor utility. Commercial translation requires maintaining analytical performance under real-world storage and operating conditions [31].

Table 1. *Classification of next-generation biosensors used in pharmaceutical analysis*

Biosensor Type	Recognition Element	Transduction Method	Pharmaceutical Application	Advantages	Limitations
Enzyme biosensor	Enzymes	Electrochemical	Antibiotic monitoring	High sensitivity	Enzyme instability
Immunosensor	Antibodies	Optical/Electrochemical	Anticancer drug detection	Excellent specificity	Expensive antibodies
Aptamer biosensor	Aptamers	Electrochemical/FET	Therapeutic drug monitoring	High stability	Aptamer optimization required
MIP biosensor	Molecularly imprinted polymers	Electrochemical	Drug impurity detection	Robustness	Template leakage
Optical biosensor	Antibodies/Aptamers	SPR/Fluorescence	Pharmacokinetic studies	Real-time monitoring	Expensive instrumentation
Wearable biosensor	Multiple	Electrochemical	Sweat drug analysis	Continuous monitoring	Calibration challenges

3. BIORECOGNITION ELEMENTS FOR DRUG DETECTION

3.1. Enzyme-Based Biosensors

Enzyme-based biosensors remain among the most widely investigated biosensing systems for pharmaceutical analysis due to their remarkable catalytic efficiency and substrate specificity. These biosensors utilize enzymes as biological recognition elements capable of selectively interacting with target analytes and generating measurable signals proportional to analyte concentration [32]. The catalytic conversion of substrates often produces electroactive species such as hydrogen peroxide, protons, or electrons, which can subsequently be detected using electrochemical transducers.

In pharmaceutical analysis, enzyme-based biosensors have demonstrated significant utility in the monitoring of antibiotics, analgesics, anticancer drugs, and metabolic biomarkers associated with drug pharmacokinetics. Oxidase- and dehydrogenase-based biosensors are particularly important because of their compatibility with amperometric sensing platforms [33]. For instance, cytochrome P450 enzyme systems have been incorporated into biosensors to investigate drug metabolism and toxicity screening, thereby enabling rapid pharmacological profiling of candidate compounds.

Recent research has focused extensively on enzyme immobilization strategies aimed at improving biosensor stability and operational lifespan. Immobilization approaches including covalent bonding, entrapment within nanomaterials, adsorption onto conductive substrates, and encapsulation in hydrogels have improved enzyme retention and catalytic activity [34]. Nanostructured materials such as graphene oxide, gold nanoparticles, and carbon nanotubes enhance electron transfer efficiency while preserving enzymatic functionality.

Despite their excellent specificity, enzyme-based biosensors are associated with several limitations. Enzymatic activity may decline because of pH variations, thermal instability, denaturation, and inhibitor interference [35]. Long-term storage stability also remains problematic for many enzyme systems. Consequently, contemporary biosensor research increasingly explores engineered enzymes, recombinant protein stabilization, and hybrid biomimetic systems to overcome these constraints.

The integration of enzyme biosensors into microfluidic and wearable devices has expanded their applicability for real-time therapeutic monitoring. Sweat-based enzymatic biosensors capable of detecting therapeutic compounds and metabolic products have shown promise for personalized healthcare applications [36]. Such developments highlight the growing importance of enzyme biosensors in decentralized pharmaceutical analysis.

3.2. Antibody-Based Immunosensors

Antibody-based immunosensors exploit the high specificity of antigen–antibody interactions to detect pharmaceutical compounds with exceptional selectivity. These biosensors are particularly valuable for detecting drugs present at low concentrations in complex biological matrices such as plasma, serum, and urine [37]. Monoclonal antibodies are frequently employed due to their uniform binding affinity and reproducibility, whereas polyclonal antibodies offer broader recognition but may suffer from batch variability.

In pharmaceutical analysis, immunosensors have been extensively applied for monitoring anticancer agents, immunosuppressants, antibiotics, and hormones. For instance, immunosensors for drugs such as methotrexate, cyclosporine, and digoxin have demonstrated high sensitivity and rapid detection compared to conventional immunoassays [38]. Optical immunosensors, particularly those based on fluorescence and chemiluminescence, provide enhanced signal amplification and multiplexing capability.

Recent advancements have focused on antibody engineering and recombinant antibody fragments, including single-chain variable fragments (scFv) and nanobodies, which improve stability and facilitate surface immobilization [39]. Coupling antibodies with nanomaterials such as gold nanoparticles or quantum dots has further enhanced signal transduction efficiency and detection limits.

However, immunosensors face limitations related to antibody stability, high production costs, and susceptibility to denaturation under non-ideal conditions [40]. Cross-reactivity with structurally similar compounds may also compromise analytical accuracy. Despite these challenges, immunosensors remain indispensable tools in therapeutic drug monitoring and pharmaceutical quality assessment.

3.3. Aptamer-Based Biosensors

Aptamer-based biosensors represent a rapidly evolving class of analytical devices that utilize synthetic oligonucleotides capable of binding target molecules with high affinity and specificity. Aptamers are selected through systematic evolution of ligands by exponential enrichment (SELEX), allowing the generation of highly selective recognition elements for a wide range of pharmaceutical compounds [41].

Compared with antibodies, aptamers offer several advantages including superior thermal stability, ease of chemical modification, low immunogenicity, and cost-effective synthesis. These characteristics make aptamer-based biosensors particularly attractive for point-of-care applications and long-term storage [42]. Aptamers have been successfully developed for detecting antibiotics, anticancer drugs, small-molecule therapeutics, and illicit substances.

Electrochemical aptasensors are among the most widely investigated platforms due to their compatibility with miniaturized electronics and rapid signal generation. Structural changes in aptamers upon target binding can be transduced into measurable electrical signals, enabling real-time drug monitoring [43]. Optical aptasensors utilizing fluorescence resonance energy transfer (FRET) and colorimetric detection have also shown promising analytical performance.

Despite their advantages, aptamers may exhibit limitations in binding affinity under physiological conditions, and their performance can be affected by complex biological matrices [44]. Ongoing research aims to improve aptamer stability and binding efficiency through chemical modifications and hybrid biosensing strategies.

3.4. Molecularly Imprinted Polymer-Based Biosensors

Molecularly imprinted polymers (MIPs) are synthetic recognition materials engineered to possess specific binding sites complementary to target analytes. These materials are fabricated through polymerization in the presence of a template molecule, which is subsequently removed to create recognition cavities [45]. MIP-based biosensors have gained attention in pharmaceutical analysis due to their robustness, chemical stability, and resistance to harsh environmental conditions. Unlike biological recognition elements, MIPs are not susceptible to enzymatic degradation or denaturation, making them suitable for long-term and reusable sensing applications [46].

Applications of MIP biosensors include detection of antibiotics, analgesics, hormones, and pharmaceutical impurities. Integration with electrochemical transducers has enabled highly sensitive detection with low limits of detection. Additionally, nanostructured MIPs incorporating nanoparticles or graphene-based materials have further enhanced analytical performance [47]. However, MIPs may suffer from template leakage, incomplete removal of the template molecule, and limited selectivity compared to biological recognition elements. Nevertheless, their durability and cost-effectiveness make them attractive alternatives for industrial and field-based pharmaceutical analysis.

3.5. Cell-Based and Whole-Cell Biosensors

Cell-based biosensors utilize living cells as sensing elements to detect biologically relevant responses to pharmaceutical compounds. These biosensors provide functional information regarding drug toxicity, pharmacodynamics, and cellular signaling pathways [48]. Whole-cell biosensors are particularly useful in drug screening and environmental pharmaceutical monitoring, where they can detect complex biological effects that cannot be captured by molecular recognition systems alone.

Genetically engineered cells expressing reporter genes enable quantification of drug-induced cellular responses through fluorescence, luminescence, or electrochemical signals [49]. Despite their advantages, cell-based biosensors require strict environmental control to maintain cell viability. Variability in cellular responses and limited operational stability remain key challenges for their widespread application [50].

3.6. Nucleic Acid- and CRISPR-Integrated Biosensing Platforms

Nucleic acid-based biosensors, including DNA and RNA sensors, have emerged as powerful tools for pharmaceutical detection, particularly for nucleic acid-targeting drugs and gene-based therapies. These biosensors rely on hybridization reactions between complementary sequences, enabling highly specific detection [51]. CRISPR-based biosensors represent a groundbreaking advancement, utilizing CRISPR-associated proteins such as Cas12 and Cas13 for highly sensitive and sequence-specific detection. These systems have demonstrated exceptional potential in detecting nucleic acid drugs, biomarkers, and pathogens [52].

Integration of CRISPR technology with microfluidics and portable detection systems has enabled rapid point-of-care diagnostic platforms. However, challenges related to scalability, cost, and regulatory approval must be addressed before widespread adoption [53].

4. TRANSDUCTION STRATEGIES IN NEXT-GENERATION BIOSENSORS

4.1. Electrochemical Biosensors

Electrochemical biosensors are the most widely used transduction systems in pharmaceutical analysis due to their simplicity, sensitivity, and compatibility with portable devices [54]. These sensors convert biochemical interactions into electrical signals such as current, voltage, or impedance. Amperometric sensors measure current generated by redox reactions, while potentiometric sensors detect potential differences between electrodes. Impedimetric biosensors evaluate changes in electrical impedance resulting from analyte binding [55].

Electrochemical biosensors are particularly suitable for therapeutic drug monitoring due to their rapid response times and ability to operate in complex biological matrices. Advances in nanomaterials and electrode design have significantly enhanced their analytical performance.

4.2. Optical Biosensors

Optical biosensors detect analyte-induced changes in optical properties such as absorbance, fluorescence, and refractive index. These biosensors offer high sensitivity and multiplexing capabilities, making them suitable for pharmaceutical applications [56]. Fluorescence-based biosensors are widely used due to their high signal-to-noise ratio. Advances in fluorescent probes and quantum dots have further improved detection limits and analytical precision.

4.3. Fluorescence and Chemiluminescence Biosensors

Fluorescence biosensors rely on emission of light upon excitation, whereas chemiluminescence biosensors generate light through chemical reactions. Both approaches provide highly sensitive detection with minimal background interference [57]. These biosensors are commonly used in drug detection assays, immunoassays, and biomarker analysis. Integration with microfluidic systems has enabled miniaturized and automated analytical platforms.

4.4. Surface Plasmon Resonance-Based Biosensors

Surface plasmon resonance (SPR) biosensors measure changes in refractive index near a sensor surface upon analyte binding. These label-free systems enable real-time monitoring of molecular interactions [58]. SPR biosensors are widely used in pharmaceutical research for studying drug–target interactions, binding kinetics, and pharmacodynamics.

4.5. Piezoelectric and Mass-Sensitive Biosensors

Piezoelectric biosensors detect mass changes on sensor surfaces by measuring variations in resonance frequency. Quartz crystal microbalance systems are commonly used for real-time monitoring of drug binding and adsorption processes [59].

4.6. Field-Effect Transistor and Nanoelectronic Biosensors

Field-effect transistor (FET)-based biosensors represent a new generation of nanoelectronic sensing devices characterized by ultra-high sensitivity and rapid signal transduction [60]. These sensors detect changes in electrical conductivity resulting from analyte binding at the sensor surface. Graphene-based FET biosensors have shown exceptional performance in detecting pharmaceutical compounds at extremely low concentrations.

5. NANOMATERIALS IN ADVANCED BIOSENSOR DESIGN

5.1. Gold and Silver Nanoparticle-Based Biosensors

Gold and silver nanoparticles play a crucial role in enhancing biosensor performance by improving electron transfer kinetics, increasing effective surface area for biomolecule immobilization, and enabling strong signal amplification. Their unique surface plasmon resonance properties further support optical detection strategies. These nanoparticles facilitate stable bioconjugation with enzymes, antibodies, and aptamers, thereby improving sensitivity and selectivity in pharmaceutical detection, especially for low-concentration drug analysis in complex biological matrices [61].

5.2. Graphene, Carbon Nanotubes, and Carbon Quantum Dots

Carbon-based nanomaterials such as graphene, carbon nanotubes, and carbon quantum dots exhibit exceptional electrical conductivity, mechanical strength, and high surface-to-volume ratios. These properties significantly enhance electron transfer rates and provide stable platforms for immobilizing biorecognition elements. Additionally, their chemical versatility enables functionalization for specific drug targets, making them highly suitable for electrochemical biosensors used in sensitive, rapid, and reliable pharmaceutical analysis and therapeutic monitoring applications [62].

5.3. Metal–Organic Frameworks and Covalent Organic Frameworks

Metal–organic frameworks (MOFs) and covalent organic frameworks (COFs) are highly porous materials characterized by large surface areas and tunable chemical functionalities. These features enable efficient analyte capture, selective binding, and enhanced signal transduction. Their structural versatility allows integration with various transducers, improving biosensor sensitivity and specificity. MOFs and COFs are increasingly explored for detecting pharmaceutical compounds, particularly in applications requiring high selectivity and multiplexed drug analysis in complex biological environments [63].

5.4. Magnetic Nanoparticles and Hybrid Nanocomposites

Magnetic nanoparticles are widely employed in biosensor systems due to their ability to facilitate efficient sample separation, target enrichment, and analyte preconcentration. When integrated with hybrid nanocomposites, they further enhance sensitivity, selectivity, and reproducibility. These systems are particularly beneficial in complex biological matrices where interference is significant. Magnetic nanomaterials also support automation and rapid processing, making them highly suitable for point-of-care pharmaceutical analysis and high-throughput drug detection platforms [64].

5.5. Quantum Dots and Upconversion Nanoparticles

Quantum dots and upconversion nanoparticles possess unique optical properties, including high fluorescence intensity, excellent photostability, and tunable emission spectra. These characteristics enable highly sensitive and multiplexed detection of pharmaceutical compounds. Their ability to emit distinct signals under specific excitation conditions allows simultaneous detection of multiple analytes. Consequently, they are widely used in fluorescence-based biosensors for advanced drug monitoring, biomarker analysis, and real-time pharmaceutical diagnostics [65].

5.6. Advantages and Limitations of Nanomaterial-Assisted Biosensors

Nanomaterial-assisted biosensors offer significant advantages, including enhanced sensitivity, reduced detection limits, faster response times, and improved signal amplification. However, challenges such as potential nanotoxicity, environmental concerns, batch-to-batch variability, and complex synthesis procedures may hinder large-scale adoption. Additionally, regulatory uncertainties and reproducibility issues remain critical barriers. Addressing these limitations through standardized fabrication and safety evaluation is essential for successful clinical and industrial translation [66].

6. POINT-OF-CARE BIOSENSORS FOR PHARMACEUTICAL ANALYSIS

6.1. Concept and Requirements of Point-of-Care Drug Testing

Point-of-care biosensors are designed to provide rapid, accurate, and user-friendly drug detection directly at or near the patient site. Key requirements include portability, minimal sample preparation, high sensitivity, specificity, and reliability under varied conditions. These systems must also be easy to operate without specialized training. By enabling immediate therapeutic decisions, point-of-care biosensors significantly improve patient outcomes, especially in emergency care, chronic disease management, and decentralized healthcare settings [67].

6.2. Portable Electrochemical Biosensors for Rapid Drug Quantification

Portable electrochemical biosensors enable real-time drug monitoring with minimal sample preparation and rapid analytical response. Their compact design, affordability, and compatibility with miniaturized electronics make them highly suitable for point-of-care applications. These devices can detect pharmaceutical compounds in blood, saliva, or sweat with high sensitivity, allowing timely dose adjustments and improved therapeutic management in both clinical and remote healthcare environments [68].

6.3. Paper-Based and Lateral Flow Biosensors

Paper-based and lateral flow biosensors provide low-cost, disposable, and easy-to-use analytical platforms that are particularly suitable for resource-limited settings. These systems rely on capillary action for fluid transport and enable rapid qualitative or semi-quantitative detection of drugs. Their simplicity, portability, and minimal infrastructure requirements make them valuable tools for field diagnostics, emergency drug screening, and decentralized pharmaceutical testing applications [69].

6.4. Lab-on-a-Chip and Microfluidic Biosensor Platforms

Lab-on-a-chip and microfluidic biosensor platforms integrate multiple analytical processes within a compact device, enabling automated and high-throughput drug analysis. These systems reduce reagent consumption, improve analytical precision, and shorten processing time. Their ability to handle small sample volumes and perform multiplexed analysis makes them highly efficient for pharmaceutical monitoring, clinical diagnostics, and personalized medicine applications [70].

6.5. Smartphone-Integrated Biosensors

Smartphone-integrated biosensors combine analytical detection with advanced digital connectivity, enabling real-time data acquisition, storage, and remote monitoring. These systems utilize mobile applications and wireless communication technologies to support telemedicine and decentralized healthcare. They enhance patient engagement, facilitate continuous monitoring, and enable healthcare professionals to make informed decisions based on real-time pharmaceutical data, improving overall treatment outcomes [71].

6.6. Disposable and Low-Cost Biosensors for Resource-Limited Settings

Disposable and low-cost biosensors are critical for expanding access to healthcare in developing regions and underserved populations. These devices prioritize affordability, ease of use, and minimal infrastructure requirements while maintaining acceptable analytical performance. By enabling widespread implementation of point-of-care drug testing, such biosensors contribute to improved disease management, early diagnosis, and equitable healthcare delivery across diverse global settings [72].

7. BIOSENSORS FOR THERAPEUTIC DRUG MONITORING

7.1. Clinical Importance of Therapeutic Drug Monitoring

Therapeutic drug monitoring (TDM) is essential for optimizing drug efficacy while minimizing toxicity, particularly for drugs with narrow therapeutic indices and high pharmacokinetic variability. Conventional TDM approaches rely on centralized laboratory techniques, which often delay clinical decision-making [73]. Biosensor-based platforms provide real-time drug quantification, enabling rapid dose adjustments and improved patient outcomes.

Biosensors facilitate continuous monitoring of drug concentrations, allowing clinicians to tailor pharmacotherapy based on individual patient responses. This approach is particularly beneficial in critical care, oncology, transplantation, and neurology, where precise drug dosing is crucial [74].

7.2. Biosensors for Antibiotic Monitoring

Antibiotic biosensors are increasingly used to monitor drugs such as vancomycin, gentamicin, and β-lactams. Rapid detection of antibiotic levels helps prevent toxicity and supports antimicrobial stewardship [75]. Electrochemical biosensors integrated with aptamers or antibodies have demonstrated high sensitivity for antibiotic detection in plasma and serum.

7.3. Biosensors for Antiepileptic and Psychiatric Drug Monitoring

Monitoring antiepileptic drugs such as carbamazepine and valproate is critical due to their narrow therapeutic windows. Biosensors enable continuous drug level monitoring, reducing the risk of seizures and adverse effects [76]. Similarly, biosensors for psychiatric medications can improve treatment outcomes by ensuring optimal dosing.

7.4. Biosensors for Anticancer Drug Monitoring

Anticancer drugs exhibit significant toxicity and interpatient variability. Biosensors capable of detecting drugs such as doxorubicin, methotrexate, and cisplatin have been developed for real-time monitoring [77]. These systems support personalized oncology treatments and minimize adverse effects.

7.5. Biosensors for Immunosuppressant Monitoring

Immunosuppressants such as tacrolimus and cyclosporine require precise dosing to prevent organ rejection while avoiding toxicity. Biosensors offer rapid and accurate monitoring, improving transplant outcomes [78].

7.6. Biosensors for Cardiovascular, Anti-Inflammatory, and Analgesic Drugs

Biosensors have also been developed for monitoring drugs such as digoxin, NSAIDs, and opioids. These platforms enable rapid detection in clinical and emergency settings, supporting overdose management and therapeutic optimization [79].

8. WEARABLE AND IMPLANTABLE BIOSENSORS FOR CONTINUOUS DRUG MONITORING

8.1. Wearable Biosensors: Design Principles and Clinical Potential

Wearable biosensors represent a transformative advancement in pharmaceutical monitoring, enabling continuous, non-invasive drug analysis. These devices integrate flexible electronics, microfluidics, and wireless communication systems [80]. Wearable biosensors facilitate real-time data collection and remote patient monitoring.

8.2. Sweat-Based Biosensors for Non-Invasive Drug Monitoring

Sweat-based biosensors have gained significant attention due to their non-invasive nature. Drugs and metabolites excreted through sweat can be quantified using electrochemical or optical sensors [81]. These systems are particularly useful for monitoring antibiotics, analgesics, and recreational drugs.

8.3. Saliva-Based and Tear-Based Biosensors

Saliva and tear fluids provide alternative matrices for drug detection. Biosensors designed for these fluids offer painless sampling and rapid analysis [82]. Tear-based biosensors integrated into contact lenses represent an emerging technology for continuous monitoring.

8.4. Microneedle-Based Biosensors for Interstitial Fluid Analysis

Microneedle biosensors penetrate the skin minimally to access interstitial fluid, providing real-time drug concentration data [83]. These systems combine the accuracy of invasive methods with the convenience of wearable devices.

8.5. Implantable Biosensors for Long-Term Monitoring

Implantable biosensors offer long-term monitoring of drug levels within the body. These devices are particularly useful for chronic disease management and personalized medicine [84]. However, challenges related to biocompatibility and biofouling remain significant.

8.6. Challenges in Calibration, Biofouling, Stability, and Patient Compliance

Wearable and implantable biosensors face challenges including signal drift, biofouling, calibration errors, and patient adherence [85]. Addressing these issues is critical for clinical adoption.

9. CLINICAL AND PRACTICAL APPLICATIONS

Biosensors support personalized medicine, emergency toxicology, bedside monitoring, home-based care, and population-specific healthcare applications [97].

10. CONCLUSION

Next-generation biosensors represent a paradigm shift in pharmaceutical analysis by enabling rapid, sensitive, and decentralized drug monitoring. Integration of nanotechnology, artificial intelligence, and wearable systems is expected to transform healthcare delivery toward personalized and real-time therapeutic management. Despite existing challenges, ongoing research and technological advancements will likely drive widespread clinical adoption and regulatory acceptance of biosensor-based analytical platforms.own exceptional performance in detecting pharmaceutical compounds at extremely low concentrations.

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