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# Chitosan Nanocomposites-Based Electrochemical Sensors: A Review

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***Authors' contributions***

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## ABSTRACT

Chitosan nanocomposites represent a promising class of materials formed by combining chitosan with various nanomaterials. This innovative approach leverages the advantageous properties of both chitosan—a biopolymer known for its biocompatibility, natural abundance, high film-formability, and tunable functionality—and nanomaterials, which exhibit enhanced properties such as high surface area, electrical conductivity, and catalytic activity. While chitosan alone is limited by its low electrical conductivity and mechanical strength, its integration with nanomaterials addresses these shortcomings, enhancing its utility in electrochemical sensing applications. This review comprehensively summarizes recent advancements in chitosan-based nanocomposites, mainly

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focusing on their application in electrochemical sensors. It discusses the various nanocomposites combined with metals, metal oxides, carbon-based materials, and other nanostructures. The review highlights the synthesis methods, performance metrics, and potential applications of these sensors across fields such as environmental monitoring, food safety, medical diagnostics, and pharmaceuticals. Emphasis is placed on the advancements over the past five years, with a discussion on the significant impact these sensors have had in detecting critical analytes like heavy metals, neurotransmitters, glucose, and reactive oxygen species.

*Keywords: Chitosan nanocomposites; electrochemical sensors; nanomaterials; environmental monitoring; biosensors; analytical chemistry.*

## 1. INTRODUCTION

Chitosan, a biopolymer derived from chitin, possesses several distinctive properties that make it a valuable material in various applications. It is recognized for its biocompatibility, biodegradability, versatility, high film-formability, tunable functionality, and gel-forming capabilities [1,2]. Certain undesirable properties of chitosan such as its non-conductivity have limited its application in the preparation of sensors of interest [3,4], therefore its combination with Nanomaterials provides an opportunity to improve sensitivity, better electron transfer kinetics and wider applications [2,5-8].

Chitosan's structure is based on two monomeric units repeating units of deacetylated D-glucosamine and Nacetyl-D-glucosamine, which are linked by glycosidic ß-bond (1→4) to form a chain polymer [2,9], as displayed in Fig. 1. Of the several biopolymers that exist, chitosan has been recognized as the most important for electrochemical purposes [10] (Vinodh et al., 2021). It is the most important derivative of chitin [11], a naturally existing polymer that forms the structural basis of all exoskeletons of arthropods (such as crabs, shrimps, and insects) and the endoskeletons of cephalopods (e.g cuttlefish) [2]. It is found more abundantly in the shells of crabs, prawns, and lobsters, making them the main source of industrial extraction [10,12]. The discovery of chitosan began by chance by Charles Hatchett in 1799 when he treated crab shells and shrimps with acetone and dilute nitric acid and found a color change in the shells into pale yellow [13].

Chitosan's ability to act as a stabilizing agent for biological components, combined with its excellent film-forming properties, has spurred significant interest in its use in electrochemical sensors [1,14].

This review provides a detailed analysis of recent advancements in chitosan-based nanocomposites for electrochemical sensing applications. It explores different types of chitosan nanocomposites, their preparation methods, and their performance in detecting various analytes, including heavy metals, neurotransmitters, glucose, and reactive oxygen species.

### 1.1 Properties of Chitosan

**Physical properties of chitosan:** Chitosan, a biopolymer derived from chitin, exhibits a range of physical properties that are influenced by factors such as the degree of deacetylation (DDA) and molecular weight (MW) [15]. These properties are crucial as they affect the polymer's applicability in various fields [16]. The physical properties of chitosan, such as its ability to form films, fibers, and gels, as well as its solution, chemical, and biological characteristics, are foundational to its use in biomedical applications [17]. Despite its versatility, chitosan films often have weaker mechanical properties than synthetic polymers. However, physical treatments like high-pressure homogenization can enhance these properties, as shown by improved tensile strength and elongation in treated chitosan films [18].

**Chemical Properties of Chitosan:** Chitosan exhibits various chemical properties influenced by its degree of acetylation and molecular weight, affecting its solubility, biodegradability, and bioactive attributes [19]. Functional hydroxyl and amine groups on Chitosan allow various chemical modifications, such as acylation, alkylation, and graft copolymerization, to tailor its physicochemical and biochemical properties for specific applications [20]. The solvation of Chitosan in different acids can alter its physico-chemical properties, as demonstrated by the acid solvation effect on the antibacterial activity and physico-chemical properties of chitosan membranes [21].

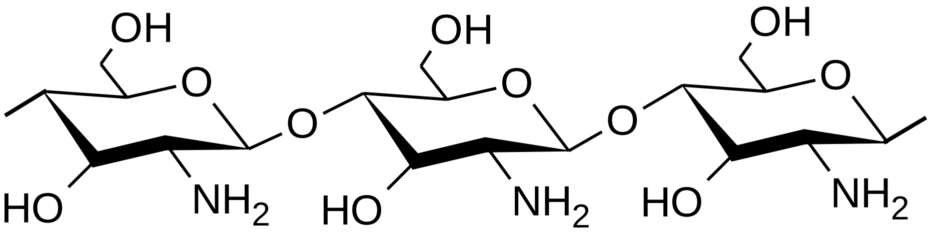

**Fig. 1. Chemical structure of chitosan biopolymer**

While Chitosan's chemical interactions and modifications can enhance specific properties, they do not necessarily predict its binding abilities, as no correlation was found between its physicochemical properties and fat- or bile acid-binding capacities [22]. Moreover, the solubilization of Chitosan in dicarboxylic acid solutions can lead to chemical crosslinking, affecting its conformational, mechanical, and thermal characteristics [23].

**Mechanical Properties of Chitosan:** The mechanical properties of chitosan, a biodegradable and biocompatible biopolymer, are of significant interest due to their relevance in various applications, such as tissue engineering and biocomposite materials [24]. Chitosan's mechanical characteristics can be enhanced by incorporating nanoparticles, which improve thermal and mechanical properties, including dynamic mechanical behavior, making it suitable for bone and wound tissue engineering [25]. Mechanical and topographical properties of chitosan hydrogels have been characterized using atomic force microscopy, revealing specific elastic modulus distributions crucial for understanding cell-material interactions [26].

Contradictorily, while chitosan films inherently possess inferior mechanical properties compared to synthetic polymers, their mechanical strength can be improved through physical methods such as high-pressure homogenization, which has been shown to significantly enhance tensile strength and elongation [27]. Moreover, adding hybrid spinel/cellulose filler to chitosan composites has improved dielectric, magnetic, and mechanical properties, including Young's modulus and tensile strength [28]. Magnetic chitosan hydrogels also benefit from including magnetic nanoparticles, which confer improved mechanical strength and other functional properties [29].

## 2. SYNTHESIS OF CHITOSAN-NANOMATERIAL

### 2.1 Synthesis of Chitosan

Chitosan is the synthetic derivative of the second most abundant polysaccharide biopolymer, chitin [30,31-32] whose structural component is based on 2-acetamido-2-deoxy-β-D-glucose linked by β-bonds (1→4). It is it's deacetylated derivative, obtained through three major stages: Demineralization, Deproteinization, and Deacetylation.

Demineralization is carried out to eliminate the mineral contents of the crude source material which consists of calcium carbonate and calcium chloride [10,31,33-34]. The deproteinization step involves the use of sodium hydroxide solution to remove protein contents before the deacetylation process to obtain chitin, whose hydrophobic nature limits its uses, owing to the presence of several acetyl groups [35,36]. The final and most important stage in the conversion of chitin to chitosan is the deacetylation process involving the use of concentrated alkali at an elevated temperature to produce at least a 70% deacetylation [10,14,37]. The degree of deacetylation of chitin also controls the proportion of acetyl groups and amine present in the polymer, which in turn influences the acid-base behavior of the resulting product [10,35]. Spectroscopic methods such as UV-vis, Infrared (IR), Nuclear Magnetic Resonance (NMR), High-performance liquid chromatography (HPLC) analysis, and Conductometric and Potentiometric [1,31]. For the resulting product to be considered chitosan, it must have a degree of deacetylation of over 50%. Fig. 2 provides a summary of the processes involved in the conversion of crab source material into chitosan.

### 2.2 Synthesis of Nanomaterials

Generally, nanomaterials are synthesized via two main approaches namely the top-down method and the bottom-up method [38].

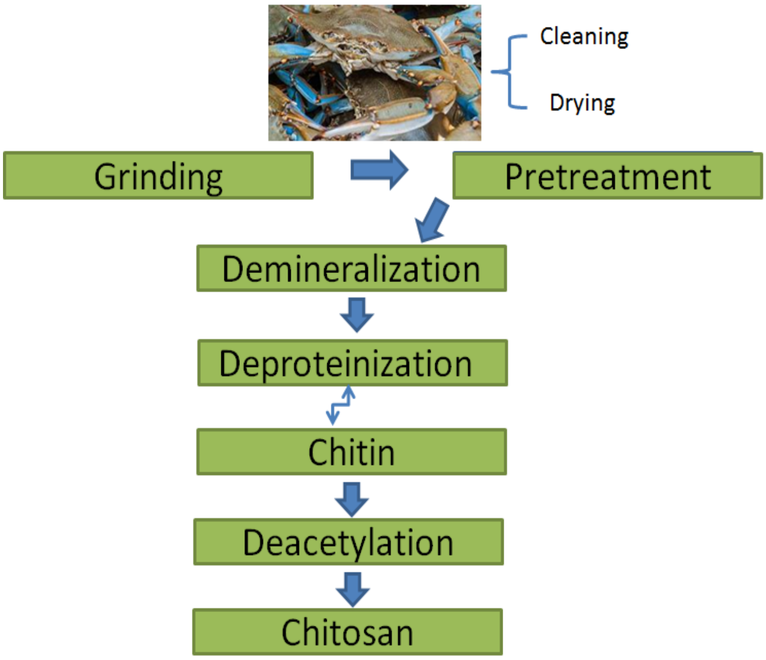

**Fig. 2. Preparation of Chitosan from Crabshell source**

The top-down approach involves breaking down bulky structures, for example, graphite into nano-sized materials with dimensions smaller than 10 nm using physical techniques such as ultrasonication, lithography, photoirradiation, radiolysis, and spray pyrolysis [38]. Other methods include laser ablation, arc discharge, and electrochemical reactions [39].

The bottom-up methods, however, depend mostly on the chemical synthesis methods using precursor molecules or polymers. Its advantage is its suitability for large-scale production. Examples include co-precipitation, solvothermal, chemical reduction and sol-gel processes [38]. Fig. 3 provides a scheme of the general bottom-up methods for synthesizing nanomaterials [40].

In the bottom-up method, both chemical and biological components may be employed in the synthesis of the nanomaterials. The green synthesis or eco-friendly approach of nanomaterial synthesis involves the use of chitosan and some other biological materials such as bacteria, fungi, plants, and plant extracts as well as enzymes [38].

The synthesis of the nanomaterials mostly requires the use of a suitable stabilizer in the reduction process. Stabilizers are typically needed to produce stable, monodispersed nanoparticles. They are employed to prevent the particles from aggregating, and when they are present, the likelihood of nanoparticle collision and coalescence lowers because the functional groups of the stabilizer and the nanoparticle interact in a way that reduces these events [41]. Fig. 3 provides a summary of some methods for the preparation of nanomaterials before they are integrated into Chitosan to form a composite.

## 2.3 Synthesis of Chitosan-Nanocomposites

The preparation of chitosan nanocomposites has been carried out through different means which involve physical, mechanical, or (electro) chemical procedures [42]. Examples of techniques previously employed in synthesizing chitosan nanocomposite include electrospinning, screen printing, ultra-sonication, phase separation, and self-assembly [14]. Fig. 4 provides some methods for the preparation of chitosan nanocomposites.

One of the most recent preparations of chitosan silver nanoparticles employed “T. portulacifolium leaf extract” as the reducing agent of the silver nitrate precursor. The mixture was incubated at 37 °C for 2 hours and the resulting silver nanoparticles solution was stirred vigorously with chitosan solution for 20 minutes to produce a “Chi-Ag NPs” hybrid [43]. The resulting product was characterized using FT-IR, FESEM, EDS analysis and TEM.

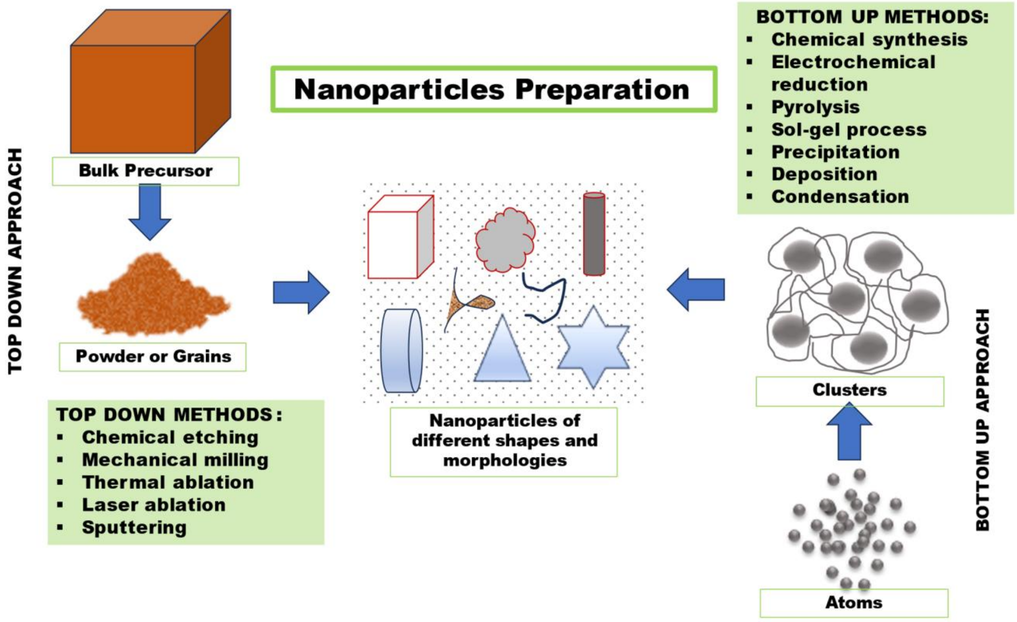

**Figure 3. Methods for nanomaterials preparation**

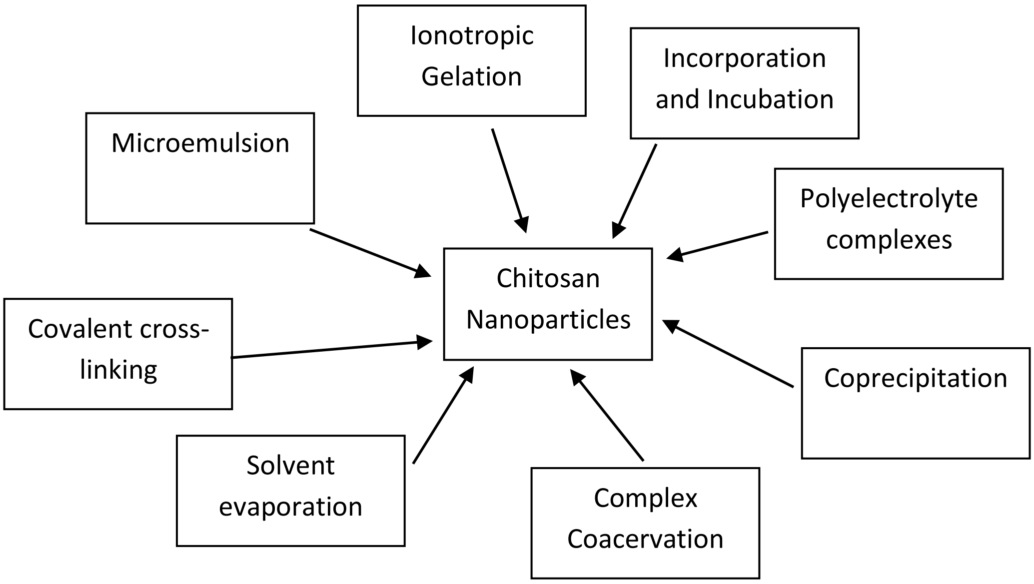

**Fig. 4. Schematic representation of some methods of chitosan nanocomposite preparation**

Another widely studied magnetic chitosan nanoparticle is magnetite ($Fe_3O_4$). According to [44] Homogen et al. (2018), it was synthesized via two methods: a single-route hydrothermal co-precipitation and a multi-synthesis route. The single-route synthesis involved dissolving $FeCl_2{\cdot}4H_2O$ and $FeCl_3$ in chitosan with magnetic stirring in a nitrogen atmosphere. The multi-procedure route first synthesized magnetite and then used ultrasound irradiation of the $Fe_3O_4$ nanoparticles in a chitosan/acetic acid solution, resulting in a $Fe_3O_4$/chitosan composite. Another study by [45] prepared a chitosan/$Fe_2O_3$/$CuFe_2O_4$ nanocomposite using a sol-gel auto-combustion process, dispersing $Fe_2O_3$ and $CuFe_2O_4$ nanostructures, stirring for 24 hours, and drying under vacuum at 60˚C for 4 hours

This review focuses on the performance of Chitosan Nanocomposite sensors synthesized using different electrochemical methods.

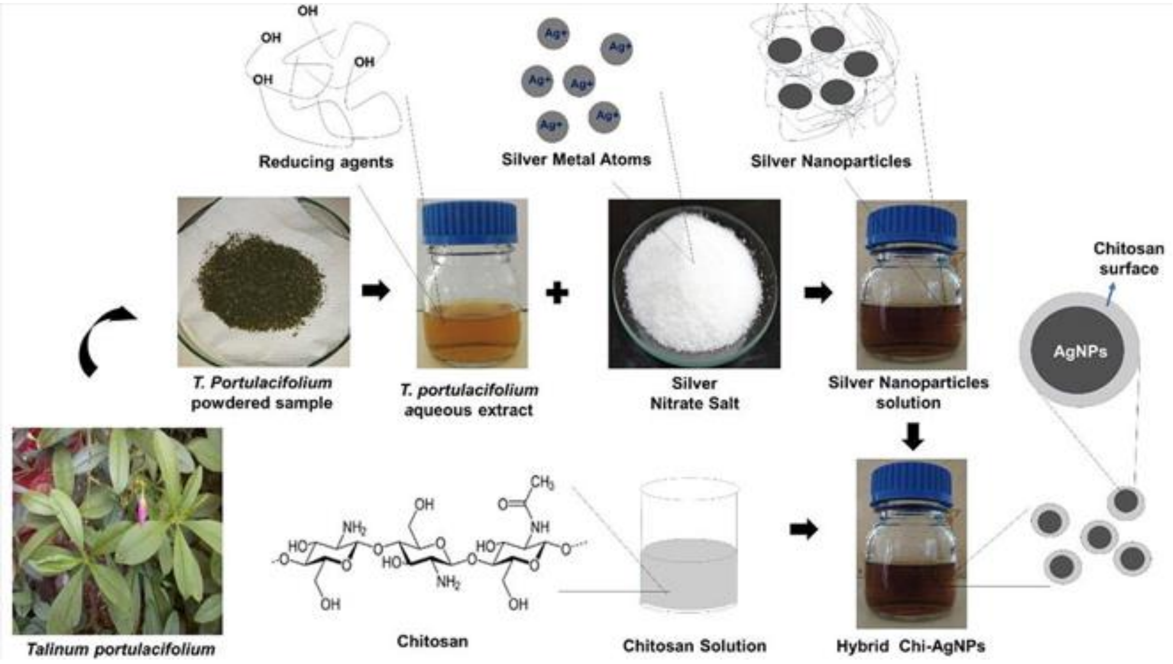

**Fig. 5. Preparation of chitosan silver nanoparticles using T. portulacifolium leaf extract [43]**

## 3. ELECTROCHEMICAL (BIO)SENSORS BASED ON CHITOSAN-NANOCOMPOSITES

Electrochemically modified electrodes using chitosan-nanocomposites have attracted growing interest due to their ease of immobilization, high sensitivity, low detection limit, and wide range of applications [46]. In this section, recent applications of chitosan nanocomposites in the manufacture of different electrochemical sensors and biosensors are discussed.

### 3.1 Chitosan-Nanocomposite Sensors Based on Silver Nanoparticles

Silver nanocomposites have been the most attractive chitosan-based nanocomposite sensor due to their remarkable features such as high electrical conductivity, thermal conductivity, nonlinear optical feature, catalytic capacity, and enhanced surface Raman scattering [47].

In the past five years, chitosan-silver nanocomposites have had a wide range of applications in several fields including agriculture [48,49] (environment [50,51], food [52-54], engineering, and most especially chemical analysis and material science.

These reports are summarized in Table 1.

Table 1 overviews various chitosan-silver nanoparticle-based sensors for detecting different analytes across diverse sample matrices. These sensors have demonstrated significant applications in water, food, and pharmaceutical sample analysis, utilizing advanced techniques such as Cyclic Voltammetry (CV), Differential Pulse Voltammetry (DPV), and Batch Injection Analysis with Multiple Pulse Amperometric Detection (BIA–MPA).

The best-performing sensor, utilizing BIA-MPA, excels in glucose detection with a linear range of 1–3500 µM and an impressive LOD of 0.05 µM, underscoring its potential for precise and reliable analytical applications***.***

### 3.2 Chitosan-nanocomposite Sensors Based on Copper and other Metallic/magnetic Nanoparticles

Recently, nanocomposites based on copper are receiving considerable attention, especially because of their wide applications in the energy field in the production of batteries, gas sensors, and electrical, optical, and solar energy exchange tools [61]. The Table 2 below shows recent work sensors designed on copper electrodes

**Table 1. Chitosan-nanocomposite sensors based on silver nanoparticles**

| **Electrode** | **Analyte** | **Application** | **Technique** | **Linear range** | **LOD** | **Reference** |
|---|---|---|---|---|---|---|
| Chitosan/Ag Nanoparticles | Nitrite | Water and ham samples | Cyclic Voltammetry (CV), Differential Pulse Voltammetry (DPV) | 4.0–1000 μm | $7.9 \times 10^{-7}$ mol $L^{-1}$ | [55] |
| “Silver nanoparticles and carbon nanotubes nanocomposite” | Diazinon (DZN) | Water and food samples | “Batch injection analysis system with multiple pulse amperometric detection (BIA–MPA)” | 0.1 to 20 μmol $L^{-1}$ | 0.35 μmol $L^{-1}$ | [56] |
| “Silver nanoparticles and carbon nanotubes nanocomposite” | Malathion (MLT) | Water and food samples | BIA–MPA | 1 to 30 Mmol $L^{-1}$ | 0.89 μmol $L^{-1}$ | [56] |
| “Silver nanoparticles and carbon nanotubes nanocomposite” | Chlorpyrifos (CLPF) | Water and food samples | BIA–MPA | 0.25 to 50 μmol $L^{-1}$ | 0.53 μmol $L^{-1}$ | [56] |
| “Silver/manganese oxide nanoparticles (Ag-mnoxnps/PAYR)” | 2,4-dichlorophenoxyacetic acid Herbicide | Water samples | CV | 22 to 11, 752 μmol $L^{-1}$ | 7.33 μmol $L^{-1}$ | [57] |
| “Silver/manganese oxide nanoparticles (Ag-mnoxnps/PAYR)” | 2,4-dichlorophenoxyacetic acid Herbicide | Water samples | DPV | 6 to 14, 308 μmol $L^{-1}$ | 2 μmol $L^{-1}$ | [57] |
| “Multiwalled carbon nanotube chitosan-functionalized silver nanoparticles (MWCNT) nitrite (Chit-agnps)” | Nitrite | River water sample | CV | 100 nmol $L^{-}$ to 50 μmol $L^{-1}$ | 30 nmol $L^{-1}$ | [58] |
| “Chitosan polymer complex derived nanocomposite (agnps/NSC)” | Glucose | Not stated | CV, chronoamperometry and EIS | 5 μmol $L^{-1}$ to 3 mmol $L^{-1}$ | 0.046 mmol $L^{-1}$ | [53] |
| “Flower-like molybd enum disulfide/Ag nanoparticle-chitosan (mos$_2$/Ag nps-CS) composite” | Butylated hydroxyanisole (BHA | Food | Molecularly imprinted electrochemical sensor | $1 \times 10^{-9}$ to $1 \times 10^{-4}$ mol $L^{-1}$ | $7.9 \times 10^{-9}$ mol $L^{-1}$ | [54] |
| “Silver nanoparticles on chitosan/polyvinylpyrrolidone modified micro-needle electrode (agnps/CTS/PVP/MNE )” | Nitrate ($NO_3^{-}$) | Seawater samples | Amperometry | 5 to 2000 μmol $L^{-1}$ | 1.2 μmol $L^{-1}$ | [51] |
| “Composite layer of silver nanowires, hydroxymethyl propyl cellulose, chitosan, and urease (agnws/HPMC/CS/Urease)” | Hg (II) | Commercial drinking water samples | Screen-Printed Carbon Electrode (SPCE) | 5 to 25 μmol $L^{-1}$ | 3.94 μmol $L^{-1}$ | [50] |
| “Silver nanoparticles using chitosan as stabilizer” | P-Nitrophenol | Surface water rice samples | DPV | $1.0\times10^{-6}$ to $1.0\times10^{-4}$ mol $L^{-1}$ | $6.0\times10^{-7}$ mol $L^{-1}$ | [59] |
| “Silver decorated chitosan nanocomposite (Ag@CTSN)” | Thiourea | Spiked samples | CV | 200 to 3600 μmol $L^{-1}$ | 18 μmol $L^{-1}$ | [49] |
| “Silver nanoparticles embedded chitosan-carbon nanotube hybrid composite (agchit-CNT)” | Clopidogrel | Urine and pharmaceutical formulations | DPV | $5 \times 10^{-8}$ to $12 \times 10^{-6}$ M. | 30 nmol $L^{-1}$ | [60] |
| “Silver nanoparticles embedded chitosan-carbon nanotube hybrid composite (Agchit-CNT)” | Clopidogrel | Urine and pharmaceutical formulations | Amperometry | $5 \times 10^{-8}$ to $12 \times 10^{-6}$ mol $L^{-1}$ | 10 nmol $L^{-1}$ | [60] |

**Table 2. Chitosan-nanocomposite sensors based on copper and other metallic/magnetic nanoparticles**

| Electrode | Analyte | Application | Technique | Linear range | LOD | Reference |
|---|---|---|---|---|---|---|
| “Copper–chitosan–black phosphorus nanocomposite CuNPs–Chit–BP” | Hydrogen peroxide | Standard samples | CV and Amperometry | 10 μmol L$^{-1}$ to10.3 mmol L$^{-1}$ | 0.390 μmol L$^{-1}$ | [62] |
| “Copper nanoparticle/C spheres composite (Cu NPs/C)” | Azathioprine (AZP) | Environ mental application | CV | 0.01 to 1401 μmol L$^{-1}$ | 3.5 nmol L$^{-1}$ | [63] |
| “Cerium oxide-copper oxide (CeO$_2$-Cu$_2$O) / chitosan (CeOC-Cu$_2$O/CH”) nanocomposites | 4-Nitrophenol | Water samples | CV | 74 to 375 μmol L$^{-1}$ | 2.03 μmol L$^{-1}$ | [64] |
| “Self-assembled chitosan capped with gold nanoparticles (Cs + AuNPs)” | Acetylsalicylic acid ASA or aspirin) | Urine samples | Voltammetric electronic tongue (VE-Tongue | 1 pg mL$^{-1}$ to 1 μg mL$^{-1}$ | 0.03 pg mL$^{-1}$ | [65] |
| “Pt-Pd nanoparticles/chitosan/nitrogen-doped graphene (N-Gra)” nanocomposite” | Oxalic acid | Drug samples | CV | 1.5 to 500 μmol L$^{-1}$ | 0.84 μmol L$^{-1}$ | [66] |
| “V$_{3.6}$Mo$_{2.4}$O$_{16}$chitosan (MV-CHT) nanocomposite chitosan-molybdenum vanadate nanocomposite” | Paracetamol | Drug samples | CV | 0.0019 to 194.0 μmol L$^{-1}$ | 0.224 nmol L$^{-1}$ | [67] |
| “Pt-Pd nanoparticles/chitosan/nitrogen-doped graphene (N-Gra) nanocomposite” | Ascorbic acid | Drug samples | CV | 2 to 400 μmol L$^{-1}$ | 0.97 μmol L$^{-1}$ | [68] |
| “Pt-Pd nanoparticles/chitosan/nitrogen-doped graphene (N-Gra)” nanocomposite | Sulfite | Drug samples | CV | 8 to 600 μ mol L$^{-1}$, | 5.5 μmol L$^{-1}$ | [68] |
| “Chitosan/SnO$_2$-SiC” | Acrylamide | Drinking water and food samples. | CV | 187 ± 12.3 ng kg$^{-1}$ to 104 ± 8.2 μg kg$^{-1}$ | 45.9 ± 2.7 ng kg$^{-1}$ | [69] |

Table 2 presents an overview of sensors based on chitosan combined with copper and other metallic/magnetic nanoparticles. These sensors have been utilized for detecting analytes such as hydrogen peroxide, azathioprine, 4-nitrophenol, acetylsalicylic acid, paracetamol, ascorbic acid, sulfite, oxalic acid, and acrylamide. The applications span standard samples, environmental monitoring, and drug sample analysis.

The best-performing sensor, utilizing CV, excels in azathioprine detection with a linear range of 0.1–60 µM and a remarkable LOD of 0.1 µM, highlighting its potential for precise and reliable analytical applications.

### 3.3 Chitosan-Nanocomposite Sensors Based on Gold Nanoparticles

Sensors based on gold-chitosan nanocomposites have also been significantly explored for sensing applicability owing to their desirable properties and outstanding performances [65,70-73].

The high compatibility of carbon nanotubes with gold nanoparticles has given rise to several chitosan-gold hybrids which has been applied in several fields for the detection of a wide range of analytes. Table 3 gives the summary of reports related to chitosan-nanocomposite-gold nanoparticles sensors.

**Table 3** provides a comprehensive overview of sensors utilizing chitosan and gold nanoparticles to detect analytes in urine, water, food, and drug samples. The employed techniques include Cyclic Voltage Metering (CV), Amperometry, Aptasensor, and Molecularly Imprinted Polymer (MIP).

The best-performing sensor, using CV, excels in Bisphenol A detection with a linear range of 0.1–25 µM and an impressive LOD of 0.005 µM, highlighting its potential for precise and reliable analytical applications.

### 3.4 Chitosan-Nanocomposite Sensors Based on Carbon Nanotubes

Table 4 provides a detailed overview of sensors composed of chitosan and carbon nanotubes, highlighting their applications in detecting analytes across biological, environmental, and pharmaceutical samples. The sensors are used for the detection of nilutamide, nitrofurantoin, histamine, hydroquinone, Mycobacterium avium, imatinib, lead, catechol, insulin, and various human metabolites such as ascorbic acid, dopamine, uric acid, tryptophan, xanthine, caffeine, and glucose.

The best-performing sensor, utilizing DPV, excels in insulin detection with a linear range of 0.01–10 mM and an impressive LOD of 0.02 nM, showcasing its potential for accurate and reliable analytical applications.

### 3.5 Chitosan-nanocomposite Sensors Based on Carbon Quantum Dots

Carbon quantum dots have amassed rising interest and attention, especially in recent years, due to many of their fascinating properties such as low cost of fabrication, high electrical conductivity, large surface area, and non-toxicity.The presence of superficial rich functional groups also provides a wealth of active, anchoring sites for the development of multi-component, high-performance composite materials [90]. A summary of the reports on applications of Chitosan-nanocomposite-carbon quantum as sensors is shown in Table 5.

Table 5 describes sensors that utilize chitosan combined with carbon quantum dots. It highlights their application in detecting analytes such as epinephrine, insulin, and Fe3+ ions in various samples, including chicken blood serum, human blood serum, and water.

The best-performing sensor, using fluorescence, excels in Fe3+ ion detection with a linear range of 0.5–100 µM and a remarkable LOD of 1 nM, emphasizing its potential for precise and reliable analytical applications.

Table 6 provides a summary of various chitosan-graphene-based sensors designed to detect a range of analytes in diverse sample types, including human serum, clinical serum samples, and tap and river water. The techniques employed include Electrochemical Impedance Spectroscopy (EIS), Linear Sweep Voltammetry (LSV), Cyclic Voltammetry (CV), and Differential Pulse Voltammetry (DPV).

The best-performing sensor, utilizing EIS and LSV, excels in detecting carcinoembryonic antigen in human serum with a linear range of $1 \times 10^{-13}$ to $1 \times 10^{-8}$ g/mL and an impressive LOD of $2.23 (\pm 0.03) \times 10^{-14}$ g/mL, highlighting its extraordinary sensitivity and extensive linear range

## Table 3. Chitosan-nanocomposite sensors based on gold nanoparticles

| Electrode | Analyte | Application | Technique | Linear range | LOD | REF |
|---|---|---|---|---|---|---|
| Gold chip surface | Amlodipine | Urine samples | CV | 0.05–150 μm | 50 nm | [74] |
| “Chitosan capped with gold” nanoparticles (SPCE/Cs + aunps ) | Acetylsalicylic acid (ASA or aspirin | Urine, saliva and pharmaceutical | VE-Tongue | 1 pg $ml^{-1}$ and 1 μg $ml^{-1}$ | 0.03 pg $ml^{-1}$ | [65] |
| “Chitosan/gold nanoparticles Nanocomposite Film (Chi/aunps)” | Bisphenol A (BPA) | Water samples | CV | 0.4 to 20 Mmol $L^{-1}$ | 0.32 μmol $L^{-1}$ | [75] |
| “Gold nanoparticle–chitosan/graphene paste modified carbon paste electrode (aunps-Chi/Gr paste)” | Activated protein C | APC in human serum samples | Aptasensor | 0.1 ng $ml^{-1}$ to 40 μg $ml^{-1}$ | 0.073 $ngml^{-1}$ | [71] |
| “Chitosan gold nanoparticles decorated molecularly imprinted polymer (Ch-aumip)” | Ciprofloxacin (CIP) antibiotic | Tap water, mineral water, milk, and pharmaceutical formulation. | MIP/CV | 1 to 100 μmol $L^{-1}$ | 210 nmol $L^{-1}$ | [76] |
| “Chitosan (CS) capped with gold nanoparticles (aunps)” | Butylated hydroxyanisole (BHA) | Food samples | MIP | 0.001 μg $ml^{-1}$ | 0.01–20 μg $ml^{-1}$ | {77] |
| “Au/Carbon Nanofibers-chitosan and Reduced Graphene Oxide. (dpau/cnfs-CS)- (RGO” | Mercury ($Hg^{2+}$) | Tap water. | Signal probe and Specific Single-Stranded DNA (ssDNA) as recognition component | 5.7 × $10^{-5}$ nmol $L^{-1}$ | 0.0001–460 mol $L^{-1}$ | [73] |
| “Au-W bimetallic nanoparticles decorated graphene-chitosan nanocomposite (aunps-wnps@Gr-Chi/PGE)” | Nitrite | Water, milk, and natural fruit juice samples. | CV | 0.12 μmol $L^{-1}$ | From 10 to 250 μmol $L^{-1}$ | [72] |
| “Molecularly imprinted polymer (mips) made of chitosan (CS) biopolymer electrochemically deposited onto a gold microelectrode” | Glyphosate (N-(phosphonomethyl-glycine (GLY) | River water sample | EIS | 0.31 pg $ml^{-1}$ to 50 ng $ml^{-1}$ | 0.31 pg $ml^{-1}$ to 50 ng $ml^{-1}$ | [31] |
| “Nitrogen-doped graphene quantum dots (N-gqds Au-N-gqds were stabilized with chitosan” | Glucose | Standard samples | Amperometry | 10 nmol $L^{-1}$ to 5.0 μmol $L^{-1}$ | 3.3 n μmol $L^{-1}$ | [78] |
| “Chitosan (CS) biopolymer electrochemically deposited onto a gold microelectrode” | Glyphosate | River water, Soybean sprout | EIS | 0.31 pg $ml^{-1}$ to 50 ng $ml^{-1}$ | 5 fg $ml^{-1}$ | [35] |

**Table 4. Chitosan-nanocomposite sensors based on carbon nanotubes**

| Electrode | Analyte | Application | Technique | Linear range | LOD | Reference |
|---|---|---|---|---|---|---|
| “MWCNTs- nitrogen doped graphene (NGr) and chitosan (CTS) with electrodeposited copper (Cu)” | Anticancer drug, nilutamide | Biological environment and pharmaceutical commercial preparations | CV and DPV | 0.005 to 20 µmol L$^{-1}$ and 20 to 900 µmol L$^{-1}$ | 1.6 nmol L$^{-1}$ | [79] |
| “Nano-hydroxyapatite incorporated MWCNT-chitosan scaffolds (HANPs/MWCNTCS/GCE)” | Nitrofurantoin | Tap water | CV, EIS and amperometry | 0.005 to 982.1 µmol L$^{-1}$ | 1.3 nmol L$^{-1}$ | [80] |
| “Chitosan–gold nanoparticles composite cryogel on Prussian blue-coated multi-walled carbon nanotubes” | Histamine | Fish and shrimp sample | CV, SPE | 2.50 to 125.0 µmol L$^{-1}$ and 125.0 to 400.0 µmol L$^{-1}$ | 1.81 µmol L$^{-1}$. | [81] |
| “NanoAu/Poly(ABSA)-MWCNTs/GCE” | Hydroquinone | Lake water | CV , DPV | 2 ~ 200 mmol L$^{-1}$ | 1.0 µmol L$^{-1}$ | [82] |
| glassy carbon electrode | Mycobacterium avium subspecies paratuberculosis (MAP) | real media | CV , DPV | $1.0 \times 10^{-15}$–$1.0 \times 10^{-12}$ mol L$^{-1}$ | $1.53 \times 10^{-13}$ mol L$^{-1}$ | [83] |
| (chitosan/rGO/GCE) | Imatinib | Human serum samples | DPV | 7.3 nM | 1–300 µM | [84] |
| “Multi-walled carbon nanotubes (MWCNTs-graphene (GR)/ gold nanoparticles (AuNPs)/Nafion” | Lead (Pb$^{2+}$) | Water and milk samples | Ion-imprinted polymers (IIPs), CV | $1.0 \times 10^{-9}$ to $5.0 \times 10^{-5}$ mol L$^{-1}$ | $2.83 \times 10^{-10}$ mol L$^{-1}$. | [85] |
| “Gold nanoparticle (AuNP)-decorated multiwalled carbon nanotubes (MWCNT) encapsulated in a polymeric chitosan (CS) CS /AuNPs / MWCNT” | Catechol | Wine | CV | 0 to 1 mmol L$^{-1}$ | $3.7 \times 10^{-5}$ mol L$^{-1}$ | [86] |
| “CoNPs/chitosan-MWCNTs” | Insulin | Blood samples | SPCE, CV | 0.05 µmol L−1 to 5 µmol L$^{-1}$ | 25 nmol L$^{-1}$ | [87] |
| “Ferricyanide-doped chitosan and multi-walled carbon nanotubes (FC/Chi-MWCNT)” | Ascorbic acid | Human serum and urine samples | DPV | 10 to 2056.8µmol L$^{-1}$ | 5.3 µmol L$^{-1}$ | [88] |
| “FC/Chi-MWCNT” | Dopamine | Human serum and urine samples | DPV | 1 to 94.1 µmol L$^{-1}$ | 1.1 µmol L$^{-1}$ | [88] |
| “FC/Chi-MWCNT” | Uric acid | Human serum and urine samples | DPV | 1 to 193.7 µmol L$^{-1}$ to 2.7 nmol L$^{-1}$ | 2.7 µmol L$^{-1}$ | [88] |
| “FC/Chi-MWCNT” | Tryptophan | Human serum and urine samples | DPV | 1 to 198.9 µmol L$^{-}$ | 3.7 µmol L$^{-1}$ | [88] |
| “FC/Chi-MWCNT” | Xanthine | Human serum and urine samples | DPV | 1 to 191.3 µmol L$^{-1}$ | 7.3 nmol L$^{-1}$ | [88] |
| “FC/Chi-MWCNT” | Caffeine | Human serum and urine samples | DPV | 10 to 2.4 µmol L$^{-1}$ | 2.2 µmol L$^{-1}$ | [88] |
| “Glucose-oxidase-chitosan-carbon nanotube hybrid (GOx-Chit-CNT)” | Glucose | Dialysis samples | CV | Not stated | Not stated | [89] |

**Table 5. Chitosan-nanocomposite sensors based on carbon quantum dots**

| Electrode | Analyte | Application | Technique | Linear range | LOD | Reference |
|---|---|---|---|---|---|---|
| “Carbon quantum dots/ copper oxide nanocomposite (CQDs/CuO)” | Epinephrine | Chicken blood serum | CV | 10 to 100 μmol $L^{-1}$ | 15.99 μmol $L^{-1}$ | [91] |
| “Carbon quantum dots (cqds) synthesized from candle soot” | Insulin detection | Human blood serum | Differential-Pulse Adsorptive Anodic Stripping Voltammetry (DPAdASV) | 0.5 nmol $L^{-1}$ to 10 nmol $L^{-1}$ | 106.8 pmol $L^{-1}$ | [92] |
| “Nitrogen-doped carbon quantum dots (N-CQDS)” | Fluorescent sensor | $Fe^{3+}$ ions in water samples | Fluorescent sensor | Not stated | 0.15 lμmol $L^{-1}$ | [93] |
| “Graphene quantum dots, chitosan, and nickel molybdate ($NiMoO_4$)” | Diazinon | Cucumber and tomato samples | CV | 0.1 to 330 μmolμmol $L^{-1}$ | 30 nmol $L^{-1}$ | [94] |
| “Cu-doped carbon dots (Cu-CDS) with chitosan” | $H_2O_2$ | Human serum samples spiked with glucose. | Colorimetry | 0.625 to 40 μM | 0.12 μM | [90] |
| “Cross-linked chitosan/thiolated graphene quantum dots modified by gold nanoparticle (Au-NSS/GQDS-CS/Cysteamine | Ractopamine | Biological samples | DPV | 0.0044 fmol $L^{-1}$ to 19.55 μmolμmol $L^{-1}$ L | 0.0044 fmol $L^{-1}$ | [95] |
| Polypyrrole-chitosan/graphene quantum dots nanocomposite layer deposited on gold-coated glass” | Glucose detection | Biological samples | Surface plasmon resonance sensor | Not stated | 1 ppm | [96] |
| “Nitrogen-doped graphene quantum dots | Triclocarban | Personal care Products | CV | 0.05 to 8.0 μmol $L^{-1}$ | 17.0 nmol $L^{-1}$, | [97] |
| “Γ-Cyclodextrin-graphene quantum dots-chitosan modified SPE | Fluoroquinolones | Animal source products e.g. broths, bouillon cubes and milkshakes | CV and DPV | 4 to 250 μmol $L^{-1}$ | 1.2 μmol $L^{-1}$ | [98] |
| “Integrated chitosan, poly(diallyldimethylammonium chloride)-functioned multi-walled carbon nanotubes and graphene quantum dots-gold nanoparticles (CS, PDDA-MWCNTs and GQDs-AuNPs)” | Glucose | Human serum samples | Closed bipolar electro chemiluminescence (C-BP-ECL) | 0.1 to 5000 μmolμmol $L^{-1}$ L | 64 nmol $L^{-1}$ | [99] |
| “Carbon black and CdTe quantum dots in chitosan film” | Norfloxacin | Pharmaceutical formulation, synthetic urine and spiked serum. | Square Wave Adsorptive Stripping Voltammetry (SWADSV) | 0.2 to 7.4 μmol L−1 | 6.6 nmol $L^{-1}$ | [100] |
| “Graphene quantum dots, chitosan, and nickel molybdate nanocomposites” | Diazinon | Cucumber and tomato samples. | DPV | 0.1 to 330 μmolμmol $L^{-1}$ L | 30 nmol $L^{-1}$ | [94] |
| “Gold -Nitrogen-doped graphene quantum dots (Au-N-GQDS) stabilized with chitosan” | Glucose | Standard samples | Electrochemiluminescence (ECL) | 10 nmol $L^{-1}$ to 5.0 μmolμmol $L^{-1}$ L | 3.3 nmol $L^{-1}$ | [78] |
| “Graphene quantum dots” | Epinephrine | Human serum | CV | 0.36 to 380 μmolμmol $L^{-1}$ L | 0.3 nmol $L^{-1}$ | [106] |

## Table 6. Chitosan-nanocomposite sensors based on graphene

| Electrode | Analyte | Application | Technique | Linear range | LOD | REF |
|---|---|---|---|---|---|---|
| glassy carbon electrode/gold nanoparticle/gold nanodendrites/chitosan-reduced graphene oxide/Anti-CEA antibody | carcinoembryonic antigen | Human serum | Electrochemical Impedance Spectroscopy (EIS) and Linear Sweep Voltammetry (LSV) | 1 × $10^{-13}$ to 1 × $10^{-8}$ g/mL | 2.23 (±0.03) x $10^{-14}$ g/mL | [107] |
| glass carbon electrode (GCE) | Aflatoxin $B_1$ | CV, DPV, and Electrochemical Impedance Spectroscopy (EIS) | | 0.05 to 25 ng/mL | 0.021 ng/mL | [108] |
| “Chitosan-reduced graphene oxide (CS-rGO) Fe-hemin-MOFs/CS-rGO” | $H_2O_2$ | Human serum samples | Amperometry | 1 to 61 lμmol L$^{-1}$ | 0.57 μmol L$^{-1}$ | [63] |
| “Reduced graphene oxid e-chitosan-ferrocene carboxylic acid/platinum nanoparticle (RGO-CS-Fc/Pt NPs)” | $H_2O_2$ | Clinical serum samples | Amperometry | 0.5 to 4.0 mg mL$^{-1}$ | 5.70 μg mL$^{-1}$ | [109] |
| “Ion-imprinted chitosan-graphene nanocomposites (IIP-S)” | Cr(VI) | Tap water and river water | CV, EIS and DPV | 1.0 × $10^{-9}$ to 1.0 × $10^{-5}$ mol/L | 6.4 × $10^{-1}$ mol/L | [110] |
| “Reduced graphene oxide-chitosan-ferrocene carboxylic acid/platinum nanoparticle (RGO-CS-Fc/Pt NPs)” | Cholesterol | Clinical serum samples | Amperometry | 0.5 to 4.0 mg mL$^{-1}$ | 5.70 μg mL$^{-1}$ | [109] |
| “Nitrogen-doped graphene quantum dots (N-GQDs Au-N-GQDs), stabilized with chitosan” | glucose | Grape juice samples | CV, Electrochemiluminescence (ECL): and EIS | 10 nmol L−1 to 5.0 μmolμmol L$^{-1}$ L | 3.3 nmol L−1 | [78] |
| “Reduced graphene oxide (RGO) and carbon black (CB) in Chitosan” (rGO-CB-CS) | Dopamine | Urine samples | Square Wave Voltammetry (SWV) | 3.2 × $10^{-6}$ to 3.2 × $10^{-5}$ mol L$^{-1}$ | 2.0 × $10^{-7}$ mol L$^{-1}$ | [111] |
| RGO-CB-CS | Paracetamol | Urine samples | SWV | 2.8 × $10^{-6}$ to 1.9 × $10^{-5}$ mol L$^{-1}$ | 5.3 × $10^{-8}$ mol L$^{-1}$ | [111] |
| “Graphene nanoplatelets (GNPs)-multiwalled carbon nanotube (MWCNTs) and chitosan (CS) (GNPs-MWCNTs-CS)” | Bisphenol A BPA | Milk samples | DPV | 0.1 to 100 μmolL$^{-1}$ | 0.05 nmol L$^{-1}$ | [22] |
| “Sulfur-doped reduced graphene oxide (S-rGO)” | Mercury ($Hg^{2+}$) | Fish muscle | DPAdASV | 0.125 to 6 μmol L$^{-1}$ | 1.6 nmol L$^{-1}$ | [112] |
| “Functionalized Graphene (f-graphene) doped chitosan (CS)” | Ochratoxin A (OTA) | Grape juice samples | DPV | 1 μgmL$^{-1}$ to 1 fg mL$^{-1}$ | 1 fg mL$^{-1}$ | [113] |
| “Graphene, and titanium dioxide (CS/RGO/$TiO_2$)” | Lead ($Pb^{2+}$) | Food samples | CV | 1 ng L$^{-1}$ to 1000 ng L$^{-1}$ | 0.33 ng L$^{-1}$ | [51] |
| “Imprinted chitosan/gold nanoparticles/graphene modified glassy carbon electrode (CS/AuNPs/GR/GCE)” | Cd(II) | Drinking water and milk samples. | Voltammetry | 0.1 to 0.9 μmolμmol L$^{-1}$ L. | 1.62 × $10^{-4}$ μmolμmol L$^{-1}$ L | [85]. |
| “Chitosan–Graphene Glassy Carbon Modified Electrode” | Hydroxyflavonoid Morin | Food samples. | CV | 0.30 μmol L$^{-1}$ to 1.0 μmol L$^{-1}$ | 0.30 μmol L$^{-1}$ | [114] |
| “Ag-reduced graphene oxide (rGO) and chitosan (CS)” | Carbaryl pesticide | Pesticide residues | CV | 1.0 × $10^{-8}$ to 1.0 μg mL$^{-1}$ | 1.0 × $10^{-9}$ μg mL$^{-1}$. | [115] |
| "Chitosan-graphene oxide composites polymer modified glassy carbon electrode (CS/GO-IIP)" | Cu (II) | Tap and river water samples | DPAdASV | 0.5 to 100 μmol L$^{-1}$ | 0.15 μmol L$^{-1}$ | [116] |

| **Electrode** | **Analyte** | **Application** | **Technique** | **Linear range** | **LOD** | **REF** |
|---|---|---|---|---|---|---|
| “Graphene oxide-chitosan composite (GO-chit)” | Phorate | Fresh vegetables | DPV | 0.1 to 800 nmol L$^{-1}$ | 0.1 nmol L$^{-1}$ | [117] |
| “GO-chit” | Isocarbophos | Fresh vegetables | DPV | 0.01 to 1000 nmol L$^{-1}$ | 0.01 nmol L$^{-1}$ | [117] |
| “GO-chit” | Omethoate | Fresh vegetables | DPV | 0.1– 100 nmol L$^{-1}$ | 0.1 nmol L$^{-1}$ | [117] |

## Table 7. Chitosan-nanocomposite sensors based on carbon black/carbon paste

| **Electrode** | **Analyte** | **Application** | **Technique** | **Linear range** | **LOD** | **REF** |
|---|---|---|---|---|---|---|
| “Double imprinted Monomer acryloylated graphene oxide-carbon black composite polymer (aGO/CBOMNiDIP/SPE)” | Dopamine (DA)<br>Epinephrine (EP) | Blood serum, urine and pharmaceutical samples | DPAdASV | DA- 0.115 to 5.909 ng mL$^{-1}$ EP- 0.079 to 1.307 ng mL$^{-1}$ | “Dopamine: 28 pg mL$^{-1}$ (Water), 28 pg mL$^{-1}$ (Serum), 61 pg mL$^{-1}$ (Urine) and 29 pg mL$^{-1}$ (Pharmaceutical sample) Epinephrine: 17 pg mL$^{-1}$ (Water), 18 pg mL$^{-1}$ (Serum), 19 pg mL$^{-1}$(Urine) and 20 pg mL$^{-1}$ (Pharmaceutical sample)” | [118] |
| “Carbon black and CdTe quantum dots in a chitosan film” | Norfloxacin | Urine and spiked serum. | SWAdASV | 0.2 to 7.4 µmol L$^{-1}$ | 6.6 nmol L$^{-1}$ | [100] |
| “Carbon black -chitosan-stabilized platinum nanoparticles (CB-Ch-PtNP )” | H$_2$O$_2$ | Natural water samples | Chronoamperometry | | 10 µmol L$^{-1}$. | [101] |
| “Carbon black - chitosan-stabilized platinum nanoparticles (CB-Ch-PtNP)” | Bisphenol A (BPA). | Natural water samples | DPAdASV | | 7.9 nmol L$^{-1}$ | [101] |
| “Super P carbon black particles and chitosan” | Macrolide antibiotics, environmental samples | Water and pharmaceutical samples | CV | 1.0–190.0 µmol | Not stated | [102] |
| Carbon paste | | | | | | |
| “Gold nanoparticle–chitosan/graphene paste modified carbon paste electrode. AuNPs-CS/Gr/CPE electrode” | Activated protein C (APC) | Human serum samples | CV, DPV & EIS | 0.1 ng·mL$^{-1}$ - 40 µg·mL$^{-1}$ | 0.073 ng·mL$^{-1}$ | [71] |
| “A carbon paste electrode, modified with chitosan-based magnetic molecularly imprinted Polymer (CS-MIP)” | Lactic acid | Milk samples | CV and DPV | 0.01–10.0 µM and 10.0–500.0 µM | 0.005 µm | [68] |
| “Poly (chitosan) (P (CS))” | Riboflavin | Commercial multivitamins | CV, DPV, and SWV | 24.6 to 176µM | 24.6µM | [103] |
| “Sn/Cs/PGE” | Riboflavin | Food samples. | CV and EIS | 10 to 1200 nmol L$^{-1}$ | 5.56 nmol L$^{-1}$ | [104]. |
| “Mung bean-derived porous carbon@ chitosan (MBC@CTS) composite” | Carbendazim | Juices | CV | 0.1 to 20 lµmol L$^{-1}$ | 20 nmol L$^{-1}$ | [105] |
| “Carbon paste electrode, modified with chitosan-based magnetic molecularly imprinted polymer (CS-MIP)” | Lactic acid | In real milk samples | CV and DPV | 0.01–10.0 µmol L$^{-1}$ and 10.0–500.0 µmol L$^{-1}$ | 0.005 µmol L$^{-1}$ | [68] |
| “Pentoxide (V$_2$O$_5$) into the carbon paste electrode (CPE)” | H$_2$O$_2$ | Cosmetic and personal care products. | EIS | 5.0 to 1400.0 µmol L$^{-1}$ | 2.5 µmol L$^{-1}$ | [69] |
| “Hemoglobin–Iron Magnetic | Acrylamide | French fries | CV | 10 to 171 nmol L$^{-1}$ | 0.06 nmol L$^{-1}$ | [70] |

| **Electrode** | **Analyte** | **Application** | **Technique** | **Linear range** | **LOD** | **REF** |
|---|---|---|---|---|---|---|
| Nanoparticle–Chitosan Modified Carbon Paste Electrode” | | | | | | |
| “Three-dimensional hierarchical porous carbon coupled with chitosan” | Niclosamide | Food samples | CV | 0.01 to 10 μmol $L^{-1}$ | 6.7 nmol $L^{-1}$ | [71] |
| “$V_{3.6}Mo_{2.4}O_{16}$-chitosan (MV-CHT) nanocomposite” | Paracetamol | Drug samples | CV | 0.0019 to 194.0 μmol $L^{-1}$ | 0.224 nmol L−1 | [67]. |
| “Pt-Pd nanoparticles/chitosan/nitrogen-doped graphene (N-Gra) nanocomposite” (Pt-Pd-CS-N-Gra) | Ascorbic acid | Drug samples | CV | 2 to 400 lμmol $L^{-1}$ | 0.97 μmol $L^{-1}$ | [68] |
| Pt-Pd-CS-N-Gra | Sulfite | Drug samples | CV | 8 to 600 μmol $L^{-1}$ | 5.5 μmol $L^{-1}$ | [68] |
| Pt-Pd-CS-N-Gra | Oxalic acid | Drug samples | CV | 1.5 to 500 lμmol $L^{-1}$ | 0.84 μmol $L^{-1}$ | [68] |
| “Chitosan/$SnO_2$-SiC” | Acrylamide | Drinking water and food samples. | Immunosensor | 187 ± 12.3 ng $kg^{-1}$ to 104 ± 8.2 μg $kg^{-1}$ | 45.9 ± 2.7 ng $kg^{-1}$ | [69] |

Table 7 details chitosan-nanocomposite sensors that utilize carbon black and carbon paste to detect various analytes across different applications, including blood serum, urine, pharmaceutical samples, and natural water samples. The techniques employed include Differential Pulse Adsorbtive Stripping Voltammetry (DPAdASV), Square Wave Adsorbtive Stripping Voltammetry (SWAdASV), and Chromatoamperometry.

The best-performing sensor, using SWAdASV, excels in norfloxacin detection in urine and spiked serum with a linear range of 0.2 to 7.4 μmol/L and an impressive LOD of 6.6 nmol/L, showcasing its remarkable sensitivity and precise detection capabilities.

## 4. CONCLUSIONS AND FUTURE PERSPECTIVES

This review article has successfully presented many of the latest developments in the vast application of chitosan-based nanocomposite sensors within the past 5 years. The study of chitosan-based material is robust, proving its wide applicability and modifiability because chitosan possesses several unique properties that make it very desirable in electrochemical studies. On another hand, nanomaterials, in the past few decades, have been one of the most studied topics in science. Their combination with chitosan has opened up a non-exhaustible vista in the production of novel materials with highly enhanced performances, which are utilized in all fields of life.

This review further emphasizes the importance and great prospects of chitosan-based nanocomposites as excellently promising materials in the production of sensors and biosensors.

In the very near future, developments in this area will continue to evolve for application in diverse fields and industries such as food, environmental, health, pharmaceuticals, agriculture, biotechnology and so much more. Sensors based on chitosan nanocomposites can be engineered and miniaturized into disposable, field testing kits in all of these field, allowing for easy, quick and reliable measurements without the need for bulky laboratory experiments.

These materials can also be integrated into microfluidic systems which would enable higher efficiency, lower reagent consumption and facilitate high throughput analysis.

As research in this field continue to evolve, eco-friendlier environmentally sustainable methods for their preparation continues to evolve, and this will help eliminate the effect of hazardous chemical practices in our world today.

By continuing to explore the versatility of sensors based on chitosan nanocomposites, their contributions to the advancement of chemical technology and solutions to critical societal challenges will remain boundless.

## DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during the writing or editing of manuscripts.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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