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Nanotechnology in the sports athlete community based on its application in doping detection: a systematic literature review and meta-analysis

Nanotecnología en la comunidad de deportistas basada en su aplicación en la detección de dopaje: una revisión sistemática de la literatura y meta-análisis

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Abstract. This study examines the effectiveness and accuracy of nanotechnology applications in doping detection within the athlete community. Nanotechnology offers a novel approach with potential in detecting doping substances more efficiently and accurately. The method used in this study is a Systematic Literature Review (SLR) and meta-analysis, with articles selected from the Scopus and Web of Science (WoS) databases covering the years 2020-2024. The selection process employs the PRISMA method and includes only research articles relevant to the topic. A total of 13 studies were selected for further analysis. The meta-analysis results indicate that the Differential Pulse Voltammetry (DPV) and Enzyme-Linked Immunosorbent Assay (ELISA) methods provide highly accurate and reliable results in doping detection. No significant differences were found between the use of serum and urine as test samples. Additionally, nanocomposite sensors proved to be more effective than regular sensors in detecting doping substances with high accuracy. Key findings from the results include no significant effect distinguishing between the DPV and ELISA methods ($Z = 0.53$, $P = 0.60$), no significant heterogeneity among the studies analyzed concerning serum and urine ($Chi^2 = 0.90$, $df = 2$, $P = 0.64$; $Tau^2 = 0.00$), and nanocomposite sensors proving to be more effective than regular sensors ($Z = 4.14$, $P < 0.0001$; $I^2 = 0\%$). In conclusion, nanotechnology has great potential to enhance doping detection in sports. The use of nanomaterials and nanosensors can improve the sensitivity, specificity, and accuracy in detecting doping substances, making it a highly effective tool for maintaining the integrity and health of athletes. This study provides a strong foundation for the development of more efficient and effective nanotechnology-based doping detection technologies in the future.
Keywords: Nanotechnology, doping, sensors, sports, athletes.

Resumen. Este estudio examina la efectividad y precisión de las aplicaciones de la nanotecnología en la detección de dopaje dentro de la comunidad de atletas. La nanotecnología ofrece un enfoque novedoso con potencial para detectar sustancias dopantes de manera más eficiente y precisa. El método utilizado en este estudio es una Revisión Sistemática de la Literatura (RSL) y un meta-análisis, con artículos seleccionados de las bases de datos Scopus y Web of Science (WoS) que cubren los años 2020-2024. El proceso de selección emplea el método PRISMA e incluye solo artículos de investigación relevantes para el tema. Un total de 13 estudios fueron seleccionados para un análisis más detallado. Los resultados del meta-análisis indican que los métodos de Voltametría de Pulso Diferencial (DPV) y Ensayo de Inmunoabsorción Ligado a Enzimas (ELISA) proporcionan resultados altamente precisos y fiables en la detección de dopaje. No se encontraron diferencias significativas entre el uso de suero y orina como muestras de prueba. Además, los sensores de nanocompuestos demostraron ser más efectivos que los sensores regulares en la detección de sustancias dopantes con alta precisión. Los hallazgos clave de los resultados incluyen la ausencia de un efecto significativo que distinga entre los métodos DPV y ELISA ($Z = 0.53$, $P = 0.60$), la falta de heterogeneidad significativa entre los estudios analizados en relación con suero y orina ($Chi^2 = 0.90$, $gl = 2$, $P = 0.64$; $Tau^2 = 0.00$) y los sensores de nanocompuestos demostrando ser más efectivos que los sensores regulares ($Z = 4.14$, $P < 0.0001$; $I^2 = 0\%$). En conclusión, la nanotecnología tiene un gran potencial para mejorar la detección de dopaje en el deporte. El uso de nanomateriales y nanosensores puede mejorar la sensibilidad, especificidad y precisión en la detección de sustancias dopantes, convirtiéndolo en una herramienta altamente efectiva para mantener la integridad y salud de los atletas. Este estudio proporciona una base sólida para el desarrollo de tecnologías de detección de dopaje basadas en nanotecnología más eficientes y efectivas en el futuro.
Palabras clave: Nanotecnología, dopaje, sensores, deportes, atletas.

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Introduction

Sports play an important role in society due to the values of effort, dedication, and excellence they convey. However, sports are often tainted by the illicit use of doping substances to enhance athlete performance under the pressure of success. This undermines fair play and poses serious health risks to athletes (Lissavetzky, 2011; Reardon & Creado, 2014). This issue extends beyond the act of doping itself, encompassing its widespread dissemination, significant impact on athletes' careers (Stukova et al., 2023; Sepriadi et al., 2024), and various perspectives on doping across different fields and social groups (Babaskin et al., 2024). Currently, steroids are the most frequently detected substances by WADA-accredited laboratories (Aguilar et al., 2017). The approach to detect steroid abuse in the field of Anti-Doping is governed by the World Anti-Doping Agency through technical documents and guidelines (WADA, 2016). Although some athletes exhibit a comprehensive understanding of anti-doping rules, the majority remain unaware of key aspects, potentially leading to unintentional doping violations (Listiani et al., 2024). Similarly, numerous individual, social, and sport-specific factors can influence doping practices (García-Grimau et al., 2020). There are even studies that validate the reliability and validity of an instrument called CUPIAD,

which measures the knowledge, beliefs, and attitudes of Spanish adolescents towards doping (Medina et al., 2017).

Nanotechnology has the potential to be implemented in every aspect of life. This includes nanomaterial science, nanoelectronics, and nanomedicine, which span all dimensions of chemistry, the physical world, and biological sciences (Singh, 2017; Chaeroni et al., 2024). Currently, with the advancement of nanotechnology, nanomaterials such as inorganic nanomaterials, organic polymer nanomaterials, nanocomposites, and bionic nanomaterials are continuously being developed and used in the biomedical field (Xing, 2022; Okilanda et al., 2024; Irawan et al., 2024). Some nanosensors also function similarly to phagocytes in clearing toxic pathogens from the bloodstream without causing septic shock conditions, particularly due to the inhalation of illicit drugs and prohibited substances (Comini et al., 2013; Erkoc & Ulucan-Karnak, 2021; Jahangirian et al., 2017). This technology is also used for dosage specification and to neutralize overdose incidents (Jahangirian et al., 2017; Chaeroni et al., 2024; Ihsan et al., 2024).

The use of nanomaterials in sports engineering has resulted in scientific advancements in the field of sports (Ćibo et al., 2020; Chaeroni et al., 2023). NT applications in sports primarily involve the use of nanomaterials such as carbon nanotubes (CNT), silica nanoparticles (SiO_2), fullerenes, and carbon nanoparticles (NP), which provide many properties to various sports equipment (Harifi & Montazer, 2017, Yendrizal., 2024). While nanoparticle-based colorimetric sensors provide high accuracy and precision in measuring pharmaceuticals and chemicals, they are also considered simple and very fast techniques (G. Liu et al., 2018; Sabela et al., 2017). The MIPs nanomaterial approach used in pseudo-ELISA can significantly enhance and modernize anti-doping systems (Cáceres et al., 2022).

Based on the theories mentioned in the background, this research aims to conduct a Systematic Literature Review (SLR) and meta-analysis on the application of nanotechnology in doping detection within the sports athlete community. Specifically, this study has several main objectives, including identifying and evaluating the latest scientific literature related to the use of nanotechnology for doping detection, providing a comprehensive summary of advancements in nanosensor technology, nanomaterials, and nanocomposites in detecting doping substances, analyzing the effectiveness of nanotechnology-based detection methods, and revealing potential publication biases and heterogeneity among the studies analyzed. Through this research process, it is expected that this study will contribute significantly to the development of more efficient and effective doping detection technologies, as well as support efforts to maintain the integrity and health of the athletes.

Materials and Methods

This study adopts the Systematic Literature Review (SLR) method, which is an approach designed to search for, evaluate, and interpret all relevant information in the literature or references with the aim of comprehensively answering research questions (Snyder, 2019; Xiao & Watson, 2019). SLR helps in providing a summary of current knowledge or topics related to the research question (Kurniati et al., 2022) and serves as a valuable source of information where the author needs to summarize and evaluate reliable scientific literature using an organized method based on predefined objectives, making it useful for other researchers (Gopalakrishnan & Ganeshkumar, 2013).

The data sources for this study were obtained from searches in the Scopus and WoS databases. The literature review employed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) method (Page et al., 2021). Introduced in 2009 (Moher et al., 2009), PRISMA is one of the best methods that can help authors conduct systematic reviews and meta-analyses correctly and also assist in reviewing the structure like a roadmap. The PRISMA method is also the most frequently used method in articles such as literature reviews (Hutton et al., 2016; Moher et al., 2016; Shamseer et al., 2015; Stewart et al., 2015).

Table 1.
Inclusion and Exclusion Criteria

Inclusion criteria	Exclusion criteria
English Language	Articles written in other languages
Years 2020-2024	Before the year 2020
Type of empirical research articles indexed in Scopus and WoS	Types of book chapters, theses, short reports, non-empirical studies and literature reviews, not indexed in Scopus and WoS
Related to nanotechnology for doping detection	Not related to nanotechnology for doping detection

The search strategy employed the use of the query (athlete* or sportsman* or sport) and (nanotechnology* or nanoparticle* or nanomaterial* or nanocomposite* or nano*) and (detect* or sensor*) as the search strategy. Article selection was limited to new publications within the last five years (Paul et al., 2021), specifically from 2019 to the current year, 2024. Eligibility criteria were required to select appropriate articles (Ahmadi et al., 2018). Articles were screened based on inclusion and exclusion criteria as detailed in table 1. The data extraction process was conducted meticulously to ensure the accuracy and consistency of the information obtained from each included study. The study characteristics data included preparation and fabrication, characterization, electrochemical measurement, real sample preparation, and real sample analysis.

The data analysis was performed using RevMan 5.4 and JASP 0.18.3. Given the considerable variability in several

experimental endpoints, we employed a random effects model for all outcomes. Mean Differences (MD) and standard deviations from baseline to final outcomes were extracted and entered into the database for analysis within each group, with 95% confidence intervals (95% CIs) used for comparison. Heterogeneity among studies meeting the inclusion criteria was measured using the Q test and the I^2 inconsistency test. I^2 values of 25%, 50%, and 75% indicate low, moderate, and high levels of heterogeneity, respectively (Higgins et al., 2003).

Statistical significance was determined at $p < 0.05$, and effect sizes along with 95% confidence intervals were graphically displayed through forest plots. Additionally, Funnel plots, the Rank Correlation Test, and Egger's Test were utilized to evaluate the potential for publication bias. Funnel plots aid in visualizing the distribution of effect sizes among studies, and asymmetry in these plots can indicate the presence of publication bias. The Rank Correlation Test is used to detect asymmetry in the Funnel plot by calculating the correlation between effect size and standard error. Egger's Test provides an additional statistical test for asymmetry in the funnel plot, which may indicate publication bias.

Result

The literature search was completed on July 28, 2024, resulting in an initial identification of 660 records from the Scopus database and 1,568 records from the WoS database. As shown in figure 1, during the initial screening stage, we selected literature with the type of research articles. From the filtered database, 1,734 records met the inclusion criteria, meaning that 494 records were excluded due to being types of books, book chapters, theses, short reports, conference papers, and literature reviews. Additionally, 743 records were excluded because the specified query was not fully present in the abstract, leading to their exclusion. Thus, the initial screening resulted in 991 articles meeting the inclusion criteria.

In the subsequent screening stage, 14 records were removed because they were not in English, and 209 records were marked as ineligible by automation tools for the years 2019-2024. Therefore, out of the total 2,228 initial records identified in the two databases, 33 records were deemed eligible for further analysis.

The monitoring of articles was conducted by investigating the titles and abstracts based on the relevance of the articles to the topic of the current SLR and meta-analysis. These articles were analyzed, and relevant information was compiled considering several classifications and criteria aligned with the information needs we sought (Table 1). Data extraction was organized to categorize, evaluate, and summarize the articles that met the specified criteria. Through the analysis of the collected data, we were able to reach recommendations and findings relevant to the topic. The analysis of articles that met the inclusion criteria revealed that at least 13 articles were suitable based on the analysis (see table 2).

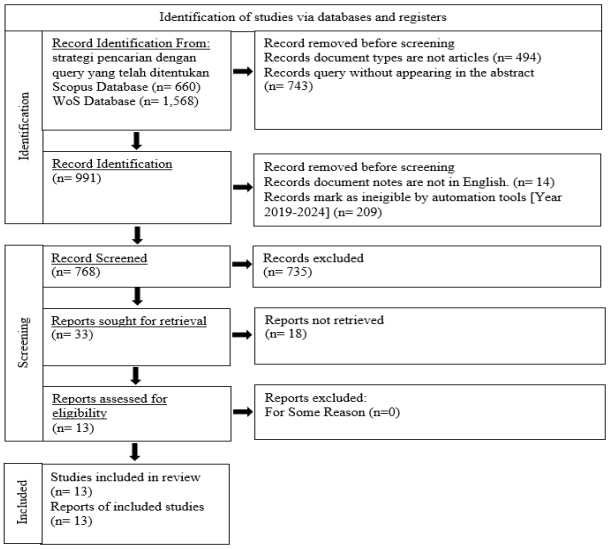

Figure 1. PRISMA flow diagram showing the study identification and selection process.

Table 2.
Characteristics of included studies

Study	Nanomaterial Preparation	Characterization	Electrochemical Measurement	Real Sample Preparation	Real Sample Analysis
(Peng et al., 2023)	Nanocomposite, solvothermal method: Mix 30 mL of ethylene glycol and 2 mL of 0.4 M $Ce(NO_3)_3$ solution, heat at 135 °C for 10 hours, centrifuge, wash, and dry. Mix 2.0 mg of CeO_2 nanoparticles with 2.0 mg/mL CNT suspension, apply on GCE.	FE-SEM Method: CeO_2 nanoparticles with an average size of 50 nm were successfully anchored on the CNT surface. XRD Method: Diffraction peaks of CeO_2 and CNTs were identified, indicating successful binding of CeO_2 to the CNT matrix.	DPV method: Measurement at -1.2 V to -0.5 V, scan rate 30 mV/s in 0.1 M PBS.	Centrifugation method: Athlete's blood at 1500 rpm for 10 minutes, filtration, mix with 0.1 M PBS.	ELISA and DPV methods. DPV results: Recovery 94.50–98.00%, RSD 3.97–5.03%. ELISA results: Recovery 94.50–98.83%, RSD 3.96–5.11%. Indicating good accuracy and application for MT detection in real blood serum samples.
(Ma & Tian, 2023)	N-CNP, microwave-assisted method: Mix 1 mM D-fructose and 3 mM urea, heat with a microwave at 750 W for 5 minutes, dry, and dialyze for 24 hours.	FE-SEM Method: The electrode surface contains evenly distributed pores and spherical	DPV method: Measurement at potential range -1.20 V to -0.50 V,	Centrifugation method: Blood samples from 5 bodybuilders (age	ELISA and DPV methods. DPV results: Recovery >98.53%, RSD <5.08%. ELISA results: Recovery

Table 2.
Characteristics of included studies

Study	Nanomaterial Preparation	Characterization	Electrochemical Measurement	Real Sample Preparation	Real Sample Analysis
		structures with an average diameter of 60-80 nm. XRD Method: Diffraction peak at $2\theta = 25.92°$ indicates a hexagonal graphite structure. EDS Method: Carbon framework doped with nitrogen atoms.	scan rate 25 mV/s in 0.1 M PBS.	25-30 years) centrifuged at 10,000 rpm for 10 minutes, serum separated, filtered, and mixed with 0.1 M PBS as electrolyte.	98.53-99.60%, RSD 3.81-5.08%. Indicating good accuracy and application for TZ detection in real blood serum samples.
(Kong & Wang, 2023)	ZnO@carbon nanocomposite, calcination method: Mix zinc acetate dihydrate and glucose in a 3:2 weight ratio, heat in a muffle furnace at 400 °C for 60 minutes. Apply ZnO@carbon on GCE, then dry at room temperature.	FE-SEM Method: ZnO nanorod surface shows an evenly distributed carbon layer. XRD Method: Diffraction peaks indicate a hexagonal wurtzite ZnO structure. EDS Method: Presence of carbon (C), oxygen (O), and zinc (Zn) elements in the ZnO@carbon nanocomposite.	CV and DPV methods: Measurement conducted in 0.1 M PBS electrolyte solution at potential range from 0.2 V to 1.1 V with scan rate 40 mV/s.	Centrifugation method: Six blood samples from young cyclists (age 21-29 years) centrifuged at 2000 rpm for 10 minutes, serum separated, filtered, and mixed with 0.1 M PBS solution.	ELISA and DPV methods. DPV results: Recovery 94.75–99.45%, RSD <5.04%. ELISA results: Recovery 94.00–99.66%, RSD 3.26–5.14%. Indicating good accuracy and application for TER detection in real blood serum samples.
(Y. Liu & Quan, 2023)	ZnO Sol Synthesis via Sol-Gel Method: Zinc ethanoate dihydrate mixed with ethylene glycol methyl ether, ethanolamine added, stirred at 60°C for 1 hour, and let stand for 48 hours. TiO_2 Sol Synthesis via Sol-Gel Method: Anhydrous ethanol and deionized water mixed, butyl titanate, acetylacetone, and deionized water added, stirred and stabilized with HCl, polyethylene glycol 800 added, let stand for 24 hours. Thin Film ZnO-TiO_2 Preparation via Spin-Coating: ZnO sol and TiO_2 sol mixed, spin-coated on ITO, dried and annealed at various temperatures (400°C, 500°C, 600°C).	XRD Method: Diffraction peaks for anatase TiO_2 and wurtzite ZnO phases observed at 400-500°C, and $ZnTiO_3$ phase at 600°C. UV-Vis Method: Absorbance increases with annealing temperature; optical bandgap decreases to 3.33 eV at 600°C. EIS Method: Lowest charge transfer resistance (R_{ct}) observed at ZnO-TiO_2-500/ITO (784.1 Ω).	Potentiostat/galvanostat method: Measurement with three electrodes. Modified working electrode, Ag/AgCl reference electrode, and platinum counter electrode. EIS measurement conducted at frequency 0.1 Hz to 100 kHz with AC voltage amplitude 10 mV. DPV method: Concentration range 0.005–50 μM, detection limit 2.7 nM.	Urine and serum samples from athletes were taken, prepared, and tested using ZnO/TiO2-500/ITO sensor. Urine from cyclists (age 21-29 years) and serum from bodybuilders (age 25-30 years).	DPV method. Results: recovery 98.70% to 102.50%, RSD <4.05%. Urine and serum show high recovery and precision values.
(B. Li & Wang, 2024)	Synthesis of Hematite Nanoparticles (NPs) via Hydrothermal Method: Iron(III) chloride hexahydrate ($FeCl_3·6H_2O$) was dissolved in ethylene glycol. Sodium acetate was then added to the solution, which was subsequently heated at 200°C for 12 hours. The resulting product was washed thoroughly with distilled water and dried to obtain hematite nanoparticles. Synthesis of Magnetite (Fe_3O_4) Nanoparticles via Solvothermal Method: Iron(III) chloride hexahydrate ($FeCl_3·6H_2O$) and iron(II) chloride tetrahydrate ($FeCl_2·4H_2O$) were dissolved in ethylene glycol. Sodium acetate was added to the mixture, and the solution was heated at 200°C for 10 hours. The resultant Fe_3O_4 nanoparticles were washed and dried. Synthesis of Fe_3O_4/Polyaniline (PANI) Composite via In Situ Oxidative Polymerization: Magnetite (Fe_3O_4) nanoparticles were dispersed in hydrochloric acid (HCl). Aniline was added to the dispersion, and in situ oxidative polymerization was carried out using ammonium persulfate as the oxidizing agent to form the Fe_3O_4/PANI composite.	XRD Method: Diffraction peaks for Fe_3O_4 and hematite structures observed. UV-Vis Method: Absorbance at 350 nm for hematite. PL Method: Emission at 450 nm for hematite. SEM Method: Fe_3O_4 microspheres with a diameter of 200 nm; hematite nanoparticles with a diameter of 38 nm. EIS Method: Lowest charge transfer resistance (R_{ct}) observed at Fe_3O_4/PANI-Cu(II)/α-Fe_2O_3/CILE.	DPV method. Serum results: Recovery 97.5-102.8%, RSD <3.2%. Urine results: Recovery 98.2-103.5%, RSD <3.5%. Indicating good accuracy and application for dexamethasone detection in real serum and urine samples.		DPV method. Serum results: Recovery 97.5-102.8%, RSD <3.2%. Urine results: Recovery 98.2-103.5%, RSD <3.5%. Indicating good accuracy and application for dexamethasone detection in real serum and urine samples.

Table 2.
Characteristics of included studies

Study	Nanomaterial Preparation	Characterization	Electrochemical Measurement	Real Sample Preparation	Real Sample Analysis
	Copper(II) Loading on Fe_3O_4/PANI Composite via Adsorption Method: The Fe_3O_4/PANI composite was dissolved in a copper(II) chloride ($CuCl_2$) solution. The mixture was heated and stirred for 1 hour, after which the product was dried, yielding the Cu(II)-loaded Fe_3O_4/PANI composite. Electrode Modification via Drop-Casting Method: A carbon ionic liquid electrode (CILE) was modified by drop-casting a suspension containing Fe_3O_4/PANI-Cu(II) composite and hematite nanoparticles onto the electrode surface.				
(Zhang, 2024)	ZnO Nanorods (NRs) Synthesis via Hydrothermal Method: Zinc nitrate hexahydrate and hexamethylenetetramine dissolved in equal volume ratio, indium nitrate hydrate (1-9% vol) added, heated at 90°C for 12 hours, centrifuged, washed, and dried at 60°C. Electrode Modification via Drop-Casting: Indium-doped ZnO NRs suspension was dropped on the GCE surface, and dried, then LOx and GA were applied on the electrode surface, and dried at room temperature.	XRD Method: Shows wurtzite ZnO structure with a diffraction peak shift due to indium doping. SEM Method: Reveals morphological changes of ZnO nanorods (NRs) after doping. FT-IR Method: Displays Zn-O and In-O absorption bands. XPS Method: Confirms the presence of In^{3+} in ZnO.	CV method: Measurement in 0.1 M PBS with a scan rate of 50 mV/s. Amperometry method: Concentration range 0.1-36 mM, detection limit 0.8 µM.	Centrifugation method: Blood and urine from athletes (age 23 years) centrifuged at 1000 rpm for 15 minutes, supernatant collected, diluted with 0.1 M PBS containing 1 mM HMF.	DPV and Amperometry methods. Serum results: Recovery 96.00-99.28%, RSD 3.77-4.25%. Urine results: Recovery 94.00-98.58%, RSD 3.55-4.62%. Indicating good accuracy and application for lactate detection in biological samples.
(Mundaca-Uribe et al., 2019)	Carboxylation of Carbon Nanofibers (CNFs): CNFs dissolved in a mixture of sulfuric acid and nitric acid (3:1), ultrasonicated for 5 hours, centrifuged at 14,000 rpm, washed to pH 7, and dispersed in ultrapure water. Electrode Modification via Drop-Casting: GCE polished with alumina slurry, cleaned and ultrasonicated. 10 µL of CNFs suspension drop-cast on GCE and dried at 41°C, then 5 µL Nafion® added and dried.	XRD Method: Shows CNFs crystal structure. FT-IR Method: Displays absorption bands of carboxyl groups and CNFs. FE-SEM Method: Reveals CNFs fibre morphology.	CV method: Measurement in 0.1 M KCl with redox mediator K3[Fe(CN)6], scan rate 60 mV/s. DPV method: Concentration range 1-17 µM, detection limit 0.06 µM.	.	DPV and Standard Addition methods. Serum Sample: Recovery 95.04-97.01%, RSD <1.01%. Pharmaceutical Tablets: Recovery 98.8-99.7%, RSD <1.1%. Indicating good accuracy and application for ACZ detection in serum and tablet samples. 4o
(Guo & Fan, 2021)	Fe_3O_4 Nanoparticles (NPs) Synthesis via Hydrothermal Method: $FeCl_3$, sodium acetate, and sodium citrate dihydrate mixed in ethylene glycol, heated at 180°C for 24 hours. CuO Nanoparticles (NPs) Synthesis via Hydrothermal Method: Copper(II) nitrate trihydrate ($Cu(NO_3)_2 \cdot 3H_2O$), hydrazine hydrate ($N_2H_4 \cdot H_2O$), and sodium borohydride ($NaBH_4$) dissolved in deionized water, heated at 160°C for 10 hours. Carbon Nanotubes (CNTs) Functionalization via Ultrasonication Method: CNTs functionalized with sulfuric acid and nitric acid at 80°C for 4 hours, washed with deionized water, and dried. Fe_3O_4-CuO@functionalized-CNTs (f-CNTs) Composite via Ultrasonic Mixing Method: f-CNTs, CuO NPs, and Fe_3O_4 NPs mixed in deionized water, deposited on CPE surface and dried at room temperature.	XRD Method: Shows diffraction patterns for Fe_3O_4 and CuO. SEM Method: Displays Fe_3O_4 and CuO nanoparticle morphology on the porous functionalized carbon nanotubes (f-CNTs) structure.	CV method: Measurement in 0.1 M PBS pH 7.0 at scan rate 10 mV/s. Amperometry method: Concentration range 0-3100 µM, detection limit 0.003 µM.	Centrifugation method: Human serum sample free of DXM taken, precipitated with methanol, centrifuged at 1500 rpm, supernatant filtered and diluted with 0.1 M PBS.	Amperometry method. Recovery 94.35-99.66% for pharmaceutical tablets, RSD <3.73%; recovery 96.36-99.50% for serum, RSD <3.71%. Indicating good accuracy and application for DXM detection in pharmaceutical and real serum samples.
(Y. Li & Xiong, 2021)	Graphene Oxide (GO) Synthesis via Modified Hummers Method: Graphite powder mixed with sulfuric acid (H_2SO_4) and nitric acid (HNO_3), potassium permanganate ($KMnO_4$) added, stirred at 35°C, hy-	FE-SEM Method: Shows graphene oxide (GO) with fluctuating layers and a porous molecularly imprinted polymer (MIP) structure.	DPV method: Measurement in 0.1 M PBS pH 7 at scan rate 10 mV/s.	Centrifugation method: Prednisolone-free plasma sample taken, precipi-	DPV method. Recovery 96-99.38% for pharmaceutical tablets and human plasma, RSD <3.89%. Indicating good accuracy and

Table 2.
Characteristics of included studies

Study	Nanomaterial Preparation	Characterization	Electrochemical Measurement	Real Sample Preparation	Real Sample Analysis
	drogen peroxide (H_2O_2) added, centrifuged, and dispersed in 0.1 M phosphate-buffered saline (PBS) at pH 7. Molecularly Imprinted Polymer (MIP) via Electrochemical Polymerization: GCE/GO modified with tetrabutylammonium perchlorate (TBAP) and acetonitrile (ACN), 4-vinylphenol (4-VP) deposited at 1.0 V for 15 minutes, and oxidized through cyclic voltammetry (CV) at pH 9.0. Electrode Modification via Electroplating: GCE cleaned and polished, electrodeposited with GO in 0.1 M PBS at pH 7, applying a potential range of -0.1 to 0.9 V for 50 cycles.	DPV Method: Measures prednisolone with a linear range of 1-120 µM and a detection limit of 0.004 µM.		tated with methanol, centrifuged, supernatant filtered and diluted with 0.1 M PBS.	application for prednisolone detection in clinical samples.
(Ni, 2023)	Graphene Oxide (GO) Synthesis via Modified Hummers Method: Graphite powder is added to a mixture of sulfuric acid (H_2SO_4) and nitric acid (HNO_3), followed by the addition of potassium permanganate ($KMnO_4$) and hydrogen peroxide (H_2O_2), centrifuged, and dispersed in 0.1 M phosphate-buffered saline (PBS). Molecularly Imprinted Polymer (MIP) Modification on GO via Electro-deposition Method: Tetrabutylammonium perchlorate (TBAP) and acetonitrile (ACN) are applied to the GCE/GO surface, then poly(ionic liquid) (PIL) deposited on MIP/GO/GCE. Electrode Modification via Electro-deposition Method: GO deposited on the GCE surface using the cyclic voltammetry (CV) technique in 0.1 M PBS at pH 7.0.	FE-SEM Method: Shows graphene oxide (GO) surface morphology and porous poly(ionic liquid)/molecularly imprinted polymer (PIL/MIP)/GO structure. XRD Method: Displays the crystal structure of GO and PIL/MIP. FT-IR Method: Shows characteristic absorption bands for GO and PIL/MIP. XPS Method: Reveals the elemental spectra of GO and PIL/MIP.	DPV method: Measurement in 0.1 M PBS pH 7.0 at scan rate 10 mV/s, concentration range 1-60 µM, detection limit 0.003 µM.	Centrifugation method: Human plasma sample free of testosterone centrifuged at 1500 rpm, supernatant diluted with 0.1 M PBS.	DPV method. Recovery 96.05-99.41% for plasma, RSD <3.87%; indicating good accuracy and application for testosterone detection in pharmaceutical and real plasma samples.
(Al Omar et al., 2023)	CeO_2 and ZnO Nanoparticles (NPs) Synthesis via Green Method: Barley and rice husk extracts heated at 60°C, mixed with cerium nitrate hexahydrate or zinc sulphate solution, heated at 80°C for 2 hours, precipitated, filtered, and dried. PTD-RK Sensor Fabrication via Membrane Layering Technique: PTD-RK (10 mg), poly(vinyl chloride) (PVC) (190 mg), and ortho-nitrophenyl octyl ether (o-NPOE) (0.4 mL) mixed with 50 mL tetrahydrofuran (THF), poured into a Petri dish, allowed to dry, and layered on aluminium wire.	XRD Method: Shows diffraction patterns for CeO_2, ZnO, and CeO_2/ZnO nanocomposites. UV-Vis Method: Displays absorption peaks at 310 nm, 362 nm, and 334 nm. FT-IR Method: Shows absorption bands for O-H, C=O, Ce-O, and Zn-O. SEM Method: Reveals spherical morphology for CeO_2 and hexagonal shape for ZnO. EDX Method: Shows elemental composition of cerium (Ce), zinc (Zn), and oxygen (O).	Potentiometric method: Linear range $1.0 \times 10{-}9$-$1.0 \times 10{-}2$ mol/L. Detection limit $4.8 \times 10{-}10$ mol/L. Response time 10 seconds.	Centrifugation method: PTD injection sample diluted to various concentrations ($1.0 \times 10{-}7$-$1.0 \times 10{-}2$ mol/L) and analyzed using the developed sensor.	Potentiometric method. Recovery 98.92-99.76%, RSD <0.7%; indicating good accuracy and application for PTD detection in real pharmaceutical and biological samples.
(Alterary, 2023)	Al_2O_3 and CuO Nanoparticles (NPs) Synthesis via Co-precipitation Method: Salvia officinalis leaf extract mixed with aluminium nitrate nonahydrate or copper nitrate trihydrate solution, heated at 80°C for 30 minutes, precipitated with sodium hydroxide (NaOH), centrifuged, and dried at 60°C. NBP-PM Sensor Material via Ion-Pair Reaction Method: NBP mixed with phosphomolybdic acid (PMA) to form NBP-PM, precipitated, filtered, and dried. Membrane Fabrication via Mixing Method: NBP-PM mixed with poly(vinyl chloride) (PVC), ortho-nitrophenyl octyl	XRD Method: Shows diffraction patterns for Al_2O_3 and CuO. FT-IR Method: Displays characteristic absorption bands for Al_2O_3 and CuO. SEM Method: Reveals nanoparticle morphology of Al_2O_3 and CuO. EDX Method: Shows the elemental composition of aluminium (Al), copper (Cu), and oxygen (O).	Potentiometric method: Linear range $1.0 \times 10{-}9$-$1.0 \times 10{-}2$ mol/L. Detection limit $5.0 \times 10{-}10$ mol/L. Response time 40-60 seconds.	Centrifugation method: NBP injection sample diluted to various concentrations ($1.0 \times 10{-}9$-$1.0 \times 10{-}2$ mol/L) and analyzed using the developed sensor.	Potentiometric method. Recovery 98.79-99.52%, RSD <0.64%; indicating good accuracy and application for NBP detection in real pharmaceutical samples.

Table 2.
Characteristics of included studies

Study	Nanomaterial Preparation	Characterization	Electrochemical Measurement	Real Sample Preparation	Real Sample Analysis
	ether (o-NPOE), and Al_2O_3 or CuO nanoparticles in tetrahydrofuran (THF), then layered on polished copper wire.				
(Al-Mohaimeed et al., 2023)	Al_2O_3 Nanoparticles (NPs) Synthesis via Green Method: Lavandula spica flower extract heated at 80°C, mixed with aluminium nitrate solution, heated, precipitated, filtered, and dried. Electroactive Material via Ion-Pair Reaction: AC mixed with phosphomolybdic acid (PMA) to form AC-PM, precipitated, filtered, and dried. Sensor Membrane Fabrication via Mixing Method: AC-PM mixed with graphite powder, ortho-nitrophenyl octyl ether (o-NPOE), and multi-walled carbon nanotubes (MWCNTs)-Al_2O_3 nanocomposite in tetrahydrofuran (THF), then layered on polished copper wire. MWCNTs Functionalization via Wet Impregnation Procedure: MWCNTs washed with hydrochloric acid (HCl) solution, oxidized with nitric acid (HNO_3) solution, washed with water to pH 7, and dried. Oxidized MWCNTs mixed with Al_2O_3 NPs in water, sonicated, stirred, heated to 80°C, and then calcined at 350°C for 4 hours.	XRD Method: Shows diffraction patterns for Al_2O_3 and multi-walled carbon nanotubes (MWCNTs). FT-IR Method: Displays characteristic absorption bands for Al_2O_3 and MWCNTs. SEM Method: Reveals Al_2O_3 nanoparticle morphology on the MWCNTs surface. EDX Method: Shows the elemental composition of aluminium (Al), carbon (C), and oxygen (O).	Potentiometric method: Linear range 1.0 × 10^-8-1.0 × 10^-2 mol/L. Detection limit 4.8 × 10^-9 mol/L. Response time 20 seconds.	Centrifugation method: AC injection sample diluted to various concentrations (1.0 × 10−7-1.0 × 10−2 mol/L) and analyzed using the developed sensor.	Potentiometric method. Recovery 98.86-99.67%, RSD <0.81%; indicating good accuracy and application for AC detection in real pharmaceutical samples.

Table 2 shows various synthesis and characterization methods of nanomaterials used for electrochemical sensor applications in the detection of biological analysis. Characterization techniques such as FE-SEM, XRD, UV-Vis, FT-IR, and EIS were used to confirm the structure, morphology, and composition of the synthesized nanomaterials. Electrochemical measurements such as DPV, CV, and potentiometry were used to assess the sensor's performance under various conditions. Real sample preparation was conducted through centrifugation and filtration to separate the desired components. The analysis results demonstrated high recovery and precision, with recovery values ranging from 94.00% to 103.50% and RSD (Relative Standard Deviation) ranging from 0.64% to 5.11%. This indicates good accuracy and applicability of the developed sensors in detecting analytes in real biological and pharmaceutical samples.

Table 3.
Meta-Analysis for Fixed and Random Effects

Category	Fixed and Random Effects					Test for overall effect				Residual Heterogeneity Estimates	
	Residual			SMD	Std. Error	z	p-value	95% CI		I^2 (%)	τ
	Chi^2	df	p-value					Lower	Upper		
DPV and ELISA	0.68	7	1.00	0.11	0.20	0.53	0.60	-0.30	0.51	0	0.00
Urine and Serum	0.90	2	0.64	0.20	0.38	0.53	0.60	-0.56	0.97	0	0.00
Tablet and Serum	3.17	3	0.37	0.10	0.67	0.25	0.80	-0.70	0.91	5	0.04
Sensor and Sensor Nanocomposites	1.17	3	0.76	1.11	0.26	4.14	<0.0001	0.58	1.63	0	0.00

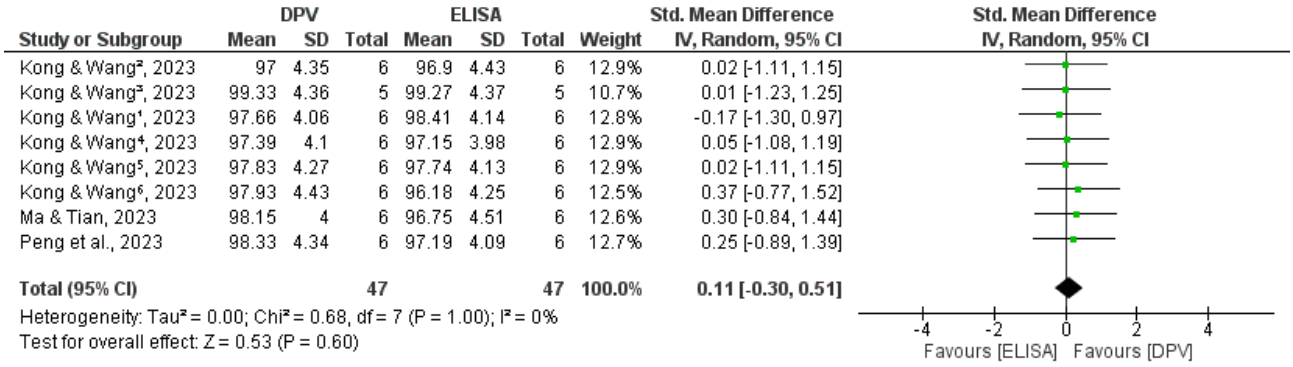

Figure 2. Findings of the DPV and ELISA analysis for the determination of doping substances in prepared sample specimens. 1) Age Group 21, 2) Age Group 23, 3) Age Group 26, 4) Age Group 27, 5) Age Group 29, 6) Age Group 29.

The forest plot analysis results in figure 2 indicate that there is no significant heterogeneity among the analyzed studies, with $Tau^2 = 0.00$, $Chi^2 = 0.68$, $df = 7$, $P = 1.00$, and $I^2 = 0\%$, meaning the results from these various studies are quite consistent. The overall effect test yielded a Z value of 0.53 with $P = 0.60$, indicating no statistically significant effect in differentiating between the Differential Pulse Voltammetry (DPV) and Enzyme-Linked Immunosorbent Assay (ELISA) methods for determining doping substances. The interpretation of the Forest Plot shows that all confidence intervals (CI) from each study include zero (0), indicating no significant difference between the DPV and ELISA methods. The standardized mean difference (SMD) comparison shows a value of 0.11 with a confidence interval of -0.30 to 0.51, indicating a slight but non-significant tendency towards DPV. The Rank Correlation Test results (Kendall's $\tau = 0.429$, $P = 0.179$) and the Regression Test (Egger's Test) with a z value of -0.090 and $P = 0.928$, indicate no evidence of significant publication bias.

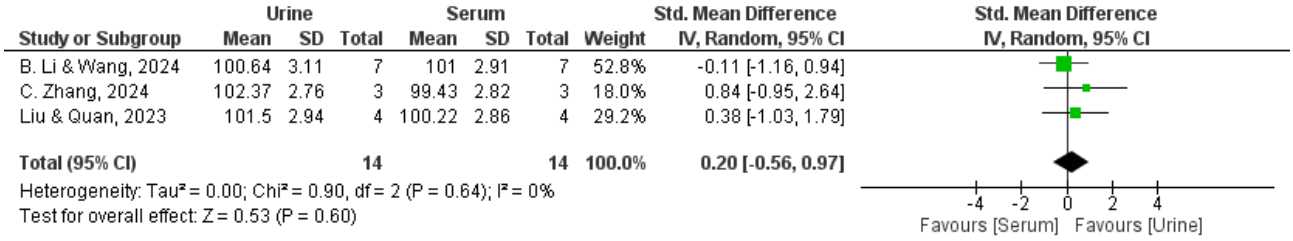

Figure 3. Forest plot of recovery results for the determination of doping substances in human serum and urine samples enriched with nanoparticles.

The Forest plot results are shown in figure 3, with the diamond shape at the bottom of the plot indicating the overall 95% CI values ranging from -0.56 to 0.97, demonstrating that the overall standardized mean difference is not statistically significant. The Chi^2 value of 0.90 with $df = 2$ and $P = 0.64$ indicates that there is no significant heterogeneity among the analyzed studies, meaning the differences between studies can be considered random variations. The results of this plot show that there is no significant difference between serum and urine in the context of doping substance determination using nanoparticles. Additionally, the asymmetry tests of the funnel plot using Kendall's τ and Egger's test showed consistent results. Kendall's τ value of 1.000 with a p-value of 0.333, and a z-value of 1.178 with a p-value of 0.239, indicate no significant evidence of asymmetry in the funnel plot.

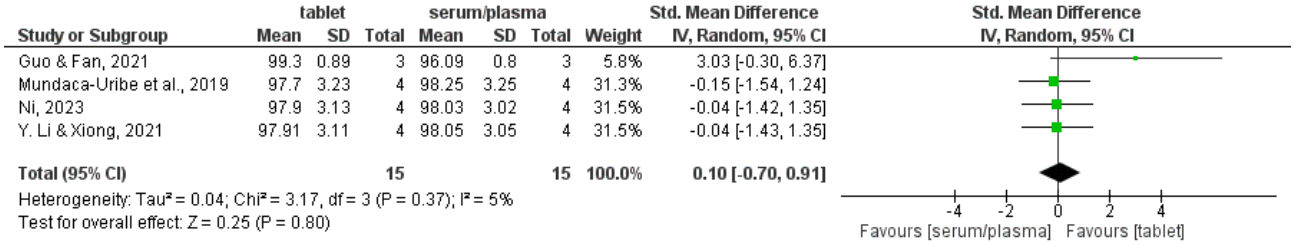

Figure 4. Analytical findings of the forest plot for nanomaterials in determining doping substances in real specimens of human tablets and serum that have been prepared.

In this study, the forest plot shown in figure 4 indicates that the average test results for tablets range from 97.7 to 99.3, while serum/plasma ranges from 96.09 to 98.25. The heterogeneity among studies is low, with a Tau² value of 0.04, Chi² of 3.17 (df = 3, P = 0.37), and I² of 5%, indicating consistent results across the studies. The overall effect test (Z = 0.25, P = 0.80) shows no significant difference between tablets and serum/plasma. This is supported by the Standard Mean Difference (SMD) calculated using the IV Random method with a 95% confidence interval (CI) of 0.10 [-0.70, 0.91], where the confidence interval crosses zero, indicating no statistical significance. The Kendall's rank correlation test (Kendall's τ = 0.000, P = 1.000) shows no significant asymmetry, indicating no evident publication bias. However, the regression test for funnel plot asymmetry (Egger's Test) indicates the presence of publication bias with a z-value of 2.719 and a P-value of 0.007. These results suggest that although publication bias was not detected based on Kendall's rank correlation test, Egger's Test results indicate potential publication bias that warrants further attention. Overall, the results from various studies show no significant difference between tablets and serum/plasma in doping substance testing, with low heterogeneity among studies and high consistency in results.

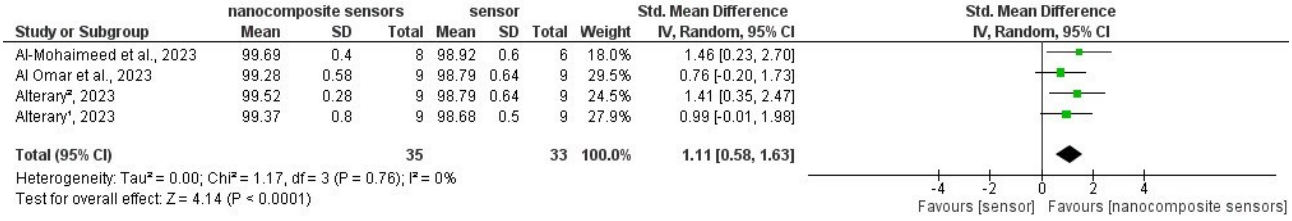

Figure 5. Estimated results from the use of conventional sensors and nanocomposite sensors for doping tests in actual samples.

Table 4.
Rank correlation test for funnel plot asymmetry and regression test for funnel plot asymmetry

Category	Kendall's		Egger's test	
	τ	p	z	p
DPV and ELISA	0.429	0.179	-0.090	0.928
Urine and Serum	1.000	0.333	1.178	0.239
Tablet and Serum	0.000	1.000	2.719	0.007
Sensor and Sensor Nanocomposites	1.000	0.083	0.981	0.327

The forest plot shown in figure 5 compares the performance of conventional sensors with nanocomposite sensors in the context of doping tests on actual samples. The statistical heterogeneity analysis results are Tau² = 0.00; Chi² = 1.17, df = 3 (P = 0.76); I² = 0%. An I² value of 0% indicates no heterogeneity among the analyzed studies, demonstrating consistency in results across the studies. Additionally, the overall effect test results show Z = 4.14 (P < 0.0001), indicating a significant overall effect and supporting the superiority of nanocomposite sensors over conventional sensors. The rank correlation test results show Kendall's τ = 1.000 with p = 0.083.

Although the τ value indicates a very high correlation, the p-value greater than 0.05 suggests no strong evidence of publication bias based on this test. The regression test (Egger's Test) shows a result of z = 0.981 with p = 0.327, indicating no significant evidence of publication bias based on the regression test. The data show that nanocomposite sensors are significantly more effective than conventional sensors in doping tests on actual samples. The absence of significant heterogeneity (I² = 0%) indicates that the study results are very consistent. Furthermore, the funnel plot analysis and the results of Kendall's τ and Egger's tests suggest a low likelihood of publication bias, thus the study results can be considered reliable.

Discussion

This study aims to evaluate the effectiveness and accuracy of nanotechnology applications in doping detection within the athlete community through the analysis of 13 selected studies. The results of the meta-analysis and systematic review reveal several key findings that reinforce the potential use of nanomaterials and nanosensors in anti-doping systems. The study by Peng et al. (2023), which utilized the Solvothermal method to produce CeO_2/CNTs nanocomposites, demonstrated high accuracy in the detection of methamphetamine (MT) in blood serum samples with a recovery rate of 94.50% to 98.00% and a relative standard deviation (RSD) between 3.97% and 5.03%. These results indicate that nanocomposites can be used for precise and accurate doping detection. These findings support the meta-analysis results showing that Differential Pulse Voltammetry (DPV) and Enzyme-Linked Immunosorbent Assay (ELISA) methods provide highly accurate and reliable results in doping detection.

The study by Ma & Tian (2023) used the microwave-assisted method for synthesizing N-CNP, showing excellent results in detecting trenbolone (TZ) in the blood serum of bodybuilder athletes with a recovery rate of over 98.53% and an RSD of less than 5.08%. This confirms that carbon-based nanosensors have very high detection capabilities, supporting the findings that there is no significant difference between serum and urine in doping determination using nanoparticles. Kong & Wang (2023) used ZnO@carbon nanocomposites synthesized through the Calcination

method. Test results indicated that these nanocomposites were highly effective in detecting tetrahydrogestrinone (TER) with recovery rates ranging from 94.75% to 99.45% and an RSD of less than 5.04%. This suggests that the use of carbon-based and metal-oxide nanomaterials can enhance the sensitivity and specificity of doping detection, supporting the findings that nanocomposite sensors are more effective than conventional sensors in doping tests on actual samples.

The study by Y. Liu & Quan (2023) used the Sol-gel method for the synthesis of ZnO and TiO_2, showing that the combination of these nanomaterials is effective in detecting lactate in the serum and urine of athletes with high recovery rates and low RSDs. These results reinforce the potential of nanomaterial applications in developing more efficient and reliable doping detection sensors. Furthermore, B. Li & Wang (2024) demonstrated that the synthesis of Hematite NPs and Fe_3O_4 NPs via Hydrothermal and Solvothermal methods resulted in nanomaterials with high accuracy in detecting dexamethasone in serum and urine. This indicates that nanomaterials can be used for doping substance detection with almost the same accuracy across various types of biological samples.

The study by C. Zhang (2024) utilized the hydrothermal method for the synthesis of indium-doped ZnO NRs, showing lactate detection capabilities in serum and urine with recovery rates ranging from 94.00% to 98.58% and RSDs ranging from 3.55% to 4.62%. This suggests that indium doping in ZnO NRs can enhance detection efficiency and provide more consistent results in field applications. The research by Mundaca-Uribe et al. (2019) highlighted the use of carbonized CNFs for detecting acetazolamide (ACZ) in serum and tablets with excellent recovery and low RSDs. This demonstrates that CNFs can be used for doping detection applications in various sample forms, offering greater flexibility in field testing.

Guo & Fan (2021) investigated Fe_3O_4-CuO@f-CNTs composites, which showed high accuracy in detecting dexamethasone (DXM) in serum and pharmaceutical tablets. These results indicate that the combination of nanomaterials and CNTs can enhance sensor sensitivity and specificity, making them more effective for anti-doping applications. Y. Li & Xiong (2021) used the modified Hummers method for the synthesis of GO and demonstrated that GO-modified MIP has very accurate prednisolone detection capabilities in human plasma, with recovery rates between 96% and 99.38% and RSDs of less than 3.89%. These results highlight the great potential of nanomaterial-based MIP techniques in anti-doping applications that require high accuracy. Ni (2023) showed that GO synthesized via the modified Hummers method is effective in detecting testosterone in human plasma, with excellent recovery results and low RSDs. This indicates that GO-based nanomaterials can be used to detect doping hormones with high accuracy.

Al Omar et al. (2023) used a green method for the synthesis of CeO2NPs and ZnONPs, which showed excellent results in detecting parathion-methyl (PTD) in pharmaceutical and biological samples with high recovery rates and low RSDs. This demonstrates the great potential of metal oxide-based nanomaterials in doping detection applications. Alterary (2023) demonstrated that the co-precipitation method for the synthesis of Al2O3NPs and CuONPs resulted in nanomaterials with high accuracy in detecting nifedipine (NBP) in pharmaceutical samples. These results confirm that metal oxide-based nanomaterials can be used for doping detection applications with high and consistent accuracy.

Al-Mohaimeed et al. (2023) used a green method for the synthesis of Al2O3NPs, which showed excellent detection capabilities in real pharmaceutical applications with high recovery rates and low RSD. This strengthens the argument that metal oxide-based nanomaterials can be used for efficient and accurate doping detection applications. Meta-analysis indicates that there is no significant difference between the DPV and ELISA methods in doping detection. This is demonstrated by the overall effect test results, which show a Z value of 0.53 with $P = 0.60$, and confidence intervals that include zero, indicating that both methods have similar effectiveness in the context of doping detection.

In the comparison between serum and urine samples, the forest plot results show no significant heterogeneity among the analyzed studies. A Chi^2 value of 0.90 with $df = 2$ and $P = 0.64$, as well as a Tau^2 value of 0.00, indicate consistent results across various studies and no significant difference between serum and urine in doping determination using nanoparticles. This study also evaluated the effectiveness of nanocomposite sensors compared to conventional sensors in the context of doping tests on actual samples. The results show that nanocomposite sensors are significantly more effective than conventional sensors, with a Z value of 4.14 and $P < 0.0001$, as well as no significant heterogeneity ($I^2 = 0\%$). Funnel plot analysis and the results of Kendall's τ and Egger's tests indicate a low likelihood of publication bias, suggesting that the study results can be considered reliable.

Overall, this study demonstrates that nanotechnology has great potential to enhance doping detection in sports. The use of nanomaterials and nanosensors in doping detection systems shows highly accurate and reliable results. The results from various studies indicate that nanomaterials can improve the sensitivity, specificity, and accuracy of doping substance detection, making them a highly effective tool in maintaining the integrity and health of the athletes. This research provides a strong foundation for the further developments of this technology and its application in future anti-doping systems.

Conclusion

This study explores the effectiveness and accuracy of nanotechnology applications in doping detection among athletes. Through a systematic literature review and meta-

analysis of 13 studies, it was found that methods such as Differential Pulse Voltammetry (DPV) and Enzyme-Linked Immunosorbent Assay (ELISA) provide highly accurate and reliable results in detecting doping substances. The study results indicate that there is no significant difference between the use of serum and urine as test samples, confirming that both types of samples can be used effectively. Nanocomposite sensors have proven to have advantages over regular sensors, with higher accuracy and sensitivity in detecting doping substances. The analysis results show no significant heterogeneity among the studies analyzed and a low likelihood of publication bias. The use of carbon-based nanomaterials, metal oxides, and other nanomaterial combinations has been shown to increase specificity and accuracy in doping detection, making them effective tools for maintaining athletes' integrity and health.

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