E-ISSN: 2664-6773
P-ISSN: 2664-6765
Impact Factor: RJIF 5.6
IJCBS 2024; 6(1): 126-132
www.chemicaljournal.org
Received: 07-02-2024
Accepted: 10-03-2024

Qasim Mezban Salih
College of Science, Wasit University, Kut, Iraq

Corresponding Author:
Qasim Mezban Salih
College of Science, Wasit University, Kut, Iraq

Nano chemistry and its importance

Qasim Mezban Salih

DOI: https://doi.org/10.33545/26646765.2024.v6.i1b.94

Abstract
Background: Biological samples as cells, nucleic acids, proteins, and metabolites are related to physiological and pathological processes in organism. Even though, the portion responsible for diseases are embedded in environment of high-abundance proteins and salts which lead to direct analysis obstacles for them. Nano-materials with easy formulation and manipulation are made to solve the problem.
Materials and Methods: Data are extracted from online databases including Science direct, PubMed and Google Scholar from 2013 till 2022. Then eligibility of reference lists was assessed.
Results: AuNPs and magnetic graphene nanocomposites are signal amplification immune sensors for tissue polypeptide antigen detection. AuNPs SPCE and silver nanoparticles loaded nanohydroxyapatite used for apolipoprotein-A1 detection. For squamous cell carcinoma antigen detection, a Sandwich-type EC immunosensor was created. As immunosensing probes, poly(o-phenylenediamine) (POPD)/Au nano-composite and poly(vinylferrocene-2-aminothiophenol) (poly (VFcATP))/Au nanocomposites are utilized for detecting CEA and AFP, respectively. For detecting tumor markers, PEC serves as immunosensors. When it comes to detecting of viruses, bacteria, and toxins, gold nano-particles (AuNPs) are becoming increasingly popular.
Aim of the study: Within the scope of our research, we wanted to evaluate the formulation of novel nanomaterials for the detection of certain elements in biological samples.

Keywords: Immunosensing probes, poly(o-phenylenediamine), nanocomposites

Introduction

Lately, determination regarding metals ions and organic species and quantification of their concentration in biological as well as environmental samples have achieved important concern (Jin *et al*., 2012) [23]. Analytical methods have limitations of low sensitivity because of interferent(s) with other elements in the matrix samples (Namieśnik, 2002) [42]. The concentration of trace elements is too low to be detected by traditional analytical instruments (Hashemi *et al*., 2018) [15]. Solid phase microextraction (SPME) and solid phase extraction (SPE) processes are utilized for the purpose of facilitating enrichment of elements (Souza-Silva *et al*., 2015) [51].

Based on the study by Hashemi *et al*. (2018) [15], biological samples such as hair, urine, blood, and plasma consist of a complex matrix of the organic and inorganic moieties such as amino acids and salts, and the presence of relevant analyte has been found in insufficient amounts. Which is why, prior to the instrumental detection, there is a high importance in isolating and improving target compounds from complex matrix. This is due to the fact that analytes or interferences' concentration level is rather low. SPE as well as SPME have been considered superior pretreatment procedures for extracting and evaluating various analytes from a wide range of biological media.

According to Lara and Perez-Potti (2018) [28], nanomaterials are objects that range in size from one nanometer to one hundred nanometers. According to Kim *et al*. (2014) [26], they have the ability to offer both chemical and physical features due to their compact dimensions, which allow them to offer a substantial surface area to volume ratio. The continuous advancements that have been made over the course of the last decade have made it possible to make them in a wide range of chemistries, shapes, and core compositions.

Managing the design of NPs to suit drug delivery (Gao *et al*., 2017) [10], imaging (Chowdhuri *et al*., 2016) [6], and diagnostics (Pelaz *et al*., 2017) [46] is a field that is developing in fields, like cancer and diagnosis and treatment of cancer as well as several pathologies, like autoimmune diseases.

Materials and Methods

Strategy

We assessed online databases including Science Direct, PubMed and Google Scholar from 2013 till 2022. We also reviewed the literature using the following Key words Nano, Nano-materials, Nanoparticles, biological samples, determination, and detection. We assessed the titles and abstracts of all papers recognized from this search for applicability. The references of related articles were also searched to identify eligible papers, if paper was theoretically related to our review, we then investigated eligibility of all paper. Finally, we assessed the eligibility of reference lists.

Study eligibility

Our inclusion criteria were those papers or studies which described synthesis and preparation of nanomaterials and used it in biological samples characterization. All study designs were considered. Results of cross-sectional and cohort study designs. We excluded unpublished reports, theses.

Results and Discussion

Immune sensors based on nanomaterials

Electrochemical immunosensing is a simple, easily operated, low cost, highly sensitive and accurate analysis method for tumor marker detection.

Carbon Nanomaterials

Carbon containing nanomaterials like graphene (Xu *et al*., 2015) [69] and carbon nanotubes, offer large surface-to-volume ratio, excellent mechanical property, as well as conductivity. They could be substituted by organic moieties in different sites in their structures. Wang *et al*., (2015) [56] utilized a new nanomaterial which bear AuNPs and magnetic graphene that used for discovery of tissue polypeptide antigen (TPA). Yang *et al*., (2017) [43] described nitrogen-doped graphene (NG) as highly streptavidin-functionalized group that can be applied to EC immunosensing for detection of CEA. Lai *et al*., (2018) [27] confirmed that by mentioning that the biofunctionalized NG detected large number of antibodies because of large surface area. Zhang *et al*., (2016) [74] used multiwalled carbon nanotubes as a sensor for latent membrane protein 1 detection.

Noble Metal Nanomaterials

Gold, silver and platinum are noble metals (Wang *et al*., 2017) [59]. AuNPs, due to excellent heat and electrical conductivity, its high electron density, good biocompatibility was commonly employed in sensors to augment their electron transfer ability (Jolly *et al*., 2017) [24]. According to Wang *et al*. (2015) [56], silver NPs loaded with nanohydroxyapatite (Ag-nHAP) and AuNPs modified SPCE were successfully utilized in the detection of apolipoprotein-A1 (ApoA11). Squamous cell carcinoma antigen (SCCA) detection was accomplished by Liu *et al*. (2016) [37] through the utilization of a sandwich-type EC immunosensor that contained noble metal.

Polymer Nanomaterials

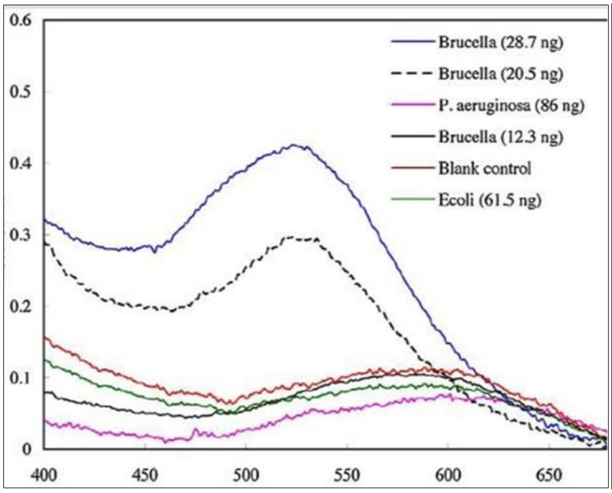
According to Niu *et al*. (2017) [43], and Yuan *et al*. (2015) [72], polymer nanomaterials, such as polyaniline, hyperbranched polymers, and polypyrrole are reported to have simple synthesis, exceptional redox-activity, easy synthesis, and good cell and biocompatibility. The researchers Liu *et al*. (2015) [38] created nanomaterials consisting of poly(o-phenylenediamine) (POPD)/Au and poly(vinylferrocene-2-aminothiophenol) (poly (VFcATP))/Au. These nanomaterials retained immunosensors for detecting the AFP and CEA in an instantaneous manner.

PEC Immunosensors Based on Nanomaterials

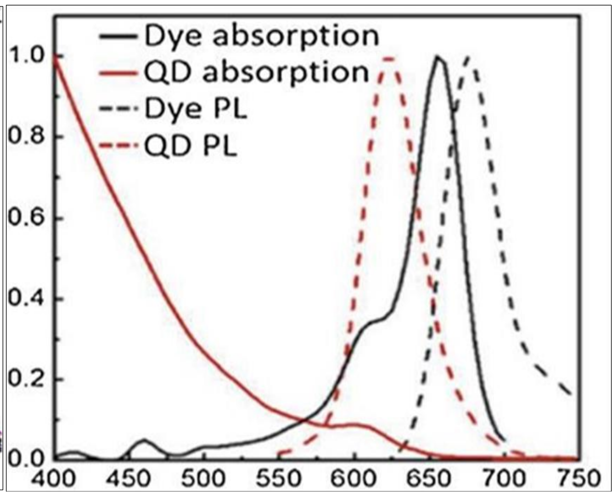
PEC sensors are type of analytical tools depend on light converting character to electricity. The improvement of photoactive materials for manufacturing immunosensors for detection of tumor markers is becoming more and more.

Detection of biological threat agents

According to Rowland *et al*. (2016) [48], detecting viruses, bacteria, and toxins is a practice that frequently makes use of AuNPs. The size of the AuNPs ranged from 2 to 100 nanometers, and they exhibited a phenomenon known as LSPR, which resulted in exceptional optical absorption capabilities. The analyses can be completed in any time between one and ten minutes. According to Rowland *et al*. (2016) [48], it is simple to modify by modifying the surface functional group to other elements, DNA sequences, or antibodies. According to Algar *et al*. (2011) [1], coating AuNPs with reactive ligands makes it possible to use covalent attachment of DNA, proteins, and antibodies. This could be accomplished through methods such as NHS- ester, maleimide-thiol, carbodiimide coupling (EDC), cycloaddition (click) chemistry, as well as non-covalent methods such as biotin or NTA or passive adsorption. In the case of Brucella species, complementary oligonucleotide was utilized in cell examination (Sattarahmady *et al*., 2015) [50]. In a case of M. tuberculosis carbon nano-tubes, complementary oligonucleotide impedance was utilized.



(Sattarahmady *et al*., 2015) [50]

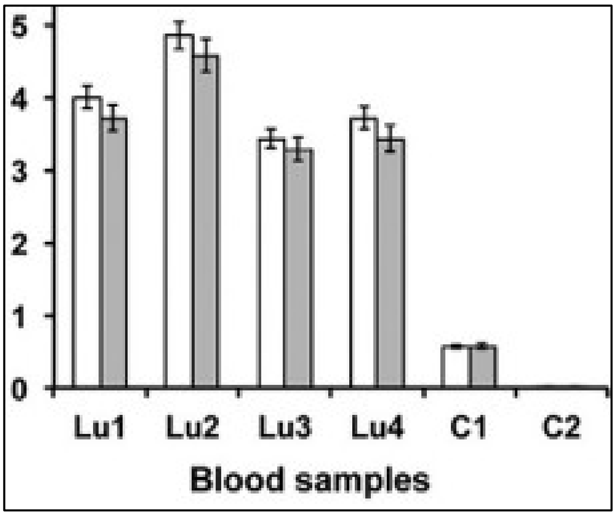


(Lee *et al*., 2015) [30]

Circulating tumor cells

When it comes to immunoaffinity approaches, nanomaterials that are based on antibodies are utilized quite frequently. On the surface of cancerous cells, there are, in most cases, distinct markers. Epidermal receptor 2 (HER-2) is discovered in high concentrations in ovarian, breast, and gastric cancers. Epithelial cell adhesion molecule (EpCAM) is also found in high concentrations in various epithelial cancers (Munz *et al*., 2009) [41]. Glypican-3 (GPC3) has been demonstrated to be present in hepatocellular carcinoma, among other cancers (Ismail, 2010) [22]. There are a lot of benefits that come along with selecting the functional groups of the antibodies produced by these particular markers with a high affinity.

According to Li *et al*. (2015) [31], Hammond and his colleagues were successful in constructing a biodegradable nanofilm composed of alginate and poly (allylamine hydrochloride). Taking into consideration a healthy sample as the control group, Stott *et al*. (2010) [53] chose lung cancer cells (H-1650 and H-1975) to use as model samples. In accordance with the findings of earlier research, they discovered that the number of CTCs that were identified in a sample of lung cancer ranged between 2.50 to 5.90 in 1 milliliter.



CTCs from blood samples of lung cancer with the use of biodegradable nano-film. The number of the CTCs that have been captured as well as released through biodegradable nano-film.

Low-abundance ordinary proteins/peptides

In Hong *et al*., (2018) [18] study, they prepared DMSNs@PDA-Ti4þ and proved that it revealed high sensitivity and high selectivity. In HeLa cell extracts, DMSNs@PDA- Ti4þ exhibited enrichment specificity of 96.30% and detected 993 multi- and1429 mono-phosphopeptides.

MOAC-based nanomaterials

A different method of separation technology is known as metal oxide affinity chromatography, or MOAC for short. Recent years have seen the development of several methods for the production of nanomaterials based on TiO2. In the year 2017, Hong and his team developed magnetic nanomaterials by using Fe_3O_4 as the core, TiO_2 as the middle layer, and NiO as the outermost layer. When compared to Fe3O4- HeTiO2, which only recognized 837 phosphopeptides with a lower enrichment specificity of 60.2%, Fe3O4@HeTiO2@f-NiO was able to detect 972 phosphopeptides with 91.90% of enrichment specificity from HeLa cell extracts. This was a significant improvement.

MOAC-based nanomaterials

A different method of separation technology is known as metal oxide affinity chromatography, or MOAC for short. Recent years have seen the development of several methods for the production of nanomaterials based on TiO_2. In the year 2017, Hong and his team developed magnetic nanomaterials by using Fe_3O_4 as the core, TiO_2 as the middle layer, and NiO as the outermost layer. When compared to Fe3O4- HeTiO2, which only recognized 837 phosphopeptides with a lower enrichment specificity of 60.2%, Fe3O4@HeTiO2@f-NiO was able to detect 972 phosphopeptides with 91.90% of enrichment specificity from HeLa cell extracts. This was a significant improvement.

Carboxyl functionalized materials the key benefit of carboxyl functionalization is the high adsorption of elements. Fathi *et al*., (2017) [9] synthesized graphene contain groups which detect Cr in water. A SiO2 covering was utilized by Wang *et al*. (2020) [60] for the purpose of Cd adsorption. The capability of poly-m-phenylenediamine

(PmPD) coated carboxyl-functionalized MNPs to adsorb aspartic acid was demonstrated by Wu *et al*. (2017) [34]. Core-shell composite of NH2–Fe3O4-NTA has been instrumental in detection and adsorption of Cu (II) and Sb (III), as reported by Hao *et al*. in 2019 [14].

The amino functionalized magnetic sorbents: Nonkumwong *et al*., (2016) [44] stated that amine-functionalized ferrite MNPs with surface modifier (ethanolamine) and MgFe2O4 efficiently detect Pb (II) in water. In their 2018 study, Ghasemi and colleagues demonstrated that the combination of MNPs, dioctyl phthalate (DOP), and TETA produced a sorbent that was able to remove zinc (II) from aqueous solutions. Wanna *et al*., (2016) [63] utilized polymethyl methacrylate onto the iron oxide nanoparticles' surface as well as polyethylene glycol diamine, which resulted in materials with great performance in Co (II), Hg (II), Cu (II), and Pb (II) removal. This is in line with the findings that they obtained.

Polyaniline (PANI) modified MNPs

He *et al*., (2020) [16] Se and Te were extracted using polyaniline modified MNPs as the extraction medium. For the purpose of Cr detection, magnetic sorbents have been utilized (Wei *et al*., 2017) [64]. The adsorption of Au and Ag ions has been accomplished by Zhao *et al*. (2018) [18] through the utilization of poly(1-vinylimidazole) (PVIM).

Mercapto functionalization

According to Kanatzidis and Manos (2016) [39], sulfhydryl functionalization is well-known for its attraction to various elements, including Cd, Pb, and Hg, as well as noble metals. According to Aljerf (2018) [2], the increased electronegativity of sulfur causes sorbents that include sulfur to have a stronger affinity to trace elements than sorbents that contain enzymes that contain amino groups.

Thiol group Zhu *et al*., (2017) [75] selected γ-MPTS sulfhydrylation reagent for functionalization of Fe3O4@SiO2, attaining Hg adsorption. Huang *et al*., (2012) [19] stated that similar sorbents were used in Se elements analysis. Wang *et al*. (2018) [27] got effective Cr removal from water samples by nano-magnetic semi-siloxane sorbent of Fe3O4-POSS-SH. Anbia, & Rahimi, (2017) [4] in their study achieved entire adsorption of Pt by magnetic cellulose material, functionalized by thiourea and glycerol methacrylate. Odio *et al*., (2016) [45] have synthesized a magnetic sorbent that adsorb Pb and Cd. Other post-functionalization methods: Wang *et al*., (2020) [60] got adsorption and analysis of Ti by preparing phosphoric acid functionalized MNPs (Fe3O4@SiO2@GMA-PO4). Additionally, Yang *et al*. (2019) [17] used organophosphorus materials to eliminate U from water. Ionic liquid-encapsulated nanomaterials was used by Davudabadi Farahani, & Shemirani (2012) [8] for of Cd and Pb adsorption. It is reported that Fe3O4@SiO2@TiO2 sorbent and used analyzing Zn, Cd, Cu, and Pb (Habila *et al*., 2016) [13]. Similarly, natural magnetic resin was used as sorbent for Cd, Pb and Cu extraction (Soylak & Erbas, 2018) [52].

Adsorption mechanism

Since N-containing functionalized sorbents have good binding effects with some of the trace elements like Bi, Pb, and Cu, they have complicated adsorption. Guo *et al*. (2014) [12] confirmed that N on amino group has the capacity to bind lead. It has been demonstrated that materials with amino functionalization could be mixed with Cu and Sb (Hao *et al*., 2019) [14]. Furthermore, as a sorbent for the removal of Hg, chitosan/cellulose composite sponge was created (Zhang *et al*., 2019) [73].

S-containing functionalized sorbents can be particularly combined with Hg and Ag, which enable them to take part in their analyses. Wang *et al*., (2018) [27] assessed thiol-functionalized magnetic materials ability in adsorption of Cr.

O-containing sorbent has high electronegativity so it can be used as general sorbent. Moreover, Liu *et al*., (2013) [36] mentioned that ability of magnetic titanate composite nano-materials to adsorb Pb is due to Pb binding to O in the structure of the titanate

Electrostatic adsorption: Al-suhybani *et al*., (2020) [3] synthesized AGPA- functionalized phthalic acid-coated magnetic nano-particles for the adsorption of Pb. Pb adsorption return to electrostatic effect. Moerover, carbon materials that contain metal oxides can adsorp trace elements by electrostatic effects (Kazak & Tor, 2020) [25]. It is also mentioned that CeO2–MoS2 used for removing Pb in water (Li *et al*., 2019) [34].

Other adsorption forces: Adsorption can appear due to ion exchange (Kazak & Tor, 2020) [25] or ion diffusion (Yang *et al*., 2019) [17]. Wang *et al*., (2019) [14] mentioned that bentonite-chitosan was used in removal of Cs+ in water. (Kazak & Tor, 2020) [25] used carbon materials prepared from red mud for Pb adsorbtion.

Conventional magnetic solid phase extraction: it was used in separation and pre-concentration of trace elements in sample solution (Xie *et al*., 2014) [68]. Lately, conventional MSPE was commonly used in trace element analysis in the drinking waters (Huang *et al*., 2010) [20], river/lake waters (Munonde *et al*., 2017) [40], industrial wastewater (Li *et al*., 2015) [31], tea waters (Leal *et al*., 2018), and urine blood samples. Wierucka, & Biziuk, (2014) [65] mentioned that MNPs have quick elution kinetics and large specific surface area which is advantageous in extraction methods. Peng *et al*., (2017) [47] utilized sulfur-magnetic carbon material for Hg^{2+} determination in environmental waters. Besides, Chen *et al*., (2019) [5] synthesized ZnFe2O4 carbon nano-tubes for analyzing earth elements in the environmental samples. Interestingly. Munonde *et al*., (2017) [40] used Fe3O4@MnO2,Al2O3@AAPTMS MNPs for Cr extraction from environmental waters. Li *et al*., (2011) [35] applied MNPs functionalized by mercapto group in analysis of trace metals.

Conclusion

In traditional methods, detecting biologocal sample elements can be achieved with excellent but these techniques are usually slow and require time consuming steps of sample preparation and laboratory conditions. Detection of these trace elements is of great concern. Many immunogenic protocols depend on the dispersability of nanomaterials to lessen assay time. Another use of nanomaterials was as a detection way in biological samples to attain lower limits of detection that couldn't be reached by traditional protocols. The multiplicity and diversity of nanomaterials and conjugate biochemistries promote sustained advance in bioagent detection accomodation in the laboratory, or in complex matrices.

References

1. Algar WR, Prasuhn DE, Stewart MH, Jennings TL, Blanco-Canosa JB, Dawson PE, *et al*. The controlled display of biomolecules on nanoparticles: a challenge suited to bioorthogonal chemistry. Bioconjugate chemistry. 2011 Sep 21;22(5):825-58.
2. Aljerf L. High-efficiency extraction of bromocresol purple dye and heavy metals as chromium from industrial effluent by adsorption onto a modified surface of zeolite: kinetics and equilibrium study. Journal of Environmental Management. 2018 Oct 15;225:120-32.
3. Alsuhybani M, Alshahrani A, Algamdi M, Al-Kahtani AA, Alqadami AA. Highly efficient removal of Pb (II) from aqueous systems using a new nanocomposite: Adsorption, isotherm, kinetic and mechanism studies. Journal of Molecular Liquids. 2020 Jan 1;301:112393.
4. Anbia M, Rahimi F. Adsorption of platinum (IV) from an aqueous solution with magnetic cellulose functionalized with thiol and amine as a nano-active adsorbent. Journal of Applied Polymer Science. 2017 Oct 15;134(39):45361.
5. Chen S, Yan J, Li J, Lu D. Magnetic ZnFe2O4 nanotubes for dispersive micro solid-phase extraction of trace rare earth elements prior to their determination by ICP-MS. Microchimica Acta. 2019 Apr 1;186(4):1-7.
6. Chowdhuri AR, Bhattacharya D, Sahu SK. Magnetic nanoscale metal organic frameworks for potential targeted anticancer drug delivery, imaging and as an MRI contrast agent. Dalton Transactions. 2016 Feb 21;45(7):2963-73.
7. Das M, Dhand C, Sumana G, Srivastava AK, Vijayan N, Nagarajan R, *et al*. Zirconia grafted carbon nanotubes based biosensor for M. Tuberculosis detection. Applied Physics Letters. 2011 Oct 3;99(14):143702.
8. Davudabadi Farahani M, Shemirani F. Supported hydrophobic ionic liquid on magnetic nanoparticles as a new sorbent for separation and preconcentration of lead and cadmium in milk and water samples. Microchimica Acta. 2012 Feb 1;179(3):219-26.
9. Fathia S, Kalantaryb RR, Rashidic A, Karbassid A. Synthesis and characterization of magnetic nano-porous graphene functionalized with carboxyl for hexavalent chromium adsorption in aqueous solution. Desalination and Water Treatment. 2017 Jul 20;82:241-51.
10. Gao Y, Xie X, Li F, Lu Y, Li T, Lian S, *et al*. A novel nanomissile targeting two biomarkers and accurately bombing CTCs with doxorubicin. Nanoscale. 2017 May 7;9(17):5624-40.
11. Ghasemi N, Ghasemi M, Moazeni S, Ghasemi P, Alharbi NS, Gupta VK, *et al*. Zn (II) removal by amino-functionalized magnetic nanoparticles: Kinetics, isotherm, and thermodynamic aspects of adsorption. Journal of industrial and engineering chemistry. 2018 Mar 25;62:302-10.
12. Guo X, Du B, Wei Q, Yang J, Hu L, Yan L, *et al*. Synthesis of amino functionalized magnetic graphenes composite material and its application to remove Cr (VI), Pb (II), Hg (II), Cd (II) and Ni (II) from contaminated water. Journal of hazardous materials. 2014 Sep 15;278:211-20.
13. Habila MA, ALOthman ZA, El-Toni AM, Labis JP, Soylak M. Synthesis and application of Fe3O4@ SiO2@ TiO2 for photocatalytic decomposition of organic matrix simultaneously with magnetic solid phase extraction of heavy metals prior to ICP-MS analysis. Talanta. 2016 Jul 15;154:539-47.
14. Hao H, Liu G, Wang Y, Shi B, Han K, Zhuang Y, *et al*. Simultaneous cationic Cu (II)–anionic Sb (III) removal by NH2-Fe3O4-NTA core-shell magnetic nanoparticle sorbents synthesized via a facile one-pot approach. Journal of hazardous materials. 2019 Dec 15;362:246-57.
15. Hashemi B, Zohrabi P, Shamsipur M. Recent developments and applications of different sorbents for SPE and SPME from biological samples. Talanta. 2018 Sep 1;187:337-47.
16. He M, Su S, Chen B, Hu B. Simultaneous speciation of inorganic selenium and tellurium in environmental water samples by polyaniline functionalized magnetic solid phase extraction coupled with ICP-MS detection. Talanta. 2020 Jul 1;207:120314.
17. Hong Y, Pu C, Zhao H, Sheng Q, Zhan Q, Lan M. Yolk–shell magnetic mesoporous TiO 2 microspheres with flowerlike NiO nanosheets for highly selective enrichment of phosphopeptides. Nanoscale. 2017 Nov 23;9(43):16764-72.
18. Hong Y, Yao Y, Zhao H, Sheng Q, Ye M, Yu C, *et al*. Dendritic mesoporous silica nanoparticles with abundant Ti4+ for phosphopeptide enrichment from cancer cells with 96% specificity. Analytical chemistry. 2018 Jun 19;90(12):7617-25.
19. Huang C, Xie W, Liu X, Zhang J, Xu H, Li X, *et al*. Highly sensitive method for speciation of inorganic selenium in environmental water by using mercapto-silica-Fe 3 O 4 nanoparticles and ICP-MS. Analytical Methods. 2012 Jan 7;4(11):3824-9.
20. Huang YF, Li Y, Jiang Y, Yan XP. Magnetic immobilization of amine- functionalized magnetite microspheres in a knotted reactor for on-line solid-phase extraction coupled with ICP-MS for speciation analysis of trace chromium. Journal of Analytical Atomic Spectrometry. 2010 Sep 1;25(9):1467-74.
21. Hühn J, Carrillo-Carrion C, Soliman MG, Pfeiffer C, Valdeperez D, Masood A, *et al*. Selected standard protocols for the synthesis, phase transfer, and characterization of inorganic colloidal nanoparticles. Chemistry of Materials. 2017 Jan 24;29(1):399-461.
22. Ismail MH. Glypican-3-Expressing Hepatocellular Carcinoma in a Non-Cirrhotic Patient with Nonalcoholic Steatohepatitis: Case Report and Literature Review. Gastroenterology Research. 2010;3(5):223.
23. Jin B, Xie L, Guo Y, Pang G. Multi-residue detection of pesticides in juice and fruit wine: A review of extraction and detection methods. Food research international. 2012;46(1):399-409.
24. Jolly P, Zhurauski P, Hammond JL, Miodek A, Liébana S, Bertok T, *et al*. Self-assembled gold nanoparticles for impedimetric and amperometric detection of a prostate cancer biomarker. Sensors and Actuators B: Chemical. 2017;251:637-643.
25. Kazak O, Tor A. In situ preparation of magnetic hydrochar by co-hydrothermal treatment of waste vinasse with red mud and its adsorption property for Pb (II) in aqueous solution. Journal of hazardous materials. 2020;393:122391.

26. Kim BH, Hackett MJ, Park J, Hyeon T. Synthesis, characterization, and application of ultrasmall nanoparticles. Chemistry of Materials. 2014;26(1):59-71.
27. Lai Y, Wang L, Liu Y, Yang G, Tang C, Deng Y, *et al*. Immunosensors based on nanomaterials for detection of tumor markers. Journal of Biomedical Nanotechnology. 2018;14(1):44-65.
28. Lara S, Perez-Potti A. Applications of nanomaterials for immunosensing. Biosensors. 2018;8(4):104.
29. Leal PM, Alonso EV, Guerrero ML, Cordero MS, Pavón JC, de Torres AG. Speciation analysis of inorganic arsenic by magnetic solid phase extraction on-line with inductively coupled mass spectrometry determination. Talanta. 2018;184:251-259.
30. Lee J, Brennan MB, Wilton R, Rowland CE, Rozhkova EA, Forrester S, *et al*. Fast, ratiometric FRET from quantum dot conjugated stabilized single chain variable fragments for quantitative botulinum neurotoxin sensing. Nano letters. 2015;15(10):7161-7167.
31. Li P, Chen YJ, Hu X, Lian HZ. Magnetic solid phase extraction for the determination of trace antimony species in water by inductively coupled plasma mass spectrometry. Talanta. 2015;134:292-297.
32. Li R, Deng H, Zhang X, Wang JJ, Awasthi MK, Wang Q, *et al*. High-efficiency removal of Pb (II) and humate by a CeO2–MoS2 hybrid magnetic biochar. Bioresource Technology. 2019;273:335-340.
33. Li W, Reátegui E, Park MH, Castleberry S, Deng JZ, Hsu B, *et al*. Biodegradable nano-films for capture and non-invasive release of circulating tumor cells. Biomaterials. 2015;65:93-102.
34. Li X, Yu M, Chen Z, Lin X, Wu Q. A sensor for detection of carcinoembryonic antigen based on the polyaniline-Au nanoparticles and gap-based interdigitated electrode. Sensors and Actuators B: Chemical. 2017;239:874-882.
35. Li Y, Huang YF, Jiang Y, Tian BL, Han F, Yan XP. Displacement solid-phase extraction on mercapto-functionalized magnetite microspheres for inductively coupled plasma mass spectrometric determination of trace noble metals. Analytica Chimica Acta. 2011;692(1-2):42-49.
36. Liu F, Jin Y, Liao H, Cai L, Tong M, Hou Y. Facile self-assembly synthesis of titanate/Fe3O4 nanocomposites for the efficient removal of Pb2+ from aqueous systems. Journal of Materials Chemistry A. 2013;1(3):805-813.
37. Liu Y, Ma H, Gao J, Wu D, Ren X, Yan T, *et al*. Ultrasensitive electrochemical immunosensor for SCCA detection based on ternary Pt/PdCu nanocube anchored on three-dimensional graphene framework for signal amplification. Biosensors and Bioelectronics. 2016;79:71-78.
38. Liu Z, Rong Q, Ma Z, Han H. One-step synthesis of redox-active polymer/AU nanocomposites for electrochemical immunoassay of multiplexed tumor markers. Biosensors and Bioelectronics. 2015;65:307-313.
39. Manos MJ, Kanatzidis MG. Metal sulfide ion exchangers: superior sorbents for the capture of toxic and nuclear waste-related metal ions. Chemical Science. 2016;7(8):4804-4824.
40. Munonde TS, Maxakato NW, Nomngongo PN. Preconcentration and speciation of chromium species using ICP-OES after ultrasound-assisted magnetic solid phase extraction with an amino-modified magnetic nanocomposite prepared from Fe_3O_4, MnO_2 and Al_2O_3. Microchimica Acta. 2017;184(4):1223-1232.
41. Munz M, Baeuerle PA, Gires O. The emerging role of EpCAM in cancer and stem cell signaling. Cancer Research. 2009;69(14):5627-5629.
42. Namieśnik J. Trace analysis—challenges and problems. Critical Reviews in Analytical Chemistry. 2002;32(4):271-300.
43. Niu Y, Yang T, Ma S, Peng F, Yi M, Wan M, *et al*. Label-free immunosensor based on hyperbranched polyester for specific detection of α-fetoprotein. Biosensors and Bioelectronics. 2017;92:1-7.
44. Nonkumwong J, Ananta S, Srisombat L. Effective removal of lead (II) from wastewater by amine-functionalized magnesium ferrite nanoparticles. RSC Advances. 2016;6(53):47382-47393.
45. Odio OF, Lartundo-Rojas L, Palacios EG, Martínez R, Reguera E. Synthesis of a novel poly-thiolated magnetic nano-platform for heavy metal adsorption. Role of thiol and carboxyl functions. Applied Surface Science. 2016;386:160-177.
46. Pelaz B, Alexiou C, Alvarez-Puebla RA, Alves F, Andrews AM, Ashraf S, *et al*. Diverse applications of nanomedicine. ACS Nano. 2017;11(3):2313-2381.
47. Peng C, He M, Chen B, Huang L, Hu B. Magnetic sulfur-doped porous carbon for preconcentration of trace mercury in environmental water prior to ICP-MS detection. Analyst. 2017;142(23):4570-4579.
48. Rowland CE, Brown III CW, Delehanty JB, Medintz IL. Nanomaterial-based sensors for the detection of biological threat agents. Materials Today. 2016;19(8):464-477.
49. Rüschoff J, Hanna W, Bilous M, Hofmann M, Osamura RY, Penault-Llorca F, *et al*. HER2 testing in gastric cancer: a practical approach. Modern Pathology. 2012;25(5):637-650.
50. Sattarahmady N, Tondro GH, Gholchin M, Heli H. Gold nanoparticles biosensor of Brucella spp. genomic DNA: Visual and spectrophotometric detections. Biochemical Engineering Journal. 2015;97:1-7.
51. Souza-Silva ÉA, Jiang R, Rodríguez-Lafuente A, Gionfriddo E, Pawliszyn J. A critical review of the state of the art of solid-phase microextraction of complex matrices I. Environmental analysis. TrAC Trends in Analytical Chemistry. 2015;71:224-235.
52. Soylak M, Erbas Z. Vortex-assisted magnetic solid phase extraction of Cd (II), Cu (II) and Pb (II) on the Nitroso–R salt impregnated magnetic Ambersorb 563 for their separation, preconcentration and determination by FAAS. International Journal of Environmental Analytical Chemistry. 2018;98(9):799-810.
53. Stott SL, Hsu CH, Tsukrov DI, Yu M, Miyamoto DT, Waltman BA, *et al*. Isolation of circulating tumor cells using a microvortex-generating herringbone-chip. Proceedings of the National Academy of Sciences. 2010;107(43):18392-18397.
54. Taleat Z, Cristea C, Marrazza G, Mazloum-Ardakani M, Săndulescu R. Electrochemical immunoassay based on aptamer–protein interaction and functionalized

polymer for cancer biomarker detection. Journal of Electroanalytical Chemistry. 2014;717:119-124.
55. Tu MC, Chen HY, Wang Y, Moochhala SM, Alagappan P, Liedberg B. Immunosensor based on carbon nanotube/manganese dioxide electrochemical tags. Analytica Chimica Acta. 2015;853:228-233.
56. Wang H, Li G, Zhang Y, Zhu M, Ma H, Du B, *et al*. Nanobody-based electrochemical immunoassay for ultrasensitive determination of apolipoprotein-A1 using silver nanoparticles loaded nanohydroxyapatite as label. Analytical Chemistry. 2015;87(22):11209-11214.
57. Wang K, Ma H, Pu S, Yan C, Wang M, Yu J, *et al*. Hybrid porous magnetic bentonite-chitosan beads for selective removal of radioactive cesium in water. Journal of Hazardous Materials. 2019;362:160-169.
58. Wang X, Peng R, He H, Yan X, Zhu S, Zhao H, *et al*. Nanomagnetic polyhedral oligomeric silsesquioxanes composite derived sulfur-containing adsorbents for effective elimination of hexavalent chromium and organic cationic dyes from water. Colloids and Surfaces A: Physicochemical and Engineering Aspects. 2018;550:1-8.
59. Wang X, Zhang B, Li J, Chang H, Wei W. A simple and fast chromogenic reaction based on Ag3PO4/Ag nanocomposite for tumor marker detection. Talanta. 2017;175:229-234.
60. Wang Y, Chen B, Wang B, He M, Hu B. Phosphoric acid functionalized magnetic sorbents for selective enrichment of TiO2 nanoparticles in surface water followed by inductively coupled plasma mass spectrometry detection. Science of The Total Environment. 2020;703:135464.
61. Wang Y, Wang Y, Pang X, Du B, Li H, Wu D, *et al*. Ultrasensitive sandwich-type electrochemical immunosensor based on dual signal amplification strategy using multifunctional graphene nanocomposites as labels for quantitative detection of tissue polypeptide antigen. Sensors and Actuators B: Chemical. 2015;214:124-131.
62. Wang Y, Zhou R, Wang C, Zhou G, Hua C, Cao Y, *et al*. Novel environmental-friendly nano-composite magnetic attapulgite functionalized by chitosan and EDTA for cadmium (II) removal. Journal of Alloys and Compounds. 2020;817:153286.
63. Wanna Y, Chindaduang A, Tumcharern G, Phromyothin D, Porntheerapat S, Nukeaw J, *et al*. Efficiency of SPIONs functionalized with polyethylene glycol bis (amine) for heavy metal removal. Journal of Magnetism and Magnetic Materials. 2016;414:32-37.
64. Wei W, Zhao B, He M, Chen B, Hu B. Iminodiacetic acid functionalized magnetic nanoparticles for speciation of Cr (iii) and Cr (vi) followed by graphite furnace atomic absorption spectrometry detection. RSC Advances. 2017;7(14):8504-8511.
65. Wierucka M, Biziuk M. Application of magnetic nanoparticles for magnetic solid-phase extraction in preparing biological, environmental and food samples. TrAC Trends in Analytical Chemistry. 2014;59:50-58.
66. Wu J, Zhu H, Liu G, Tan L, Hu X, Chen C, *et al*. Fabrication of core–shell CMNP@ PmPD nanocomposite for efficient As (V) adsorption and reduction. ACS Sustainable Chemistry & Engineering. 2017;5(5):4399-4407.
67. Wu YW, Zhang J, Liu JF, Chen L, Deng ZL, Han MX, *et al*. Fe_3O_4@ ZrO_2 nanoparticles magnetic solid phase extraction coupled with flame atomic absorption spectrometry for chromium (III) speciation in environmental and biological samples. Applied Surface Science. 2012;258(18):6772-6776.
68. Xie L, Jiang R, Zhu F, Liu H, Ouyang G. Application of functionalized magnetic nanoparticles in sample preparation. Analytical and Bioanalytical Chemistry. 2014;406(2):377-399.
69. Xu T, Ma J, Ma Z. Dual tumor markers assay based on surface charged graphene. New Journal of Chemistry. 2015;39(2):1006-1012.
70. Yang P, Liu Q, Liu J, Chen R, Li R, Bai X, *et al*. Highly efficient immobilization of uranium (VI) from aqueous solution by phosphonate-functionalized dendritic fibrous nanosilica (DFNS). Journal of Hazardous Materials. 2019;363:248-257.
71. Yang Z, Lan Q, Li J, Wu J, Tang Y, Hu X. Efficient streptavidin-functionalized nitrogen-doped graphene for the development of highly sensitive electrochemical immunosensor. Biosensors and Bioelectronics. 2017;89:312-318.
72. Yuan G, He J, Li Y, Xu W, Gao L, Yu C. A novel ultrasensitive electrochemical immunosensor based on carboxy-endcapped conductive polypyrrole for the detection of gypican-3 in human serum. Analytical Methods. 2015;7(5):1745-1750.
73. Zhang D, Wang L, Zeng H, Yan P, Nie J, Sharma VK, *et al*. A three-dimensional macroporous network structured chitosan/cellulose biocomposite sponge for rapid and selective removal of mercury (II) ions from aqueous solution. Chemical Engineering Journal. 2019;363:192-202.
74. Zhang X, Zhou D, Sheng S, Yang J, Chen X, Xie G, *et al*. Electrochemical immunoassay for the cancer marker LMP-1 (Epstein-Barr virus-derived latent membrane protein 1) using a glassy carbon electrode modified with Pd@ Pt nanoparticles and a nanocomposite consisting of graphene sheets and MWCNTs. Microchimica Acta. 2016;183(6):2055-2062.
75. Zhu S, Chen B, He M, Huang T, Hu B. Speciation of mercury in water and fish samples by HPLC-ICP-MS after magnetic solid phase extraction. Talanta. 2017;171:213-219.