Recent Progress in Screen-printed Electrochemical Sensors and Biosensors for the Detection of Estrogens

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Abstract: Estrogens have become increasingly prevalent in environmental samples across the world, posing a serious threat to human health. They have received considerable public attention due to their harmful effect on the normal endocrine functions of humans and animals. Over the last twenty years, electrochemical sensor and biosensors for monitoring of estrogenic endocrine disrupting chemicals (EDCs) have seen considerable improvement in performance. This review summarizes developments in screen-printed electrochemical sensor and biosensors published over the period 2000 to 2020. Emphasis is given to reports focused on the application of nanomaterials as modifiers for screen printed electrodes for electrochemical (bio) sensor development and outlook for the future development of sensors for monitoring estrogens in the environment.

Keywords: screen-printed electrodes; estrogens; synthetic receptors; molecularly imprinted polymers (MIPs); electrode modification; aptamers; environmental samples; Estrogenic endocrine disrupting chemicals (EEDCs); biosensors.

1. Introduction

The last two decades saw an increased awareness of the danger posed by the pollutants from various human activities. There is a growing body of literature that recognizes anthropogenic activities from agricultural, pharmaceuticals and other chemical-intensive industries substantially contribute to environmental pollution. A list of up to 1000 priority substances has been identified as emerging pollutants (EPs) that require close monitoring by world regulatory bodies [1]. Among these emerging pollutants are estrogenic endocrine disrupting chemicals (EEDCs) that effect the normal functioning of the endocrine system even at low concentrations [2]. The endocrine system consists of the hormone producing glands in the body that play a critical role in growth, metabolism and reproduction [3]. These estrogens include Estrone (E1), 17-β-estradiol (E2), estriol (E3) and 17-a-ethinylestradiol (EE2) and diethylstilbesterol (DES), which are part of the EU Watch List of emerging substances to be monitored (European Decision EU 2015/495) [4].

Analysis of these pollutants is usually undertaken using techniques such as liquid chromatography mass spectrometry (LC-MS), as well as biological assays and immunoassays [5] and electrochemiluminescence (ECL) [6], [7], [5]. However, these approaches suffer from the requirements of complex sample preparation, protracted assay time, expertise, and high cost; all of which hinder their potential application in routine environmental monitoring. Another challenge is the occurrence of these pollutants at very low concentrations in complex environmental matrices.

Analytical approaches generally require off-line pre-concentration and clean-up steps followed by chromatographic or electrophilic separation. The low limits of detection necessitate selective and sensitive detection systems and, for this reason, tandem mass spectrometry as well as LC-MS are commonly employed. There are presently no reported electroanalytical methods capable of measuring these compounds at both linearity values of 0.035 to 2.24 ng L^{-1} and limit of quantification (LOQ) levels of 0.035-0.1 ng L^{-1}

[4]. The development of miniaturized tools that will replace the routine analytical means of measuring estrogens is still a subject of investigation, despite the volume of literature published. The features of electrochemical sensors have the potential to deliver point-of-test measurement in a variety of real matrices, the result of which would transform the whole sector [8]. Electroanalytically, pharmaceuticals including estrogens were commonly measured using mercury-based electrodes, such as the dropping mercury electrode (DME) and the hanging mercury drop electrode (HMDE). These were replaced by graphitic and metallic macroelectrodes [9] and carbon paste electrodes [10], which then led to the current configuration of macroelectrodes constructed from ordered pyrolytic graphite, glassy carbon and boron-doped diamond electrodes with various modifications [11,12]. In designing any sensor, sensitivity and selectivity are the hallmark of any electroanalytical technique. In addition, miniaturization from screen-printing of electrodes is vital in the fabrication of (bio)chemical sensors [13]. This approach allows a cost-effective device to be produced in large volume and a customized sensitivity and selectivity for a particular application to be achieved [14].

These stringent requirements indicate the amount of work that is required to produce a sensor suitable for monitoring estrogens in surface water. Consequently, the research area is very active, with numerous publications [1,4,15–24]. Some of the earlier reviews like Jaffrezic-Renault *et al*. [25] described analysis of EDCs in various matrices using different techniques from conventional methods to electrochemical techniques. They highlight trends in the design of sensors, with many types of sensor materials and structures from nanomaterial-based, to aptamer-based and molecular imprinted polymers (MIPs) based sensors estrogens included [25].

Herein, we review the recent developments in the deployment of screen-printed electrodes (SPE) in the fabrication of electrochemical sensors and biosensors for both natural and synthetic estrogens namely estrone (E1), 17β-estradiol (E2), estriol (E3), and synthetic forms ethinylestradiol (EE2), diethylstilbesterol (DES) (Figure 1). This includes unmodified SPE, polymer film-

modified SPE, aptamer-modified SPE, enzyme-modified SPE and antibody-modified. The review describes recent works related to SPEs, including major highlights, current state of the art and key challenges yet to be overcome, as well as the future perspectives of SPEs. While these studies are highly valuable in demonstrating how far the research in this area has matured, there are no reviews dedicated to the use of screen-printed electrochemical sensors for estrogens. The reader is pointed towards reviews published on sensors and biosensor using other approaches for a holistic synopsis on the state of the art of estrogenic EDC detection [26–29].

1.1 Toxic effects of estrogens and their environmental recalcitrance

As knowledge has increased on the endocrine disrupting activities of estrogens in the environment, methods capable of monitoring low concentrations in environmental samples have become increasingly important. For example, EE2 that is widely used in contraceptive pills and hormone replacement therapy is resistance to degradation and hence, it accumulates in aquatic bodies [30]. These compounds therefore pose a threat to our food chain as they can be present in soil, water, and plants [30,31]. A well-documented aspect is the feminization of fish as they upset physiology and can affect reproductive development [31,32]. This is also the same for other aquatic and wild animals.

Toxic effects associated with these compounds are not fully understood, and as a result they are referred to as pollutants of emerging concern or contaminants of emerging concern that require monitoring [30]. The work of Celik et al. reported [33] the attachment of EDCs to the endocrine receptor in the tissues, causing problems in the endocrine, metabolism, and reproduction systems [33,34]. Other health issues, such as the hindrance of sulfotransferase enzyme by EDC was linked possibly to an increase in estradiol levels in humans [35]. Other studies reported the link between excess estrogens with metabolic disturbances [36], Parkinson disease [37], breast cancer [38] and risk of Alzheimer disease [39]. All these issues reinforce the requirement for platforms for monitoring of these pollutants [40].

1.2 Electrochemical Sensors

A chemical sensor is a self-contained device that provides real time analytical information (concentration of chemical species) about a test sample [41]. Chemical sensors consist of two major parts; one for recognition through the interaction with the analyte and a second for transduction, *i.e.* translating the interaction into readable signal [41]. The recognition or sensing element must be sensitive and specific to the analyte of interest. It is composed of distinct units, known as recognition receptors. Several strategies have been reported within each category of electrochemical sensor and biosensor utilizing various transducers and detection techniques. Electrochemical sensors are seen as the panacea for on-spot, *in situ* monitoring and point-of-care testing in the field of biomedical, pharmaceutical, and environmental application, removing pre-treatment and cleaning steps from routine analytical measurement [42].

1.2 Biosensors

An electrochemical biosensor is a self-contained integrated device, which is capable of providing specific quantitative or semi-quantitative analytical information using a biological recognition element (biochemical receptor) which is retained in direct spatial contact with an electrochemical transduction element [41]. A number of electrochemical techniques, from potentiometric, amperometric, conductometric, impedimetric to field effect, have been used for determination of various types of analyte [41]. The biosensors market is rapidly growing, specifically the blood glucose sensor, which recorded revenue of USD 12.8 billion in 2018 with projection of reaching USD 23.7 billion by 2022 [43]. This is an indicator of the viability of screen-printed electrodes (SPEs) in electrochemical devices. SPEs offer a direct means of measurement of various analytes such as using stripping voltammetry for heavy metals, lactate, glucose, *etc.* [14,44–47]. The ideal SPE-based chemical sensor should have the following properties: (i) inexpensive, (ii) portable, (iii) simple/easy-to-use device that can respond sensitively and instantly to a target chemical substance (analyte) with good selectivity in any medium. In addition, it must produce a quantifiable signal

output for that required analyte. Realizing such sensors is still ongoing to respond to the growing need to perform rapid in-situ analyses as an alternative to the traditional electrodes [48].

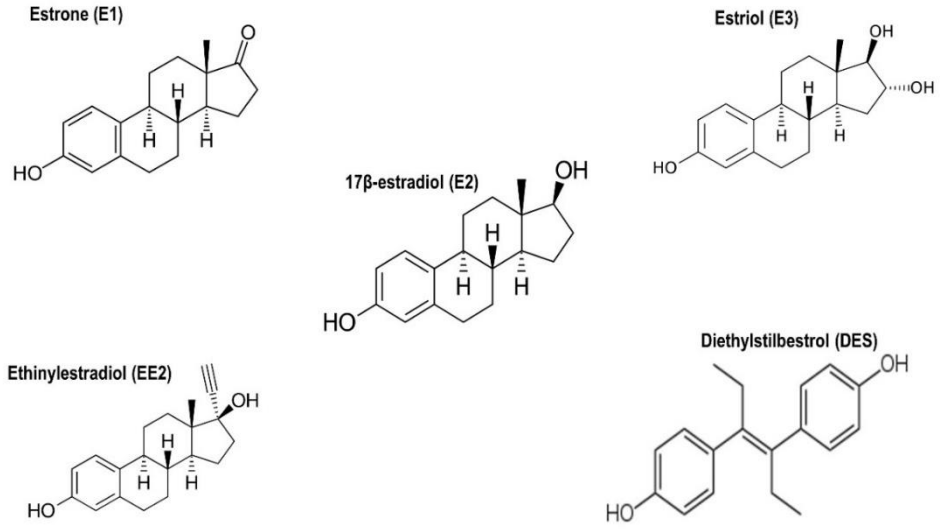


Figure 1. Structures of estrogens investigated in this review.

2. Design and fabrication Screen-printed electrode

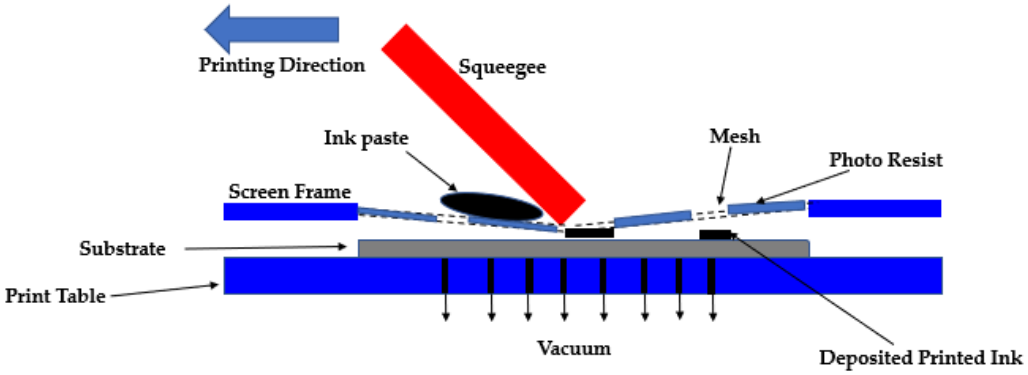
Screen printing techniques were seen as subset of thick-film technology that was believed to have originated in China during the Song dynasty [49,50] and have their traces in the construction of the Great Wall of China as well as in ancient Egyptian cloth. In recent times, the production of 'thick film' printed electronic circuits is performed by screen printing technology [51]. Screen printing technology was part of the "New frontier in the Renaissance of electroanalysis" [52]. In addition to screen-printing, printed sensors have been produced by other fabrication methods, such lithography and ink-jet printing. Recently, Honeychurch *et al.*[52] reported the application of three-dimensional (3-D) printing technology (rapid prototyping) as an alternative means of fabricating electrodes, using carbon nanofiber–graphite–polystyrene electrodes with a carbon pseudo-reference electrode [52]. Whilst the Rotogravure printing process has been used in the past by [54,55]. All these technologies are helping in revolutionizing the field

of low cost and mass-produced sensors as effective routes for environmental monitoring of emerging pollutants.

Since the 1990s, screen-printing technology, adapted from the microelectronics industry, has offered high-volume production of inexpensive, and yet highly reproducible and reliable sensors [56,57]. Screen-printing technology allows the production of various forms of SPEs to be used as transducers in electrochemical sensors [58–60]. This allows the printing of both working electrodes as well as counter and reference electrodes in different geometries, using inks modified with different catalysts, mediators, and other materials. The technique facilitates the fabrication of low-cost electrochemical sensors thus offering economic and practical benefits, as it is viable for the sensor to be disposable.

In general, screen-printing technique to produce SPEs involves forcing suitable ink formulations in form of paste through a patterned stencil or screened mesh of specific size and shaped onto a planer substrate [42]. The formulation paste contains graphite, carbon, gold, silver, or platinum, as well as binders, polymers, plasticizers and solvents, plus additives such as metals, metal oxides, enzymes, and ion exchange resins [61]. In the screen-printing process, ink is forced through the open regions of a mesh screen, using squeegee, to form the desired design on a substrate surface, (see Figure 2). The screen is then detached from the substrate, leaving the ink behind in the desired design. This process produces electrodes with a thickness, typically, between 10-20 μm. Subsequently, the printed electrodes are cured under various regimes, for example at approximately 60°C for between 30-60 min. Depending on the proposed application of the electrode, different types of meshes can be used to print the electrodes. Substrate materials usually are either ceramic or plastic-based [62]. The process is amendable to fabrication of large numbers of sensors on a single sheet. Additionally, the process can then be repeated, to produce large numbers of reproducible devices. An in-depth description of the screen-printing process is given by Fletcher (2016), in which the physical and chemical properties of screen-printing of a carbon electrode are discussed [63].

A



B

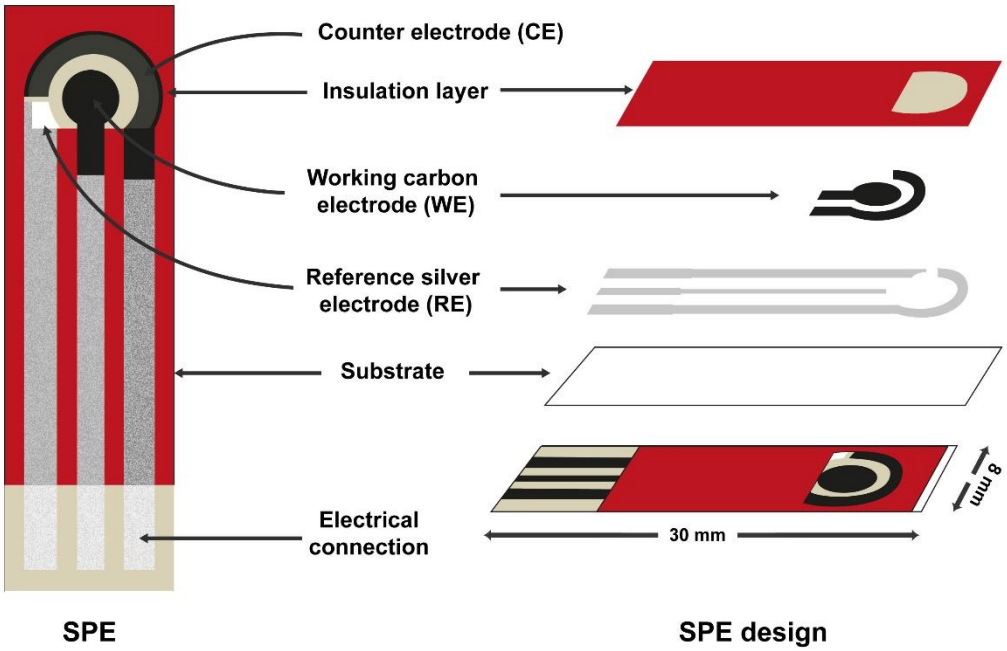


Figure 2. **A**. Representation of the screen-printing process for the fabrication of SPEs. **B**. Representation of a screen-printed electrode design.

Almost all types of carbon materials, such as carbon black (activated form inclusive), graphite nanotubes, graphene, fullerenes, and quantum dots have been screen-printed. Three important features of the screen-printed process make it an attractive fabrication technique: (1) the ability to control the electrode area, thickness, and composition. (2) Reproducible results can be obtained and statistically validated and (3) almost any materials, such as biologically compatible materials, *e.g.* carbon, metallic nanoparticles,

polymers, can be incorporated into the screen-printing process. A SPE consists of a solid support with two, three or more electrodes, *viz* a working electrode (WE), a pseudo reference electrode (RE) and a counter electrode (CE) [11,13], as shown in the representation in Figure 2.

Normally in an electrochemical measurement (electroanalytical), one or more of the following parameters – potential (E), current (i), charge (Q) and time (t) are measured. Within the field of electroanalysis, various methods such as voltammetric and amperometric are utilised for the sensing of a range of analytes by measuring the change in the oxidation state (oxidized or reduced) of the electroactive species (Faradaic current), which is directly proportional to the analyte's concentration [64].

Plotting different above parameters in several ways, forming the basis of the derived information. The versatility of SPEs allowed them to be used in electroanalytical systems employing techniques such as: (1) amperometry, in which changes in output current are measured [29,65], (2) voltammetric techniques, such as differential pulse voltammetry (DPV) [66,67], square wave voltammetry (SWV)[19,24,68], cyclic voltammetry (CV) and linear sweep voltammetry (LSV) [69–71], potentiometric [72] and (3) impedance spectroscopy [73]. Analytes of interest are oxidized or reduced at the surface of the WE based on their redox potentials [45,74]. These are techniques used to study the concentration of an analyte in a sample, giving an understanding of the electrochemical behaviour of the analyte under investigation through the generation of a readable signal [75,76], which is directly proportional to the concentration of the compound in the sample [77].

3. Applications of electrochemical sensing for analysis of estrogens

Estradiol is of great concern and is the target analyte in 80% of the publications devoted to the analysis of estrogens. This is a result of it being the most potent of all estrogens [78,79]. A recent work of Lu *et al.* [26] highlighted research from 2017 - 2019 which reported the use of biosensors for estrogen measurement in both food and the environment using various electrode

surfaces [26]. They concluded that, the application of nanomaterials to enhanced biosensor performance is common, with the use of various materials such as metal nanomaterials, metal oxide nanomaterials, carbon nanomaterials etc. Biosensors are mostly applied in the detection of estrogen in environmental water samples, but also infrequently in food samples, like honey or milk, which need further evaluation. Finally, there remains the need to move from the lab to the market in order to make the ideal estrogen sensor a reality [26]. Dong and co-workers [80] reported, a sensitive and low-cost alternative sensor to commonly applied methods for estradiol determination using Biochar nanoparticles obtained via pyrolysis of sugarcane bagasse (fibrous residue remaining after juice extraction). The particle size of biochar was shown to be important in the construction of the electrochemical sensor. Their study highlighted the use of numerous materials in the fabrication of electrochemical sensors for estradiol. It was shown that pyrolyzing bagasse at 800°C gave the optimum adsorptive biochar allowing for a limit of detection (LOD) of 11.0 nM to be obtained. The developed sensor showed good agreement with the results gained from the established HPLC based method [80]. The study by Ji *et al.* [81] utilised a composite of a metal-organic framework (MOFs) and 1,3,5-benzenetricarboxylic acid ligand as a sensor for estradiol. MOFs are crystalline porous material that composed of a three-dimensional (3D) network of metal ions held in place by multidentate organic molecules [81]. MOFs have been reported in the design of electrochemical sensors as an electroactive materials or signal labels [82]. Ji et al. [81] described the measurement of E2 and EE2 using the copper (II) benzene-1,3,5-tricarboxylate (Cu-BTC) framework as a reportedly rapid, simple and sensitive sensor, giving a LOD of 2.7 nM and 1.1nM for E2 and EE2 respectively. Recoveries of 97.27 – 102.9% were obtained for the practical application of these sensors for measurement of E2 and EE2 in water samples. An interesting aspect of this study is the comparison table given for E2, EE2 using other methods and materials [83]. Liu *et al.* [84] used a factorial design optimization technique for the design of the experimental factors required for the development of electrochemical sensors based on carbon nanotube -

Nafion modified glassy carbon electrode (GCE). The final step of the sensor design involved the electropolymerisation of Ni(Cyclam) to enhance the electrocatalytic properties of the sensor. Electrocatalytic detection of estradiol gave a reported linear range of 0.5 to 40 µM for E2 with an associated LOD of 60 nM [84]. The evaluation of three factors namely, amount of CNTs, thickness of Nafion layer, and the thickness of the Ni(cyclam) reveal that the amount of Nafion and surface coverage of Ni(cyclam), in addition to their interaction, result in a statistically significant optimum peak current for determination of estradiol [84]. Most studies reported an issue of a weak, ill-defined oxidation peak associated with E2. In the study of Luo et al. [85], the weak, ill-defined oxidation peak associated with E2 was overcome by combining poly (l-proline)-ordered mesoporous carbon materials to enhance the signal response. More specifically an ordered mesoporous carbon (OMC) and L-proline modified GCE was utilised for the fabrication of electrochemical sensor. The OMC - L-proline were electropolymerized by CV scanning in a solution containing 1 mg/ml of OMC and 10 mM proline in 0.1 M phosphate buffer, using 10 cycles over the potential scan range of -0.8 V to 2.4 V. CV, SWV, and electrochemical impedance spectroscopy (EIS) were used to characterize the developed sensor. Under the optimised conditions, the sensor exhibited a linear range of 1 x 10^{-8} to 2 x10^{-6} M with a LOD of 5 x 10^{-9} M for E2 [85].

Masikini *et al.* [86] developed an estradiol sensor via the combination of multiwalled carbon nanotubes and gold nanoparticles composite on a GCE [86]. The two materials improved the electrochemical activity of the sensor for E2 measurement relative to the bare GCE. This was due to increasing the speed of electron transfer and reduction of the requirement for a high input potential. Real water samples were investigated using the developed sensor and a linear range of 1 x 10^{-6} M to 20 x 10^{-6} M, LOD of 7.0 x 10^{-8} M was reported [86]. Moraes *et al.* [87] reported the use of reduced graphene oxide (RGO) as a modifier for electrochemical detection of estradiol in river water by DPV. This study combines RGO with metal porphyrins to a complex that can overcome the low current of estradiol oxidation to be sensitive enough to

deliver a portable sensitive, low cost sensor. The author compared the sensitivity of the electrochemical sensors with established HPLC method. RGO amplifies the oxidation signal to overcome the low oxidation current of estradiol on GCEs. Reduced graphene oxide (RGO) has been used with other materials such as quantum dots to enhanced oxidation of estradiol as reported by this author in one of their previous studies. A linear range of 0.1 - 10. µM estradiol with an associated LOD of 5.4 nM was reported in river water samples [87]. In another study, Ngundi *et al.* [88] reported a comparative mechanism for estradiol oxidation using a rotating disk electrode. The work described oxidation of estradiol, bisphenol A, and DES using CV using bulk electrolysis with controlled potential coulometry (CPC) [88]. Raymundo-Pereira *et al.* [174] reported the use of carbon black doped with silver nanoparticles for sensitive determination of estriol in creek water. This paper showed the possibility of the sensing platform application in real sample analysis. Carbon-based nanostructures are employed mostly to increase electron transfer, surface area and reduction in overpotential in electrochemical sensor design. The sensor exhibited a linear range of 0.2 - 0.3 µM with a LOD of 0.16 µM [174]. This is part of a series of work carried out on the measurement of estradiol anodically at a bare GCE. Salc *et al.* [89] offered an explanation on the electrooxidation redox behaviour of estradiol and the chemical and electrochemical parameters affecting it, including pH, supporting electrolyte and mechanism of the oxidation process. It serves a general guide to an understanding of estradiol oxidation in sulphuric acid (0.05 M) supporting electrolyte. Even though the linear range and sensitivity is not an improvement on the standard HPLC method, serum sample analysis was carried using tablets and Transdermal therapeutic system (TTS) strips. This showed the potential of the application of the sensor for estradiol analysis [89]. Sun *et al.* [90] reported using a Cu-BDC framework using 1,4-benzenedicarboxylic acid as a ligand with copper-based metal-organic frameworks (MOFs). The paper highlighted the need for an E2 sensor which is rapid, sensitive, and low-cost in order to compete with the presently employed techniques, which required both technical know-how as well as

well-equipped laboratories for their implementation. A linear range of 5 - 650 nM was reported with LOD of 3.8 nM. The water samples tests gave a recovery of 96.5 - 101% showing the practical application of the designed sensor. An interesting aspect of this study is the comparison table given for estradiol using other methods and materials [90].

4. Screen-printed electrochemical sensors

Different SPEs, modified with various materials, such as enzymes and nanomaterials have been characterized, and compared for use as sensing platforms for environmental applications. Common challenges include the near identical electrochemical behaviour of different analytes on SPE surfaces due to the various composition of the ink used in fabrication of the SPE. A number of studies have already been reported for commercial ink supplied by various companies [61,91] with each of the electrodes giving a different response to various analytes. This is due to different composition and printing techniques, together with the curing process protocols. Active surface area and roughness factors are contributors to the performance of SPEs. Calculating the surface area has been somewhat difficult due to non-uniform material composition and printing processes. Redox systems [92] used include both inner and outer sphere redox probes, such as potassium ferricyanide (III), ascorbic acid (AA) and NADH. The results of this experiment [61] revealed the nature of each SPE response in all the redox systems is linked to the amount of graphite in the ink composition, functionalization of the surface, the curing process, the binder and the wettability of the surface. Honeychurch *et al*, looked at redox characteristics of lead (Pb) at modified screen-printed carbon electrodes (SPCEs) [93]. The roughness contributes to the possible edge plane sites available. The higher the roughness, the more edge plane sites which eventually leads to better performance for reversibility [61]. This is a subject of debate as other researchers hold different views on this [94–97]. There is yet to be a clear prevailing view on this, but we tend to support the view Kadara *et al.* [61] based on the current study currently being undertaken in our laboratory. Screen printed electrodes

have been modified using various materials to make them selective by adapting the sensing element to respond specifically to the analytes of interest. Nanomaterials, coated with relevant biological receptors have not only been used to increase the sensitivity but also the selectivity of various sensor designs to overcome this key sensing challenge, as can been seen in sections 4 and 5 [98].

In addition to biological receptors, synthetic receptors called molecularly imprinted polymers (Section 5.4) have been reported to impart selectivity to screen printed electrodes. Peveler et al. [98] highlighted the advantages and disadvantages in respect of selectivity and specificity in sensing approaches in the two domains for specific sensing and selective sensing [98].

4.1 Electrochemically pretreated Screen-printed electrode

Electrochemically pre-treated Screen-printed electrode have been put forward to increase their sensitivity towards numerous analytes. Pre-treatment of the SPE can be perform electrochemically or using other means such as soaking in various solutions that will dissolve the binder and solvent that remains on the surface after the final product of the screen-printing process. Electron transfer as well as charge resistance transfer are commonly compared between pre-treated and untreated SPCE using both inner and outer sphere redox systems. These pre-treatment methods are aim at conditioning the electrode surface in order to promotes fast reaction kinetics (both electron and proton transfer) [99] - thus, the name activated or pre-treated electrode. Edge plane activity was found to influence the electrocatalytic activity of pre-treated screen-printed electrodes when compared with untreated ones. Several methods reported suggested that the edge plane and basal plane of treated SPE behave differently with the former showing better activity towards biological compounds [99].

Little information on the estrogens behaviour at pre-treated SPE has been reported [100]. Raymundo-Pereira *et al.* [58], demonstrated the simple electrochemical pre-treatment of SPCEs using cyclic voltammetry in a

potential range -2.5 and 2.5 V at 100 mVs in 0.5 M H_2SO_4 (two scans) for sensor in determination of emerging pollutants; of estradiol (E2), hydroquinone (HQ) and paracetamol (PARA) simultaneously determination in tap water, with detection limits of 185, 218 and 888 nM, respectively, within a linear range between 0.5 and 10.0 µM. The result of this study was compared with HPLC showing the validity of the pre-treated sensor as an economic, rapid, and sensitive method for environmental protection [58].

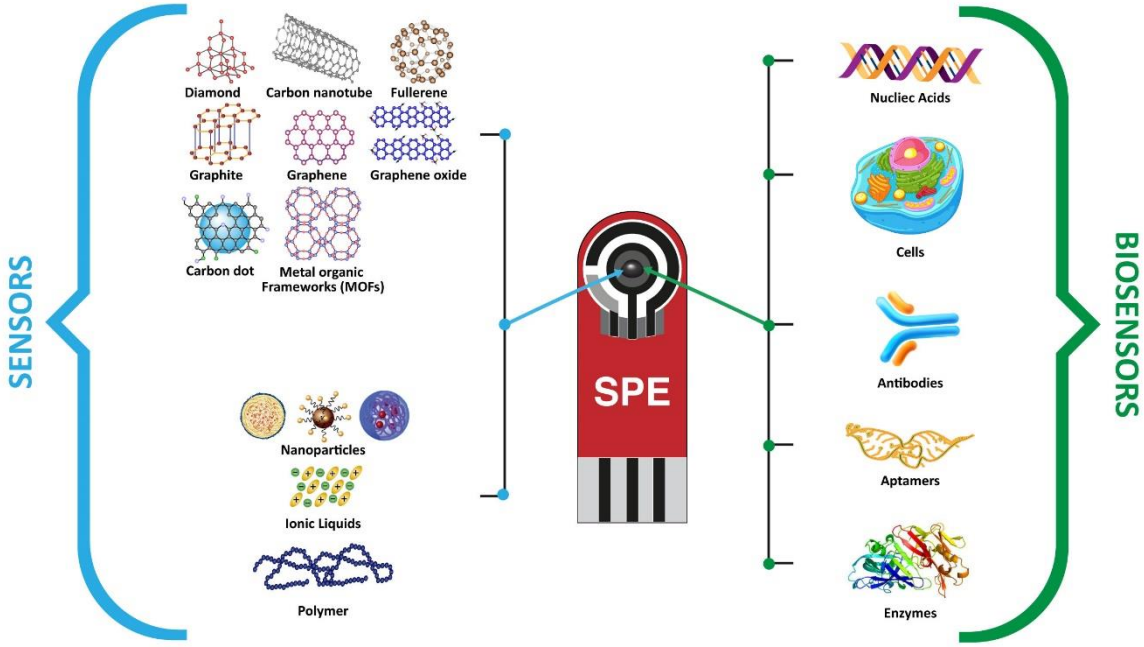


Figure 3. Schematic representation of some the various materials employed for modification of SPEs

4.2 Carbon-based Screen-printed electrode

Carbon-based nanomaterials have been incorporated in to the working electrode design in various sensor platforms [101]. For bioelectrochemical platforms, Sanati *et al.* [102] reviewed modification of screen-printed electrodes with the carbonaceous material in the field in electrochemical biosensing, such as graphene and its derivatives, carbon nanotubes, mesoporous carbon, carbon nanofibers and carbon nanospheres [102].

Cesarino *et al.* [103] applied tristimulus analysis to measure two estrogens based on differential pulse voltammetry measurement in order to overcome

the lack of specificity of the sensor to a single chemical species. Carbon nanostructures, namely graphene oxide, reduced graphene oxide, and reduced graphene oxide doped with antimony nanoparticles were utilized for E2 and E3 detection in water [103]. Mazzaracchio *et al.* [104] investigated the use of various types of carbon nanomaterials as modifiers for improving the performance of SPEs. The work also explored various forms of carbon black as a cheap modifier for this purpose. A notable increase in anlytical performance compared with unmodified bare electrode was reported. The authors reported improvements, such as lower applied potential, greater peak-to-peak separation and increased peak signal intensity. This resulted from enhance material properties including high electron transfer as the dimensions, onion like carbon structure, and availability of high numbers of defect sites [104].

A rapid, efficient and sensitive sensor based on adsorptive stripping voltammetry (AdSV) was reported for the determination of E2 and EE2 in pharmaceutical formulations and urine samples. A comparative study on the realtive sensitivity between HMDE, SPE, and screen-printed carbon nanotube electrodes was undertaken for the oxidation of each of the analytes. The major parameters in AdSV are the adsorption potential, time and pH. LODs of 0.3 µg/L (E2) and 9.7 µg/L (EE2) for HMDE were obtained, while values of 242 and 182 µg/L were measured using SPE [78].

Wong *et al.* [105] developed an E2 electrochemical sensor using SPE modified with copper phthalocyanine (CuPc), Printex 6L carbon and Nafion film. The author compared the various SPEs (SPE, SPE_F, CuPc-P6LC-Nafion/SPE_F) before and after modification with the various materials with linear range of 8 x 10^{-8} M to 7.3 x 10^{-6} M and LOD of 5 x 10^{-9} M. The electrochemical oxidation of E2 was evaluated using cyclic voltammetry. A single oxidation peak was observed for the anodic potential scanning, at a potential of 0.39 V. After optimizing experimental conditions, a more sensitive DPV technique was used to evaluate the sensor at linear concentration range between 8.0×10^{-8} to 7.3×10^{-6} M, and detection limit of 5.0×10^{-9} M was obtained. Synthetic urine samples analysis revealed the application of the

sensor in different matrices [105]. Mesoporous carbon and graphene are among the materials employed for electrochemical sensor development by [105]. This study reports the combination of the two materials for determination of E1, E2, and E3. The sensor was fabricated by the deposition of each material at 0.1 mg/ml in phosphate buffer (pH 7). Factors such as the influence of pH, electrodeposition cycles, and accumulation time were optimized in designing the sensor. Square wave voltammetry was utilized as the method for the determination of estradiol practically in human serum. A linear range of 5.0 x 10^{-9} M - 2 x 10^{-6} M and LOD of 2 x 10^{-9} M were obtained [106].

4.3 Graphene-based Screen-printed electrodes

Features such a large surface area and high electrical conductivity are among the attributes of graphene that make it an excellent electrode modifier for promotion of fast electron transfer between a target analyte and the electrode. Karuwan *et al.* [107] reported the addition of graphene into the ink formulation in screen printing process [107]. In another study, [108] a SPCE was modified using multi-walled carbon nanotubes (MWCNT) and graphene (GP) [108]. A dedicated review based on the application of graphene -carbon nanotubes modified electrochemical sensors can be found elsewhere [109]. Cinti *et al.* [110] provides an overview on modification of SPEs using the graphene based materials [110].

Barton *et al.* [111] demonstrated the analysis of E1, E2 and EE2 using graphene screen printed electrode (G-SPE). The PANI/Graphene-SPE-devices displayed linear responses to estrogenic substances, in EIS assays, over a concentration range of 0.0975 ng/L to 200 ng/L in water samples. Detection limits of 0.043 pg/L for E1, 0.19 ng/L for E2 and 0.070 pg/L for EE2 were obtained. which is lower than other current technique such as commercial ELISA [111].

4.4 Carbon nanotubes (CNTs)-based Screen-printed electrode

Carbon nanotube (CNT) is a well reported electrode modifier that increases the electrocatalytic activity of a number of analytes in sensing design [112]. Ochiai and co-workers used a combination of microflow device and a SPE modified with CNT for measurement of estriol to produce a device that combines low sample use and fast amperometric determination estriol [113]. A linear response was observed for a concentration range of 1.0 to 1000 µM with LOD and LOQ of 0.53 µM and 1.77 µM respectively. The proposed methodology was applied for determination of estriol in commercial samples and results were compared with those provided by spectrophotometric methodology. The obtained results agreed at a 95 % of confidence level [112].

Wang *et al.* [79] reports a novel disposable electrochemical doped with MWCNTs/Al_2O_3/poly-L-lysine film for measurement of 17β-estradiol in clinical samples. Under optimized conditions, the sensor was able to detect estradiol with a linear range of 0.5 nM to 50 nM and low detection limit of 0.014 nM [79]. One interesting aspect of this work is that, the author reports the use of cyclic voltammetry for this sensitive sensor. This requires a look into contributions by changes in the double layer capacitance as CV does not have background correction ability for changes in the capacitive layer [114]. Gan *et al.* [115] employed multiwalled carbon nanotubes for the enhancement of oxidation signal 17a-ethynylestradiol determination. The screen-printed modified electrodes were able to achieve high sensitivity under optimized conditions [115]. Hao and co-workers produced a layer-by-layer assembly of Polyethyleneimine (PEI), Polyacrylic acid (PAA) and f-MWCNT with graphite clay, together with pencil graphite electrode. The sensor has a LOD of 1 x10^{-8} M [116].

4.5 Miscellaneous materials-modified Screen-printed electrode

Pradela-Filho *et al.* [117], investigates the suitability of incorporating glass varnish (an alkyd resin) into carbon conductive inks for disposable electrochemical SPE sensors. The SPE sensors were used to measure a range

of analytes including estriol in the range 0.1 - 8.0 µM, with LOD 0.08 µM. The new material has the potential as an inexpensive material in the design of disposable SPE to enhanced analytical performance. This is due to the efficient dispersion of the graphite particles with functional groups of the glass varnish (alkyl resin) as a promising binder leading to high electrical conductivity and excellent adhesion without aggregation [117].

Moreira *et al.* [19] reports the application of a carbon paste electrode modified with magnetite nanoparticles and the ionic liquid, 1-butyl-3-methylimidazolium hexafluorophosphate in the electroanalytical determination of E2 and E3. Typical to the irreversible nature of 17β-estradiol and estriol, peaks at +0.320 V and +0.400 V were observed, which was triple the values of the unmodified SPE. Optimization of the measurement parameters i.e. scan increment, amplitude, and frequency, was carried out using Box-Behnken factorial design for each estrogen. For 17β-estradiol, the calibration plot was linear from 0.10 to 1.0 µM, with a detection limit of 50.0 nM, while for estriol the range was 1.0 to 10.0 µM, with a detection limit of 300.0 nM. Statistical comparison was made between these results and those obtained using Ultraviolet–visible (UV/VIS) spectrometry with no significant difference, hence demonstrating the quality of the modified sensors [19].

5. Screen-printed biosensors for estrogens

Electrochemical biosensors are a subclass of electrochemical sensors, which provide analytical information using a biological recognition element (biochemical or biological mechanisms) of the analyte. Electrochemical biosensors are already being deployed in diagnostic, agri-food and environmental applications [118]. Application of biosensors in detecting estrogenic EDCs has seen a large increase in interest. A review presented by Lu *et al.* [26] gives an update on the recent progress (2017-2019) with respect to biosensors for monitoring of estrogens in the environment and in food. The review covers all biosensor transduction methods, not only electrochemical sensors and makes a brief reference to SPEs [26]. Jaiswal *et al.* [119] reviewed the recent advancements in the biosensor technology based on carbon

nanomaterial-modified SPEs [119], but only briefly mentions estrogen detection. Generally, when designing an electrochemical sensor or biosensor, limit of detection (LOD) and time of analysis, in addition to sensitivity and selectivity are vital. A trade-off is required for signal improvement and time taking for the measurement to be taken. As such careful consideration of the application in mind is needed when deciding to either use an electrochemical sensor or a biosensor. In addition to portability, cost, and ease of operation (with or without sample preparation). Table 1 presents a range of reported approaches for the detection of estrogens employing screen-printed electrochemical sensor and screen-printed biosensors. The table provides the sensor and biosensors for estrogens analysis and the various modifying materials used in the design, with sensitivity evidently at the heart of improving the performance of the sensors.

5.1 Enzyme-modified Screen-printed electrode

Enzymatic biosensors are well developed group of sensors that have been applied in health, environmental and food analysis applications [120]. Thanks to the adoption of recombinant DNA technology that allows their production [121]. This is applied in enhancing the SPE development as simple and effective technique for electrochemical enzyme-based biosensors [122,123]. Aromatase enzyme have been applied in biosensing of various analyses from the first work by [124]. Laccase has also been exploited for the estrogen estradiol detection [125,126]. Using SPE as transducer, Kuzikov group [127] described the electrocatalytic activity of CYP19A1 (aromatase) on screen-printed electrodes modified by didodecyldimethylammonium bromide (DDAB). The reaction pathways of CYP19A1 produce products (estrone and estradiol) of the induced CYP19A1 reactions was determined by direct electrochemical oxidation on the electrode. Sensitivity values obtained were 0.1 A/M for estrone and 0.12 A/M estradiol respectively. Limits of detection were calculated to be 11 nM and 3.4 nM for estrone and estradiol [127].

5.2 Antibody-modified Screen-printed electrode

Immunosensors are one of the most reported type of biosensors that use antigens or antibodies that are specific to a target. A transducer measures the binding of a complementary target with the bioreceptor in sample under investigation both as labelled and Label-free assays, as shown in Figure 4 [128]. This antibody/antigen binding interaction is specific and selective. This interaction can be determined by electrochemical, optical, and mass techniques. Immunoassay kits are available for a number of pollutants in the environment [129]. Combining screen-printing production methods and immunoassay allows the low cost, high volume production required for environmental analysis to be achieved.

In 2005, one of the first studies to investigate the possibility of the integration immunoassay with an electrochemical method for rapid analysis of E2 was described by Pemberton *et al.* [129]. For an E2 concentration range of 25–500 pg/mL a LOD of 50 pg/mL was recorded [130].

Kanso *et al.* [24] describe an immunosensors using magnetic beads attached to a carboxylic or amine functionalized estrogen derivative on SPEs for sensitive detection of E2 and EE2. SWV was used as the electrochemical technique for quantification. The electrochemical immunosensors showed a highly sensitive response to E2 and EE2, with respective detection limits of 1.0 and 10 ng/L, in addition to offering an easy, and rapid assay protocol; an assay time of 120 minutes compared to 280 minutes for conventional immunoassays [24]. Scala-Benuzzi *et al.* [130] reported a paper-based immunocapture assay (EPIA) for ethinyl estradiol (EE2) determination in water samples. The sensor combined paper microzones on a SPE, which had been modified with electrochemically reduced graphene (RG). LOD and linear range values of 0.1 ng L^{-1} and 0.5-120 ng L^{-1}, respectively were obtained [131]. Disposable immunosensors based on SPEs, as a direct enzyme-linked immunosorbent assay (ELISA) for estradiol detection in bovine serum, used a polyclonal antibody to compete with 17β-estradiol–alkaline phosphatase

conjugate (17β-E2–AP) [132]. The prototype sensors recorded a LOD below the Action Limit of 40 pgmL^{-1} for estradiol, as described by EU criteria (2002/657/EC) for qualitative and quantitative screening methods.

Ma *et al.* [133] employed a multiplexed immunoassay method for determination of DES and E2 based on disposable SPCE. The immunosensor has different antibodies attached on the SPE with Platinum nanoparticle functionalized mesoporous silica nanoparticles (Pt@SBA-15) Pt@SBA-15 as the label for the secondary antibodies. Platinum catalytic properties and Mesoporous silica (SBA-15) allowed a strong signal towards the analytical antigens. The sensor response to DES and E2 showed wide linear ranges with detection limits of 0.28 and 1.2 pg/mL respectively [133]. Liu *et al*. [78] reported an immunosensor the determination of E2 and EE2 in pharmaceutical drug formulations and urine samples. The work serves as comparison of different types of electrode, namely HMDE, SPE and screen-printed carbon nanotube electrodes (SPCNTE). The LODs were 0.3 µg/L for E2, 14.8 µg/L for EE2 at −0.23 V, and 9.7 µg L^{-1} for EE2 for HMDE, at −1.20 V. Whilst the LOD was 242 µg/L for E2, 277, 182, and 191 µg L^{-1} for SPE and SPCNTE at 0.30, 0.31, 0.32, and 0.33 V potentials [78]. These results supported the claim of Barek et al. [134], that mercury-based electrodes "are probably the best sensors for the determination or trace amounts of electrochemically reducible organic compounds"[134].

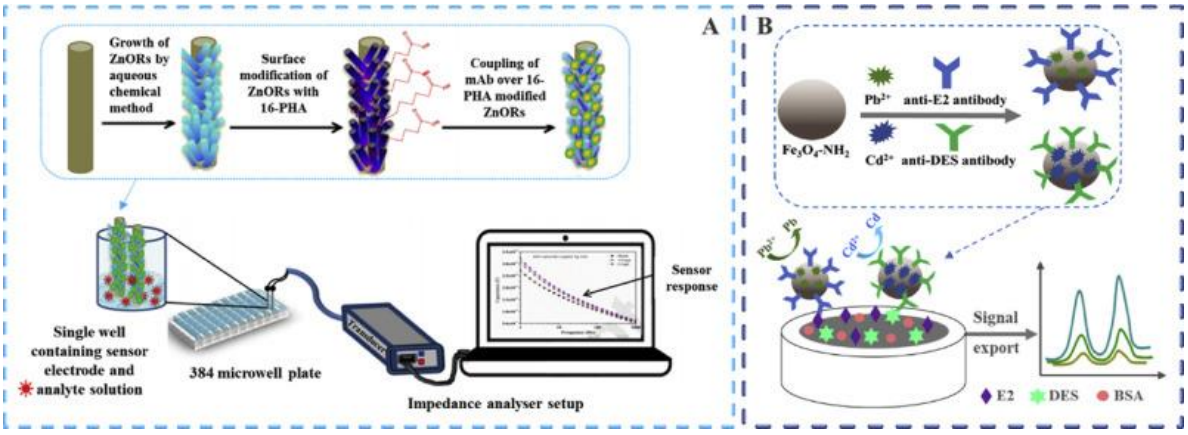


Figure 4. Schematic diagram of electrochemical immunosensors. A. Label-free immunosensor based on ZnONRs modified silver wire electrode [10]. B. Immunosensor based on Fe_3O_4–NH_2–Cd^{2+} and Fe_3O_4–NH_2–Pb^{2+} labeled antibodies (Reproduced with permission from elsevier ref. [26]. Copyright 2021 elsevier.).

An immunosensor for estradiol was reported via the -based formation biotin-streptavidin linkage using *p*-aminobenzoic acid modified screen-printed carbon electrode [135]. Covalently bound streptavidin serves as the bridge for the biotinylated anti-estradiol. Analysis was carried out by a competitive immunoassay with peroxidase-labelled estradiol (HRP–estradiol) using amperometry at -0.2V with hydroquinone (HQ) as redox mediator. The calibration curve exhibited a linear range between 1 - 250 pg/mL and LOD of 0.77 pg/mL. The fabricated immunosensor were tested in both serum and urine samples with good results [135]. Mistry *et al.* [77] provides a useful review of amperometric detection technique for immunosensors based on SPEs, specifically explaining the principle behind the measurement means and the design of the sensors and modification, explaining both the strength and weakness. However, estrogen detection is not covered [77].

5.3 Aptamer based- Screen-printed electrode

Aptamers are an alternative bio-recognition element, synthesized chemically with the target, giving them an advantage over other biological recognition element/materials, such as antibodies, peptides, and enzymes, due to their high stability and exceptional affinity to wide variety of targets. For biorecognition elements, such as antibodies, a short shelf-life, issues with stability and nonspecific analytical response in electrochemical biosensors are some of the reasons for the use of aptamer as a substitute [43]. Discovered almost around the same time by three separate independent research groups, this paved the way to the active engagement in nucleic acid research we are witnessing now [136,137]. Aptamers are single strand DNA/RNA produced by in vitro selection process known as "Systematic

evolution of ligands by exponential enrichment" (SELEX) (shown in Figure 5). The consist of 20 to 120 nucleotides compose of a nitrogenous base, a five-carbon sugar (ribose or deoxyribose), and phosphate group [138]. Systematic evolution of ligands by Exponential Enrichments allows for the generation of aptamers that bind with high affinity and specificity to the compound. The process starts with the generation of a large oligonucleotide library consisting of randomly generated sequences of specific length with constant sequence at position 5' and 3' ends that serve as primers as shown in Figure 5. Nezami *et al.* [28] provides an overview of the applications of aptamer-based biosensors, as well as bioaffinity sensors, in analysis and monitoring of estradiol [28]. Gatel *et al.* [139] published a detailed report on the use of nucleic acid in sensor technology for detection of EDC in the environment [139].

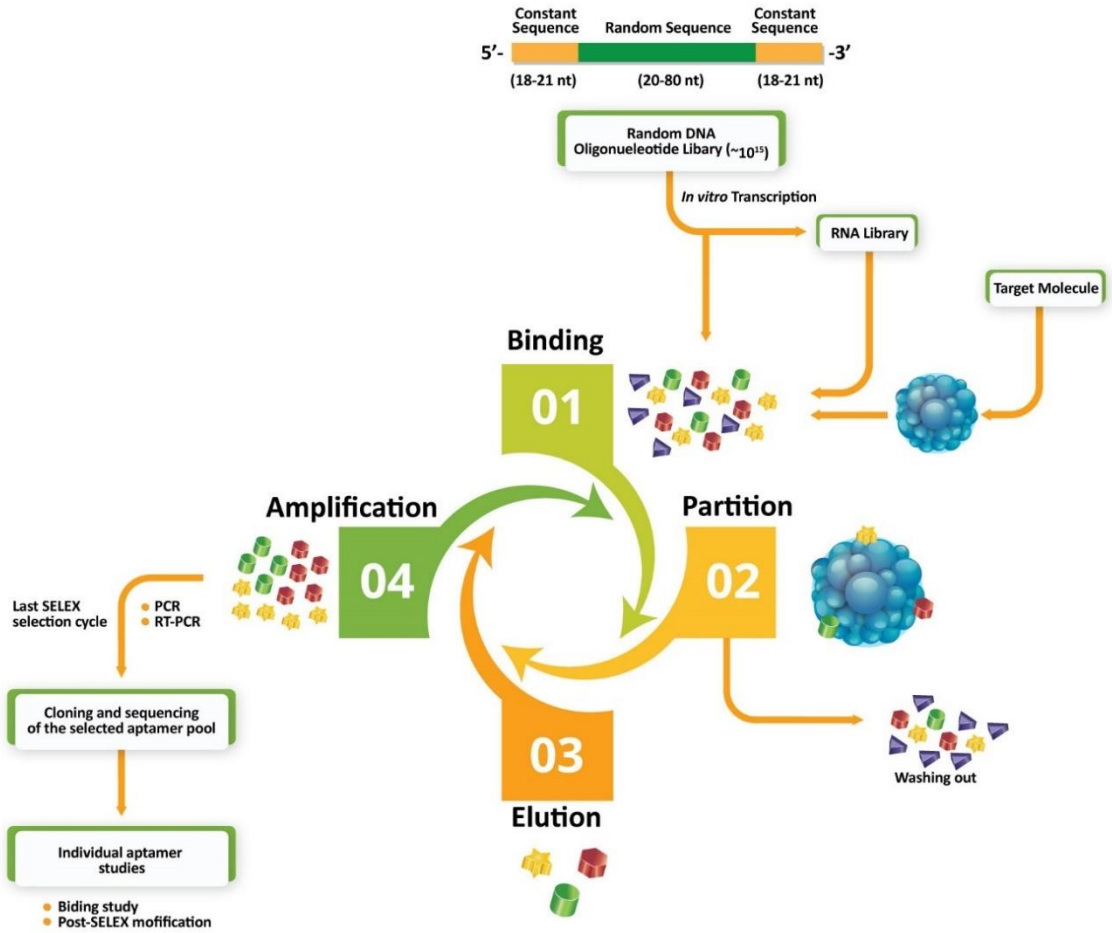


Figure 5. Schematic of the Systematic evolution of ligands by Exponential Enrichments (SELEX) process.

Kim and his group reported the first aptamer (a 76-mer and 23 kDa sequence) for 17β-estradiol produced by SELEX process [140]. From 2007, the sequence has been studied extensively with a series of modifications [6,141–146] on various electrode surfaces and using various transduction techniques. Zaid *et al.* [146] utilised the same sequence aminated at the 5'-end with –NH2 to develop an electrochemical aptasensor on screen-printed electrode (SPCE) modified by electrodeposition of carbon nanodots as an immobilization platform probe for the detection of estradiol (E2). The E2 aptamer-based biosensors was tested in various concentrations of E2 with linear range of 1.0×10^{-7} to 1.0×10^{-12} M and a detection limit of 5.0×10^{-13} M. Furthermore, it was used to measure real river water samples and the selectivity of the fabricated sensor was tested against bisphenol A (BPA), estriol (E3) and progesterone (P4) with good selectivity toward E2 and excellent discrimination respectively. E2 spiked water samples gave recoveries from 98.2% - 103.8%, relative standard deviations (RSD) of 1.1% - 3.8%, revealing the feasibility of the application of the aptasensor for E2 measurement in water samples [147]. Immobilization of aptamers on gold substrates for various sequence modification such as thiol-Au bond, EDC/NHS attachments is shown below (Figure 6). These are some of the ways of combing aptamer on transducer surfaces with other emerging strategies even in the absence of secondary aptamer [148]. No aptamer development has been reported for estrogens E1, E3 and EE2 as yet due to limitation of molecular diversities of libraries [149,150].

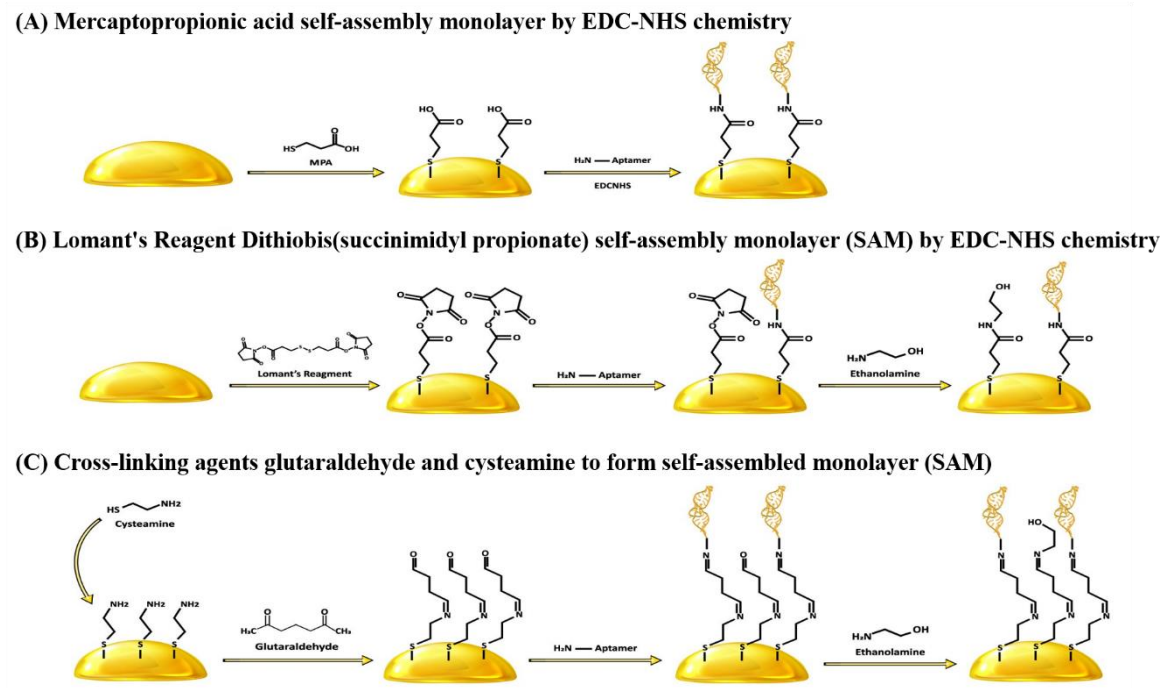


Figure 6. Schematic illustration of aptamer Immobilization strategies on gold electrode.

5.4 MIP-modified Screen-printed electrode

Synthetic receptors have been explored as a replacement for biological receptors [138]. The main drive for this include reduce costs, increase sensor shelf-life and to eliminate issues of denaturation, making the sensors more suitable for measurement in complex environmental matrices [151–153].

Molecularly imprinted polymers (MIPs) are among the most promising alternatives to natural receptors being presently investigated [154]. Molecular imprinting is a technique for creating binding sites within a polymer network having the same shape, size and functional groups as the target (template). Molecular imprinting technology (MIT) was first reported by Polyakov more 80 years ago, but its applications remains in immunoassays, affinity separation, and sensors makes it relevant to date [155]. In MIPs synthesis, a template (target analyte), monomer, initiator and cross-linker undergoes polymerization to form a polymer complex between the target molecule and functional monomers in a solvent. Template removal after polymerization leaves a vacant site in the porogen that is utilized for

(mimicking) molecular recognition ability of natural receptor within the polymer network [156,157] making it selective to the template (analyte of interest).

Polymerization can be perform by bulk imprinting or surface imprinting depending on the nature of the analyte [152,156,158–161]. Improved backside-surface imprinting, has also been utilised [162]. Back-side surface imprinting approach allows the polymerization mixture to form uniform binding site without aggregation of the template within the whole polymer matrix. This is achieved by the contact with the outer surface hence the ability to exit the imprinted matrix, thus generating surfaces with a high density of rebinding sites [162]

The combination of MIP and electrochemistry to produce "Molecularly imprinted electrochemical sensors (MIECS)" has shown improvement of sensor capabilities [158], using different analytical methods, such as amperometry, potentiometry, conductometry and voltammetry. Figure 7, Indicates the various analytical methods reported on molecularly imprinted electrochemical sensors (MIECS). It allows both direct and indirect methods of redox probe use as the basis of the detection. Beluomini *et al.* [163], reviewed the application of molecularly imprinted polymers on nanostructured carbon materials. Carbon-based materials with MIECS are compatible with number of materials such as carbon nanotubes, graphene *etc*., increasing sensitivity, selectivity and stability due to the combination of properties of the two materials instead of standalone material [163]. Lahcen and co-workers [164] developed a MIP-sensor based (Fe_3O_4-MIP) using aniline and dimethacrylate (EGDMA) as the monomer, for the detection estradiol. Fe_3O_4 nanoparticles were utilized as aprt of the prepolymerization mixture for signal amplification due to high surface area. Cyclic voltammetry and electrochemical impedance spectroscopy (EIS) were employed to probe the fabricated sensor. Parameters such pH, incubation time *etc.* were optimized. The MIP based sensor increased the oxidation current, as shown using square wave voltammetric measurements, delivering a linear range of 0.05–10.0 μM and a LOD of 20 nM [164].

A molecularly imprinted polymeric microspheres MWCNT–gold nanoparticles (AuNPs) modified SPE for the rapid detection of E2 hormone in serum samples has been developed by Futra *et al.* [165]. Both MWCNT and AuNPs aid the accelaration of electron transfer while the microspheres were designed to bind specifically to E2. A photopolymerization technique was employed for depositing the MIP on SPCE. Under optimal conditions, the sensor could detect the concentrations of 17b-estradiol from 1.0 x 10^{-9} to 1 µM with a detection limit of 2.5 x 10^{-10} µM [165]. A similar polymerization method was reported by [166] for antibiotics using thermocouple as for the thermal measurements of the MIP Sensors. Screen-printed electrodes were doped with gold nanoparticles in order to provide a suitable platform for the development of a MIP receptor for estradiol detection. The rationale for this was to create a platform with high surface areas which was stable enough to generate a uniform polymer matrix on the electrode surface. Truong et al. report the electrodeposition fo AuNPs onto SPEs followed by electropolymerization of funtional monomer for E2 analysis. The rationale is to increase the specific area of electrode of the membrane MIP , thus increases the imprinted site with reported LOD of 2 fM. This demonstrated the use of gold nanoparticles instead of gold ink on carbon SPE platform resulted in simplicity of manufacture and high reproducibility [167]. Recently, Jiang *et al.* [168] reported a signal-on type electrochemiluminescence (ECL) hybrid sensor for diethylstilbestrol (DES) detection, employing magnetic surface. The surface comprised a magnetic molecular imprinted polymer (MMIP), coupled with an aptamer labeled cadmium selenide quantum dots (CdS QDs) conjugated probes [168]. The MMIPs-DES-CdS-Apt composite was attached to a SPE using an external magnetic field. The sensor emitted an electrochemical luminescence signal at a potential −1.1 V. The signal intensity was proportional to the DES concentrations in the range of 0.3 to 1.0 × 10^{-5} pg ml^{-1}, with the LOD of 0.1 pg ml^{-1}. The rationale behind the use of the E2 aptamer was not given, just the statement that "it served as a tag". However, it is assumed it was use as the E2 to aptamer binding has higher affinity than antibody to antigen [169]. This is the first concept of a hybrid

Apta-MIP sensor for estrogen, although this type of sensor has been reported previously for the detection of lipopolysaccharide [170].

Lee group in 2019, [171] reported the integration of MIPs and screen-printed gold electrodes for electrochemical determination of steroidal hormones cortisol, progesterone, testosterone and 17β-estradiol in urine simultaneously. A four-channel system was established to enable simultaneous determination of the hormones by CV. The range of concentration, detection limit were 0.001–1000 fg·mL^{-1} and 9 ag·mL^{-1} [171]. One year later, the same group published measurements from a MIP-SPE sensor, which had a tungsten disulfide coating formed by electropolymerization of aniline and a metanilic acid conductive polymer on to SPE to create a 17β-estradiol sensor. Tungsten, as a class of transition metal dichalcogenide (TMD), serves as a dopant due to its direct band gaps and hence improves the electrochemical signal. The MIP-SPE sensor was applied to eel serum samples with various estradiol concentrations in the range 28.2±3.6 to 73.0±11.6 pg/mL and LOD of 0.06 fg/mL was obtained [172].

The commercial viability of MIPs in sensors has still not been proven, although the technology has been applied successfully in separation methods [138]. There is an increase in the work undertaken in application of MIPs in the area of sensors with different detection methods and formats(See Figure 7), with 50% of total articles published from (1962–2015) coming from the five years between 2010 and 2015 [173]. Investigations of the MIPs research repository (http://www.mipdatabase.com), in the last two years alone, has seen the publication of more 600 articles related to sensor applications [156].

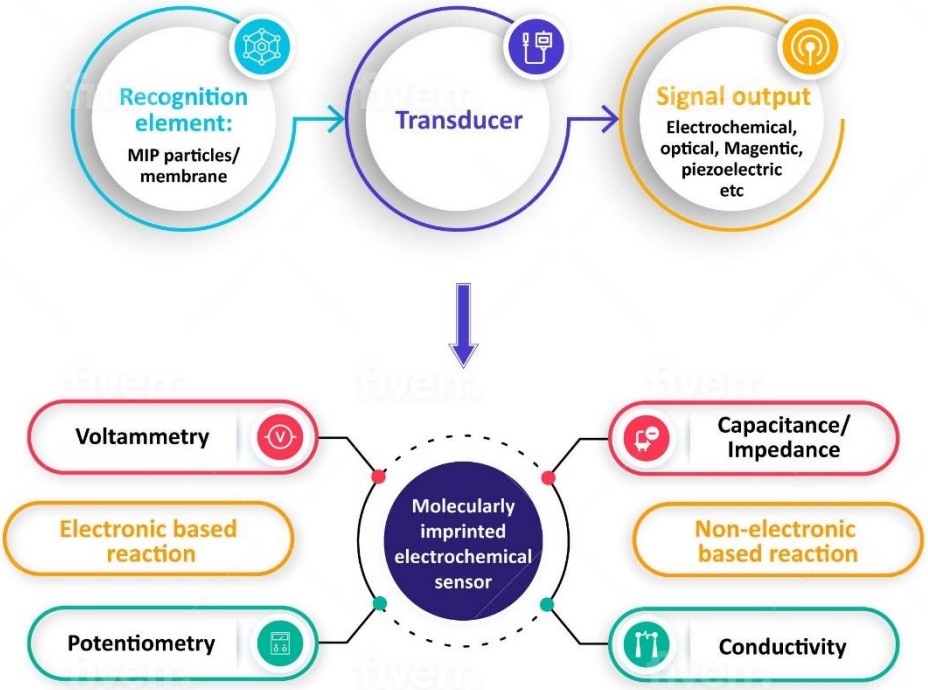


Figure 7. Mechanisms of molecularly imprinted electrochemical sensors (MIECS).

Table 1. Summaries some recent developments in the application of screen-printed electrochemical sensor & biosensors for the determination of estrogens

SPE-Design	Modifier	Applied Technique	Sensor type	Linear range	Detection limit	Estrogens	Samples	Ref.
Screen printed carbon electrode	Aptamer/ Carbon Nanodots	electrochemical impedance spectroscopy	impedimetric biosensor	1.0×10^{-7} to 1.0×10^{-12} M	5.0×10^{-13} M	Estriol (E3)	River water samples	[147]
Screen printed carbon electrode	Reduced graphene oxide/silver nanowires (AgNWs) and silver nanoparticles (AgNPs)	differential pulse voltammetry	Electrochemical sensor	1 - 90 µM	0.58 µM	Estriol (E3)	urine	[174]
Screen printed carbon electrode	Glass varnish-based carbon conductive ink	square wave voltammetry	Electrochemical sensor	0.1 - 8.0 µM	0.08 µM	Estriol (E3)	Water and Vaginal cream	[117]

Screen printed carbon electrode		Square wave voltammetry	Electrochemical sensor	1.7 mg/ L	242μgL^{-1}	Estradiol (E2)	urine	[78]
Screen printed carbon electrode		Square wave voltammetry	Electrochemical sensor	2.0 mg/L	277μgL^{-1}	Ethinylestradiol (EE2)	urine	[78]
Screen printed carbon nanotube electrode (SPCNTE)	carbon nanotubes	Square wave voltammetry	Electrochemical sensor	1.2 mg /L	182μg L^{-1}	Estradiol (E2)	urine	[78]
Screen printed carbon nanotube electrode (SPCNTE)	carbon nanotubes	Square wave voltammetry	Electrochemical sensor	1.6 mg /L	191 μgL^{-1}	Ethinylestradiol (EE2)	urine	[78]
Gold-Screen printed electrode (Au-SPE)	MIP Coated poly (ANIco-MSAN) s	cyclic voltammetry	Electrochemical sensor	0.001–1000 fg·mL^{-1}	9 ag·mL^{-1}	Estradiol (E2)	urine	[171]

Gold-Screen printed electrode (Au-SPE)	(TSMEIPs) poly (AN-co-MSAN)	cyclic voltammetry	Electrochemical sensor	28.2-3.6 to 73.0-11.6 pg/mL	9 ag·mL^{-1}	Estradiol (E2)	serum	[172]
Screen-printed electrode	antibody	differential pulse voltammetry	Immunosensor	25–500 pg/ml	50 pg/ml	Estradiol (E2)	serum	[130]
screen-printed electrodes	Electrochemical pre-treatment	differential pulse voltammetry	Electrochemical sensor	0.5 - 10.0 µM	888 nM	Estradiol (E2)	Tap water	[175]
screen-printed electrodes	CuPc-P6LC-Nafion/SPE$_F$	differential pulse voltammetry	Electrochemical sensor	8.0×10^{-8} to 7.3×10^{-6} M	5.0×10^{-9} M	Estradiol (E2)	River Water samples	[105]
Screen-printed electrodes	Fe_3O_4-MIP/SPCE	Square wave voltammetry	Electrochemical sensor	0.05–10 µM	20 nM	Estradiol (E2)	River water samples	[164]
Screen-printed electrodes	MIP-AuNPs-SPCE	EIS	Electrochemical sensor	100 fM to 10 nM.	2 fM	Estradiol (E2)	PBS Buffer	[167]
Screen-printed electrodes	MWNTs/Al2O3/poly-L-lysine	cyclic voltammetry	Electrochemical sensor	0.5 to 50 nM	0.014 nM	Estradiol (E2)	Blood and urine samples	[79]

Screen-printed electrodes	MWCNT–AuNP-SPE	differential pulse voltammetry	Electrochemical sensor	1.0 x 10_{-15} to 1.0 x10_{-6} M	2.5 x 10_{-16}M	Estradiol (E2)	serum	[176]
Screen printed electrode	E2-hexa-Magnetic Beads	square wave voltammetry	Immunosensor	0.1 - 100 ng/L	1 ng/L	Estradiol (E2)	Water samples	[24]
Screen printed electrode	EE2-hexa-Magnetic Beads	square wave voltammetry	Immunosensor	0.1 - 100 ng/L	10 ng/L	Ethinylestradiol (EE2)	Water samples	[24]
Screen printed electrode	Anti-estradiol-Biotin/Strept-ABA-g-SPCE.	EIS	Immunosensor	1- 250 pg mL^{-1}	0.77 pg/mL	Estradiol (E2)	human serum and urine.	[135]
Screen printed electrode	Anti-17ß-estradiol antibody Au-protein-SPCE	cyclic voltammetry	Immunosensor	0.1 - 20 µg/L	0. 035 µg/L	Estradiol (E2)	Serum	[177]

Screen printed electrode	Anti-rabbit IgG-17ß-estradiol antibody-SPCE	differential pulse voltammetry	Immunosensor			Estradiol (E2)	Serum	[132]
Screen printed electrode	Anti-17ß-estradiol antibody-SPCE	amperometry	immunosensor		0.25 pg/ml	Estradiol (E2)	serum	[178]
Screen-printed electrodes	[C8py][PF6]-MWCNTs	Linear sweep voltammetry	Electrochemical sensor	0.05 to 2.0 mM,	2 nM	Ethinylestradiol (EE2)	phosphate buffer solution (pH 7.0)	[115]

screen-printed electrodes	Pt@SBA-15-Ab2	cyclic voltammetry	immunosensor	0.005–8.0 ng/mL	1.2 pg/mL	Estradiol (E2)	River water samples	[133]
screen-printed electrodes	Pt@SBA-15-Ab2	cyclic voltammetry	immunosensor	0.001–10.0 ng/mL	0.28 pg/mL	Ethinylestradiol (EE2)	River water samples	[133]
screen-printed electrodes	MMIPs-QDs-Apt	Electrochemiluminescence (ECL)		0.3 - 1.0 × 10^5 pg/ml	0.1 pg/ml	diethylstilbestrol	Serum	[168]

screen-printed electrodes	Enzyme electrodes (SPE/DDAB/CYP19A1)	square wave voltammetry	Biosensor		11 nM	Estrone (E1)	Buffer	[127]
screen-printed electrodes	Enzyme electrodes (SPE/DDAB/CYP19A1)	square wave voltammetry	Biosensor		3.4 nM	Estradiol (E2)	Buffer	[127]
screen-printed electrodes	Reduced-Graphene oxide-SPCE	square wave voltammetry	Biosensor	0.5-120 ng L^{-1}	0.1 ng L^{-1}	ethinyl estradiol (EE2)	water samples	[131]

screen-printed electrodes	Multiwalled Carbon nanotube	Amperometry	Electrochemical	1.0 - 1000 µM	0.53uM	Estriol (E3)	pharmaceutical sample	[113]
screen-printed electrodes	Anti-E1/ Polyaniline (PANI)/Gr-SPE	Electrochemical Impedance Spectroscopy (EIS)	Biosensor	0.0975 ng/L to 200 ng/L	0.043 pg/L	estrone (E1)	River water samples	[111]
screen-printed electrodes	Anti-E1/ Polyaniline (PANI)/Gr-SPE	Electrochemical Impedance Spectroscopy (EIS)	Biosensor	0.0975 ng/L to 200 ng/L	0.19 ng/L	estradiol (E2)	River water samples	[111]

screen-printed electrodes	Anti-EE2/ Polyaniline (PANI)/Gr-SPE	Electrochemical Impedance Spectroscopy (EIS)	Biosensor	0.0975 ng/L to 200 ng/L	0.070 pg/L	ethinyl estradiol (EE2)	River water samples	[111]
screen-printed electrodes	graphene quantum dots (GQD)/SPE	Linear Sweep voltammetry	Electrochemical sensor	0.05 -7.5 µM	8.8 nM	diethylstilbestrol (DES)	Urine and tap water	[179]

6. Conclusion and future trends

Research in the field of electrochemical sensors and biosensors for estrogen determination is very active, as evidenced by the number of published works. However, application of SPEs is still limited, if we are to correlate this with the number of articles obtained from Scopus database and other databases. Screen-printed electrode-based immunosensors seem to be particularly attractive in terms of research activity. This is not new looking at the commercial immunoassay kits already available. No SPEs based sensors for estrogens are available on the market - we are still at the lab research and development stage. Nanomaterials, including carbon nanomaterials, metal, metal oxide and ionic liquid materials, as modifiers for screen-printed electrochemical estrogens sensors, are said to improve the sensitivity, selectivity, and repeatability compared to the traditional screen-printed electrochemical sensors, and even can detect multiple analytes. However, the work of Raymundo-Pereira *et al.* shows that the sensitivity of the pre-treated SPEs is comparable with that of some nanomaterials reported [58]. This means we need to have a better understand of ink formulation as well the use additional tools, such tristimulus analysis, in understanding the behaviour of estrogens on SPEs. On the other hand, the portability of SPE systems is verified to enable *in situ* detection. A large number of works on estradiol have been carried out with various material to improve the sensitivity of the sensor but only a few are available with SPE. More importantly, such sensors are still in the development stage, so there is still much research space. In addition, the LOD reported by standard methods, as well as regulatory standard enhances the challenges in this field.

Nevertheless, to achieve higher performance, more research into the utilization of other composite materials as a modifier, such as alloys of various forms, needs to be explored to overcome the limitations of using a single material. In addition to this, the modification of the methods using various materials to create the SPEs may also play a key role in performance

improvement. However, there are challenges, for example simple drop coating technique that is mainly reported on other electrodes cannot be directly employed for SPE. One of the noticeable differences is the reference electrode (termed pseudo reference electrode) that is commonly used can degrade even before measurement, therefore affecting the potential of the electrochemical oxidation of the sample.

Mixing of the nanomaterials directly into the ink is practical and convenient but the ink formulation changes must be investigated especially the ratio of components. However, even this method may cause the nanomaterials or other functional materials doped in the ink formulation not to be completely exposed to the surface of the electrode, resulting in the poor performance. A typical example is the carbonaceous nanomaterial where the edge plane and basal plane is vital for creating a uniform film on the working electrode [56,97,100,180]. Surface modification seems easier and more straightforward, but the reproducibility is vital. An alternative is to employ an automatic dispensing system, such as Biodot, which will accurately disperse equal volume with high accuracy and repeatedly. If SPEs are to serve as the replacement of conventional methods, a lot of factors need to be considered. From the point of conceptualization, the protocol for transfer from lab-based to field-based research should be in mind. Back-to-back screen-printing of working electrodes, as mentioned by Metters *et al.* [11], needs to be consider where appropriate in the construction of the SPE [11]. Real samples are complex and having this in mind will surely see a focus on optimization for the relevant application and ensuring that the developed screen-printed electrochemical (bio) sensors will have integrated the advantages of rapidity of testing, portability, and sensitivity. Still, the screen-printed electrochemical sensors based on various nanomaterials face enormous challenges. New nanomaterials need to be developed for the fabrication of screen-printed electrochemical sensors to provide more convenient and effective tools for the detection of estrogens in the future. If we are to see the "true Renaissance in electroanalysis" using SPEs, additional tools such as chemometric must be embedded in the process of data

analysis. The same applies to synthetic materials like MIPs and aptamer. There is need for a next generation of monomers based on insilico designs, as well new aptamer sequence designs.

Finally, market requirements are now shifting toward not only designing sensor with good sensitivity and specificity but a continuous, real-time, wash-free, antifouling and calibration-free sensing platforms as reported by [181].

Acknowledgments: This work has been supported by the University of the West of England.

References

[1] V. Geissen, H. Mol, E. Klumpp, G. Umlauf, M. Nadal, M. van der Ploeg, S.E.A.T.M. van de Zee, C.J. Ritsema, Emerging pollutants in the environment: A challenge for water resource management, Int. Soil Water Conserv. Res. 3 (2015) 57–65. https://doi.org/10.1016/J.ISWCR.2015.03.002.

[2] E. Özgür, E. Yılmaz, G. Şener, L. Uzun, R. Say, A. Denizli, A new molecular imprinting-based mass-sensitive sensor for real-time detection of 17β-estradiol from aqueous solution, Environ. Prog. Sustain. Energy. 32 (2013) 1164–1169. https://doi.org/10.1002/ep.11718.

[3] G. Csaba, The Immuno-Endocrine System: Hormones, Receptors and Endocrine Function of Immune Cells. The Packed-Transport Theory, Adv. Neuroimmune Biol. 1 (2011) 71–85. https://doi.org/10.3233/NIB-2011-007.

[4] S. Barreca, M. Busetto, L. Colzani, L. Clerici, D. Daverio, P. Dellavedova, S. Balzamo, E. Calabretta, V. Ubaldi, Determination of estrogenic endocrine disruptors in water at sub-ng L −1 levels in compliance with Decision 2015/495/EU using offline-online solid phase extraction concentration coupled with high performance liquid chromatography-tandem mass spectrometry, Microchem. J. 147 (2019) 1186–1191. https://doi.org/10.1016/j.microc.2019.04.030.

[5] L. Zhao, J.-M. Lin, Z. Li, X. Ying, Development of a highly sensitive, second antibody format chemiluminescence enzyme immunoassay for the determination of 17β-estradiol in wastewater, Anal. Chim. Acta. 558 (2006) 290–295. https://doi.org/10.1016/J.ACA.2005.11.034.

[6] K.J. Huang, Y.J. Liu, J.Z. Zhang, J.T. Cao, Y.M. Liu, Aptamer/Au nanoparticles/cobalt sulfide nanosheets biosensor for 17β-estradiol detection using a guanine-rich complementary DNA sequence for

signal amplification, Biosens. Bioelectron. 67 (2015) 184–191. https://doi.org/10.1016/j.bios.2014.08.010.

[7] J.-J. Zhang, J.-T. Cao, G.-F. Shi, K.-J. Huang, Y.-M. Liu, Y.-H. Chen, Label-free and sensitive electrochemiluminescence aptasensor for the determination of 17β-estradiol based on a competitive assay with cDNA amplification, Anal. Methods. 6 (2014) 6796. https://doi.org/10.1039/C4AY01147C.

[8] L.E. Sofen, A.L. Furst, Perspective—Electrochemical Sensors to Monitor Endocrine Disrupting Pollutants, J. Electrochem. Soc. 167 (2020) 037524. https://doi.org/10.1149/2.0242003jes.

[9] V.K. Gupta, R. Jain, K. Radhapyari, N. Jadon, S. Agarwal, Voltammetric techniques for the assay of pharmaceuticals-A review, Anal. Biochem. 408 (2011) 179–196. https://doi.org/10.1016/j.ab.2010.09.027.

[10] M.M. Charithra, J.G. Manjunatha, Poly (l-Proline) modified carbon paste electrode as the voltammetric sensor for the detection of Estriol and its simultaneous determination with Folic and Ascorbic acid, Mater. Sci. Energy Technol. 2 (2019) 365–371. https://doi.org/10.1016/j.mset.2019.05.002.

[11] J.P. Metters, E.P. Randviir, C.E. Banks, Screen-printed back-to-back electroanalytical sensors, Analyst. 139 (2014) 5339–5349. https://doi.org/10.1039/c4an01501k.

[12] G. Liu, Y. Lin, Nanomaterial labels in electrochemical immunosensors and immunoassays, Talanta. 74 (2007) 308–317. https://doi.org/10.1016/j.talanta.2007.10.014.

[13] J.P. Metters, R.O. Kadara, C.E. Banks, New directions in screen printed electroanalytical sensors: An overview of recent developments, Analyst. 136 (2011) 1067–1076. https://doi.org/10.1039/c0an00894j.

[14] J.P. Hart, A. Crew, E. Crouch, K.C. Honeychurch, R.M. Pemberton, Some

Recent Designs and Developments of Screen-Printed Carbon Electrochemical Sensors/Biosensors for Biomedical, Environmental, and Industrial Analyses, Anal. Lett. 37 (2004) 789–830. https://doi.org/10.1081/AL-120030682.

[15] X. Liu, K. Deng, H. Wang, C. Li, S. Zhang, H. Huang, Aptamer based ratiometric electrochemical sensing of 17β-estradiol using an electrode modified with gold nanoparticles, thionine, and multiwalled carbon nanotubes, Microchim. Acta. 186 (2019). https://doi.org/10.1007/s00604-019-3465-y.

[16] H. Pu, Z. Huang, D.W. Sun, H. Fu, Recent advances in the detection of 17β-estradiol in food matrices: A review, Crit. Rev. Food Sci. Nutr. 59 (2019) 2144–2157. https://doi.org/10.1080/10408398.2019.1611539.

[17] A. Azzouz, S.K. Kailasa, P. Kumar, E. Ballesteros, K.-H. Kim, Advances in functional nanomaterial-based electrochemical techniques for screening of endocrine disrupting chemicals in various sample matrices, TrAC Trends Anal. Chem. 113 (2019) 256–279. https://doi.org/10.1016/J.TRAC.2019.02.017.

[18] P. Gamache, I. Acworth, Measurement of Environmental Estrogens in Water Using a Gradient HPLC-EC-UV Method, (2014). https://assets.thermofisher.com/TFS-Assets/CMD/Application-Notes/AB-160-HPLC-EC-UV-Estrogens-Water-AB71224-EN.pdf (accessed June 20, 2020).

[19] F. Moreira, E.R. Santana, A. Spinelli, Ionic liquid-supported magnetite nanoparticles as electrode modifier materials for estrogens sensing, Sci. Rep. 10 (2020) 1–11. https://doi.org/10.1038/s41598-020-58931-6.

[20] A. Nezami, R. Nosrati, B. Golichenari, R. Rezaee, G.I. Chatzidakis, A.M. Tsatsakis, G. Karimi, Nanomaterial-based aptasensors and bioaffinity sensors for quantitative detection of 17β-estradiol, TrAC Trends Anal.

Chem. 94 (2017) 95–105. https://doi.org/10.1016/J.TRAC.2017.07.003.

[21] A. Pillon, A.M. Boussioux, A. Escande, S. Aït-Aïssa, E. Gomez, H. Fenet, M. Ruff, D. Moras, F. Vignon, M.J. Duchesne, C. Casellas, J.C. Nicolas, P. Balaguer, Binding of estrogenic compounds to recombinant estrogen receptor-a: Application to environmental analysis, Environ. Health Perspect. 113 (2005) 278–284. https://doi.org/10.1289/ehp.7522.

[22] C.L. Waller, T.I. Oprea, K. Chae, H.K. Park, K.S. Korach, S.C. Laws, T.E. Wiese, W.R. Kelce, L.E. Gray, Ligand-based identification of environmental estrogens, Chem. Res. Toxicol. 9 (1996) 1240–1248. https://doi.org/10.1021/tx960054f.

[23] M. Česen, E. Heath, Disk-based solid phase extraction for the determination of diclofenac and steroidal estrogens E1, E2 and EE2 listed in the WFD watch list by GC–MS, Sci. Total Environ. 590–591 (2017) 832–837. https://doi.org/10.1016/j.scitotenv.2017.02.222.

[24] H. Kanso, L. Barthelmebs, N. Inguimbert, T. Noguer, Immunosensors for estradiol and ethinylestradiol based on new synthetic estrogen derivatives: Application to wastewater analysis, Anal. Chem. 85 (2013) 2397–2404. https://doi.org/10.1021/ac303406c.

[25] N. Jaffrezic-Renault, J. Kou, D. Tan, Z. Guo, New trends in the electrochemical detection of endocrine disruptors in complex media, Anal. Bioanal. Chem. (2020). https://doi.org/10.1007/s00216-020-02516-9.

[26] X. Lu, J. Sun, X. Sun, Recent advances in biosensors for the detection of estrogens in the environment and food, Trends Anal. Chem. (2020) 115882. https://doi.org/10.1016/j.trac.2020.115882.

[27] C. Li, Y. Wei, S. Zhang, W. Tan, Advanced methods to analyze steroid estrogens in environmental samples, Environ. Chem. Lett. (2020). https://doi.org/10.1007/s10311-019-00961-2.

[28] A. Nezami, R. Nosrati, B. Golichenari, R. Rezaee, G.I. Chatzidakis, A.M. Tsatsakis, G. Karimi, Nanomaterial-based aptasensors and bioaffinity sensors for quantitative detection of 17β-estradiol, TrAC Trends Anal. Chem. 94 (2017) 95–105. https://doi.org/10.1016/J.TRAC.2017.07.003.

[29] L. Barreiros, J.F. Queiroz, L.M. Magalhães, A.M.T. Silva, M.A. Segundo, Analysis of 17-β-estradiol and 17-a-ethinylestradiol in biological and environmental matrices - A review, Microchem. J. 126 (2016) 243–262. https://doi.org/10.1016/j.microc.2015.12.003.

[30] I. Cabas, S. Liarte, A. García-Alcázar, J. Meseguer, V. Mulero, A. García-Ayala, 17a-Ethynylestradiol alters the immune response of the teleost gilthead seabream (Sparus aurata L.) both in vivo and in vitro, Dev. Comp. Immunol. 36 (2012) 547–556. https://doi.org/10.1016/j.dci.2011.09.011.

[31] M. Adeel, X. Song, Y. Wang, D. Francis, Y. Yang, Environmental impact of estrogens on human, animal and plant life: A critical review., Environ. Int. 99 (2017) 107–119. https://doi.org/10.1016/j.envint.2016.12.010.

[32] K.E. Arnold, A.R. Brown, A.R. Brown, G.T. Ankley, J.P. Sumpter, Medicating the environment: Assessing risks of pharmaceuticals to wildlife and ecosystems, Philos. Trans. R. Soc. B Biol. Sci. 369 (2014). https://doi.org/10.1098/rstb.2013.0569.

[33] L. Celik, J.D.D. Lund, B. Schiøtt, Exploring interactions of endocrine-disrupting compounds with different conformations of the human estrogen receptor a ligand binding domain: A molecular docking study, Chem. Res. Toxicol. 21 (2008) 2195–2206. https://doi.org/10.1021/tx800278d.

[34] G.C. Mauruto de Oliveira, E. P. de Palma, M.H. Kunita, R. Antigo Medeiros, R. de Matos, K.R. Francisco, B.C. Janegitz, Tapioca Biofilm Containing Nitrogen-doped Titanium Dioxide Nanoparticles for

Electrochemical Detection of 17-β Estradiol, Electroanalysis. 29 (2017) 2638–2645. https://doi.org/10.1002/elan.201700392.

[35] A.. Kester, M.H., Bulduk, S., Tibboel, D., Meinl, W., Glatt, H., Falany, C.N., Coughtrie, M.W., Bergman, A.K.E., Safe, S.H., Kuiper, G.G. and Schuur, Potent inhibition of estrogen sulfotransferase by hydroxylated PCB metabolites: a novel pathway explaining the estrogenic activity of PCBs, Endocrinology. 141 (2000) 1897–1900.

[36] R.P.A. Barros, J.Å. Gustafsson, Estrogen receptors and the metabolic network, Cell Metab. 14 (2011) 289–299. https://doi.org/10.1016/j.cmet.2011.08.005.

[37] M. Nitkowska, R. Tomasiuk, M. Czyzyk, A. Friedman, Prolactin and sex hormones levels in males with Parkinson's disease, Acta Neurol. Scand. 131 (2015) 411–416. https://doi.org/10.1111/ane.12334.

[38] C. Schairer, J. Lubin, R. Troisi, S. Sturgeon, L. Brinton, R. Hoover, Menopausal estrogen and estrogen-progestin replacement therapy and breast cancer risk, J. Am. Med. Assoc. 283 (2000) 485–491. https://doi.org/10.1001/jama.283.4.485.

[39] S.C. Janicki, N. Schupf, Hormonal influences on cognition and risk for Alzheimer's disease, Curr. Neurol. Neurosci. Rep. 10 (2010) 359–366. https://doi.org/10.1007/s11910-010-0122-6.

[40] M. Farré, L. Kantiani, S. Pérez, D. Barceló, Sensors and biosensors in support of EU Directives, TrAC - Trends Anal. Chem. 28 (2009) 170–185. https://doi.org/10.1016/j.trac.2008.09.018.

[41] G.S.W. Daniel R.Thevenot, Klara Toth, Richard A. Durdt, ELECTROCHEMICAL BIOSENSORS : RECOMMENDED Electrochemical biosensors : Recommended definitions and classification (Technical Report), Pure Appl. Chem. 71 (1999) 2333–2348. https://doi.org/10.1016/S0956-5663(01)00115-4.

[42] H.M. Mohamed, Screen-printed disposable electrodes: Pharmaceutical applications and recent developments, TrAC - Trends Anal. Chem. 82 (2016) 1–11. https://doi.org/10.1016/j.trac.2016.02.010.

[43] A. Villalonga, A.M. Pérez-Calabuig, R. Villalonga, Electrochemical biosensors based on nucleic acid aptamers, Anal. Bioanal. Chem. 412 (2020) 55–72. https://doi.org/10.1007/s00216-019-02226-x.

[44] K.C. Honeychurch, J.P. Hart, Screen-printed electrochemical sensors for monitoring metal pollutants, TrAC - Trends Anal. Chem. 22 (2003) 456–469. https://doi.org/10.1016/S0165-9936(03)00703-9.

[45] K.C. Honeychurch, Review of electroanalytical-based approaches for the determination of benzodiazepines, Biosensors. 9 (2019). https://doi.org/10.3390/bios9040130.

[46] K.C. Honeychurch, M. Piano, Electrochemical (bio) sensors for environmental and food analyses, Biosensors. 8 (2018) 2–4. https://doi.org/10.3390/bios8030057.

[47] K.C. Honeychurch, Screen-printed Electrochemical Sensors and Biosensors for Monitoring Metal Pollutants, Insciences J. 2 (2012) 1–51. https://doi.org/10.5640/insc.020101.

[48] R.A.S. Couto, J.L.F.C. Lima, M.B. Quinaz, Recent developments, characteristics and potential applications of screen-printed electrodes in pharmaceutical and biological analysis, Talanta. 146 (2016) 801–814. https://doi.org/10.1016/j.talanta.2015.06.011.

[49] N. Postell, J., & Gesimondo, Materiality and interior construction, John Wiley & Sons, 2011.

[50] D.T. Jenkins, D. T., & Jenkins, The Cambridge history of western textiles, Volume I, Cambridge University Press, 2003.

[51] K. Grennan, A.J. Killard, M.R. Smyth, Physical characterizations of a screen-printed electrode for use in an amperometric biosensor system,

Electroanalysis. 13 (2001) 745–750. https://doi.org/10.1002/1521-4109(200105)13:8/9<745::AID-ELAN745>3.0.CO;2-B.

[52] A. Escarpa, Food electroanalysis: Sense and simplicity, Chem. Rec. 12 (2012) 72–91. https://doi.org/10.1002/tcr.201100033.

[53] K.C. Honeychurch, Z. Rymansaib, P. Iravani, Anodic stripping voltammetric determination of zinc at a 3-D printed carbon nanofiber–graphite–polystyrene electrode using a carbon pseudo-reference electrode, Sensors Actuators, B Chem. 267 (2018) 476–482. https://doi.org/10.1016/j.snb.2018.04.054.

[54] O. Bagel, E. L'Hostis, G. Lagger, M.D. Osborne, B.J. Seddon, H.H. Girault, D. Brack, U. Loyall, H. Schäfer, Rotograved carbon electrodes for amperometric cadmium and lead determination, J. Electroanal. Chem. 469 (1999) 189–195. https://doi.org/10.1016/S0022-0728(99)00226-0.

[55] O. Bagel, G. Lagger, H.H. Girault, D. Brack, U. Loyall, H. Schäfer, Mercury free determination of lead by differential pulse anodic stripping voltammetry onto silver-plated rotograved carbon electrodes, Electroanalysis. 13 (2001) 100–103. https://doi.org/10.1002/1521-4109(200102)13:2<100::AID-ELAN100>3.0.CO;2-I.

[56] X. Ji, C.E. Banks, A. Crossley, R.G. Compton, Oxygenated edge plane sites slow the electron transfer of the ferro-/ferricyanide redox couple at graphite electrodes, ChemPhysChem. 7 (2006) 1337–1344. https://doi.org/10.1002/cphc.200600098.

[57] A.G. Tummala, R., Rymaszewski, E. J., & Klopfenstein, Microelectronics Packaging Handbook:Subsystem Packaging, 2nd ed., Springer US, 1997. https://www.springer.com/gp/book/9780412084515.

[58] P.A. Raymundo-Pereira, N.O. Gomes, S.A.S. Machado, O.N. Oliveira, Simultaneous, ultrasensitive detection of hydroquinone, paracetamol

and estradiol for quality control of tap water with a simple electrochemical method, J. Electroanal. Chem. 848 (2019) 113319. https://doi.org/10.1016/J.JELECHEM.2019.113319.

[59] K. Tyszczuk-Rotko, K. Pietrzak, A. Sasal, Adsorptive stripping voltammetric method for the determination of caffeine at integrated three-electrode screen-printed sensor with carbon/carbon nanofibers working electrode, Adsorption. 25 (2019) 913–921. https://doi.org/10.1007/s10450-019-00116-3.

[60] X. Cetó, A.M. O'Mahony, J. Wang, M. Del Valle, Simultaneous identification and quantification of nitro-containing explosives by advanced chemometric data treatment of cyclic voltammetry at screen-printed electrodes, Talanta. 107 (2013) 270–276. https://doi.org/10.1016/j.talanta.2012.12.042.

[61] R.O. Kadara, N. Jenkinson, C.E. Banks, Characterisation of commercially available electrochemical sensing platforms, Sensors Actuators, B Chem. 138 (2009) 556–562. https://doi.org/10.1016/j.snb.2009.01.044.

[62] M. Li, Y.T. Li, D.W. Li, Y.T. Long, Recent developments and applications of screen-printed electrodes in environmental assays-A review, Anal. Chim. Acta. 734 (2012) 31–44. https://doi.org/10.1016/j.aca.2012.05.018.

[63] S. Fletcher, Screen-Printed Carbon Electrodes, Adv. Electrochem. Sci. Eng. 16 (2016) 425–443. https://doi.org/10.1002/9783527697489.ch12.

[64] A. García-Miranda Ferrari, S.J. Rowley-Neale, C.E. Banks, Screen-printed electrodes: Transitioning the laboratory in-to-the field, Talanta Open. 3 (2021) 100032. https://doi.org/10.1016/j.talo.2021.100032.

[65] K. Yamanaka, M.C. Vestergaard, E. Tamiya, Printable electrochemical biosensors: A focus on screen-printed electrodes and their application,

Sensors (Switzerland). 16 (2016) 1–16. https://doi.org/10.3390/s16101761.

[66] D. Ji, N. Xu, Z. Liu, Z. Shi, S.S. Low, J. Liu, C. Cheng, J. Zhu, T. Zhang, H. Xu, X. Yu, Q. Liu, Smartphone-based differential pulse amperometry system for real-time monitoring of levodopa with carbon nanotubes and gold nanoparticles modified screen-printing electrodes, Biosens. Bioelectron. 129 (2019) 216–223. https://doi.org/10.1016/j.bios.2018.09.082.

[67] M. Franco Guzmán, G.A. Álvarez-Romero, L.H. Mendoza-Huizar, C.A. Galán-Vidal, G. Roa Morales, M.T. Ramírez-Silva, M.G. Montes de Oca Yemha, Optimization of a Differential Pulse Voltammetric Methodology for the Quantification of Diclofenac Using Paste Electrodes and Carbon Nanotubes, ECS Trans. 76 (2017) 9–18. https://doi.org/10.1149/07601.0009ecst.

[68] K.L. Westmacott, A. Crew, O. Doran, J.P. Hart, A novel electroanalytical approach to the measurement of B vitamins in food supplements based on screen-printed carbon sensors, Talanta. 181 (2018) 13–18. https://doi.org/10.1016/j.talanta.2017.12.074.

[69] A. Morrin, A.J. Killard, M.R. Smyth, Electrochemical characterization of commercial and home-made screen-printed carbon electrodes, Anal. Lett. 36 (2003) 2021–2039. https://doi.org/10.1081/AL-120023627.

[70] X. Lin, Y. Li, A sensitive determination of estrogens with a Pt nano-clusters/multi-walled carbon nanotubes modified glassy carbon electrode, Biosens. Bioelectron. 22 (2006) 253–259. https://doi.org/10.1016/j.bios.2006.01.005.

[71] A. Florea, C. Cristea, F. Vocanson, R. Săndulescu, N. Jaffrezic-Renault, Electrochemical sensor for the detection of estradiol based on electropolymerized molecularly imprinted polythioaniline film with signal amplification using gold nanoparticles, Electrochem. Commun. 59 (2015) 36–39. https://doi.org/10.1016/j.elecom.2015.06.021.

[72] Mahboubeh Vafi, G.H. Rounaghi, Z. Es'haghi, Chemometrically-Assisted Fabrication of a Potentiometric Sensor for Potassium Ion Based on Kryptofix 22 Ionophore, Russ. J. Phys. Chem. A. 92 (2018) 2795–2801. https://doi.org/10.1134/S0036024418130320.

[73] X. Liu, P.A. Duckworth, D.K.Y. Wong, Square wave voltammetry versus electrochemical impedance spectroscopy as a rapid detection technique at electrochemical immunosensors, Biosens. Bioelectron. 25 (2010) 1467–1473. https://doi.org/10.1016/j.bios.2009.10.047.

[74] K.C. Honeychurch, J.P. Hart, N. Kirsch, Voltammetric, chromatographic and mass spectral elucidation of the redox reactions of 1-hydroxypyrene occurring at a screen-printed carbon electrode, Electrochim. Acta. 49 (2004) 1141–1149. https://doi.org/10.1016/j.electacta.2003.10.025.

[75] T. Cho, J. Wang, Selective Voltammetric Measurements of Epinephrine and Norepinephrine in Presence of Common Interferences Using Cyclic Square-voltammetry at Unmodified Carbon Electrodes, Electroanalysis. 30 (2018) 1028–1032. https://doi.org/10.1002/elan.201700823.

[76] M. Mascini, S. Gaggiotti, F. Della Pelle, J. Wang, J.M. Pingarrón, D. Compagnone, Hairpin DNA-AuNPs as molecular binding elements for the detection of volatile organic compounds, Biosens. Bioelectron. (2018). https://doi.org/10.1016/j.bios.2018.07.028.

[77] K.K. Mistry, K. Layek, A. Mahapatra, C. RoyChaudhuri, H. Saha, A review on amperometric-type immunosensors based on screen-printed electrodes, Analyst. 139 (2014) 2289–2311. https://doi.org/10.1039/c3an02050a.

[78] J.J. Triviño, M. Gómez, J. Valenzuela, A. Vera, V. Arancibia, Determination of a natural (17B-estradiol) and a synthetic (17A-ethinylestradiol) hormones in pharmaceutical formulations and urine by

adsorptive stripping voltammetry, Sensors Actuators, B Chem. 297 (2019) 126728. https://doi.org/10.1016/j.snb.2019.126728.

[79] Y. Wang, Y. Xiong, H. Tian, S. Wang, Q. Zhang, M. Zhang, H. Ding, Y. Gu, A. Peng, Application of sensitive sensor modified with MWNTs/Al2O3/poly-L-lysine composite for 17β -estradiol determination in pregnant woman blood, Int. J. Electrochem. Sci. 13 (2018) 147–158. https://doi.org/10.20964/2018.01.20.

[80] X. Dong, L. He, Y. Liu, Y. Piao, Preparation of highly conductive biochar nanoparticles for rapid and sensitive detection of 17β-estradiol in water, Electrochim. Acta. 292 (2018) 55–62. https://doi.org/10.1016/j.electacta.2018.09.129.

[81] M. Eddaoudi, D.B. Moler, H. Li, B. Chen, T.M. Reineke, M. O'Keeffe, O.M. Yaghi, Modular chemistry: Secondary building units as a basis for the design of highly porous and robust metal-organic carboxylate frameworks, Acc. Chem. Res. 34 (2001) 319–330. https://doi.org/10.1021/ar000034b.

[82] F. Zhao, T. Sun, F. Geng, P. Chen, Y. Gao, Metal-organic frameworks-based electrochemical sensors and biosensors, Int. J. Electrochem. Sci. 14 (2016) 5287–5304. https://doi.org/10.20964/2019.06.63.

[83] L. Ji, Y. Wang, K. Wu, W. Zhang, Simultaneous determination of environmental estrogens: Diethylstilbestrol and estradiol using Cu-BTC frameworks-sensitized electrode, Talanta. 159 (2016) 215–221. https://doi.org/10.1016/j.talanta.2016.06.030.

[84] X. Liu, D.K.Y. Wong, Electrocatalytic detection of estradiol at a carbon nanotube|Ni(Cyclam) composite electrode fabricated based on a two-factorial design, Anal. Chim. Acta. 594 (2007) 184–191. https://doi.org/10.1016/j.aca.2007.05.043.

[85] L. Luo, F. Li, L. Zhu, Y. Ding, D. Deng, Electrochemical sensing platform of

natural estrogens based on the poly(l-proline)-ordered mesoporous carbon composite modified glassy carbon electrode, Sensors Actuators, B Chem. 187 (2013) 78–83. https://doi.org/10.1016/j.snb.2012.09.056.

[86] M. Masikini, M.E. Ghica, P.G.L. Baker, E.I. Iwuoha, C.M.A. Brett, Electrochemical Sensor Based on Multi-walled Carbon Nanotube/Gold Nanoparticle Modified Glassy Carbon Electrode for Detection of Estradiol in Environmental Samples, Electroanalysis. 31 (2019) 1925–1933. https://doi.org/10.1002/elan.201900190.

[87] F.C. Moraes, B. Rossi, M.C. Donatoni, K.T. de Oliveira, E.C. Pereira, Sensitive determination of 17β-estradiol in river water using a graphene based electrochemical sensor, Anal. Chim. Acta. 881 (2015) 37–43. https://doi.org/10.1016/j.aca.2015.04.043.

[88] M.M. Ngundi, O.A. Sadik, T. Yamaguchi, S. ichiro Suye, First comparative reaction mechanisms of β-estradiol and selected environmental hormones in a redox environment, Electrochem. Commun. 5 (2003) 61–67. https://doi.org/10.1016/S1388-2481(02)00538-6.

[89] B. Salc, I. Biryol, Voltammetric investigation of β-estradiol, J. Pharm. Biomed. Anal. 28 (2002) 753–759. https://doi.org/10.1016/S0731-7085(01)00676-8.

[90] D. Sun, Q. Deng, J. Long, Highly sensitive electrochemical sensor for estradiol based on the signal amplification strategy of Cu-BDC frameworks, J. Solid State Electrochem. 22 (2018) 487–493. https://doi.org/10.1007/s10008-017-3778-x.

[91] J. Barton, M.B.G. García, D.H. Santos, P. Fanjul-Bolado, A. Ribotti, M. McCaul, D. Diamond, P. Magni, Screen-printed electrodes for environmental monitoring of heavy metal ions: a review, Microchim. Acta. 183 (2016) 503–517. https://doi.org/10.1007/s00604-015-1651-0.

[92] R.L. McCreery, Advanced carbon electrode materials for molecular electrochemistry, Chem. Rev. 108 (2008) 2646–2687. https://doi.org/10.1021/cr068076m.

[93] K.C. Honeychurch, D.M. Hawkins, J.P. Hart, D.C. Cowell, Voltammetric behaviour and trace determination of copper at a mercury-free screen-printed carbon electrode, Talanta. 57 (1999) 565–574. https://doi.org/10.1016/S0039-9140(02)00060-7.

[94] M.I. González-Sánchez, B. Gómez-Monedero, J. Agrisuelas, J. Iniesta, E. Valero, Highly activated screen-printed carbon electrodes by electrochemical treatment with hydrogen peroxide, Electrochem. Commun. 91 (2018) 36–40. https://doi.org/10.1016/j.elecom.2018.05.002.

[95] D.M. Anjo, M. Kahr, M.M. Khodabakhsh, S. Nowinski, M. Wanger, Electrochemical activation of carbon electrodes in base: Minimization of dopamine adsorption and electrode capacitance, Anal. Chem. 61 (1989) 2603–2608. https://doi.org/10.1021/ac00198a004.

[96] J. Wang, B.A. Freiha, Extractive Preconcentration of Organic Compounds at Carbon Paste Electrodes, Anal. Chem. 56 (1984) 849–852. https://doi.org/10.1021/ac00268a069.

[97] A.N. Patel, M.G. Collignon, M.A. OConnell, W.O.Y. Hung, K. McKelvey, J. V. MacPherson, P.R. Unwin, A new view of electrochemistry at highly oriented pyrolytic graphite, J. Am. Chem. Soc. 134 (2012) 20117–20130. https://doi.org/10.1021/ja308615h.

[98] W.J. Peveler, M. Yazdani, V.M. Rotello, Selectivity and Specificity: Pros and Cons in Sensing, ACS Sensors. 1 (2016) 1282–1285. https://doi.org/10.1021/acssensors.6b00564.

[99] G.M. Swain, Handbook of Electrochemistry, Handb. Electrochem. (2007) 111–V. https://doi.org/10.1016/B978-044451958-0.50006-9.

[100] N. Karikalan, P. Sundaresan, S.-M. Chen, R. Karthik, Exploring the Electrocatalytic Edge Plane Activity of Screen Printed Carbon Electrode and Various Carbonaceous Materials towards the Catecholic Derivatives, J. Electrochem. Soc. 165 (2018) H969–H978. https://doi.org/10.1149/2.1081814jes.

[101] J.N. Tiwari, V. Vij, K.C. Kemp, K.S. Kim, Engineered carbon-nanomaterial-based electrochemical sensors for biomolecules, ACS Nano. 10 (2016) 46–80. https://doi.org/10.1021/acsnano.5b05690.

[102] A. Sanati, M. Jalali, K. Raeissi, F. Karimzadeh, M. Kharaziha, S.S. Mahshid, S. Mahshid, A review on recent advancements in electrochemical biosensing using carbonaceous nanomaterials, Microchim. Acta. 186 (2019). https://doi.org/10.1007/s00604-019-3854-2.

[103] I. Cesarino, I.A. Hümmelgen, An additional tool towards overcoming absence of specificity of carbon nanostructure-based electrochemical sensors—application to estriol and estradiol detection and distinction, J. Solid State Electrochem. 19 (2015) 3045–3050. https://doi.org/10.1007/s10008-015-2923-7.

[104] V. Mazzaracchio, M.R. Tomei, I. Cacciotti, A. Chiodoni, C. Novara, M. Castellino, G. Scordo, A. Amine, D. Moscone, F. Arduini, Inside the different types of carbon black as nanomodifiers for screen-printed electrodes, Electrochim. Acta. 317 (2019) 673–683. https://doi.org/10.1016/j.electacta.2019.05.117.

[105] A. Wong, A.M. Santos, E.L. Fava, O. Fatibello-Filho, M.D.P.T. Sotomayor, Voltammetric determination of 17β-estradiol in different matrices using a screen-printed sensor modified with CuPc, Printex 6L carbon and Nafion film, Microchem. J. 147 (2019) 365–373. https://doi.org/10.1016/j.microc.2019.03.052.

[106] Y. Zhu, X. Liu, J. Jia, Electrochemical detection of natural estrogens using

a graphene/ordered mesoporous carbon modified carbon paste electrode, Anal. Methods. 7 (2015) 8626–8631. https://doi.org/10.1039/c5ay01833a.

[107] C. Karuwan, A. Wisitsoraat, D. Phokharatkul, C. Sriprachuabwong, T. Lomas, D. Nacapricha, A. Tuantranont, A disposable screen printed graphene-carbon paste electrode and its application in electrochemical sensing, RSC Adv. 3 (2013) 25792–25799. https://doi.org/10.1039/c3ra44187c.

[108] P. Pasakon, J.P. Mensing, D. Phokaratkul, C. Karuwan, T. Lomas, A. Wisitsoraat, A. Tuantranont, A high-performance, disposable screen-printed carbon electrode modified with multi-walled carbon nanotubes/graphene for ultratrace level electrochemical sensors, J. Appl. Electrochem. 49 (2019) 217–227. https://doi.org/10.1007/s10800-018-1268-1.

[109] S. Radhakrishnan, J. Mathiyarasu, Graphene-carbon nanotubes modified electrochemical sensors, Elsevier Inc., 2018. https://doi.org/10.1016/B978-0-12-815394-9.00008-X.

[110] S. Cinti, F. Arduini, Graphene-based screen-printed electrochemical (bio)sensors and their applications: Efforts and criticisms, Biosens. Bioelectron. 89 (2017) 107–122. https://doi.org/10.1016/j.bios.2016.07.005.

[111] H. Barton, W.M. Berbel-Filho, S. Consuegra, L. Francis, C. Tizaoui, R.S. Conlan, S.R. Teixeira, Ultrasensitive environmental assessment of xeno-estrogens in water samples using label-free graphene immunosensors, Anal. Biochem. 548 (2018) 102–108. https://doi.org/10.1016/j.ab.2018.02.027.

[112] T. Rasheed, F. Nabeel, M. Adeel, K. Rizwan, M. Bilal, H.M.N. Iqbal, Carbon nanotubes-based cues: A pathway to future sensing and

detection of hazardous pollutants, J. Mol. Liq. 292 (2019). https://doi.org/10.1016/j.molliq.2019.111425.

[113] L.M. Ochiai, D. Agustini, L.C.S. Figueiredo-Filho, C.E. Banks, L.H. Marcolino-Junior, M.F. Bergamini, Electroanalytical thread-device for estriol determination using screen-printed carbon electrodes modified with carbon nanotubes, Sensors Actuators, B Chem. 241 (2017) 978–984. https://doi.org/10.1016/j.snb.2016.10.150.

[114] A. Allagui, T.J. Freeborn, A.S. Elwakil, B.J. Maundy, Reevaluation of Performance of Electric Double-layer Capacitors from Constant-current Charge/Discharge and Cyclic Voltammetry, Sci. Rep. 6 (2016). https://doi.org/10.1038/srep38568.

[115] P. Gan, J.S. Foord, R.G. Compton, Ionic liquid-carbon nanotube modified screen-printed electrodes and their potential for adsorptive stripping voltammetry, Electroanalysis. 26 (2014) 1886–1892. https://doi.org/10.1002/elan.201400214.

[116] G. Hao, D. Zheng, T. Gan, C. Hu, S. Hu, Development and application of estradiol sensor based on layer-by-layer assembling technique, J. Exp. Nanosci. 6 (2011) 13–28. https://doi.org/10.1080/17458081003752988.

[117] L.A. Pradela-Filho, I.A.A. Andreotti, J.H.S. Carvalho, D.A.G. Araújo, L.O. Orzari, A. Gatti, R.M. Takeuchi, A.L. Santos, B.C. Janegitz, Glass varnish-based carbon conductive ink: A new way to produce disposable electrochemical sensors, Sensors Actuators, B Chem. 305 (2020) 127433. https://doi.org/10.1016/j.snb.2019.127433.

[118] G. Hughes, K. Westmacott, K.C. Honeychurch, A. Crew, R.M. Pemberton, J.P. Hart, Recent advances in the fabrication and application of screen-printed electrochemical (bio)sensors based on carbon materials for biomedical, agri-food and environmental

analyses, Biosensors. 6 (2016). https://doi.org/10.3390/bios6040050.

[119] N. Jaiswal, I. Tiwari, Recent build outs in electroanalytical biosensors based on carbon-nanomaterial modified screen printed electrode platforms, Anal. Methods. 9 (2017) 3895–3907. https://doi.org/10.1039/c7ay01276d.

[120] E. Eltzov, A. Kushmaro, R.S. Marks, Biosensors for endocrine disruptors, Woodhead Publishing Limited, 2009. https://doi.org/10.1533/9781845695743.2.183.

[121] A. Economou, Enzymatic biosensors, Portable Biosensing Food Toxicants Environ. Pollut. (2013) 123–159. https://doi.org/10.1201/b15589.

[122] M. Nurul Karim, H.J. Lee, Amperometric phenol biosensor based on covalent immobilization of tyrosinase on Au nanoparticle modified screen printed carbon electrodes, Talanta. 116 (2013) 991–996. https://doi.org/10.1016/j.talanta.2013.08.003.

[123] C.C. Mayorga-Martinez, M. Cadevall, M. Guix, J. Ros, A. Merkoçi, Bismuth nanoparticles for phenolic compounds biosensing application, Biosens. Bioelectron. 40 (2013) 57–62. https://doi.org/10.1016/j.bios.2012.06.010.

[124] G. Di Nardo, S. Castrignanò, S.J. Sadeghi, R. Baravalle, G. Gilardi, Bioelectrochemistry as a tool for the study of aromatization of steroids by human aromatase, Electrochem. Commun. 52 (2015) 25–28. https://doi.org/10.1016/j.elecom.2015.01.007.

[125] A. Wang, Y. Ding, L. Li, D. Duan, Q. Mei, Q. Zhuang, S. Cui, X. He, A novel electrochemical enzyme biosensor for detection of 17β-estradiol by mediated electron-transfer system., Talanta. 192 (2019) 478–485. https://doi.org/10.1016/j.talanta.2018.09.018.

[126] E. Povedano, F.H. Cincotto, C. Parrado, P. Díez, A. Sánchez, T.C. Canevari, S.A.S. Machado, J.M. Pingarrón, R. Villalonga, Decoration of

reduced graphene oxide with rhodium nanoparticles for the design of a sensitive electrochemical enzyme biosensor for 17β-estradiol, Biosens. Bioelectron. 89 (2017) 343–351. https://doi.org/10.1016/j.bios.2016.07.018.

[127] A. V. Kuzikov, R.A. Masamrekh, T.A. Filippova, Y.I. Haurychenka, A.A. Gilep, T. V. Shkel, N. V. Strushkevich, S.A. Usanov, V. V. Shumyantseva, Electrochemical oxidation of estrogens as a method for CYP19A1 (aromatase) electrocatalytic activity determination, Electrochim. Acta. 333 (2020) 135539. https://doi.org/10.1016/j.electacta.2019.135539.

[128] K. Mahato, S. Kumar, A. Srivastava, P.K. Maurya, R. Singh, P. Chandra, Electrochemical immunosensors: Fundamentals and applications in clinical diagnostics, Elsevier Inc., 2018. https://doi.org/10.1016/B978-0-12-811762-0.00014-1.

[129] J. Castro-Jiménez, C. Gonzalez, Immunoassay-based screening of polychlorinated biphenyls (PCB) in sediments: Requirements for a new generation of test kits, J. Environ. Monit. 13 (2011) 894–900. https://doi.org/10.1039/c0em00569j.

[130] R.M. Pemberton, T.T. Mottram, J.P. Hart, Development of a screen-printed carbon electrochemical immunosensor for picomolar concentrations of estradiol in human serum extracts, J. Biochem. Biophys. Methods. 63 (2005) 201–212. https://doi.org/10.1016/j.jbbm.2005.05.002.

[131] M.L. Scala-Benuzzi, J. Raba, G.J.A.A. Soler-Illia, R.J. Schneider, G.A. Messina, Novel Electrochemical Paper-Based Immunocapture Assay for the Quantitative Determination of Ethinylestradiol in Water Samples, Anal. Chem. 90 (2018) 4104–4111. https://doi.org/10.1021/acs.analchem.8b00028.

[132] G. Volpe, G. Fares, F. delli Quadri, R. Draisci, G. Ferretti, C. Marchiafava,

D. Moscone, G. Palleschi, A disposable immunosensor for detection of 17β-estradiol in non-extracted bovine serum, Anal. Chim. Acta. 572 (2006) 11–16. https://doi.org/10.1016/j.aca.2006.05.008.

[133] H. Ma, K. Mao, H. Li, D. Wu, Y. Zhang, B. Du, Q. Wei, Ultrasensitive multiplexed immunosensors for the simultaneous determination of endocrine disrupting compounds using Pt@SBA-15 as a non-enzymatic label, J. Mater. Chem. B. 1 (2013) 5137–5142. https://doi.org/10.1039/c3tb20932f.

[134] J. Barek, Possibilities and limitations of mercury and mercury-based electrodes in practical electroanalysis of biologically active organic compounds, Port. Electrochim. Acta. 31 (2013) 291–295. https://doi.org/10.4152/pea.201306291.

[135] I. Ojeda, J. López-Montero, M. Moreno-Guzmán, B.C. Janegitz, A. González-Cortés, P. Yáñez-Sedeño, J.M. Pingarrón, Electrochemical immunosensor for rapid and sensitive determination of estradiol, Anal. Chim. Acta. 743 (2012) 117–124. https://doi.org/10.1016/j.aca.2012.07.002.

[136] L. Gold, SELEX: How It Happened and Where It will Go, J. Mol. Evol. 81 (2015) 140–143. https://doi.org/10.1007/s00239-015-9705-9.

[137] T. Mairal, V. Cengiz Özalp, P. Lozano Sánchez, M. Mir, I. Katakis, C.K. O'Sullivan, Aptamers: Molecular tools for analytical applications, Anal. Bioanal. Chem. 390 (2008) 989–1007. https://doi.org/10.1007/s00216-007-1346-4.

[138] M. Menger, A. Yarman, J. Erdossy, H.B. Yildiz, R.E. Gyurcsányi, F.W. Scheller, MIPs and aptamers for recognition of proteins in biomimetic sensing, Biosensors. 6 (2016). https://doi.org/10.3390/bios6030035.

[139] L. Gatel, A. Cuprys, P. Kumar, G. Suresh, F. Bendourou, M. Chaali, K. Hegde, S.K. Brar, Recent advances in oligonucleotide-based sensor

technology for detection of endocrine-disrupting chemicals (EDC) in the environment, Elsevier Inc., 2019. https://doi.org/10.1016/b978-0-12-814679-8.00007-8.

[140] Y.S. Kim, H.S. Jung, T. Matsuura, H.Y. Lee, T. Kawai, M.B. Gu, Electrochemical detection of 17β-estradiol using DNA aptamer immobilized gold electrode chip, Biosens. Bioelectron. 22 (2007) 2525–2531. https://doi.org/10.1016/j.bios.2006.10.004.

[141] R.A. Olowu, O. Arotiba, S.N. Mailu, T.T. Waryo, P. Baker, E. Iwuoha, Electrochemical aptasensor for endocrine disrupting 17β-estradiol based on a Poly(3,4-ethylenedioxylthiopene)-gold nanocomposite platform, Sensors (Switzerland). (2010). https://doi.org/10.3390/s101109872.

[142] H. Ke, M. Liu, L. Zhuang, Z. Li, L. Fan, G. Zhao, A Fetomolar Level 17β-estradiol Electrochemical Aptasensor Constructed On Hierachical Dendritic Gold Modified Boron-Doped Diamond Electrode, Electrochim. Acta. 137 (2014) 146–153. https://doi.org/10.1016/J.ELECTACTA.2014.06.014.

[143] D. Zhang, W. Zhang, J. Ye, S. Zhan, B. Xia, J. Lv, H. Xu, G. Du, L. Wang, A label-free colorimetric biosensor for 17β-estradiol detection using nanoparticles assembled by aptamer and cationic polymer, Aust. J. Chem. 69 (2016) 12–19. https://doi.org/10.1071/CH14735.

[144] G. Zhang, T. Li, J. Zhang, A. Chen, A simple FRET-based turn-on fluorescent aptasensor for 17B-estradiol determination in environmental water, urine and milk samples, Sensors Actuators, B Chem. 273 (2018) 1648–1653. https://doi.org/10.1016/j.snb.2018.07.066.

[145] K. Vanschoenbeek, J. Vanbrabant, B. Hosseinkhani, V. Vermeeren, L. Michiels, Aptamers targeting different functional groups of 17β-estradiol., J. Steroid Biochem. Mol. Biol. 147 (2015) 10–16.

https://doi.org/10.1016/j.jsbmb.2014.10.013.

[146] K.J. Huang, Y.J. Liu, G.W. Shi, X.R. Yang, Y.M. Liu, Label-free aptamer sensor for 17β-estradiol based on vanadium disulfide nanoflowers and Au nanoparticles, Sensors Actuators, B Chem. 201 (2014) 579–585. https://doi.org/10.1016/j.snb.2014.05.055.

[147] M.H.M. Zaid, J. Abdullah, N. Rozi, A.A.M. Rozlan, S.A. Hanifah, A sensitive impedimetric aptasensor based on carbon nanodots modified electrode for detection of 17ß-estradiol, Nanomaterials. 10 (2020) 1–14. https://doi.org/10.3390/nano10071346.

[148] Z. Li, M.A. Mohamed, A.M. Vinu Mohan, Z. Zhu, V. Sharma, G.K. Mishra, R.K. Mishra, Application of electrochemical aptasensors toward clinical diagnostics, food, and environmental monitoring: Review, Sensors (Switzerland). 19 (2019). https://doi.org/10.3390/s19245435.

[149] H.Y. Kong, J. Byun, Nucleic acid aptamers: New methods for selection, stabilization, and application in biomedical science, Biomol. Ther. 21 (2013) 423–434. https://doi.org/10.4062/biomolther.2013.085.

[150] O. Rabal, F. Pastor, H. Villanueva, M.M. Soldevilla, S. Hervas-Stubbs, J. Oyarzabal, In Silico Aptamer Docking Studies: From a Retrospective Validation to a Prospective Case Study'TIM3 Aptamers Binding, Mol. Ther. - Nucleic Acids. 5 (2016) e376. https://doi.org/10.1038/mtna.2016.84.

[151] J.K. Stroble, R.B. Stone, S.E. Watkins, An overview of biomimetic sensor technology., Sens. Rev. Pp. 29 (2009) 112–119.

[152] M.F. Frasco, L.A.A.N.A. Truta, M.G.F. Sales, F.T.C. Moreira, Imprinting technology in electrochemical biomimetic sensors, Sensors (Switzerland). 17 (2017). https://doi.org/10.3390/s17030523.

[153] G. Díaz-Díaz, D. Antuña-Jiménez, M. Carmen Blanco-López, M. Jesús Lobo-Castañón, A.J. Miranda-Ordieres, P. Tuñón-Blanco, New materials

for analytical biomimetic assays based on affinity and catalytic receptors prepared by molecular imprinting, TrAC - Trends Anal. Chem. (2012). https://doi.org/10.1016/j.trac.2011.09.011.

[154] M. Hussain, J. Wackerlig, P.A. Lieberzeit, Biomimetic strategies for sensing biological species, Biosensors. 3 (2013) 89–107. https://doi.org/10.3390/bios3010089.

[155] R. Viveiros, S. Rebocho, T. Casimiro, Green Strategies for Molecularly Imprinted Polymer Development., Polymers (Basel). 10 (2018). https://doi.org/10.3390/polym10030306.

[156] O.S. Ahmad, T.S. Bedwell, C. Esen, A. Garcia-Cruz, S.A. Piletsky, Molecularly Imprinted Polymers in Electrochemical and Optical Sensors, Trends Biotechnol. 37 (2019) 294–309. https://doi.org/10.1016/J.TIBTECH.2018.08.009.

[157] F. Canfarotta, J. Czulak, A. Guerreiro, A.G. Cruz, S. Piletsky, G.E. Bergdahl, M. Hedström, B. Mattiasson, A novel capacitive sensor based on molecularly imprinted nanoparticles as recognition elements, Biosens. Bioelectron. 120 (2018) 108–114. https://doi.org/10.1016/j.bios.2018.07.070.

[158] C. Zhong, B. Yang, X. Jiang, J. Li, Current Progress of Nanomaterials in Molecularly Imprinted Electrochemical Sensing., Crit. Rev. Anal. Chem. 48 (2018) 15–32. https://doi.org/10.1080/10408347.2017.1360762.

[159] C. Malitesta, E. Mazzotta, R.A. Picca, A. Poma, I. Chianella, S.A. Piletsky, MIP sensors - The electrochemical approach, Anal. Bioanal. Chem. 402 (2012) 1827–1846. https://doi.org/10.1007/s00216-011-5405-5.

[160] S. Piletsky, S. Piletsky, I. Chianella, MIP-based Sensors, Mol. Imprinted Sensors. (2012) 339–354. https://doi.org/10.1016/B978-0-444-56331-6.00014-1.

[161] M.M. Titirici, B. Sellergren, Thin molecularly imprinted polymer films via

reversible addition-fragmentation chain transfer polymerization., Chem. Mater. Pp. 18 (2006) 1773–1779.

[162] G. Cabral-Miranda, M. Gidlund, M.G.F. Sales, Backside-surface imprinting as a new strategy to generate specific plastic antibody materials, J. Mater. Chem. B. 2 (2014) 3087–3095. https://doi.org/10.1039/c3tb21740j.

[163] M.A. Beluomini, J.L. da Silva, A.C. de Sá, E. Buffon, T.C. Pereira, N.R. Stradiotto, Electrochemical sensors based on molecularly imprinted polymer on nanostructured carbon materials: A review, J. Electroanal. Chem. 840 (2019) 343–366. https://doi.org/10.1016/j.jelechem.2019.04.005.

[164] A.A. Lahcen, A.A. Baleg, P. Baker, E. Iwuoha, A. Amine, Synthesis and electrochemical characterization of nanostructured magnetic molecularly imprinted polymers for 17-β-Estradiol determination, Sensors Actuators, B Chem. 241 (2017) 698–705. https://doi.org/10.1016/j.snb.2016.10.132.

[165] D. Futra, L.Y. Heng, M.Z. Jaapar, A. Ulianas, K. Saeedfar, T.L. Ling, A novel electrochemical sensor for 17β-estradiol from molecularly imprinted polymeric microspheres and multi-walled carbon nanotubes grafted with gold nanoparticles, Anal. Methods. 8 (2016) 1381–1389. https://doi.org/10.1039/c5ay02796a.

[166] O. Jamieson, T.C.C. Soares, B.A. de Faria, A. Hudson, F. Mecozzi, S.J. Rowley-Neale, C.E. Banks, J. Gruber, K. Novakovic, M. Peeters, R.D. Crapnell, Screen Printed Electrode Based Detection Systems for the Antibiotic Amoxicillin in Aqueous Samples Utilising Molecularly Imprinted Polymers as Synthetic Receptors, Chemosensors. 8 (2019) 5. https://doi.org/10.3390/chemosensors8010005.

[167] T.N.L. Truong, P. Van Toan, N.Q. Hao, Using AuNPs-modified screen-

printed electrode in the development of molecularly imprinted polymer for artificial bioreceptor fabrication to improve biosensor sensitivity for 17β-estradiol detection, Adv. Nat. Sci. Nanosci. Nanotechnol. 10 (2019). https://doi.org/10.1088/2043-6254/ab0d1b.

[168] Q. Jiang, D. Zhang, Y. Cao, N. Gan, An antibody-free and signal-on type electrochemiluminescence sensor for diethylstilbestrol detection based on magnetic molecularly imprinted polymers-quantum dots labeled aptamer conjugated probes, J. Electroanal. Chem. 789 (2017) 1–8. https://doi.org/10.1016/j.jelechem.2017.02.020.

[169] M.R. Gotrik, T.A. Feagin, A.T. Csordas, M.A. Nakamoto, H.T. Soh, Advancements in Aptamer Discovery Technologies, Acc. Chem. Res. 49 (2016) 1903–1910. https://doi.org/10.1021/acs.accounts.6b00283.

[170] J.L. Bowen, Detection of lipopolysaccharide pyrogens by molecularly imprinted polymers, PQDT - Glob. (2011) 226.

[171] M.H. Lee, J.L. Thomas, W.C. Liu, Z.X. Zhang, B. Da Liu, C.H. Yang, H.Y. Lin, A multichannel system integrating molecularly imprinted conductive polymers for ultrasensitive voltammetric determination of four steroid hormones in urine, Microchim. Acta. 186 (2019). https://doi.org/10.1007/s00604-019-3797-7.

[172] M.H. Lee, J.L. Thomas, Z.L. Su, Z.X. Zhang, C.Y. Lin, Y. Sen Huang, C.H. Yang, H.Y. Lin, Doping of transition metal dichalcogenides in molecularly imprinted conductive polymers for the ultrasensitive determination of 17β-estradiol in eel serum, Biosens. Bioelectron. 150 (2020) 111901. https://doi.org/10.1016/j.bios.2019.111901.

[173] L. Uzun, A.P.F. Turner, Molecularly-imprinted polymer sensors: realising their potential., Biosens. Bioelectron. 76 (2016) 131–144. https://doi.org/10.1016/j.bios.2015.07.013.

[174] Q. Zhao, Y. Faraj, L.Y. Liu, W. Wang, R. Xie, Z. Liu, X.J. Ju, J. Wei, L.Y. Chu,

Simultaneous determination of dopamine, uric acid and estriol in maternal urine samples based on the synergetic effect of reduced graphene oxide, silver nanowires and silver nanoparticles in their ternary 3D nanocomposite, Microchem. J. 158 (2020) 105185. https://doi.org/10.1016/j.microc.2020.105185.

[175] P.A. Raymundo-Pereira, N.O. Gomes, S.A.S. Machado, O.N. Oliveira, Simultaneous, ultrasensitive detection of hydroquinone, paracetamol and estradiol for quality control of tap water with a simple electrochemical method, J. Electroanal. Chem. 848 (2019). https://doi.org/10.1016/j.jelechem.2019.113319.

[176] D. Futra, L.Y. Heng, M.Z. Jaapar, A. Ulianas, K. Saeedfar, T.L. Ling, A novel electrochemical sensor for 17β-estradiol from molecularly imprinted polymeric microspheres and multi-walled carbon nanotubes grafted with gold nanoparticles, Anal. Methods. 8 (2016) 1381–1389. https://doi.org/10.1039/c5ay02796a.

[177] D. YANG, Y., MU, J., DING, Y., WANG, J., LI, J., DU, X., & CHANG, An Immunosensor for Detection of 17β-Estradiol Based on Screen-Printed Electrode with Nano-Gold and Protein-A, Chinese J. Sensors Actuators. 4 (2012) 2.

[178] D. Butler, G.G. Guilbault, Disposable amperometric immunosensor for the detection of 17-β estradiol using screen-printed electrodes, Sensors Actuators, B Chem. 113 (2006) 692–699. https://doi.org/10.1016/j.snb.2005.07.019.

[179] A. Gevaerd, C.E. Banks, M.F. Bergamini, L.H. Marcolino-Junior, Graphene Quantum Dots Modified Screen-printed Electrodes as Electroanalytical Sensing Platform for Diethylstilbestrol, Electroanalysis. 31 (2019) 838–843. https://doi.org/10.1002/elan.201800838.

[180] C.E. Banks, T.J. Davies, G.G. Wildgoose, R.G. Compton, Electrocatalysis

at graphite and carbon nanotube modified electrodes: Edge-plane sites and tube ends are the reactive sites, Chem. Commun. (2005) 829–841. https://doi.org/10.1039/b413177k.

[181] S. Campuzano, M. Pedrero, M. Gamella, V. Serafín, P. Yáñez-Sedeño, J.M. Pingarrón, Beyond sensitive and selective electrochemical biosensors: Towards continuous, real-time, antibiofouling and calibration-free devices, Sensors (Switzerland). 20 (2020) 1–22. https://doi.org/10.3390/s20123376.