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Nanomaterial-based aptasensors and bioaffinity sensors for quantitative detection of 17β-estradiol

Alireza Nezami [a, c], Rahim Nosrati [b, c], Behrouz Golichenari [b, c], Ramin Rezaee [d], Georgios I. Chatzidakis [e], Aristides M. Tsatsakis [e], Gholamreza Karimi [a, *]

[a] Pharmaceutical Research Center, Pharmacy School, Mashhad University of Medical Sciences, Mashhad, Iran
[b] Department of Pharmaceutical Biotechnology, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
[c] Biotechnology Research Center, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
[d] Clinical Research Unit, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
[e] Department of Forensic Sciences and Toxicology, Faculty of Medicine, University of Crete, Heraklion 71003, Greece

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ABSTRACT

One of the most important endogenous estrogens is 17β-estradiol, which disturbed the endocrine system, and causing adverse effects on the growth, reproduction and development of the body. It is necessary to develop a convenient and rapid analytical method to detect estradiol with high sensitivity and selectivity. For determination of 17β-estradiol, methods such as high performance liquid chromatography/mass spectrometry and gas chromatography/mass spectrometry were used. However, these methods often need expensive instruments, complex pretreatment, large volumes of harmful solvents and professional operation. Aptamers have been used as a new biosensor platform for detection of 17β-estradiol in different samples. This article provides an overview of the applications of aptasensors in analysis and monitoring of 17β-estradiol. After a brief description of the steroids, recent advances and applications of aptamer-based biosensors are presented. We have paid attention to the potential role of bioaffinity systems in the detection and quantitative determination of 17β-estradiol.

1. Introduction

Steroids are naturally found in animals, microorganisms and plants and possess a construction of three cyclohexane carbon rings in companion with one pentagonal carbon ring (arranged in a 6–6–6–5 structure), which is attached to various functional groups and side chains. All steroidal compounds derived from cholesterol. Some examples of steroid hormones and their source compound are shown in Table 1. Estrone (E1), 17β-estradiol (E2) and estriol (E3) (main natural estrogens) are C18 steroids that have different oxidation state of their rings. These compounds induce female secondary sexual characteristics and reproductive structures. Moreover, mestranol (MES) or ethinylestradiol (EE2) are synthetic estrogens that are derived from estradiol. Estrogens have been used in animal fattening because of their anabolic effects [1].

One of the most important environmental endogenous estrogens is 17β-estradiol (E2), which is disturbed in the endocrine system, and can cause adverse effects on the growth, reproduction and development of the body and endanger the offspring health [2]. 17β-Estradiol has the strongest estrogen effect when it enters the organism [3]. This entrance can lead to immunological diseases, gender imbalance at birth and reproductive system diseases, etc. [4–9]. Water samples with content of estradiol have been reported by numerous studies [10–14]. Dairy farms, aquaculture facilities, and surface waters with actively spawning fish are the most important sources of environmental pollution. The investigation results indicated that dairy wastes contain up to 650 ng L^{-1} of endogenous estrogens 17β-estradiol, estrone, androgens testosterone and androstenedione. These hormones have been also found around 1 mg L^{-1} in nearby groundwater, nearby surface waters and tile drain likely impacted by animal wastes. Samples from rivers containing spawning adult Chinook salmon have been similar concentrations. Detectable concentrations of steroid hormones in these sources can cause adverse effect on human and other animals because of accumulation capacity [15]. When E2 in water reaches 10–12 mol L^{-1} [16–18], male fish may be feminized [19]. Afterward humans would be greatly affected due to bioaccumulation through food chain even at low concentration of estradiol. In this way, the effect of low dose 17β-estradiol on bone turnover, sex hormone levels, and side effects in older women were studied. According to

* Corresponding author.
E-mail address: karimig@mums.ac.ir (G. Karimi).

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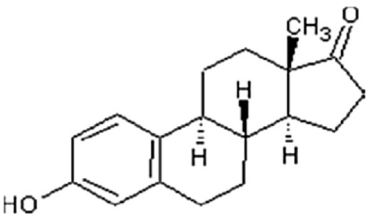
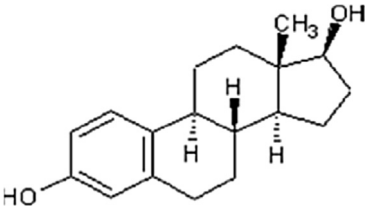
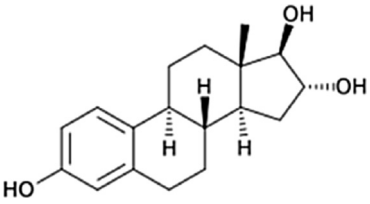
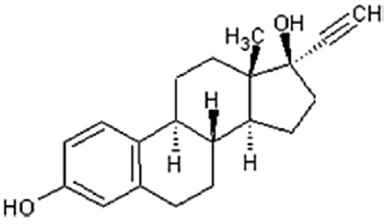
Table 1
Chemical structures and properties of some estrogens.

Name	Systematic name	Synthetic/natural (S)/(N)	Summary structure	Structure
Estrone (E1)	Estra-1,3,5(10) trien-17-one	N	$C_{18}H_{22}O_2$	
17β-estradiol (E2)	Estra-1,3,5(10)-triene-3,17diol	N	$C_{18}H_{24}O_2$	
Estriol (E3)	(16-alpha, 17-beta)estra 1,3,5(10)-triene-3,16,17 triol	N	$C_{18}H_{24}O_3$	
Ethynylestradiol (EE2)	19-norpregna 1,3,5(10)-triene 20-yn-3,17-diol	S	$C_{20}H_{24}O_2$	

the results, low dose of estrogen (0.25 mg/day) lead to reduced bone turnover, increased E2 and estrone levels and increased side effects [20]. Hence, it is necessary to develop a convenient and rapid analytical method for characterization of estradiol with high sensitivity and selectivity to control public and environmental health [10].

Common methods such as HPLC/MS [21], GC/MS [22] and HPLC [23] analysis are sensitive and selective techniques in determination of estradiol; however, these, often need expensive instrumentations, complex pretreatment, usage of large volumes of harmful solvents and professional operation [24]. In the past decade, several biosensors have been established for monitoring and management of 17β-estradiol [25,26]. These biosensors can detect estrogenic compounds, such as 17β-estradiol with notable sensitivity, despite the fact that their specificity is compromised raised from their high affinity to other xenoendocrines and lack of specificity [27,28]. Recently, nanobiosensors and immunosensors have also been broadly used for rapid and sensitive detection of 17β-estradiol along utilizing antibodies or functional polymers.

Among afore-mentioned developed detection strategies, aptamer-based biosensors have attracted considerable attention due to their objectivity that can prepare a specific, sensitive, portable and simple set up for detection [29,30]. Aptamers are short RNA or DNA fragments capable of binding to target molecules with high affinity and specificity [31,32]. The three-dimensional (3D) stability of aptamers offers feasibility in different conditions, which may not be presented by antibody based biosensors. In this article, we pay deep attention to the recent advances in DNA-based aptasensors developed for 17β-estradiol detection. DNA aptamers have some advantage to RNA aptamers. DNA aptamers are easier to handle and identify and more stable than RNA aptamers. The first report of specific DNA aptamer binding to 17β-estradiol, which was selected by the SELEX process, was presented by Kim et al. The selected DNA aptamer probe used in their study was: 5′-Biotin GCTTCCAGCTTATTGAATTACACGCAGAGGGTAGCGGCTCTGCGCATT-CAATGCTGCGCGCTGAAGCGCGGAAGC-3′. This DNA strand was 76-mer and 23 kDa [33]. In other studies, generally same probe is used and some modification employed to increase affinity to 17β-estradiol. Various methods and different approach, such as aptamer modification, as well use of Au and/or other nanoparticles, result in different affinity, accuracy, sensitivity and selectivity. The present review discussed about these methods in the following sections. We classified 17β-estradiol DNA-based aptasensors according to their signal-harvesting methods, including optical and electrochemical approaches.

A summary of the reports on 17β-estradiol aptasensors based on electrochemical and optical methods are provided in Table 2.

2. Aptamer-based 17β-estradiol biosensors

A biosensor provides selective quantitative or semi-quantitative measurement of an analyte by incorporating a biological