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# A novel colorimetric aptasensor for ultrasensitive detection of cocaine based on the formation of three-way junction pockets on the surfaces of gold nanoparticles

Khalil Abnous [a, b, 1], Noor Mohammad Danesh [c, 1], Mohammad Ramezani [a], Seyed Mohammad Taghdisi [d, e, *], Ahmad Sarreshtehdar Emrani [f, **]

[a] Pharmaceutical Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran
[b] Department of Medicinal Chemistry, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
[c] Research Institute of Sciences and New Technology, Mashhad, Iran
[d] Targeted Drug Delivery Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran
[e] Department of Pharmaceutical Biotechnology, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
[f] Cardiovascular Research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

## HIGHLIGHTS

- Cocaine is one of the most illegally abused drugs worldwide.
- A novel colorimetric aptasensor was introduced for detection of cocaine based on the formation of three-way junction pockets on the surfaces of gold nanoparticles (AuNPs).
- Simplicity and rapid detection of cocaine (only 35 min) are some of the unique features of the proposed sensing strategy.
- The sensing strategy showed good specificity and a limit of detection (LOD) of 440 pM for cocaine.
- The sensing method was also successfully applied to detect cocaine in spiked human serum samples.

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## ABSTRACT

Herein, a novel colorimetric aptasensor was introduced for detection of cocaine based on the formation of three-way junction pockets on the surfaces of gold nanoparticles (AuNPs) and the catalytic activity of the surfaces of AuNPs. Simplicity and detection of cocaine in a short time (only 35 min) are some of the unique features of the proposed sensing strategy. In the presence of cocaine, triple-fragment aptamer (TFA) forms on the surfaces of AuNPs, leading to a significant decrease of the catalytic activity of AuNPs and the color of samples remains yellow. In the absence of target, TFA does not form on the surfaces of AuNPs and 4-Nitrophenol, as a colorimetric agent, has more access to the surfaces of AuNPs, resulting in the reduction of 4-Nitrophenol and the color of sample changes from yellow to colorless. The sensing strategy showed good specificity, a limit of detection (LOD) of 440 pM and a dynamic range over 2 −100 nM. The sensing method was also successfully applied to detect cocaine in spiked human serum samples with recovery of 94.71−98.63%.



## 1. Introduction

Cocaine is one of the most illegally abused drugs worldwide which acts as a strong brain stimulant [1,2]. Cocaine abuse can lead to many adverse effects on the human body and even result in cardiac arrest [3,4].

Existing analytical techniques for cocaine detection include gas chromatography (GC), capillary electrophoresis, mass spectrometry

* Corresponding author. Targeted Drug Delivery Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran.
** Corresponding author.
*E-mail addresses:* taghdisihm@mums.ac.ir (S.M. Taghdisi), ahmad_sarreshtedar@yahoo.com (A.S. Emrani).
[1] These authors contributed equally to the work.

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(MS) and high-performance liquid chromatography (HPLC). These methods are sensitive for cocaine detection, but high cost, complicated and time-consuming operation restrict their broad applications [3,5–7]. So, it is highly desirable to introduce sensitive, rapid and cost-effective analytical methods for quantification of cocaine especially in pharmacy and forensic science.

Aptamers are synthetic oligonucleotides which are selected by a technique named systematic evolution of ligands by exponential enrichment (SELEX) [8,9]. Aptamers have the capability to form defined tertiary structures for specific target binding, such as metal cations, organic small molecules, peptides and cells [10–12]. Aptamers exhibit a variety of advantages compared to antibodies, including rapid production, easy synthesis, high stability in different temperatures and pHs and low cost [13–16]. Due to these unique features, aptamers have great potential in development of biosensors.

Among different analytical methods, aptamer-based colorimetric sensors have attracted great attentions due to their simplicity and convenience. Moreover, the results can be observed by the naked eye [17–19].

Gold nanoparticles (AuNPs) are one of the most desired nanoparticles which have been extensively applied in optical sensors, owing to their unique optical characteristics like high extinction coefficient and size-dependent optical characteristics [20–22]. Also, AuNPs can show catalytic activity like reduction of 4-Nitrophenol to 4-Aminophenol in the presence of $NaBH_4$ [23,24].

Target-induced conjugation of cocaine split aptamer fragments has been reported previously [25]. Herein, we developed a novel colorimetric aptasensor for recognition of cocaine, based on the formation of three-way junction pockets on the surfaces of AuNPs and the enzyme-like activity of the surfaces of AuNPs. One of the great benefits of the developed aptasensor is detection of cocaine in a short time (35 min). Furthermore, the three-way junction pockets on the surfaces of AuNPs can warrant that the AuNPs lose their catalytic activity in the presence of cocaine.

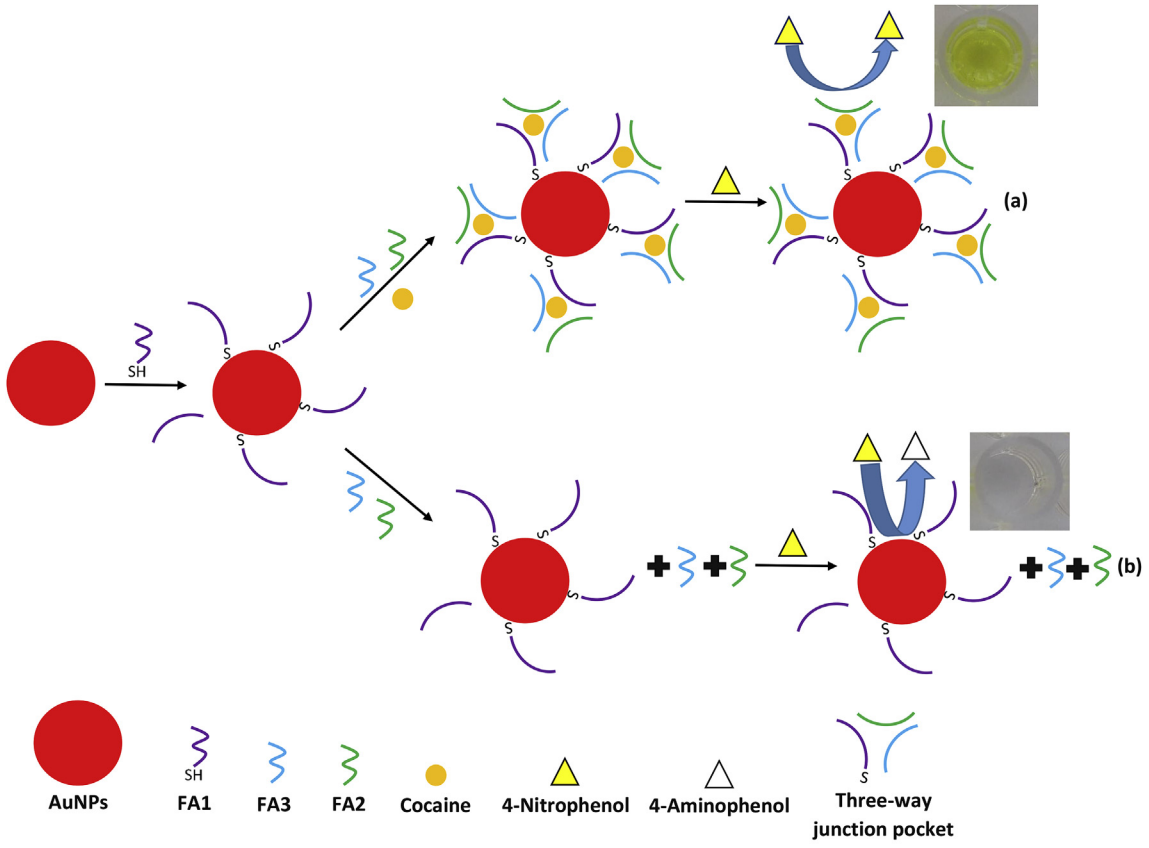
## 2. Experimental section

### 2.1. Reagents and materials

The cocaine triple-fragment aptamer (TFA) [25], including 5′-Thiol-GGGAGTCAAGAAC-3’ (FA1), 5′-GTTCTTCAAT-3’ (FA2) and 5′-AGTGGGACGACA-3’ (FA3) were purchased from Bioneer (South Korea). Gold (III) chloride trihydrate ($HAuCl_4$), cocaine, diazepam, diclofenac, amoxicillin, propranolol, adenosine triphosphate (ATP), Tris(2-carboxyethyl) phosphine hydrochloride (TCEP), 4-Nitrophenol, human serum and sodium borohydride ($NaBH_4$) were obtained from Sigma-Aldrich (USA).

### 2.2. Preparation of gold nanoparticles (AuNPs)

The AuNPs were synthesized by chemical reduction of $HAuCl_4$ with sodium citrate following a literature procedure [26]. In brief, 1 mL $HAuCl_4$ solution (50 mM) and 49 mL deionized water were added into a round-bottom flask. Then, 5 mL sodium citrate solution (38.8 mM) was rapidly added to the above boiled solution and




**Scheme 1.** Schematic illustration of cocaine determination by the three–way junction pockets-based colorimetric aptasensor. In the presence of cocaine, three-way junction pockets forms on the surfaces of AuNPs and prohibit the catalytic activity of the surfaces of AuNPs. Thus, the color of sample remains yellow following the addition of 4-Nitrophenol (a). Without introduction of cocaine, only the FA1 is immobilized on the surfaces of AuNPs and 4-Nitrophenol has access to the surfaces of AuNPs. So, the color of sample changes from yellow to colorless (b).