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Colorimetric detection of sodium ion in serum based on the G-quadruplex conformation related DNAzyme activity

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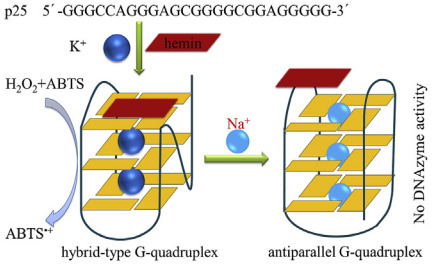
HIGHLIGHTS

- A new insight for developing Na^+ detection technology is provided.
- The mechanism relies on G-quadruplex conformation-related DNAzyme activity.
- The Na^+ sensor can effectively avoid the interference of K^+.
- Detection of the Na^+ level in serum is proved.

GRAPHICAL ABSTRACT



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ABSTRACT

There has been a big challenge in developing the Na^+ sensor that can be practically used in the physiological system with the interference of large amounts of K^+. In this research, a novel Na^+ sensor has been designed based on the G-quadruplex-conformation related DNAzyme activity. The sensor exhibits high selectivity and sensitivity with the detection limit of 0.6 μM, which enables the sensor to be practically used in determination of the Na^+ level in serum. The research not only provides a simple Na^+ sensor but also opens a new way for developing the detection technology of Na^+.

1. Introduction

Sodium (Na) is an essential element in biological systems and important to both cellular and electrical function. The normal range for blood sodium levels is 135–145 mM. The abnormal concentration of Na^+ is related with many diseases such as adrenal gland problems, diabetes insipidus, heart failure, kidney diseases, cirrhosis of the liver, ketonuria, and so on. In many cases, quantitative detection of Na^+ is urgently required which will be an important basis for diagnoses and treatment. Driven by this demand, many techniques focused on Na^+ detection have been developed. The mechanisms are mainly based on ion selective

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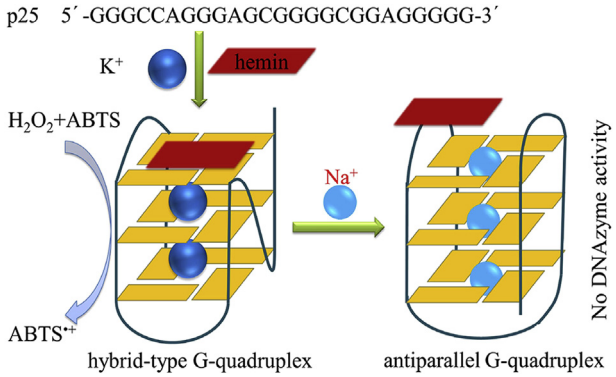

Scheme 1. The schematic illustration for the mechanism of sensing Na^+ based on the G-quadruplex conformation-related DNAzyme activity.

electrodes [1], the complexation of Na^+ with crown ethers [2–5] and other organic molecules [6]. Nevertheless, a simple technology that can accurately quantify Na^+ in the real samples with excessive K^+ present is still a challenge.

Recently, G-quadruplex, a special four-stranded DNA secondary structure formed by G-rich oligonucleotides, has attracted great attention in developing ion and biomolecule detection technology/sensors owing to its structural sensitivity towards some specific ions [7–12]. A typical technology is using the complex of G-quadruplex and hemin to mimic DNAzyme [13–17]. The main mechanism is that G-rich oligonucleotide is induced by a specific metal ion to form a parallel or hybrid-type G-quadruplex structure, which binds with hemin and catalyzes the H_2O_2-mediated oxidation of 2,2-azinobis(3-ethylbenzothiazoline)-6-sulfonic acids (ABTS) or luminol [18]. Many sensors of K^+ [19,20], Pb^{2+} [21,22], Hg^{2+} [23], and Ag^+ [24,25] have been developed based on this mechanism. But no Na^+ sensor has been proposed based on the G-quadruplex DNAzyme. The challenge is that most G-quadruplexes are much more sensitive towards K^+ than that towards Na^+ [26,27], and thus selective detection of Na^+ is difficult in the physiological system with a large amount of K^+ present.

However, there are specific G-quadruplexes exhibiting different conformations responding to K^+ and Na^+ [28], and a conformational transition of G-quadruplexes will happen with increasing amounts of Na^+ in the presence of K^+. The G-quadruplexes with different conformations may have different binding affinity towards hemin and thus show a great discrepancy in DNAzyme activity. Thus a decrease of DNAzyme activity will happen with the Na^+-induced conformational transition of G-quadruplexes. According to this mechanism, design of a Na^+ sensor is possible.

To design such a Na^+ sensor, the G-quadruplex (named p25) that shows a hybrid-type conformation with K^+ but an antiparallel conformation with Na^+ is developed to construct DNAzyme (Scheme 1). With increasing the concentrations of Na^+ in the presence of K^+, p25 G-quadruplex exhibits a conformational transition from hybrid-type to antiparallel, resulting to a decrease of the p25-hemin DNAzyme activity. A colorimetric probe of Na^+ is thus designed on the basis of this mechanism.

2. Materials and methods

2.1. Sample preparation

The oligonucleotide p25 was purchased from Invitrogen (Shanghai, China), purified by PAGE. Tris (hydroxymethyl) aminomethane (Tris), NaCl, KCl, and ethylenediaminetetraacetic acid (EDTA) are analytical grade. Ultrapure water prepared by Milli-Q Gradient ultrapure water system (Millipore) was used throughout the experiments. The G-quadruplex DNAzyme was prepared by dissolving the oligonucleotides and hemin directly into 10 mM Tris–HCl buffer solution containing 2 mM KCl.

2.2. Spectroscopy measurement

Circuit Dichroism (CD) spectra were collected from 200 to

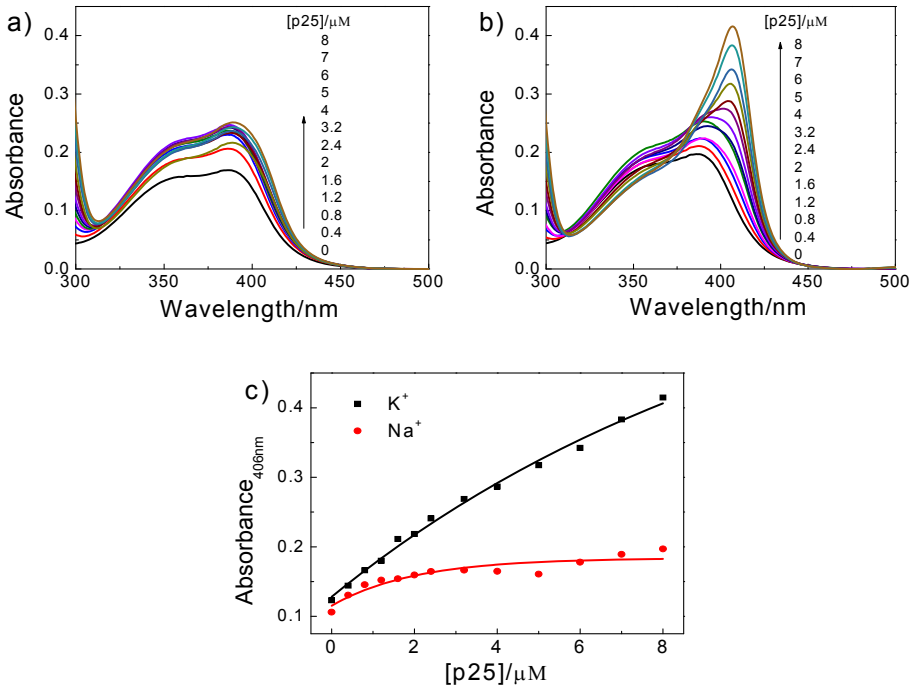

Fig. 1. a) The absorption spectra of 4 μM hemin with increasing amounts of p25 G-quadruplexes in the presence of 10 mM Na^+. b) The absorption spectra of 4 μM hemin with increasing amounts of p25 G-quadruplexes in the presence of 10 mM K^+. c) The plot of the absorbance at 406 nm versus [p25]. All the above samples are prepared in 10 mM Tris–HCl solution (pH 7.0).