Journal of Photochemistry and Photobiology A: Chemistry 348 (2017) 246–254

Contents lists available at ScienceDirect

Journal of Photochemistry and Photobiology A: Chemistry

journal homepage: www.elsevier.com/locate/jphotochem

Invited paper

A water soluble, highly sensitive and selective fluorescent probe for Al^{3+} ions and its application in live cell imaging

Shraddha Rani Gupta[a], Priya Singh[b], Biplob Koch[b], Vinod P. Singh[a,*]

[a] Department of Chemistry, Banaras Hindu University, Varanasi 221005, India
[b] Department of Zoology, Banaras Hindu University, Varanasi 221005, India

ARTICLE INFO

Article history:
Received 16 June 2017
Received in revised form 31 July 2017
Accepted 20 August 2017
Available online 24 August 2017

Keywords:
Aminothiazole
Fluorescent probe
^{1}H NMR titration
Binding constant
Detection limit
Live cell imaging

ABSTRACT

An efficient, aminothiazole based, fluorescent probe (*E*)-2-(2-aminothiazol-5-yl)-*N*'-((2-hydroxynaphthalen-1-yl)methylene)acetohydrazide (NTH) for the detection of Al^{3+} ions was synthesized and characterized by different physico-chemical and spectroscopic tools. An attractive glowing blue color was observed in the presence of Al^{3+} with single channel emissions for NTH (λ_{em} 451 & λ_{ex} 391 nm). NTH, selectively detected Al^{3+} ions among various other ions without any significant interference in Tris-HCl buffer solution (10 mM, pH ~ 7.4). The >C=N— isomerization was responsible for the turn 'on' fluorescence response after Al^{3+} binding. The stoichiometry of NTH with Al^{3+} was determined to be 1:1 by Job's plot. The binding constant and limit of detection (LOD) were observed as $3.65 \times 10^9\ M^{-1}$ and 1.09×10^{-9} M, respectively. The ^{1}H NMR titration and DFT studies were also performed in support of binding details of NTH-Al^{3+} complex. MTT assay on live A549 cells suggested viability of the probe to A549 cells even at higher concentration (100 μM) with no serious cytotoxicity in cells. Live cell imaging study clearly indicated that the accumulation of Al^{3+} in the cytoplasm of cells could be detected by NTH.

1. Introduction

Design of chemosensors, which can selectively recognize and signal the presence of specific analytes through the naked eye and optical responses, has received significant attention over the years because of their potential use in medicine, environment and biology [1]. Aluminium is the most abundant element in the earth's crust after oxygen and silicon, and is the second most widely used metal after iron for the manufacture of electrical equipments, automobiles, packaging materials, clinical drugs, building construction, cookware, drinking water supplies, antiperspirants, antacids and computers etc [2,3]. Detection of aluminium in mixed metal environment is of general concern. On the basis of their difference of responses in fluorescence emission, Schiff bases and related heterocyclic compounds are generally used for the detection of aluminium ions [4–7]. The use of Schiff bases in homogeneous or heterogeneous conditions may have long standing impact to design probes for detection of aluminium ions [8–11]. Schiff bases, having one or two azomethine (>C=N—) groups are among the most important ligands used in modern coordination chemistry due to their well-known coordinating capability [12–15]. These Schiff bases and their complexes have wide applications in different areas of electrochemistry, catalysis, extraction of metal ions and various types of polymerization [16–20]. Moreover, they are also used as corrosion inhibitors, highly selective polymer membrane electrodes, optical sensors and biological probes [21].

Previously, our group has reported a number of sensors based on an aromatic platform, which had imine, hydroxyl and hydrazides as probes for sensing [22–26]. In the present investigation, we have synthesized a new fluorescent probe which is superior over other similar synthesized probes [27–29]. The selected probe, (*E*)-2-(2-aminothiazol-5-yl)-*N*'-((2-hydroxynaphthalen-1-yl)methylene)acetohydrazide (NTH) has strong binding affinity for Al^{3+} in complete water medium with very low detection limit. All the sensing studies of NTH for the detection of Al^{3+} ions have been carried out at physiological pH of ~7.4. NTH can easily be synthesized by a simple and one step condensation reaction. The components used for the synthesis of NTH are inexpensive, biocompatible and provide binding sites for the target metal ions. The selection of 2-hydroxy-1-naphthaldehyde as a second moiety of the Schiff base is due to its short fluorescence lifetime, low quantum yield and ability to act as a donor as well as an acceptor [30]. 2-Hydroxy Schiff base ligands are of interest mainly due to the

* Corresponding author.
E-mail address: singvp@yahoo.co.in (V.P. Singh).

http://dx.doi.org/10.1016/j.jphotochem.2017.08.055
1010-6030/

existence of O—H···N or O···H—N type hydrogen bonds and tautomerism between phenol-imine and keto-amine forms [31]. From the literature survey, it appears that very few work on Schiff bases of 2-aminothiazole have been reported as fluorescent probe for Al^{3+} [32]. The present work on 2-aminothiazole derived Schiff base as a probe for selective detection of Al^{3+} in Tris-HCl buffer (10 mM, pH ~ 7.4), follows chelation enhanced fluorescence (CHEF) mechanism [33] and is reported for the first time. In addition, NTH has found practical application in the estimation of Al^{3+} in live human lung cancer cells (A549) using a confocal microscope.

2. Experimental

2.1. Materials and methods

All analytical reagent grade chemicals were obtained from the commercial sources. All metal chloride salts were purchased from Merck Chemicals, India. 2-Hydroxy naphthaldehyde, 2-(2-aminothiazol-5-yl)acetohydrazide and tris (hydroxymethyl) aminomethane (Tris-HCl buffer) were purchased from Sigma–Aldrich Chemicals, USA. Triple distilled water was used after checking its purity thoroughly by UV–vis and fluorescence spectral techniques. Dulbecco's Modified Eagle's Medium (DMEM), Fetal Bovine Serum (FBS) were purchased from Gibco, antibiotic solution (Penicillin 1000 IU and Streptomycin 10 mg/ml) from cell clone, trypsin-EDTA was purchased from Genetix and MTT [3-(4,5-dimethylthiazolyl-2)-2,5-diphenyltetrazoliumbromide] from Himedia Laboratories, India and DMSO from Merck, India.

2.2. Instrumentation

C, H, N contents were determined on an Exeter Analytical Inc. CHN Analyzer (Model CE-440). ^1H and ^{13}C NMR spectra were recorded in DMSO-d_6 on a JEOL AL-500 FT-NMR multinuclear spectrometer. Chemical shifts were reported in parts per million (ppm) using tetramethylsilane (TMS) as an internal standard. Infrared spectra were recorded in KBr on a Perkin Elmer FT-IR spectrophotometer in the 4000–400 cm^{-1} region. UV–vis spectra were recorded in Tris-HCl buffer (10 mM, pH ~ 7.4 maintained by adding HCl) on a Shimadzu spectrophotometer, Pharmaspec UV-1700 model. Fluorescence spectra were recorded on a Cary-Eclipse Fluorescence spectrophotometer (Agilent Technologies). Mass spectrometric analysis was carried out in acetonitrile on a Waters-Q-Tof Premier-HAB213 mass spectrometer.

2.3. General methods

UV-vis, fluorescence and ^1H NMR titration experiments were carried at room temperature. For UV–vis titration experiment, 10 μM solution of NTH in Tris-HCl buffer (pH ~ 7.4) was used and for fluorescence titration studies, 5 μM NTH in Tris-HCl buffer (pH ~ 7.4) was used. The solutions of metal chloride salts were prepared in triple distilled water. ^1H NMR titration was performed by treating 10^{-2} M solution of NTH in DMSO-d_6 with 10^{-2} M solution of Al^{3+} in D_2O and varying the equivalents (0.2, 0.5, 0.7 and 1.0) of Al^{3+}.

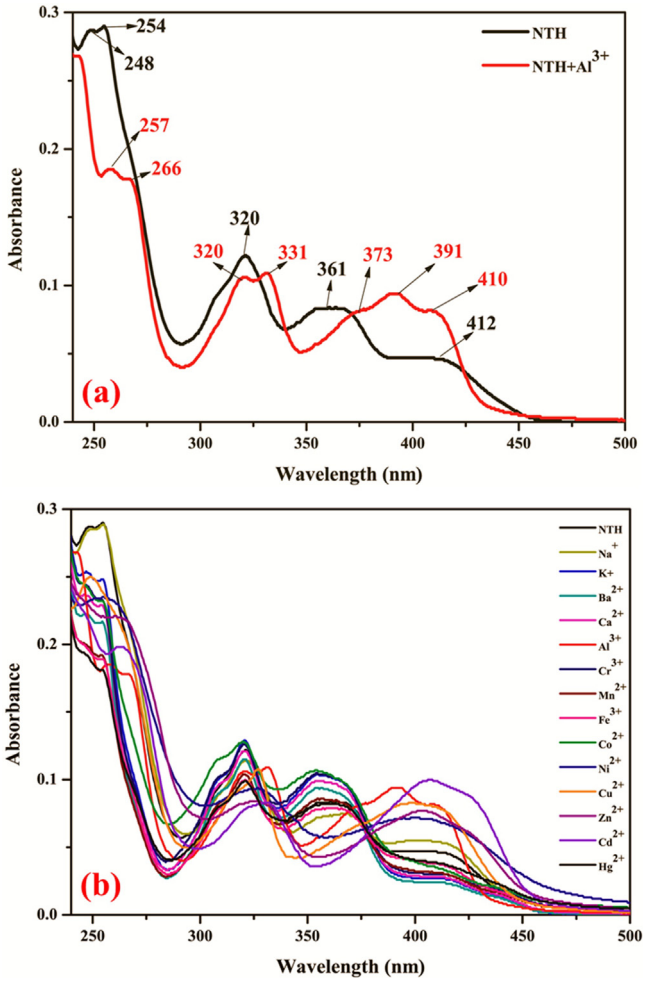


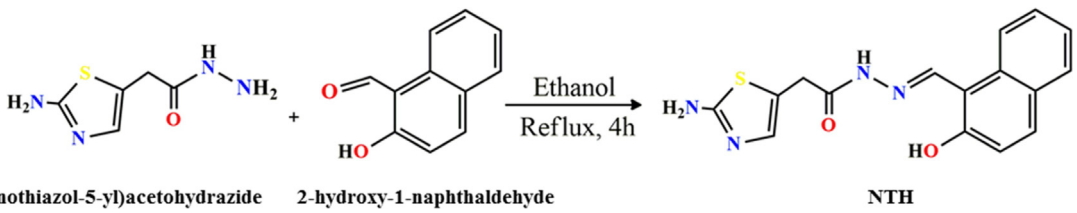
Fig 1. (a) Absorption spectra of NTH and NTH + Al^{3+} in Tris-buffer (10 mM, pH ~ 7.4) (b) Effect of addition of various metal ions (1 equivalent) on the UV–vis spectra of 10 μM NTH in Tris-HCl buffer solution (10 mM, pH ~ 7.4).

NTH-Al^{3+} binding ratio was determined by Job's plot, while the binding constant (K_B) was analyzed by the linear fitting of fluorescence titration curve in modified Benesi-Hildebrand equation for spectro-fluorometric titration (Eq. (1))

$$I_o/I - I_o = (a/b - a)\,(1/K_B\,[\text{substrate}] + 1) \quad (1)$$

Where, I_o and I are fluorescence intensities of NTH at 451 nm in the absence and presence of Al^{3+}; a & b are constants; [substrate] is the concentration of the Al^{3+}.

The detection limit of NTH probe for the analysis of Al^{3+} was determined from a plot of fluorescence intensity as a function of the concentration of the added Al^{3+} ions. To determine the S/N



Scheme 1. Synthesis of probe NTH.