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Novel chemical sensor for detection Ca(II) ions based on ferutinin

Sayed M. Saleh [a,b,*], Eman M. Elkady [c], Reham Ali [a,d], Fahad Alminderej [a], Tarik A. Mohamed [e]

[a] Chemistry Department, Science College, Qassim University, Buraidah, Saudi Arabia
[b] Chemistry Branch, Department of Science and Mathematics, Faculty of Petroleum and Mining Engineering, Suez University, 43721 Suez, Egypt
[c] Marine Chemistry lab, National Institute of Oceanography & Fisheries, Suez, Egypt
[d] Chemistry Department, Science College, Suez University, 43518 Suez, Egypt
[e] Chemistry of Medicinal Plants Department, National Research Centre, 12622, 33 El Bohouth St., Dokki, Giza, Egypt

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ABSTRACT

A new optical chemical sensor based on medicinal compound, jaeschkeanadiol *p*-hydroxyben-zoate (Ferutinin), has been designed and utilized for Ca(II) ions detections. This natural optical sensor exhibits immense selectivity including fluorescence and absorption ratiometric for Ca(II) ions within precious physiological pH range. Further, the chelation process of the Ca(II) ions with the medicinal optical sensor ferutinin yields a 1:1 (metal: ligand) complex which is accompanied by fluorescence enhancement of the main emission band centered at 355 nm of the medicinal probe. The fluorescence "turn-on" effect is a clear evidence for the chelation process between ferutinin medicinal probe and Ca(II) ions and this could be simply detected. The new sensor was proposed depending on significant fluorescence mechanism, (MLCT, metal-ligand charge transfer). However, the interaction of the medicinal optical sensor with Ca(II) in presence of other cations was examined without any significant interference. Also, the new developed optical sensor consecutively exhibits low limit of detection (LOD) 1.5 nM for Ca(II) which is detected in very significant physiological pH range ($pH = 7.4$). Also, the probe provides high binding affinity towards Ca(II) with large binding constant K_b 5.97×10^4 M^{-1}. As a result, this optical sensor may apply for detection Ca(II) in cell or biological samples.

1. Introduction

Much considerable attentions were provided for detection several types of metal ions utilizing optical chemosensor techniques [1]. Memorable, several metal ions exist in man blood plasma significantly Ca(II) ions [2], the design and development of optical sensor in order to detect and measure the content of this biologically vital metal ion has been attracted more attentions in clinical analysis [3]. Chemical sensors based on significant dye or chemical probe exhibit distinctive optical properties and have the ability to change their fluorescence or absorption properties upon chelation process with the analyte ions or gust molecules [4]. Many researches were applied to improve the sensitivity and selectivity of the chemosensor for recognition and detection numerous metal ions especially Ca(II) ions, which take a significant part in distinct biological systems and attract more consideration [5]. Additionally, these ions showed prospective extreme value in several fields such as food [6], medicinal science and cellular applications [7]. Several chemical probes were developed and designed for measuring and recognition Ca(II) ions based on diverse molecular structures involving organic probes [8–11], nanomaterials [12–14] and protein [15]. Also, chemical sensors provide a unique technique in sensing because they offer easy naked eye recognition of Ca(II) ion. Therefore, several chemical and colorimetric molecules have been developed and used in order to detect Ca(II) ions [16], but there are some important limitations confront with utilizing of these chemical probes such as presence of different metal ions in the environment medium especially Zn(II) [17].

The crucial requisite for the development and designing of suitable materials for usage as chemical sensor or bio-sensor in numerous fields, involving in-vitro and in-vivo, food science and medicine [18,19], has presently inspired huge number of scientists to develop and apply chemical probes able to tracing a specified molecule or metal cations. Between the plentiful applied detection techniques performed, much more consideration has been offered to chemical sensors that have the attendance to change their fluorescence in the presence of gust molecules. These optical sensors show unique advantages such as sigh sensitivity, rapid detection, distinctive resolution and biological applications [20–22]. One of the most sensing applications is the usage of the fluorescence alteration which is accompanied by enhancement or quenching of the emission intensity of the chemical probes due to addition of gust molecule or metal ions [23–27].

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* Corresponding author at: Chemistry Branch, Department of Science and Mathematics, Faculty of Petroleum and Mining Engineering, Suez University, 43721 Suez, Egypt.
E-mail addresses: sayed.saleh@suezuniv.edu.eg e.saleh@qu.edu.sa (S.M. Saleh).

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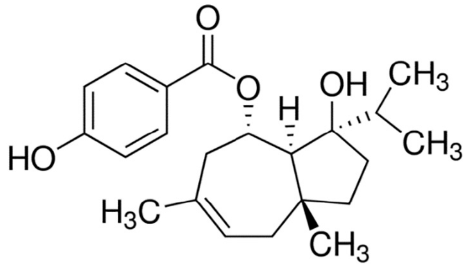

Fig. 1. Chemical structure of ferutinin isolated from *Ferula hermonis*.

On the other hand, many significant factors control the efficiency of the fluorescence sensor including photo-bleaching of the utilized chemical probe, limit of concentration of the guest molecule, the pH of the surrounding medium, solvent polarity and temperature. Ratiometric measurement is one of the most considerable sensing techniques [28]. This can be established by utilizing two different probes or dyes, where one of these dyes works as a reference signal and the other uses for analyte detection [29]. The emission intensities ratio between the sensitive and reference dyes is utilized as a function of analyte concentration. The selection of the two dyes is typically critical because they have to be excited under the same wavelength. However, the ratiometric technique is proposed with utilizing one dye or chemical probe, which has considerable alterations in the fluorescence intensities or UV–vis absorption at two separated wavelengths [30]. Thus, several optical chemosensor provide signal ratiometry based on significant probes [31]. Moreover, the ratiometric techniques increase the dynamic range and decrease the effects of surrounding factors.

Simultaneous recognitions of the significant analyte based on the alteration of optical properties is often used technique that conducted by fluorescence quenching “switching off” mechanism [32] or fluorescence enhancement “switching on” mechanism. Further, the mechanism of the chemosensor could be attributed to the replacement of hydrogen protons of the chemosensor probe during the chelation process of Ca (II) ions. Switching on sensing mechanism displays distinctive advantages with respect to switching off mechanism [33] including low detection limit of gust ions and the low interfering with the background fluorescence of the chemical probe which is inversely proportional to the analyte concentration [34]. These two factors mainly neglect the pseudo signal probability and control the chemosensor efficiency, selectivity and sensitivity. In case of both mechanisms of “switching on” [35] or “switching off” [36], MLCT has been widely applied to deduce the optical interaction of many chemosensors [37–40].

In this paper we introduce a novel optical chemical sensor based medicinal probe for Ca(II) detection. The new optical sensor is based on the utilization of jaeschkeanadiol *p*-hydroxybenzoate (Ferutinin) medicinal probe. The interaction mechanism could be attributed to MLCT mechanism between the medicinal probe and Ca(II) during chelation process [41]. The UV–vis absorption and fluorescence measurements of the free ligand (ferutinin) and in the presence of Ca(II) have been studied. The new sensor shows high selectivity with good value of LOD, high sensitivity and rapid reversibility for detection Ca(II) ions.

2. Instruments and Materials

Pre-coated silica gel plates (Merck, Darmstadt, Germany, Kieselgel 60 F_{254}, 0.25 mm) were used for TLC analyses. Spots were visualized by heating after spraying with 5% H_2SO_4 and 1% vanillin. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNMECA 600 spectrometer (600-MHz for ^1H and 150-MHz for ^{13}C) with reference to TMS as an internal standard. The melting point was measured using a Kofler microhot stage apparatus. The mass spectra of the isolated compound were recorded with an API QSTAR pulsar mass spectrometer. The UV–vis spectra were obtained using a 1-cm quartz cell utilizing (Evolution™_200-series/UV–Visible) spectrophotometer. Fluorescence spectra were determined on a (JASCOFP6300-spectrofluorometer) using a 1 cm quartz cell for the emission and excitation spectral measurements. Chemicals were obtained from (Sigma-Aldrich).

3. Extraction of Ferutinin

The extraction and isolation process of ferutinin was carried out according to recent literature [42]. The air-dried aerial part of *Ferula hermonis* (500 g) was extracted with CH_2Cl_2/MeOH (1:1) at 25 °C for 48 h. After solventremoval,10 g of the dried yield (45 g) was exposed to gravity chromatography in a silica gel column (100 cm × 3 cm), eluted with *n*-hexane followed by gradient of *n*-hexane/Et-OAc up to 100% Et-OAc. Fractions were combined (2 g) based on TLC similarities, concentrated in vacuo, followed by re-purification on silica gel CC, eluted with 10% of hexane/Et-OAc to afford Ferutinin (800 mg). The structure of ferutinin was confirmed by spectroscopic analysis especially NMR spectra. Ferutinin: ^1H NMR (600 MHz):$\delta_{\mathbf{H}}$ 0.87 (3H, d, $J = 6.5$ Hz, H-12), 0.96 (3H, d, $J = 6.5$ Hz, H-13), 1.10 (3H, s, H-15), 1.85 (3H, s, H-14), 1.96 (1H, m, H-10a), 2.01 (1H, d, $J = 10.0$ Hz, H-5), 2.05 (1H, dd, $J = 13.5$, 7.5 Hz, H-10b), 2.25 (1H, dd, $J = 13.5$, 2.5 Hz, H-7b), 2.55 (1H, dd, $J = 13.5$, 7.5 Hz, H-7a), 5.24 (1H, ddd, $J = 10.0$, 10.0, 2.5 Hz, H-6), 5.56 (1H, br, H-9), 6.90 (2H, d, $J = 8.6$ Hz, H-3′, H-7′), 7.95 (2H, d, $J = 8.6$ Hz, H-4′, H-6′). ^{13}C NMR (150 MHz): $\delta_{\mathbf{C}}$ 167.1 (C-1′, C=O), 161.0 (C-5′), 133.5 (C-8), 132.0 (C-3′, C-7′), 125.3 (C-9), 122.0 (C-2′), 115.5 (C-4′, C-6′), 86.9 (C-4), 71.2 (C-6), 60.1 (C-5), 41.5 (C-7), 41.2 (C-2), 40.1 (C-10), 37.1 (C-11), 31.5 (C-3), 26.5 (C-14), 20.1 (C-15), 18.6 and 17.6 (C-12, C-13).

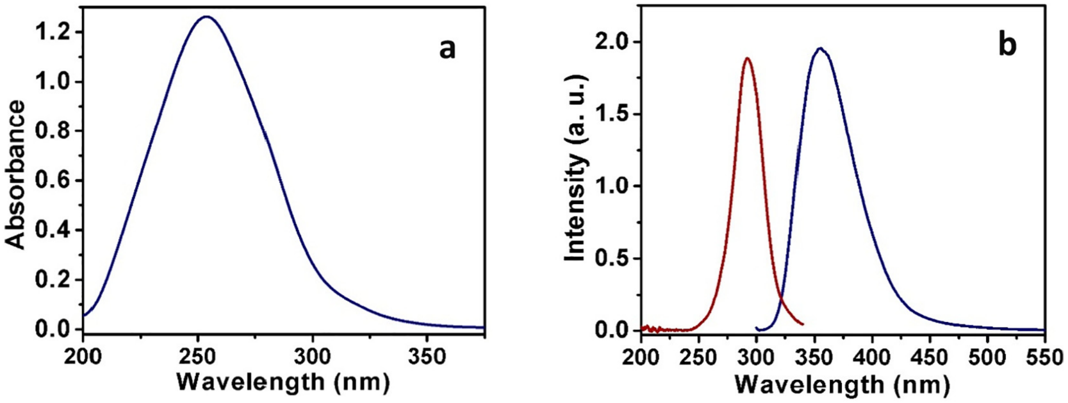

Fig. 2. The optical properties of the ferutinin optical sensor in aqueous medium (a) UV–vis absorption; (b) Fluorescence spectrum.