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# Nicotine – Metal ion interactions in solutions: Potentiometric, cyclic voltammetry investigations and quantum chemical calculations

Ahmed E. Fazary [a,b,*], Yi-Hsu Ju [c], Khaled F. Fawy [a], Ayed S. Al-Shihri [a], Mutasem Z. Bani-Fwaz [a], Mohammad Y. Alfaifi [d], Ali A. Shati [d], Serag Eldin I. Elbehairi [b], Hisham S.M. Abd-Rabboh [a,e]

[a] *Chemistry Department, Faculty of Science, King Khalid University, Abha 9004, Saudi Arabia*
[b] *Applied Research Sector, Egyptian Organization for Biological Products and Vaccines (VACSERA Holding Company), 51 Wezaret El-Zeraa St., Agouza, Giza, Egypt*
[c] *Chemical Engineering Department, National Taiwan University of Science and Technology, 43 Keelung Rd., Taipei, Taiwan, ROC*
[d] *Biology Department, Faculty of Science, King Khalid University, Abha 9004, Saudi Arabia*
[e] *Department of Chemistry, Faculty of Science, Ain Shams University, Cairo 11566, Egypt*

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## ABSTRACT

The experimental protonation and complex formation equilibrium constants of nicotine (NIC) with trivalent (iron (III), and chromium (III)) and divalent (copper (II), and nickel (II)) metal ions have been investigated at 310.15 $^{o}$K in water solutions at ionic strength of 13.60 g·dm$^{-3}$ $NaNO_3$ using pH-potentiometric and cyclic voltammetry techniques, and by means of Hyperquad 2008 estimation model program. Also, the dissociation constants of NIC and the equilibrium constants of its binary complexes with the studied metal ions in 13.60 g·dm$^{-3}$ $NaNO_3$ water solutions were observed at different temperatures such as (298.15, 310.15, 318.15 and 328.15) K. The theoretical calculations of overall protonation and stability constants of the metal ion-nicotine complex species in aqueous solutions were predicted as the Gibbs energy change associated with the nicotine protonation, and metal ion – nicotine complex formation equilibria using *ab initio* and density function theory calculations by applying Gaussian 09 software molecular modeling. The usage of the experimental potentiometry/spectrophotometry techniques and theoretical predictions provides a complete picture of the microscopic equilibria of the studied systems (metal ions -nicotinate). Precisely, this theoretically predications could be useful to control the most real protonation constants of nicotine ligand in which the binding sites changes due to the ligand protonation/deprotonation equilibria. Also, the complexing capacities of different metal ions towards nicotine in solutions were evaluated and discussed. From the determined experimental stability constants of different metal complex species, the concentration distribution diagrams of the various metal ions - nicotine complex species in solutions were estimated using HySS 2009 software.

## 1. Introduction

Nicotine (NIC) is an oxygenic alkaloid compound which consists of a pyridine ring, substituted at the 3-position with an N-methylpyrrolidine ring (Scheme 1) [1] is extracted mainly from the *Nicotiana tabacum* plant, although it is found in smaller amounts amongst other plants of the *Solanaceae* family [1]. It functions as an parasympathomimetic, stimulant drug, antiherbivore, insecticide, imidacloprid, nicotinic acetylcholine receptor agonist, and recently chromatin-modifying enzymes inhibitor [1]. Nicotine was considered to be one of the most biologically important compounds [1], for which information about their metal ions complexation properties are very rare in the literature. A few detailed crystal structures of metal complexes of (S)-(-)-nicotine had been found in the literature such as nicotine complexes of Hg(II) [2–4], Cu(II) [5–11], Ag(I) [12], Zr(III) [13], Zn(II) [7,14,15], Pt(IV) [16], Mn(II) [10], La(II), Pr(III), and Nd(IV) [17,18], Pd(II) [4], Co(II) [19] metal ions. Most of these previous X-ray crystal structures indicates that only two of the possible three bonding modes of nicotine (Scheme 2) have been observed; coordination of the pyridine nitrogen, and coordination of both the pyridine and pyrrolidine nitrogen, where the nicotine molecule acts as a bridging ligand.

Zinc(II) complexation with pure nicotine was used in a simple, economical and quick method for extraction of pure nicotine from *Nicotiana tabacum* and subsequent removal of the metal as ZnS [20]. The chemical investigation of the interaction mechanisms of

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* Corresponding author at: King Khalid University, Chemistry Department, Faculty of Science, 9004, Saudi Arabia.

*E-mail addresses:* afazary@kku.edu.sa, aefazary@gmail.com (A.E. Fazary).

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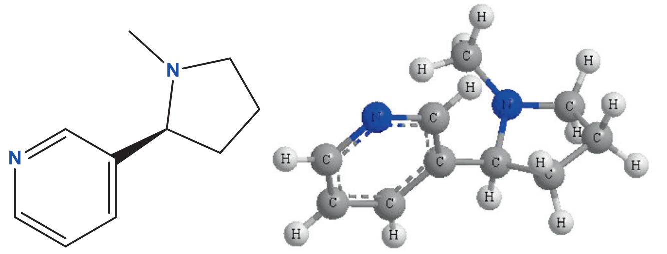
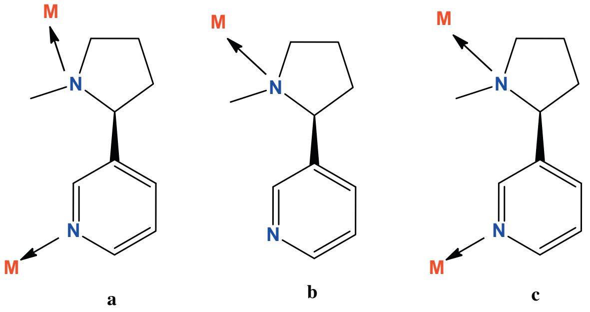


**Scheme 1.** Molecular Structure of Optically active (S)-Nicotine and its Computer Generated Model.



**Scheme 2.** Three Possible Coordination Modes of (S)-Nicotine Molecule. (a) Monodentate Coordination via the Pyridine Nitrogen. (b) Monodentate Coordination via the Pyrrolidine Nitrogen. (c) Bidentate Coordination via both Nitrogen atoms.

nicotine with some divalent metal ions such as Pb(II), Fe(II), and Cu (II) [21] were investigated recently by Professor Manfredi [21] at room temperature, in solutions using UV/Vis spectrophotometric and potentiometric techniques [21]. Several transition metals such as iron (Fe), chromium (Cr) cobalt (Co), nickel (Ni), and copper (Cu) are known to play important roles in biochemical functions such as acting as cofactors for many enzymes, helping nerve transmission and maintaining the nutrition balance [22]. As known, the deficiency of essential metals initiates several undesirable health problems and may also affect daily performance. However, the nutrient balance problems not only occur due to nutrients deficiency but also when the nutrients are taken excessively. The *d*-block elements are often become a health concern since their present easily exceeds the require amount in the body and cause poisoning [23]. Herein, with the continuation of my research on the interactions of bioactive ligands with different metal ions [24–34], the interaction of nicotine with different metal ions was conducted. The experimental protonation and complex formation equilibrium (pKa, and log β values) constants of nicotine (NIC) with trivalent (iron (III), and chromium (III)) and divalent (copper (II), and nickel (II)) metal ions have been investigated at 310.15 K in aqueous solutions and in fixed ionic strength (13.60 g·dm$^{-3}$ $NaNO_3$) using pH-potentiometric, and cyclic voltammetry techniques. The dissociation constants of NIC ligand as well as the stability constant of its binary complexes with the studied metal ions in aqueous solution with ionic strength (13.60 g·dm$^{-3}$ $NaNO_3$) were observed at different temperatures of (298.15, 310.15, 318.15 and 328.15) K. The metal ion complexing capacities of nicotine and their overall stability constants in aqueous solutions were obtained by the HYPERQUAD 2008 program from the potentiometric data. The molecular structures of nicotine –metal complexes formed in solutions were determined based on some spectral methods, and molecular modeling computer programs such as Gaussian 09. The graphic representation of the complex species concentration curves was given by the distribution diagram performed by means of HySS 2009 modeling program, which furnishes a variety of data presentations, including tables of concentrations of all species present in solution in the selected pH ranges.

## 2. Experimental

### 2.1. Materials, chemicals and solutions

All the chemicals, materials, and organic solvents used in this work were of analytical reagent grade and were used without further purifications (Table 1). An optically active form of nicotine having *S*-configuration, ((S)-3-(1-methylpyrrolidine-2-yl) pyridine, NIC, $C_{10}H_{14}N_2$, 0.99999 mass fraction purity) and sodium nitrate ($NaNO_3$, >0.9900 mass fraction purity) were purchased from Sigma-Aldrich (USA). Sodium hydroxide (NaOH, >0.9900 mass fraction purity) was provided by Acros Organics (Belgium). Copper chloride dihydrate ($CuCl_2{\cdot}2H_2O$, >0.990 mass fraction purity) was a product of Kanto Chemical Co., Inc. (Japan). Nickel chloride hexahydrate ($NiCl_2{\cdot}6H_2O$, 0.9700 mass fraction purity) was obtained from Acros Organics, USA. Chromium(III) chloride anhydrous ($CrCl_3$, 0.9999 mass fraction purity) purchased from Sigma Aldrich (USA) was weighted accurately before preparing its solutions, and iron(III) chloride hexahydrate ($FeCl_3{\cdot}6H_2O$, 0.9700 mass fraction purity) salts were supplied from Sigma-Aldrich, UK. Standard pH buffering solutions from Acros Organics (USA) were used. Carbonate-free sodium hydroxide solution was prepared by dissolving NaOH pellet (Across Organics, Belgium) with ultra-pure water and the solution was potentiometrically standardized against potassium hydrogen phthalate with mass fraction purity 0.9900 (Aldrich, USA). Nitric acid was purchased from Pancreac (Spain). All solutions were freshly prepared daily. Chemicals were accurately weighed then dissolved in ultra-pure water obtained from a nano pure ultrapure water system in which water was distilled and deionized with a resistance of 18.3 MΩ·cm$^{-1}$.

**Table 1**
Supplier, purities and pretreatments of the chemicals used.

| Chemical Substance | Supplier | Mass fraction purity | Pretreatment |
|---|---|---|---|
| (S)-Nicotine (NIC) | Sigma Aldrich (USA) | ≥0.9900 | Storage in vacuum desiccator at room temperature |
| Chromium(III) chloride anhydrous | Sigma Aldrich (USA) | ≥0.9900 | Storage in vacuum desiccator at room temperature |
| Sodium nitrate | Sigma Aldrich (USA) | ≥0 . 9900 | Storage in vacuum desiccator at room temperature |
| Sodium hydroxide | Acros Organics (Belgium) | ≥0.9799 | Storage in vacuum desiccator at room temperature |
| Copper chloride dihydrate | Kanto Chemical Co., Inc. (Japan) | ≥0.9900 | Storage in vacuum desiccator at room temperature |
| Nickel chloride hexahydrate | Across Organics (USA) | ≥0.9900 | Storage in vacuum desiccator at room temperature |
| Standard pH buffering solutions | Across Organics (USA) | ~0.9800 | Storage at room temperature |
| Iron(III) chloride hexahydrate | Sigma Aldrich (USA) | ≥0.9900 | Storage in vacuum desiccator at room temperature |
| Potassium hydrogen phthalate | Sigma Aldrich (USA) | ≥0.9800 | Storage in vacuum desiccator at room temperature |
| Nitric acid | Panreac (*Spain)* | ~0.6500 | Storage at room temperature |