A new spectrophotometric study with ortho hydroxy schiff base for the determination of aluminum in drug

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Abstract

In this study, a Schiff base called (E)-2-((2- hydroxy -3- methoxy benzylidene)amino)-5-methylphenol (L) was used as a ligand. Spectrophotometric properties of the ligand have been defined and the optimum conditions for determining aluminium by complex by UV-Vis. spectrophotometry. The absorbance of Al(III)-L complex obeys Beer’s law between 1.4 µg mL⁻¹ and 13.5 µg mL⁻¹ for the aluminium in the optimum conditions. Under optimum conditions, the determination of aluminium in Kompensan® drug was done successfully. The LOD and LOQ values of the developed method were 0.01139 µg mL⁻¹ and 0.0345 µg mL⁻¹, respectively for the ligand.

1. Introduction

Aluminium is used in a many area, so it can enter the living body through inhalation, contact and nutrition. Searches have shown that aluminum has toxic effects in humans. Certain diseases are thought to be associated with high aluminium content in human tissues. Although there are many ways of exposure to aluminum, nutrition is seen as the main source of intaking aluminum. It is estimated that 20% of the aluminum taken into the body in one day comes from cooking and preserving containers. Certain antacid drugs used for stomach disorders contain significant amounts of aluminium compounds. For these reasons, it is important to determine aluminium [1, 2]. AAS [3-5], Chromatography [6, 7], Fluorescence [8], X-ray fluorescence spectrometry [9], Voltametry [10], Polarography [11], and ICP-MS [12, 13] methods are used for the determination of aluminium apart from UV-Vis. method. Although these methods give positive results for the qualitative and quantitative analysis, they need an expert and extra pre-treatment. UV-visible method has been the choice for this study because of less cost and ease-of-use in comparison to the other methods. Certain spectrophotometric methods have been proposed for the determination of aluminium in the last decade [14-22]. Although the azo compound-based methods have high sensitivity and selectivity, they have certain disadvantages such as difficulties in the synthesis of azo compounds and low synthesis efficiency [14-17]. Schiff bases are known to be a particular class of chelating ligands for metal ions and they are widely used as receptors due to their easy synthesis with a high yield [23]. Moreover, the structures of Schiff bases can be easily characterized. Schiff bases have attracted much attention of researchers due to their certain properties such as nonlinear optical properties, polymerization, metal bond formation abilities and superior biological activities [24, 25]. Schiff bases derived from aromatic o-hydroxyaldehydes have received attention due to their biological properties. These properties are antifungal, antibacterial, antimalarial, antitumor, antiproliferative, anti-inflammatory, antiviral, antipyretic, herbicide properties and anti-tumor activity [24-28]. The purpose of the study is to develop a new UV-Vis. method to determine aluminium. To the best of our knowledge, (E)-2-((2- hydroxy -3- methoxy benzylidene)amino)-5- methylphenol (L) has not been used for the determination of aluminium (Fig. 1).

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Figure 1. Chemical structure of (E)-2-((2- hydroxy -3-methoxy benzylidene)amino)-5- methylphenol (L).
2. Materials and Methods

2.1. Chemical and instruments

All the reagents used were ACS grade with ≥95%. These chemicals were purchased from Sigma, Merck and Alfa Aesar. Their solutions were prepared with bi-distilled deionized water. A stock solution of aluminum solution of 1000 mg L\(^{-1}\) (ICP, Merck) was used. By dissolving 0.2032 g of ligand in 500 mL of deionized water, it was prepared [29]. The solution is stable for a one month at ambient temperature. Shimadzu UV-3150 UV-Vis spectrophotometry (Shimadzu Corporation, International Marketing Division, Tokyo, Japan) using a 1.00 cm quartz cell was used for the spectrophotometric measurements. Mettler Toledo Inlab Expert Pro-ISM pH meter (Mettler-Toledo GmbH, Analytical CH-8603 Schwerzenbach, Switzerland) was used for the pH measurements.

2.2. General procedure

The Al (III)-(E)-2-((2- hydroxy -3- methoxy benzylidene)amino)-5- methylphenol complex has been formed in optimum conditions detailed in ‘Results and discussion’ section. Transfer Al (III) solution (last concentration was in the range of 1.4-13.5 μg mL\(^{-1}\)) into a 10 mL calibrated flask. Add 1 mL 1.0 × 10\(^{-3}\) M ligand and dilute to the mark with pH 5 buffer solution. Measure the absorbance at 413.5 nm against the reagent blank. Since the concentration of ligand affects the formation of the complex, the concentration of the ligand was identical in blank and tests solutions. The ligand solution, whose concentration and pH were the same with those of the complex, has been used as a blank. A calibration curve is obtained and the unknown amount of Al (III) is determined with similar method.

2.3. Analytical applications of the method

2.3.1. Determination of aluminium in artificial mixture

The developed method was successfully applied to the artificial mixture. The artifical mixture was prepared as in the below:

0.54 mg Al\(^{3+}\) + 0.30 mg Mn\(^{2+}\) + 0.13 mg Cr\(^{3+}\)

The mixture was diluted with pH 5 buffer solution up to 100 mL. The aliquot parts of the solution was taken, then 1.0 mL of 1.0 × 10\(^{-3}\) M ligand was added into the solution. The mixture was diluted to the appropriate volume with pH 5 buffer solution. The absorbances of the solution was measured.

2.3.2. Application of the method to drug

Kompensan® is a tablet. It includes 62.826 mg of aluminum in per g of tablet. A stock solution of the tablet was prepared by complying the pharmacopeia procedure (USP XXIV) [30]. The aliquot part of this solution (last concentration was in the range of 1.4-13.5 μg mL\(^{-1}\)) and a 1.0 × 10\(^{-3}\) M ligand (1.5 mL) reagent were added. Then, the mixture was diluted up to 10 mL with a buffer solution of pH 5. The absorbance of the solution was measured at 413.5 nm.

3. Results and Discussion

3.1. Working wavelength and pH

The selection of the measurement wavelength is the most important step of the determination of metals using UV–Vis spectrophotometry. Due to all the experimental measurements performed at the false selected wavelength, all experimental results are negative affected.

In this work, the UV–Vis. spectra of Al\(^{3+}\)–L complex at different pH values were examined against water and ligand. This complex gave maximum absorbance at 420.0 nm and pH 9. Since Aluminium can precipitate or forms hydroxyl complex in alkaline medium, pH 5 was selected as an optimum pH and 413.5 nm was selected as working wavelength (Fig. 2 and Table 2).

| pH  | 1     | 2     | 3     | 4     | 5     | 6     | 7     | 8     | 9     | 10    | 11    | 12    |
|-----|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Abs | 0.619 | 0.796 | 0.730 | 0.745 | 0.824 | -     | -     | -     | 0.887 | 0.705 | 0.700 | 0.425 |
Figure 2. Absorption spectra, pH=5; (1) ligand (comparison standard: water), C_L=2.0×10^-4 M; (2) Al-L complex (comparison standard: water), C_{Al}=5.0×10^{-5} M, C_L=2.0×10^{-4} M; (3) Al-L complex (comparison standard: ligand), C_{Al}=5.0×10^{-5} M, C_L=2.0×10^{-4} M, l=1 cm.

3.2. The ligand concentration

The absorbance of the Al^{3+}-L complex increased by increasing concentrations of ligand at constant metal concentration, and the absorbance of the complex became constant on the 1.5 × 10^{-4} mol L^{-1} ligand at 413.5 nm. So, the 1.5 × 10^{-4} mol L^{-1} ligand was used in this study.

3.3. Temperature and time on complex formation

The data concerning complex formation depending on the time and temperature was given in the slight. The complex is stable up to 40 min. All the studies were done at room temperature. The complex was stable for more than 30 minutes.

3.4. Complex stoichiometry

Job’s method of continuous variation and mole-ratio methods were used for determining the molar composition of the complex. The stoichiometry of the complex was determined as (M:L) is 1:2 by Job method (Figure 3). The conditional stability constant (K) was computed as 2.68 × 10^{6} by Job’s method.

3.5. Calibration curve

Absorbance of the Al^{3+}-L complex obeys Beer’s law between 1.4 µg mL^{-1} and 13.5 µg mL^{-1} for the aluminium in the optimum conditions. The molar absorption coefficient of aluminium was 1.47 × 10^{4} L mol^{-1} cm^{-1}. The Sandell’s sensitivity [31, 32] is computed for the developed method and it was 1.84 × 10^{3} µg cm². The correlation coefficient for the Al^{3+}-L is 0.9964. The values of slope are 0.0579 and the intercept is + 0.0062. Thus, the calibration equation was y = 0.0579x + 0.0062.

Figure 3. Determination of Al-L Complex formation stoichiometry by Job method, 413.50 nm, comparison standard: ligand, l=1 cm, pH=5; (I) C_L=C_{Al}=1.0×10^{-3} M; (II) C_L=C_{Al}=5.0×10^{-4} M

3.6. The investigation of interfering species

The possible interference effects on the determination of aluminum were investigated under the optimum conditions and the quantities did not cause any interfering effects. In the complexization study using the ligand, the ligand, it was masked with iron (III) and bismuth (III) ascorbic acid, copper (II) thiourea, mercury (I) urea, and manganese (II) KSCN (Table 4.2).

3.7. Analytical performance

The developed method was successfully applied on the three artificial mixtures. The artificial mixtures include aluminium with spiked aluminium (Section 2.4.1). The results are summarized in Table 4. The values of standard deviation, absolute and relative errors were acceptable levels. Then, the developed method was applied to the ‘Kompensan®’ drug. The developed method has high accuracy. There is no meaningful difference (|\bar{X} - X_{true}| < \frac{t_s}{\sqrt{N}})(Table 5).
Table 3. Interference effects for the determination of Al$^{3+}$ with ligand at pH=3.5, 485 nm

| Interfering species (I) | Limiting mass ratio (Al$^{3+}$: I) | Interfering species (I) | Limiting mass ratio (Al$^{3+}$: I) |
|------------------------|----------------------------------|------------------------|----------------------------------|
| K$^+$                  | 1:385                            | NO$_3^-$               | -                                |
| Na$^+$                 | 1:85                             | CH$_3$COO$^-$          | 1:35                             |
| Pb$^{2+}$              | -                                | SO$_2^-$               | 1:420                            |
| Mg$^{2+}$              | 1:4                              | MnO$\_4^-$             | -                                |
| Zn$^{2+}$              | 1:160                            | NaO$_2^3^-$            | 1:155                            |
| Bi$^{3+}$              | -                                | SCN$^-$                | 1:74                             |
| Ni$^{2+}$              | 1:14                             | B$_2$O$_5^2^-$         | 1:300                            |
| Cd$^{2+}$              | 1:27                             | NaO$_3^-$              | 1:305                            |
| Cu$^{2+}$              | -                                | Thio Urea              | 1:370                            |
| Cr$^{3+}$              | 1:4                              | Ascorbic Acid          | 1:370                            |
| Fe$^{3+}$              | -                                | Tartaric Acid          | -                                |
| Hg$^+$                 | -                                | Urea                   | 1:740                            |
| Sr$^{2+}$              | 1:150                            | EDTA                   | -                                |
| Co$^{2+}$              | 1:17                             | Cr$^{3+}$ + Urea       | -                                |
| As$^{3+}$              | 1:210                            | Cu$^{2+}$ + Urea       | -                                |
| Sn$^{2+}$              | -                                | Cd$^{2+}$ + Urea       | -                                |
| Mn$^{2+}$              | -                                | Bi$^{3+}$ + Urea       | -                                |
| Ag$^+$                 | -                                | Cr$^{3+}$ + Thio Urea  | -                                |
| Ga$^{3+}$              | 1:0,300                          | Ni$^{3+}$ + Urea       | -                                |
| In$^{3+}$              | 1:1                              | Zn$^{2+}$ + Urea       | -                                |
| NH$_4^+$               | -                                | Fe$^{3+}$ + Ascorbic Acid | 1:5 |
| F$^-$                  | -                                | Bi$^{3+}$ + Ascorbic Acid | 1:30 |
| Cl$^-$                 | 1:350                            | Cu$^{2+}$ + Thio Urea  | 1:19                             |
| Br$^-$                 | 1:245                            | Hg$^+$ + Urea          | 1:25                             |
| I$^-$                  | 1:565                            | Mn$^{2+}$ + KSCN       | 1:240                            |

Table 4. Determination of aluminium in artificial mixture ((0.54 mg Al$^{3+}$+0.30 mg Mg$^{2+}$+0.13 mg Cr$^{3+}$)/100 mL) (n=5).

| Taken, sample (A), mL | Amount of Al$^{3+}$, µg 10 mL$^{-1}$ | Added standard Al$^{3+}$, µg 10 mL$^{-1}$ | Found, Al$^{3+}$, µg 10 mL$^{-1}$ | Standard deviation, s | Absolute Error, AE$^a$ | Relative Error, % (RE%)$^b$ |
|------------------------|----------------------------------|--------------------------------|--------------------------------|------------------------|----------------|--------------------------|
| 1.0                    | 5.400                            | -                             | 5.540                          | 0.151                  | 0.140          | 2.593                     |
| 1.0                    | 5.400                            | 2.700                         | 8.230                          | 0.059                  | 0.130          | 1.605                     |
| 1.5                    | 8.100                            | -                             | 8.020                          | 0.192                  | 0.070          | 0.865                     |
| 1.5                    | 8.100                            | 2.700                         | 10.750                         | 0.270                  | 0.040          | 0.370                     |

$^a$ Absolute error, AE = |X̄ - X$_{true}$|

$^b$ Relative error, %, (RE%) = (|X̄ - X$_{true}$| / X$_{true}$) * 100

Table 5. Determination of aluminium in drug suspension (Kompensan®)

| Certified value of Al (X$_{true}$), mg | Found Al (X), (CL) | Standard deviation, s | Relative standard deviation (RSD%)$^a$ | Relative Error, % | [X̄ - X$_{true}$] | ts√N |
|---------------------------------------|--------------------|-----------------------|---------------------------------------|-------------------|------------------|-------|
| 62.800                                | 62.750± 0.054      | 0.089                | 0.080                                 | 0.050             | 0.067            |

4. Conclusions

A new UV–Vis. spectrophotometry has been developed to determine aluminium. In the range of 1.4-13.5 µg ml$^{-1}$ Al(III), the method obeys Beer’s law. The developed method is an alternative method with molar extinction coefficient of the Al(III)-L complex (M:L;1:2) is 1.474 × 10$^{4}$ L mol$^{-1}$ cm$^{-1}$. The developed method has high selectivity.
and sensitivity. The developed method is an alternative to the present methods [14, 18, 19, 21]. In the certain spectrophotometric methods, the synthesis of azo compounds has difficulties for the determination of aluminum and some others have low reaction efficiency. So, our developed method has certain advantages in terms of the use of easily synthesized ligand and the high reaction efficiency compared to the other methods [14-17]. It does not require any separation technique in this study. Our method; neither surfactant nor time consuming extractant solvent usage in dispersive liquid-liquid microextraction or immobilization procedure [20, 22] requires to increase the selectivity and sensitivity. As a conclusion, the proposed method is simple, reproducible, easy and sensitive to determine aluminium. Moreover, the method can be successfully applied on artificial mixture and drug suspension to determine aluminium.

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**Conflicts of interest**

The authors state that did not have conflict of interests

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