Synthesis of a new organic probe
4-(4 acetamidophenylazo) pyrogallol for
spectrophotometric determination of Bi(III) and Al(III) in pharmaceutical samples

Abstract: A modern development discusses the synthesis and validity of simple, sensitive, and versatile spectrophotometric methods for Bi(III) and Al(III) determination in pharmaceutical formulations have been conducted. In the present paper, 4-(4 acetamidophenylazo) pyrogallol has been synthesized as a new organic compound, 4-APAP, by coupling pyrogallol in a regulated pH medium with diazotized p-aminoacetanilide. 4-APAP was identified by methods of FT-IR, 1H-NMR, 13C-NMR, and thermal analysis (thermogravimetry and differential scanning calorimetry). Solvatochromic activity was also studied in solvents with different polarities. The Kamlet and Taft linear solvation energy relationship was used to correlate shifts in UV-Visible spectra of 4-APAP with Kamlet-Taft parameters (α, β, and π*). The optimum assay conditions showed linearity from 0.3-13 to 0.5-11 μg‧mL⁻¹ for Bi(III) and Al(III), respectively. Molar absorptivity values were 3.365 × 10⁴ and 0.356 × 10⁴ L‧mol⁻¹‧cm⁻¹ for Bi(III) and Al(III), with similar Sandell’s sensitivity measures of 0.006 and 0.008 μg‧cm⁻². Detection limits and quantification limits were 0.013 and 0.043 μg‧mL⁻¹ for Bi(III), respectively, and 0.018 and 0.059 μg‧mL⁻¹ for Al(III) with the relative standard deviation for determination of both metal ions using 4-APAP probe being <2.0%. The validity, accuracy, and efficiency of the approaches were demonstrated by the determination of Bi(III) and Al(III) in different formulations.

Keywords: synthesis, pharmaceutical applications, pyrogallol, p-aminoacetanilide, Bi(III), Al(III)

1 Introduction

For quite a long time, organic reagents play a vital role of the chemical methodologies of analysis. They are dedicated to the qualitative and quantitative determination of chemical components and compounds (inorganic and organic) in addition to other useful methods that pave the way or perform the method of analysis. Theoretically speaking, the planning scope for new organic materials for analytical objectives is boundless; in reality, nevertheless, only a few tens of chemical compound denominations are usable as organic reagents [1]. Organic reagents are currently widely used not only in the analysis of spectrophotometry [2-4] and luminescence [5,6], but also in a number of analytical techniques [7-9]. The need for the organic reagent is met by the analytical process used. Nevertheless, the synthesis of an organic reagent to react with particular tests, primarily tests involving metals, is a major challenge. First of all, a proper functional analytical group should be used in the reagent for the determination of metals, enabling its interaction with the determined material and, subsequently, detection of the corresponding analytical signal.

Now that an organic reagent that displays reaction only with aluminum (III) and bismuth (III) has been synthesized. It is known that both of the elements are of significant value in various fields such as: medicine, agriculture, industry, and nanoscience [10-15].

The present paper investigates the role of the organic reagent, 4-(4 acetamidophenylazo) pyrogallol, in an enhanced analytical process giving special attention to its utilization in the spectrophotometric analysis.
2 Experimental

2.1 Instruments and devices

UV-Visible (UV-Vis) spectrum was recorded using 1 cm quartz cells of the same size by T80 UV-visible spectrophotometer. PG instruments Ltd., UK. Prestige-21 FT-IR, Shimadzu, Japan, was used for infrared spectra recording. SMP30 Stuart melting point apparatus, UK was used to measure melting points and they were uncorrected while measurements of pH were achieved via WTW 340i pH-meter, Germany. Using Stapt-1000 Linseis, the thermal analysis was performed by thermogravimetry and differential calorimeter scanning. The synthesized compound and its starting materials were investigated thermally in a constantly purged atmosphere of nitrogen (flow rate 50 mL/min). The device was adjusted using indium to measure temperature and enthalpy. The samples were crimped into non-hermetic aluminum pans and screened at a heating rate of 10°C/min in a platinum crucible from 30°C to 500°C. The 1H- NMR spectrum was measured in DMSO using the 300 MHz operating NMR Bruker DPX 400 spectrophotometer. As an internal norm, TMS was used, and the chemical changes reported in ppm.
2.2 Reagents

All of the chemicals used were provided from the companies stated and all were of analytical-reagent grade. Bismuth chloride and aluminum chloride were supplied from Sigma Aldrich; ethyl acetate, 2-propanol, n-propanol, and HCl were supplied from G.C.C: 4-aminoacetanilide and DMSO from C.D.H; while butanol and pyrogallol

Figure 3: FTIR of pyrogallol.

Figure 4: FTIR of 4-APAP.
from Fluka. Acetone, acetonitrile, acetic acid, benzene, 1,4-dioxane, ethanol, methanol, cyclohexanol, sulphuric acid, NaOH, and THF were supplied from B.D.H; chloroform, sodium nitrite, ethylenechloride, and toluene from Merck. Ultra-distilled water has been used through most of the experiment.

2.3 Synthesis of 4(4-acetamidophenylazo) pyrogallol

A 3.02 g (0.02 mol) of p-amino acetanilide was dissolved in a mixture of 5 mL conc. HCl, 20 mL of glacial acetic acid, and 25 mL DW. The solution of the primary amine was kept in an
ice bath at a temperature that did not exceed 5°C and was diazotized by an additional solution of sodium nitrite which was made by dissolving 1.38 g (0.02 mol) of sodium nitrite in 10 mL D.W. Slow addition was followed, and the diazotization process was continued with constant stirring for 45 min. Then the solution of pyrogallol, as a coupling component, was added slowly to diazonium salt (Compound 1, Figure 1). Pyrogallol solution was formed by dissolving 2.52 g (0.04 mol) of pyrogallol in 50 mL of D.W. The addition was also made in an iced condition, slowly, with constant stirring at a controlled pH value of less than 6.0. The product, 4-APAP, was left overnight; then it was filtered and treated with absolute ethanol (Compound 2, Figure 1). The yield of the product was 53%.

2.4 Spectrophotometric assay for determination of Bi(III) and Al(III)

In a series of 10 mL standard volumetric flasks, aliquot volumes of stock solutions of Bi(III) and Al(III) were
transferred to satisfy a working concentration range of 0.3-13 μg/mL for Bi(III) and 0.5-11 μg/mL for Al(III), followed by addition of 2.5 mL of 4-APAP reagent solution at room temperature (25 ± 1°C). The contents of each volumetric flask were mixed well then diluted to volume with ethanol after optimizing reaction time (5 min) and pH of medium (pH = 6.5). The absorbance was measured at 506 and 497 nm as $\lambda_{\text{max}}$ for Bi(III) and Al(III) complexes, respectively, versus the reagent blank prepared similarly except for the metal ions.

Figure 9: TG and DSC curves for 4-aminoacetanilide thermal decomposition (heating rate 10°C/min).

Figure 10: TG and DSC curves for 4-APAP thermal decomposition (heating rate 10°C/min).
2.5 Procedure for the determination of Bi and Al in drug formulations

2.5.1 Procedure for tablets

The average weight of 10 finely powdered tablets was accurately weighed (tablets used Aciloxplus 200 mg, Cadila Pharmaceuticals Ltd, India, and Antespin 1000 mg, Pharmacy2U Limited, UK, and Sucralfate 1000 mg, Eipico, Egypt). It was dissolved in a 50 mL solution prepared by addition of 20 mL distilled water, 20 mL ethanol, and 10 mL of 6 M hydrochloric acid. The mixture was left for 10 min to allow complete dispersion, then, filtered and transferred into a 100 mL calibrated flask and was filled to the mark with distilled water. The determination of metals present was accomplished via the recommended spectrophotometric method for the metal ion.

2.5.2 Procedure for ointment

A 1 g of ointment (from two sources: PROCTO-CINOLONE 50, Medico Labs, Syria and Proctoyat 50, Promofarma, Spain) was accurately weighed and dissolved in distilled water. The residue of sample was well rinsed and filtered. Then, the filtrate was transferred quantitatively into a 100 mL calibrated flask and the was filled to the mark with distilled water. The determination of metals present was accomplished via the recommended spectrophotometric method for the metal ion.

2.5.3 Procedure for syrup

The syrup made by commercial company was packaged in bags which each weighed 1 g. Therefore, contents of one bag were equivalent to 1000 mg strength of the definite metal ion and was easily dissolved in distilled water. The mixture was transferred quantitatively into a 100 mL calibrated flask and then filled to mark. The concentration of

### Table 1: Effect of temperature on mass changes TG curves of materials

<table>
<thead>
<tr>
<th>Materials</th>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Loss on ignition (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$T_{\text{onset}}$ (°C)</td>
<td>$T_{\text{offset}}$ (°C)</td>
<td>Mass changes (%)</td>
<td>$T_{\text{onset}}$ (°C)</td>
</tr>
<tr>
<td>pyrogallol</td>
<td>30.0</td>
<td>305.631</td>
<td>-69.8284</td>
<td>305.631</td>
</tr>
<tr>
<td>4-aminoacetanilide</td>
<td>200</td>
<td>500</td>
<td>-97.38</td>
<td>-</td>
</tr>
<tr>
<td>4-APAP</td>
<td>25</td>
<td>95</td>
<td>-6.96</td>
<td>180</td>
</tr>
</tbody>
</table>

$T_{\text{onset}}$ – the initial temperature of thermal degradation for each stage, $T_{\text{offset}}$ – the final temperature at which the degradation process for each stage ends, mass loss (W%) and residue at the end of decomposition processes.

### Table 2: Effect of temperature on DSC curves of materials

<table>
<thead>
<tr>
<th>Materials</th>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Loss on ignition (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$T_{\text{onset}}$ (°C)</td>
<td>$T_{\text{offset}}$ (°C)</td>
<td>Mass changes (%)</td>
<td>$T_{\text{onset}}$ (°C)</td>
</tr>
<tr>
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<tr>
<td>4-APAP</td>
<td>25</td>
<td>95</td>
<td>-6.96</td>
<td>180</td>
</tr>
</tbody>
</table>

Figure 11: Absorption spectrum of 4-APAP in ethanol.
metal ion was determined from regression equation using the calibration curve.

3 Results and discussion

3.1 Physical and chemical features of 4-APAP

The organic reagent is a powder of dark-brown color that can slightly dissolve in water. 4-APAP is soluble in methanol, ethanol, acetone, cyclohexanol, 1,4-dioxane, DMSO, 2-propanol, n-propanol, ethylacetate, acetonitrile, butanol, acetic acid, tetrahydrofuran (THF), and slightly soluble in ethylenechloride, toluene, chloroform, and benzene. It produces a red solution in alkali, turning to orange in neutral media and yellow in acidic solutions depending on the protonation state (which is described in Figure 14). The measured melting point falls in the range 196-198°C; and the other spectroscopical techniques, such as FT-IR, UV-Vis, 1H-NMR, and 13C-NMR combined with the gravimetric analyses, were performed in order to assess the chemical characterization and purity. Regarding FT-IR


Figure 13: Effect of pH on 4-BPAP; selected spectra from Figure 12 which shows isobestic point at 365 nm.
spectroscopy, the structure of 4-APAP contains aromatic systems of –C=C– bonds, aromatic –CH, and a single –C–N bond. Absorption of these groups in the infrared region location are indistinguishable frequencies. However, 4-aminoacetanilide showed in its FTIR spectrum (Figure 2) a sharp band at 3461-3364 cm\(^{-1}\) belonging to the primary aromatic amine of 4-aminoacetanilide. For pyrogallol, the spectrum (Figure 3) shows the broadband due to intramolecular hydrogen bonding at 3343 and 3341 cm\(^{-1}\), that is due to the widening vibrations of three adjacent –OH groups.

Figure 4 showed absorption at 1271 cm\(^{-1}\), belonging to aromatic –C–O and a medium band at 1553 cm\(^{-1}\) attributed to widening of –N=N– group. In similar result, FTIR spectrum of 4-APAP shows no presence of specific bands for –NH\(_2\) group, a broadband at 3322 cm\(^{-1}\) belonging to the widening vibration of –OH group, and 2982 cm\(^{-1}\) for C–H (aro)\[16\].

Figure 5 shows the \(^1\)H-NMR spectrum of 4-APAP having a band at \(\delta = 7.8\) ppm (4H) for the 4-aminoacetanilide moiety. 4-APAP showed a broad band at \(\delta = 7.6\), referring to the proton of OH involved in strong intramolecular hydrogen bonding. Further, a broad peak at \(\delta = 7.4\) was observed for the –NH proton. Two doublet peaks at 6.5 and 7.3 ppm belong to the 4H of benzene ring moiety of 4-aminoacetanilide and that observed at 4.8 belongs to the proton of OH of pyrogallol. A singlet peak at \(\delta = 2.2\) ppm refers to protons of the methyl group and that at \(\delta = 3.3\) ppm refers to the proton of OH of pyrogallol [17,18].

Figure 6 illustrates the spectrum of \(^{13}\)C-NMR of 4-APAP, the band at \(\delta = 170\) ppm due to the carbon of the carbonyl group. The \(^{13}\)C-NMR spectrum of 4-APAP showed 12 signals from \(\delta = 110\) to 150 ppm which refer to 12 carbons of two benzene moieties. A peak at about 23 ppm belongs to the carbon of the methyl group.

Figure 7 illustrates the spectrum of MS of 4-APAP. Peaks at 125 and 164 m/z belong to fragments of pyrogallol and 4-aminoacetanilide, respectively. In the MS
Figure 16: Compilation of the spectra for 4-APAP measured in the referred solvents.
Figure 16: (Continued)
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The spectrum, other fragments of the synthesized compound are demonstrated in a variety of peaks. Either this fragmentation effect was not evident in the mass spectrum on the molecular ion peak or the molecular ion is indeed very unstable [19,20].

3.2 Thermal analysis of 4-APAP, thermogravimetric analysis (TG), and differential scanning calorimetry (DSC)

The thermal analysis includes several techniques where the properties of the material are investigated against temperature and time. Thermal analytical approaches essentially permit the analysis of decomposition, pyrolysis, ignition, phase changes, calorimetry, and other properties on a minimal sample and in a way that is highly automated. Figures 8-10 demonstrate the combined analysis of TG-DSC pyrogallol, 4-aminoacetanilide, and 4-APAP, respectively.

The DSC and TG of the starting compounds and the product synthesized, 4-APAP, were substantially different. At low temperatures, however, as opposed to inorganic materials, organic compounds indicate deterioration; consequently, thermal information collected from thermograms shown in Tables 1 and 2 indicate that the preliminary temperature initiates with low stability [21,22].

Stages of degradation with initial and final temperatures of thermal decomposition for pyrogallol, 4-aminoacetanilide, and 4-APAP presented in Table 1. In the synthesized compound, the TG curve of Figure 10 shows that the compound decomposed in two stages. The 1st stage is associated with dehydration or loss of water from the powder sample surface and pores. Changes occur in large amount because of the high percent loss seen in the 2nd stage from around 200-400°C that alluded to the most extreme measure of degradation of the organic reagents.

The data collected from the temperature effect on DSC curves of the three materials involved in the synthesis reaction were tabulated in Table 2. For the synthesized compound (Figure 10), two peaks are shown on the DSC curve: exothermic and endothermic. The broad range of the endothermic peak is associated with loss of water from the powder sample surface and pores. Changes occur in large amount because of the high percent loss seen in the 2nd stage from around 200-400°C that alluded to the most extreme measure of degradation of the organic reagents.

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![Graph demonstrating variation of λ_max of 4-APAP as a function of solvent dielectric constant.](image)

**Figure 17:** Variation of λ_max of 4-APAP as a function of solvent dielectric constant.

**Table 3:** Absorption maxima of azo compound in various solvents and selective Kamlet-Taft solvent parameters (ε: dielectric constant) for 4-APAP

<table>
<thead>
<tr>
<th>Solvent</th>
<th>λ_max (nm)</th>
<th>ν (cm⁻¹)</th>
<th>π*</th>
<th>β</th>
<th>α</th>
<th>ε</th>
</tr>
</thead>
<tbody>
<tr>
<td>acetic acid</td>
<td>469</td>
<td>21322.0</td>
<td>0.64</td>
<td>0.45</td>
<td>1.12</td>
<td>6.2</td>
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<tr>
<td>methanol</td>
<td>390</td>
<td>25641.0</td>
<td>0.6</td>
<td>0.63</td>
<td>0.93</td>
<td>32.6</td>
</tr>
<tr>
<td>ethanol</td>
<td>391</td>
<td>25575.4</td>
<td>0.54</td>
<td>0.75</td>
<td>0.83</td>
<td>24.6</td>
</tr>
<tr>
<td>n-propanol</td>
<td>437</td>
<td>22883.3</td>
<td>0.52</td>
<td>0.9</td>
<td>0.84</td>
<td>20.33</td>
</tr>
<tr>
<td>2-propanol</td>
<td>391</td>
<td>25575.4</td>
<td>0.48</td>
<td>0.84</td>
<td>0.76</td>
<td>19.92</td>
</tr>
<tr>
<td>butanol</td>
<td>392</td>
<td>25510.2</td>
<td>0.47</td>
<td>0.84</td>
<td>0.84</td>
<td>18</td>
</tr>
<tr>
<td>1,4-dioxane</td>
<td>391</td>
<td>25575.4</td>
<td>0.49</td>
<td>0.37</td>
<td>0</td>
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<tr>
<td>ethyl acetate</td>
<td>389</td>
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<td>0.45</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>DMSO</td>
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<td>24813.9</td>
<td>1</td>
<td>0.76</td>
<td>0</td>
<td>47</td>
</tr>
<tr>
<td>acetonitrile</td>
<td>387</td>
<td>25839.8</td>
<td>0.66</td>
<td>0.4</td>
<td>0.19</td>
<td>37.5</td>
</tr>
</tbody>
</table>

**Table 3:** Absorption maxima of azo compound in various solvents and selective Kamlet-Taft solvent parameters (ε: dielectric constant) for 4-APAP
3.3 UV-Visible spectrum of 4-APAP

The orange-colored solution of 4-APAP, which was dissolved in ethanol, reached the highest point at 391 nm which was assigned to absorption of N=N group (Figure 11). Moreover, such absorption emphasizes that the compound was created because this band is not present in any of the reacting molecules.

Figures 12 shows the effect of pH on 4-APAP with a range of 2-11 and Figure 13 shows the isobestic point for 4-APAP. Depending on the level of medium acidity, 4-APAP solution contains three different forms of acid-base, which are: \( \text{LH}_4 \), \( \text{LH}_3^- \), and \( \text{LH}_2^- \) (Figure 14). The neutral species which are fully protonated \( \text{LH}_4 \) are of yellow colour (390, 424 nm) and occur for 4-APAP in the medium of low pH up to 1.0. The orange-colored neutral type was predominant while the pH varied from 5.0-7.0, and showed the highest absorption at 458 nm for 4-APAP. In pH > 8.0 media, the 4-APAP spectrum reveals an absorption peak at 470 nm with an isopestic point at 365 nm. This activity demonstrates the existence of a chemical equilibrium amid neutral and ionic 4-APAP formulas [23,24].

3.4 Constant dissociation of 4-APAP

The 4-APAP constant dissociation was determined using a spectrophotometric technique [25,26], from the individual regions of formation of the absorbance-pH curves, and by graphical analysis in Figure 15. The pKa1 and pKa2 values were estimated to be 1.2 and 6.5, respectively.

3.5 Solvent effect

Spectra of absorption of the azo substance being studied was tested in different solvents of various polarities including ethanol, n-propanol, methanol, acetic acid, 2-propanol, and butanol that are protic solvents as well as acetone, ethylene chloride, ethyl acetate, chloroform, benzene, dioxane cyclohexanol, toluene, DMF, and DMSO THF as aprotic solvents as shown in Figure 16.

The characteristics of electronic spectra are investigated in various solvents. To put it in another way, various phenomena occur in different media. Some idealized theories [27,28] suggest that the dielectric solvent constant is a quantitative way of measurement of the polarity of solvents. This perspective is not sufficient as researchers have limited resources to deal with only certain solute-solvent interactions such as hydrogen bonding and donor/electron pair/electron pair acceptor (EPD/EPA) interactions, which have a significant impact on those interactions.

Depending on the concept of solvent polarity already defined and Figure 17 that demonstrates \( \lambda_{\text{max}} \) variation as a feature of solvent dielectric constant in 4-APAP, it is obvious that a single physical amount is not capable of
representing such a solvent dielectric constant. Therefore, the linear solvation energy relationship (LSER) as a multiparameter scale of solvent polarity is considered an important and insightful method to solvation results as proposed by Kamlet and Taft. It requires major interactions between a solute and its surroundings and may allow an estimation of bonds formation of hydrogen for the compounds under analysis. The following equation represents Kamlet and Taft solvatochromism [29]:

\[ \nu = \nu_o + s\pi^* + b\beta + a\alpha \]  

(1)

where: \( \pi^* \) – represents the solvent polarizability/polarity, \( \beta \) – represents measure of the solvent hydrogen-bonding acceptor (HBA) basicity, \( \alpha \) – represents measure of the solvent hydrogen-bonding donor (HBD) acidity and \( \nu_o \) – represents the solute property regression value for cyclohexane as the reference solvent. The coefficients of regression \( s, b, \) and \( \alpha \) in Eq. 1 measure relative susceptibility of the absorption frequency ranges to the indicated solvent parameters.

Table 3 shows parameters of the solvent [30]. The spectroscopic data correlations were achieved using multiple linear regression analysis methods. It has indeed been documented that azo compounds absorption frequencies in various solvents demonstrate an acceptable association with parameters of \( \pi^* \), \( \beta \), and \( \alpha \). The multiple regression findings are presented in Table 4, and \( \nu_o, s, b, \) and \( \alpha \) coefficients have a significant level of 95% of confidence intervals. The degree of success of Eq. 1 is expressed in Figure 18 using a plot of the measured absorption wave number (\( \nu_{calc} \)) as a feature of the theoretical values in question. For synthesized azo compounds in the chosen ten solvents, the \( s \) and \( b \) negative
mark coefficients signify a bathochromic change with an increase in solvent polarizability/dipolarity and solvent hydrogen bond acceptor basicities. It means that the electronic stabilization of the excited state is relative to the ground state. The positive sign of a coefficient points out a hypsochromic change with an increase in acidity of the donor solvent hydrogen bond [31] which means that the ground-stabilization in relation to the electronically excited state.

### 3.6 Application of 4-APAP: An analytical approach

Preliminary investigations for 4-APAP with element ions under definite conditions such as concentration, temperature and pH were conducted. Ions tested with 4-APAP are: Sn$^{2+}$, Al$^{3+}$, Ag$^{+}$, Mg$^{2+}$, K$^+$, Ni$^{2+}$, Mn$^{2+}$, Co$^{2+}$, Cr$^{3+}$, Cu$^{2+}$, Cu$^{+}$, Zn$^{2+}$, Hg$^{2+}$, La$^{3+}$, Sr$^{2+}$, Pd$^{2+}$, Cr$^{6+}$, Ca$^{2+}$, Cd$^{2+}$, Pb$^{2+}$, Fe$^{3+}$, Bi$^{3+}$, NH$_4^+$, Na$^+$, K$^+$, Ti$^{4+}$, Li$^+$, Pt$^{4+}$.

Depending on the appearance of the new color after mixing the reactants, these ions showed no reaction with

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**Figure 20:** Absorption spectrum (a) and calibration curve for aluminum complex (b).

**Table 5:** The best volume of the reagent required to complete the reaction of Bi(III) and Al(III) with 4-APAP

<table>
<thead>
<tr>
<th>Volume of reagent (mL)</th>
<th>Bi$^{3+}$ at 506 nm</th>
<th>Al$^{3+}$ at 497 nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>0.012</td>
<td>0.160</td>
</tr>
<tr>
<td>1</td>
<td>0.342</td>
<td>0.252</td>
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<tr>
<td>1.5</td>
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<tr>
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<td>0.990</td>
</tr>
<tr>
<td>2.5</td>
<td>1.504</td>
<td>1.357</td>
</tr>
<tr>
<td>3</td>
<td>1.422</td>
<td>1.398</td>
</tr>
<tr>
<td>3.5</td>
<td>1.515</td>
<td>1.356</td>
</tr>
<tr>
<td>4</td>
<td>1.512</td>
<td>1.360</td>
</tr>
</tbody>
</table>
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4-APAP except Al$^{3+}$ and Bi$^{3+}$. Therefore the synthesized compound, 4-APAP, acts as a specific reagent for these two metal ions.

A maroon-colored product of Bi(III) and Al(III) complexes was scanned within 200-800 nm range without any modification of pH. The absorption maximum for the complexes was found to be 506 and 497 nm, respectively (Figures 19a and 20b).

This reaction is devoted to develop a spectrophotometric approach for Bi(III) and Al(III) assessments. The experimental conditions for the reaction between these ions and 4-APAP were optimized. The optimized conditions were the volume of the synthesized reagent (Table 5), temperature (Figure 21), time (Figure 22), pH (Figure 23), and the calculation of the M:L ratio (complex stoichiometry) by both the method of continuous variations and the method of mole ratio (Figures 24 and 25). The standard calibration curves were subsequently constructed for the determination of Bi(III) and Al(III) using 4-APAP (Figures 19b and 20b). In addition, analytical parameters have been computed and provided in (Table 6). The structural formula of the complexes formed has been proposed (Figure 26). The obtained results make the proposed analytical method with good performance, high precision,
Further, to examine the validity of the present method, it has been implemented to the identification of bismuth ion and aluminum ion in pharmaceutical forms. The recovery experiments tested the reliability of the system used to evaluate these real samples using the normal addition process (Tables 7 and 8). A measured amount of pure medication was used to formulate tablets for this purpose, syrup and ointment in two different amounts, and the nominal concentration of drug was confirmed by the suggested method. Each selected level of concentration was measured five times. The results show that the recovery is close to 100% and satisfactory accuracy for Bi(III) and Al(III) determination at low concentrations.

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indicates, by applying the proposed procedure, good recovery is obtained with low SD and RSD. Further, such good results illustrate that common excipients do not show interference on determination of desired analyses.

### 4 Conclusion

The reagent 4-APAP showed its specificity to react only with Bi(III) and Al(III). The spectrophotometric approach performed, based on a 4-APAP reaction with the two metal ions, has been proved to be simple, rapid, precise, low cost, and sensitive for Bi(III) and Al(III). Successful application of the Kamlet-Taft equation to show the effect of a solvent of different polarities was utilized. Applying this equation correlates effects other than the solvent dielectric constant contribute their effects on electronic spectra. The procedure did not involve any critical steps; hence it can be used routinely for the determination of Bi and Al in their pharmaceutical preparations with good recoveries.

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