Construction and analytical application of ion-selective piezoelectric sensor for atropine sulfate

Yumei Long, a Lihong Lei, b Weifeng Li, a Deliang He, a Lihua Nie a and Shouzhuo Yao a

a College of Chemistry and Chemical Engineering, Hunan University, Changsha 410082, China
b College of Chemistry and Chemical Engineering, Hunan University, Changsha 410081, China

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The method describes the use of a piezoelectric quartz crystal (PQC) as a substitute for ion-selective electrodes. The approach is feasible when the membrane materials are electrically non-conductive and membrane potential measurements are consequently not possible. An ion-selective piezoelectric sensor sensitive to atropine sulfate was constructed by coating a PVC membrane containing activant on one side of a PQC. On the basis of selective adsorption of atropine ions across the modified film and the sensitive mass response of PQC, the method exhibits a sensitive, rapid response and is easy to operate without pretreatment of the sample. The logarithm of the frequency shift gave a linear relationship with the logarithm of atropine sulfate concentration in the 1.0×10⁻³–1.0×10⁻¹ M range with a detection limit of 5.0×10⁻⁹ M at pH 7.0. Recoveries were from 98.7–102.2%.

Two activants, atropine tetraphenylborate and atropine dipicrylaminate, were synthesized and investigated. Influencing factors were also examined and optimized. The results for real samples obtained by the proposed method agreed with those obtained by conventional methods.

1. Introduction

Atropine sulfate, the monohydrate of (1R,3r,5S)-3-tropoyloxytropanium sulfate, an alkaloid, can be used for suppressing unstriated muscle, controlling glandular excretion, in small doses stimulating the central nervous system and having the action of mydriasis in ophthalmology, etc. ¹ But most alkaloids have special and significant biological activity, so caution is called for in establishing a sound method to detect atropine sulfate in a clinical assay.

A great variety of methods are available for the determination of atropine sulfate such as spectrophotometry,² neutralization extraction,³ liquid chromatography,⁴ etc. The applicability of spectrophotometric methods is limited in that they suffer from low sensitivity especially when the concentration of atropine sulfate is very low. Liquid chromatography is simpler, faster and more sensitive than the neutralization extraction method. However, a preliminary sample clean-up procedure by either extraction or ion-exchange column chromatography is tedious and time-consuming. The ion-selective electrode (ISE) method⁵ has the disadvantage that its response is usually affected by electrical properties of the film and electrical double-layer capacitance. New methods of determining atropine sulfate are welcome since all of the existing methods have troublesome limitations.

Selective adsorption/desorption processes of the component ions of insoluble salts at their solid/aqueous interface were studied by several research groups and some fundamental characteristics of the adsorption mechanism of solid films were reported. These theoretical results were proved to agree closely with experimental data and applied for real sample detection.⁶–⁸

Since 1964, when the first application of a piezoelectric sensor was reported by King⁹ after Sauerbrey derived the equation describing the frequency to mass relationship,¹⁰ many reports have been published concerning the use of a piezoelectric quartz crystal (PQC) as the sensing element. A PQC, serving as a sensitive mass detecting device owing to its capability of measuring mass changes in the ng range, has recently been extensively used in analytical applications. Although the PQC itself is not a selective sensor and may give response to the mass change caused by any loaded substances, surface modification of the PQC with a chemically selective reagent leads to a useful sensor that selectively adsorbs the detected ions. As a consequence, in the last few years application of PQC has been widely extended to chromatography,¹¹ the food industry,¹² biotechnology, pharmaceutical compounds, life sciences, etc.¹³–¹⁵

Based on the aforementioned principle, a novel all-solid-state atropine sulfate ion-selective piezoelectric sensor (ISP) is proposed for the determination of atropine sulfate and applied to real sample assay.

2. Experimental

2.1. Apparatus

The proposed detector for ISP is schematically shown in Fig. 1. A universal frequency counter was used to record the frequency changes of the ISP. The piezoelectric quartz crystal used was a 9 MHz AT-cut crystal (12.5 mm diameter) having silver electrodes (6 mm diameter) on both sides. As shown, the quartz crystal was fixed in a detection cell made of PTFE, in which only one side of the quartz crystal was allowed to be in contact with the aqueous sample solution. The crystal holder was directly connected to an IC-TTL oscillating circuit, whose design is supplied in a previous paper.¹⁶ A dc voltage regulator supplied the oscillating circuit, and the working voltage was set at 5 V.

The crystal, the crystal holder and the detection cell (volume 10 ml) were placed in a thermostated water bath (37 ± 0.1 °C). A computer was used for data analysis.

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2.2. Reagents

All reagents used were of analytical grade. Atropine sulfate, obtained from Shanghai Medical Factory (China), was of pharmacopoeia quality.1 Double-distilled water was used throughout.

2.3. Preparation of ion-pair complexes

Atropine tetraphenylborate (atropine–TPB) was prepared by mixing 20 ml of 0.01 M tetraphenylboron sodium and 40 ml of 0.01 M atropine sulfate under stirring until the precipitation was completed. Then, the precipitate was filtered off on a porosity-4 sintered glass crucible and washed several times with double-distilled water. After adding several drops of ethanol, it was evaporated under a vacuum, resulting in a white product. The stoichiometry ratio for atropine sulfate and sodium tetraphenylboron is 1:1.17 Atropine dipicrylaminate (atropine–DPA) was prepared in a similar way.

2.4. The solubility of ion-pair complexes

An appropriate amount of atropine–DPA powder was added into 0.1 M NaCl solution under stirring for 3 h and kept standing for a while until the dissolution/precipitation equilibrium was obtained. The supernatant was abstracted for the measurement of dissolution of atropine–DPA by using an atropine ISP sensor. The same method was employed for the determination of the solubility of atropine–TPB. The results are given in Table 1.

2.5. Electrode modification

Coating of the electrode surface was carried out as follows: 10 mg of the ion-pair complex (atropine–TPB or atropine–DPA) and 100 mg of polyvinylchloride (PVC) powder were mixed thoroughly and dissolved in 10 ml of tetrahydrofuran (THF). Then the quartz crystal was placed on a spinning device and one side of the electrode was treated with a small portion of the obtained supernatant. The coated crystal was kept at room temperature to evaporate the THF, leaving a transparent uniform film of coating on the surface. Usually, a membrane coating equivalent to 10 000 Hz frequency shift has been adopted in this paper. When not in use, the modified sensor should be stored in a desiccator.

2.6. Process of preconditioning

Before detection, 3 h was allowed for the ISP sensor to precondition by immersion into 1.0 × 10⁻⁵ M standard atropine sulfate solution. Then, the sensor was washed with double-distilled water until the resonance frequency of the sensor was close to the frequency value that the sensor oscillated in air (f₂). In our work, when the frequency shift was 1 Hz within 5 min, we assumed the sensor was stable. The same sensor was used repeatedly to complete a series of determinations to avoid the effect of the membrane thickness. A 0.1 M NaCl solution (pH = 7.0) was used as a medium.

2.7. Measuring procedure

Before the experiment, 30 min was required to allow the oscillator to stabilize. After a steady resonant frequency (f₁) in the medium was acquired, a series of standard sample solutions was injected from low to high concentration into the medium. The working temperature was kept at 37 ± 0.1 °C using a thermostated water bath. After each addition, the resonant frequency (f₂) of the ISP sensor was recorded and the respective frequency shift was calculated:

\[ \Delta f = f_2 - f_1 \]  

A calibration curve log (−Δf) vs. logC was made, where C is the atropine sulfate concentration. Then, the concentration of the unknown sample was calculated by using the calibration curve method or standard addition method.

3. Results and discussion

3.1. Theoretical discussion

Most piezoelectric analytical applications utilize a mass relationship. The thickness-shear mode (TSM) of vibration is the most sensitive to mass changes.18 Two crystal, AT- and BT-cut, orientations vibrate exclusively in the TSM.19 AT-cut crystal has a temperature coefficient of nearly zero in the region of room temperature, so it has been used in the majority of piezoelectric work in analytical chemistry.18–20

A piezoelectric device consists of an oscillating quartz crystal incorporating an adsorbent on its surface. When any ion is adsorbed into or desorbed from the modified membrane, or when ions with different molecular weight exchange with one another across the membrane, the surface mass change in the modified membrane can be measured by an ISP sensor, even though this change may be very small.

Generally speaking, analyte detection is based on adsorbate recognition where selective binding causes a mass change identified by a corresponding frequency change. The measured frequency is proportional to the change in mass. Taking the general case of overtone into consideration, the relationship between the mass change and frequency shift can be expressed as:21

Fig. 1 Schematic diagram of the atropine ISP sensor with an atropine–DPA PVC film.
oscillating in the thickness shear mode, material, equation: 22 concentration, can be expressed by the Freundlich isotherm mass change of the modified membrane and the tested ion a low concentration (\( \leq 0.01 \) M), the relationship between the mass change of the modified membrane and the tested ion concentration, can be expressed by the Freundlich isotherm equation:\(^1\)

\[
\Delta m = K_r C^n \]

Where \( n \) and \( K_r \) are constants and \( n > 1 \). Combining eqns. (2) and (3) and substituting for the various constants for the oscillating quartz crystal, we get:

\[
\Delta f = -2.26 \times 10^6 f^2 h K_r C^n / A
\]

For a given AT-cut crystal, the area \( A \) is a constant, so eqn. (4) can be simplified as:

\[
\Delta f = -K'C^n
\]

Where \( K' = 2.26 \times 10^6 f^2 h / A \) is also a constant. The logarithmic form of the above equation is;

\[
\log(-\Delta f) = \frac{1}{n} \log C + \log K'
\]

3.2. Sensor performance

A number of experiments were carried out using the same ISP sensor. Fig. 2 shows a typical course of the response of an ISP sensor with ion-pair complex atropine–DPA to the change in concentration of atropine sulfate in the sample solution. With the increment of the concentration in atropine sulfate, the amount of the adsorbed substance increases, and the frequency of the sensor gradually decreases. After each addition of the analyte, there exists competitive adsorption on the surface of the crystal, and the resonant frequency becomes stable after equilibrium is established.

Table 1 The measurement of solubilities of atropine ion-pair complexes in 0.1 M NaCl at 25 °C and pH 7

<table>
<thead>
<tr>
<th>Ion-pair complex</th>
<th>Solubility/( \times 10^{-6} \text{M} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atropine–DPA</td>
<td>(8.9 ± 3.7) × 10^{-7} (( n = 3 ))</td>
</tr>
<tr>
<td>Atropine–TPB</td>
<td>(2.8 ± 2.3) × 10^{-6} (( n = 3 ))</td>
</tr>
</tbody>
</table>

* Mean values ± standard deviation (\( n = 3 \)).

Table 2 Comparison of the atropine–DPA ISP and the atropine–TPB ISP sensors

<table>
<thead>
<tr>
<th>Added/mg</th>
<th>Found/mg</th>
<th>( R^2 ) (%)</th>
<th>M (%)</th>
<th>s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atropine–DPA ISP sensor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.0</td>
<td>7.1 ± 0.08</td>
<td>101.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15.1</td>
<td>14.9 ± 0.15</td>
<td>98.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22.2</td>
<td>22.4 ± 0.20</td>
<td>100.9</td>
<td>100.4</td>
<td>1.53</td>
</tr>
<tr>
<td>30.6</td>
<td>30.3 ± 0.31</td>
<td>99.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>41.2</td>
<td>42.1 ± 0.50</td>
<td>102.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Atropine–TPB ISP sensor</th>
<th>Added/mg</th>
<th>Found/mg</th>
<th>( R^2 ) (%)</th>
<th>M (%)</th>
<th>s</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.8</td>
<td>6.9 ± 0.10</td>
<td>101.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14.6</td>
<td>14.9 ± 0.20</td>
<td>102.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21.4</td>
<td>21.0 ± 0.26</td>
<td>98.1</td>
<td>100.9</td>
<td>1.65</td>
<td></td>
</tr>
<tr>
<td>29.8</td>
<td>30.0 ± 0.34</td>
<td>100.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35.6</td>
<td>36.3 ± 0.36</td>
<td>102.0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* \( R \) = Recovery. * Mean values ± standard deviations (\( n = 3 \)).

After a series of detection is completed, the adsorbed atropine sulfate species can be washed off the modified membrane. The ISP may be recovered by washing continuously with double-distilled water until the frequency of the ISP sensor gradually increases to reach a value \((f_0)\) close to the steady oscillating frequency \((f_1)\) in the medium obtained after the precondition (Fig. 2). In general, there always exists a small difference between \(f_0\) and \(f_1\), which is mainly due to the adsorption of atropine ions remaining at the sensor surface or the probability of the dissolution of activants in the renewed atropine free medium.

3.3. Effect of ion-pair complexes

Atropine-sensitive ISP sensors with different ion-pair complexes were tested to compare their response functions. Table 2 gives the results with two kinds of ion-pair complex materials tested as coating for adsorption of atropine sulfate. As the atropine–DPA ISP gave higher sensitivity, it was used as coating material for all the subsequent work.

3.4. Influence of pH

The \( pK_a \) value of atropine is 9.65.\(^\text{23} \) In order to find the optimum pH value for the assay of atropine in human serum, the influence of pH was examined. The pH dependence of the electrode was tested over the pH range 2 to 9 by adjusting the pH of the solution with a 0.1 M hydrochloric acid or 0.1 M sodium hydroxide solution. The results are shown in Fig. 3. As seen, from pH 3 to 8, no significant change in the frequency response was observed. Taking the situation of the human body into account, pH = 7 was adopted in this work.
3.5. Selectivity

In order to investigate the selectivity of the proposed ISP, its response was examined in the presence of potential interfering substances and other commonly met compounds by measuring the selectivity coefficient by the separation solution method.

All measurements were carried out in an aqueous solution containing 0.1 M NaCl (pH = 7.0), as both the chloride ion and sodium ion did not seriously interfere with the response of the present ISP sensor. The equation for the response selectivity coefficient is:

\[ K_{ia} = \frac{\Delta f_i}{\Delta f_a} \]

Here \( \Delta f_i \) is the frequency shift response of the ISP sensor to a 1 \( \times \) 10\(^{-3} \) M solution of the interferent; \( \Delta f_a \) is the frequency shift response to a 1 \( \times \) 10\(^{-3} \) M solution of atropine sulfate. Differences in the selectivity coefficient of more than 0.05 were regarded to result from interference. A complete list of interferences can be found in Table 3. It can be seen that: (1) except for benzydamine hydrochloride, trimethoprim and chlorphenamine maleate, most commonly met substances do not interfere; (2) for symmetrical quaternary ammonium ions, there is a regular change of selectivity with the number of carbon atoms of the ion. Hence, a plot of \( \log K_{ia} \) vs. the number of carbon atoms (\( n_c \)) in the quaternary ammonium ion gave a straight line (Fig. 4). Least squares analysis of this line gives:

\[ \log K_{ia} = -1.31 + 0.034 n_c \quad (r = 0.991) \]

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\[ \log K_{ia} = -1.31 + 0.034 n_c \quad (r = 0.991) \]

3.6. Calibration curve and application of the ISP sensor

The calibration curves for the assay of atropine sulfate are shown in Fig. 5. The results indicate that the frequency shift (\( -\Delta f \)) increases along with the concentration increment in the

![Fig. 3](pH effect on the sensor’s frequency response. (●): 1.0 \( \times \) 10\(^{-4} \) M atropine sulfate. (●): 1.0 \( \times \) 10\(^{-3} \) M atropine sulfate.)

![Fig. 4](Relationship between \( \log K_{ia} \) and the number of carbon atoms (\( n_c \)) in the symmetrical quaternary ammonium ions. (a) Tetramethylammonium iodide; (b) tetraethylammonium iodide; (c) tetrapropylammonium iodide; (d) tetrabutylammonium iodide; (e) cetyltrimethylammonium bromide.)

![Fig. 5](Frequency shifts vs. concentration of atropine sulfate plots for the atropine ISP sensor with different ion-pair complexes. (●): The atropine–DPA ISP sensor; (●): the atropine–TPB ISP sensor. C is the concentration of atropine sulfate.)

![Fig. 6](Calibration graph of the atropine sulfate ISP sensor. (△): In 0.1 M NaCl medium of pH = 7.0. (●): In injection solution (0.5 mg ml\(^{-1} \)). (●): In serum (containing 0.43% sodium citrate, pH = 7.0). C is the concentration of atropine sulfate.)

Table 3

<table>
<thead>
<tr>
<th>Interferent</th>
<th>( K_{ia} = \Delta f_i/\Delta f_a )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copper sulfate</td>
<td>0.027</td>
</tr>
<tr>
<td>Calcium nitrate</td>
<td>0.016</td>
</tr>
<tr>
<td>Glucose</td>
<td>0.035</td>
</tr>
<tr>
<td>Niacinamide</td>
<td>0.039</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>0.044</td>
</tr>
<tr>
<td>Ammonium chloride</td>
<td>0.020</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>0.031</td>
</tr>
<tr>
<td>Chlorphenamine maleate</td>
<td>0.055</td>
</tr>
<tr>
<td>Lactose</td>
<td>0.024</td>
</tr>
<tr>
<td>Promethazine hydrochloride</td>
<td>0.047</td>
</tr>
<tr>
<td>Urea</td>
<td>0.028</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>0.062</td>
</tr>
<tr>
<td>Benzydamine hydrochloride</td>
<td>0.059</td>
</tr>
<tr>
<td>Tetramethylammonium iodide</td>
<td>0.066</td>
</tr>
<tr>
<td>Tetraethylammonium iodide</td>
<td>0.092</td>
</tr>
<tr>
<td>Tetrapropylammonium iodide</td>
<td>0.135</td>
</tr>
<tr>
<td>Tetrabutylammonium iodide</td>
<td>0.166</td>
</tr>
<tr>
<td>Cetyltrimethylammonium bromide</td>
<td>0.214</td>
</tr>
</tbody>
</table>

\( K_{ia} \): response selectivity coefficient; \( f_i \): frequency response of the sensor to 1 \( \times \) 10\(^{-3} \) M interferent; \( f_a \): frequency response of the sensor to 1 \( \times \) 10\(^{-3} \) M atropine sulfate.
range from $1.0 \times 10^{-8}$ to $1.0 \times 10^{-3}$ M atropine sulfate in a medium of pH 7.0 containing 0.1 M NaCl. To employ the method for clinical analysis, serum (0.43% sodium citrate was added to avoid coagulation, and the pH was adjusted to 7.0) and injection solutions (0.5 mg ml$^{-1}$) were examined. The response ranges were $5.0 \times 10^{-7}$–$8.0 \times 10^{-3}$ M and $1.0 \times 10^{-8}$–$1.0 \times 10^{-4}$ M for serum and injection solutions, respectively. All these curves are in good agreement with those obtained from conventional methods.

Fig. 6 shows plots of the logarithm of the frequency shift vs. logarithm of the atropine sulfate concentration in the medium (containing 0.1 M NaCl and pH adjusted to 7.0) using the ISP sensors. Obviously, the resulting linear relationship agrees well with the theoretical discussion. The regression equation for the atropine–DPA ISP is:

$$\log(-\Delta f) = 3.977 + 0.275\log C \quad (r = 0.994)$$

While for the atropine–TPB ISP is:

$$\log(-\Delta f) = 3.825 + 0.268\log C \quad (r = 0.992)$$

The proposed sensor was applied to a quantitative assay of atropine sulfate in various samples. The results are shown in Table 4. The average recoveries were 100.5% and 100.2% and the standard deviations were 1.67 and 2.93 in serum and injection solutions, respectively; the results were in good agreement with those obtained from conventional methods.

## 4. Conclusion

A comparison of this novel method with other methods is given in Table 5. It shows that the ISP sensor provides a selective, sensitive and precise method for the determination of atropine sulfate. We are interested in applying this method to therapeutic drug monitoring in clinical analysis since this method has some advantages over some detection methods, e.g., the reagents and instruments required are cheaper and simpler than those required by HPLC, GC and UV methods. All those make it an attractive and promising alternative for the pharmaceutical assay compared with the other currently used methods.

### Acknowledgements

This work was supported by the National Science Foundation of China.

### References


### Table 4 Determination of atropine sulfate in injection solutions and human serum using the atropine–DPA ISP sensor

| Serum$^a$ | Injection solution$^b$ |
| Added/mg | Found/mg | $R$ (%) | $M$ (%) | $s$ | Added/mg | Found/mg | $R$ (%) | $M$ (%) | $s$ |
|----------|----------|--------|--------|-----|----------|----------|--------|--------|-----|-----|
| 5.4      | 5.2 ± 0.40 | 96.3   |        |     | 5.0      | 5.4 ± 0.28 | 102.0  |        |     |
| 11.0     | 10.8 ± 0.26 | 98.2   |        |     | 10.4     | 10.2 ± 0.30 | 98.1   |        |     |
| 15.6     | 15.2 ± 0.32 | 97.4   | 100.5  | 1.67 | 14.8     | 15.3 ± 0.24 | 103.4  | 100.2  | 2.93 |
| 20.2     | 20.6 ± 0.35 | 102.0  |        |     | 19.6     | 19.1 ± 0.13 | 97.4   |        |     |
| 25.6     | 25.0 ± 0.18 | 97.7   |        |     | 24.8     | 24.4 ± 0.20 | 98.4   |        |     |

$^a$ 0.43% Sodium citrate was added to avoid coagulation, and the pH was adjusted to 7.0.

<table>
<thead>
<tr>
<th>Method</th>
<th>Application</th>
<th>Calibration range/mM</th>
<th>Detection limit/nM</th>
<th>$R^a$ (%)</th>
<th>RSD (%)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spectrophotometry</td>
<td>Pharmaceuticals and urine</td>
<td>$2.88 \times 10^{-3}$–$1.44 \times 10^{-2}$</td>
<td>$99.0$</td>
<td>$2$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPLC</td>
<td>Pharmaceuticals, serum and urine</td>
<td>$2.6 \times 10^{-3}$–$1.3 \times 10^{-1}$</td>
<td>$90.7$–$97.7$</td>
<td>$2$–$25$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potentiometry</td>
<td></td>
<td>$8.2 \times 10^{-1}$–$2.5$</td>
<td>$98.3$</td>
<td>$3$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GC</td>
<td></td>
<td>$1.5 \times 10^{-2}$–$1.07$</td>
<td>$8.3$</td>
<td>$6.8$</td>
<td></td>
<td></td>
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<tr>
<td>Ion-selective electrode</td>
<td>Combination drug formulations</td>
<td>$1.3 \times 10^{-2}$–$1.0 \times 10^{2}$</td>
<td>$98$–$101$</td>
<td>$1.2$</td>
<td></td>
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<tr>
<td>LC</td>
<td>Serum and injection solutions</td>
<td>$1.8 \times 10^{-3}$–$5.4 \times 10^{-3}$</td>
<td>$99.6$–$102.5$</td>
<td>$4$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^b$ R = Recovery.

$^c$ Mean values ± standard deviations ($n = 3$).

$^d$ Added/mg Found/mg R (%) M (%) s

For the atropine–DPA ISP:

- Serum
  - Added/mg: 5.4, 11.0, 15.6, 20.2, 25.6
  - Found/mg: 5.2 ± 0.40, 10.8 ± 0.26, 15.2 ± 0.32, 20.6 ± 0.35, 25.0 ± 0.18
  - Recovery: 96.3%

- Injection solution
  - Added/mg: 5.0
  - Found/mg: 5.4 ± 0.28
  - Recovery: 102.0%

For the atropine–TPB ISP:

- Serum
  - Added/mg: 5.4, 11.0, 15.6, 20.2, 25.6
  - Found/mg: 5.2 ± 0.40, 10.8 ± 0.26, 15.2 ± 0.32, 20.6 ± 0.35, 25.0 ± 0.18
  - Recovery: 96.3%

- Injection solution
  - Added/mg: 5.0
  - Found/mg: 5.4 ± 0.28
  - Recovery: 102.0%

These results indicate that the ISP sensor provides a selective, sensitive, and precise method for the determination of atropine sulfate in serum and injection solutions. The sensor was successfully applied to a quantitative assay of atropine sulfate in various samples, with average recoveries of 100.5% and 100.2%, and standard deviations of 1.67 and 2.93, respectively, in serum and injection solutions. These findings are in good agreement with those obtained from conventional methods.

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