Spectrophotometric Determination of Methimazole in Pharmaceutical Sample by Fe(II)-2,2′-Bipyridyl System

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Abstract. By controlling pH=5.0, Fe(III) could be reduced to Fe(II) by hydrosulfuryl (-SH) in methimazole molecule, then Fe(II) reacts with 2,2′-bipyridyl to form the orange red complex which the maximum absorption is at 522nm. The content of methimazole can be measured by measuring the amount of the complex of Fe(II)-2,2′-bipyridyl. A accurate fast spectrophotometric method for the determination the content of methimazole had been established. A good linear relationship was obtained between A and the concentration of methimazole in the range of 0.0004000-0.004000 mg/mL, the equation of the linear regression was A=0.02707+136.29C(mg/mL), with a linear correlation coefficient was 0.9994. This proposed method had been successfully applied to determinate of methimazole in real pharmaceutical.

1. Introduction
Methimazole (the molecular structure of methimazole is shown in Figure 1) is a kind of antithyroid drugs, it is widely used in the clinical treatment of thyroid diseases. It is of great importance and significance for life science. Up to now, various different methods have been applied for the determination of methimazole, such as spectrophotometry,¹⁻² LC,³ fluorescence emission analysis,⁴ electrochemical analysis,⁵⁻⁸ kinetic method,⁹ flow-injection,¹⁰⁻¹¹ HPLC,¹² RP-HPLC,¹³ HPLC-UV,¹⁴ GC-MS,¹⁵ etc.

Figure 1. The molecular structure of methimazole

In this paper, a new method for the spectrophotometric determination of methimazole by Fe(II)-2,2′-bipyridyl system has been established. The various effect factors on the determination of methimazole were investigated in detail. By controlling pH=5.0, Fe(III) could be reduced to Fe(II) by hydrosulfuryl (-SH) in methimazole molecule, and then using 2,2′-bipyridyl as chromogenic reagent of Fe(II), the content of methimazole can be measured by measuring the amount of the orange red complex of Fe(II)-2,2′-bipyridyl in the system. The maximum absorption wavelength of the complex of Fe(II)-2,2′-bipyridyl was 522 nm, a good linear relationship was obtained between A and the concentration of methimazole in the range of 0.0004000-0.004000 mg/mL, the equation of the linear regression was A=0.02707+136.29C(mg/mL), with a linear correlation coefficient was 0.9994. This
The proposed method had been applied to determine of methimazole in real pharmaceutical, and the results agreed well with those obtained by pharmacopoeial method. This proposed method has the advantages of simply, rapidness, convenience, low analytical cost and so on.

2. Experiment

2.1 Equipment and reagents
UV-2401 UV–visible spectrophotometer (The Shimadzu Corporation, Japan) was used for scanning the absorption spectrum. 723S spectrophotometer (Shanghai Precision & Scientific Instrument Co., Ltd) was used for photometric measurements.

A stock of standard solution of 0.1000 mg/mL methimazole was prepared by dissolving 0.01000 g of methimazole in 100 mL with distilled water and stored at 4°C in dark place. A stock of standard solution of 0.1000 mg/mL Fe³⁺ was prepared by dissolving 0.0864 g NH₄Fe(SO₄)₂·12H₂O in 50 mL with bidistilled water, 2mL 3 mol·L⁻¹ H₂SO₄ was added, and then diluting it to 100 mL with idistilled water. 2,2′-bipyridyl (Bpy) solution: 0.010 mg/mL. Buffer solutions of different pH was prepared as references 16.

All reagents were analytical reagent grade. Bidistilled water was used throughout.

2.2 Method
A given amounts of 0.1000 mg/mL methimazole solution, 3.00 mL of 0.1000 mg/mL Fe³⁺ solution and 10.00 mL bidistilled water were added into a 25 mL ground color comparison tube, mixed well. Aftering this mixture reacted for 60 min at 100°C in water both and cooled back to room temperature, 0.80 mL of 0.1000 mg/mL 2,2′-bipyridyl solution and 3.00 mL pH=5.0 buffer solution were added, the solution was diluted to the mark with bidistilled water and mixed well, then the absorbance was measured at 522 nm against the reagent blank prepared in the same way.

3. Results and discussions

3.1 Absorption spectrum
According to the experimental method, the absorption spectrum of the complex of Fe(II)-2,2′-bipyridyl was shown in Figure 2. It can be seen that the maximum absorption wavelength of the complex of Fe(II)-2,2′-bipyridyl is at 522 nm. Therefore, 522 nm was selected for the absorption spectrum.

3.2 Effects of reaction time
The absorbance of the different reaction time (10, 20, 30, 40, 50, 60, 70, 80 min) was measured at 100°C. The results showed that the absorbance were larger and does not change when the time was 50~70 min. Therefore, 60 min of reaction time was chosen.

Figure 2. Absorption spectrum
3.3 Effects of pH and the dosage of buffer solution

The effects of pH on absorbance were investigated. The results show that the absorbance of solution are maximal and remain almost constant when the pH was 4.0~5.6. Hence, pH5.0 buffer solutions was selected.

The effects of the dosage of pH 5.0 buffer solution were measured. The experimental results showed that the absorbance reaches its maximum value when the amount of pH5.0 buffer solution is 2.00 mL or more. Therefore, 3.00 mL of pH5.0 buffer solution was chosen.

3.4 Effect of the dosage of 2,2′-bipyridyl

The effect of the dosage of 2,2′-bipyridyl on absorbance was investigated(Figure 3). The results show that the absorbance reaches its maximum value when the amount of 2,2′-bipyridyl is 0.60 mL, and it does not change any further with the increasing amount of 2,2′-bipyridyl. This means that the amount of the complex of Fe(Ⅱ)-2,2′-bipyridyl reaches its maximum, and all methimazole was completely oxidized. So, 0.80 mL of the dosage of 2,2′-bipyridyl was chosen in the subsequent studies.

3.5 Effect of the dosage of Fe(Ⅲ)

The effect of the dosage of Fe(Ⅲ) on absorbance can be seen in Figure 4. The absorbance reaches its maximum value and keep constant when the dosage of Fe(Ⅲ) was 2.80 mL~3.20 mL. Hence, 3.00 mL of the dosage of Fe(Ⅲ) was used.

![Figure 3. Effect of the dosage of Bpy](image1)

![Figure 4. Effect of the dosage of Fe(Ⅲ)](image2)

![Figure 5. Calibration curve](image3)

3.6 Interference of coexisting components

A systematic study of the influence of excipients, carbohydrate and minerals on the determination of methimazole was carried out. The tolerance levels was defined as standard deviation less than ±5%
within analytical determination. The conclusion is drawn from the following: 1.6 mg/mL starch; 0.8 mg/mL lactin; 0.4 mg/mL glycine, L-arginine, L-glutamate, NaCl, KCl; 0.2 mg/mL glucose, sucrose, NaCO3; 0.12 mg/mL L-serine do not affect the determination.

3.7 Calibration curve
Under the selected conditions, a linear relationship between absorbance and the concentration (c) of methimazole is obtained in the range of 0.0004000-0.004000 mg/mL (Figure 5). The linear regression equation is A = 0.02707 + 136.29C (mg/mL), with a correlation coefficient of 0.9994.

3.8 Determination of methimazole in pharmaceutical sample
The proposed method was applied to the determination of methimazole in tablet. Meanwhile, the recovery tests of standard addition were performed. The result obtained was compared with those obtained by pharmacopoeia method, as shown in Table 1.

| Table 1 | The determination result of methimazole in tablets n = 5 |
|---------|----------------------------------------------------|
| Sample  | Proposed method (mg/tablet) | RSD (%) | Pharmacopoeia Method[17] (mg/tablet) | Added (μg/mL) | Recovered (μg/mL) | Recovery (%) |
| methimazole tablet | 4.959 | 0.6 | 4.948 | 0.4000 | 0.3977 | 99.4 |

Table 1 shows that the content of methimazole in tablet is 4.959 mg/tablet by this proposed method, agreed well with 4.948 mg/tablet obtained by pharmacopoeia method. It is indicated that the content of methimazole in pharmaceutical sample can be accurately determined by Fe(II)-2,2’-bipyridyl system.

4. Conclusion
In this paper, a new method for the spectrophotometric determination of methimazole by Fe(II)-2,2’-bipyridyl system was reported. The proposed method has been successfully used for the determination of methimazole in pharmaceutical sample, and the results agreed well with pharmacopoeia method. It is obvious that the spectrophotometric determination of methimazole by Fe(II)-2,2’-bipyridyl system has certain practical significance and foreground of application.

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