Determination of Methimazole by Potassium Permanganate Spectrophotometry

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Abstract. In H₂SO₄ medium, oxidation-reduction reaction can be happened between methimazole and potassium permanganate, which results in the fading of potassium permanganate solution. The Beer’s law is obeyed between the concentration of methimazole and the decrease value of absorbance, and the content of methimazole can be indirectly measured by measuring the decrease value of absorbance. A new method for the determination of methimazole by potassium permanganate spectrophotometry is established. The optimum conditions for the determination of methimazole is confirmed. The maximum absorption wavelength of the discoloring system is 525 nm. In the range of 0.001600-0.009600 mg/mL, the linear regression equation is \( \Delta A =-0.0061+34.518 C \) (mg/mL), and the linear correlation coefficient of 0.9992. This method is applied to the determination of methimazole in drugs, and the results are satisfactory.

1. Introduction
Methimazole(Figure 1) is an imidazole antithyroid drugs, it is widely used in the clinical treatment of thyroid diseases. It has been found that overdose of methimazole may cause some side effects such as nephritis, skin allergy, gastrointestinal discomfort and hepatobiliary injury, etc. Thus, it is of great significance for life science to determinate the content of methimazole.

There are many literatures have been reported for the determination of methimazole, such as spectrophotometry,¹⁻² fluorescence emission analysis,³ electrochemical analysis,⁴⁻⁶ flow-injection,⁷⁻⁸ HPLC,⁹ LC,¹⁰ etc.

![Figure 1. The molecular structure of methimazole](image)

In H₂SO₄ medium, potassium permanganate can be reduced by hydrosulfuryl(-SH) in methimazole molecule, which results in the fading of potassium permanganate solution. The Beer’s law is obeyed between the concentration of methimazoletea and the decrease value of absorbance, and the content of
methimazole tea can be indirectly measured by measuring the decrease value of absorbance. A new method for the determination of methimazole tea by potassium permanganate spectrophotometry is established. The maximum absorption wavelength of the discoloring system is 525 nm. In the range of 0.001600-0.009600 mg/mL, the linear regression equation is $\Delta A = -0.0061 + 34.518C$ (mg/mL), the linear correlation coefficient is 0.9992. This method is applied to the determination of methimazole in drugs, and the results are satisfactory.

2. Experimental

2.1 Equipment and reagents

UV-2401 UV-visible spectrophotometer (The Shimadzu Corporation, Japan); 723S spectrophotometer (Shanghai Precision & Scientific Instrument Co., Ltd).

KMnO4 standard solution: $2.3 \times 10^{-3}$ mol/L; Methimazole standard solution: 0.4000 g/L; H2SO4 solution: 3.0 mol/L.

All reagents are of analytical reagent grade, and bidistilled water are used.

2.2 Method

$2.3 \times 10^{-3}$ mol/L KMnO4 solution (2.00 mL), 3 mol/L H2SO4 solution (3.40 mL) are transferred into the two comparison tubes (25 mL). Then 0.4000 g/L methimazole standard solution (0.50 mL) or methimazole sample solution (appropriate amount) is added into one of the two comparison tubes (25 mL). These solutions are diluted to 25 mL with distilled water, mixed well and reacted for 10 min at 35°C in water both and cooled back to room temperature. After placing 10 min, the absorbance ($A_1$) of the blank solution (KMnO4+H2SO4) and the absorbance ($A_2$) of the determination solution (KMnO4+H2SO4+methimazole) are measured at 525 nm against water. The $\Delta A (A_1 - A_2)$ is calculated.

3. Results and discussion

3.1. Absorption spectrum

Based on experimental method, the absorption spectrums of the blank solution (KMnO4+H2SO4) and the determination solution (KMnO4+H2SO4+methimazole) in the range of 400–600 nm are plotted, the absorption spectrums can be seen in Figure 2. Figure 2 shows that the maximum absorption wavelength of the blank solution and the determination solution are at 525 nm. So, 525 nm is selected for determination wavelength.

![Figure 2. Absorption spectrum](image-url)
1-the blank solution (KMnO₄+H₂SO₄); 2- the determination solution (KMnO₄+H₂SO₄+methimazole) 
KMnO₄ solution:2.00 mL; H₂SO₄ solution:3.40 mL; methimazole standard solution:0.50mL; 
reaction temperature:35℃; reaction time:10 min; placing time:10min.

3.2. Reaction temperature, reaction time and placing time
According to the proposed method, KMnO₄ solution(2.00 mL), H₂SO₄ solution(3.40 mL), methimazole 
standard solution(0.50 mL) are added. 
The effect of the reaction temperature (20~60℃) on the absorban ce(∆A) is seen in Figure 3. 
Figure 3 shows that the ∆A reaches maximum value and fix constant when the temperature is 
35~40℃. Therefore, 35℃ is chosen.

![Figure 3 Effect of the reaction temperature](image)

KMnO₄ solution:2.00 mL; H₂SO₄ solution:3.40 mL; methimazole standard solution:0.50mL; reaction 
time:10 min; placing time:10min.

The effect of the reaction time(5~45 min) on the absorbance(∆A) is studied at 35℃. The results 
show that the ∆A of solution reaches maximum value and maintain stability when the reaction time is 
5~15 min. So, 10 min is selected.

When the reaction time is 10 min, the effect of the placing time (5~120 min) on the absorbance(∆A) 
is researched at 35℃. This researchs show that the absorbance(∆A) of solution remains constant 
when the placing time is 5~50 min. Hence, 10 min is used.

3.3. H₂SO₄ solution amount
The effect of the H₂SO₄ solution amount on the absorbance(∆A) can be seen in Figure 4. The ∆A 
reaches its larger value and maintain stability when the H₂SO₄ solution amount is 3.20 mL~3.80 mL. 
Therefore, 3.40 mL of the dosage of H₂SO₄ solution is employed.

3.4. KMnO₄ solution amount
The effect of KMnO₄ solution amount on the absorbance(∆A) is studied (Figure 5). The ∆A reaches 
its maximum value and it does not change when the KMnO₄ solution amount is 1.50 mL~2.00 mL. So, 
2.00 mL KMnO₄ solution is selected.
3.5 Calibration curve

Under optimum conditions, methimazole standard solutions (0.001600, 0.003200, 0.0048, 0.0064, 0.0080, 0.0096 mg/mL) are prepared. The absorbance ($\Delta A$) is measured at 525 nm, the calibration curve is shown in Figure 6. In the range of 0.001600-0.009600 mg/mL, the linear regression equation is $\Delta A = -0.0061 + 34.518C$ (mg/mL), and the correlation coefficient is 0.9992.

3.6 Determination of methimazole in drugs

30 tablets of methimazole tablet are weighed 2.2660 g, 1.4450 g powder of methimazole is weighed after grinding and blending. The powder of methimazole is dissolved by bidistilled water and is transferred into a volumetric flask (250 mL), it is diluted to the 250.0 mL and mixed well. This is the methimazole sample solution, and the solution is preserved at 4°C, shielding from light.
When $2.3 \times 10^{-3}$ mol/L KMnO$_4$ solution (2.00 mL), 3 mol/L H$_2$SO$_4$ solution (3.40 mL) and methimazole sample solution (0.30 mL) are added. The content of the methimazole in methimazole tablet is determined by controlling the reaction temperature is 35℃, reaction time is 10 min and placing time is 10 min, and the recovery tests of standard addition are completed. Meanwhile, the content of the methimazole in methimazole tablet is determined by pharmacopoeia method. The results can be seen in Table 1.

| Sample             | Proposed method (mg tablet$^{-1}$) | RSD (%) | Pharmacopoeial method [11] (mg tablet$^{-1}$) | Added (μg mL$^{-1}$) | Recovered (μg mL$^{-1}$) | Recovery (%) |
|--------------------|------------------------------------|---------|---------------------------------------------|----------------------|--------------------------|--------------|
| Methimazole tablet | 4.623                              | 0.3     | 4.652                                       | 1.600                | 1.564                    | 97.8         |

The results show that the content of methimazole is 4.623 mg·tablet$^{-1}$ by this proposed method, and the result is 4.652 mg·tablet$^{-1}$ by pharmacopoeial method.

### 4. Conclusion

A new method for the determination of methimazole by potassium permanganate spectrophotometry is established. The content of methimazole in methimazole tablet is determined by this method and pharmacopoeial method, and the results are similar. Therefore, the determination of methimazole by potassium permanganate spectrophotometry has certain practical significance and application prospect.

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