Spectrophotometric Determination of Methimazole by Silicomolybdenum Blue

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Abstract. Under optimum reaction conditions, Ammonium silicomolybdate could be quantitatively reduced to silicomolybdenum blue by hydrosulfuryl(-SH) in methimazole molecule, and the content of methimazole was determinated indirectly through determinating the absorbance of the silicomolybdenum blue. A novel method for the spectrophotometric determination of methimazole by silicomolybdenum blue has been established. The results showed that the maximum absorption wavelength of silicomolybdenum blue is 730 nm, good linear relationship is obtained between the absorbance of silicomolybdenum blue and the concentration of methimazole in the range of 8.000-160.0μg/mL, and the equation of the linear regression is A=0.0757+11.547ρ（mg/mL）with a linear correlation coefficient is 0.9998. This proposed method has been applied to determinate of methimazole in tablets, and the results agree well with those obtained by pharmacopoeial method.

1. Introduction

Methimazole is a kind of antithyroid drugs, which is widely used in the clinical treatment of thyroid diseases. But methimazole may cause side effects such as nephritis, liver injury,skin allergy or the decrease of white blood cells in the blood, etc. Thus, the development of methods for the determination of methimazole is obviously of great importance and significance for life science.

Up till now, a number of methods to determine methimazole have been developed, such as spectrophotometry,[1-2] fluorescence emission analysis,[3] electrochemical analysis,[4-7] HPLC,[8] kinetic method,[9] flow-injection,[10-11] RP-HPLC,[12] HPLC-UV,[13] LC,[14] GC-MS,[15] etc. However, some of the methods mentioned above need either complicated and expensive equipment or tedious procedures. This problems limit the practical application of these method.

In this paper, a novel method for the determination of methimazole in pharmaceutical samples by silicomolybdenum blue spectrophotometry has been established. The various effect factors on the determination of methimazole by silicomolybdenum blue spectrophotometry are investigated in detail. Under the optimum reaction conditions, ammonium silicomolybdate could be quantitatively reduced to silicomolybdenum blue by hydrosulfuryl(-SH) in methimazole molecule, the content of methimazole can be determined by determinating the absorbance of silicomolybdenum blue at maximum absorption wavelength (730 nm). This proposed method has been successfully applied to the determination of methimazole in pharmaceutical samples, and the results agree well with those obtained by pharmacopoeial method. This proposed method does not need complicated or expensive equipment,and 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.

Standard solution of methimazole:1.000 mg/mL, was prepared by dissolving 0.1000 g of methimazole in 100 mL bidistilled water and stored at 4°C, shieding from light. Na_2SiO_3 solution: 4.293 mg·mL^{-1}. Mo(VI) solution: 16.30 mg·mL^{-1}, was prepared by dissolving 7.5000 g of ammonium molybdate ($(NH_4)_6Mo_7O_{24}\cdot 4H_2O$) in bidistilled water, transferring into a 250 mL standard flask, diluting to the mark with distilled water. HCl solution:1.0 mol·L^{-1}. NH_3-NH_4Cl buffer solution: pH=10.

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

2.2. Method

2.00 mL of 16.30 mg·mL^{-1} Mo(VI) solution, 15.00 mL bidistilled water, 0.80 mL of 4.293 mg·mL^{-1} Na_2SiO_3

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solution, 0.60 mL of 1.0 mol·L^{-1} HCl solution and 1.00 mL of 1.000 mg·mL^{-1} methimazole solution were added into a 25 mL volumetric flask, mixed well. Aftering this mixture reacted for 15 min at 30℃ in water both and cooled back to room temperature, 1.20 mL of pH=10 NH_3-NH_4Cl buffer solution were added into the 25 mL volumetric flask, the solution was diluted to the mark with bidistilled water and mixed well. The absorbance was measured at 730 nm against the reagent blank after placing 10 min.

3. Results and discussions

3.1. Absorption spectrum

According to the experimental method, in the range of 550 ～ 850nm, the absorption spectrum of silicomolybdenum blue formed from the reaction of ammonium molybdate, Na_2SiO_3 and methimazole is shown in Fig.1. It can be seen that the maximum absorption wavelength of silicomolybdenum blue is at 730 nm. Therefore, 730 nm was selected for the absorption wavelength.

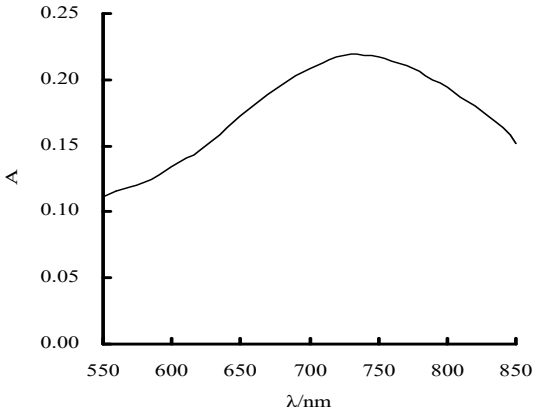

Figure 1. Absorption spectrum Mo(VI):1.00mL;Na_2SiO_3:1.00mL;HCl:0.50mL; methimazole:0.50mL;pH=10 NH_3-NH_4Cl: 2.00mL; reaction time:5min.

3.2. Reaction temperature and time

The effect of reaction temperature on absorbance was studied, the results is shown in Fig.2. It is found that the absorbance keeps constant when the temperature was 30℃～40℃. Hence, 30℃ has been selected for all further studies.

The effect of different reaction time on absorbance showed that the absorbance keeps constant when the reaction time was 10～15min. Therefore, 15 min of reaction time has been chosen.

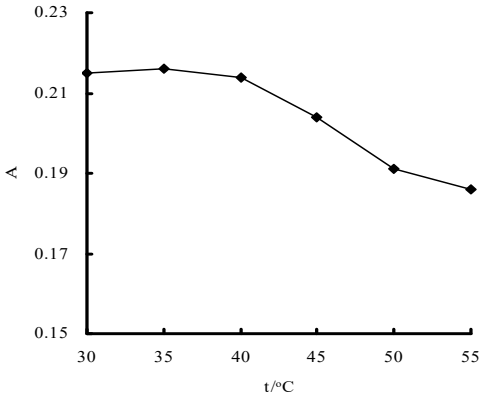

Figure2. Effect of reaction temperature Mo(VI):1.00mL;Na_2SiO_3:1.00mL;HCl:0.50mL; methimazole:0.50mL;pH=10 NH_3-NH_4Cl: 2.00mL;reaction time:5min.

3.3. Place time

The effect of different place time on absorbance was studied. The results show that the absorbance keeps constant when the place time was 10～30min. So, 10 min of place time is chosen.

3.4. The dosage of Na_2SiO_3

The effect of the dosage of Na_2SiO_3 on absorbance can be seen in Fig.3. Fig.3 show that the absorbance reaches its maximum value when the dosage of Na_2SiO_3 was 0.80 mL and remains constant in the range of 0.80 mL～1.40 mL. Hence, 0.80 mL of Na_2SiO_3 was chosen in the subsequent studies.

3.5. The dosage of ammonium molybdate

The effect of the dosage of ammonium molybdate (0.60 mL～2.40 mL) on absorbance can be seen in Fig.4. The results show that the absorbance reaches its maximum value when the amount of ammonium molybdate is 2.00 mL, and it does not change any further with the increasing amount of ammonium molybdate. Therefore, 2.00 mL of ammonium molybdate has been selected.

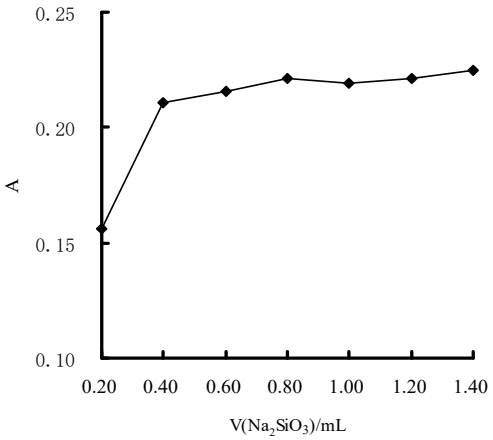

Figure 3. Effect of the dosage of Na_2SiO_3 Mo(VI):1.00mL; HCl:0.50mL; methimazole: 0.50mL;pH=10 NH_3-NH_4Cl:2.00mL; reaction temperature:30°C; reaction time:15 min.

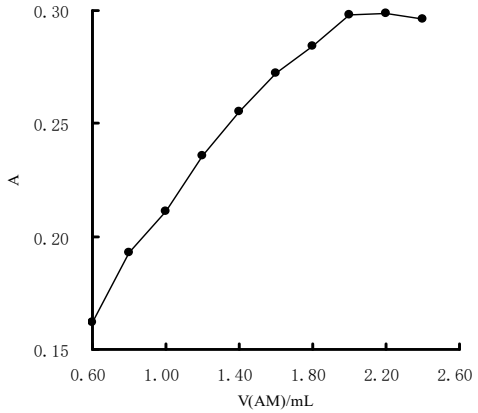

Figure 4. Effect of the dosage of ammonium molybdate Na_2SiO_3:080 mL; HCl:0.50mL; methimazole: 0.50mL;pH=10 NH_3-NH_4Cl:2.00mL;reaction temperature:30°C; reaction time:15 min.

3.6. The dosage of HCl

The effect of the dosage of HCl(from 0.20 mL to 0.65 mL) on absorbance was studied. The results show that the absorbance reaches greater and keeps constant when the dosage of HCl is 0.55 mL～0.65 mL. So, 0.60 mL of the dosage of HCl has been selected.

3.7. The dosage of pH=10 NH_3-NH_4Cl buffer solution

The effect of the dosage of pH=10 NH_3-NH_4Cl buffer solution(from 0.40 mL to 2.00 mL) on absorbance was studied. It is found that the absorbance remains constant when the dosage of pH=10 NH_3-NH_4Cl buffer solution was 1.00 mL～1.80 mL. Hence, 1.20 mL of pH=10 NH_3-NH_4Cl buffer solution was chosen in the subsequent studies.

3.8. Interference of coexisting components

A systematic study of the influence of excipients, aminoacids and carbohydrate on the determination of methimazole was carried out. The tolerance levels are defined with an error of the determination less than ±5%.A conclusion can be drawn from the following: 8.00 mg/mL glucose, sucrose, lactose, fructose; 2.00 mg/mL starch; 0.40 mg/mL serine, arginine, proline, L-glutamate do not affect the determination.But a certain amount of glycine and tyrosine affect the determination.

3.9. Calibration curve

Under the chosen conditions, a linear relationship between absorbance (A) of silicomolybdenum blue and the concentration (C) of methimazole is obtained in the range of 8.000-160.0μg/mL (Fig.5). The linear regression equation is A=0.0757+11.547C(mg/mL), with a correlation coefficient of 0.999

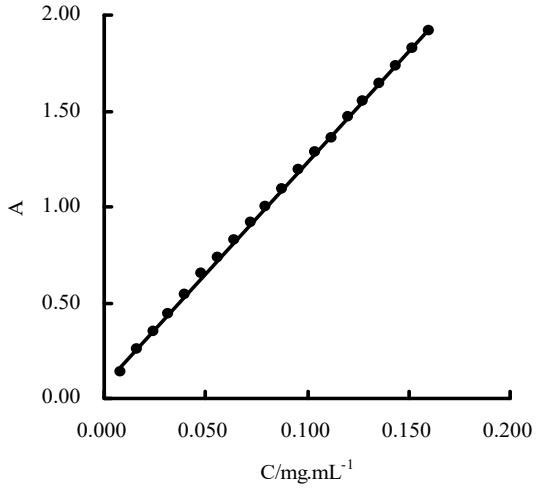

Figure 5. Calibration curve
Mo(VI):2.00mL; Na_2SiO_3:080 mL;
HCl:0.60mL; pH=10 NH_3-NH_4Cl:1.20mL;
reaction temperature:30°C; reaction time:15 min.

3.10. Determination of methimazole in pharmaceutical samples

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

Table 1 The determination result of methimazole in tablet n = 5

Sample	Proposed method ($mg \cdot tablet^{-1}$)	RSD (%)	Pharmacopoeia Method[16] ($mg \cdot tablet^{-1}$)	Added ($\mu g \cdot mL^{-1}$)	Recovered ($\mu g \cdot mL^{-1}$)	Recovery (%)
methimazole tablet	4.957	0.3	4.998	3.20 6.40	3.19 6.35	99.7 99.2

Table 1 shows that the content of methimazole in methimazole tablet is 4.957 $mg \cdot tablet^{-1}$ by this proposed method, and the content of methimazole is 4.998 $mg \cdot tablet^{-1}$ by pharmacopoeial method. Obviously, the result of this proposed method agreed well with those obtained by pharmacopoeial method. It is indicated that the content of methimazole in tablet can be accurately determined by silicomolybdenum blue spectrophotometry.

4. Conclusion

A novel method for the spectrophotometric determination of methimazole is established by silicomolybdenum blue. The proposed method has been successfully applied to the determination of methimazole in pharmaceutical samples with satisfactory results. It is indicated that the content of methimazole in real pharmaceutical can be accurately determined by silicomolybdenum blue spectrophotometry.

References

1. Skowron,M.; Ciesielski,W. *J.Anal.Chem*.2011, 66(8), 714.
2. Dong,C.-H.; Zhang,Yan.; Guo,Li.; Li,Q.-M. *J.Anal.Chem*,2010,65(7),707.
3. Dong,F.; Hu,K.-W.; Han,H.-Y.; Liang,J.-G. *Microchim.Acta*.2009,165(1-2), 195.
4. Shahrokhian,S.; Ghalkhani,M. *Electroanalysis*.2008,20(10),1061.
5. Zbigniew,F.;Petr,Z. *Anal.Lett*.1990,23(7),1213.
6. Aslanoglu,M.; Peker,N. *J.Pharm.Biomed.Anal*.2003,33(5),1143.
7. Wang,Y.-Z. *Bioelectrochemistry*,2011,81(2),86.
8. Meulemansa,A.; Manuelb,C.; Ferrierec,C.; Valpillatd,M.*J.Liq.Chromatogr*.1980,3(2),287.
9. Ma,S.-G.;Ma,I.-A.;Concepción,S.-P.;Lorenzo,T. *Analyst*.1995, 120, 129.
10. Anastasios,E.;Paraskevas,D.-T.;Maria,N.;Demetrius,G.-T. *Anal.Chim.Acta*.2004,505(1), 129.

11. Pedreño,C.-S.; Albero,M.-I.; García,M.-S.; Ródenas,V. *Anal.Chim.Acta*.1995,308(1-3), 457.
12. Hollosi,L.; Kettrup,A.; Schramm,K.-W. *J.Pharm.Biomed.Anal*.2004,36(4),921.
13. Pan,M.-F.; Wang,J.-P.; Fang,G.-Z.; Tang,W.-W.; Wang,S. *J.Chromatogr.,B*.2010,878(19),
14. Krzysztof,K.;Edward,B. *Talanta*.2007,71(5),2121.
15. Susanne,F.;Kerstin,L.;Björn,L. *J.Chromatogr.,B*.1980,182(1),63.
16. The Pharmacopeial Committee of China.*The Pharmacopoeia of the People's Republic of China*(*second-part*);Chemical Industry Press;Beijing,2005, p128. (In Chinese)