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Spectrophotometric Determination of Mesna in Commercial Injections

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A new visible spectrophotometric method for the determination of mesna was carried out based on the reaction of ferric solution with mesna to produce ferriferrous ion. The dependence of the absorbance on pH, temperature and reaction time was investigated. In Clark-lubs buffer medium, the red complex with the absorbance decreased obviously at 480 nm. The decrease value of the absorbance (ΔA), due to the presence of mesna was correlated with its concentration. Linear relationship with good correlation coefficient (0.9991) was found between ΔA and the concentration of mesna in a concentration range of 1-30 μg mL^{-1}. The assay limit of determination was 0.31 μg mL^{-1}. The proposed method was successfully applied to the determination of the investigated drug in injections with the recoveries of the range from 99.4 to 100.2 %.

Key Words: Mesna, Spectrophotometry, Injection.

INTRODUCTION

Mesna is an important thiol compound. The chemical name is sodium 2-mercaptoethanesulfonate. As a non-toxic compound, mesna prevents hemorrhagic cystitis in patients who receive oxazaphosphorine treatment, such as ifosfamide or cyclophosphamide, by neutralizing the highly reactive urotoxic metabolites of oxazaphosphorines locally in the urine[1]. Several procedures have been reported in the literature for the determination of mesna. These methods are HPLC[2-6], flow injection method with chemiluminescence detection[7], solid-phase microextraction gas chromatography-mass spectrometry[8], voltammetry[9] and vibrational spectroscopy[10]. In this work, a new spectrophometric method for the assay of mesna is developed, which is based on the reaction between mesna and ferric solution, then the colour reaction of excess of ferric ion with potassium rhodanate to produce the red complex with the absorption peak at 480 nm. In the proposed method, there are no complicated sample separation and extraction steps with satisfactory analytical results.

EXPERIMENTAL

Measurements were performed using a 722-N spectrophotometer (Shanghai Precision & Scientific Instrument Co., Ltd., China) equipped with 1 cm matched quarz cells. The stock solution of mesna (1000 μg mL^{-1}) was prepared by dissolving 0.5000 g of mesna in 500 mL volumetric flask and filling it up with water. 100 μg mL^{-1} mesna standard working solution was obtained by diluting the stock solution with water. 100 μg mL^{-1} ferric solution was prepared by dissolving 0.8640 g of $NH_4Fe(SO_4)_2 \cdot 12H_2O$ in 15 mL 4 mol L^{-1} HCl solution and diluting the solution to 1000 mL with water. Potassium rhodanate solution was prepared by dissolving 25.0 g of potassium rhodanate in 250 mL volumetric flask and filling it up with water. Clark-Lubs solutions were prepared at pH range from 2.00 to 4.00 based on the described procedure[11]. Distilled water used in this study and all the reagents were of analytical grade.

Experimental procedure: A suitable amount of sample solution or standard mesna working solution and 1.50 mL of 100 μg mL^{-1} ferric solution were transferred into a 10 mL colorimetric tube. Then the tube was heated for 15 min at 90 ºC in water-bath and cooled to room temperature with following water, 2.00 mL potassium rhodanate solution and 2.00 mL pH = 1.4 Clark-lubs buffer solution were added to the hot solution then cooled solution, diluted to the mark with water. After lying aside for 15 min at room temperature, the absorbance A of the complex solution was measured with 1.0 cm cell at 480 nm. The measurement was repeated in the absence of mesna to obtain the absorbance A_0 of the reagent blank. The absorbance difference was defined as $\Delta A = (A_0 - A)$.

RESULTS AND DISCUSSION

Absorption spectra and reaction mechanism: Mesna (sodium 2-mercaptoethanesulfonate) is an important thiol compound which can be used as the reducing agent on the

reaction between mesna and ferric solution,whereas the excess of ferric ion can react with potassium rhodanate solution to produce the red complex with the absorbpton peak at 480 nm in Clark-lubs buffer medium with pH value at 1.4. The reaction mechanism was as followed in reaction eqns. 1 and 2:

$$2HSCH_2CH_2SO_3Na + 2Fe^{3+} = 2Fe^{2+} + NaO_3S\ CH_2CH_2S\text{-}SCH_2CH_2SO_3Na + 2H^+ \quad (1)$$

$$Fe^{3+} + 6SCN^- = [Fe(SCN)_6]^{3-} \quad (2)$$

(red complex, 480 nm)

The absorption spectra of the reagent blank and the solution contain of mesna are shown in Fig. 1. From Fig.1, it is found that the absorbance of the reagent decreased obviously at the presence of mesna. The absorbance difference (ΔA) reached a maximum at 480 nm. Hence, 480 nm is selected for further studies.

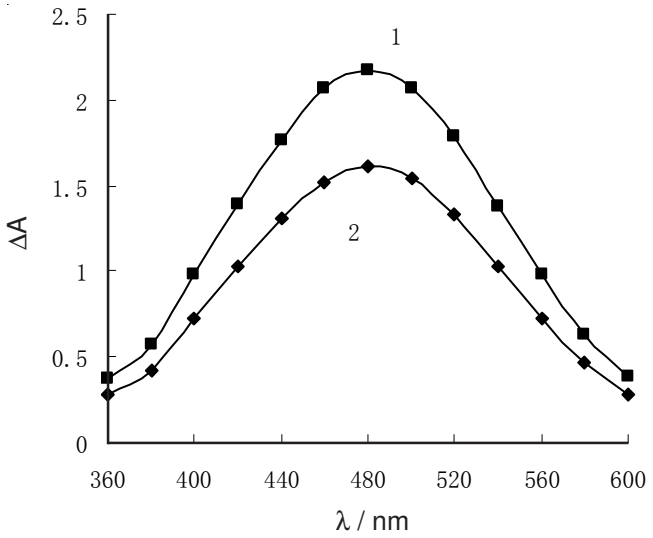

Fig. 1. Absorption spectra: (1) the reagent blank *vs.* water; (2) the solution containing mesna *vs.* water; [mesna] = 10 μg mL^{-1}

Effect of heating temperature: The reaction between mesna and ferric solution is slow at room temperature. Thus the effect of heating temperature on ΔA in the range of 40-95 °C for the reaction between mesna and ferric solution, is investigated and the results are shown in Fig. 2. It is observed that ΔA was almost constant at 80-95 °C. For the reason of simple operation, 90 °C is chosen as optimum temperature for further study.

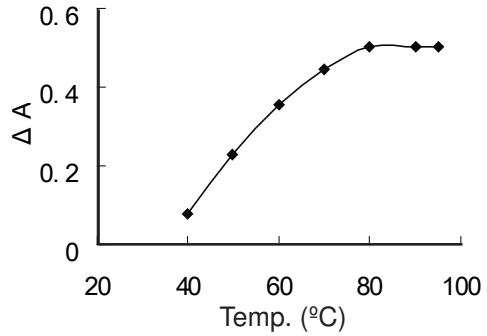

Fig. 2. Effect of heating temperature: [mesna] = 10 μg mL^{-1}

Effect of reaction time: The effect of heating time for the reaction between mesna and ferric solution is studied. As shown in Fig. 3, mesna reacted with ferric solution within at most 8 min at 90 °C. The formed red complex $[Fe(SCN)_6]^{3-}$ remained steady at least 1 h. Therefore 10 min of heating time is chosen in the experiments.

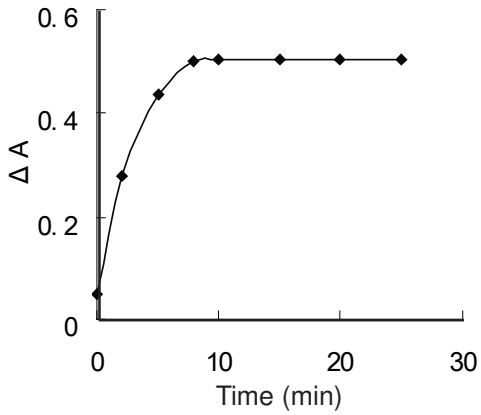

Fig. 3. Effect of heating time: [mesna] = 10 μg mL^{-1}

Effect of pH: The effect of various pH values in Clark-lubs buffer solution was investigated on the reaction of excess of ferric with potassium rhodanate solution after the reaction of mesna with ferric solution and the results were given in the Fig. 4. It was obvious from Fig. 4 that pH value at 1.4 was the best medium with the maximum absorbance ΔA. Further study shows that 0.50-2.50 mL pH 1.4 Clark-lubs buffer solution will give the maximum absorbance ΔA. Therefore 2.00 mL pH 1.4 Clark-lubs buffer solution is chosen for further studies.

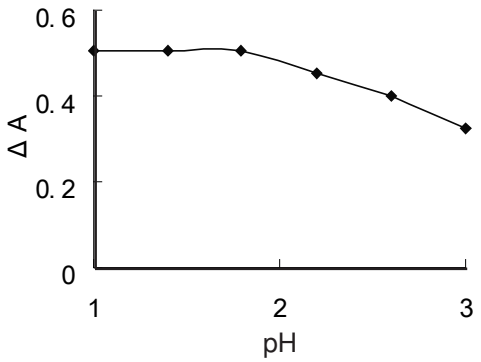

Fig. 4. Effect of pH: [mesna] = 10 μg mL^{-1}

Effect on volume of ferric solution: As the oxidizer of mesna, the concentration of ferric solution may effect on the absorbance ΔA of the reaction system. From Fig. 5, 100 μg mL^{-1} 1.00-2.00 mL ferric solution given the maximum absorbance ΔA for the system, so 1.50 mL 100 μg mL^{-1} ferric solution was chosen in the experiments.

Effect on volume of potassium rhodanate solution: It is known that the potassium rhodanate is the colour reagent for ferric ion. From Fig. 6, 1.75-2.50 mL potassium rhodanate solution could give the maximum absorbance ΔA for the system, so 2.00 mL potassium rhodanate solution is chosen in the experiments.

TABLE-1
ANALYTICAL RESULTS OF MESNA

Injections	Labeled amount (mg)	Percentage of labeled value[a] (w/%)	RSD (%)	Added (μg mL^{-1})	Recovered (μg·mL^{-1})	Recovery (%)
Meian[b]	200	99.86	1.4	50.0	49.80	99.80
Meian[b]	400	100.1	1.2	50.0	50.10	100.2
Yidizheng[c]	400	99.78	1.6	50.0	49.70	99.40

[a]Each value is the mean of five measurements; [b]Meian from Jiangsu Hengrui Medicine Co. Ltd;
[c] Yidizheng from Shengzheng Wanle Medicine Co. Ltd.

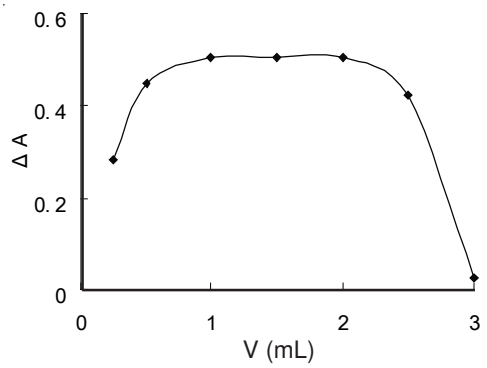

Fig. 5. Effect on volume of ferric solution: [mesna] = 10 μg mL^{-1}

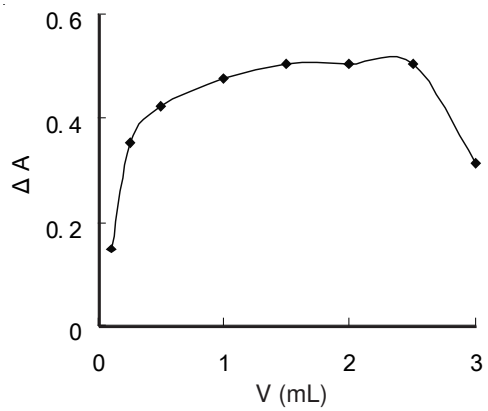

Fig. 6. Effect on volume of potassium rhodanate solution: [mesna] = 10 μg mL^{-1}

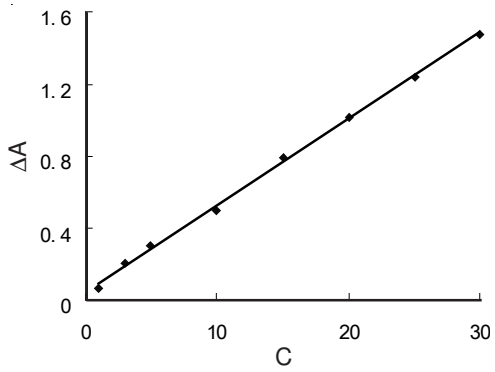

Fig. 7. Working curve

Working curve and detection limit: A series of standard mesna solutions with different concentration were prepared. Under the chosen experimental conditions, ΔA of these solutions was measured. The working curve was drawn and shown in Fig. 7. The results showed that Beer's law was obeyed in the concentration range of 1-30 μg mL^{-1} for mesna. The linear regression equation was $\Delta A = 0.048C + 0.0446$ with the regression coefficient $\gamma = 0.9991$. The reagent blank was determined 11 times and the detection limit of assay was 0.31 μg mL^{-1} by 3S/K method (S = standard deviation of the reagent blank for 11 times determination, K = slope of the working curve).

Application: The proposed method was applied to the determination of mesna in commercial mesna injections. Five commercial injections, which were obtained from local drug store, were homogeneously mixed and 1.00 mL mixed solution containing 100 mg of mesna were dissolved in 1000 mL with water. Then 1.00 mL of the diluted solutions were analyzed in five replicate determinations by the proposed method. Satisfactory results were obtained as shown in Table-1. Moreover, to check the validity of the proposed method, the standard addition method was applied by adding mesna to the previously analyzed injections. The recovery was calculated and shown in Table-1.

Conclusion

This paper demonstrated that colour reaction can be utilized as a useful method for the spectrophotometric determination of mesna. The proposed method has the advantages of being simple, cheap, accurate and requires minimum equipments and chemicals. These advantages encourage the application of the proposed method in routine quality control of the investigated mesna in industrial laboratories.

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