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Fading Spectrophotometric Quantification of Mesna in Commercial Injections with Ferric Salicylate Complex System

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A new simple fading spectrophotometric quantification of mesna was developed, which based on the reaction of ferric solution with mesna (2-mercapto ethane sulfonate) to produce ferriferrous ion, whereas result from the red complex with the maximum absorption peak at 530 nm by the reaction of excess of ferric ion with sodium salicylate. The dependence of the absorbance on acidity, temperature and reaction time was investigated. In the diluted HCl solution, the decrease value of the absorbance (ΔA) at 530 nm, due to the presence of mesna was correlated with its concentration. Beer's law was obeyed in a mesna concentration range of 1-30 μg mL^{-1} with good correlation coefficient (0.9987). The proposed method was successfully applied to the quantification of mesna in commercial injections with the recoveries of the range from 99.68 % to 101.0 %.

Key Words: Quantification, Mesna, Fading spectrophotometry, Injection.

INTRODUCTION

As an important non-toxic thiol compound, the chemical name of mesna is sodium 2-mercaptoethane sulfonate, which 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].

Some procedures have been reported in the literature for the quantification of mesna,such as voltammetry[2], vibrational spectroscopy[3], solid-phase microextraction GC-MS[4], flow injection method[5], HPLC method[6-10] and spectrophotometry[11].

Visible spectrophotometric methods have been widely applied to the quantification of organic compounds of pharmaceutical preparations for faster and cheaper than HPLC method and more precise than voltammetry. In this work, a new fading spectrophometric method for the quantification of mesna was developed, which was based on the reaction between mesna and ferric solution, then the colour reaction of excess of ferric ion with sodium salicylate to produce the red complex with the maximum absorption peak at 530 nm. There are no complicated sample separation and extraction steps with satisfactory analytical results in this proposed method.

EXPERIMENTAL

722-N spectrophotometer (Shanghai Precision and Scientific Instrument Co. Ltd., China).

All the reagents used were of analytical reagent grade and the solutions were prepared with distilled water unless otherwise specified.

A stock solution of mesna (500 μg mL^{-1}) was prepared by dissolving 0.1250 g of mesna in 250 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 ferriammonium sulfate in 15 mL 4 mol L^{-1} hydrochloric acid solution and diluting the solution to 1000 mL with water. Sodium salicylate solution was prepared by dissolving 1.0 g of sodium salicylate in 100 mL volumetric flask and filling it up with water. 0.1 mol L^{-1} hydrochloric acid solution was employed as reaction medium.

Appropriate amount of the sample solution or standard mesna working solution and 3.50 mL of 100 μg mL^{-1} ferric solution were transferred into a 10 mL colourimetric tube. Then the tube was heated 15 min. in 90 ºC water-bath and cooled to room temperature with following water, 1.50 mL 0.1 mol/L hydrochloric acid solution and 2.00 mL sodium

salicylate solution were added to the heated 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 cm cell at 530 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: Mesna is sodium 2-mercaptoethanesulfonate and an important thiol compound. As we know, the mercapto or thiol compound can be used as the reducing agent in the redox reaction. So the redox reaction between mesna and ferric solution is used in this work,whereas the excess of ferric ion can react with sodium salicylate solution to produce the red ferric salicylate complex with the absorption peak at 530 nm in the hydrochloric acid solution medium. The reaction mechanism is as followed in reaction equation (1) and (2):

$$2HSCH_2CH_2SO_3Na + 2Fe^{3+} = 2Fe^{2+} + NaO_3SCH_2CH_2S\text{-}SCH_2CH_2SO_3Na + 2H^+ \quad (1)$$

ferric ion + salicylate = red ferric salicylate complex (530 nm) (2)

The absorption spectra of the reagent blank and the solution contain of mesna were shown in Fig. 1. From Fig. 1, it was found that the absorbance of the reagent decreased obviously at the presence of mesna. The absorbance difference (ΔA) reached a maximum at 530 nm. Hence, 530 nm was selected for further studies.

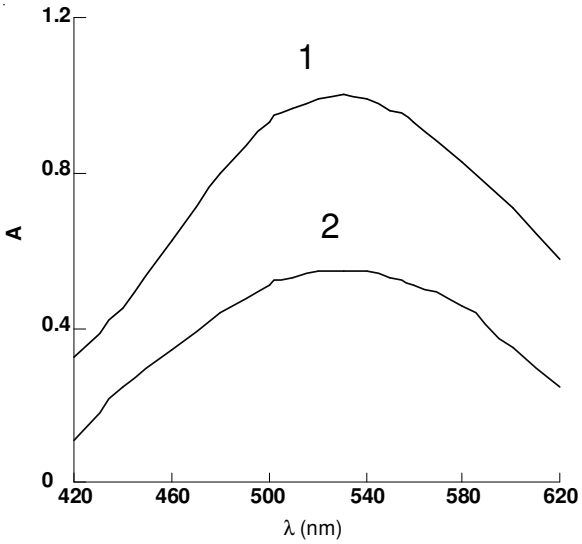

Fig. 1. Absorption spectra: (1) the reagent blank *vs.* water; (2) the solution containing mesna *vs.* water; [Mesna] = 20 μg mL^{-1}

Effect of heating temperature: At room temperature the redox reaction between mesna and ferric solution is very slow. Thus the heating condition was investigated. It was found that effect of heating temperature on ΔA in the range of 40-95 ºC for the redox reaction between mesna and ferric solution in Fig. 2. It was seen that ΔA was almost constant at 80 -95 ºC. For the reason of simple operation, 90 ºC was chosen as optimum temperature for further study.

Effect of reaction time: The effect of heating time for the redox reaction between mesna and ferric solution was studied. As shown in Fig. 3, mesna reacted with ferric solution within at most 10 min at 90 ºC. The formed red ferric salicylate complex remained steady at least 1 h. Therefore 15 min of heating time was chosen in the experiments.

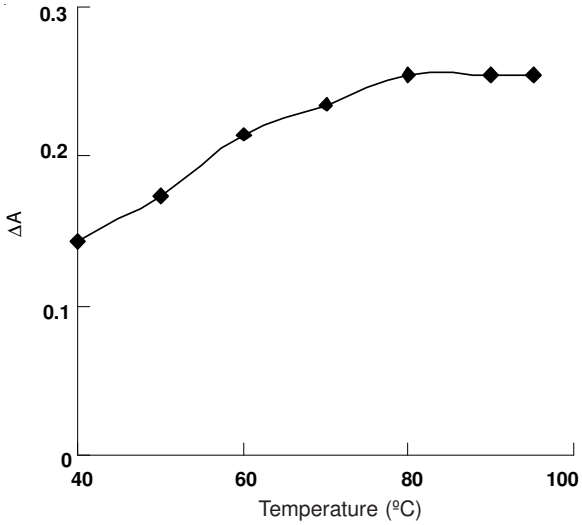

Fig. 2. Effect of heating temperature: [Mesna] = 20 μg mL^{-1}

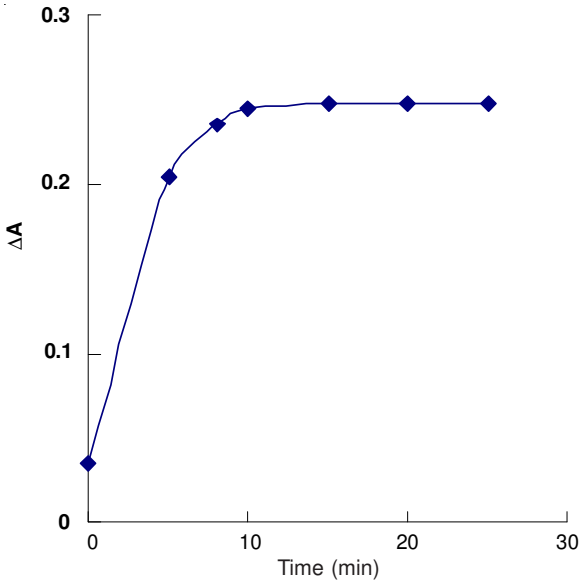

Fig. 3. Effect of heating time: [Mesna]= 20 μg mL^{-1}

Effect of hydrochloric acid solution: The effect of hydrochloric acid solution was investigated on the reaction of excess of ferric with sodium salicylate solution after the reaction of mesna with ferric solution and the results were given in the Fig. 4. It was obvious from Fig. 4, the best volume range of 0.10-2 mL hydrochloric acid solution will give the maximum absorbance ΔA. Therefore 1 mL 0.1 mol L^{-1} hydrochloric acid solution was chosen for further studies.

Effect on ferric solution: As the oxidizer of mesna, the concerntration of ferric solution will effect on the absorbance ΔA of the redox reaction system. From Fig. 5, the ferric concerntration range from 30 to 45 μg mL^{-1} will give the maximum absorbance ΔA for the system, so 3.50 mL 100 μg mL^{-1} ferric solution was chosen in the experiments.

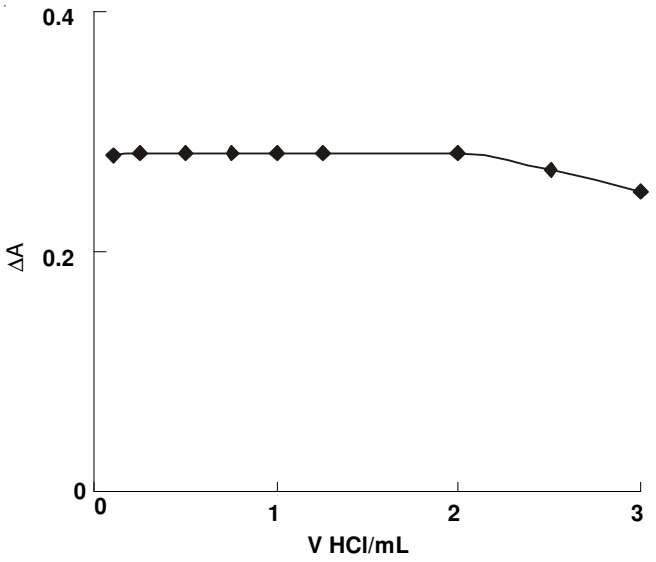

Fig. 4. Effect of volume ammount of hydrochloric acid solution: [Mesna] = 20 μg mL^{-1}

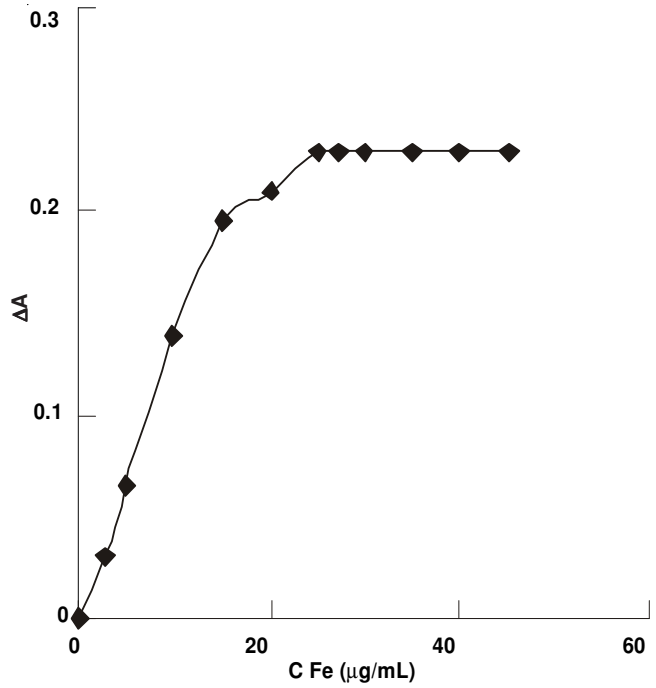

Fig. 5. Effect on ferric concerntration: [Mesna]= 20 μg mL^{-1}

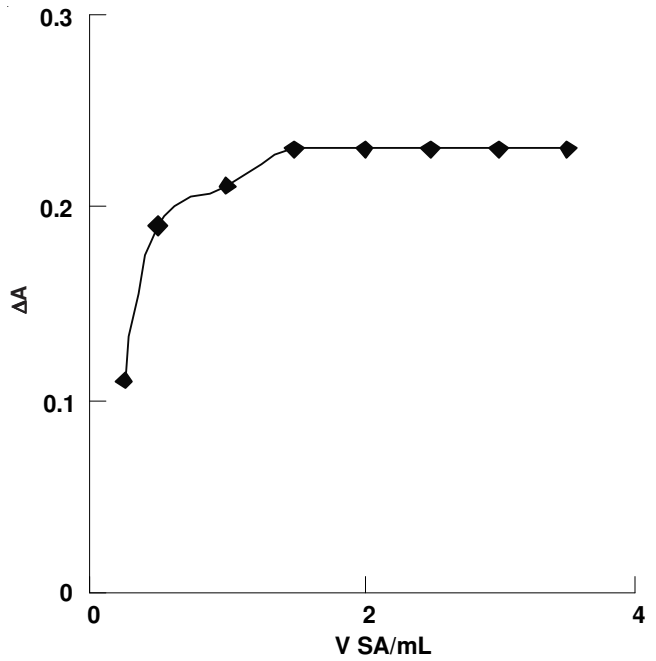

Fig. 6. Effect on volume of sodium salicylate solution: [Mesna] = 20 μg mL^{-1}

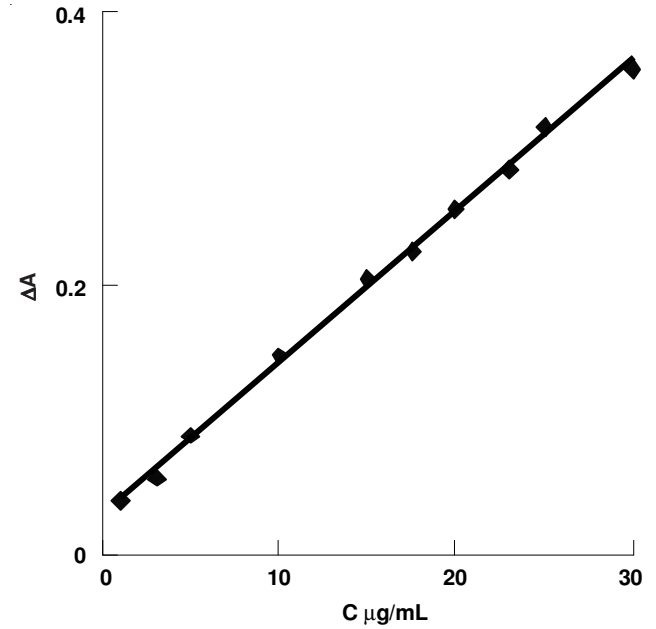

Fig. 7 Calibration graph

Effect on volume of sodium salicylate solution: As we know, sodium salicylate solution is the colour reagent of ferric ion. From Fig. 6, 2-3.5 mL sodium salicylate solution could give the maximum absorbance Δ*A* for the system, so 2.5 mL sodium salicylate solution was chosen in the experiments.

Calibration graph: A series of standard mesna solutions with different concentration were prepared. Under the chosen optimum experimental conditions,the calibration graph was linear in the range 1-30 μg mL^{-1} for mesna (Fig. 7). The calibration equation is $\Delta A = 0.01114C + 0.0263$ with the regression coefficient $\gamma = 0.9987$.

Sample analysis: The proposed method was applied to the quantification of mesna in commercial mesna injections. Five commercial injections, which were obtained from local drug store, were homogeneously mixed and 2.00 mL mixed solution containing 200 mg of mesna were dissolved in 1000 mL with water. Then 1 mL of the diluted solutions were analyzed in five replicate quantifications 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

A new simple fading spectrophotometric quantification of mesna has been proposed with the advantages of being simple, cheap, accurate and requires minimum equipments and chemicals. It is well suited for routine quality control of the investigated mesna in industrial laboratories.

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	99.78	1.7	50.0	49.84	99.68
Meian[b]	400	100.2	2.1	50.0	50.16	101.0
Yidizheng[c]	400	99.88	1.8	50.0	49.92	99.84

[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.

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