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# Application of Argent Metric in the Estimation of Mesna in Tablets and Injections. Application to Content Uniformity Testing

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**ABSTRACT**

A new, accurate, sensitive and simple indirect spectrophotometric method for the estimation of sodium 2-mercaptoethanesulfonate (mesna) has been developed. This procedure base on the reaction of mesna with excess of silver nitrate and a known amount of methyl orange and the increase in absorbance at 520 nm, caused by a decrease in pH due to release of nitric acid, is measured and related to drug concentration .The absorbance results increased with increasing concentration of mesna . Beer' s law is obeyed and linear at the concentration range of 2-28µg/ml. Apparent molar absorbance, Sand ell's sensitivity values were $7.16\times10^3$ Lmol-1cm$^{-1}$. And 22.93 ng.cm$^{-2}$ respectively, The present method is considered to be simple because it does not need either heating or hydrolysis or solvent extraction steps. The ingredients often formulated with Metoclopramide hydrochloride have been shown not to interfere, and the proposed method is suitable for the routine determination of mesna. The (RSD) of this method was less than 2 and average recovery (accuracy) is 100 ± 0.75. The method applied successfully for estimation of mesna in (tablets and injections pharmaceutical formulations).and Application to Content Uniformity Testing.

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## Introduction

Mesna is an important thiol compound. The chemical name is sodium 2-mercapto ethane sulfonate (Figure 1).


$C_2H_5NaO_3S_2$=164.2

**Figure 1:** Chemical Structure of Mesna

Mesna used as antioxidant for prevention of urothelial toxicity in patients treated by antineoplastic, cyclophosphamide or ifosfamide. In the kidney, by neutralizing the highly reactive urotoxic metabolites of oxazaphosphorines locally in the urine, mesna recently used as antioxidant against acetaminophen toxicity [1-4]. Mesna oxidized to disulfide, and stabilized using EDTA, sodium hydroxide and inert gas atmosphere in pharmaceutical formulation . The reducing character of mesna should be considered in the design of any analytical methods [5]. The literature revealed that mesna has been determined by means of a few analytical methods. These include: HPLC [5-7]. Chemiluminescence-flow injectio, spectrophotometric methods, Spectrofluorimetric [14]. BP and USP described a tedious titrimetric estimations [15,16]. The present method work is accurate, simple, sensitive spectrophotometric method for estimation of mesna in pure, pharmaceutical dosage forms ,provided from the state company for drug industries and medical appliances Mosul-Iraq (NDI). Utilize silver nitrate – methyl orange as new reagents.

## Experimental

### Apparatus

Optima SP 3000 plus UV-Visible spectrophotometer with 1.0 cm quartz cells was used (OPTIMA USA, INC).

### Reagents

The chemical reagents used were of pharmaceutical and analytical purity grade, and double distilled water was used throughout. Standard solution of mesna (100 ppm): Prepared by dissolving 0.1 g of mesna in 1 L distilled water.

$AgNO_3$ solution (0.25%): was prepared by dissolving 250 mg silver nitrate in 100 ml of distilled water in a volumetric flask. and stored in a dark bottle methyl orange A 0.01% :was prepared by dissolving 0.01g of methyl orange in 100ml of distilled water.

### Recommended Procedure

Aliquots of standard solution of mesna(5-70 µg) were transferred into a series of 25 ml calibrated flasks, added 2 ml of 0.25% AgNO3solution, mixed well and let stand for 5 min with occasional shaking, and then added 2 ml of 0.01% methyl orange was added to each flask, diluted to volume with distilled water and the absorbance was measured at 520 nm against the reagent as a blank.

### Procedures for Pharmaceutical Dosage Forms

Tablets: To minimize a possible variation in the composition of

the tablets (were provided from the company for pharmaceutical industries (NDI) Mosul-Iraq). The mixed content of 10 tablets (Mesnan tablets 400 mg of Mesna / tablet), were weighed and grounded, then powder equivalent to 100 mg of mesna was dissolved well in 1 L distilled water, filtered by filter paper and 3 mL of this solution was treated as under recommended procedure.

Injection: Ampoule of 100 mg of mesna (provided from (NDI) Mosul- Iraq). The content of 5 ampoules was mixed well in 500 mL beaker. An aliquots equivalent to 100 mg of mesna was transferred into 1 L volumetric flask and diluted up to the mark with distilled water, and 3 mL of this solution was treated as recommended procedure.

## Results and Discussion

Spectrophotometric methods development for the determination of drugs has been increased considerably in recent years because of their importance in pharmaceutical analysis [17,18] . A new method has been developed for the spectrophotometric determination of mesna.

The proposed method was based on the reaction of Mesna which contains a -SH group, and converted to a mercantile by treatment with excess AgNO3 and a known amount of methyl orange,which have basic form (yellow) and change to its acidic form (red) and the increase in absorbance at 520 nm, caused by a decrease in pH due to release of nitric acid, The formation of the results might be written as

**$HS\text{-}CH_2\text{-}CH_2\text{-}SO_3Na + AgNO_3$ (Known excess) → $Ag\text{-}S\text{-}CH_2\text{-}CH_2\text{-}SO_3Na + HNO_3$**

Beer's law is obeyed over the concentration range 2 - 28µg/ml .Linear regression equation: Y=0.0436X+0.0115 (r = 0.998, n = 8). Where Y is the absorbance and X is the concentration in µg\ml as shown below Figure 2 .The apparent molar absorptivity was 7.16×103 l/mol.cm , and Sandell sensitivity 22.93 µg/cm2

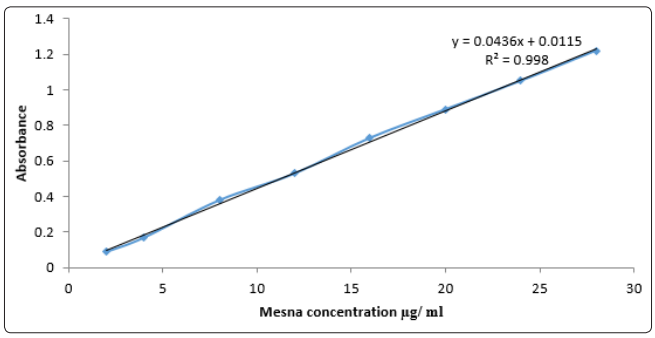


**Figure 2:** Calibration curve of mesna

The optical characteristics such as absorption maxima, Beer's law limits, Molar absorptivity and Sandell's sensitivity for this method are presented in Table 1.

## Accuracy and Precision

The accuracy and precision of the method were established by analyzing the pure drug solution at three different levels. The average recovery which is a measure of accuracy is 100±0.75% revealing high accuracy of the method. The relative standard deviation (RSD), which is an indicator of precision, is less than 2% the results are compiled in Table 1.

**Table 1: Optical characteristics and statistical data for regression equation of the proposed method**

| Parameters | Value |
|---|---|
| λ max (nm) | 520 |
| Beer's law limits, (µg.ml$^{-1}$) | 2-28 |
| Molar absorptivity, (l.mol-1.cm$^{-1}$) | $7.16\times10^3$ |
| Sandell's sensitivity, (ng\cm$^2$) | 22.93 |
| Correlation coefficient (r) | 0.998 |
| Regression equation (y= a + bx) | Y=0.0436X+0.0115 |
| Intercept (a)<br><br>Slope (b) | 0.0115<br><br>0.0436 |
| Recovery (%) | 100 ±0.75 |
| Relative standard deviation (%) | < 2 |

## Interference Studies

In order to assess the possible applications of the proposed method, the effect of substance that often accompany with mesna in pharmaceutical preparations were studied by adding various amounts of substances to 20µg of mesna. An attractive feature of the method is its relative freedom from interference by the usual diluents and excipients in amounts for in excess of their normal occurrence in pharmaceutical preparations. The results are given in Table 2.

**Table 2: Determination of 2µg / ml of Mesna in the presence of excipients and other substances.**

| Interfering substances | Amount added (mg of nterfering) | Amount of drug found*,µg | Recovery, % |
|---|---|---|---|
| Corn starch | 40 | 20.06 | 100.3 |
| Microcrystalline cellulose | 20 | 19.9 | 99.5 |
| Mannitol | 1000 | 20.05 | 100.25 |
| Talc | 1000 | 20.15 | 100.75 |
| Propylene glycol | 1000 | 20.16 | 100.8 |
| Lactose | 30 | 19.96 | 99.8 |
| Magnesium stearate | 40 | 20.18 | 100.9 |
| Polyethylene glycol | 20 | 20.15 | 100.75 |

*Average of six determinations

## Analytical application

The proposed method was satisfactorily applied to the determination of Mesna in its pharmaceutical preparations tablets and ampoules samples the results of the assay of the pharmaceutical preparations revels that there is close agreement between the results obtained by the proposed method and the label claim Table 3.

**Table 3: Determination of mesna in pharmaceutical formulations**

| Pharmaceutical formulations | Label amount (mg) | Found* (mg) | % Recovery(n=6) |
|---|---|---|---|
| Mesnan tablet(NDI) | 400 | 402 | 100.5 |
| Mesnan ampoule(NDI) | 100 | 99.9 | 99.9 |

*Mean value of six determinations.

Application of the proposed method to content uniformity [19,20] Content uniformity or the Uniformity of dosage unit was defined as the degree of uniformity in the amount of active substance among dosage units. The risk assessment strategy underlying content uniformity testing is the assumption that some pre-specified limits exist where safety and efficacy outcomes may change if content uniformity fails. The proposed method proved to be suitable for the content uniformity test, where a great number of assays on individual tablets are required. Data presented in table indicate that the proposed method cans accurately and precisely quantitative Nitrofurantoin in its commercially available tablets [4]. The mean percentage (with RSD) of the labeled claim found in ten tablets was 100.12(0.12%) which fall within the content uniformity limits specified by the Japanese Pharmacopoeia [20] .

**Table 4: Content uniformity testing of Mesna tablets using the Proposed method**

| Parameter | % of the label claim |
|---|---|
| Tablet No.1 | 100.33 |
| Tablet No.2 | 99.87 |
| Tablet No.3 | 100.20 |
| Tablet No.4 | 100.30 |
| Tablet No.5 | 99.86 |
| Tablet No.6 | 100.10 |
| Tablet No.7 | 99.98 |
| Tablet No.8 | 100.30 |
| Tablet No.9 | 100,11 |
| Tablet N0.10 | 99.98 |
| Mean(X) | 100.103 |
| %RSD | 0.12 |
| Max. allowed unit value[20] | ±15% |

## Conclusion

The developed method is found to be sensitive, accurate ,simple ,precise economical ,and can be used for routine quality control analysis of Mesna in pure form ,pharmaceutical formulations (tablets and injections) and application to content uniformity testing..

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