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FULL PAPER

Spectrophotometric determination of Mesalazine by formation of ion pair complex

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A simple, developed, fast, and accurate spectrophotometric method was examined to determine Mesalazine (MES) in its pure form and pharmaceutical preparation (Pentasa). It was based on the formation of an ion pair complex between MES and the Amaranth (AMA) reagent to give a purple color product which gives its highest absorption at the wavelength of 556 nm. The best conditions for complex formation were found (time, temperature, optimal reagent concentration, and pH). The linearity of the method for the complex consisting ranged from 5-45 µg/mL, the Sandell's index was 0.01934 µg/cm², the molar absorption coefficient was 7917.338 L/mol.cm and the detection limit was 0.03772 µg/mL, the quantitative limit was 0.11432 µg/mL, the percent recovery range was Rec% between (100.9671-95.5512) %, and the relative standard deviation rate RSD% between (0.3752-0.2926)%. It was found that the method is accurate and precision and has been successfully applied to estimate the MES in its pharmaceutical preparation, in direct methods, and in multi standard additions.

KEYWORDS

Ion pair; mesalazine; amaranth.

Introduction

Mesalazine is known as mesalamine according to the American nomenclature as well as 5-amino-2-hydroxybenzoic acid according to the regular label [1]. Mesalazine is an anti-inflammatory drug. It is used in the treatment of inflammatory bowel disease, such as ulcers of the colon, anus or rectum, and protects against Crohn's disease through the development of cancer in people who suffer from inflammatory bowel disease [2]. Figure 1 displays the chemical structure of mesalazine [3].

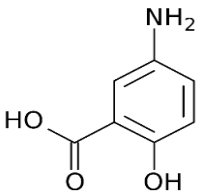


FIGURE 1 Mesalazine chemical structure [3]

MES can reduce the production of pro-inflammatory prostaglandins and leukotrienes [4], whereas ulcerative colitis is a condition that causes long-lasting inflammation along with sores (ulcers) in the large intestine (colon) and rectum [5]. Commonly effects result in colon cancer, skin, eye, and joint inflammation, which usually occurs due to IBD flare-ups [6,7].

MES also exhibits various significance in controlling mucosa by inhibiting bacterial peptides and cell injury through trapping most reactive oxygen species resulting in reducing its toxicity thereby blocking the production of prostaglandins [8,9].

With its significance in the pharmaceuticals industry, quality control in pharmacopeia through various analytical methods has been used to analyze MES in actual samples, such as chromatographic [10,11.12,15], fluorescence spectroscopyic

[13], electrochemical [14,16], and spectrophotometric [15] methods. Among these, electrochemical methods were found to be useful for rapid response, sensitive and selective determination of various pharmaceutical applications [17].

The aim of the present study is to develop a simple and economy method for determination of MES in pure and in pharmaceutical form. This method is based on the ion pair formation.

Practical part

Apparatuses used

Many devices were used in this method such as: Sensitive balance (with four digits) Sartorius- Germany, Uv-Vis Spectrophotometer Double Beam, Shimadzu -1650- Japan, Uv-Vis Spectrophotometer Single Beam, Spectrophotometer-200705044, China. pH-meter, Jenway-3310, and Ultrasonic water bath, LabTech-Korea.

The chemical materials

High-purity materials were used as: Mesalazine (Sigma-Aldrich), Amaranth (Trisodium (4E)-3-oxo-4-[(4-sulfonato-1-naphthyl) hydrazono] naphthalene-2,7-disulfonate has a chemical formula ($C_{20}H_{11}N_2Na_3O_{10}S_3$) from (Sigma-Aldrich), Ethanol (GCC-England), Hydrochloric acid (BDH-U.K), and Sodium hydroxide (Fluka-Switzerland).

Standard solutions

Standard Mesalazine solution (1000 µg/mL)

Solution was prepared by dissolving 0.1 g of Mesalazine in a specific volume of hot distilled water in a 100 mL volumetric flask, and then the volume was completed to the limit of the mark with the same solvent so that the concentration becomes 1000 µg/mL as a stock solution. Next, 10 mL of the solution was withdrawn and transferred to a 100 mL volumetric flask, and the solution was diluted with distilled water to the limit of the mark, so that the concentration was 100 µg/mL as a working solution.

Amaranth (AMA) reagent solution (100 µg/mL)

It was prepared by dissolving 0.1 g of the dye in a specific volume of ethanol in a 100 mL volumetric flask, and then the volume was completed to the limit of the mark with the same solvent, to be the concentration to 1000 µg/mL as a stock solution. Then 10 mL of the solution was transferred to a 100 mL volumetric flask, and the solution was diluted with ethanol to the limit of the mark, so that the concentration was 100 µg/mL as a working solution.

Hydrochloric acid solution (0.01M)

The solution was prepared by diluting 0.08 mL of concentrated acid (11.86 M) in volumetric flask with a capacity of 100 mL, and then the volume was completed to the mark with distilled water.

Sodium hydroxide solution with an approximate concentration (0.01 M)

Solution was prepared by dissolving 0.04 g of solid sodium hydroxide in a specific volume of distilled water in a 100 mL volumetric flask, then the volume was filled up to the mark of the same solvent.

Pharmaceutical solution (Pentasa) (1000 µg/mL)

10 Tablets of Pentasa, manufacturing site ferring international center–Germany, and the average weight of one tablet containing 500 mg of Mesalazine was taken, the powder was placed in a volumetric flask of 500 mL, then a certain amount of hot water was added and the volumetric flask was shaken and put it in an ultrasound water bath for 10 min. The volume was filled up by the same solvent and

filtered it by Whatman No.42 filter paper. From the filtrated solution (1000 µg/mL Mesalazine) transferred 10mL to a 100 mL volumetric flask and diluted with distilled water up to the mark so that the concentration was 100 µg/mL.

Preparation of the ion pair complex

Prepare the ion pair complex for Mesalazine by mixing 1 mL of Mesalazine (100 µg/mL) with 1 mL of AMA dye (100 µg/mL) in a 10 mL volumetric flask, then complete the volume to the mark by distilled water. A range of wavelengths was between 190 to 800 nm and it was scanned, and then the resulting complex gave a new peak at 556 nm, which was adopted in subsequent experiments.

Experimental conditions

Optimum concentration of dye

In order to choose the best dye concentration with the resulting complex giving the highest absorption, the increased concentration (2-16 µg/mL) of standard AMA dye solution (100 µg/mL) were added in 10 mL volumetric flask containing a fixed volume of 1 mL of standard Mesalazine solution (100 µg/mL), the volume was filled up by water to the mark level. Then, the absorption values for the complex formed versus the blank solution were recorded, as indicated in Table 1.

TABLE 1 The optimum dye concentration for the ion association complex of MES

Conc.of AMA µg/mL	Absorbance
2	0.211
4	0.449
6	0.722
8	0.899
10	**0.920**
12	0.465
14	0.258
16	0.221

Table 1 illustrates that (10 µg/mL) was the optimum dye concentration through which the resulting complex gives the highest absorption, so it was chosen as the best dye concentration.

The pH effect

A study was conducted to choose the optimum pH at which the complex formed giving the highest absorption. This study was conducted at different pH values ranging (6.7-9.2) and the absorption values for the complex formed at each of these values were recorded and depicted in Table 2.

TABLE 2 The effect of the acid function on the ionic association complex of MES

Addition	Volume(mL)	Absorbance	pH
HCl (0.01)M	0.1	0.984	6.7
	0.2	0.972	6.2
	0.3	0.940	5.9
Without addition	-----	0.999	7.3
NaOH (0.01)M	0.1	0.998	7.6
	0.3	0.999	8.1
	0.5	0.997	8.5
	0.7	0.998	9.2

The results in Table 2 demonstrate that adding the acid led to a decrease in the absorption of the colored product so its use was avoided, and that adding the base did not have a noticeable effect on the value of the complex absorption which was formed, so the acid and base addition was dispensed and the natural pH of the complex was adopted (7.3) without any addition.

The optimum temperature

In order to choose the optimum temperature at which the resulting complex gives the highest absorption, the measurement process was performed for the complex with a temperature range of 5-60 °C which was depicted in Table 3.

TABLE 3 The effect of temperature on the ion pair complex of MES

Temperature	Absorbance
5	1.087
10	1.097
15	1.104
20	1.105
25	**1.107**
30	1.106
35	1.100
40	1.102
45	1.104
50	1.105
55	1.106
60	1.102

It is clear from the results of this study and as indicated in Table 3 that the maximum absorption was at the laboratory temperature, while the decrease in the absorption of the colored product formed when the temperature is increased. The laboratory temperature was therefore adopted in subsequent experiments, as high heat causes decrease absorbance gradually.

Time effect

A study was conducted to find the constancy and stability of the complex formed between MES and the AMA dye by choosing the optimal time at which the complex formed gives the highest absorption, and Table 4 demonstrates the values of complex absorption at different times, ranging from the beginning of preparing the complex to a limit of 60 min.

TABLE 4 The effect of time on the ionic association complex of MES

Time(min)	Absorbance
0	**1.235**
5	1.232
10	1.230
15	1.227
20	1.226
25	1.226
30	1.227
35	1.227
40	1.227
45	1.226
50	1.228
55	1.227
60	1.227

It was found from the Table 4 that there is no significant effect of the time factor on the formation process of the complex, that is, the compound was almost stable from the moment of the reaction until 60 min, and the time of the reaction moment was adopted in subsequent experiments.

Job method

A study was conducted to determine the ratio of the drug to the ratio of the (AMA) dye in the ionic complex, according to the Job method for continuous changes. The absorption values for the complex formed were measured against the blank's solution as displayed in Figure 2.

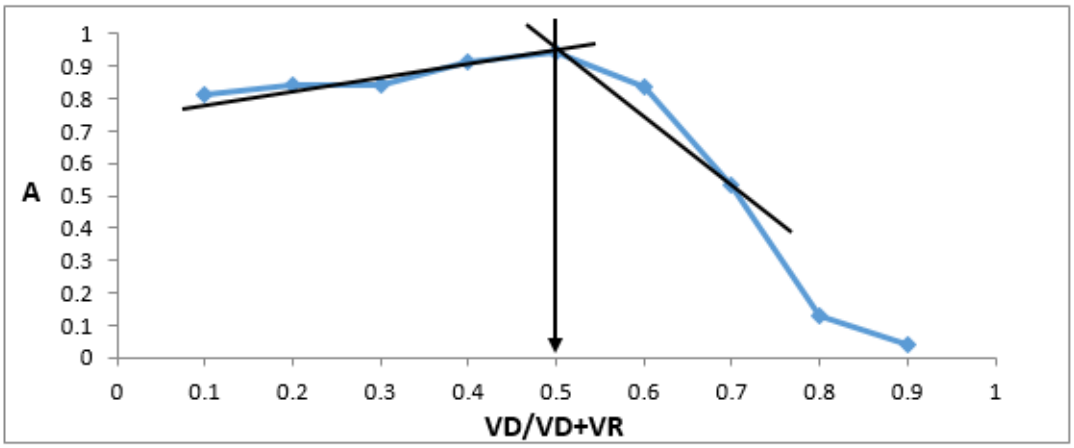


FIGURE 2 The correlation ratio of the MES complex

Through the results obtained from the Job method, it was found that the complex formed under the best conditions is composed of equal molar ratios of the drug and the dye at a ratio of (1:1), respectively.

Calibration curves

The calibration curve for the MES ion pair complex with AMA was constructed under the pre-established best conditions. The linearity of the method was between 5-45 µg/mL, the Sandell's index was 0.01934 µg/cm², and molar absorption coefficient was 7917.338 L/mol.cm. The detection limit was 0.03772 µg/mL and the quantitative limit was 0.11432 µg/mL. Figure 3 displays the calibration curve for the MES complex.

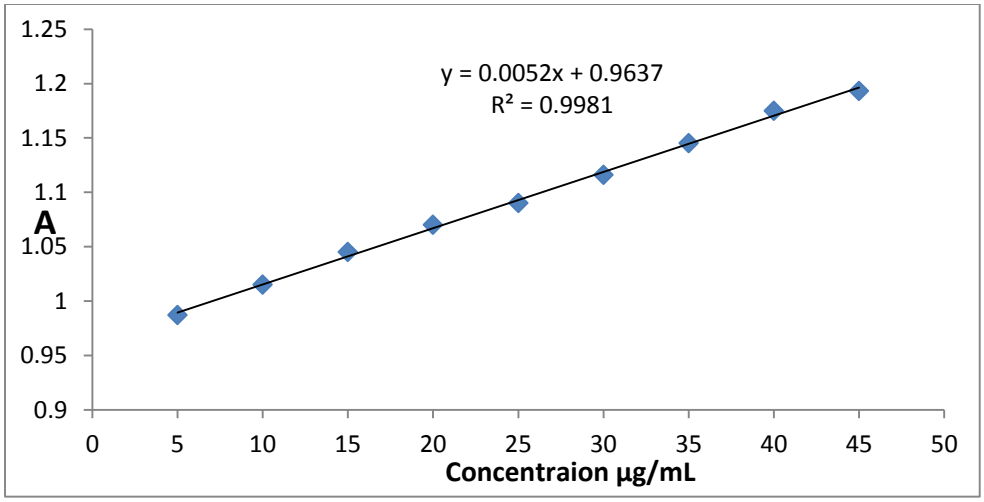


FIGURE 3 The calibration curve for MES complex

Accuracy and precision for method

A study was conducted to calculate the accuracy and precision of the proposed method, by calculating the Rec% value to express the accuracy of the results, and the RSD% for expressing the precision of the results and for three concentrations (15,25,45 µg/mL) of the calibration curve, and by performing six readings for each measurement process conducted in which the values of Rec% ranged were found between (95-100.3846)% and the values of RSD% between (0.2926-0.3752)%, as indicated in Table 5.

TABLE 5 The accuracy and precision of MES ion pair complex

Conc.of MES taken µg/mL	A	Conc.of MES found µg/mL	Rec %	RSD %
15	1.045	15.0576	100.3846	0.3752
25	1.090	23.75	95	0.2926
45	1.193	44.6730	99.2735	0.3412

Applications

Direct

Method

The proposed method was applied at pharmaceutical preparation (Pentasa), with different concentrations (20, 30, and 40) µg/mL of the drug, and by performing six readings for each measurement. To express the accuracy of the results, used Rec%, in which it was between (95.4807-99.1825)%, and to express the precision of the results, used RSD% and it was between (0. 2040-0.2370)%, which is shown in Table 6.

TABLE 6 Applying the direct method of the ionic complex of the drug

Conc.of MES taken µg/mL	A	Conc.of MES found µg/mL	Rec %	RSD %
20	1.063	19.0961	95.4807	0.2040
30	1.113	28.7115	95.7051	0.2253
40	1.170	39.6730	99.1825	0.2370

Standard additions method

Mesalazine was determinate in the Pentasa pharmaceutical preparation using the multiple standard additions method. (0.5) mL of the prepared solution of the pharmaceutical preparation with a concentration of (100 µg/mL) was added to a series of volumetric flasks (seven flasks) of 10 mL capacity. Increasing volumes of MES standard solution (100 µg/mL) were added ranged from (0.5-3) mL, and the seventh volumetric flask was left without addition. Then, a fixed volume of 1 mL of the standard solution of the dye was added and the volume was filled up by water to the mark. The concentration of the added solution was plotted against absorption at 556 nm wavelength. The results were displayed in Figure 4. The Rec% and RSD% were (102.2972)% and (0.15475)%, respectively which indicates that the method is accurate and precise.

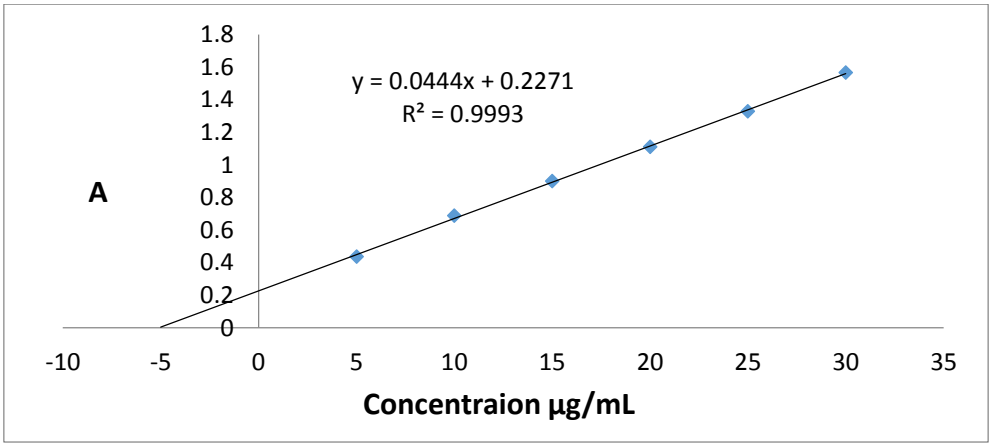


FIGURE 4 Standard additions curve

Final absorption spectrum for MES complex

According to the obtained optimum conditions, the final absorption spectrum of the MES complex versus the blank solution was recorded to confirm the result, as a new peak of the complex appeared at the wavelength 556 nm while the value of (λ_{max}) of the pigment was AMA 494 nm and MES 298 nm, as depicted in Figure 5.

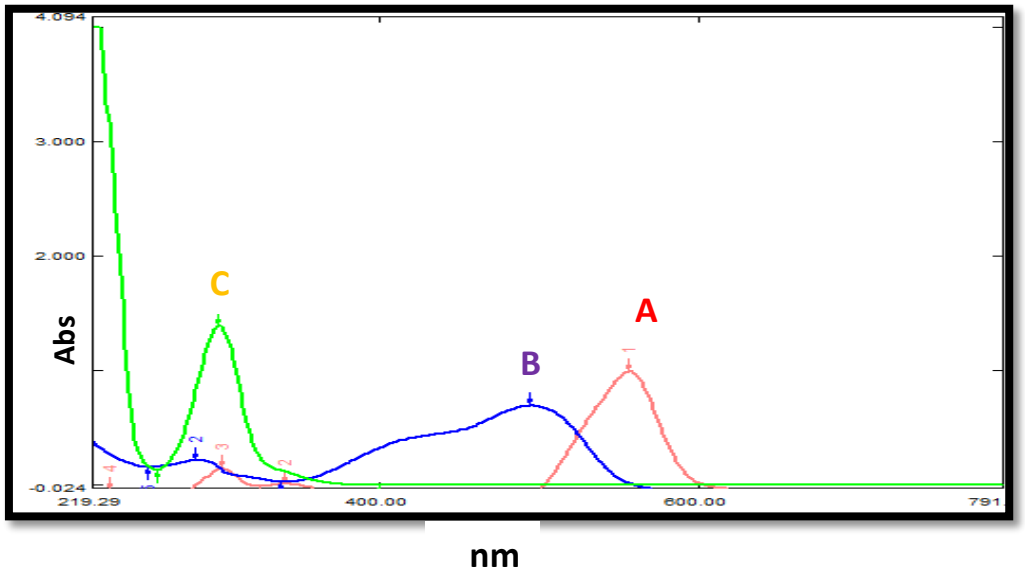


FIGURE 5 The absorption spectrum of ion pair complex (A), AMA spectrum (B) and MES spectrum (C)

Comparing the analytical properties of the proposed method

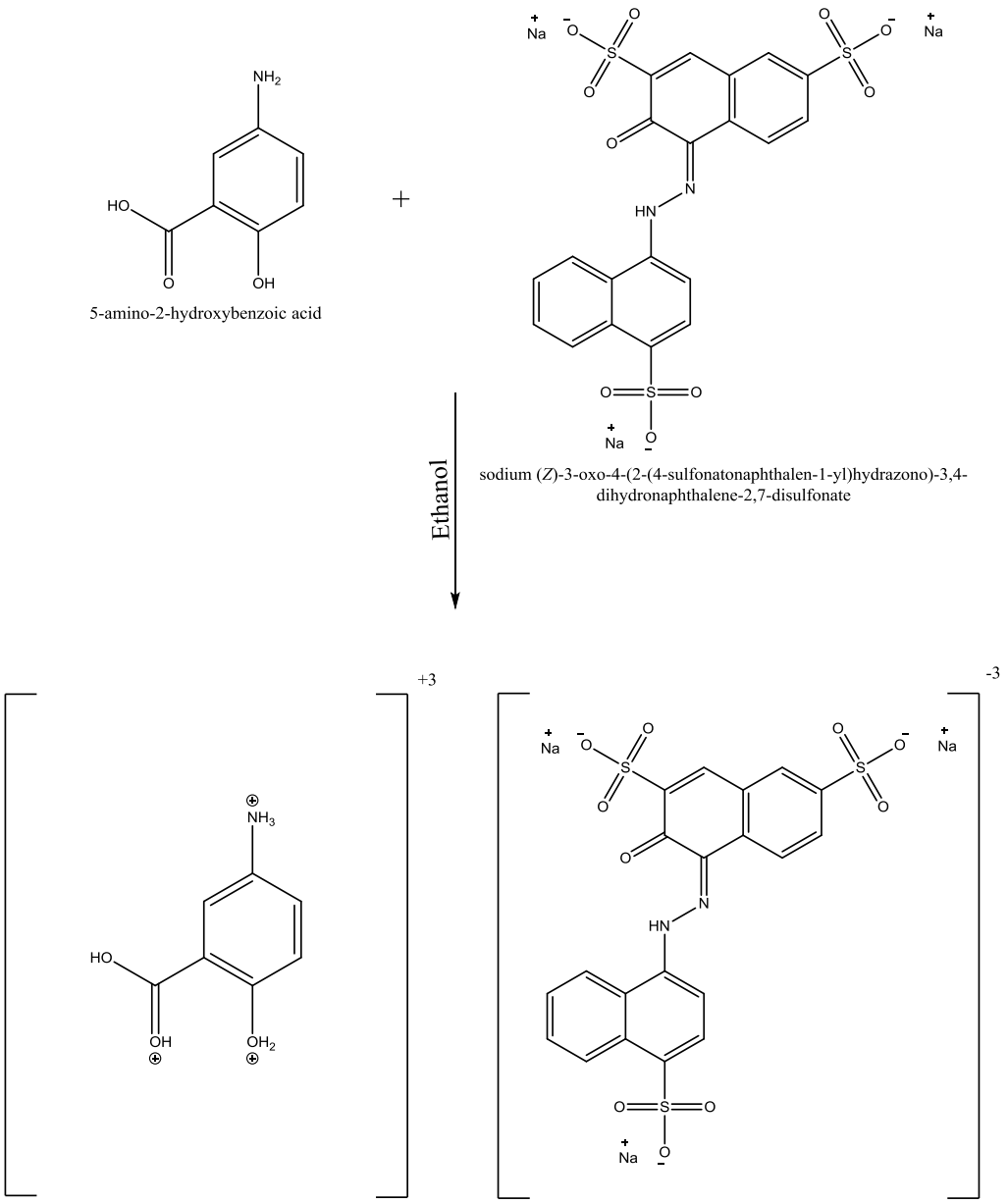
The proposed method was compared with another spectroscopic method is shown in Table 7.

TABLE 7 Comparing the proposed method with another spectral method

Parameters	Present Method	Other Method[1]
λ_{max} (nm)	556	346
Beer's law range (µg/mL)	5-45	0.48-12
T (^{0}C)	25	40
L.O.D (µg/mL)	0.03772	0.053
L.O.Q (µg/mL)	0.11432	0.176
Correlation coefficient (R^2)	0.9981	0.9987
Sandell's index (µg/cm^2)	0.01934	0.02356
ε (L/mol.cm)	7917.338	6500
Rec% Average	100.3905	98.04
RSD%	0.3752- 0.2926	1.70

Suggested reaction equation

From the results obtained from the study of the ratio of the complex binding formed and according to Job's method for continuous changes, an equation for the interaction of mesalazine with AMA was proposed, as demonstrated in the following diagram.



Ion pair complex

Conclusion

The ion pair method was used to determine MES in its pure drug and Pentasa pharmaceutical form. This method was based on the reaction of MES with AMA reagent to formation of a purple complex. The highest absorption was given at 556 nm wavelength, and the obtained results showed the percentile recoveries values, the relative standard deviation, the detection limit, and the quantitative limit that the method is accurate and precise, which indicates the success of the proposed method for MES determination.

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