Tikrit Journal of Pure Science Vol. 29 (3) 2024

TJPS

https://doi.org/10.25130/tjps.v29i3.1542

IASJ

المجلات الاكاديمية العراقية

Tikrit Journal of Pure Science

ISSN: 1813 – 1662 (Print) --- E-ISSN: 2415 – 1726 (Online)

Journal Homepage: http://tjps.tu.edu.iq/index.php/j

4-aminosalicylic acid as a coupling reagent for spectrophotometric determination of mesalazine in an alkaline medium

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ARTICLE INFO.

Article history:

-Received: 28 / 8 / 2023

-Received in revised form: 5 / 10 / 20 23

-Accepted: 18 / 10 / 20 23

-Final Proofreading: 15 / 2 / 2024

-Available online: 25 / 6 / 2024

Keywords: 4-aminosalicylic acid, mesalazine, oxidative coupling, spectrophotometric, pharmaceutical preparation.

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ABSTRACT

A sensitive, rapid, and inexpensive spectrophotometric method for the determination of mesalazine in an alkaline medium by an oxidative coupling reaction was developed. At a wavelength of about 600 nm, mesalazine could be estimated in the range (0.1–14.0) µg/mL with high sensitivity, since the molar absorption was 7.6×10^3 $L.mol^{-1}.cm^{-1}$ and the Sandell index was 0.0201 $\mu g/cm^2$, with a recovery rate of 101.6% and a lower relative standard deviation from 1.1%. The synthesis ratio of the dye product was tested and found to be 1:1 (mesalazine:4-aminosalicylic acid) and the dye stability constant value was 8.51×10^5. The method was successfully applied to the determination of mesalazine in its pharmaceutical preparations, which were in the form of compressed tablets, and the results agreed with the authentic contents of the pharmaceutical preparation and the British Pharmacopoeia-approved method.

حامض 4–أمينوساليسيليك ككاشف اقتران للتقدير الطيفي للميزالازين في وسط قاعدي

محمد يحيى ضمرة ، اسراء عبد الحميد احمد

قسم الكيمياء، كلية التربية للعلوم الصرفة، جامعة الموصل، الموصل، العراق

الملخص

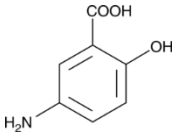
تم تطوير طريقة طيفية حساسة وسريعة وغير مكلفة لتقدير الميزالازين في وسط قلوي عن طريق تفاعل الاقتران المؤكسد. التأكسدي عند طول موجة يبلغ 600 نانومتر، يمكن تقدير الميزالازين في النطاق (0.1–14) ميكروغرام / مل مع حساسية عالية، حيث اذ ان قيمة الامتصاصية المولارية 7.6×10^3 لتر مول $^{-1}$ سم $^{-1}$ ودلالة ساندل كانت 0.0201 ميكروغرام / سم^2، بمعدل استرداد 101.6٪ وانحراف قياسي أقل نسبيًا من 11٪، تم اختبار نسبة طبيعة الناتج ووجد أنها 1: 1 (ميزالازين زين: حمض 4–أمينوساليسيليك) وكانت قيمة ثابت التكوين الناتج الملون 8.51×10^5. كما طبقت الطريقة بنجاح لتقدير الميزالازين في مستحضراته الصيدلانية، والتي كانت على شكل أقراص مضغوطة، ووافقت النتائج مع المحتويات الأصلية للمستحضر الصيدلاني وطريقة دستور الأدوية البريطانية المعتمدة.

Introduction

Mesalazine, a powerful medication in the field of gastroenterology, stands as a beacon of hope for individuals battling chronic [1]. With its remarkable ability to alleviate symptoms and improve the quality of life for patients, mesalazine has appeared as a brave warrior in the fight against conditions such as ulcerative colitis and Crohn's disease. For the mucous membranes of the colon, therefore, it is given in the form of enteric-coated tablets with resin to be dissolved in the large intestine to play its effective role instead of being absorbed in the small intestine, also given in the form of suppositories or enemas to

https://doi.org/10.25130/tjps.v29i3.1542

relieve colic Ulcerative colitis or enteritis by inhibiting the formation of prostaglandins and arachidonic acid metabolites [2]. Mesalazine did not record any side effects on pregnant women, but low concentrations of it were found in samples of breast-feeding milk, and it was found to have side effects such as intestinal gas, headache, diarrhea, and abdominal pain, so it is forbidden to give it to children under the age of two years, as well as to people who suffer from kidney diseases and people who suffer from Allergy to aspirin [3]. Mesalazine has the following chemical structural:



5-aminosalicylic acid

Mesalazine was estimated using a variety of reactions that relied on different techniques, including chromatography [4-6], electric [7-9], polarographic [10-12], and fluorometric [13-15] in addition to spectrophotometric [16-20] methods and other methods.

Materials and solutions

Instrument

Absorbance and spectral measurements were performed using a 1.0 cm thick quartz cuvette and a PG Instruments-England T92+ UV spectrophotometer.

Mesalazine Solution 100 ppm

The solution was prepared by dissolving 0.01 g of neat mesalazine in 5 mL of absolute ethanol in a 100 mL volumetric flask, making up to the mark with distilled water and placing the solution on an ultrasonic shaker became complete dissolution, then kept in the refrigerate.

4-aminosalicylic acid 2.0×10^{-3} M solution

The solution was prepared by dissolving (0.0305) g of the pure substance in five milliliters of absolute ethanol, then transferred to a 100 mL volumetric flask completed up to the mark with distilled water and completing the dissolution process in an ultrasonic stirrer.

Oxidizing Solutions

Potassium Metaperiodate 5×10^{-3} M

The solution was prepared by dissolving (0.115) g of the pure substance in distilled water in a 100 mL volumetric flask and then bringing the volume up to the mark with distilled water in the flask was placed in an ultrasonic stirrer for complete dissolution and diluted as needed. The other oxidants were also prepared at the same concentration 5.0 x 10^{-3} M by dissolving the proper amount of each oxidant in distilled water in a 100 mL volumetric flask. Make up to volume and dilute if necessary.

Sodium Hydroxide Solution 1.0 M

The solution was prepared by dissolving (4.0) g of pure material in distilled water in a 100 mL volumetric flask and making up to the mark with distilled water.

Potassium hydroxide solution 1.0 M

The solution was prepared by dissolving (5.611) g of the pure substance in distilled water in a 100 mL volumetric flask and making up to the mark with distilled water.

Surfactant Solutions

Prepared at 1.0% concentration by dissolving in hot distilled water.

Preliminary study

To develop a spectral method of estimating mesalazine, preliminary experiments were conducted to test the possibility of using 4-amino salicylic acid as a coupling detector in the oxidative coupling reaction, by adding micrograms of mesalazine with 1ml of 4- aminosalicylic acid at 2.0×10^{-3} M and with 1 mL of oxidizing agent potassium metaperiodate at 2.0×10^{-3} M. According to the literature, oxidative coupling often takes place in the basal medium. The initial experiments showed that the blue tint had maximum absorption at 600 nanometers, While the blank solution was colorless and did not give the absorption spectrum at the wavelength above thus,- 4-aminosalicylic acid is a chromogenic reagent that can be used in the spectral estimation of mesalazine in the water medium.

Optimization of the conditions for the reaction.

In all the next studies, a mesalazine concentration of 8.0 µg/mL was used using 10 mL volumetric flasks**.**

Effect of oxidant type:

Distinct types of oxidants represented by potassium metaperiodate, N-Bromosuccinimide, potassium iodate, potassium dichromate, potassium permanganate, ammonium sulfate, and ferric potassium trihydrate were tested by adding 1.0 ml of each oxidant at a concentration of 2.0×10^{-3}M. Each individually with 8.0 µg/ml mesalazine in a 10 ml volumetric flask and in the presence of 1 ml of 2.0×10^{-3} M 4-aminosalicylic acid reagent, followed by the addition of 1 ml of 1 sodium hydroxide, and the absorbance was measured after 5 minutes of dilution. Table 1 shows that potassium metaperiodate is the best oxidant and was therefore adopted in further studies.

Table 1: Effect of oxidant type

Type of oxidant	Wavelength, nm	Absorbance
KIO_4	600	0.248
KIO_3	570	0.004
NBS	458	0.023
$KMnO_4$/base medium	Turbid	Turbid
KMnO4/acidic medium	350	0.138
Ammonium ferric sulphate	304	0.098

Effect of concentration and volume of potassium metaperiodate

Solutions with different concentrations of potassium metaperiodate in the range (3.0×10^{-4} - 2.0×10^{-2}) M were prepared and their effect on the intensity of absorbance of the resulting dye was tested by adding (1.0 mL) of each concentration into a 10 ml

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volumetric flask with 8 µg/mL of mesalazine and 1 ml of 4-aminosalicylic acid at 2.0×10^{-2} M plus 1 mL of sodium hydroxide at 1.0 M, and the absorbance was measured at 600 nm after 5 minutes of volume completing, as evident from the results obtained. In table 2 the concentration of the oxidizing agent 5.0×10^{-3} M is reasonable and has therefore been used in subsequent studies.

Table 2: Effect of concentration of potassium metaperiodate

Molarity of potassium metaperiodate	3.0×10^{-4}	1.0×10^{-3}	2.0×10^{-3}	5.0×10^{-3}	1.0×10^{-2}	2.0×10^{-2}
Absorbance	0.160	0.220	0.248	0.305	0.288	0.265

The effect of adding increasing volumes in the range (0.2-2.0) mL of potassium metaperiodate at a concentration of 5.0 x 10^{-3} M on the absorption of the product formed was also studied. Figure (1) shows that a volume of 0.8 mL of potassium metaperiodate gave the highest absorbance value. Therefore, it was accepted in later studies.

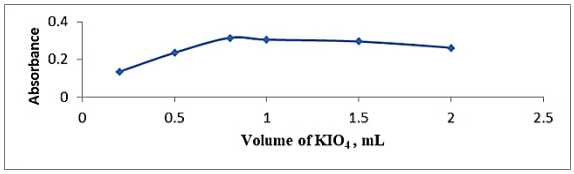

Figure **1: Effect of volume of potassium metaperiodate**

The influence of the base type

Based on initial experiments indicating that the reaction occurs in an alkaline medium, the impact of various types of bases was investigated at a concentration of 1.0 M. To conduct the tests, 1.0 mL of each base was individually placed in a 10.0 mL volumetric flask after adding the other ingredients, as outlined in table 3. The results confirmed that potassium hydroxide (KOH) is the best suitable base for the proposed reaction.

Table 3: The influence of the base type

Type of base	**Wavelength, nm**	**Absorbance**
NaOH	600	0.315
KOH	600	0.360
Na_2CO_3	472	0.148
$NaHCO_3$	458	0.143

Effect of medium or pH

Considering the earlier paragraph showing that the reaction occurs in a basic medium and the resulting pH value of 13, more investigations were carried out to further confirm this finding. Basic buffer solutions with pH values ranging from 9 to 13 were prepared to see the effect of different pH levels on the reaction. Upon adding the optimal quantities, it was observed, as depicted in table (4), that the reaction favored the medium with potassium hydroxide. To find the ideal volume of potassium hydroxide, a secondary study was conducted, visualized in figure (2). The results showed that 1 ml of potassium hydroxide is the optimal volume, thereby establishing its use in subsequent studies.

Table 4: Effect of alkaline medium

Type of buffer (1.0 mL)	**PH**	**Wavelength, nm**	**Absorbance**
Borate buffer	9	480	0.137
Sodium bicarbonate	10	476	0.210
Sodium bicarbonate	11	476	0.231
Potassium chloride	12	592	0.314
Potassium chloride	13	600	0.320
Without buffer	13	600	0.360

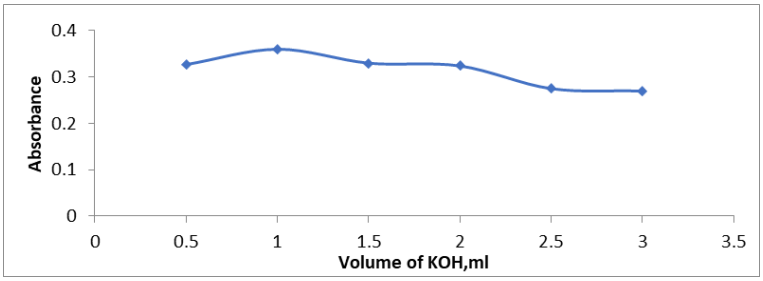

Fig. 2: The effect of potassium hydroxide volume

Effect of concentration and volume of 4-amino salicylic acid

The impact of varying concentrations of 4-amino salicylic acid, ranging from (1.0×10^{-4} to 2.0×10^{-2}) M, on the absorbance of the resulting product was investigated. All experiments were conducted in a 10.0 mL volumetric flask using the optimal quantities. After diluting with distilled water up to the mark, the absorption was measured at 600 nm after a 5-minute interval. The results, as shown in table 5, indicate that a concentration of 2.0×10^{-3} M yields the highest value. Consequently, this concentration was adopted for subsequent studies.

Table 5 Effect of concentration of 4-amino salicylic acid

Molarity of 4-ASA	1.0×10^{-4}	3.0×10^{-3}	2.0×10^{-3}	3.0×10^{-3}	1.0×10^{-2}	2.0×10^{-2}
Absorbance	0.296	0.325	0.360	0.330	0.248	0.240

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The investigation also included examining the impact of varying volumes of the reagent 4-amino salicylic acid at a concentration of 2.0 $\times 10^{-3}$ M. Different volumes ranging from 0.5 to 3.0 mL were added to the reaction. Based on the study's findings, it was determined that the highest absorption is obtained when mesalazine is conjugated with 4-amino salicylic acid to form the dye. Specifically, using a volume of 1.5 milliliters of the reagent yielded optimal results, as illustrated in figure 3. Consequently, this volume was deemed suitable for subsequent studies.

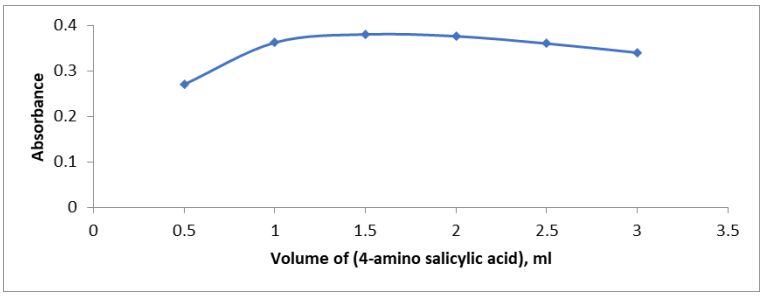

Fig. 3: Effect of volume of 4-amino salicylic acid

The effect of temperature on the stability of the reaction

The stability of the colored product in the proposed reaction between mesalazine and 4-amino salicylic acid in a basic medium was investigated at various temperatures ranging from 0 to 40 ºC. The effect of temperature on the reaction was analyzed, as portrayed in figure 4. The results revealed that the highest intensity of absorption was achieved after 20 minutes, with a settling time of 120 minutes. Therefore, these specific conditions were selected and adopted for subsequent studies, considering the laboratory temperature.

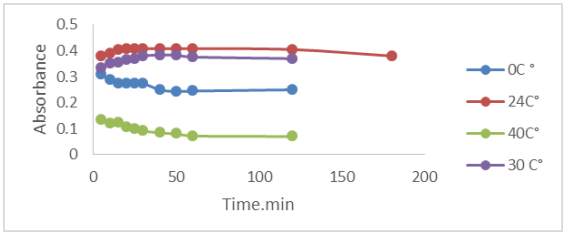

Fig. 4: The effect of temperature on the stability of the reaction

The effect of surface tension agents

The impact of surface tension agents was investigated in this study by adding 1 ml of positive, negative, and neutral surfactants to a 10 ml volumetric flask containing the optimal quantities of other additives. It was observed that surface tension agents negatively affected the absorption of the colored product. As a result, they were excluded from further studies, table 6.

Table 6: The effect of surface tension agents

Type of surfactant	Wavelength, nm	Absorbance
Tween	584	0.226
SDS	586	0.293
Trix-100	586	0.278
CETAB	586	0.166
Without	600	0.408

Addition sequence effect

The impact of altering the sequence of adding the reaction components on the absorbance of the colored product was investigated. It was determined that the sequence utilized in previous studies is suitable and, as a result, it was adopted for subsequent studies. Where (S) represents mesalazine solution, (R) 4-amino salicylic acid solution, (O) potassium metaperiodate solution, and (B) potassium hydroxide solution. Table (7).

Table 7: The effect of the Addition sequence effect

Order number	Reaction components	Absorbance
I	S+R+O+B	0.408
II	S+O+R+B	0.328
III	S+B+R+O	0.379
IV	S+R+B+O	0.391
V	O+B+S+R	0.385
VI	S+O+B+R	0.360

The Effect of Solvents

To experience the effect of the different types of solvents on the absorption of the color product, after adding all the optimum quantities, complete the volume using the solvents listed in table 8, showing the usage of Water as a solvent proved to be the best, as well as figure 5, which shows the absorption spectrum of water and other solvents and was therefore used in subsequent studies.

Table 8: The Effect of Solvents

Type of solvent	Wavelength, nm	Absorbance
Ethanol	480	0.212
e Aceton	608	0.169
acetonitrile	596	0.202
Dimethylformamide	476	0.041
Water	600	0.408

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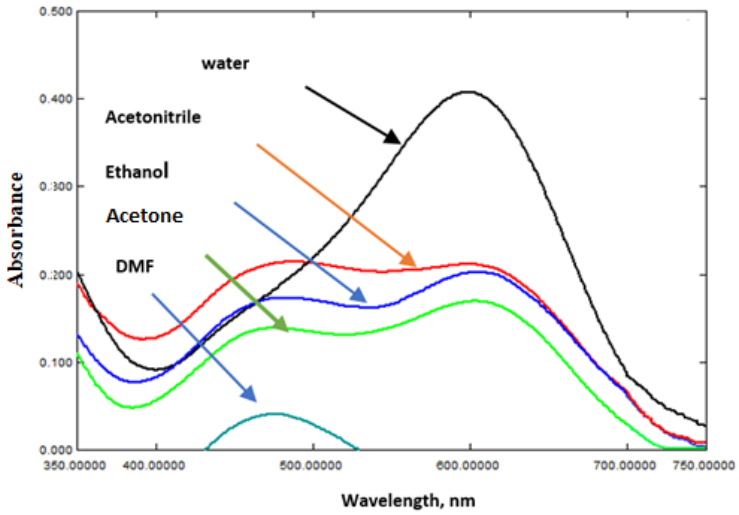

Fig. 5: The Effect of Solvents

Final absorbance spectrum

After fitting all optimal conditions, the final absorbance spectrum for the product formed was recorded as it gave the maximum absorbance at 600 nm as shown in figure (6) and table 9 a summary of the optimal conditions.

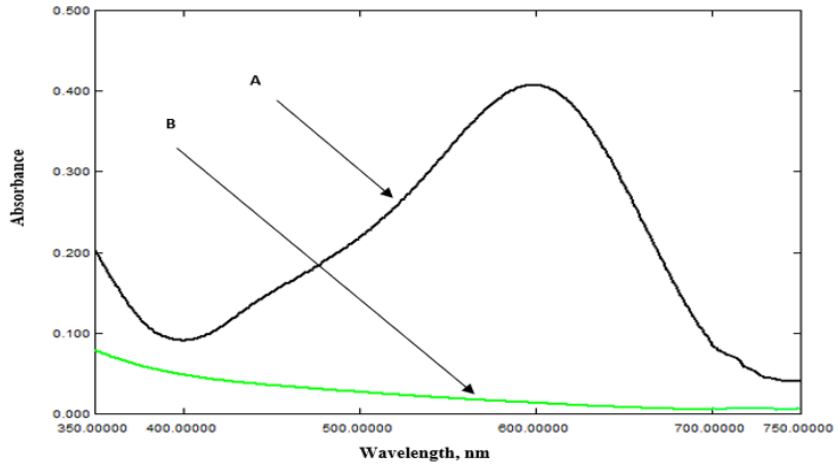

Fig. 6: Final absorbance spectrum

A: Absorption spectrum of 8.0 µg/mL of mesalazine against blank solution.
B: absorption spectrum of a blank solution against distilled water.

Table 9: Summary of the optimal reaction conditions obtained for the determination of mesalazine

Material solution	Concentration	Optimum amount (ml)
4-amino salicylic acid	2.0×10^{-3}M	1.5
KIO_4	5.0×10^{-3}M	0.8
KOH	1.0 M	1.0
Wavelength	600nm	
Color	Blue	
Standing time	min20	
Stability period	120 min	
Temp. (°C)	Room temperature	

Standard curve of mesalazine

Based on the optimal conditions listed in table (9), the standard curve of mesalazine in aqueous solution was constructed as follows:

For a group of 10 mL volumetric flask, increasing volumes of mesalazine was used at a concentration of 100 µg/ mL, in the range (0.05-1.4)µg/ mL to cover the concentration ranges given in table (9), then 1.5 mL of 4-aminosalicylic acid and 0.8 mL of potassium metaperiodate at a concentration of 5.0×10^{-3} M and in the presence of 1.0 mL of potassium at a concentration of 1.0 M, the absorbance was measured 20 minutes after filling up the volumes with water distilled at 600 nm against its blank solutions and after plotting the absorbance against the concentrations, the standard curve shown obtained.

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This is illustrated in figure (7), which shows that the proposed method obeys Beer's law in the interval (0.5-14.0) µg/mL, as the correlation coefficient was 0.9994, showing that the standard curve has excellent linear performance. Table (10) shows the estimated range, limits of detection, and the limit of quantification, molar absorbance, slope, cross-section, and correlation coefficient. The limit of Detection, LOD, LOQ were calculated for six replicates of the blank solution. From the molar absorbance value, the detection limit, and the quantitative limit, it was concluded that the proposed method allows an estimation of the high sensitivity of mesalazine.

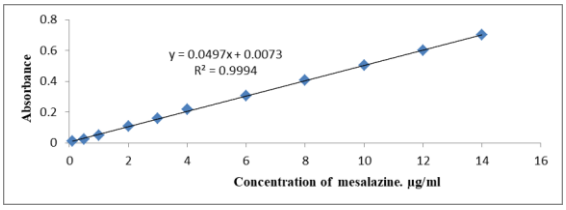

Fig. 7: Standard curve of mesalazine

Table 10: Analytical parameter for mesalazine

Analytical parameter	Value
Linearity range µg/mL	0.5-14
Molar absorptivity ($L.mol^{-1}.cm^{-1}$)	7.6×10^3
Intercept	0.0073
slope	0.0497
Determination coefficient (R)	0.9994
Limit of detection (LOD) µg/mL	0.177
Limit of quantitation (LOQ) µg/mL	0.539
Sandell sensitivity µg.cm^2	0.0201

Method Accuracy and precision

To calculate the recovery rate and its standard deviation, the method accuracy and agreement were evaluated in five replicates at three different mesalazine concentrations as shown in table 11. The results of the method show good accuracy and agreement as the recovery with its standard deviation was less than 1.1%.

Table 11: Method Accuracy and precision

Conc. of mesalazine µg/mL	Recovery %	Average of recovery %	RSD %
2	99.00	99.29	1.05
6	100.03		1.06
12	98.86		0.59

Tablet analysis for Mesalazine (Pentasa)

Five tablets were weighed (one tablet equals 500.0 mg of mesalazine), crushed, and mixed well, then the equivalent of 0.5 grams was weighed from it and dissolved in 5.0 mL of ethanol then transferred to a 250 volumetric flask and completely dissolved in distilled water, the solution was filtered to produce a concentration of 2000 µg/mL, then a concentration of 100 µg/mL was prepared from it by dilution with distilled water in a 100 mL volumetric flask, then equivalent concentrations (2, 4, 8) µg/mL of were prepared in 10.0 mL volumetric flask. They were processed according to the previous paragraphs and the results obtained are summarized in table (12).

Tablet Analysis for Mesalazine (Mezacol)

Five tablets (one tablet having 400 mg of mesalazine) were weighed, crushed, and mixed well, then 0.4 g of them were weighed, dissolved in 5.0 mL of ethanol, transferred to a 250 mL volumetric flask, and topped up to the mark with distilled water to yield a concentration of 1000 µg/mL. After other dilutions, concentrations equivalent to (2.0,4.0 and 8.0) µg/ml were taken in a volumetric flask of 10.0 mL and treated according to the standard curve method. The results obtained were included in table (12).

Table 12: Determination of mesalazine in pharmaceutical preparations

Pharmaceutical preparation	Certified value	Amount present	Drug content found* (mg)	Recovery* (%)	Average recovery (%)
Pentasa tablet Turkey	500mg	2	1.94	97.00	99.16
		4	4.08	102.00	
		8	7.88	98.50	
Mesacol tablet Syria	400mg	2	1.92	96.00	98.95
		4	4.03	100.75	
		8	8.01	100.12	

Evaluation of the results of the proposed method

To demonstrate the effectiveness of the proposed method and its degree of success in determining mesalazine and its non-interference, the standard addition method to two different concentrations of pharmaceutical preparations (pentasa and mesacol) was used due to the lack of requirements for using the British Constitution method, which is based on high-performance liquid chromatography. Tables (13) and figures (8) and (9) show the results obtained, indicating that the standard addition method agrees well with the proposed method, indicating that the method has good selectivity.

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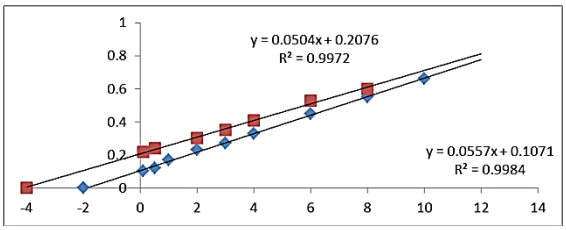


Fig. 8: Curve the standard addition of the Pentasa tablet

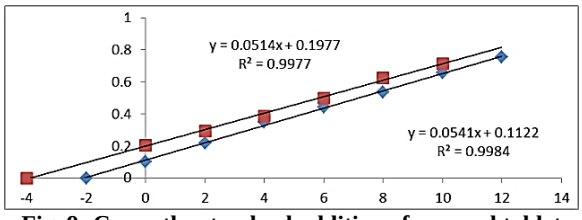


Fig. 9: Curve the standard addition of mesacol tablet

Table 13: Determination of mesalazine in pharmaceutical preparations by the standard addition method

Pharmaceutical preparation	Certified value (mg)	Amount present (µg/ml)	Recovery* (%)	Drug content found (mg)	
				Present method	Standard addition
Pentasa tablet Turkey	500	2	96.14	485.00	480.70
		4	102.97	510.00	514.85
Mesacol tablet Syria	400	2	103.69	384.00	414.76
		4	96.15	403.00	384.60

Job method (Continuous changes)

This method consisted of studying the evolution of the absorbance of solutions with different volume ratios at similar molar concentrations (1×10^{-3}) mol/ml of mesalazine and 4-aminosalicylic acid, such that the total volume was 3.0 mL in a 10ml volumetric flask optimal amount of potassium meta periodate and potassium hydroxide was then added to volt ml dosing vials and the absorbance measured at 600 nm against the test solution, observing that the dye was formed in a ratio of 1:1 (mesalazine:4-aminosalicylic acid), as shown in figure (10).

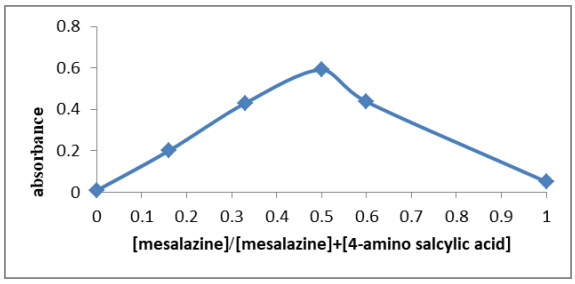


Figure **10**: **Job method (Continuous changes)**

Slope ratio Method

This method is suitable for weak complexes and is only applicable to systems in which only one complex is formed. The method assumes that the complex formation reaction can be completed by a significant excess of metal ions or reactive ligand and that Beer's law is observed. Equal concentration solutions (1.0 x 10^{-3}) M of mesalazine and the 4-aminosalicylic acid were prepared. Increasing volumes (0 to 3) mL of 4-aminosalicylic acid solution were added to a fixed volume of mesalazine in 10 mL volumetric flasks. Optimal amounts of potassium metaperiodate and potassium hydroxide were then added and absorbances were measured compared to their blank solutions at 600 nm after dilution with distilled water, figure 10, which shows the product formed with a molar ratio of 1:1 Mesalazine: 4-aminosalicylic acid.

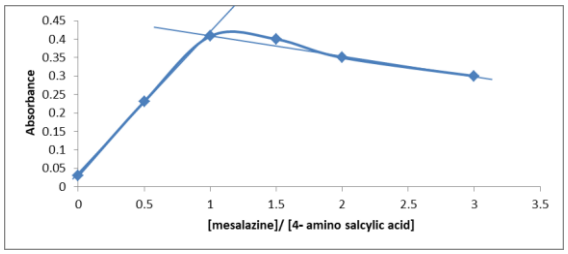


Fig. 10: Slope ratio Method

The stability constant of the formed dye

The value of the degree of dissociation α and the stability constant of the formed dye in a 1:1 molar ratio between mesalazine and 4-aminosalicylic acid were calculated in an alkaline medium such that the concentration of each of the two solutions was 1.0×10^{-3}M. Three solutions were prepared with equal volumes of drug and reagent. Under these conditions, the product is in the dissociated state and the absorbance value is expressed as Subsequently, three more solutions were prepared to have the same amount of mesalazine but in the presence of a large amount of 4-aminosalicylic acid since the product does not dissociate and the absorbance value, in this case, is expressed by the symbol Am. by using the relationship:

$\alpha = (Am-As)/Am$

The degree of dissociation value was calculated. Next, the stability constant Kst was calculated from the relationship that holds when the type of complex formed is (1:1).

$K_{st} = (1-\alpha)/(\alpha 2.C)$

where C is the concentration of the product formed, which corresponds to that of mesalazine. Table 14 shows the average values of the stability constant are 8.51×10^{5} l.mol^{-1}, showing that the colored product has high stability.

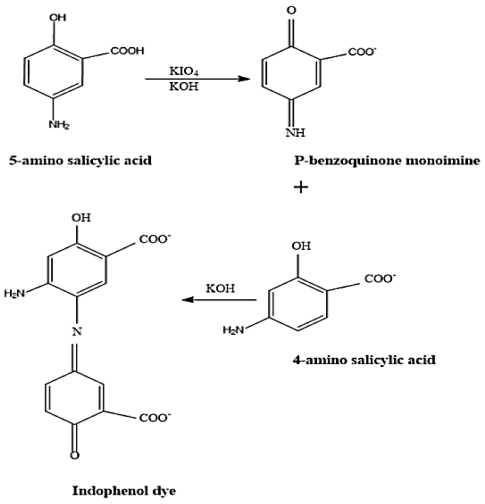
https://doi.org/10.25130/tjps.v29i3.1542

Table 14: The stability constant of the formed dye

Conc. of mesalazine M	Absorbance		α	K l. mole^{-1}	Average of K l. mole^{-1}
	As	Am			
2×10^{-5}	0.066	0.193	0.658	0.39×10^{5}	8.51×10^{5}
4×10^{-5}	0.294	0.325	0.095	2.5×10^{6}	
5×10^{-5}	0.305	0.441	0.308	0.14×10^{6}	

proposed chemical reaction

Depending on the mechanism proposed by Berthelot [21], the reaction is oxidized by mesalazine in an aqueous solution by potassium metaperiodate to form (p-benzoquinone monoamine) which is coupled with 4-amino salicylic acid as a chromogenic reagent to form a blue colored product. Measured at 600 nm and depending on the molar ratio of the product 1:1 (mesalazine: 4-amino salicylic acid), the interaction between them can be expressed as shown in Scheme 1.



Scheme 1: proposed chemical reaction

Comparison of the method with another spectrophotometric method

Some spectral variables of the proposed method for the determination of mesalazine were compared with those of two other methods found in the scientific literature, as shown in the following table 15

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Table 15: Comparison of the method with another spectrophotometric method

Analytical parameters	Present method	Literature method Alsafar, 2021	Literature method Theia'a, N., 2014
Type of pH	KOH	Na_2CO_3	9
Temperature	24	24	40
Development time (min)	5	10	20
Stability period (min)	120	60	50
Wavelength	600	440	346
Reagent	4-amino salicylic acid	Amoxicillin	p-Chloranil
Beer's law rang mL /gμ	0.1-14	2-70	1-30
Molar absorptivity l.mol^{-1}.cm^{-1}	7.6×10^{3}	2.86×10^{3}	4.60×10^{3}
Recovery (%)	99.2	99.99	98.80
RSD (%)	2.23	Less than 0.6	≤ 2.07
Colour of the product	Blue	yellow	-

Conclusion

A sensitive, rapid, and inexpensive spectrophotometric method was developed for the determination of mesalazine in alkaline media using an oxidative coupling reaction. At a wavelength of 600 nm, it was possible to analyze mesalazine in the range (0.1–14.0) μg/mL with high sensitivity as the molar absorbance was 7.6 x 10^3 L mol^{-1}cm^{-1} and the sandal mean was 0.0201 μg/cm^2, with a recovery rate of 101.6%. The relative standard deviation is less than 1.2%, the ratio of synthetic product to color product is 1:1 (mesalazine: 4-aminosalicylic acid) and the stability value is dye-tested. The constant was 8.51×10^5, and the method succeeded in estimating mesalazine in its pharmacological formulations, which was in tablet form, the results were in complete

https://doi.org/10.25130/tjps.v29i3.1542

agreement with the original content of the medicinal preparation and the method approved in the British Pharmacopoeia.

Acknowledgments

The writers like to thank the employees for their assistance during this research of Mosul University for their inspiration and support.

Author's Statement

The manuscript is an original work that has not been published elsewhere or submitted for publication. Citations have been made for all sources used in this work. We acknowledge full responsibility for the content of this manuscript, including all errors and omissions, and certify that the author made all changes. Furthermore, we have confirmed that all ethical considerations related to the studies described in this manuscript have been addressed. You have been considered and respected. This also includes obtaining the consent of the study participants. We understand that any violation of these statements may result in your manuscript being removed from publication.

Author Contributions

All individuals named in the study contributed equally to the work and writing

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