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DETERMINATION OF MESALAZINE SPECTROPHOTOMETRICALLY BY THE OXIDATIVE COUPLING METHOD USING A COUPLING REAGENT

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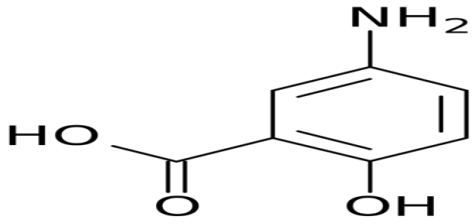
Abstract: The goal of the research is to create a spectroscopic technique that uses an oxidative coupling reaction with the reagent 4-amino antipyrine in a basic media to estimate the medication mesalazine. Potassium iodate forms a light, nutty result when dissolved in water in the presence of the oxidizing agent, and it absorbs lightest at 438 nm. 6.25–62.5 ug/ml of mesalazine was the range of concentrations when Beer's law reached its limitations. The Sandel significance (0.067 ug/cm2) and the molar absorptivity (2281 L/mole/cm). The quantitative detection limit was 0.0513, the qualitative detection limit was 0.0155, and the relative standard deviation value ranged from 0.1868%. This technique has been effectively used to measure the amount of mesalazine in tablet medicinal formulations. With 98.1766% recoverability.

Keywords: mesalazine, 4-amino antipyrine, oxidative coupling, spectroscopic determination.

Introduction:

Mesalazine, sometimes referred to as 5-amino-2-hydroxybenzoic acid chemically is used to treat Crohn's disease and non-specific ulcerative colitis, two conditions involving the inflammatory bowel. N-acetylmesalazine is produced during the in vivo metabolism of MES by acetylating enzymes [1], which aid in the removal of oxygen-derived free radicals, which inflammatory bowel disease patients frequently produce [2]. For a lot of ulcerative colitis patients, MES is the first line of therapy. It is believed to have a positive anti-inflammatory effect by causing gastrointestinal epithelial cells to express more peroxisome proliferator-activated receptors [3]. Mesalazine is in the form of a white to pink crystalline powder. It is slightly soluble in cold water and alcohol. It is highly soluble in hot water as well as in hydrochloric acid. Mesalazine has the chemical formula (C7 H7NO3) with a molecular weight of 153.135 gm/mole. It has the chemical formula as shown in Figure (1) [4].



The chemical formula is shown in Figure (1) [4].

Several analytical methods, such as spectrofluorometry [5], high-pressure liquid chromatography (HPLC) [6], microfluidic device-based liquid phase microextraction-HPLC [7], cyclic voltammetry [8], and liquid chromatography-mass spectrometry [9], were described in the literature for the MES determination. Spectrophotometry [11–16], FIA [10], and spectroscopy [9]. Flow injection analysis (FIA) techniques have gained a lot of attention and are frequently utilized because of their great repeatability, ease of use, and low cost of apparatus. The FIA method is widely applied to the examination of several organic and inorganic substances [17]. There is extensive discussion of the regular and reverse modes of the different FIA processes. Considerations [18, 19]. There are several methods for drug determination; Spectrophotometric methods [20-23]. The scientific name: is 5-amino-2-hydroxybenzoic acid.

EXPERIMENTAL PART:

Materials and methods

Shimadzu UV-Visible Spectrophotometer UV-160, Ultrasonic with a water bath, UNISONICS, Hot Plate with Magnetic Stirrer (BIOSAN MSH 300), Sensitive scale (with four decimal places). 2_5 Solutions for the materials utilized:

1.2_ 250 ppm mesalazine solution

Prepare by dissolving (0.02gm) of mesalazine powder in ethanol while stirring continuously. Fill a volumetric bottle (200ml) to the brim with distilled water.

1.3_4- Amino antipyrine

Prepare by dissolving (0.120115 gm) of reagent powder in water, then supplement the volume with distilled water to the mark in a volumetric bottle (100 ml).

1.4_Sodium hydroxide concentration (1M)

Prepare by dissolving 4 grams of sodium hydroxide powder in water, and then top up the volume in a volumetric vial (100 ml) with distilled water.

1.5_Potassium iodate at a concentration (0.1M)

To prepare, dissolve 2.14 grams of potassium iodate powder in distilled water, and then fill a volumetric vial (100 ml) to the brim with distilled water.

Results and discussion:

Initial tests:

When potassium iodate was present in a basic medium and mesalazine solution was combined with the 4-amino antipyrine reagent solution, an observation was made. After some shaking, a compound with a light walnut hue developed. At a wavelength of 438 nm, it displayed maximum absorption, and the photo solution looked colourless. Since there is minimal absorption at the wavelength above, research has been done to determine the appropriate conditions for the coupling process to produce an accurate and straightforward spectroscopic approach for mesalazine identification.

Enhancement of the Experimental Setup:

The oxidizing agent solution (1 ml) with a concentration of 0.1M, the reagent solution (1 ml), the sodium hydroxide base solution (1 ml), and the mesalazine solution (2 ml) with a concentration of 250 ppm were used in the subsequent experiments. The final volume of 20 ml was used, and the absorption of the solutions was measured at a wavelength (438 nm) in comparison to the mock solution.

Choose the best coupling agent:

Several chemical compounds that can be used as coupling reagents, such as (N, N_di phenyl _p_ phenyl hydrochloride, Tri fluor pyrazine, 2,4-di chloro aniline, and dapsone (at a concentration of 0.01 M) were used in the determination of mesalazine in the presence of the oxidizing agent.

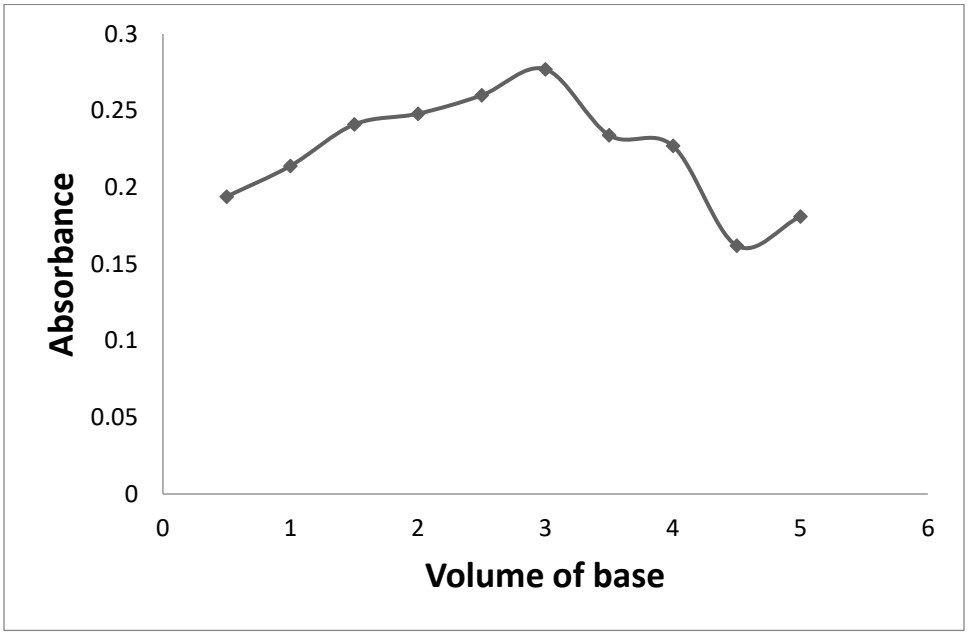
The concentration of potassium iodate (0.1 M) and sodium hydroxide (1 ml) were measured, and the wavelength range of each model's absorption was compared to its fake solution. Since 4-amino antipyrine produced the maximum absorption of the product at the wavelength (438 nm), it was selected as the coupling agent at a concentration of 0.01M. Select the ideal base:

A group of bases such as sodium hydroxide and potassium hydroxide ammonium were tried and gave sodium hydroxide the highest absorption so it was chosen better as the base as in the table below.

Absorbance	Bases
0.196	NaOH
0.184	KOH
0.129	NH4OH

The effect of the base volume:

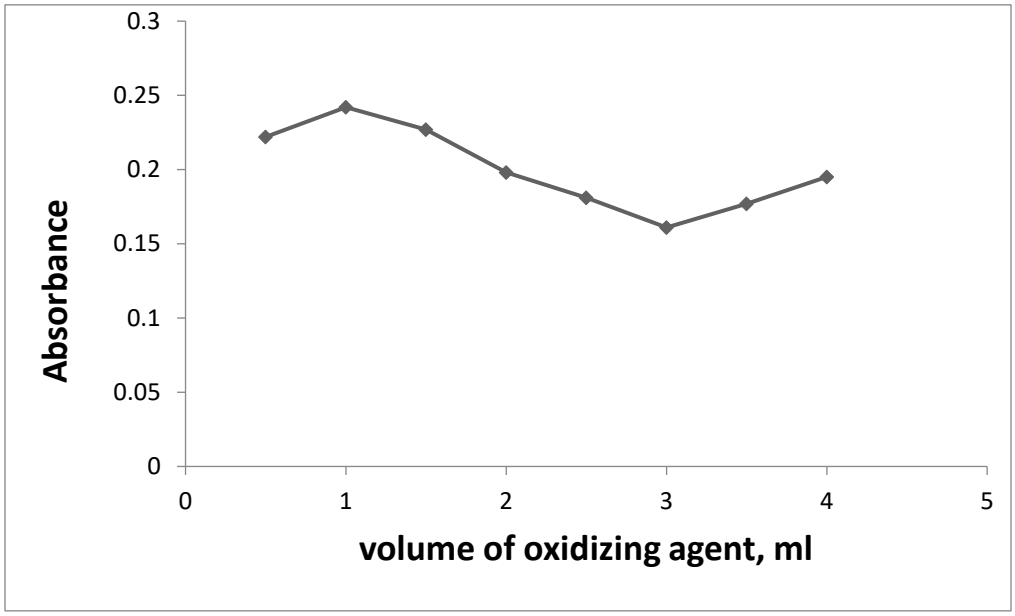
The effect of the base volume on absorption was studied by adding different volumes (0.5-5mL) from the base concentration solution (1M) to a series of volumetrics (20ml) Each of them contains (2ml) of Messalazin with a concentration (250ppm) in volumetrics (20ml) and 1 ml (from the oxidized worker, potassium Iodate with a concentration (0.1 m) Then add (4ml) from the 4-amino anti pyrine concentration of (M 0.1) then the solutions were diluted with distilled water, then the absorption was measured at the wavelength (438 NM) its mock solutions. As in the figure below (4-2).



Selecting an optimal oxidizing agent:

Several oxidizing agents were used, such as (potassium iodate, N-bromosuccinimide, ammonium sulfate, ferric potassium cyanide, ammoniated cerium sulfate, ferric chloride) at a concentration of (0.1M) for each, added to (2ml) of mesalazine at a concentration of (250 ppm), then (1ml) of 4_amino anti pyrine reagent solution at a concentration of (0.01M) was added into a 20ml volumetric bottle, and the appropriate amount

of distilled water was added to finish the capacity. The best oxidizing agent was discovered to be potassium iodate since it had the maximum absorption at the wavelength (438 nm), and it was used in the following tests. The absorbance of each model was then tested against its mock solution in a wavelength range between (200 - 800 nm).



Based on the data shown in Figure (4-1), it was determined that 1 millilitre is the ideal amount of the oxidized factor solution for optimal absorption. This information was utilized in the following situations.

Impact of the oxidation period:

To determine how long it takes for potassium iodate to oxidize mesalazine, a series of volumetric bottles with a capacity of 20 ml were used. Each bottle held 2 ml of mesalazine at a concentration of 250 ppm, and 1 ml of a potassium iodate solution with a concentration of 0.1M was added to it. Following varying times for the solutions, 4 ml of the 0.01M concentration 4 amino antipyrine reagent solution was added. It was then diluted with 20 ml of distilled water, and the solutions' absorption at 438 nm was measured in comparison to their mock solutions. The ideal duration was found to be ten minutes. as shown in Table (4-3).

Absorbance	Time minutes
0.472	0
0.371	5
0.380	***10***
0.310	15
0.362	20
0.252	25
0.298	30
0.278	35

Table (4-3) Effect of oxidation time on absorption.

Effect of a sequence of additions:

Since the order of addition affects the colour intensity of the final chemical, the impact of altering the order of additions to the solutions used in the reaction was investigated. As a result, several tests were carried out

using various addition sequences, taking care to ensure that the components' sizes and concentrations remained constant throughout. The first configuration was utilized in future studies since it was shown from the data shown in Table (4-4) to offer the largest absorption at a wavelength of 438 nm.

No	Order of additions	Absorbance
1	***M + O + R+B***	***0.382***
2	M+R + O +B	0.107
3	O+R+B+M	0.01 K8
4	M+O+B+R	0.051

Table (3-3) Effect of the sequence of additions on absorption.

- ✓ Mmesalazine (M)
- ✓ KIO3 (O)
- ✓ Reagent (R)
- ✓ NaOH (B)

The ability of the resulting output:

The stability of the resulting product was traced using the optimal conditions obtained in previous experiments by taking a volume of (2ml) of mesalazine at a concentration of (250ppm) in volumetric bottles of (20ml), adding (1ml) of the oxidizing agent potassium iodate at a concentration of (0.1M) and abandoning the bottles. The oxidation process was allowed to finish for ten minutes, after which two millilitres of a 0.01M concentration solution of the 4-amino antipyrine reagent was added. The volume was then adjusted with distilled water in volumetric bottles containing twenty millilitres, and the absorption of the coloured solutions was measured after being left for the designated amounts of time in minutes. It is evident from the findings in Table (4-6) that the stability of the coloured product was demonstrated at a wavelength of 438 nm in comparison to its mock solutions after 5 minutes and for a minimum of 60 minutes, which is a suitable amount of time to conduct measurements. The results are displayed in Table (4-6).

Time (min)	Absorbance
0	0.472
5	0.325
10	0.370
15	0.375
20	0.372
25	0.371
30	0.373
35	0.372
40	0.316
45	0.384
50	0.312

Table (4-6) Stability of the resulting output.

Effect of solvent type:

Various solvents were employed to fill volumetric bottles to the mark after all reaction components were added by the ideal values from the prior tests (20ml), so water was chosen as the best solvent because it is

available in the laboratory, economical, and the highest absorption at (438nm). The results are as follows: Shown in Table (4-7).

Solvent	λ_{max}(nm)	Absorbance
Water	***438***	***0.3860***
Ethanol	438	0.233
Acetone	438	0.107
Methanol	438	0.046

Table (3-6) Effect of solvent type

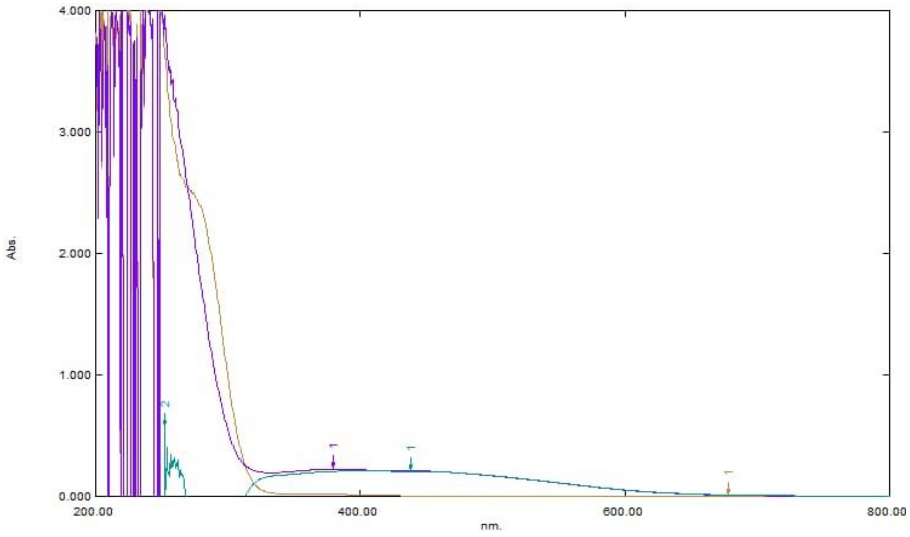
Temperature effect:

Table (4-5) displays the findings of a study conducted at temperatures ranging from 5 to 50°C to examine the impact of temperature on the absorption and stability of the resulting coloured product.

Temperature ^{o}C	Absorbance
0	0.236
5	0.169
10	0.253
15	0.247
20	0.381
25	0.379
30	0.386
35	0.295
40	0.276
45	0.216
50	0.198

Table (4-5) Effect of temperature on absorption.

Absorption spectrum:



Optimum Conditions	Volume of mL
Mesalazine	2ml
4-amino anti pyrine	4ml
KIO_3	1ml
NaOH	3ml

The working method adopted in the calibration curve

Following the establishment of the ideal parameters for mesalazine determination, the following standard curve was created:

A series of 20 ml volumetric bottles were filled with varying volumes (0.5–4.5 ml) of mesalazine solution at a concentration of (250ppm). One ml of the potassium iodate oxidizing agent solution at a concentration of (M0.1) was then added, and the solutions were left for 10 minutes to finish the oxidation reaction.

Then add (4 ml) of 4-amino antipyrine reagent solution at a concentration of (2-10 x 1M) and (3 ml) of sodium hydroxide at a concentration of (1M), After adding distilled water to the volume of the appropriate level, each solution's absorbance at 438 nm was measured in comparison to the fake solution. The procedure yielded a molar absorbance of (L\mole.cm 2281) and a Sandel significance of (ug\cm 0.067). The standard curve for a range of mesalazine concentrations between (ug\ml) 6.25 – 56.25) is shown in Figure (4-5), which exhibits Beer's law.

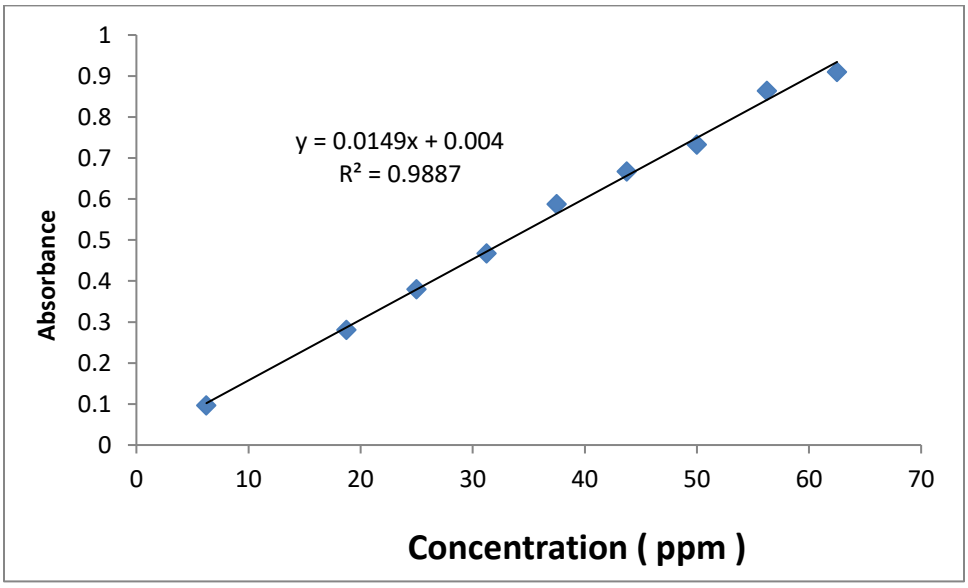


Figure (4-5) Standard curve for determination of mesalazine.

Accuracy and Compatibility:

Amount of Measalazine taken (ppm)	RE, %	Recovery, %	Average recovery,%	RSD, %	
6.25	0.671141	99.33		0.004062	
25	0.9396	100.9664	99.38739	2.174448	
50		97.86577		0.655164	

Accuracy and compatibility of the method:

By computing the recall and the relative standard deviation of three distinct mesalazine concentrations, 0.000254, the accuracy and compatibility of the suggested technique for determining mesalazine were determined in the ideal circumstances outlined in the working procedure.

,0.008263,0.004803(ug\ml) by averaging each measurement over six. With a recall rate of 99.387% and a relative standard deviation below 0.1868%, the approach demonstrated good agreement and excellent accuracy. The following mathematical formula was used to determine the recall, its rate, and the relative standard deviation:

RE% =O-T/T×100

RE = relative error

= O practical value

= T true value

The recovery value is calculated from the following law

Recovery % =RE % + 100

As for calculating the percentage value of the relative standard deviation, the following law is applied (70):

S = standard deviation

= reading rate

The results are shown in Table (4-9).

Amount of Measalazine taken (ppm)	RE, %	Recovery, %	Average recovery,%	RSD, %
6.25	0.671141	99.33		0.004062
25	0.9396	100.9664	99.38739	2.174448
50		97.86577		0.655164

Table (4-9) Method accuracy and compatibility:

Detection limit and quantity limit:

The quantitative and qualitative detection limits were calculated by measuring the absorbance of 3 solutions to the lowest concentration (6.25ppm).

In the calibration curve, within the limits of Beer's law and at optimal conditions, the limits of qualitative and quantitative detection were, respectively

(0.0155), (0.0513) as in Table (4-10) and it was calculated from the following mathematical relationship:

LOD=3.3S/B

LOQ=10S/B

Since:

DOD=Specific limit of detection

LOQ = limit of detection of quantitation

S = standard deviation of the lowest concentration

B=slope

Conncentration (ppm)	*B*	*S*	*LOD µg /ml*	*LOQ µg /ml*
6.25	*0.0149*	*0.0005*	*0.0155*	*0.0513*

Table (4-10) detection limit:

The nature of the resulting product:

The two techniques of continuous changes (Job method) and the molar ratio approach were used to determine the type of the resultant product and the rate of drug-reagent binding. The concentration of the reagent solution 4 amino acid pyridine (2 ml) and the mesalazine solution (0.0016M) in both procedures, respectively.

(Job's approach) involved adding 1 ml of a 0.1M potassium iodate solution and 3 ml of sodium hydroxide with a concentration of 1M to 20 ml volumetric flasks containing varying quantities of the drug solution, ranging from 1 to 9 ml. Following the appropriate diluting with distilled water, these solutions' absorbance at 438 nm was evaluated in comparison to respective mimic solutions. The ratio of mesalazine to the reagent is 1:1, as seen in Figure (4-6).

Figure (4-6) Curve of the continuous changes method (Job's method).

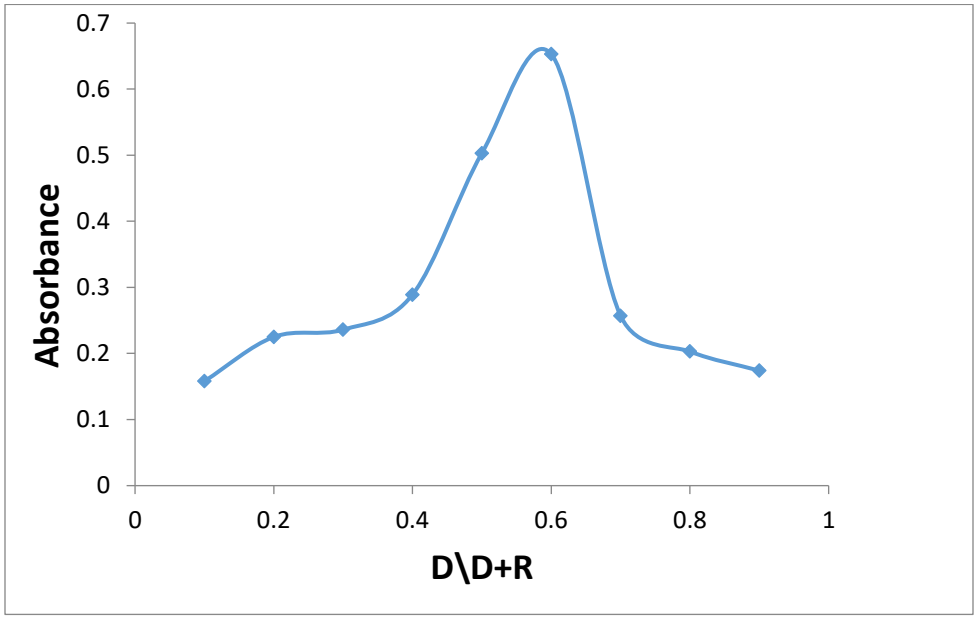


Figure (4-6) CurVe of the continuous changes method (Job's method).

The molar ratio approach was employed to guarantee that the reaction ratio between reagent 4_amino anti pyrene is 1:1. A succession of volumetric bottles with a capacity of 20 ml were filled with 2 ml of the medication mesalazine solution. The reagent solution was then added to it in various quantities (0.25–4 ml), and the remaining additions were finished. The ideal sizes were diluted to the appropriate length (438 nm) using distilled water, and the absorption of these solutions was compared to the fake solution for each of them. The molar ratio was determined to be consistent with the modification procedure, and Figure (4-7) validates the 1:1 ratio between the reagent and mesalazine.

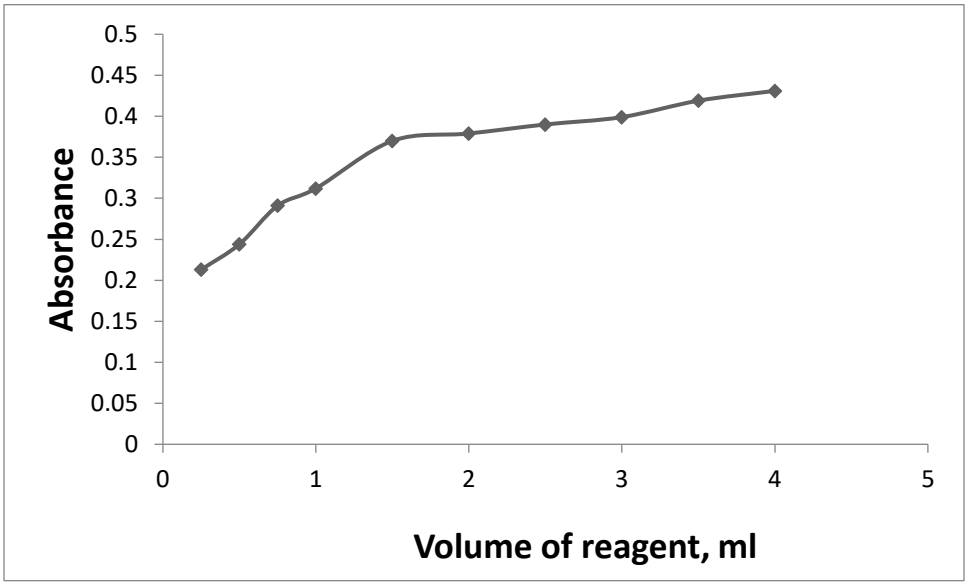


Figure (4-7) Molar ratio method curve.

Therefore, the proposed reaction equation is as follows:

The effect of interferences:

TTo examine the selectivity of the method and the possibility of its application to pharmacological formulations, a series of volumetric bottles with a capacity of 20 ml that contained 2 ml of solution were filled with varying amounts of these agents (2.4 ml) at a concentration of 1000 ppm to study the agents' effects. 3 ml of sodium hydroxide at a concentration of 1 M, 4 ml of the oxidizing agent at a concentration of 0.1 M, and mesalazine. Ten minutes were given to the solutions to finish the reaction.

Following the addition of 4 ml of the reagent solution (4 amino aniline pyridine) at a concentration of 0.01M, all solutions' absorbance was measured at 438 nm in comparison to respective mock solutions. The solutions were then diluted with distilled water to the appropriate level. It was feasible to apply the procedure to pharmaceutical formulations and display the findings by calculating the recoverability of each addition and finding that the interferences utilized did not influence the absorption. Table (4-11).

Foreign Compound	Recovery (%) of Measalazine (250 ppm) and Foreign Compound Added		
	100	200	300
Starch	103.1	100.1	103.6
Lactose	100.4	100.7	101.5
Sucrose	100.4	99.33	101.2
Na_2CO_3	100	100.4	99.6

Applied part:

Determination of mesalazine in a 400 mg tablet by the direct method

Different volumes (1, 2, 3) ml of the prepared medicinal tablet solution (400 mg) were taken to obtain concentrations (ppm 6.25, 25, 50). These volumes were treated according to the optimal working method, as these volumes were placed in three Volumetric bottles of 20 ml, and to each bottle I added (4 ml) of the oxidizing agent potassium iodate at a concentration of (0.1M), and added (4 ml) of the reagent 4-amino anty pyridine at a concentration of (0.01M) and (3 ml) of sodium hydroxide at a concentration (1M), and the

solutions were left for 10 minutes for the reaction to complete. The absorbance (average of six readings) of each solution was measured against its mock solution at the wavelength (438 nm), and the recall and RSD were calculated, and the results are shown in Table (4-12).

Amount of Measalazine taken (250ppm)	RE, %	Recovery*, %	Average recovery,%	RSD, %
6.25	0.886	99.11	98.1766	1.772
25	0.537	100.5		2.183
50	5.078	94.92		5.635

***** Average of six determinations

Table (4-12) Determination of mesalazine in pharmaceutical tablets (400 mg) by the direct method.

Conclusions:

A new spectroscopic method was developed for the determination of mesalazine, simple and highly sensitive, based on the direct determination of mesalazine using oxidative coupling reactions with the reagent 4-amino anty pyridine at a concentration of (0.01M) in the presence of the oxidizing agent potassium iodate at a concentration of (0.1M). The reaction was carried out in a basic medium. (Sodium hydroxide at a concentration of M1) and a green-coloured product appeared, dissolved in water and stable, and gave the highest absorption at the wavelength (438 nm). The method follows Beer's law in the range (6.25-56.25 ppm). A deviation occurs at higher concentrations, and the molar absorption reaches (2281 L\mole). .cm) and the Sandel significance (0.067 ug\cm), and the relative standard deviation does not exceed (0.1868%), and the detection limit was the qualitative and quantitative detection limit, respectively. (0.0155), (0.0513) The method was successfully applied in the determination of mesalazine in pharmaceutical preparations (tablets), with a recovery rate of 99.387%.

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