How to Cite:

Mohammed, G. F., & Omar, F. K. (2022). Indirect spectroscopic determination of esomeprazole using malachite green dye in the presence of N-bromosuccinimide. *International Journal of Health Sciences*, 6(S5), 10344–10353. https://doi.org/10.53730/ijhs.v6nS5.12034

Indirect spectroscopic determination of esomeprazole using malachite green dye in the presence of N-bromosuccinimide

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Abstract---A simple, fast and sensitive spectrophotometric method has been developed for the determination of esomeprazole in its pure form and also in the form of a pharmaceutical preparation. The highest absorption was found at a wavelength of 618 nm and the limits of Beer were (2_24) μ g/ml. The molar absorbance (2.1070 \cdot 10⁴) L.mol⁻¹ .cm⁻¹, Sandell sensitivity 0016. μ g.cm⁻², and limits of detection LOD 0.0153 μ g/ml, LOQ 0.0510 μ g/ml were determined the method was also applied to pharmaceutical preparations, and the validity of the method was confirmed by standard addition.

Keywords---esomeprazole, malachite green dye, pharmaceutical preparation.

Introduction

Esomeprazole (S-isomer of omeprazole). Chemically, it is (S)-5-methoxy-2-[[[4-methoxy-3,5-dimethyl-2- pyridinyl]methyl]sulfiny]-1H-benzimidazole as show in fig(1). ⁽¹⁾. Esomeprazole (ESO) is a proton pump inhibitor (PPI) (1) because it inhibits gastric acid secretion ^(3,2)., including Zollinger-Ellison syndrome, as well as the treatment and prevention of gastric and duodenal ulcers and erosive esophagitis ^(4,5) and also works to eliminate stomach germs (helicobacter pylori) and heartburn ⁽⁶⁾.

Esomeprazole is used in the treatment of inflammation resulting from the work of gastric and esophageal endoscopy ⁽⁷⁾, and esomeprazole helps to prevent esophageal cancer ⁽⁸⁾. Esomeprazole also inhibits placental autophagy because it relieves symptoms of pre-eclampsia (PE), which plays a major role in causing preeclampsia in pregnant women ⁽⁹⁾. As for the side effects of esomeprazole, studies have shown that it is simple for people who do not suffer from

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.

Manuscript submitted: 9 April 2022, Manuscript revised: 18 June 2022, Accepted for publication: 27 July 2022 10344

cardiovascular diseases and includes simple headaches, diarrhea and abdominal pain that disappear when treatment is stopped ⁽¹⁰⁾ On the other hand, studies have warned against giving it to patients who suffer from cardiovascular diseases. Blood and high level of cholesterol in the blood, because of the weakness in the metabolism of fats, even if its effect is small ⁽¹¹⁾ Regarding the effect of this drug on the liver, studies have shown that the effect of esomeprazole is limited and the study did not confirm its toxicity to the liver ⁽¹²⁾.



Figure 1: Esomeprazole

Practical part Equipment and tools "used":

- 1. Shimadzu(UV/Vis) 1800 spectrophotometer, Japan
- 2. (BL 210S- sensitive) Scientific balance.
- 3. Quartz cell of (1.0) cm for absorbance measurements.

Reagents and chemical materials used

All chemicals were of(high purity) and from(known sources) and their solutions It was prepared as follows:

1. Standard Esomeprazole solution, (200 ppm)

The solution was prepared by dissolving 0.0200 g) of pure Esomeprazole (prepared by the General Company for Pharmaceuticals and Medical Appliances - SDI Samarra - Iraq) in 5 ml of ethanol, then the volume was completed with distilled water to Limit the mark to a 100-mL volumetric vial .

2.malachite green dye solution ,(100 ppm).

The solution was prepared by dissolving 0.0100 g of malachite green salt in distilled water using a 100 ml volumetric flask.

3. N_bromosuccinimde solution,(300 ppm).

 $0.03~{\rm g}$ of the substance is dissolved in distilled water in a volumetric flack of 100 ${\rm ml}$

4. hydrochloric acid solution, (1M).

The acid was prepared by diluting 8.5 ml of concentrated acid using a volumetric bottle of 100 ml and completing the volume with distilled water.

5. Pharmaceutical solutions Esomeprazole capsules solution, (200 ppm)

A mixture of powder of five esomeprazole in capsules was prepared, each containing 40 mg of esomeprazole, the weight of each one was 0.044, then 0.0200 of it was weighed and dissolved in 5 ml of ethanol, and the volume was completed with distilled water in a volumetric flask of 100 m

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The principle of the method

The principle of the method depends on the oxidation of the drug (ESO) by the oxidizing agent in an acidic medium, after which the dye solution is added, so that the resulting solution is green, indicating that the oxidizing agent has run out.

Preliminary study

1ml of (ESO) was added, then 1 ml of the oxidizing agent N_bromosuccinimde was added, then 1 ml of hydrochloric acid was added, and finally 1 ml of malachite green dye was added, All of this was done using volumetric bottles of 25ml capacity. It was noticed that the color of the dye appeared as an indication of the depletion of the oxidizing agent The highest absorption was at a wavelength of 618 nm.

Study the optimal conditions

For the reaction In order to obtain a colored product with high absorption and sufficient stability to complete the measurements, the optimal conditions were studied.

Study of the effect of the oxidizing agent N_bromosuccinimide (NBS)

The effect was studied by adding increasing volumes of (0.25 ± 2.0) ml of (NBS) solution and it was found that 1.0 ml is the appropriate volume.

Table No.	(1)	Effect of the oxidizing agent N_bromosuccinimide	(NBS))
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Volume of (NBS) (0.03%)(ml)	Absorbance
0.25	0.102
0.5	0.186
1.0	0.293
1.25	0.221
1.5	0.175
2.0	0.116

Study of the effect of the amount of green dye malachite

The effect of the dye was studied by adding different volumes of (0.25 - 2.5) ml at a concentration of (0.01%) of the dye, as shown by the results in Table (2)

Table No. (2) Effect of the amount of dye				
a of dya (0.01%) (m1)	Absorbance			

Volume of dye (0.01%) (ml)	Absorbance
0.25	0.141
0.5	0.198
1.0	0.292
1.25	0.378
1.5	0.409
2.0	0.275
2.25	0.265
2.50	0.194

Study the type of acid

Preliminary experiments showed that the process is carried out in an acidic medium to form a colored product, so the effect of several strong and weak acids was studied in the estimation of esomeprazole by adding fixed amounts of 1 ml of (1M) to each of them separately. It is clear from the table below that hydrochloric acid is the best

Type of acid (1M) (ml)	H_2SO_4	HC1	CH ₃ COOH	HNO ₃
Absorbance	0.293	0.405	0.113	0.201

Table No. (3) Study the type of acid

Study the effect of the amount of HCl

The effect was studied by adding different volumes of HCl with a concentration of 1M to the reaction mixture, then the absorbance of these solutions was measured against the blank solution and the following table shows the results.

Table (4) Studying the effect of the amount of HCl

Volume of HCl (1M)	0.25	0.5	0.75	1.0	1.5	2.0
Absorbance	0.190	0.245	0.301	0.490	0.401	0.220

Oxidation time study

The effect of oxidation time on the intensity of absorption was studied by adding the calculated amount of the oxidizing agent to (ESO) in an acidic medium and leaving it for different periods of time (0_30) minutes, then adding a calculated amount of dye and completing the volume with distilled water, then the absorbance was measured.

Time of oxidation (min)	Absorbance	
0	0.321	
5	0.491	
10	0.475	
15	0.405	
20	0.322	
25	0.312	
30	0.278	

Table (5) studying the effect of oxidation time

Study the effect of surfactants

The effect of surfactants was studied, where different volumes $(0.5_2.0)$ ml of each of the surfactants were added to the reaction, and then the absorbance was measured at a wavelength of 618 nm, and the results showed that it had a negative effect on the reaction.

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	Absorbance /ml of surfactant used				
Surfactant	0.5	1.0	1.5	2.0	
CTAB 0.1%	0.324	0.355	0.316	0.301	
CPC 0.1%	0.275	0.294	0.319	0.271	
SDS 0.1%	0.241	0.276	0.232	0.211	
TritonX-100	0.401	0.422	0.418	0.391	
0.1%					
Without	0.490				

Table (6) Effect of surfactants

Study of the effect of dye stability time

The effect of time on the stability of the resulting dye was studied by using the approved method and the optimal conditions obtained from previous experiments by using a volumetric bottle of 25 ml and completing the volume with distilled water after that, then measuring the absorbance of the colored solution with different time periods at a wavelength of 618 nm.

Esomeprazole 8µgml ⁻¹ Room Temp.	Absorbance/time (min)	
After addition	0.491	
5	0.493	
10	0.493	
15	0.493	
20	0.491	
25	0.491	
30	0.491	
35	0.491	
40	0.490	
45	0.490	
50	0.489	
55	0.489	
60	0.489	
90	0.489	
Over night	0.482	

Table (7) Effect of time on dye stability

Table No.8 Summary of optimal conditions

Material solution	Concentration	Optimum amount (ml)
Malachite Green	%0.01	1.5
NBS	%0.03	1
HCL	1 M	1
λ_{max} (nm)	618	
Temp.	35 C°	
Stability period	min)60 (

Final absorption spectrum:

Esomeprazole is oxidized by a known amount of oxidizing agent (NBS) in an acidic medium, and the excess of the oxidizing agent leads to shortening the dye at a wavelength of 618 nm.



Fig(.2) final absorption spectrum of (8ppm) Esomeprazole solution: A-(versus blank), B(versus distilled water), C-(blank versus distilled water).

Calibration curve

By following the previously mentioned method and under optimal conditions, increasing amounts of esomeprazole are taken in volumetric flask 25 ml to make the standard curve and measure the absorbance of the solutions against the blank solution at a wavelength (618 nm). The following figure shows the standard curve for the determination of esomeprazole, which follows Beer's law in the range Concentration (2_24) μ g/ml, and the value of the correlation coefficient indicates that the linear specifications are good



Fig.3: The standard curve for determination of esomeprazole

The values of ε max LOD, LOQ, Sandel's sensitivity and correlation coefficient were calculated as shown in the table. It is clear that the method has "good" sensitivity, and the correlation coefficient value shows the high linear specifications of the calibration curve.

Table No.9 Emax LOD, LOQ, Sandel's sensitivity and correlation coefficient

Beer's law range(ppm)	(2-24)
Molar absorptivity (l.mol ⁻¹ .cm ⁻¹)	2.1070 ×10 ⁴
Sandell's sensitivity (µg.cm ⁻²)	0.016
LOD (µg/ml)	0.0153
LOQ (µg/ml)	0.0510
slope	0.061

The accuracy and compatibility of the method

To calculate the accuracy of the calibration curve, several concentrations of esomeprazole were taken as shown in the following table

Table No.10 The accuracy and compatibility of the method

Amount of ESO µg/ml	Amount of ESO µg/ ml	Recovery %	Rrelative error,%	Relative standard deviation %
2	1.986	99.3	0.7	0.967
4	3.938	98.45	1.55	0.900
6	6.019	100.3	-0.3	0.190

Application of the method to pharmaceutical preparations

The proposed method was applied to the pharmaceutical preparations of esomeprazole, which were in the form of a capsule. Three different concentrations of the solution were taken. All the steps mentioned in the method were applied in the optimal conditions. The value of the recall ratio, relative error, and relative standard deviation was calculated. The following table shows that the proposed method is successful with an estimate Esomeprazole is in the capsule form and has good accuracy and compatibility.

AwaNex	Amount of	Amount of	Recovery %	Relative	Relative
capsules 40	ESO µg/ml	ESO μg/		error,%	standard
mg/capsule	present	ml found			deviation,%
Iraq	2	1.970	98.50	1.50	0.569
	4	3.970	99.25	0.75	0.574
	6	6.019	100.31	-0.3	0.465

Standard addition method

Because of the difficulty in providing the necessary tools and chemicals for the standard method in the British Constitution, and in order to clarify the efficiency of the method and prove its accuracy, the standard addition method was applied to the pharmaceutical preparation of esomeprazole by adding fixed volumes (0.25_0.50) of the solution of the 200 μ g/ ml preparation to two series of 25 ml volumetric flask and then adding Increasing volumes of the standard solution of esomeprazole at a concentration of 200 μ g/ ml under all optimum conditions were applied and the absorbance was measured at a wavelength 618 nm The results shown in the figure and the table below showed that the method is compatible with the developed method and has an acceptable selectivity.





Fig - 4. Standard addition method curves for determination of esome prazole in pharmaceutical preparation at concentration (2,4 $\mu g/$ ml).

Table No.12	The results	of the	standard	addition	method	according	to	the
		propos	ed metho	d of work	C			

pharmaceutical preparation	esomeprazole present µg/ml	esomeprazole measured µg/ml	Recovery %
esomeprazole	2	2.008	100.4
AwaNex capsules	4	3.979	99.47
40 mg/capsule			
Iraq			

Conclusions

A new developed spectrophotometric method has been proposed for the determination of esomeprazole using malachite green dye and the oxidizing agent N bromosuccinimde

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