Chemical Methodologies 6(2022) 6(3) 228-236

Chemical Methodologies

Journal homepage: http://chemmethod.com

Original Research Article

A Simple Spectrophotometric Method for the Determination of Famotidine *via* Reaction with Alizarin Red S

Safaa A. Zakaria[1], Rana S. Al-Saffar[2], Nabeel S. Othman[1,*]

[1]*Department of Chemistry, College of Science, University of Mosul, Mosul, Iraq*
[2]*Northern Technical University, Mosul Technical Institute, Mosul, Iraq*

ARTICLE INFO

Article history

Submitted: 2021-11-13
Revised: 2022-01-14
Accepted: 2022-01-16
Manuscript ID: CHEMM-2111-1393
Checked for Plagiarism: **Yes**
Language Editor:
Ermia Aghaie
Editor who approved publication:
Dr. Vahid Khakyzadeh

DOI:10.22034/chemm.2022.313691.1393

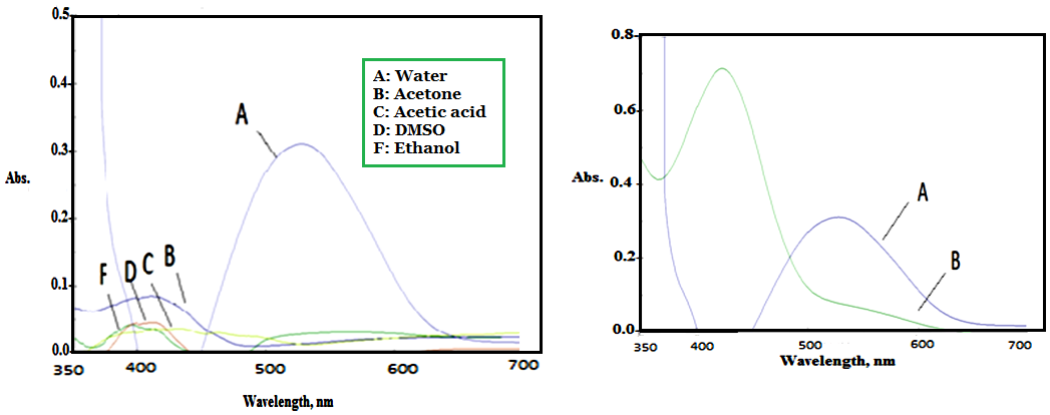
KEYWORDS

Alizarin red S
Famotidine
Famosam tablets
Spectrophotometric

ABSTRACT

A simple, quick, and sensitive spectrophotometric method was proposed to determine famotidine (FAMT) in its pure form and pharmaceutical preparation (tablet). The method involves the reaction of FAMT with alizarin red S to produce a stable, water-soluble red complex with the maximum absorption signal at 528 nm, Beer's law is followed for standard FAMT solutions in the range of 6.0-80 µg/mL with a negative deviation at concentrations higher than 80 µg/mL. The method is sensitive. The molar absorptivity and Sandell's sensitivity index values are 3.3 × 10 4 l/mol.cm and 0.0109 µg /cm^2 respectively. Two approaches were applied to determine the amount of FAMT in its pharmaceutical formulation (famosam tablets), the one depending on a regression equation and the second on the standard addition method. The results were obtained with sufficient precision and accuracy, with negligible effects from excipient interference.

GRAPHICAL ABSTRACT



* Corresponding author: Nabeel S. Othman
✉ E-mail: nsn20002004@uomosul.edu.iq

Introduction

The FAMTs are histamine H2-receptor antagonists that are reversible and inexpensive histamine blockers at the H2-receptors. Because H2-receptors are found in the stomach, their stimulation causes gastric acid to be released. They compete for H2-receptors with histamine and prevent gastric acid secretion and some of the histamine's effects [1]. FAMT FAMT ($C_8H_{15}N_7O_2S_3$, 3-[[[2-[(diaminomethylene) amino] thiazol-4-yl]methyl] sulphanyl] -*N*-sulphamoylpropanimidamide) is a white or yellowish-white color, very slightly soluble in water, soluble in acetic acid (glacial), and mineral acids. Figure 1 reveals the chemical structure of FAMT [2].

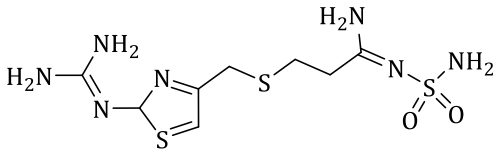


Figure 1: Chemical structure of FAMT

Numerous analytical methods were performed for the determination of FAMT in pure and formulation products, including UHPLC [3], SPE-LC-MS/MS, [4], HPLC [5-9], spectrofluorometric [10-12], and electrochemical [13].

In assessing active chemicals in pharmaceutical formulations, UV-Vis spectrophotometric approaches are inexpensive, simple to use, and rapid to detect, involving only a few minutes in some instances [14--19].

This work established a simple and accurate spectrophotometric method for determining FAMT, based on only one primary rapid chemical reaction between FAMT and alizarin red S reagent. The effective use for the estimate of FAMT in its formulation tablets, on the other hand, revealed no influence from any excipients commonly utilized in tablet manufacturing.

Material and Methods

A Jasco UV Spectrophotometric (JascoV-630) with a pair of glass cells was employed for the experiment. The pH was measured with a HANA pH meter.

Reagents

For analytical studies, all chemicals used are as pure as possible.

Preparation of solutions

Working famotidine solution (FAMT), 200 µg. mL^{-1}

0.0200 g of FAM (SDI) dissolved in 100 mL distilled water (with 1 drop of concentrated HCl) in a calibrated flask.

Alizarin Red S (ARS) (0.05%w/v).

0.0500 g of ARS dissolved in 10 mL distilled water, then diluted to 100 mL with absolute ethanol in a calibrated flask.

Pharmaceutical preparation

Famosam tablet solution, 200 ($\mu g.mL^{-1}$).

A solution of 200 $\mu g.mL^{-1}$ concentration was prepared by taking a weight equivalent to one tablet (40 mg/tablet) from five tablets powder then dissolved in a 100 mL calibrated flask with distilled water (with 1 drop of concentrated HCl), followed by proper dilution to prepare 200 $\mu g.mL^{-1}$.

General Procedure and Calibration Graph

A 0.3 to 4 mL of FAMT solution (200 $\mu g/mL^{-1}$) were transferred to a set of 10 mL volumetric flasks. Then 1.5 mL of ARS was added, the solutions were raised at room temperature for 10 min, and then all solutions were diluted to the mark with distilled water. The absorbance was measured at 528 nm versus the blank. The calibration graph was linear over the concentration range of 60-800 µg FAMT /10 mL (6.0- 80 µg. mL^{-1}), and concentration above 80 µg /ml gave a negative deviation from Beer's law (Figure 2). The molar absorptivity and Sandell's sensitivity index were calculated and equal 3.3×10^4 $l.mol^{-1}cm^{-1}$ and 0.0109 $\mu g/cm^{2,}$ respectively.

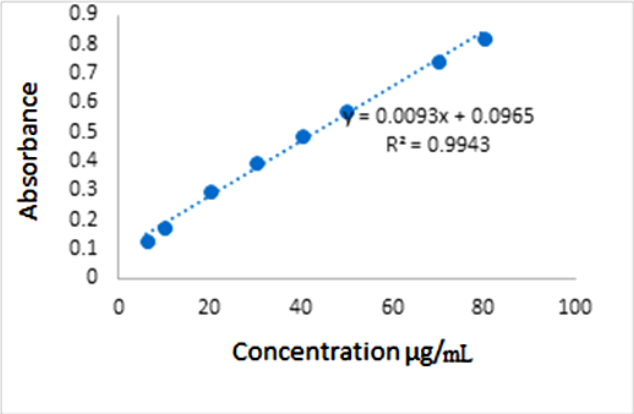


Figure 2: The calibration curve of the estimation FAMT according to the suggested method

Results and Discussion

A set of parameters that influenced the increase of colored products were investigated.

Effect of pH

The addition of acid (0.01 M HCl) and base (0.01 M NaOH) was investigated. As a result, adding acid or base to lower or raise the pH of the final solution of reaction components (pH =5.5) was not advised. The highest absorbance was reached when the pH in the reaction medium was equal to 5 without the addition of acid or basic (Table 1).

Table 1: The effect of pH on absorbance signal

V NaOH(0.01M)	Absorbance	pH
0	0.309	5.5
0.01	0.295	5.67
0.02	0.287	5.74
0.03	0.250	5.97
0.04	0.175	6.05
0.05	0.140	6.11
V HCl(0.01M)	Abs.	pH
0	0.309	5.5
0.01	0.290	5.1
0.02	0.266	4.95
0.03	0.219	4.86
0.04	0.096	4.76
0.05	0.068	4.68

Effect of Buffer Solutions

The pH of the standard FMAT solution was found to be 6.9. After adding 1.5 of the reagent solution and diluting, the pH became 5.5. Buffer solutions with an acidic function (phthalate buffer solution and citrate buffer solution) were prepared, and their effect on the formation of the colored product was studied. The result showed that buffer solutions negatively affected the absorption of the colored product (turbid solutions after 10 min), so it would not be recommended to occupy any buffer solution in the subsequent experiments.

Effect of Reagent Amount

The effect of ARS amount on the absorbance of a colored product has been studied by adding various amounts of 0.5 – 2 mL of 0.05 % ARS solution to several FAM 100-400 µg/10 mL solutions.

Table 2: The effect of the reagent amount on absorbance

ARS 0.05% (mL)	Absorbance /µg of FAM in 10 mL.					
	100	150	200	300	400	r
0.5	0.140	0.178	0.208	0.254	0.355	0.9925
1	0.172	0.239	0.296	0.381	0.443	0.9895
1.5	0169	0.235	0.305	0.426	0.498	0.9924
2	0.179	0.249	0.285	0.457	0.499	0.9801

The results in Table 2 reveal that 1.5 mL of ARS was sufficient to give the highest intensity and the highest value of correlation coefficient (r). It was fixed in the subsequent experiments.

Effect of Time

The effect of time on the progress and formation of the colored product has been studied by mixing FAMT (200 µg) with ARS and leaving it for various times before dilution with distilled water (see Table 3).

Table 3: Effect of time on formation of the colored product

Time, minute	Absorbance
Immediately	0.278
5	0.288
10	0.309
15	0.306
20	0.307

The results in Table 3 indicated that only 10 minutes of standing time before dilution is required to get the highest intensity of the colored product, so it is recommended. The results in Table 3 indicated that only 10 of standing time before dilution is required to get the highest intensity of the colored product, so it is recommended.

Effect of Surfactant

A 1.5 mL of three different surfactants were added to the reaction mixture to evaluate the impact on the color product intensity. Surfactants were added to obtain a higher absorbance of the formed colored product or a redshift. The addition did not cause an increase in the absorbance or the maximum wavelength of the measurement. The results (Table 4) are shown to have no useful effect (turbid solutions with CTAB and CPC will SDS a decrease in absorbance). As a result, it was not reliant on the results of subsequent tests.

Table 4: Effect of adding surfactants on absorbance

Surfactant ($1x10^{-3}$M**),** order*	Absorbance
Cetyltrimethylammonium bromide(CTAB)	Turbid
Sodium dodecyl sulfate (SDS)	0.198
Cetylpyridinium chloride (CPC***)***	T
Without	0.305

*FAMT+ ARS+ surfactant

Solvent Effect.

In addition to water, various solvents have been used to dilute the flasks to the mark after adding all components of the reaction (Figure 3).

Figure 3 shows that all solvents resulted in a blue shirt and reduced absorbance, except water. As a result, water should be utilized as a diluting solvent in future tests.

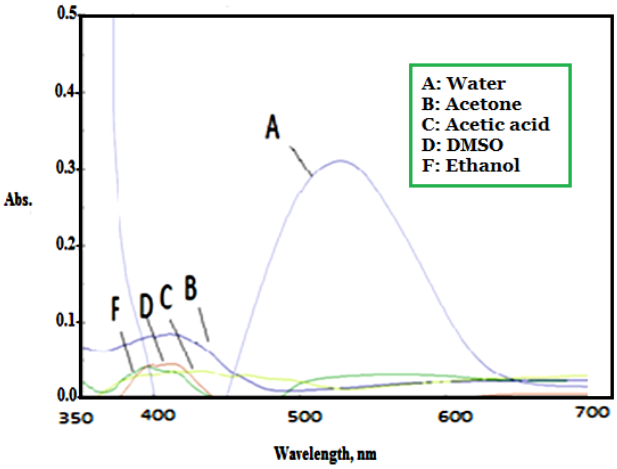


Figure.3: The effect of different solvents on the absorbance of colored products

Stability of Colored Product

Because the stability of the colored product is so crucial, the stability of three different quantities of FAMT was investigated by monitoring absorbance every 5 min (after dilution) for three different concentrations of FAMT (Table 5).

Table 5: Effect of time on the stability of the color

Time (minute)	Absorbance / µg of FAMT present		
	100	200	400
Immediately	0.168	0.310	0.484
5	0.168	0.315	0.490
10	0.169	0.315	0.490
15	0.171	0.316	0.489
20	0.171	0.319	0.488
30	0.174	0.319	0.498
40	0.174	0.321	0.497
50	0.174	0.321	0.494
60	0.175	0.321	0.493

The results in Table 5 show that the formed product's red color has stability for at least 60 minutes.

Absorption Spectra

When FAMT in an aqueous solution is treated with ARS reagent solution, an absorption peak is obtained, showing an intense red dye with maximum absorption at 528 nm. The reagent blank shows little absorption at this wavelength. The absorption of the blank solution is less, and it is an acceptable analytical result. Figure 3 shows that the blank peak is far from the peak of the colored product and the color contrast is good (Figure 4).

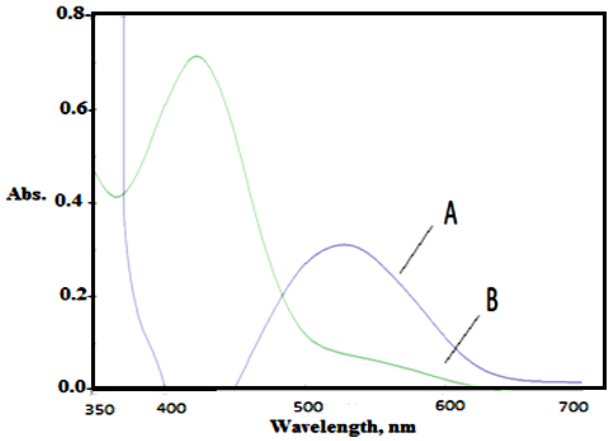


Figure 4: Absorption spectrum of 20µg FAMT/mL with ARS proceed under suggested method (A) the colored product against the blank, (B) blank against distilled water

Nature of the Dye

The stoichiometric of the complex resulting from coupling FAMT with ARS has been studied using the mole ratio method (Figure 5). By taking a fixed amount of FAMT (1 mL of 4 × 10 $^{-3}$M) and various amounts of ARS (0.5-5 mL of 4 × 10 $^{-3}$M), the ratio of coupling FAMT with ARS is equal to 1:1.

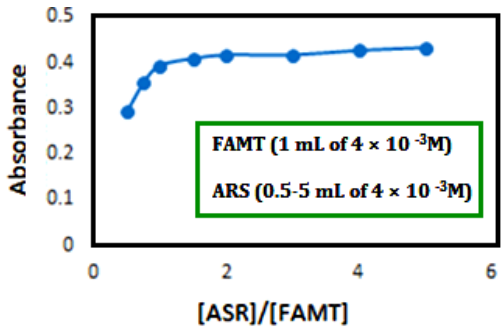


Figure 5: Mol. –ratio plot for FAMT-ARS

The mole ratio method determined the stoichiometric ratio of the two reactants in the present work [20]. The plot for the interaction of FAMT and ARS reagent shows that the contact occurs between an equimolar of FAMT and ARS. So that the complex was formed in the ratio of 1:1. Based on the obtained results, it is possible to suggest the mechanism of the reaction of FAMT and ARS reagent according to the proton transfer reaction [21] to produce a red complex is proposed and presented in Figure 6.

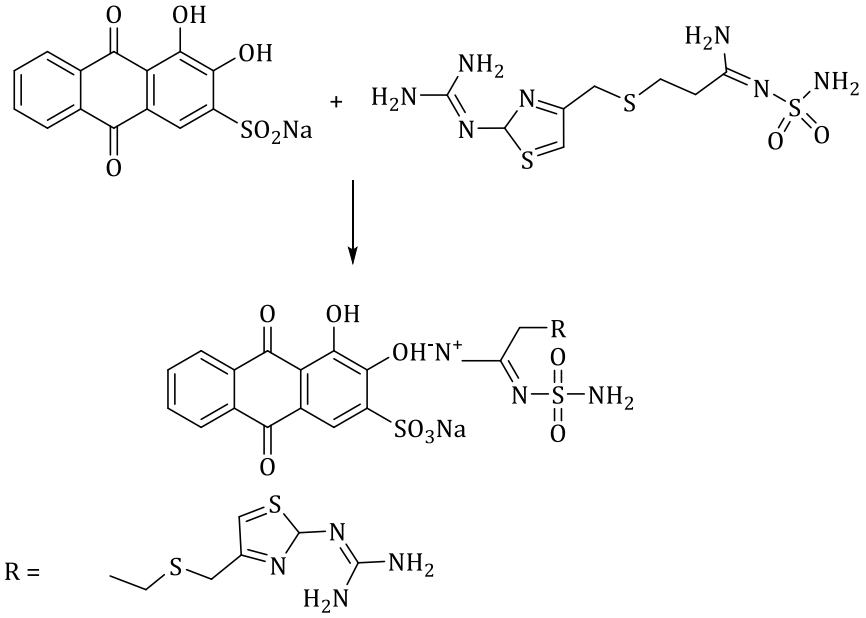


Figure 6: The suggested reaction mechanism of red –complex product

Application of the Method

The current method has been used to determine FAMT in pharmaceutical preparations (Famosam Tablet) to predict its applicability. Satisfactory analytical results were achieved in terms of acceptable accuracy and precision (Table 7).

Table 6: Application of the method

Drug	Amount taken µg/ml	Recovery%*	E%	RSD%	Drug Contained, mg
Famosam, 40 mg /tablet SDI	20	98.06	+1.94	1.02	39.224
	40	99.79	+0.21	0.82	39.916

*Average of five determinations

Also, the standard addition method has been used in determining two concentrations of drug solution (20 and 40 µg/mL to prove that the suggested method is free from interferences of the additives used in manufacturing formulations (Figure.7).

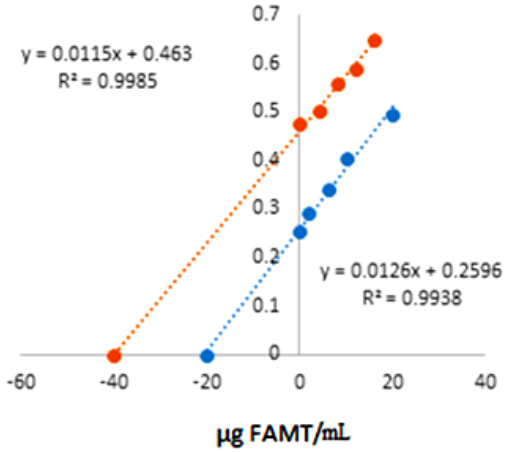


Figure7: Calibration standard addition method for the determination of 20 and 40 µg/mL FAMT in pharmaceutical preparation (tablet).

Table 7 presents the results obtained from Figure 7.

Table 7: The results of the standard addition method

Pharmaceutical preparation	FAMT taken (µg/ml)	FAMT measured (µg/m)	Recovery%	Drug Contained (mg)
Famosam 40mg/tablet SDI	20	20.602	103.01	41.204
	40	40.260	100.65	40.260

The results in Table7 show that the method successfully determined FAMT in its pharmaceutical drug tablet.

Comparison of the Methods

Table 8: The main variables of the present method compared with the same of another spectrophotometric method

Analytical variables	Present method	Literature method [22]	Literature method [14]
Reaction type's	Proton transfer	Redox reaction	Diazo-coupling
Reagent used	ARS	Permanganate	Diazotized metoclopramides
Maximum wavelength, nm	528	545	478
molar absorptivity (l/mol.cm.)	3.3 x 10^4	1.62 x 10^4	2 x 10^4
Beer's law, µg/ml	6.0-80	2.5-20	1-40
Medium type	Acidic	Acidic	Neutral
LOD µg/mL	0.069	0.22	0.1
LOQ µg/mL	0.209	0.65	---

The results in Table 8 indicate that the present method is more sensitive than other methods, and has an extensive range of determination.

Conclusion

An easy and simple spectrophotometric method has been suggested to determine FAMT in tablet formulation with accepted analytical results. The method involves only one step of reaction between FAMT and ARS to give the colored product, followed by spectroscopically.

Acknowledgments

The measurements required for the current work were made in the analytical research laboratories of the Department of Chemistry / College of the Science / University of Mosul. We would like to extend our thanks and appreciation to them for facilitating work difficulties.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

We have no conflicts of interest to disclose.

ORCID

Safaa A. Zakaria:
https://www.orcid.org/0000-0002-2622-9239
Rana S. Al-Saffar:
https://www.orcid.org/0000-0002-2622-9239
Nabeel S. Othman:
https://www.orcid.org/0000-0002-5930-3925

References

[1]. Sweedman S.C., *Martindale: The Complete Drug Reference,* 36th Edition, Martindale The Pharmaceutical Press London, 2009 [Google Scholar], [Publisher]

[2]. *British Pharmacopeia*, CD – Rom, 3rd ed. System Simulation Ltd., the Stationary Office, London, 2000 [Publisher]

[3]. Myhal A., Marksa M., Golovchenko O., Gubar S., Georgiyants V., Ivanauskas L., *In 20th anniversary of BaltPharm Forum (BPhF 2017): April 28-30, 2017 Jūrmala, Latvia: abstracts/Pharmacists' Society of Latvia (PSL). Jūrmala: Pharmacists' Society of Latvia*, 2017 [Google Scholar], [Publisher]

[4]. Kiszkiel-Taudul I., *Microchem. J.*, 2021, **162**:105874 [Crossref], [Google Scholar], [Publisher]

[5]. Safila N., Farya Z., *Am. J. Pharm. Pharmacol.*, 2014, **1**:28 [Crossref], [Google Scholar], [Publisher]

[6]. Muhammad H., Nida N., Vesh C. and Usman Z., *Trop. J. Pharm. Res.*, 2016, **15**:605 [Crossref], [Google Scholar], [Publisher]

[7]. Nita A., Tit D., Copolovici L., Melinte C., Copolovici D., Bungau S., Iovan C., *Rev. Chim.*, 2018, **69**:297 [Google Scholar], [Publisher]

[8]. Kiszkiel-Taudul I., Starczewska B., Karpińska J., Kasabuła M., *J. Surfactants Deterg.*, 2017, **20**:1401 [Crossref], [Google Scholar], [Publisher]

[9]. Abass S., Walash M., Ibrahim F., *Pharm Anal Acta*, 2016, **7**:476 [Crossref], [Google Scholar], [Publisher]

[10]. Walash M.I., El-Brashy A., El-Enany N., Wahba M.E., *J. Fluoresc.,* 2009, 5:333 [Crossref], [Google Scholar], [Publisher]

[11]. Shen Y.M., Tian R., Ma H.Y., Sun X.H., *Luminescence*, 2021, **36**:705 [Crossref], [Google Scholar], [Publisher]

[12]. Saeed A., Salih E., *Baghdad Sci. J.*, 2020, **17**:1 [Crossref], [Google Scholar], [Publisher]

[13]. Vais R.D., Yadegari H., Heli H., *Iranian Journal of Pharmaceutical Research (IJPR)*, 2020, **19**:120 [Crossref], [Google Scholar], [Publisher]

[14]. Al-Abachi M.Q., Mohmmed S.S., Hadi A.J., *Baghdad Sci, J.*, 2015, 12 [Crossref], [Google Scholar], [Publisher]

[15]. Ariavand S., Ebrahimi M., Fooladi E. *Chem. Methodol.*, 2020, **5**:82 [Crossref], [Google Scholar], [Publisher]

[16]. Alhelfi A., Abd Aljabar R., *Kerbala J Pharm Sci*., 2016, **11**:15 [Google Scholar], [Publisher]

[17]. Wadher S.J., Kalyankar T.M., Kshirsagar J.R., Anitha K., *Res. J. Pharm. Technol.*, 2017, **10**:408 [Crossref], [Google Scholar], [Publisher]

[18]. Yevstahiyovych B.M., Yuriivna S.Y., Pavlivna K.S., Osypivna D.L., *Ars Pharm. (Internet)*, 2018, **59**:69 [Crossref], [Google Scholar], [Publisher]

[19]. Taghizade M., Ebrahimi M., Fooladi E., Yoosefian M., *Microchem. J.*, 2021, **160**:105627 [Crossref], [Google Scholar], [Publisher]

[20]. Winefordner J.D., Spectrochemical Methods of Analysis". Wiley Intersience, New York, 1971 [Crossref], [Google Scholar], [Publisher]

[21]. Al-Ghabsha T., Saeed A., *J. Educ. Sci.*, 2012, **25**:1 [Crossref], [Google Scholar], [Publisher]

[22]. Basavaiah K., Zenita Devi O., *J. Mex. Chem.*, 2010, **54**:182 [Crossref], [Google Scholar], [Publisher]

HOW TO CITE THIS ARTICLE
Safaa A. Zakaria, Rana S. Al-Saffar, Nabeel S. Othmana, A Simple Spectrophotometric Method for the Determination of Famotidine via Reaction with Alizarin Red S. *Chem. Methodol.*, 2022, 6(3) 228-236
DOI: 10.22034/chemm.2022.313691.1393
URL: http://www.chemmethod.com/article_143552.html