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Development of a Spectrophotometric Technique for The Estimation of Sulfamethoxazole (SMX) in its Pure also in Pharmaceutical Formulation, using organic reagent (A1)

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ABSTRACT

A sensitive, simple, as well as accurate spectrophotometric technique to the estimation of Sulfamethoxazole (SMX) drug in pure also pharmaceutical formulations was developed. It was created by the reaction of (SMX) and organic reagent (A1) after oxidation by iron chloride and potassium periodate in acidic medium. The absorption of the product of SMX and A1 was measured at 423 nm. Linearity ranged between (0.5-22.5 µg. mL-1), molar absorptivity was (6.839 $*10^{+3}$L / mol.cm), limits of detection and quantification were (0.204, 0.612 µg/ml), respectively, the method was applied successfully to the estimation of SMX in pure and pharmaceutical formulations.

1. Introduction

Sulfamethoxazole is N1-(5-methylis -oxasole -3-il) sulfanilamide. It is an isoxazole (1,2-oxazole) compound there is in it a methy l substituent at the 5-positionanda 4-aminobenzenesulfonamido group at the 3-position. It has apart as an antibacterial agent (Amali et al.,2019). Its formula (C10H11N3O3S) and M.Wt 253.3 g.mol-1,mp.169°C (Yin R.,et al .,2018) (Khalaf.H.,etal.,2017) White & yellowish white colored, cryst allized powder (Brand name: Bactrim, Septra, Sulfatrim Pediatric) product branded as Bactrim(Hasan H. ,2017)(Mahmoud T.,et al., 2017)

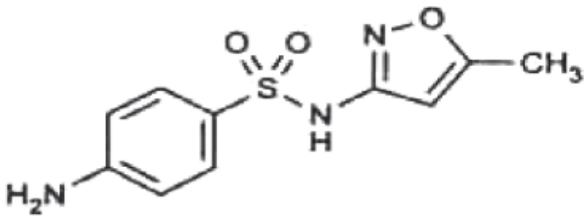

Figure 1. Sulfamethoxazole structure (Mahmoud T.,et al., 2017)

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As of its low cost plus high efficiency against various gram-positive and gram negative bacteria, they are used largely to the treatment of urinary infectious diseases (Liu Yu W., et al., 2013) Sulfamethoxazole (SMX) is a wide-spectrum antibiotic that has been broadly used as a growth promoter in the breeding industry (GaoNet.al .,2018) SMX has been usually sensed in effluents, soils, and surface waters (Yang B. et al ., 2023). However, SMX drug estimated by a few methods for example:
Spectrophotometric Determination (Noor Ghaib et al, 2021) (Al-Okab R. A., et al., 2018) (ALRashidy A. et al., 2020), oxidation reaction (Ding Y. et al., 2021) (Yang B. et al., 2023) Transformation and detoxification of sulfamethoxazole (Gu Q. et al., 2021) (Huang Y. & Yang J. 2022) electrochemical oxidation (Li S., et al., 2022).
The aim of this paper to run an enhanced spectrophotometric technique to produce color solution by reaction between SMX drug and new organic reagent of N- (3-mercapto-5-(pri-yl) - 4,2,1- triazole-4-yl) hydrazine carbothioamides A1 (AL Rashidy A. et al., 2022) and also in Pharmaceutical Formulation.

2. Methodology

2.1. Apparatus

PG Instrumental Ltd UV-Visible Spectrophotometer, UK T90 using 10-3 m quartz cell for all spectrophotometric quantities, 210 S kern sartorius balance using all weight measurements were used.

2.2. Chemicals

Sulfamethoxazole was provided by the state Company for Drugs Industry and Medical Appliances Samarra-Iraq. The solutions were prepared by using A 500 µg. mL^{-1} SMX of solution ready by dissolving the exact weights of in 10mL absolute ethanol then added distilled water to the mark in volumetric bottle 100 mL, kept in dark place then used, for at least 10 days , as standard solution. More dilute working solutions of the SMX solution prepared by serial distilled water; as 1000 µg.ml^{-1} of A1 was ready via dissolving 0.05 gm in 50ml of hot distill water with a stirrer in volumetric bottle 50mL.
dilutions by distilled water Solutions of iron chloride and potassium periodate (with 0.01M for each) were prepared and used,0. 1M of each of hydrochloric acid , sulfuric acid nitric acid and acetic acid prepared then used .

2.3. Solutions of Interference 1000 µg/mL

These solutions ready via dissolving 0.1gm of (glucose, fructose, lactose, sucrose and vanillin) in right solvent (water or ethanol) completed volume to 100ml by D.W**.**

2.4. General procedure for estimation of Sulfamethoxazole SMZ with A1 reagent

The primary test for the present method involved oxidation of 0.3ml A1 organic reagent 250µg/mL by 0.1ml $FeCl_3$ 0.1ml KIO_4 of $1x10^{-2}$M and then add 0.5ml of SMX drug 250 µg/mL in acid medium the contents were diluted to the mark with D.W in 10 ml volumetric bottle. Absorbance and ʎmax of brown color solution at 423nm against blank organized in same manner without SMX Figure2 shows that the maximum absorption was obtained at a wavelength 423 nm.

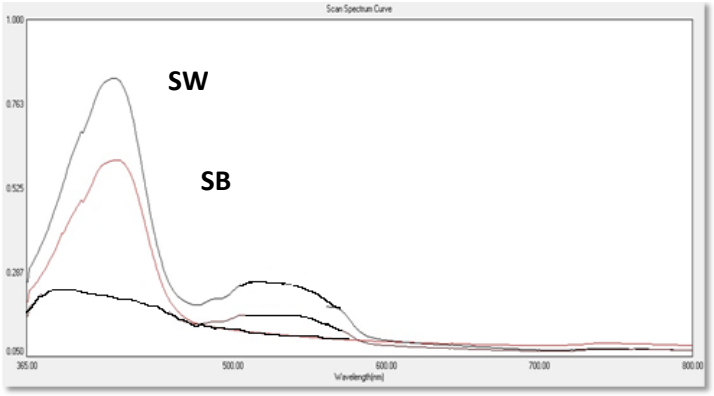

Figure 2. SB: Spectrum of sample solution against blank, and SW: Spectrum of solution against water.

2. 6. Sample preparation

A standardized powder prepared from 10 exactly weighed metheprim tablets (0.4934gm). A suitable quantity of the powder dissolved in absolute ethanol and added D.W to the mark in volumetric bottle 100mL. Dissolution of sample by an ultrasonic bath. the mixture filtered and made up to the mark with D.W in 100mL volumetric bottle to obtain solution (250 µg/mL)

2.7. Condition's reaction optimization

Numerous conditions studied are affecting remove of the absorbance. The effect of the kind of acids and reagent of oxidation, the quantity of (HCl, , potassium periodate, $FeCl_3$ and A1 reagent) was studied. Result that use 1.00 ml of 0.1 M HCl i.e pH=4,0.500 ml of 0.01M of KIO_4, and 0.6 ml of $FeCl_3$ and 0.6 of 250µg.ml^{-} ofA1 reagent give best results Figures.3-5 respectively.

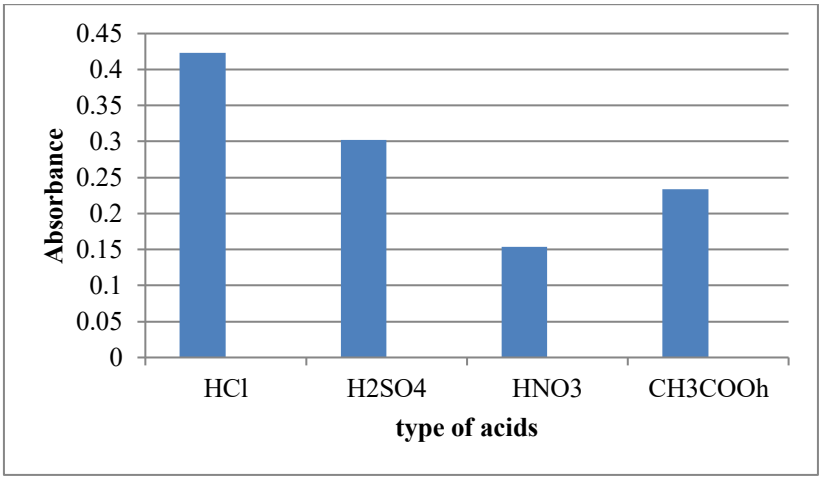

Figure.3 Effect of type of acid at 423nm

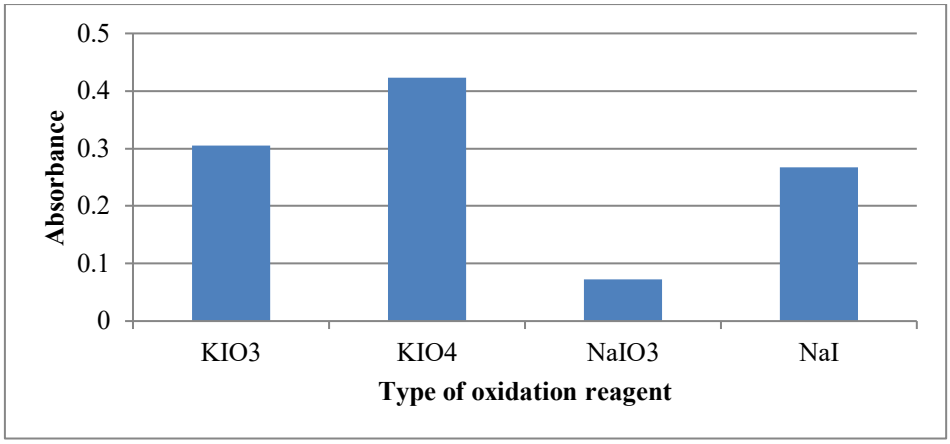

Figure.4 Effect of type of oxidation reagent at 423nm

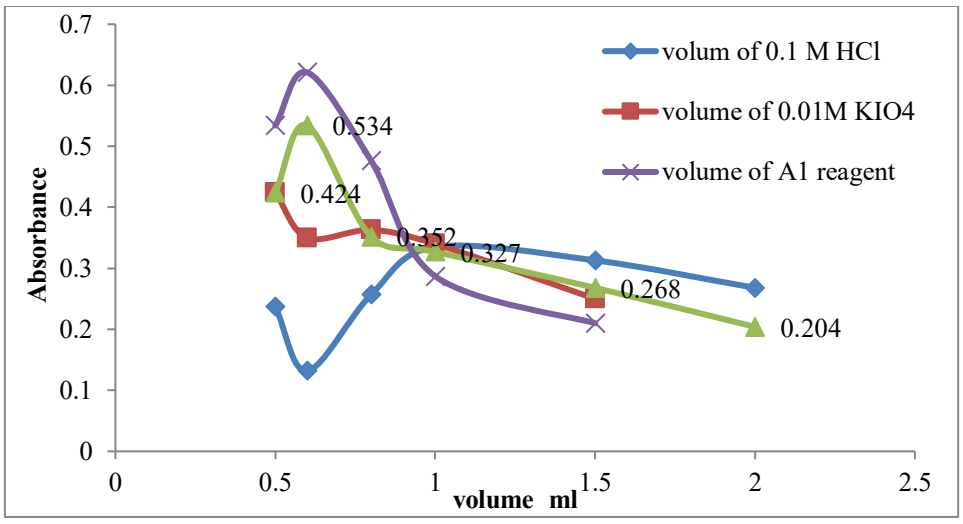

Figure. 5 Effect volume of HCl, KIO_4, $FeCl_3$and A1 at 423nm

The order of adding reactants must be followed as mentioned in the mentioned procedure solution was left 5 minutes before adding distilled water. Figure.6.

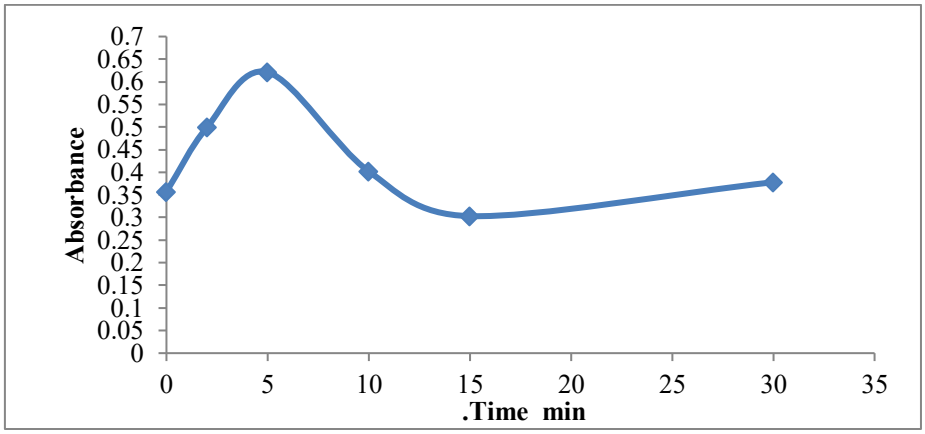

Figure.6 Effect of time on absorbance at 423nm.

3. Result and discussion

The Calibration curve was fabricated Using-conditions Figure .7 product follows Beer's law in A variety of The method's efficiency was statistically calculated by evaluating accuracy as relative error percentage (Erel % and precision as RSD percent of the suggested methods. Table 2 shows that the results found for 6 repeats at 3 concentrations of SMX

3.1. The statistical data &calibration curve

concentrations 0.5– 22.5 µg/ml SMX. Table 1.

3.2. Precision and accuracy

sample which show that the suggested methods ensure a good accuracy and precision. Tabte 1 illustrate the statistical information to the calibration curve such wave length , linear rang ,Molar absorptivity …etc.

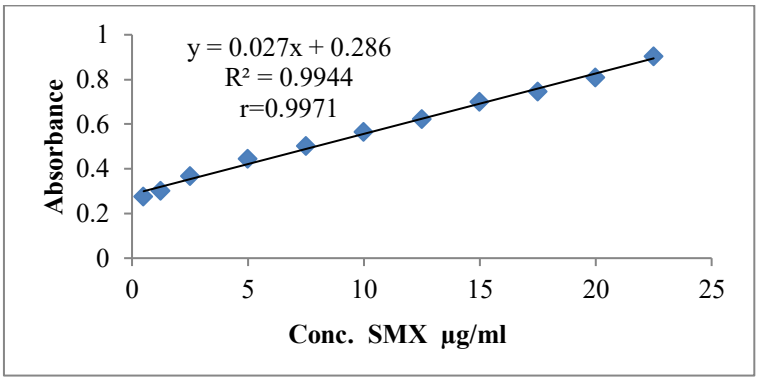

Figure. 7 Calibration curve for the estimation of SMX**.**

Table1. Statistical information to the calibration curve

Parameter	**Value**
λ max	423 nm
Linear range µg.mL^{-1}	0.5-22.5
Regression equation	A= 0.027[SMX] + 0.286
Molar absorptivity (L/mol.cm)	6.839 *10^{+3}
Sandell's sensitivity µg.cm^{-2}	0.0370
Correlation coefficient	0.9971
Intercept	0.286
Slope	0.027
LD (µg.mL^{-1}) (Ahmed A .Z & Asmaa A.A.,2022)	0.204
LOQ (µg.mL$^{-1)}$ (Mohammed A& Asmaa A.A.,2022)	0.612

Table. 2 Valuation of accuracy and precision.

Conc of SMX µgml^{-1} Taken	found*	Erel %	*RSD %
12.5	12.4	-0.74	0.54
15	15.3	2.22	0.29
20	19.4	-2.96	0.10

*n=6

3.4 Stoichiometry of reaction

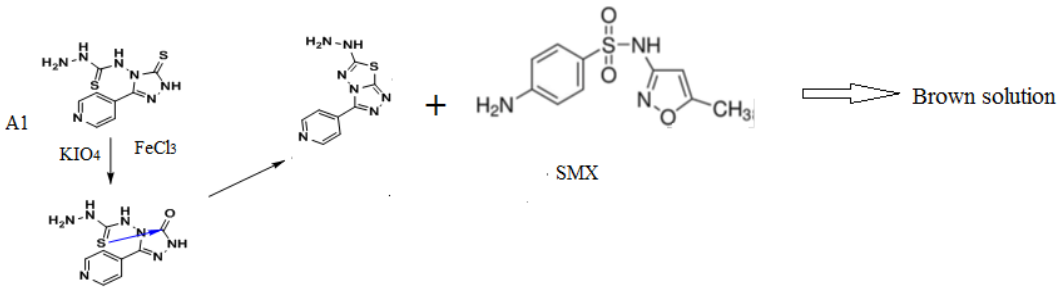

Figure 8 Proposed mechanism of reaction.

3.5. Study of Interference

For test selectivity towards excipients added to the pharmaceutical formulation, such as (glucose, fructose, lactose, sucrose and vanillin), which do not interfere the estimation of SMX and do not affect the reaction (10µg.ml^{-1}) of SMX. Thus, interference was analyzed. The results in Table 3.

Table.3 Rec. for (10µg.ml^{-1}) of SMX in the presence of diverse concentration of excipients

Excipients	Concentration µg/ml	SMX Conc. Taken 10 µg/ml	
		Conc. found* µg/mL	Recovery* %
Sucrose	1000	10.06	100.6
Vanillin		10.08	100.8
Glucose		10.04	100.3
Lactose		9.97	99.7
Starch		9.95	99.5

*n = 3

4. Applications

4.1. Direct Method

Diverse Conc. 10 ,15,20 µg mL^{-1} of a pharmaceutical form like in Conc. Calibration curve. Absorbance restrained 3 times at 423 nm, Erel% calculated Table.4 .

Table. 4 Estimation SMX in formulation pharmaceutical

Conc of SMX µg.mL^{-1}	**Observed µgmL^{-1} * Conc of SMX**	**Erel%**
10	10.1	1
15	15.12	0.8
20	19.66	1.7-

n=3

5. Conclusion

Results confirmed that a proposed technique is simple with sensitivity to the estimation of SMX. Colored product showed an absorption maximum at 423 nm. It was found that the proposed method was highly efficient and recoverable with a high linear range. It did not use solvent extraction or organic solvents. It could be applied successfully to the estimation of SMX in formulations of pharmaceutics.

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