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Micro Spectrophotometric Determination and Cloud Point Extraction of Sulphadimidine Sodium in Pure form and Pharmaceutical Drug

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Abstract:

Two simple, rapid, and useful spectrophotometric methods were suggest or the determination of sulphadimidine sodium (SDMS) with and without using cloud point extraction technique in pure form and pharmaceutical preparation. The first method was based on diazotization of the Sulphdimidine Sodium drug by sodium nitrite at 5 ºC, followed by coupling with α –Naphthol in basic medium to form an orange colored product . The product was stabilized and its absorption was measured at 473 nm. Beer's law was obeyed in the concentration range of (1-12) $\mu g \cdot ml^{-1.}$ Sandell's sensitivity was 0.03012 $\mu g \cdot cm^{-1}$, the detection limit was 0.0277 $\mu g \cdot ml^{-1}$, and the limit of Quantitation was 0.03605$\mu g \cdot ml^{-1}$.The second method was the cloud point extraction (CPE) using Trtion X-114 as surfactant. Beer's law was obeyed in the concentration range of (1-12) $\mu g \cdot ml^{-1.}$ Sandell's sensitivity was 0.02958 $\mu g \cdot cm^{-1}$, the detection limit was 0.01745 $\mu g \cdot ml^{-1}$, and the limit of quantitation was 0.028303 $\mu g \cdot ml^{-1.}$ All variables including the reagent concentration, reaction time, color stability period, and mole ratio were studied in order to optimize the reaction conditions. The mole ratio for the composition of product is (1:1). Both methods were effectively useful to the determination of sulphdimidine sodium in pharmaceutical dose form. The attained results were in a good agreement with the official and other methods in the literature .No interference were observed from the commonly encountered additives and excipients.

Key words: Cloud Point Extraction, α –Naphthol, Sulphdimidine Sodium, Triton X-114.

Introduction:

Sulfonamides are one of the oldest groups of pharmacologically energetic material used in veterinary medication to day(1) .Their discovery in 1935, suggested the start of a new era in the treatment of a varied range of bacterial diseases and a number of protozoan toxicities(2).

The pharmaceutical sulfa of the first antibiotics, terms of manufacturers folic acid were discovered by tincture known as Prontosil (3) which are effective in the body work antibiotics. Sulfonamide preparation authority Sodium salt has temperate solubility(4).

Sulphadimidine Sodium (SDMS), famous as sulfamethazine Sodium, is one of the greatest broadly used sulfonamides in animals. It has supposedly been effectually used contrary to a wide-ranging of contagious diseases, a public healing medication, particularly for livestock, pigs and fowls. It is accepted for healing coccidiosis and has been used as a growing fields in pigs and livestock.

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It is not agreed for use in lactating dairy cows and placing chickens of age less than 16 weeks(5). Over-all characterizes of sulfadimidine Sodium are certain in fig. 1 (6).

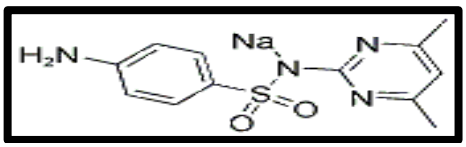

Figure 1. Structure of sulphadimidine sodium

Diazonium salts are important raw materials for the preparation of some aromatic compounds, drugs, dyes, and other organic compounds. These salts are useful in the analysis process. They have electrolytic properties that enable them to be combined with other high-density electronic compounds such as phenols and amino acids(7), consisting of colored compounds that are suitable for use in estimating very small amounts of organic compounds, light absorption or polygraphy by measuring the propagation current.

These salts can be extracted by cloud point extraction method(8) .Cloud point extraction (CPE)

is based on the phase behavior of non- ionic surfactants in aqueous solution(9), which exhibits phase separation after an increase in temperature or the addition of a salting out agent (10).Separation and preconcentration based on (CPE) are becoming an important and practical application of surfactant in analytical chemistry(11).This study focuses to developing easy method and sensitive to determination of SDMS. The experimental conditions are free of heating and environmental friendly because small amounts of chemicals are used (12).

Materials and Methods:

Instruments:

UV-Vis spectrophotometer: SHIMADZU, Double beam UV-Vis, model UV-1800 made in Japan. The range of wavelength (190-1100) nm, quartz cell with 1cm path., Water Bath: A thermostat water bath, Memmert, made in Germany, Electric Balance: Sartorius (0.0000), made in Germany, Centrifuge: Triup International Corp. TRIU 800 Centrifuge, made in Korea & PH meter: HANNA, PH meter, HI 83141.

Preparation Standard Solutions

All reagents and materials used in this work were of high purity materials. Distilled water was used to dissolve and prepare solutions. Stock solution of Sulphadimidine Sodium (SDMS) 1000µg. ml^{-1} was prepared by dissolving 0.1gm in a small amount of distilled water then completed to100ml by distilled water. Stock solution of reagent [α-Naphthol] 1000µg. ml^{-1} was prepared by dissolving 0.1gm in 25ml ethanol then diluting to the mark in 100ml volumetric flask by distilled water. (1%) Sodium nitrite solution was prepared by dissolving 1g from $NaNO_2$ in distilled water and diluting to the mark in 100 ml volumetric flask. (1%) Sulfamic acid solution was prepared by dissolving 1g from H_3NSO_3 with distilled 100 ml.(10% V/V) Different surfactants[TritonX-100, TritonX-114, Tween 20,Tween 80,STAP, SDS] were prepared by diluting 10 ml with distilled to 100 ml volumetric flask.1000 µg.ml^{-1} stock solution of interferences were prepared by dissolving the organic compound 0.1gm from the following [Lactose, Starch, Arabic Gum, Glucose, Talc, Trimethoprim] and inorganic compound [0.2579gm, 0.2500gm, 2.9 gm] of $Ca_3(PO_4)_2$, $CaCO_3$, $FeCl_3$ in distilled water and diluting to the mark in 100 ml volumetric flask.1M from Phosphoric acid, Nitric acid, Sulphuric acid, Hydrochloric acid and Acetic acid were prepared by proper dilution.

General Procedure for Azo Coupling:

The prepared Azo Coupling product are added in volumetric flask (10ml) in ice bath, 1ml of Sulphadimidine Sodium (SDN) (1000 µg ml^{-1}), 1ml for hydrochloric acid, 1ml for sodium nitrate (1%), 1ml for sulphamic acid (1%), 1ml for α-Naphthol(1000µg ml^{-1}), at last 1ml is added for sodium hydroxide and the volume is commpleted by distilled water. Then absorbance is measured by UV-VIS. Absorption spectra with maximum wavelength are shown in fig.2

General procedure for CPE:

A typical experiment of cloud point includes the following steps: taking the volumetric flask (10ml) and use the optimum condition of azo coupling. Add 1ml for surfactant (10%) and complete the volume by distilled water. The content of volumetric flask is transferred to centrifuge test tube then the mixture is placed in a water bath for 20 minutes at 60 ^oC and separated by centrifugation for 20 minutes at 4000 rpm. Test tube is taken in ice bath to increased viscosity micelles layer for 1minutes, then become easily separated. The separated sediments dissolved by 1ml of ethanol and its absorption spectrum are recorded in Fig. 2.

Results and Discussion:

First Methods: Spectrophotometric Determination of Sulphadimidine Sodium (SDMS) by Oxidation Coupling Reactions.

Optimization Parameters for Reaction.

All of the factors that affect the absorbance of azo dye product are optimized to improve the sensitivity and detection limit for the determination of the drugs .All optimization work under wavelength at 473 nm.

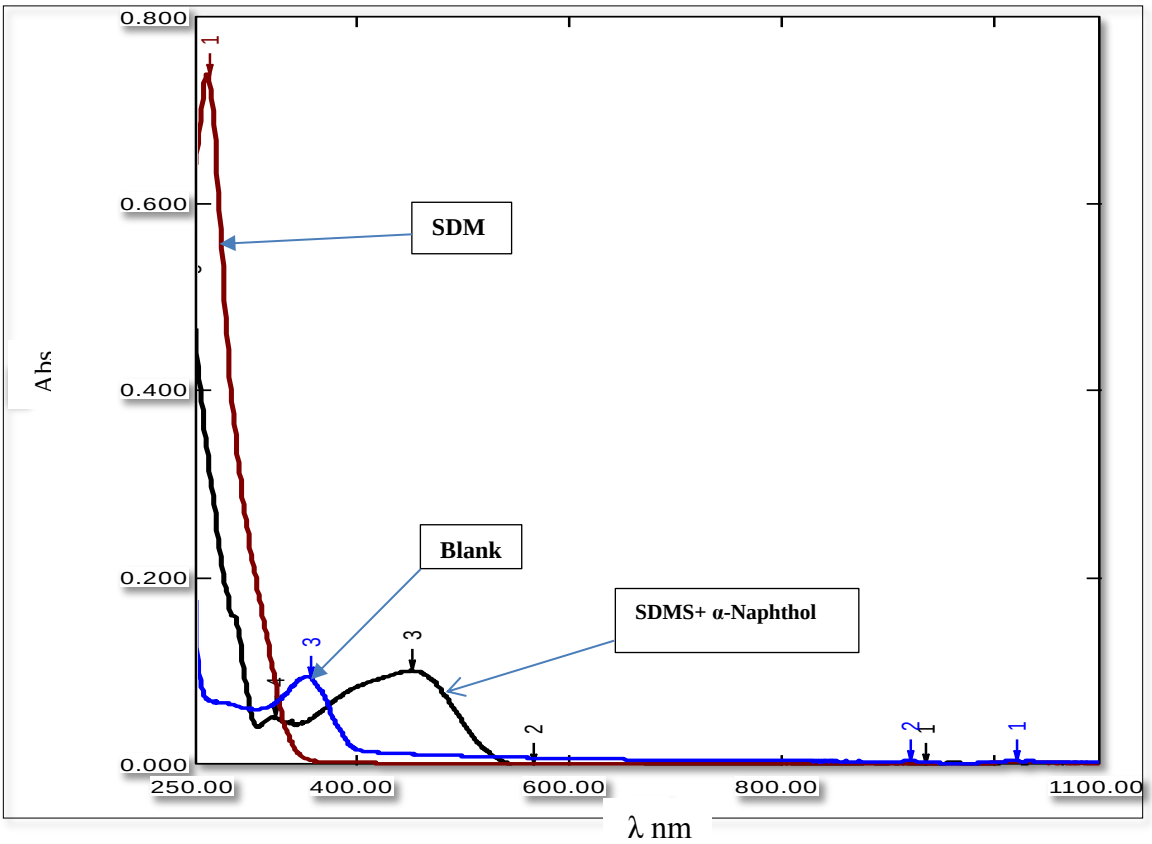

Figure 2. Absorbance spectra of the Resulting Dye. SDMS

Effect of Acid Type.

In this study, 0.5 M of different acid [HCl , H_2SO_4, HNO_3 ,H_3PO_4 and CH_3COOH] are used. The same procedure that [1ml of drug SDMS , 1 ml of each acid, 1ml of $NaNO_2$, 1ml of H_3NSO_3, 1ml α-Naphthol and 1ml of KOH] are mixed in 10-mL volumetric flask and volume is completed by distilled water to–form the diazonium salt. After that, the absorbance is measured at maximum wavelength for drug.

It is clear from this study that the acetic acid gives higher absorbance for SDMS, this acid is a few of uses in subsequent experiments as shown in the Table 1 and Fig .3.

Table 1. The absorbance of different acid with SDMS

0.5 M (acid) 1ml	Abs.
HCl	0.140
HNO_3	0.053
H_2SO_4	0.128
H3PO4	0.039
CH_3COOH	0.153

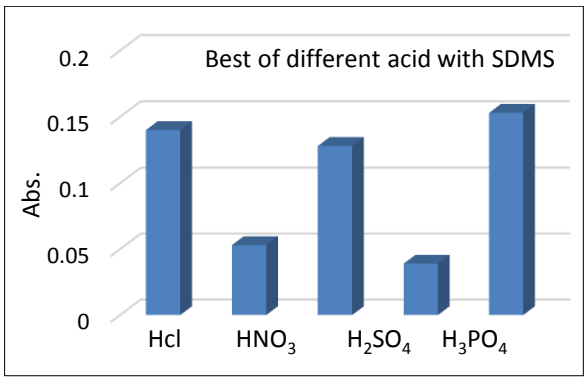

Figure 3. Absorbance of different acid

Effect of Optimum Volume of 0.5M Acetic Acid

The same addition for SDMS is [1ml drug, with varying volumes of 0.5 CH_3COOH from (0.1-1) ml , 1 ml $NaNO_2$, 1ml H_3NSO_3, 1ml α-Naphthol and 1ml of KOH in 10 ml volumetric flask and the volume is completed by distill water .Then the absorbance are measured and the optimum volume for higher absorbance that fixed for sequence experiment 0.5 ml as shown in Table 2 and Fig. 4.

Table 2. Data of the absorbance of different volume to acetic acid with SDMS.

Volume of (CH_3COOH) 0.5 M	Abs.	Volume of (CH_3COOH) 0.5 M	Abs.
0.1	- 0.013	0.6	0.157
0.2	0.061	0.7	0.155
0.3	0.108	0.8	0.152
0.4	0.166	0.9	0.150
0.5	0.192	1	0.148

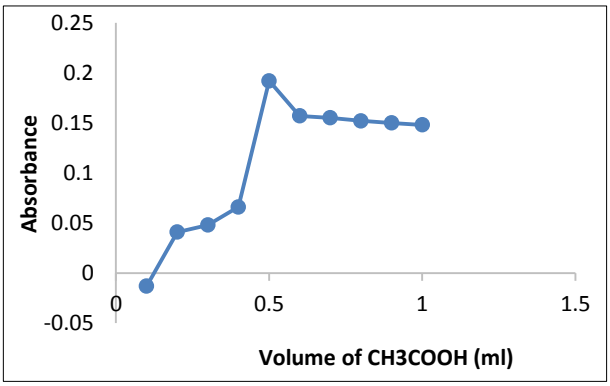

Figure 4. The Volume of 0.5 M CH3COOH ml with SDMS

It is obvious that absorbance increase with increasing the volume of acid, suddenly the absorbance decrease because the primary amine becomes inactive (13) .

Effect of Base Type

In this experiment using different basic [NaOH, KOH, K_2CO_3, Na_2CO_3, NH_4OH, $NaHCO_3$] and that follow the addition [1ml SDMS, 0.5ml CH_3COOH, 1ml $NaNO_2$, 1ml H_3NSO_3, 1ml α-Naphthol and 1ml of each base] in 10 ml volumetric flask. Then maximal absorbance for the base is KOH as shown in Table 3 and Fig. 5.

Table 3. Data of the absorbance of different base with SDMS

0.5 M (base) 1ml	Abs.
NaOH	0.183
KOH	0.272
NH_4OH	0.004
Na_2CO_3	0.123
K_2CO_3	0.174
$NaHCO_3$	0.061

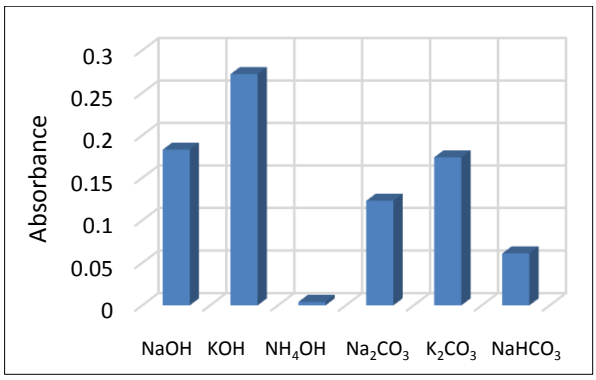

Figure 5. The absorbance different base with SDMS

It is clear the potassium hydroxide gives the higher absorbance, this base is fixed in subsequent(14).

Effect of Optimum Volume of 0.5M KOH.

The same addition for SDMS is [1ml drug, **0.5** ml CH_3COOH, 1 ml $NaNO_2$, 1ml H_3NSO_3, 1ml α-Naphthol and (0.1-1) ml of KOH in 10 ml volumetric flask and the volume is completed by distill water .Then the absorbance and the optimum volume for higher absorbance that fixed at 1ml for sequence experiment are measured as shown in Table4 and Fig. 6.

Table 4. Data of the absorbance of different volume of KOH.

(KOH) 0.5 M	Abs.
0.1	.0.069
0.2	0.106
0.3	0.119
0.4	0.124
0.5	0.158
0.6	0.220
0.7	0.246
0.8	0.291
0.9	0.301
1	0.312
1.1	0.094
1.2	0.074

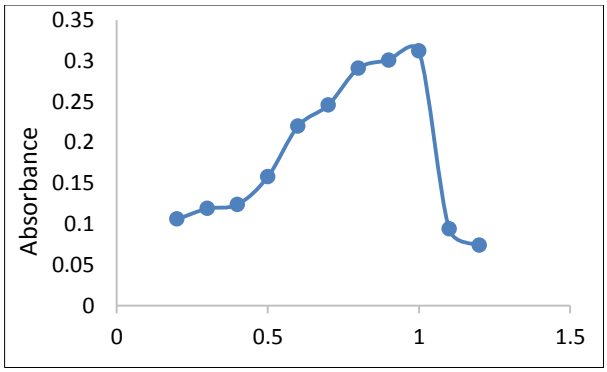

Figure 6. Different Volume of KOH with SDMS

It is evident that absorbance increases with increasing the volume of KOH, but suddenly decrease the absorbance because the decomposition happens when increased basicity and formation

diazotate ions that may couple and agree with previous studies (15) .

Effect of Optimum Volume of 1% Sodium nitrite.

The same additions [1ml for SDMS, **0.5** ml CH_3COOH with varying volume of 1% $NaNO_2$ from (0.1-1) ml, 1ml H_3NSO_3, 1ml α-Naphthol and **0.5** ml KOH are put in volumetric flask 10 ml and the higher absorbance of optimum volume fixed at 0.3 ml for sequence experiment, as shown in Table 5 and Fig.7.

Table 5. Data of the absorbance of different volume of Sodium nitrite.

1% Sodium nitrite	Abs.
0.1	0.336
0.2	0.347
0.3	0.357
0.4	0.350
0.5	0.323
0.6	0.271
0.7	0.264
0.8	0.216
0.9	0.194

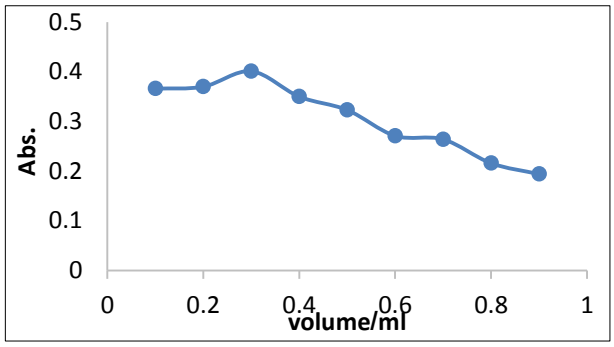

Figure 7. Absorbance of 1% NaNO2 / ml

It is clear that the absorbance increases with increasing the volume of $NaNO_2$,but the signals decrease because the nitrate toxic because a high rate of pollutants affecting on diazonium salt (16).

Effect of Optimum Volume of 1% Sulphamic acid.

The same additions [1ml for SDMS, **0.5** ml CH_3COOH, **0.3**ml $NaNO_2$ with varying volume of 1% H_3NSO_3 from (0.1-1) ml, 1ml α-Naphthol and **0.5** ml KOH are put in volumetric flask 10 ml and the higher absorbance of optimum volume is fixed at 0.09 ml for sequence experiment as shown in Table 6 and Fig. 8.

Table 6. Data of the absorbance of different volume of Sulphamic acid.

Volume of 1% Sulphamic acid	Abs.	Volume of 1% Sulphamic acid	Abs.
0.07	0.199	0.3	0.194
0.08	0.241	0.4	0.177
0.09	0.363	0.5	0.164
0.1	0.286	0.6	0.154
0.2	0.202		

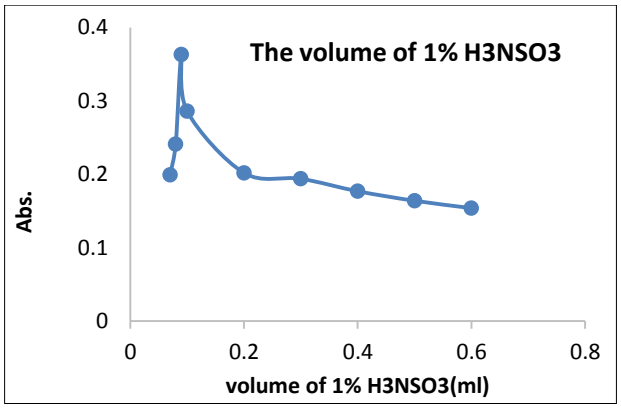

Figure 8.the volume of 1% H_3NSO_3

In this graph. it is clear that the absorbance increases with increasing the volume of Sulphamic acid , but the signals decrease suddenly because this volume of sulphamic acid is used to removes nitrite and escape of nitrogen gas(17).

Effect of Optimum Volume of (100 µg mL^{-1}) Reagent

The same additions [1ml for SDMS,0.5 ml CH_3COOH, 0.3ml $NaNO_2$,0.09ml H_3NSO_3, with varying volume from (0.1-0.9) ml α-Naphthol and 0.5 ml KOH are put in volumetric flask 10 ml and the higher absorbance of optimum volume 0.4 ml at maximum wavelength is fixed for sequence experiment as shown in Table7 and Fig.9.

Table 7. Data of the absorbance of different volume of α-Naphthol with SDMS

Volume of α-Naphthol	Abs.	Volume of α-Naphthol	Abs.
0.1	0.178	0.6	0.365
0.2	0.237	0.7	0.357
0.3	0.333	0.8	0.340
0.4	0.402	0.9	0.329
0.5	0.374		

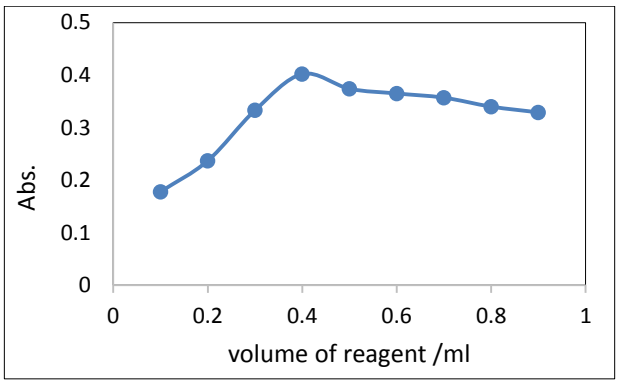

Figure 9. volume of reagent /ml with SDMS

The absorbance increases with increasing the volume of reagent but suddenly decreases because this is required volume for coupling with SDMS.

Effect of Reaction Time on the of Stability of the Product

The optimum volumes are going to be applied for the color product of SDMS [1ml SDMS,0.5ml CH_3COOH, 0.3ML $NaNO_2$, 0.09 ml H_3NSO_3, 0.4ml α-Naphthol, 1ml KOH] in volumetric flask 10 ml. The stability of the product is one of the important factors that diazotization and clouding reaction depend on, so the time needed is (0-60) minutes Then the absorbance is measured and the high reader at a high maximum wavelength is taken and recorded. It is clear that the time of product remains stable for SDMS is 50 minutes show in Table 8 and Fig. 10.

Table 8. The absorbance of different time of SDMS.

Time	Abs.	Time	Abs.
0	0.430	35	0.496
5	0.450	40	0.497
10	0.460	45	0.498
15	0.461	50	0.499
20	0.463	55	0.483
25	0.469	60	0.475
30	0.478	65	0.465

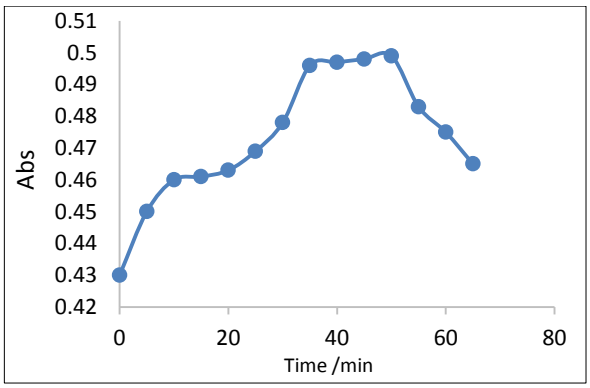

Figure 10. Time stability color /minutes of SDMS

Effect of the Order of Addition

In this study, the effect of sequence of addition with optimum volumes depends on the same procedure is applied. The absorbance is measured and recorded in Table 9.

R: α-Naphthol, **H**: acid (CH_3COOH), **N**: NaNO2, **S**: H2NSO3, D: Drug (SDMS), **B**: Base (KOH). It is evident that the best addition is the order two because it gives the upper absorbance as shown in Fig. 11.

Table 9. Data of different addition of SDMS

No.	Addition	Abs.
1	R+H+N+S+D+B	0.264
2	D+H+N+S+R+B	0.521
3	D+H+N+B+R+S	0.301
4	D+B+R+N+H+S	0.151
5	R+B+D+H+N+S	0.165
6	R+H+N+B+D+S	0.027

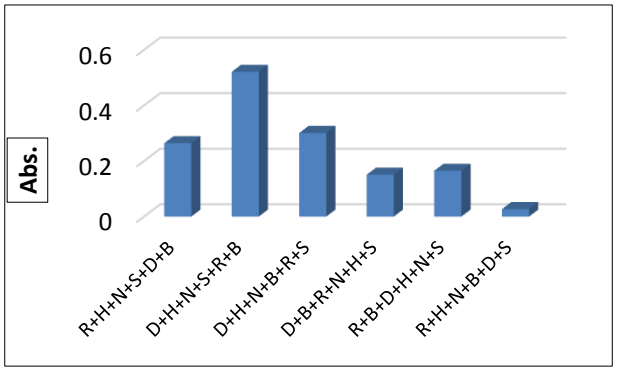

Figure (11): Different addition with SDMS.

Effect of Solvent:

All the compounds of the optimum parameters for SDMS are dissolved in a volumetric flask and this volume is completed for different solvents and the absorbance is measured.

In this study shows the best solvent is water. It is sensitive, cheap, economical and nontoxic as shown in Table 10 and Fig .12.

Table 10. Data of different solvent with SDMS.

NO.	Solvent	Abs.
1	Water	0.520
2	Ethanol	0.408
3	Methanol	0.342
4	Acetonitril	0.437
5	1-Propanol	0.442
6	Acetone	0.054

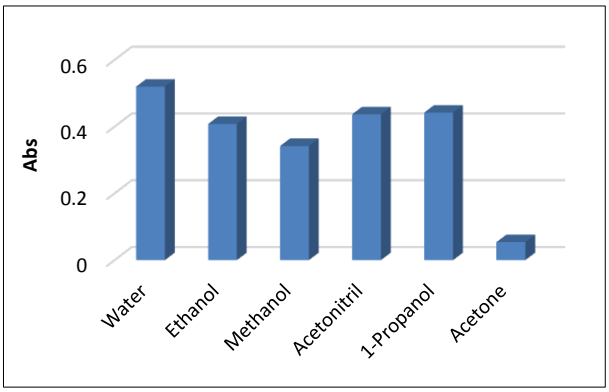

Figure 12. Different solvent with SDMS

Effect of Temperature:

The rest additions are optimal conditions then diluted with distilled water in volumetric flask in 10 ml ,then the effect of different temperature on the color product have been (5-60) ^{O}C . The absorbance is measured and this result is recorded in Table 11.

It is evident the best temperature is 20C^{O} because is give the best absorbance shown in Fig.13.

Table 11. Data of Absorbance to Temperature in the formation of color product and stabilization

Time	Abs.
5	0.350
15	0.482
20	0.521
30	0.493
40	0.484
50	0.439
60	0.419

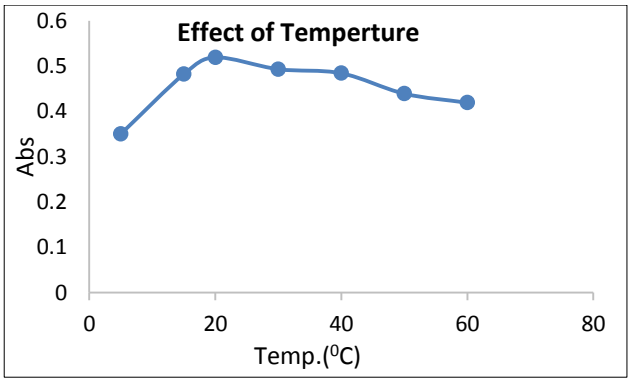

Figure 13. Effect of Temperature with SDMS

Stoichiometric Determination of Product Continuous Variation Method (18)

A series of different volumes of reagent and drug are prepared (0.1-0.9) ml, with concentration (4x10^{-4} M) in volumetric flask 10 ml .The additions are optimal condition and the volume is complete by distilled water (10). Then absorbance is measured by UV-VIS at λmax =473 nm. The stoichiometric ratio between reagent[R] and drug [D] result 1:1as shown in Table 12 and Fig .14

Table 12. Data of absorbance for Continuous Variation Method Result for SDMS

Volume of Drug/ml	Volume of Reagent/ ml	Abs.
0.1	0.9	0.039
0.2	0.8	0.090
0.3	0.7	0.132
0.4	0.6	0.170
0.5	0.5	0.203
0.6	0.4	0.185
0.7	0.3	0.155
0.8	0.2	0.114
0.9	0.1	0.070

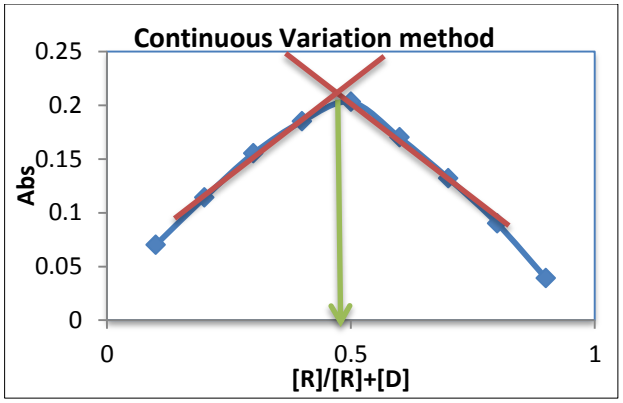

Figure 14. Continuous Variation method of SDMS

Mole Ratio Method

In this method the volume of drug is fixed at I ml with concentration (4x10^{-4}M) and the volume of reagent changes (0.5-4.5 ml). The optimum of addition is completed by distilled water in volumetric flask 10 ml and the absorbance is measured by UV-VIS at λmax =473 nm. The stoichiometric ratio between reagent[R] and drug [D] result 1:1as shown in Table 13 and Fig 15

Table 13. Data of Absorbance Mole Ratio Method.

Volume of Reagent/ ml	Abs.
0.5	0.151
1	0.333
1.5	0.399
2	0.401
2.5	0.410
3	0.415
3.5	0.425
4	0.427
4.5	0.433

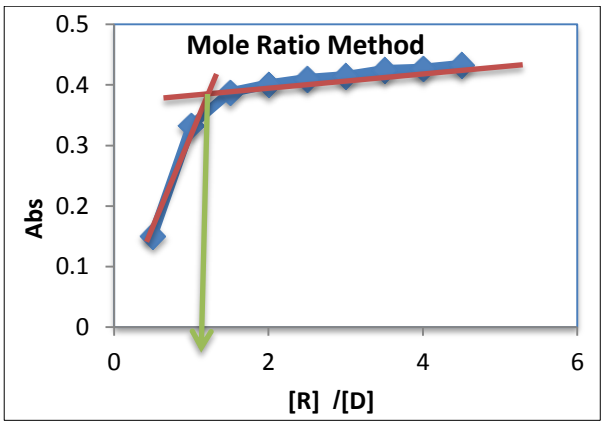

Figure 15. Mole Ratio Method of SDMS.

Calibration **Curve for complex of SDMS - α-Naphthol**

In this study, the solution is prepared in volumetric flask 10 ml containing increasing concentration of SDMS (1-12) µg mL^{-1} by taken [0.5 ml **CH_3COOH**, 0.3 ml **$NaNO_2$**, 0.09 ml **H_2NSO_3**, 0.4 ml **α-Naphthol**, 1ml **KOH**]. The volume is completed by distilled water and the absorbance is measured by UV-VIS at maximum wave length against a blank solution prepares same condition without the drug. Linear calibration graph is established by blotting absorbance against concentration of SDMS, it found (1-12) µg mL^{-1} obeys Bear Law. The molar absorption coefficient of product equals ($9,970x10^3 L.mol^{-1}.cm^{-1}$) and sandell's sensitivity (0.03012 µg mL^{-2}). The result as shown in Fig 16.

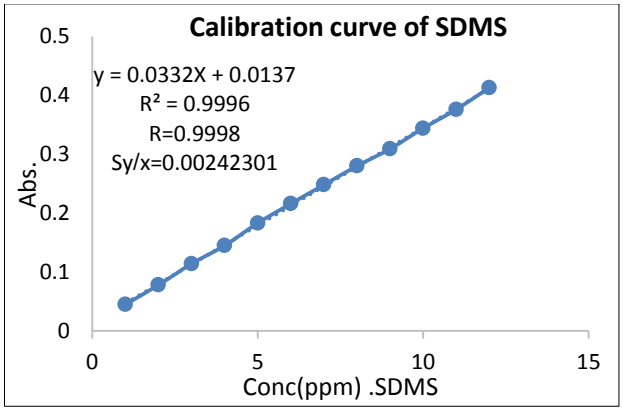

Figure 16. Calibration Curve of SDMS.

Effect of interference.

In this study effect of interference expected are present with SDMS by adding 1ml (1000 ppm), and the rest of optimum addition in volumetric flask 10 ml and complete by distilled water. Then the absorbance is measured by UV-VIS.

Table 14. Data of Absorbance of interference

NO.	100ppm interference	Abs.	Recovery %	E_{rel}%
1	Lactose	0.337	97.54	-2.46
2	Starch	0.341	98.77	-1.23
3	Arabic Gum	0.343	99.25	-0.75
4	Glucose	0.342	99.038	-0.962
5	Talc	0.334	96.73	-3.27
6	$Ca_3(PO_4)_2$	0.325	93.769	-6.231
7	$CaCl_3$	0.315	90.79	-9.21
8	$FeCl_3$	0.320	92.422	-7.578
9	$CoCl_2$	0.326	94.068	-5.932
10	$CaCl_2$	0.316	91.05	-8.956
11	$NiCl_2$	0.313	90.04	-9.956
12	Tri methyprine	0.323	93.468	-6.532
13	Without interference	0.347	100.4006	0.04006

This result showed in Table 14 indicate there is no interaction between interference and SDMS (19).

The Stability Constant of Color Product.

The stability constant K is shown in the Table15.

Table 15. Data of the Stability Constant of Color Product of SDMS.

Volume of $4x10^{-4}$M of SDMS / ml	Final con. SDMS /M	As*	Am*	α	K(L..Mol^{-1})	Mean of K ($L.Mol^{-1}$)
0.3	$1.2X10^{-3}$	0.108	0.111	0.02703	$4.01X10^5$	$2.22\ X10^6$
0.5	$2X10^{-3}$	0.186	0.189	0.01587	$1.17\ X10^6$	
0.7	$2.8X10^{-3}$	0.259	0.261	$7.6628\ X10^{-3}$	$5.09\ X10^6$	

It is clear the stability constant is high, so the dye formed is very stable.

Am= the high absorbance, as = the few absorbance.

Accuracy and Precision Test

The Table 16 shows the accuracy and precision of SDMS, which is studied at different concentration

(12, 9, 6, 3). It is clear that this result has a good accuracy and precision.

Table 16. Accuracy and Precision Test of SDMS

Amount of SDMS / µg mL^{-1}	*Found	Recovery %	Average Recovery %	E_{rel}%	Average E_{rel}%	RSD%
12	11.097928	99.8267	103.3793	-0.1733	3.3786	1.3021
9	9.54438	106.0478		6.0477		0.9192
6	5.9556	99.26		-0.74		0.82005
3	3.25149	108.383		8.38		3.0562

*= Average for five determination.

6- Application:

sThe proposed method is applied on [Montajat Pharmaceuticals. Saudi Arabia] injection (SULJAT) that contains (200mg) from Sulphadimidine Sodium in100ml) .The result is good and summarized in Table (17).

Table 17. Data of Accuracy and Precision Test.

Amount of SDMS / µg mL^{-1}	*Found	Recovery %	Average Recovery %	E_{rel}%	Average E_{rel}%	RSD%
12	11.9728	99.773	98.474	-0.2266	-1.5253	0.4134
9	9.0090	100.1		0.1		0.5982
6	5.8765	97.94		-2.058		0.6678
3	2.8825	96.0833		-3.9166		1.585

*= Average for five determination.

Second Method: Spectrophotometric Determination of Sulphadimidine Sodium (SDMS) with Using Cloud Point Extraction Technique.

Effect Type of Surfactant with SDMS

The surfactant plays an important role in cloud point extraction process .The basic practical dependes of micells for extraction .The solution contains [**1**ml SDMS,**0.5**ml CH_3COOH , **0.3**ml $NaNO_2$, **0.09** ml H_3NSO_3 ,**0.4**ml α-Naphthol , **1**ml KOH]and 1ml of each surfactant is added in volumetric flask 10 ml and the volume is completed by distilled water.at 60C^O for 20 minutes then separated by centrifugated at 4000rpm for 20 minutes ,that separated and dissolved in 1 ml ethanol and measured by UV-VIS at λmax=473nm and the result is shown in Table18.

It is clear from this result that the surfactant Triton X-114 increases the absorbance and efficiently of cloud point extraction (20) in Fig.17.

Table 18. Data of Absorbance for different surfactant with SDMS.

No.	Surfactant	Abs.
1	Tween 20	0.190
2	Triton X-100	0.215
3	Tween 80	0.207
4	SDS	0.235
5	Triton X-114	0.276
6	CTAP	0.041

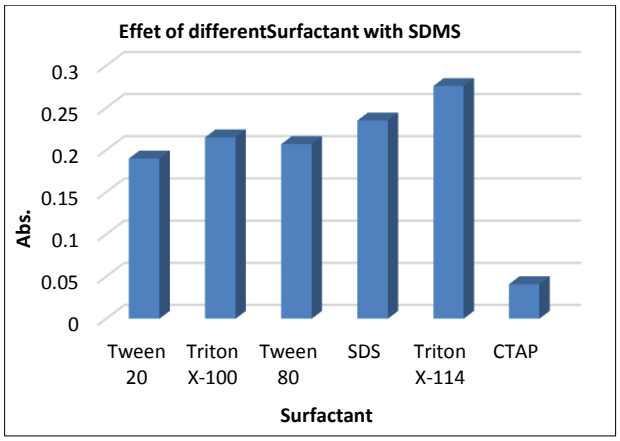

Figure 17. Effect of different Surfactant with SDMS

Effect of Triton X-114 Volume

The solution contain the former addition and uses varying volumes of 10% Triton X-114 in volumetric flask 10 ml and complete the mark by distilled water. It is heated at 60C^O for 20 minutes to form cloud point and separated by centrifugation at 4000rpm for 20 minutes, 1ml ethanol will be added and measured by UV-VIS at λmax=473nm .

It is obvious that the absorbance increases with increasing the volume of Triton X-114 ,that effects on the efficiency of extraction (21) ,suddenly this absorbance decreases below the optimum volume due to micelles catch enough the amount of hydrophopic product. The best volume of Triton X-114 is 1.4 ml as shown in Fig. 18 and Table 19

Table 19. Data of Absorbance of Volume Triton X-114.

Volume of Triton X-114	Abs.
0.2	0.156
0.4	0.162
0.6	0.235
0.8	0.252
1	0.278
1.2	0.290
1.4	0.307
1.6	0.298
1.8	0.286
2	0.236

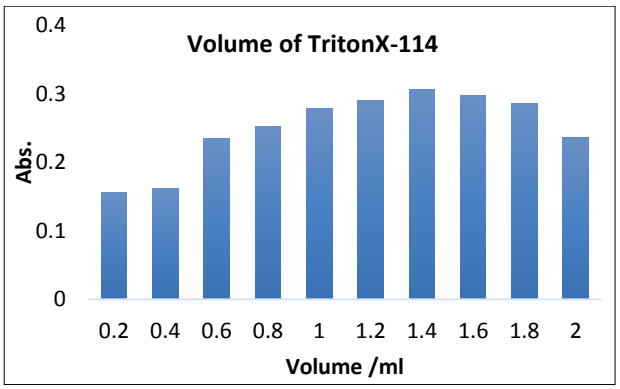

Figure 18.Volume of TritonX-114 with SDMS

Effect of Equilibrium Temperature

In series of 10 ml that contain [**1**ml SDN,**0.5**ml CH_3COOH , **0.3**ml $NaNO_2$, **0.09** ml H_3NSO_3 ,**0.4**ml α-Naphthol , **1**ml KOH,**1.4** ml Triton X114]in volumetric flask 10 ml ,then complete to the mark by distilled water. The varied temperature (35-70 ^oC) for 20 minutes to form cloud point and separated by centrifugation at 4000rpm for 20 minutes, 1ml ethanol will be added and measured by UV-VIS at λmax=473nm and recorded as shown in Fig. 20.

The result recorded that the best temperature are 50 ^oC as shown in Table 20 and Fig.19.

Table 20. Data of Absorbance of Varied Temperature.

Temperature	Abs.
35	0.217
40	0.286
45	0.301
50	0.331
55	0.290
60	0.288
65	0.276

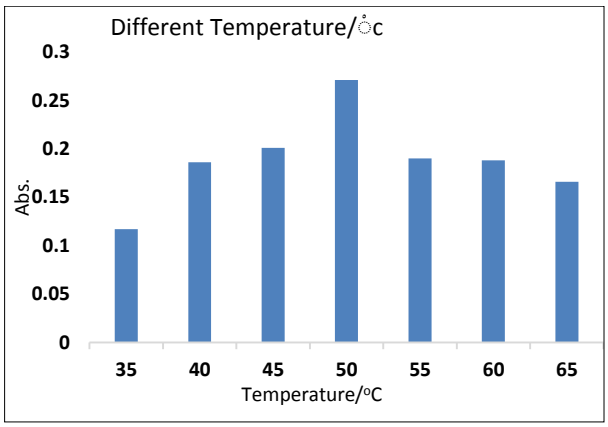

Figure 19. Different Temperature/C^0 with SDMS

Effect of Incubation Time

The solution [**1**ml SDN, **0.5ml** CH_3COOH, **0.3**ml $NaNO_2$, **0.09** ml H_3NSO_3, **0.4ml** α-Naphthol , **1**ml KOH,**1.4** ml Triton X114] is prepared in volumetric flask 10 ml and the volume is complete by distilled water at temperature 50 ^oC and the incubation time for(5-35minutes) to form cloud point and separated by centrifugation at 4000rpm for 20 minutes, 1ml ethanol will be added and measured by UV-VIS at λmax=473 nm. The best of incubation time is 20 minutes as shown in the Table 21 and Fig. 20.

Table 21. Data of absorbance of Incubation Time

Time /min	Abs.
5	0.245
10	0.268
15	0.306
20	0.341
25	0.296
30	0.273
35	0.260

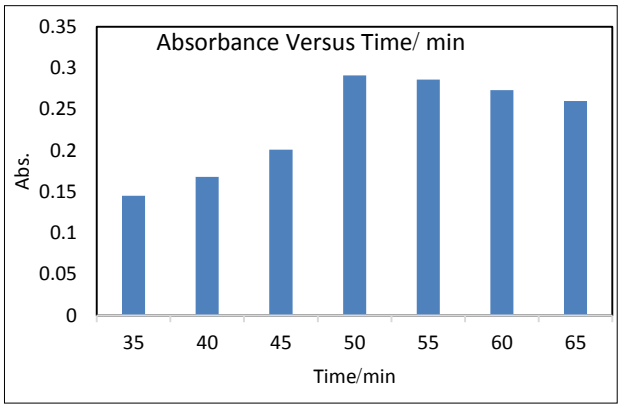

Figure 20.Absorbance of different incubation time.

Preparation of Calibration Curve in CPE

The prepared solution prepared increasing concentration(1-12 µg mL^{-1}) by taking [**0.5**ml CH_3COOH, **0.3**ml $NaNO_2$, **0.09** ml H_3NSO_3 ,**0.4**ml α-Naphthol , **1**ml KOH,**1.4** ml Triton X114],and in

volumetric flask 10 ml the volume is completed by distilled water at temperature 50°C and the incubation time for(20minutes) to form cloud point and separated by centrifugation at 4000rpm for 20 minutes, 1ml ethanol will be added and measured by UV-VIS at λmax=473nm and show the result in Fig (21).

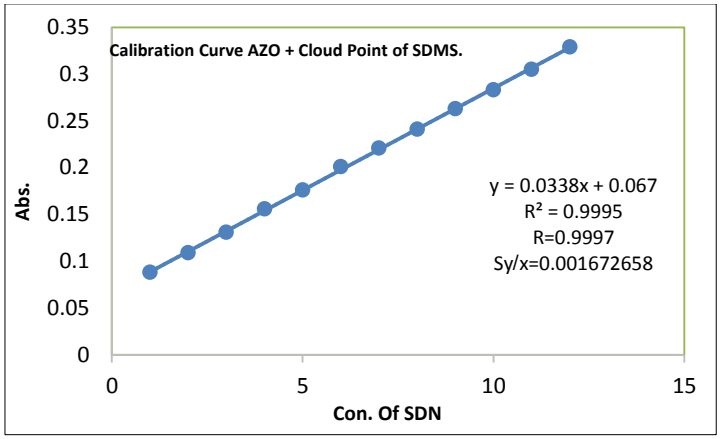

Figure 21. Calibration Curve AZO + Cloud Point of SDMS.

Accuracy and Precision Test

The table 22 show the accuracy and precision for SDMS with CPE, which are studied at different concentrations (12, 9,6,3) . It is clear that this result has a good accuracy and precision as shown in Table 22.

Table 22. Data of Accuracy and Precision Test

Amount of SDMS / µg mL^{-1}	*Found	Recovery %	Average Recovery %	E_{rel}%	Average E_{rel}%	RSD%
12	12.0118	100.0983		0.0983		0.3018
9	9.0650	100.722	100.2538	0.7222	0.2538	0.9943
6	5.9763	99.605		0.395		0.9905
3	3.0177	100.59		0.59		0.9808

*= Average for five determination.

Application:

The proposed method is applied on (silphdimidine sodium33.3% injection. Jorden), that contain (33.3 gm each 100gm) .The result is good and summarized in Table 23.

Table 23. Data of Accuracy and Precision Test

Amount of SDMS / µg mL^{-1}	*Found	Recovery %	Average Recovery %	E_{rel}%	Average E_{rel}%	RSD%
12	11.8956	99.8956		-1.1041		0.5583
9	8.9111	99.0122	99.5298	-0.9377	-0.4575	1.7135
6	5.9691	99.485		-0.515		2.0230
3	3.0218	100.7266		0.7266		2.7868

*= Average for five determination.

Comparison of the AZO-Coupling with Cloud Point Extraction Methods for SDMS.

The final result of the AZO-Coupling with Cloud Point Extraction for SDMS Methods as shown in Table 24.

Table 24. Comparison of the AZO-Coupling with Cloud Point Extraction Methods for SDMS.

Parameter	AZO-Coupling Method	CPE Method
Color of Product	Reddish orange	Red
λ max	473	473
Regression equation	y = 0.0332X + 0.0137	y = 0.0338X + 0.067
Standard deviation of regression	0.00242301	0.001672658
Correlation coefficient (r)	0.9998	0.9997
C.L for slop ($b \pm tS_b$) at 99%	0.0332±0.0064220	0.0318±0.00443
C.L for Intercept ($b \pm tS_a$) at 99%	0.0137±0.04726	0.067±0.0326
Concentration range (µg ml^{-1})	1-12	1-12
Limit of Detection (µg ml^{-1})	0.0277	0.01745
Limit of Quantitative (µg ml^{-1})	0.03605	0.028303
Sandell's Sensitivity (µg ml^{-1})	0.03012	0.02958
Molar absorbance ($L.mol^{-1}.cm^{-1}$)	$9.970x10^3$	$10.1505x10^3$
Composition of product	1:1	
Recovery %	99.8267-108.383	94.578-101.338
RSD%	0.82005-3.0562	1.3132-5.2892
C.L for con.12(µg ml^{-1})	11.9792±0.4018	12.0118±0.07453
C.L for con.9(µg ml^{-1})	9.5443±0.3506	9.0650±0.1855
C.L for con.6(µg ml^{-1})	5.9556±0.2930	5.9763±0.1218
C.L for con.3(µg ml^{-1})	3.25149±0.2051	3.0177±0.0609
Enrichment Factor		101.807

*Average five measurement

Conclusion:

Cloud point extraction is a simple, safe, and useful pre-concentration technique to determine Sulphadimidine Sodium by UV/VIS. CPE method is kindliness, selectivity and gave a good RSD and low limit of detection.

Conflicts of Interest: None.

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التقدير الطيفي المايكروي والاستخلاص بنقطة الغيمة للسلفاديمادين الصوديوم في المركبات النقية والمستحضرات الصيدلانية

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الخلاصة :

تم اقتراح طريقتين امتازت كل منهما بالبساطة والسرعة والملائمة لتقدير عقار سلفاديمادين الصوديوم في المادة النقية والمستحضرات الصيدلانية استندت طريقة الازوته للدواء (سلفاديمادين الصوديوم)بواسطة نتريت الصوديوم في الوسط الحامضي عند 5م متبوعًا بالاقتران مع الفانفثول في الوسط القاعدي لتشكيل اللون البرتقالي. تم تثبيت المنتج وقياسه عند 473 نانومتر والتي تطيع قانون بيرلامبرت في نطاق تركيز يتراوح بين (1-12) ميكروغرام / مل. كانت حساسية ساندل هي 0,03012 مايكروغرام / مل ، وكان حد الكشف 0,0277 مايكروغرام / مل ، وكان حد التقدير الكمي 0.03605 مايكروغرام / مل .

استخدمت الطريقة الثانية باستخدام الاستخلاص بنقطة الغيمة **(CPE)** المادة السطحية المستخدمة هي ترايتون اكس 114 والتي تطيع قانون بيرلامبرت في نطاق تركيز يتراوح بين (1-12) ميكروغرام / مل. كانت حساسية ساندل هي 0,02958 مايكروغرام / مل ، وكان حد الكشف 0,01745 مايكروغرام / مل، وكان حد التقدير الكمي 0.028303 متيكروغرام / مل . تمت دراسة جميع المتغيرات بما في ذلك تركيز الكاشف ، زمن التفاعل ، فترة استقرار اللون ، ونسبة مول من أجل تحسين ظروف التفاعل. تكوين المنتج **(1: 1)** طبقت الطريقتان بنجاح لتقدير عقار سلفاديمادين الصوديوم في المستحضرات الصيدلانية ،من خلال النتائج المستحصلة والخاصة بقيم الاسترجاعية المئوية اظهرت الطريقتان ان لاتاثير للمتداخلات على عملية القياس .

الكلمات المفتاحية: الاستخلاص بنقطة الغيمة، الفانفثول، سلفاديميدين الصوديوم ، ترايتون اكس 114.