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Review Article:

A Review of the Approved Data on Methods for Quantitative Determination of Sulfadiazine in Pharmaceutical Formulations

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Abstract

Background: Recently, the consumption of pharmaceutical preparations and health products has increased to treat various diseases, such as urinary tract infections, treatment of some skin conditions, burns, Alzheimer's disease, streptococcal infection, bronchitis, and eye infections. Many of these preparations have the potential to harm patients or act as emergency pollutants in the environment. Sulfadiazine is one of the most commonly used antimicrobials for both human and animal infections. **Aim:** The purpose of this paper is to show how important it is to keep an eye on sulfadiazine using simple, accurate, precise, selective, and repeatable methods for estimation. **Methods:** For measuring pharmaceutical preparation amounts, spectrophotometry, chromatography, and electrochemical methods are best. Spectrophotometric techniques possess ease, accuracy with precision, and repeatability. **Conclusion:** Chromatographic techniques are selective, and they are more than their predecessors in that they possess speed and safety, but their drawback is that they are expensive. When compared to other methods, electrochemical techniques have very high sensitivity and selectivity. However, they are not very precise, and the sensors are affected by the current. Also, the supporting medium needs to be maintained all the time before it can be used.

1. Introduction

Methotrexate Sulfa drugs, known as sulfonamides, were among the first antibiotics to be used systematically and paved the way for the antibiotic revolution in biomedicine (1). According to reports from the European Medicines Agency, sulfa antibiotics were the third most commonly used veterinary antibiotics in Europe in 2014, representing 11% of total veterinary antibiotic sales (2). They are considered one of the most important drugs that have appeared in the medical field due to its high effectiveness in treating many serious diseases, including its effect on the types of bacteria that cause tuberculosis, pneumonia, diphtheria, meningitis, tonsillitis, and scarlet fever. In addition, sulfa drugs have shown their vital effectiveness in treating other pathological conditions that affect humans, as they have been used in the treatment of trachoma (3), the urinary tract infection (4), treatment of some skin ulcers conditions, burns (5,6), fungal and bacterial infections (7), and antimicrobial (8) .In the veterinary field, it has been used to treat some cases of cholera in chickens (9) treat limb rot diseases in cows (10). Recently, sulfonamides have been used as an antitumor agent (11), as inhibitor of HIV protease (amprenavir) (12) , Also, sulfonamides have been used in the treatment of Alzheimer's disease (13) . These drugs are found in various

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derivatives that contain heterocyclic substitutes, such as sulphamethoxazol, Sulfadiazine, sulfathiazole, sulfamethazine, and sulfacetamide (14,15). Sulfadiazine (SDZ) is one of the important sulfonamides commonly used in medical sulfadiazine is a white solid that is poorly soluble in water, and dissolves in ethyl alcohol, acetone (96%), diluted mineral acids and alkali hydroxides. Its melting point is 255 °C and it is unstable when exposed to air or light (16).

1.2. Parameters of validation

Many international institutions are working together to provide the necessary means to verify chemical analysis methods:

The International Council of Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) has created validation guidelines, and the International Union of Pure and Applied Chemistry (IUPAC) regularly publishes chemical data, standard analytical methods, and the most recent process laboratories. Occasionally (17,18), the original crystal city conference report (19).

While United States Pharmacopeia "USP.", Indian Pharmacopeia "IND P." British pharmacopeia "BP.": Guidance for Innovative or developed methods provides an assurance recommendations on submitting those methods, and validation data to support the researcher and those interested in determining identity, quality, and purity. There is a possibility of relying on new methods to determine the content of the active chemical compound in the pharmaceutical preparation (20), a chemical name of sulfadiazine in IUPAC system (amino-N) -pyrimidin-2-yl-benzenesulfonamide-4) (21,22), a chemical structure (23) in **Figure 1**:

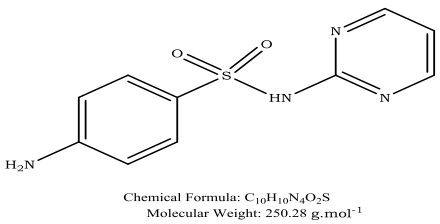

Figure1. structure of sulfadiazine

1.3. Additional parameters to evaluate the proposed methods

Additional parameters are to be presented and evaluated in this review paper when observing precision and accuracy are part of the method improvement and development process or are performed during the validation process when observing an acceptable method performance. It includes relative standard deviation, linearity, range of the method, recovery, and selectivity (24).

The quality of drug estimation methods depends on precision, accuracy, and reproducibility. Accordingly, part of this paper review looks at the results of selected methods around the principles of precision (distribution of data values), accuracy (relationship between experimental and true value), and reliability in the quantitative range resulting from the process of estimating these drugs (25,26).

1.3.1. Limit of Detection and Limit of Quantitation

Limit of Detection (LoD) : The smallest amount of analytical material that the devices can reliably sense is two or three times the baseline noise, with a confidence limit for T-test statistic σ=0.05 (27) ,Limit of Quantitation (LoQ): lowest concentration of an analyte that the devices can reliably determinated, is ten times the baseline noise (28).

1.3.2. Precision and Accuracy

This requires researchers to determine and report the precision, accuracy, sensitivity, reproducibility, and any other characteristics to validate test methods, regrettably. There is no unified approved source guideline on analytical method validation and discussion of the results reached by the researchers as the comprehensive source approved for validating the methods used in estimating the pharmaceutical preparation (29).

Two simultaneous terms. The first is a measurement of the degree to which an analyte's experimental value closely resembles its real value under identical condition. It is statistically determined through the statistical calculation of the recovery, However, the second phrase describes measurements of how closely two or more accurate measurements of the same variable match under the same conditions, It is statistically determined through the statistical calculation of the RSD which can be described as follows: precision i.e., the degree of repeatability, Accuracy, i.e., the degree of reproduction (30,31).

1.3.3. The molar absorptivity and Sandell's sensitivity

It is possible to verify and determine reliably the sensitivity of the method used to estimate the drug product by finding two values (sandell's sensitivity and molar absorptivity) (32): Sandell's sensitivity is a term that refers to the smallest concentration of an analyst that can be independently detected by a fixed-determined method. or it is the amount of analyst in µg that gives an absorbance of $1*10^{-3}$ When using a cell with a path length of 1 cm (33) . Molar absorptivity is a measure of how well a chemical compound absorbs light projection on it under given conditions at a certain wavelength (34,35).

2. Estimation methods of sulfadiazine

Pharmaceutical preparations estimation methods can be divided into two main sections. The first section is estimation methods as a protocol approved by international institutions to verify the quality, efficiency, and purity of the product. The second section is represented by alternative methods presented by

researchers and verified through approved means with high reliability.

2.1. Standard estimation methods

In Indian pharmacopoeia, sulfadiazine can be assayed by taking 0.125 g from it and transfer to separator funnel contain 20 ml 1M NaOH, shaking and extract with 4th quantities dichloromethane, every time add 50ml , each dichloromethane , with four quantities of dichloromethane in 50 ml of each, then wash each extract with 10 ml of sodium hydroxide , Combine the aqueous washings and the aqueous .Layer and dilute by D.w. in container of 250ml , filter and again dilute 10.0 ml of the filtrate to 200 ml with D.W. then take 2ml from the resulting solution and add (0.5 ml of 4M HCl and 1 ml of 0.1w/v solution of $NaNO_2$) allow to stand 2 min. Add 1m of 0.5 w/v solution. of SO_3NH_2 and allow to stand for 3min. Add 1 ml of 0.1 w/v solution of N-(l-naphthyl) ethylene diamine dihydrochloride, allow to stand for 10 min. Dilute the solution to 25ml with D.W. and measure the absorbance of the resulting solution against blank (All additives after filtration without Sulfadiazine) at 538 nm , Calculate the content of Sulfadiazine by $A_{(1\ percent,\ 1\ cm)} = abl$ (36).

In USP. used Chromatographic system (mode: LC, detector: UV 254nm, column: 4 mm × 30 cm; pa. L1,Flow rate: 2 mL/min and Injection size: 10 µL), as standard method for assay Sulfadiazine, mobile phase water, glacial acetic acid, acetonitrile (87:1:12), with two solution, standard solution: dissolved 1 mg/mL of Sulfadiazine in 0.025 N NaOH, Sample solution: dissolved 1 mg/mL of sulfadiazine from powdered Tablets in 0.025 N sodium hydroxide. Calculate the percentage of it in the portion of Tablets taken (37):

$$\textbf{Result} = (P_{Sa}/P_{St}) \times (C_{St}/C_{Sa}) \times 100$$

P: *peak response ,Sa: sample, St: standard;* ***C*** *:concentration , Acceptance criteria: 95.0%–105.0%*

In British pharmacopeia two standard methods for tablet and injection drag for determination of sulfadiazine, for tablet; wight 20 tablets , crush and grind well, shake amount of the resulting powder contain 0.15 g sulfadiazine with 50ml 0.1M NaOH ,completed the volume to 100 ml , filter, and discard the first 20 ml of filtrate, dilute only 5 ml of it with 750 ml D.W in volumetric flask , add 20ml of 0.1 M CH_3COOH. Mix well for 5min and complete volume to 1000 ml, Leave it for a while, then measure the absorbance at 359nm , in the same approach prepare the equivalent 0.15 g sulfadiazine , acceptance criteria are calculated from the obtained results.

In injection, add mixture of HCl and D.w.(10:75) ml to an amount containing the equivalent of 0.5 g of drug , add 3 g KBr, cool in ice bath for sufficient time, titrate the mixture prepared carefully with $NaNO_2$, stirring gently and continuously , set the end point electrometrically, Acceptance criteria are calculated on the principle that: Each 1ml $NaNO_2$ is equivalent to 0.02503 g of sulfadiazine (16) .

2.2. Other Methods

The pharmaceutical industry has witnessed, on a global level, a great development in the field of preparing chemical compounds with pharmacological efficacy and in different pharmaceutical forms (38,39). Therefore, it was necessary to develop methods of quality control of the drug in order to monitor the quality and effectiveness of pharmaceutical products and their suitability for human use, which must have high standards in terms of quality (40,41). Therefore, researchers in the field of analytical chemistry have turned to finding new methods for estimating pharmaceutical preparations. These methods are characterized by accuracy, precision and sensitivity and give stable results for estimating these preparations.

2.2.1. Spectrophotometric methods

Spectrophotometric methods are simple, sensitive, selective, accurate, precise, inexpensive, reproducible, and can be used in routine lab work (42). The method depends on showing a colored product by introducing the pharmaceutical preparation into a specific reaction, such as oxidation-reduction reactions, condensation reactions, diazotization and coupling, and Schiff base reactions (43). Sulfadiazine was estimated by different spectrophotometric methods and **Table1.** shows the most important parameters that verify the quality, precision, accuracy, sensitivity of method of these spectrophotometric methods.

2.2.2. *Chromatographic methods*

The effectiveness of therapy and the side effects of drugs contribute to determine human health and reduce their direct threat to people's safety. Most protocols specify a fixed dose of the drug in the treatment process, without paying attention to the other aspect represented by the possibility of the patient taking other drugs at the same time or the presence of genetic or environmental factors that may affect the absorption of the drug by the body and the extent of , distribution, metabolism and excretion of it. Therefore, it is necessary to detect drug concentrations accurately to prevent or reduce the adverse events caused by drugs (44) . Recently, laboratory techniques have developed significantly to estimate drug compounds, whether in the drug product or clinically, among these chromatographic methods (45), It is a general term for a group of techniques including: thin layer chromatography, ion exchange chromatography, column chromatography, gas chromatography, and high-performance liquid chromatography (46), Like other drugs, sulfadiazine is considered an important drug for humans and animals. Therefore, researchers have contributed to finding methods that are equivalent in accuracy, precision and sensitivity to those methods approved by the competent institutions to provide alternatives for estimating and diagnosing active

compounds in pharmaceutical preparations. **Table 2.** shows the methods obtained by a number of researchers regarding the possibility of estimating the pharmaceutical preparation using chromatography methods.

2.2.3. *Electrochemical methods*

In an indispensable role, analytical chemistry works to keep pace with the development in pharmaceutical manufacturing and design processes in order to meet the various requirements for the purpose of monitoring pharmaceutical and organic materials on a regular basis [63] (47). In the last decade, the role provided by electroanalysis techniques in the field of pharmaceutical and medical analysis has grown [64] (48) due to the high selectivity and sensitivity that techniques possess towards quantitative and qualitative estimation in addition to simple activity accompanied by a rapid response [65] (49), as the method depends in its work on the oxidation-reduction process with the availability of electrodes dedicated to measure the resulting voltage [66] (50), which are constantly being developed by researchers to reach ideal results in the estimation processes of pharmaceutical compounds. **Table 3.** shows the use of electrical techniques and developed electrodes to estimate sulfadiazine

Table 1. summary important parameter for spectrophotometric methods determination of sulfadiazine

Type reaction	Reagent	λ_{max} (nm)	linearity (µg.ml^{-1})	Sensitivity			Accuracy	Precision	References
				Molar absorptivity (l.mol^{-1}.cm^{-1})	Sandell's sens. (µg.cm^{-2})	LOD, LOQ (µg/ml)	RE%	RSD%	
first-derivative spectrophotometry	NA	272	(3× 10^{-6} – 3×10^{-5})M	NA	NA	(5.14×10^{-7}, 1.56×10^{-6}) M	99.01	NA	51
diazotization and coupling	2,6 dimethyl phenol and cloud point method	468	1-18	8.3×10^{3} 8.4×10^{3}	0.03012 0.02958	0.0277, NA 0.0745, NA	NA	NA	52
diazotization and coupling	3,5-dihydroxy benzoic acid	436	0.1-18	2.24×10^{4}	0.0100	0.329,0.411	100.122	0.648	53
oxidative coupling	ortho-amino phenol	532	5-40	5.5×10^{3}	0.04	0.175, NA	101.1	0.31	54
oxidative coupling	2,4-dinitrophenyl hydrazine	486	3-15	2.23×10^{4}	0.0222	0.03,NA	99.75	≤1.26	55
Uv-spectram	methanol	289	9.08-41	NA	NA	0.82,0.13	98.71	0.440	56
diazotization and coupling	4-amino-2-hydroxy acetophenon	410	0.5-15	2.83×10^{4}	0.008	0.443,0.249	≤100.24	≤0.562	57
diazotization and coupling	2,5-dimethoxy aniline	478	0.1-5	8.26×10^{4}	0.003	0.023,0.078	99.26	0.968	58
diazotization and coupling	2,6-dihydroxybenzoic acid	458	0.4-12	4.38×10^{4}	0.005	NA	≤102.6	≤1.21	59
diazotization and coupling	thymol	469	1-7	2.6 × 10^{4}	0.0096	0.077,0.025	100.57	0.657	60
Uv-spectram	ME:D.W (90;10)	270	5-30	2.4×10^{4}	0.0101	NA	≤100.90	0.025	61
diazotization and coupling	8-Hydroxyquinoline	500	0.1-7	3.7×10^{4}	NA	0.05,0.16	100.8	0.1	62
diazotization and coupling	Histidine	423	0.4 – 9.6	1.75×10^{4}	NA	NA	≤99.96	≤0.87	63
diazotization and coupling	α-naphthylamine	538	0.2-20	NA	NA	0.06,NA	NA	NA	64
diazotization and coupling	N-(l-naphthyl) ethylendiamine	542	0.5-50	NA	NA	NA	NA	0.003	65
Condensation reaction	p-Benzoquinone	500	5-80	5.05×10^{3}	NA	NA	NA	NA	66

Table 2. summary important parameter for chromatographic methods determination of sulfadiazine

Chromatographic type	Mobil phase	Stationary phase	Linearity (µg.ml^{-1})	Detector/λmax(nm)	Reference
LC-MS	acetonitrile :0.05 M phosphoric buffer,pH 4.5	Kinetex C_{18}, 100 mm × 4,6 mm; 2,6 µm	20-750 mg.kg^{-1}	MS/350°C	67
UPLC/MS/MS	methanol: water (90:10)	Agilent poroshell 123EC-C_{18} ,4.6 mm x 50 mm, 2.7 µm	5–2000 ng/mL	MS/MS	68
RP-HPLC	Acetonitrile: 0.05 M phosphate buffer (pH 5.0 to which added triethyl amine 0.5 ml/L), (35: 65)	X-Select C_{18} ,250 × 4.6 mm, 5 µm	0.8–100	UV, 205	69
HPLC	a. 0.08% acetic acid: acetonitrile (9:1) b.Methanol	Agilent 5 TC-C_{18}, 250 x 4.6 mm	1.15-3.84	UV, 295	70
TLC-densitometeric	chloroform :methanol: ammonia hydroxide 8.5:1.5:0.1	aluminum plates (20×10 cm) coated 0.25 mm Silica gel 60 F254	0.1-2	UV, 220	71
RP-HPLC	methanol:phosphate buffer (KH2 PO4 and K2 HPO4), phosphate pH 3 70:30	Zodiac sil C18 column (4.6×150 mm) 5µ	16-80	UV, 240	72
UHPLC–DAD	ACN/0.01 M oxalic acid,pH 3.0	on-line SPEC_{18}	0.5–100	UV, 277	73
HPLC-FLD	Ethyl acetate :methanol: acetonitrile (50:25:25)	zorbax eclipse XDB C_{18}	NA	fluorescence detection	74
LC-MS	Water:0.05% H_3PO_4	X Terra MS C_{18}	25-10000 µg.kg^{-1}	ZQ 2000 single quadrupole/24-26 °C.	75
HPLC	(%0.5–0.01)formic acid: water، 0.1%formic acid in water :acetonitrile, 12:88	nucleosil C_{18},250×4.0 mm, 5µm	0.1to 3 mg.L^{-1} for water 0.1 to 3 mg.kg^{-1} for plasma	UV,267	76
HPLC	acetonitrile and 0.5% acetic acid in purified water	Supelcosil C18 ,250 mm × 4.6 mm I.D	5.0 -100.0 ng/L	UV,272	77
RP-HPLC	Acetonitrile:0.01 M H_3PO_4(16:84)	C_{18},100×4.6 mm,5µm	5-150 ng.ml^{-1}	UV,271	78

Table 3. summary important parameter for Electrochemical methods determination of sulfadiazine

Technique types	Electrodes	The Electrolyte media, pH	Voltage	RangeμM	RSD	LOD (μM)	References
DPV	$SrWO_4$-SPCE	0.05 M Phosphate Buffer (pH 7.0)	0.93	0.05-235	NA	0.009	79
DPV	$ZnMn_2O_4$-GCE	0.05 M Phosphate Buffer (pH 7.0)	NA	0.008-1264	≤2.12	0.0021	80
i-t	SmV/CNF-GCE	0.1 M Phosphate Buffer (pH 7.0)	0.7	0.009-445	1.12	0.0013	81
CV DPV	GCE/(MWCNT-MIP)	2.0mM $K_3[Fe(CN)_6]$ solution containing 0.1 M KCl	(-0.3)-0.6 (-0.1)- 0.7	4-50	≤4.6	0.68	82
DPV	Cu2Sb-SPCE	Phosphate Buffer (0.05 M) ,pH 7.2	0.95	0.09-818.2	≤2.93	0.07	83
i-t	rGO-$OPPF_6$-GCE	0.1M sulfuric acid	0.90	0.22-63	0.93	0.07	84
DPV	MIP/GO@COF/GCE	0.2 M Na_2HPO_4 and 0.2 M NaH_2PO_4(phosphate buffer (0.2 M, pH 7.0)	NA	0.5–200	2.7	0.16	85
i-t	MoS_2eRuS_2-GCE	BrittonRobinson buffer, pH 2.0	0.92	0.01- 598.7	≤ 2.89	0.004	86
i-t	MWCNTs–PSS-GCE	0.1 M sulfuric acid	0.95	1.9-160	≤7.42	0.6	87
SWV	(CPEs)	phosphate buffer pH 6.0	0.93	1-10	4.8	0.4	88
i-t	Carboxyl-MWCNTs/GCE	Britton-Robinson Buffer, pH 2.0	0.952	0.50-110	≤3.86	0.03	89
DPV	BA-SPCEs-MWCNTCOOH	Britton-Robinson buffer, pH 1.7	-0.04	1-14	3.2	0.3	90
DPV	MIP-CPE	Britton-Robinson Buffer, pH 6.5	0.92	0.2-100	2.56	0.14	91
i-t	$OPPF_6$ -MWCNTs/GCE	NA	0.9	3.3-35.4	4.9	0.21	92
DPV	OPPY-PGE	Britton–Robinson buffer ,pH 2.5,in acetonitrile: water (50:50)	1.03	25-1500	0.64	1.76	93
SWV	GCE	0.04 M Britton-Robinson, pH 6.8	-1.49	62.7 - 340	≤1.71	10.9	94
DPV	Bismuth-film	0.05 M Britton–Robinson,acetate pH 4.5 solution	−0.74	3.2–97	1.92	2.1	95
SWV	boron-doped diamond (BDD)	Ethanol: 0.5 M H_2SO_4 ,50:50	1.1	8.01-119	1.9	2.19	96
SWV	poly(3-methylthiophene)-GCE	Britton-Robinson Buffer, pH 6.26	-1.33	5-3200	NA	4.0	97
DPP	Hg	BrittonRobinson buffer, pH 2.0	0.09	2.0-32	NA	4.90	98
DPV	GCE	Britton-Robinson Buffer, pH 4.7	0.05	15-30	4.0	5.4	99

3. Conclusion

The quantitative estimation of the drug sulfadiazine, which belongs to the sulfonamide drugs derivatives, has received great attention due to the importance of the drug in humans and veterinary medicine. It was noted that all methods generally have sensitivity, accuracy and applicability, but that the electrochemical methods were the most sensitive and had a greater range of obeyed Beer's law, which is shared with chromatographic methods. Chromatographic methods have a faster path, high selectivity, and fewer steps. As for repeatability, spectroscopic methods have achieved. high accuracy and precision, shared with chromatographic methods, on the contrary, electrochemical methods, were less precise. The financial cost of chromatographic methods was higher compared to electrochemical methods, whilst spectroscopic methods, have lower costs.

The Abbreviations

The table below shows the abbreviations included in the review paper.

Abbreviations	Means
NA	No Available
RP-HPLC	Reversed-phase high-performance liquid chromatography
UPLC/MS/MS	Ultra-performance liquid chromatography/ mass spectrometry
UHPLC–DAD	Ultra-performance liquid chromatography /diode array detection
HPLC-FLD	high-performance liquid chromatography/ fluorescence detector
TLC-densitometric	Thin layer chromatography
CV	Cyclic Voltammetry
DPV	Differential Pulse Voltammetry
i-t	Chronoamperometry
SWV	square-wave voltammetry
D.W.	distilled water
SPCE	Screen-printed electrodes
SmV/CNF-GCE	samarium vanadate/carbon nanofiber-glassy carbon electrode
MIP/MWCNT	Molecularly imprinted polymer multi-walled carbon nanotube
rGO/OPPF$_6$	reduced graphene oxide - N-octyl-pyridinium-hexafluorophosphate
GO@COF/GCE	a graphene oxide@ covalent organic framework
MWCNTs–PSS	multiwalled carbon nanotubes - sodium polystyrene sulfonate
MIP-CPE	imprinted polymer -carbon paste electrode
OPPY-PGE	overoxidized polypyrrole - pencil graphite electrodes

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مراجعة البيانات المعتمدة لطرائق التحديد الكمي للسلفاديازين في المستحضراته الصيدلانية

الخلاصة

الخلفية: في الآونة الأخيرة، زاد استهلاك المستحضرات الصيدلانية والمنتجات الصحية لعلاج أمراض مختلفة، مثل التهابات المسالك البولية، وعلاج بعض الأمراض الجلدية، والحروق، ومرض الزهايمر، والعدوى العقدية، والتهاب الشعب الهوائية، والتهابات العين. العديد من هذه المستحضرات لديها القدرة على إلحاق الضرر بالمرضى أو العمل كملوثات طارئة في البيئة. السلفاديازين هو أحد أكثر مضادات الميكروبات استخدامًا لكل من العدوى البشرية والحيوانية. **الهدف:** الغرض من هذه الورقة هو إظهار مدى أهمية مراقبة السلفاديازين باستخدام طرق بسيطة ودقيقة ومحددة وانتقائية وقابلة للتكرار للتقدير. **الطرائق:** لقياس كميات المستحضرات الصيدلانية، تعد طرق القياس الطيفي والكروماتوغرافيا والطرق الكهروكيميائية هي الأفضل. تتمتع تقنيات القياس الطيفي بالسهولة والدقة مع الدقة والقدرة على التكرار. **الاستنتاج:** تقنيات الكروماتوغرافيا انتقائية، وهي أكثر من سابقاتها من حيث السرعة والأمان، ولكن عيبها هو أنها باهظة الثمن. عند مقارنتها بالطرق الأخرى، تتمتع التقنيات الكهروكيميائية بحساسية وانتقائية عالية جدًا. ومع ذلك، فهي ليست دقيقة جدًا، وتتأثر المستشعرات بالتيار. كما يجب صيانة الوسيط الداعم طوال الوقت قبل استخدامه.

الكلمات المفتاحية : السلفاديازين، مطيافية، كروماتوغرافية، كروموكيميائية، حساسية ، الدقة ، التوافقية