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A NEW METHOD FOR DETERMINING ISONIAZID DRUG BY FLOW INJECTION ANALYSIS WITH A MERGING ZONE TECHNIQUE

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ABSTRACT. This study investigated the designing of a simple and rapid flow injection (FI) system and the determination of Isoniazid in a prepared aqueous solution. The principle of the method depended on the indirect reaction of the isoniazid drug with copper(II)-neocuproine (Cu(II)-NCPR) complex after acidifying the aqueous medium. The yellow-orange and charge transfer complex had maximum absorption at 455 nm. The optimum conditions of the FIA were studied. The calibration graph of isoniazid was constructed with a linear range of 0.10 to 10.00 mg/L, and a linearity (r^2) value of 0.9988. The detection and quantification limits were 0.073 and 0.221 mg/L, respectively. The molar absorptivity (ε) was 56.68×10^4 L/mol.cm and Sandell's sensitivity was 0.84×10^{-3} µg/cm. The manufactured local valve was characterized by inexpensive, easily running, high repeatability (n = 6) at an RSD of 2.18%, and the dead volume was zero. The dispersion coefficient values were 1.91, and 1.53 for both concentrations of 0.60, and 4.00 mg/L, respectively. The sampling rate of the analysis for the FIA system was 63.00 samples per hour. The proposed analytical flow injection method was successfully applied to standard aqueous solutions and tablets of isoniazid.

KEY WORDS: Isoniazid, Flow injection, Merging zone, Repeatability, Charge transfer complex

INTRODUCTION

Isoniazid is a synthetic antimicrobial used widely to treat tuberculosis [1]. Excess doses of this medication can cause seizures, coma, and hepatotoxicity [2]. Isoniazid reacts immediately with colorless Cu(II)-NCPR complex after acidifying the medium to form colorful complex with maximum absorption at 455 nm based on the charge transfer complex reaction [3]. Flow injection analysis is used for the determination of many pharmaceutical drugs [4, 5]. The merging-zone FIA method demands a lower quantity of chemicals [6]. Consequently, a homemade valve can be used to determine isoniazid by reacting with Cu(II)-NCPR complex via a merging-zone FIA.

Many techniques used to determine isoniazid, including voltammetry [7], colorimetry [2], high performance liquid chromatography [8], polarography [9], liquid chromatography-mass spectrometry [10], derivative spectrophotometry [11], and electrochemical [12]. Even while these techniques have significant benefits, they are typically very time-consuming, and demanding extensive sample processing. Furthermore, they are not portable, and in some instances, they are required a complex pretreatment using a high purity reagent or solvent [13, 14].

Isoniazid is estimated by several flow injection techniques. Flow injection-chemiluminescence system is used to determine Isoniazid in pharmaceutical samples [15]. In addition, it is determined by the amperometric-flow injection method using a modified carbon electrode [16]. A flow injection technique is used for the fluorimetric measurement of isoniazid

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by oxidizing with cerium(IV) [17]. Among the various flow injection techniques, merging-zone modulation is distinguished by its lower consumption of reactants [18, 19].

This article describes a novel merging-zone technique for determining isoniazid using flow injection analysis with a low-priced homemade valve. Isoniazid immediately reacts with a Cu(II)-NCPR complex forming a yellow-orange complex that absorbs at 455 nm according to the charge transfer complex reaction. This method is a precise, high throughput, and simple approach for estimating isoniazid in aqueous solutions and pharmaceutical formulations.

EXPERIMENTAL

Chemicals and reagents

All chemicals and reagents used in the present work were of analytical grade quality, including: isoniazid (4-pyridinecarboxylic acid hydrazide) (Samarra Factory), 2,9-dimethyl-1,10-phenanthroline (neocuproine reagent) (NCPR) (Merck), copper(II) nitrate tri-hydrate (BDH), hydrochloric acid (BDH), sodium hydroxide (Merck), and absolute ethanol (BDH). The preparation of aqueous solutions was conducted by using distilled and deionized water.

Instruments and apparatus

Four-channel peristaltic pump from Ismateic (Germany) was used for the aspiration of the carrier stream. Manufactured locally FI valve composed of plastic, acrylic, and four three sub-way ports, which was used for injecting sample and reagent solutions. A PD-303 (Japan) single-beam APEL UV spectrophotometric was used for the purpose of obtaining UV-VIS spectra for spectrometric measurements as a detection part of the flow injection system. To obtain data, the spectrophotometer was coupled to the kompensograph C1032 Siemens (Germany). The flow cell with volume 450.00 µL, an optical path of 1.00 cm, and two vents for outputting and inserting the sample and reagent section were employed from Helmma (UK). The pH measurements were obtained using a Philips Pw 9421 (Germany) pH meter. The λ_{max} was fixed using the double-beam spectrophotometer Shimadzu UV-1700 (Japan).

Preparation of solutions

The isoniazid solution of 100 mg/L was prepared by dissolving 0.010 g in 100 mL of deionized water. The NCPR reagent solution was obtaining by dissolving in ethanol [20]. The solution of NCPR was prepared daily at the concentration of 700 mg/L in 10% absolute ethanol. The preparation method included dissolving 0.0350 g of the NCPR reagent in 5 ml of ethanol, then the volume of the volumetric flask was completed with distilled water to 50 mL. The stock solution of Cu(II) 200 mg/L was prepared by dissolving 0.0761 g of copper(II) nitrate tri-hydrate in 100 mL of deionized water. The working solutions of Cu(II) was acquired by gradual dilution of the stock solution. The dilution process was conducted by using deionized water. The carrier solution of Cu(II) was modified to the pH = 6.00 by adding drops of 0.1 N of hydrochloric acid solution. All the working solutions were prepared by successive dilution of stock solutions.

Procedure for real sample analysis

The tablets of isoniazid pharmaceutical formulations were used to demonstrate the analytical performance of the flow injection method. About ten tablets were precisely weighed and converted to fine powder using a ceramic mortar. A stock solution of Isoniazid tablet was prepared by dissolving an appropriate amount of tablet powder with distilled water. Then solution was filtered using filter paper. After that, the filtered solution was diluted to a complete volume of 100

mL and obtained the stock solution of 100 mg/L. The real sample analysis was conducted utilizing the diluted solutions with the concentrations 0.60, 4.00, and 10.00 mg/L.

Method principle

The isoniazid determination process in the present study is based on an indirect reaction between isoniazid and uncolored Cu(II)-NCPR complex in the acidic media of HCl as equations (1) and (2). Cu(II) react firstly with NCPR reagent to give Cu(II)-NCPR uncolored complex that reacts with Isoniazid by charge transfer reaction to form Cu(I)-NCPR yellow-orange complex with maximum absorption of light at 455 nm [21]. The combination ratio of Cu(II)-NCPR complex is 1:2 [22]. Figure 1 show the charge transfer complex reaction's steps:

$$Cu(II) + 2\ NCPR + HCl \rightarrow Cu(II)\text{-}(\ NCPR)_2 \text{ uncolored complex} \quad (1)$$

$$Cu(II)\text{-}(\ NCPR)_2 + Isoniazid \rightarrow Cu(I)\text{-}(\ NCPR)_2 \text{ colored complex} \quad (2)$$

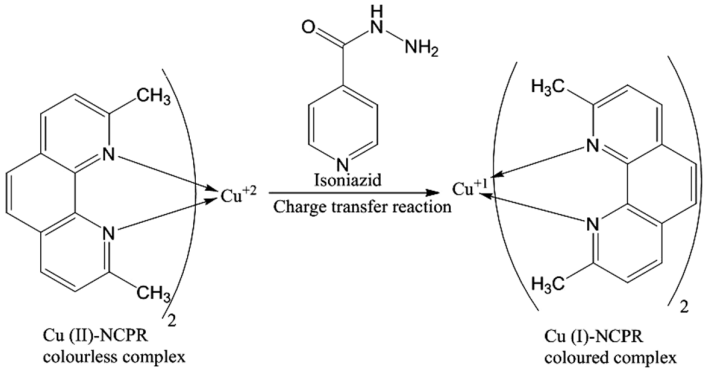

Figure 1. Charge transfer complex reaction of the Cu(I)-NCPR complex.

The mechanical operation of the valve

Figure 2 illustrates the process of mechanical operation for the manufactured local valve. In the first step, the solution of 80.00 mg/L of Cu(II) was adjusted at pH = 6.00 by hydrochloric acid as the carrier stream was propelled into all the flow injection unit parts by a peristaltic pump with a flow rate of 4.60 mL/min. The aqueous solution of Cu(II) stands for the blank and furnishes the acidic medium to complete the reaction between Cu(II) and NCPR reagent. At the second and third steps, the pumping of the Cu(II) carrier stream stopped then the solution of 110.50 µL and 350 mg/L of NCPR reagent was injected into the loop 2 followed by injecting 85.40 µL of the isoniazid sample into the loop 1. The solutions of NCPR and Isoniazid were inspired by the reaction coil of 300 cm by the carrier stream of Cu(II). The reaction between Cu(II) and NCPR occurred in acidic media to form an uncolored complex which in turn reacts with isoniazid to yield a yellow-orange complex. The complex showed maximum absorption at the wavelength (λ_{max}) of 455 nm. The change in the height response of the Kompenso graph was proportional to the concentration of isoniazid/reference carrier (Cu(II)+HCl).

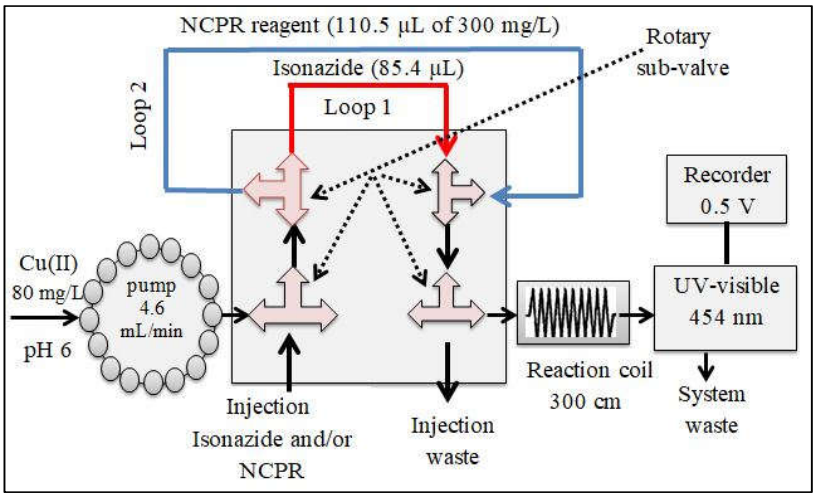

Figure 2. Diagram of the homemade-valve's mechanical operation.

RESULTS AND DISCUSSION

Effect of pH

The pH effect on the reaction was investigated between 150 mg/L NCPR, 60 mg/L of Cu(II) as a carrier solution, a coil of 2 m, and 110.50 µL of 10 mg/L isoniazid. The tested pH range was 3-11, and the flow rate of 5.30 mL/min was maintained throughout the experiment. According to the results (Figure 3), the optimal pH for the reaction was six, with a peak height of 5.90 cm. The results of the present study were consistent with the findings of Kemal [23] and Bouazzi *et al.* [24] when the determination of Isoniazid by voltammetry method and HPLC-UV, respectively.

Effect of flow rate

The effect of the flow rate was studied over the range of 2.40-7.80 mL/min. The optimal flow rate was determined to be under a pH of 6.00 for the carrier solution, 80 mg/L of Cu(II) as a carrier solution, and 350 mg/L of NCPR reagent. The other conditions included 135.70 µL for the NCPR reagent, a coil length of 2 m, and 110.50 µL of 10 mg/L of the isoniazid reagent solution. The outcomes (Figure 3) demonstrated that the lowest value 2.40 mL/min of flow rate resulted in a higher response at 11.50 cm. However, the form of the analytical response was broad and double-peaked because the sluggish flow rates causing imperfect mixing of the sample-reagent zone. The higher values of flow rate more than 2.40 mL/min, led to increasing the analytical signal sensitivity due to the perfect mixing, as well as the peak is sharp and reliable whilst the dispersion decreases the height of analytical signal at the higher flow rate. Furthermore, the result also demonstrated that the optimal flow rate is 4.60 mL/min at the peak height of 10.90 cm.

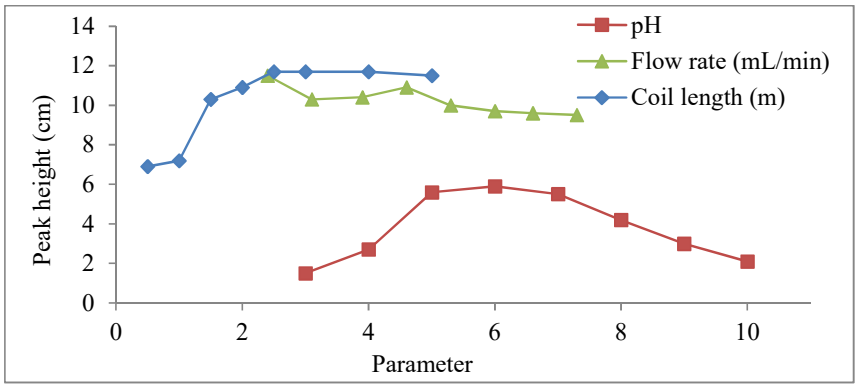

Figure 3. The effect of NCPR and Cu(II) concentration, and the effect of isoniazid and NCPR volume.

Effect of NCPR concentration

The effects of NCPR concentration on the reaction between isoniazid and Cu(II) were investigated in the range of 25-450 mg/L. The optimum conditions were found to be at a pH of 6 for the carrier, a flow rate of 5.3 mL/min, 110.50 µL of 10 mg/L isoniazid, 60 mg/L of Cu(II) as a carrier solution, 135.75 µL of NCPR, and a reaction coil of 2 m. The outcomes of the experiment (Figure 4) turned out that increasing the concentrations of the reagent from 25 to 300 mg/L increased the height of analytical signal from an initial value to 7.90 cm. It was also noted that the higher concentrations caused the response to reach an immutable value of 450 mg/L. As a result, 350 mg/L had been approved as the best concentration for the indirect interaction between Isoniazid and the Cu(II)-NCPR complex to give the highest response. That suggests the optimal concentration of the reagent to maximize the response lies in the range of 300-350 mg/L.

Effect of Cu(II) carrier stream concentration

The effect of Cu(II) carrier concentration on the reaction of the NCPR reagent was studied in the range of 5-120 mg/L. Optimal reaction conditions were identified as a pH 6.00 for the carrier solution and 350 mg/L of NCPR reagent. Additionally, the flow rate regulates at 5.30 mL/min, 110.50 µL of 10 mg/L isonazide, and 135.70 µL of 350 mg/L NCPR. Reaction coil was 2 m. The results of the study were presented in Figure 4. The reaction was found to be the most efficient when the Cu(II) carrier concentration was at a range of approximately 50-80 mg/L. The reaction time was reduced as the carrier concentration increased beyond this range while the efficiency of the reaction decreased. Furthermore, the reaction was found to be ineffective at concentrations of Cu(II) lower than 5 mg/L.

Effect of reaction coil length

The optimum length of the reaction coil for reacting Isoniazid solution with Cu(II)-NCPR was studied. The lengths of reaction coils which were used to conduct this study were 0.50, 1, 1.50, 2, 2.5, 3, 4 and 5 m after establish the optimal conditions included the pH = 6 of the carrier stream, the flow rate of 4.6 mL/min, 80 mg/L of Cu(II) as a carrier stream, 110.50 µL of 10 mg/L isoniazid solution, and 135.70 µL of 350 mg/L NCPR reagent. According to the findings (Figure 3), It was noted that the increasing coil length from 0.50 to 2.50 m promoted the sensitivity of the analytical

signal because these lengths of reaction coils allow perfect and appropriate mixing and caused a limited dispersion for the reaction components while the longer lengths of more than 2.50 cm demonstrated that there was no effect on the sample-reagent zone where the reaction between Isoniazid and Cu(II)-NCPR occurred. At the peak height of 11.70 cm, the reaction coil of the length of 3 m was manifested to be the optimum length of reaction coil.

Effect of isoniazid volume

The optimal Isoniazid solution volume was determined using the different loop lengths of the homemade flow injection valve in the range of 35.10–135.70 µL. The conditions represented by pH of 6.00 for the carrier stream, flow rate 4.6 mL/min, 80 mg/L Cu(II) as carrier solution, reaction coil length 3 m, 10 mg/L Isoniazid, and 135.70 µL of 350 mg/L NCPR reagent. The results (Figure 4) showed that the response first enhanced with increasing volume of isoniazid from 35.10 to 85.40 µL, then relative invariability was occurred at 110.50 µL whereas the height of peak was reduced with increasing volume of Isoniazid because higher volumes created dilution of Isoniazid within the volume of NCPR and carrier stream. The optimal volume of isoniazid was set at 85.40 µL with a peak height of 11.80 cm and a proved by sharp peak.

Effect of NCPR volume

The effect of NCPR volume on intentional analytical signal was in the range of 85.40–185.90 µL. Under optimal physical and chemical conditions characterized by a pH of 6.00 for the carrier stream, the flow rate was 4.60 mL/min, 80 mg/L copper(II) as carrier stream solution, the volume of 85.40 µL at the concentrations of 10 mg/L for the isoniazid, 350 mg/L for the NCPR reagent, and the length of the coil was 3 m. The outcomes (Figure 4) demonstrated that an increasing in peak height from 9.30 to 12.30 cm when the NCPR volume increased from 85.40 to 110.50 µL. There was decreasing in peak height to 9.20 cm due to the dilution factor, as the sample-reagent zone was dispersed over the considerable excess reagent volume. Hence the amount of 110.50 µL was represented the optimal volume of NCPR at the highest response value of 12.30 cm.

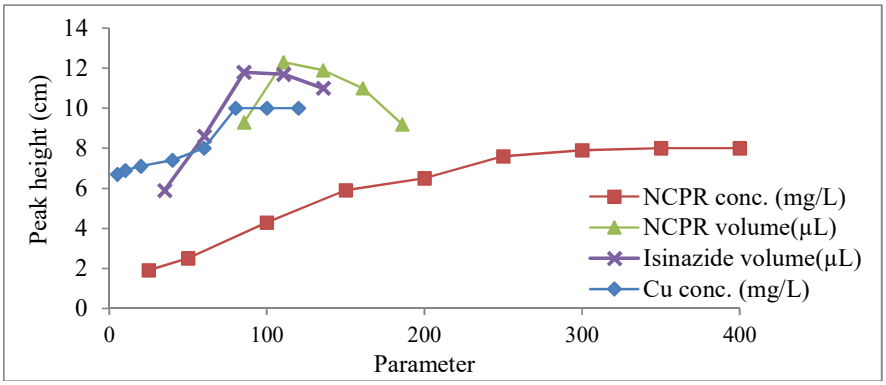

Figure 4. The effect of NCPR and Cu(II) concentration, and the effect of isoniazid and NCPR volume.

Calibration curve

A calibration curve was generated by performing the measurements under ideal physical and chemical conditions. The ideal parameters for the flow injection system to determine the

concentration of isoniazid are as follows: a carrier stream pH of 6.00, a flow rate of 4.60 mL/min, isoniazid sample and NCPR reagent volumes of 85.70 and 110.50 µL respectively, a reaction coil length of 3.00 m, a copper (II) concentration of 80 mg/L, and NCPR reagent concentration of 350 mg/L. The graph (Figure 5) was produced using serial concentrations of Isoniazid. The calibration curve demonstrated that linearity of Beer's Law (R^2) was over the range of 0.10–10.00 mg/L. This value indicates that the method is acceptable and has low errors over a wide estimation range. Table 1 shows the analytical data obtained from the curve.

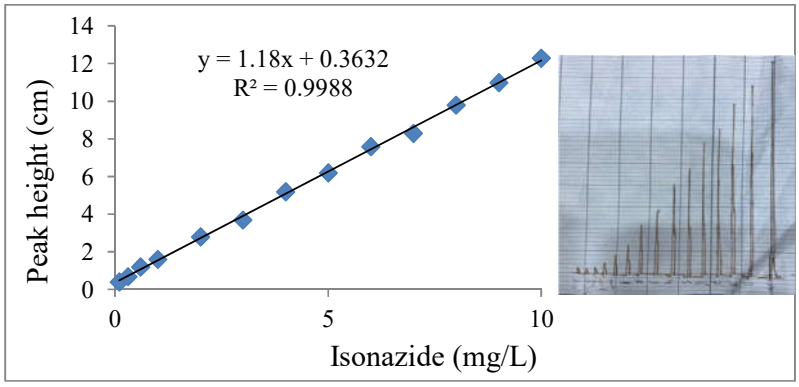

Figure 5. The calibration curve of Isoniazid drug.

Repeatability

The successive injections of the Isoniazid sample at least six times (n = 6) determined the precision and efficiency of the flow injection system by the so-called repeatability experiment. Six consecutive injections of Isoniazid solution at the concentrations of 0.60, 4.00, and 10.00 mg/L were utilized to examine the repeatability of injections after fixation of the optimal conditions. The acquired RSD values for the mentioned concentrations were 2.18, 0.49, and 0.22%, respectively. The results presented in Table 1 proved the efficiency and accuracy of the flow injection system design for Isoniazid determination.

Table 1. The repeatability and calibration curve data for determining isonazide by FIA system.

Calibration curve data		Repeatability (n = 6)			
Parameter	Value	Isonazide (mg/L)	0.40	4.00	10.00
Range(mg/L)	0.10-10.00	Peak height(cm)	1.20	5.20	12.30
Molar absorptivity (L/mol.cm)	56.68×10^{4}		1.20	5.20	12.35
Sandal sensitivity (µg/cm^2)	0.84×10^{-3}		1.15	5.25	12.30
Detection limit (mg/L)	0.073		1.20	5.25	12.35
Quantification limit (mg/L)	0.221		1.20	5.25	12.30
Intercept	36.32×10^{-2}		1.15	5.25	12.35
Slop	1.18	R.S.D$\times10^{-1}$	21.81	4.93	2.22
r^2	0.9988				

Dispersion coefficient (D)

The measurements of dispersion coefficient were performed at the optimal conditions to calculate the values of the factor D which is calculated by dividing H^o by H_{max} [25]. The first experiment was conducted outside the flow injection system through mixing the components of reaction in a beaker, afterwards the product was measured as a carrier stream solution, and the recorded signal refers to H^o which was found to be equal to 2.30 and 8.00 at concentrations of 0.60 and 4.00 ppm, respectively. The second measurement involved the injection of isoniazid and NCPR into their specified loops of the valve, with the stream solution of Cu(II) solution at pH 6.00 In this case, the recorded signal indicates H_{max} which was found to be equal to 1.20 and 5.20 at concentrations of 0.60 and 4.00 ppm, respectively. The dispersion coefficient values were 1.91 and 1.53 at concentrations of 0.60 and 4.00 ppm, respectively. The low dispersion coefficient (D) values lead to accurate results.

Dead volume

The distilled water was loaded in replace of the isoniazid reagent solution as the first step of the dead volume determination. The second step was loading the loop of NCPR with distilled water. It was found that no appearance of a peak in both steps, but when Isoniazid and NCPR were injected into their specific loops at the same time, the peak was evident. It´s worth recalling that the carrier solution in the previous two steps was Cu(II) solution at the optimal conditions. The result of the current study leads to the following conclusion, no volume of isoniazid solution sample or NCPR reagent solution was residual in the loops before performing the second analysis. Thus, the valve operated at zero dead volume. Several designs of home-produced valves achieved zero dead volume operating in preceding articles [21, 26].

Comparison of sampling throughput

The required time to inject the Isoniazid sample and NCPR reagent into the loops of the home-made valve was 21 seconds. The time required for the peak to appear starting from the baseline ascending to the maximum height, then descending repeatedly to the baseline was 36 seconds. Thus, the flow injection system's throughput was 63 samples per hour. Table 2 shows a comparison between the sampling rate for the flow injection system under study comparatively to other techniques' sampling rates for isoniazid determination.

Comparison of DL, QL, and range

By comparing with other techniques that determined isoniazid, using the merging-zone flow injection system for Isoniazid determination has several advantages according to the obtained low values of detection limit and quantification limit and the widely ranging concentration of isoniazid determination. Table 2 summarizes a comparison between the current analytical system for isoniazid determination and other methods.

Table 2. Comparison of the present FI system with previous methods of isoniazid determination

Technique	Sampling rate (h)	Ref.	Technique	DL (mg/L)	Range (mg/L)	Ref.
HPLC	6	27	Spectrophotometry	0.68	2.00-22.00	33
HPLC	12	28	Spectrophotometry	0.23	13.40-53.70	31
HPLC	16	29	Spectrophotometry	0.88	-	34
LC-MS	5	30	Electrochemical	0.20	1.37 - 480	35
Spectrophotometric	12	31	Electrochemical	0.03	1.37-10.90	36

Spectrophotometric	9	32	HPLC	0.16	0.50-20.00	37
FIA- amperometric	24	16	Voltammetry	0.25	0.68-241.30	7
FIA-fluorescence	50	17	LC-MS/MS	-	0.20-10.00	38
FIA-chemiluminescence	65	15	FIA-amperometric	0.35	0.68-68.50	16
merging-zone FIA	63	Present study	Merging-zone FIA	0.073	0.10 – 10.00	Present study

Comparison of sample volume

The merging-zone method is the leading flow injection technique for reducing the volume of sample and reagent, as it outperforms other techniques. Table 3 compares the utilized volume of isoniazid and reagent of various methods with the current merging-zone FIA method.

Table 3. Comparison the volume of isoniazid and reagent.

Technique	Isoniazid volume (µL)	Reagent volume (µL)	Ref.
VIS- Spectrophotometry	500	500	31
UV- Spectrophotometry	100	-	37
Polarography	100-1000	-	9
UV-VIS	1400	300	39
LC-MS/MS	950	-	38
HPLC-UV	100	-	8
Merging-zone FIA	85.70	110.50	Present study

Method validation [40]

When all experimental parameters of the flow injection technique as pH, flow rate, sample and reagent volumes, dead volume (residence time), and dispersion are well controlled and time-matched from the point of sample injection to the appearance of the peak, the method is highly selective.

A linear relationship was found between the peak heights and concentrations of isoniazid. In order to confirm the method linearity, one way ANOVA and student "t" test were conducted at the 95% confidence level. The statistical analysis data are shown in Table 4. The coefficient of determination (r^2) was higher than 0.9900 for Isoniazid, and no significant deviation of linearity was observed. The data shows that t_{cal} is greater than t_{tab} (95.79 >> 2.20), so the null hypothesis (H_0), when t_{tab} is greater than t_{cal} and r = 0, is rejected because r = 0.9994 and the alternative hypothesis (H_1) which indicates linearity between peak height (cm) and isoniazid concentration (mg/L). It's worth mentioning that the tabulated value for F_{tab} ($F_{11}^{1} = 4.747$) is lower than the value calculated for F-statistic (F_{stat} = 9220.02). The results demonstrated the linear case as shown in Table 4. Because of the significant difference at the 95% confidence interval between variance due to regression and variance due to error.

The results in Table 4 showed that RSD values decrease less than 3% for intraday analysis ensure the precision of the method. It has to be noted from the results that the relative standard deviation RSD% values decrease with concentrations higher than 0.60 mg/L to become less than one. Also, the relative error E_r% value decreases with the increase of the concentrations, the same mentioned concentrations, to become less than one. The recovery % values for isoniazid were over the range of 98.32–101.67%. Therefore, the results confirmed that the FIA method has sufficient accuracy and precision for isoniazid drug determination.

Table 4. ANOVA test and linear regression equation results of the formula y = bx + a.

Linear regression equation results of the formula y = bx + a						
Linear range µg/mL	No. of measurements (n)	Straight line equation $\hat{Y} = (a \pm s_a t) + (b \pm s_b)[X]$	Correlation coefficient (r)	Coefficient of determination (r^2)	Calculated t-value = $\frac{/r/\sqrt{n-2}}{\sqrt{1-r^2}}$	Tabulated t-value at 95% confidence interval
0.10-10.00	13	$\hat{Y}$ =0.03±0.44+0.11±23.07 [Isoniazid]	0.9994	0.9988	95.79	2.20
ANOVA test results for straight-line equation y = bx + a						
Source of variance	Sum of squares (SSq)	Degree of freedom (Df)	Mean squares (MSq)	F-statistic	F-tabulated	P > F
Due to regression	$\sum(\hat{Y}_i - \bar{Y})^2$ = 200.812	ν_1=1	S_1^2 =200.812	9220.02	4.74	0.00000
Due to error (about regression)	$\sum(Y_i - \hat{Y}_i)^2$ = 0.239	ν_2 (n-2)=11	S_0^2 =0.021			
Total	201.052	ν_{Total} (n-1)=12				
$\hat{Y}$= Estimated response, [isoniazid] = the concentration of isoniazid						

Application

Isoniazid drug was indirectly determined with uncolored Cu(II)-NCPR complex after acidifying the aqueous medium by the FI unit depending on the charge transfer reaction principle. Standard solutions were prepared at 0.60, 4.00, and 10.00 mg/L from isoniazid were analyzed. Table 5 demonstrates dependable results for the designed merging-zone flow injection unit based on RSD values of less than 3% and high agreement among the concentrations of isoniazid solutions that were acquired from the constructed calibration graph of the merging-zone FI system.

Table 5. Determination of isoniazid drug in standard solutions and tablets.

Taken concentration mg/L	Recovered concentration mg/L	R.S.D%	$E_r\% = \frac{(Tak. - Recov.)}{Tak.}$	Recovery%
Standard solutions of isoniazid				
0.60	0.59	2.54	1.67	98.32
4.00	3.99	0.57	0.25	99.75
10.00	10.02	0.24	-0.20	100.20
Isoniazid tablets preparations				
0.60	0.61	2.39	-1.67	101.67
4.00	4.02	0.55	-0.50	100.50
10.00	9.98	0.24	0.20	99.80

CONCLUSION

A convenient, rapid, simple, and inexpensive system was developed for Isoniazid determination by flow injection method using the merging zone technique. The rapidity of the system is evident with a sampling rate of 63 samples per hour. Simplicity of the system including isoniazid determination via indirect reaction between an isoniazid and Cu(II)-NCPR charge transfer

complex in an acidic medium. The new method had a high sampling rate compared to other reported techniques. The approach was very sensitive to low concentrations, with a detection limit of 0.073 and a broad range of 0.1 to 10. The advantages of the homemade valve were the low cost of raw materials, virtually no perpetuation, easy handling, and residual volume of zero value. The repeatability of the measurements for the flow injection system was of high precision at low RSD values less than 2.1%. Therefore, the results of this new system are reliable for the determination of isoniazid in aqueous solutions and tablets preparations in a wide concentration range at a maximum error of no more than 1.67%.

Recommendations

Utilizing the flow injection system for the determination of isoniazid in other pharmaceutical tablets and related drugs, human blood, urine samples, saliva samples and the metal ions which have important biological role (trace elements).

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