Muthana Saleh Mashkoor et al /J. Pharm. Sci. & Res. Vol. 10(2), 2018, 248-253

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

A New Design Micro Total Analysis System for Determination Hydrazine in Pharmaceutical Samples

Muthana Saleh Mashkoor[*], Ahmed Adnan Al-Khafagi[*], Dakhil Nassir Taha[**]
** Chemistry department-Faculty of Science /Kufa University, Iraq*
*** Chemistry department-Faculty of Science / Babylon University, Iraq.*

Abstract
The new microfluidic analysis system use to determine the hydrazine based on the reaction between Spectrophotometric reagent vanillin with sulfuric acid and hydrazine sulfate to form the hydrazone complex . Wavelength 410 nm , and give a linear range (7.685×10^{-6} - 5.379×10^{-4}) molar .The detection limit is 7.685×10^{-6} molar and the regression coefficient R^2 value is 0.9979. Reproducibility, SD, RSD, dead volume and interferences have been calculated. The reaction time, concentration of reagent and volume of sample has been optimized. The method has been successfully applied for the determination of hydrazine in water and pharmaceutical samples.
Key Words : Microfluidic analysis, Chip , Hydrazine , Vanillin , pharmaceutical samples.

1. INTRODUCTION

Hydrazine is an inorganic compound with the chemical formula N_2H_4 (likewise composed H_2NNH_2). A basic pnictogen hydride, it is a vapid combustible fluid with an alkali like scent. Hydrazine is very harmful and hazardously shaky unless dealt with in arrangement [1]. Hyd razine is predominantly utilized as a foaming specialist in planning polymer foams, however huge applications likewise incorporate its uses as a forerunner to polymerization impetuses and pharmaceuticals. Also, hydrazine is utilized as a part of different rocket energizes and to set up the gas antecedents utilized as a part of air packs.

Hydrazine is utilized inside both atomic and customary electrical power plant steam cycles as an oxygen scrounger to control groupings of broke down oxygen with an end goal to diminish erosion. Anhydrous hydrazine is destructive towards glass, in a way like hydrofluoric[2,3]. The flow analysis did in microfluidic system is now exceptionally progressed, yet expanding research movement is being centered around the plan of micro-flow system analysis or microfluidic [4] .The most punctual microfluidic gadgets exhibited that fluidic segments could be scaled down and coordinated together, prompting to the possibility that one could fit a whole lab on a chip or micro total analysis system (μTAS) [5] . Figure (1) shows the Microfluidic chip[6].

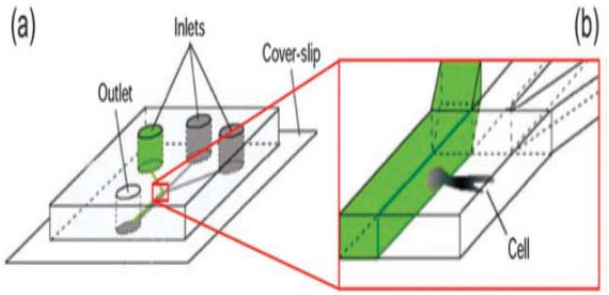


Fig. (1): (a and b) Chip channels are utilized to make laminar interfaces between fluids from various inlet .

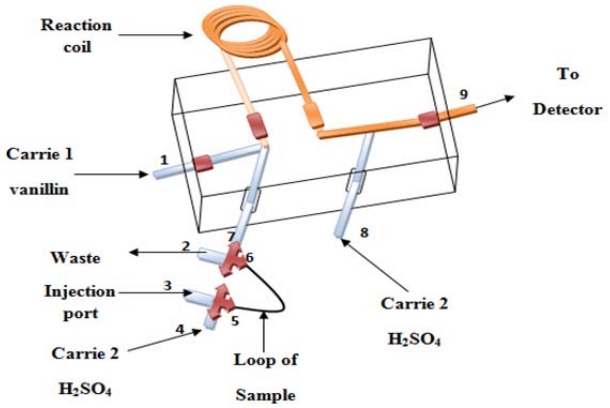
Many methods are used for the determination of hydrazine using different analytical techniques such as spectrofluorimetry[7] , voltammetry[8], titrimetry[9] , differential pulse voltametry[10], potentiometry[11], ion chromatography[12] , coulometry[13] and spectrophotometry[14]. Many techniques have been proposed for the determination of hydrazine in view of its fundamental character or reducing property[15].

2.EXPERIMENTAL

2.1. Apparatus

Spectrophotometer Labomed.inG single beam, Analytical balance sensitive Denver Instrument, USA, and a spectrophotometer Shimadzu UV-1700 spectrophotometer, peristaltic pump Germany, Ismatic, Recorder Pen Siemens C 1032,files Interaction with the radius of 0.5 mm, homemade microfluidic chip , pipes load of Teflon, flow cell volume of 450 μL.

2.2. Unit



Fig(2)

The various condition affecting the unit have been investigated and selected for a final method evaluation; the following results allow the operator to choose different operation conditions, many new designs of chips were developed by the researchers [16,26]. We have been designing new systems for microfluidic analysis, as in Fig.s 2 and 3.

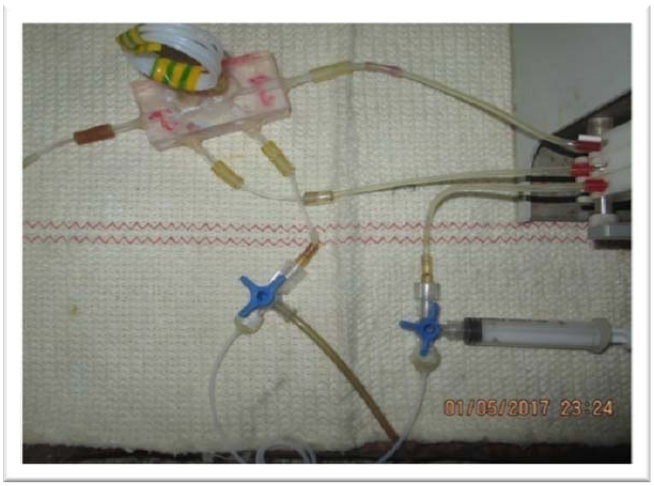


Fig. (3) : shows the injection stage in new chip

2.2. Material and reagents

A standard solution of 0.01M vanillin was prepared by dissolving weighed 7.6075 g of pure $C_8H_8O_3$ (Sigma Aldrich) was dissolved

in 50ml ethanol and transferred into a 500 mL volumetric flasksand diluted to the mark with distilled water. The solution was freshly prepared. Hydrazine prepared by dissolving weighed 0.6506 g of pureN_2H_4 • H_2SO_4(Sigma Aldrich in distilled water than transferred into a 500 mL volumetric flasks and diluted to the mark with distilled water , and serial dilutions with distilled water were made [27] . 1M H_2SO_4 was prepared by diluting 27.80 mL of 17.98 M of concentratedPhosphoric acid(BHD) with distilled water in 500 ml volumetric flasks, and then diluting to the other concentrations.

3.RESULTS AND DISCUSSION

3.1. Absorption spectra

The test solution was prepared In acidic solution, hydrazine reacts with 0.3 M sulfuric acid and 0.4 $g.L^{-1}$ vanillin at room temperature to form a yellow compound. The absorbance of the yellow compound was examined in the range of 350–800 nm by ultraviolet-visible spectrometer. The spectra obtained for the Hydrazine –Vanillin – sulfuric acid complexare presented in Figure (4) . The result showed that the maximum absorbance wavelength of the yellow compound is 410 nm, whereas the reagent shows maximum absorbance at 363nm. Therefore, 410nm was chosen as optimum wavelength for further studies.

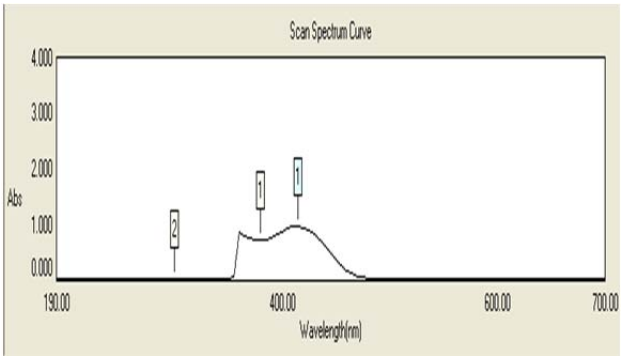


Fig. (4) : Absorbance spectrum of product

3.2. Study of optimum conditions

3.2.1. Physical Conditions

3.2.1.1. Effect of Reaction Coil Length

Study the effect of the Reaction Coil Length within the range (50-100) cm, and that the conditions of the system are Concentration of vanillin is 0.026 M ,Concentration of hydrazine sulfate is 4.611 x 10^{-4} M, Concentration of sulfuric acid is 0.2 M ,Volume of the sample is 235.650 µL loaded in the loop of sample (L_s), Flow rate for the three of carriers stream is 14.80 $ml.min^{-1}$,The length of the reaction coil is (50 – 100) cm .Results of the study showed that signal increases with the Reaction Coil Length until access to the 75 cm then begins to decline and thus the optimal Reaction Coil Length is to be 75 cm, as in the table (1) and figure (5) illustrates the results

3.2.1.2. Effect of Flow Rate

Study the effect of the flow rate within the range (3.30-6.60) ml / min, and that the conditions of the system are Concentration of vanillin is 0.026 M , Concentration of hydrazine sulfate is 4.611 x 10^{-4} M, Concentration of sulfuric acid is 0.2 M , Volume of the sample is 235.650 µL loaded in the loop of sample (L_s), Flow rate for the three of carriers stream is (3.30-6.60) $ml.min^{-1}$, The length of the reaction coil is 75 cm .Results of the study showed that the absorbance increased with increasing flow rate until access to the flow rate4.90 $ml.min.^{-1}$ then begins to decline, and this is the optimal flow rate is 4.90 $ml.min.^{-1}$, as in the table (2) and figure(6) illustrates the results

3.2.1.3. Effect of hydrazine sulfate volume

Study the effect of the hydrazine sulfate volume within the range (78.550-392.500) µL, and that the conditions of the system are Concentration of vanillin is 0.026 M , Concentration of hydrazine sulfate is 4.611 x 10^{-4} M, Concentration of sulfuric acid is 0.2 M , Volume of the sample is (78.550-392.500) µL loaded in the loop of sample (L_s), Flow rate for the three of carriers stream is 4.90$ml.min^{-1}$, The length of the reaction coil is 75 cm .Results of the study showed that signal increases with the volume of vanillin until access to the 314.200 µL then begins to decline and thus the optimal volume of vanillin is to be 314.200 µL, as in the table (3) and figure (7) illustrates the results.

Table (3-24):The effect of the change in the absorbance value with the change in Reaction Coil Length

Reaction Coil Length (cm0	Peak Height (mV)			Mean $\bar{Y}$	S.D	R.S.D
50.000	136.000	136.000	136.300	136.100	0.173	0.127
75.000	160.000	160.000	160.000	160.000	0.000	0.000
100.000	140.000	140.200	140.100	140.100	0.100	0.071

Table (2):The effect of the change in the absorbance value with the change in flow rate

Flow rate ml/min.	Peak Height (mV)			Mean $\bar{Y}$	S.D	R.S.D
3.300	312.000	312.000	312.400	312.133	0.230	0.073
4.900	328.000	328.000	328.000	328.000	0.000	0.000
6.600	280.000	280.000	279.700	279.900	0.173	0.061

Table (3):The effect of the change in the absorbance value with the change in volume of hydrazine sulfate

volume of hydrazine sulfate (µL)	Peak Height (mV)			Mean $\bar{Y}$	S.D	R.S.D
78.550	232.000	232.000	232.000	323.166	0.288	0.089
157.100	256.000	256.000	256.000	256.000	0.000	0.000
235.650	328.000	328.000	328.000	328.133	0.230	0.070
314.200	376.000	376.000	376.000	376.000	0.000	0.000
392.500	200.000	200.000	200.100	200.133	0.152	0.075

Table (4):The effect of the change in the absorbance value with the change in vanillin concentration

[Vanillin]	Peak Height (mV)			Mean Ȳ	S.D	R.S.D
$6.572x10^{-3}$	60.000	60.000	60.000	60.000	0.000	0.000
0.013	236.000	236.500	236.000	236.166	0.288	0.121
0.019	276.000	276.000	276.000	276.000	0.000	0.000
0.026	376.000	376.300	376.000	376.100	0.173	0.045
0.032	280.000	280.000	280.000	280.000	0.000	0.000

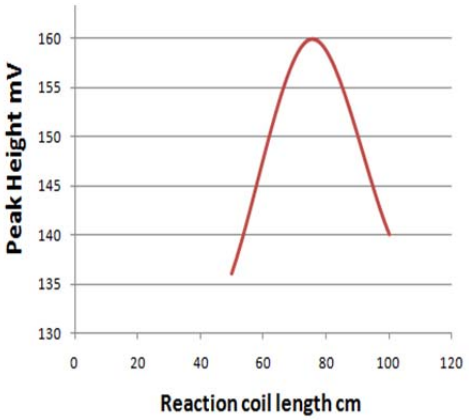


Fig.(5): Effect of Reaction Coil Length on the response

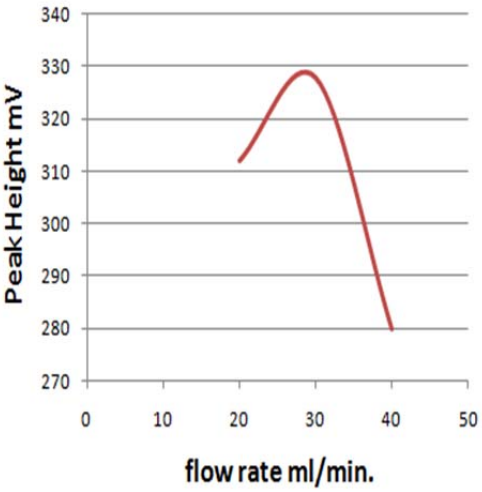


Fig. (6): Effect of flow rate on the response

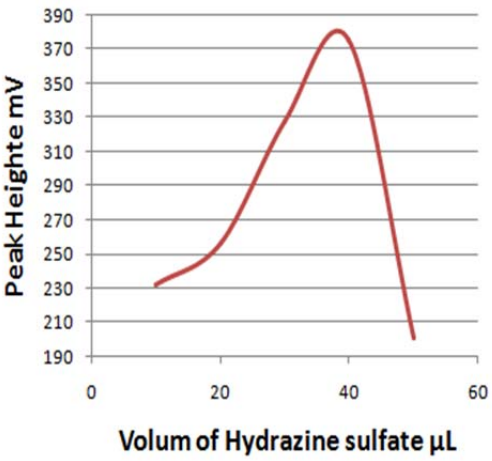


Fig. (7): Effect of hydrazine sulfate volume on the response

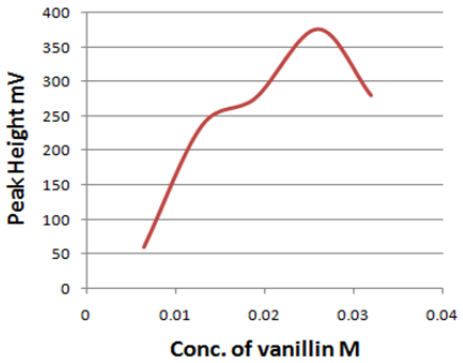


Fig. (8): Effect of vanillin concentration on the response

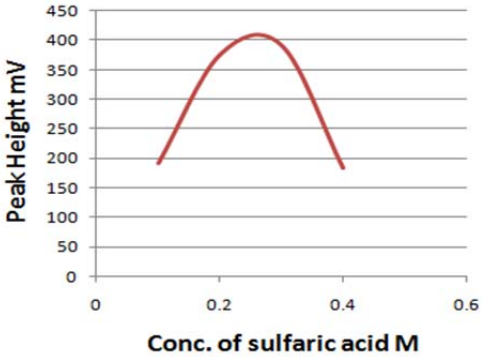


Fig. (9): Effect of H_2SO_4 concentration on the response

3.2.2. Chemical Conditions

3.2.2.1. Effect of Concentration of Vanillin :

The effect of vanillin concentration on the absorbance was studied in the range ($6.572 \times 10^{-3} - 0.032$) M, and that the conditions of the system are Concentration of vanillin is ($6.572 \times 10^{-3} - 0.032$) M , Concentration of hydrazine sulfate is 4.611×10^{-4} M, Concentration of sulfuric acid is 0.2 M , Volume of the sample is 314.200µL loaded in the loop of sample (L_s), Flow rate for the three of carriers stream is $4.90ml.min^{-1}$, The length of the reaction coil is 75 cm .Results of the study showed that signal increases with the concentration of vanillin until access to the 0.026 M then begins to decline and thus the optimal concentration of vanillin is to be 0.026 M, as in the table (4) and figure (8) illustrates the result

3.2.2.2. Effect of Concentration of sulfuric acid :

The effect of sulfuric acid concentration on the absorbance was studied in the range (0.1 – 0.4) M , and that the conditions of the system are Concentration of vanillin is 0.026 M , Concentration of hydrazine sulfate is 4.611×10^{-4}M, Concentration of sulfuric acid is (0.1 – 0.4) M, Volume of the sample is 314.200µL loaded in the loop of sample (L_s), Flow rate for the three of carriers stream is $4.90ml.min^{-1}$, The length of the reaction coil is 75 cm . Results of the study showed that signal increases with the concentration of sulfuric acid until access to the 0.3 M then begins to decline and thus the optimal concentration of sulfuric acid is to be 0.3 M, as in the table (5) and figure (9) illustrates the result

Table (5):The effect of the change in the absorbance value with the change in sulfuric acid concentration.

[H_2SO_4]	Peak Height (mV)			Mean $\bar{Y}$	S.D	R.S.D
0.1	192.000	192.000	192.200	192.066	0.011	0.005
0.2	376.000	376.200	376.100	376.100	0.100	0.026
0.3	392.000	392.000	392.200	392.066	0.115	0.029
0.4	184.100	184.100	184.000	184.066	0.057	0.030

Table (6): The reproducibility of responses

Conc. of Hydrazine sulfate (M)	Peak Height (mV) n=9									Mean $\bar{Y}$	SD	RSD%
3.94 X 10^{-4}	376.000	376.000	376.000	376.100	376.200	376.000	376.100	375.900	376.100	375.933	0.324	0.086

3.3. - Study of The dead volume

The dead volume must be studied to ensure accurate results obtained from this unit. Two experiments have been done, in the first water (H_2O) was injected into the loop instead of hydrazine sulfate and there was no response, in the second experiments water (H_2O) was passed as the carrier instead of reagent vanillin and there was no response. This shows the efficiency of the system, as illustrated in Figure (10).

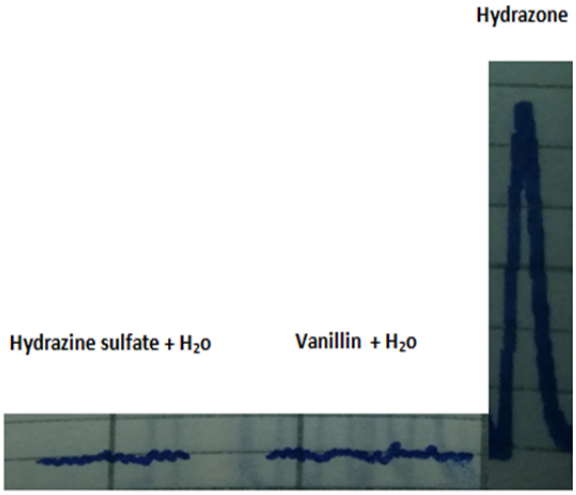


Fig. (10): Effect of dead volume on the response

3.4. Study of Reproducibility

The effect of reproducibility can be studied to know accuracy and precision of the method by using large number of repeated injections of the sample at least six injections . The concentration 3.94 x 10^{-4} M of hydrazine sulfate were used to study the reproducibility of measurements . Nine successive injections were measured under the optimum conditions the obtained results which are tabulated in table (6) and illustrated in figure (11) .

3.5. Study of Dispersion

To measure the dispersion value in different concentration of 8.544 x 10^{-5} and 1.643 x 10^{-4} molar hydrazine sulfate , two experiments were carried out. In the first experiment, after mixing of reactants (hydrazine sulfate and vanillin) that passes through manifold unit, giving a continuous response; this indicates the non - existence of a dispersion effect of convection or diffusion. This measurement represents (H^o). The second experiment includes injecting different concentration of hydrazine sulfate for microfluidic unit . The obtained value of this experiment represents the intensity response for sample injected (H^{max}) . This equation has been used to calculate dispersion (D) which was : D ° = H^o/H^{max}. These values fall in limit state of dispersion, Table (7) and Figure (12) illustrated the result.

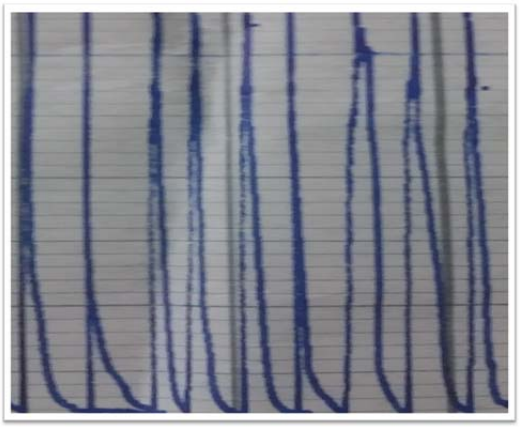


Fig. (11): The reproducibility of responses.

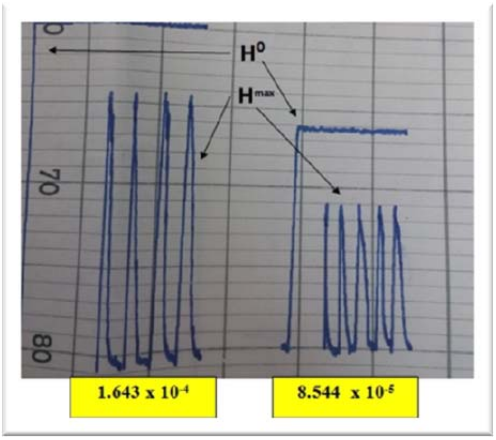


Fig.(12): The dispersion for the two concentrations

Table (7): Determination of dispersion.

Hydrazine sulfate Concentration M	Peak Height (mV)		Dispersion (D)
	H^o	H^{max}	
8.544 x 10^{-5}	140.000	92.000	1.521
1.643 x 10^{-4}	208.000	168.000	1.238

Table (8): Effect of the concentration of hydrazine sulfate with peak height.

Conc. Of hydrazine sulfate ppm	Conc. Of hydrazine sulfate M	Peak Height (mV)			Mean Ȳ	SD	RSD %
1	$7.685x10^{-6}$	16.000	16.000	16.100	16.033	0.057	0.355
5	$3.842x10^{-5}$	48.000	48.000	48.000	48.000	0.000	0.000
10	$7.685x10^{-5}$	88.000	88.200	88.100	88.100	0.000	0.000
20	$1.537x10^{-4}$	140.000	140.200	140.000	140.066	0.115	0.0821
30	$2.305x10^{-4}$	212.000	212.000	212.300	212.1	0.173	0.0815
40	$3.074x10^{-4}$	264.000	264.500	264.000	264.166	0.288	0.109
50	$3.842x10^{-4}$	308.000	308.000	308.000	308.000	0.000	0.000
60	$4.611x10^{-4}$	376.000	376.300	376.000	376.100	0.173	0.045
70	$5.379x10^{-4}$	428.000	428.000	428.000	428.000	0.000	0.000

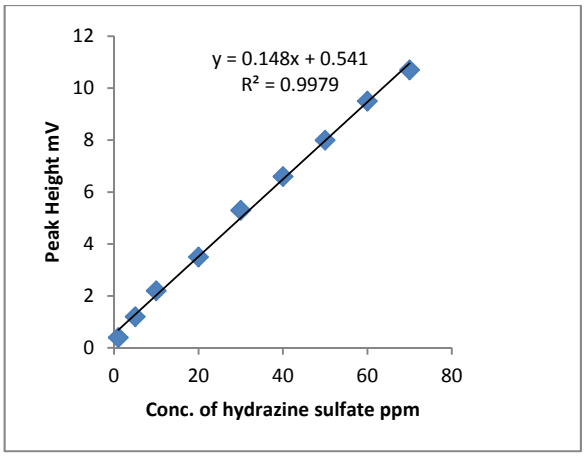


Fig. (13): The calibration graph for variable Hydrazine sulfate concentrations

3.6. Standard Calibration Graph For hydrazine sulfate

Calibration graph of hydrazine sulfate was constructed by preparing a series of solutions containing the range concentrations of it from 7.685 x 10^{-6} to 5.379 x 10^{-4} M under optimum conditions. The results are shown in table (8) and figure (13), Concentration of vanillin is 0.026 M , Concentration of hydrazine sulfate is (7.685 x 10^{-6} to 5.379 x 10^{-4}) M, Concentration of sulfuric acid is (0.3) M , Volume of the sample is 314.200µL loaded in the loop of sample (L_s), Flow rate for the three of carriers stream is 4.90ml.min^{-1} , The length of the reaction coil is 75 cm .

3.7. The sampling frequency

Sampling frequency calculation of the reaction rate after the fixing of the physical and chemical conditions and it calculates the time from the moment of injection and until appear of the maximum absorbance value of a concentration as he found that the time required for the appearance of this absorbance is (45) seconds and thus sampling frequency rate is (80) sample . h^{-1} .

3.8. Effects of interferences

To study the selectivity of the proposed methods, the effect of interferences ions on the 1.537 x 10^{-4} hydrazine sulfate was studied under the optimum condition . Table (9) shows the interferences and masking agent .

Results showed that most of the ions and compounds found in the environment does not interfere with the proposed method .

3.9. Pharmaceutical Applications

Solutions of pharmaceutical preparations were prepared. The proposed method was applied for the determination of Sulfanilamide , Ciprofloxacin , Ibuprofen and Isoniazid in tablet by analysis in triplicate of samples using the recommended procedure. The results are summarized in Table (10). The results obtained were accurate and reproducible. Table (11) the Optimum conditions and statistical treatments for the proposed method .

Table (9) :Effects of interferences

Interferences	Masking agent
NO^{2-}	sulfamic acid
Ca^{2+}, Ba^{2+}, Sr^{3+}, Pb^{2+}, Cr^{2+}, Cd^{2+}, Co^{2+}	10 % EDTA
Fe^{3+}	10% Potassium sodium tartrate

Table (10): Application of the proposed method for the determination of pharmaceutical preparations

Pharmaceutical preparation	Conc. M		E_{error}%	Rec%	RSD%
	Present	Found			
Sulfanilamide	$1.742x10^{-4}$	$1.752x10^{-4}$	0.574	100.574	0.000
	$3.484x10^{-4}$	$3.450x10^{-4}$	-0.975	99.025	0.057
Ciprofloxacin	$9.053x10^{-5}$	$9.041x10^{-5}$	-0.132	99.868	0.057
	$1.810x10^{-4}$	$1.800x10^{-4}$	-0.552	99.448	0.087
Ibuprofen	$1.454x10^{-4}$	$1.450x10^{-4}$	-0.275	99.725	0.000
	$2.908x10^{-4}$	$2.900x10^{-4}$	-0.275	99.725	0.000
Isoniazid	$2.187x10^{-4}$	$2.180x10^{-4}$	-0.320	99.68	0.015
	$4.375x10^{-4}$	$4.370x10^{-4}$	-0.114	99.886	0.000

Table (11): The Optimum conditions and statistical treatments for the proposed method

Parameters	Value
λ_{max}	410 nm
Flow rate	4.90mL/min
Reaction coil length	75.00 cm
Hydrazine sulfate volume	314.200 µL
Cons. of H_2SO_4	0.3 M
Cons. of vanillin	0.029 M
Linearity range	$7.685 \times 10^{-6} - 5.379 \times 10^{-4}$ M
Regression equation	y = 0.148x + 0.541
Regression coefficient ($R^{2)}$	0.9979
Correlation coefficient (R)	0.9968
$F_{Tab.}$	5.32
$F_{Stat.}$	2218.864
$T_{Tab.}$	2.365
$T_{Calcu.}$	627.619
Confidence limits	95%
LOD	7.685×10^{-6} M

CONCLUSIONS

The new microfluidic system to be efficient for the determination of hydrazine . this method selective, sensitive , rapidity, low cost , temperature independent, simplicity and applicable in the different samples.

ACKNOWLEDGEMENTS

The work was supported by the chemistry department-College of Science / Babylon University, Iraq and Chemistry department-College of Science / Kufa University, Iraq.

REFERENCES

[1] A.R. Slonim, J. B. Gisclard, Bulletin of Environmental Contamination &Toxicology,16, 3, 301-309,1976.
[2] A. Moliner, J. Street, "Decomposition of Hydrazine in Aqueous Solutions." ./.Environ. Qual. 18:483-487,(1989).
[3] M. R. Smith, R. L. Keys, G. L. Hillhouse, J. Am. Chem.Soc.111,8312-8314, 1989.
[4] N.L. Rosi, C.A. Mirkin, Chemical Reviews, 105,1547-1562, 2005.
[5] D. A. Skoog, D. M. West, F. J. Holler, and S. R. Crouch, "Fundamentals of Analytical Chemistry", 9th edition, brooks/cole, cengage learning, p. 168,2014.
[6] A. van den Berg and T. S. J. Lammerink, Topics in Current Chemistry, 194,22-25, 1998.
[7] A.Afkhami, A. R.Zarei, , Talanta, 62,. 559-565, 2004.
[8] A. Afkami, A. Afshar-e-Asl, AnalyticaChimicaActa, 419, 1, 101-106, 2000.
[9] Y.A. Gawargious, A. Beseda, , Talanta, 22, 9, 757-760, 1975.
[10] D. Jayasri, S.S. Narayanan, , Journal of Hazardous Materials, 144, 348-354, 2007.
[11] R. Shustina, J. H. Lesser, *J. Chromatogr. A*, 464, 28, 208-212, 1991.
[12] M. Sun, L. Bai, and D. Q. Liu, , *Journal of Pharmaceutical and Biomedical Analysis*,49, 2, 529-533, 2009.
[13] W. McBride, R. Henry, and S. Skolnik, Anal. Chem. 23, 6, 890-893, 1951.
[14] M. Yang, H.L. Li, *MicrochimicaActa*, 138, 1-2, 65-68, 2002.
[15] R. Kaveeshwar , V. K. Gupta, Fresenius J. Anal. Chem.,*344,* 114-17, 1992.
[16] H. JoB, J. Moorthy, and Beebe D. J., Kluwer Academic Publishers, Dordrecht, The Netherlands, 335-338, 2000.
[17] M. C. Potter, D. C. Wiggert, "Mechanics of Fluids", 3rd ed., Brooks/Cole: Pacific Grove, CA., 2002.
[18] G. A. Posthuma-Trumpie, J. Korf and A. van Amerongen, Anal. Bioanal. Chem., 393, 569–582,2009.
[19] D. N. Taha AL-Zerkany , Z. S. Obaid , RJPBCS, 7(6) , 2241, 2016.
[20] G. J. Abbas, M.S. Mashkour, D. N. Taha AL-Zerkany , Journal of Purity, Utility Reaction and Environment , 5 ,4, 92-105 , 2016.
[21] D. N. Taha AL-Zerkany , I.S. Samaka, J. Oleo Sci., 61,12,729-739,2012.
[22] D. N. Taha AL-Zerkany , I.S. Samaka, L.A. Mohammed, Journal of Asian Scientific Research 3, 9: 945-955, 2013 .
[23] N.A. Naser, K.H. Kadim, D. N. Taha AL-Zerkany , J. Oleo Sci. , 61,7: 387-392 , 2012.
[24] A. S. Farhood, International Journal of ChemTech Research,10(2): 854-861, 2017.
[25] L. A. Mohammed , International Journal of ChemTech Research,10(2): 829-836, 2017.
[26] A. S. Farhood, L. A. Mohammed, M. ALI AND F. F. ALI, *Orient. J. Chem.*,33(2), 944- 950 2017
[27] L. Yu, X. Zhang and L. Yu , Communications in Information Science and Management Engineering , 4, 1, 13-18, 2014.