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New Flow Injection Designed Unit for the Determination of Dapsone in some Pharmaceutical Products

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Abstract: A new, simple and rapid method is reported for the accurate and precision spectrophotometric determination of Dapsone using a new flow injection designed unit. The method included the designing a new valve. The proposed method is based on the reaction between Dapson and 1, 2-naphthoquine-4-sulfonate(NQS) at alkaline medium to form colored adduct, exhibiting maximum absorption (λ_{max}) at 485 nm. The various parameters, physical and chemical, affecting the determination have been investigated such as flow rate, reaction coil, volume of reagent (NQS), volume of sample, pH and concentration of (NQS). The linear regression equation of the calibration graph is A=0.0016+0.0708C (µg/mL), with a linear regression correlation coefficient of 0.9989, the detection limit is 5 µg/mL .The method has been successfully applied to the determination of Dapsone in pharmaceutical formulation.
Key words: Flow injection analysis, Dapsone, 1, 2-naphthoquine-4-sulfonate, pharmaceutical formulation.

Introduction

Dapsone, chemically 4,4_-diamino diphenylsulfone, has been known as an important anti-leprotic drug in addition to its anti-malarial properties. In view of its pharmacological importance, considerable work has been done for its detection and quantification. Various analytical techniques have been employed for the determination of dapsone in serum, plasma, urine, pharmaceutical dosage, and so on, such as dead-stop titration[1,2], micellarelectroki-netic capillary chromatography[3], capillary supercritical fluid chromatography[4], GC–MS[5], TLC[6], HPLC [7], spectrofluorimetry[8], and spectrophotometry[9-11].

This paper reports a rapid and selective flow-injection spectrophotometric analysis (FIA)method for determining the content of dapsone in some pharmaceutical products., which is based on a replace reaction[11], i.e. sodium1,2-naphthoquinone-4-sulfonic reacts with amino of dapsone molecule to form colored compound. λ_{max} of the compound is at 485 nm. The reaction equation reads as follows:

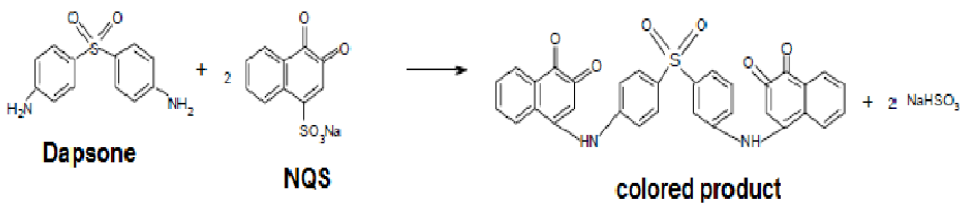

Fig. 1: The reaction equation between Dapsone and NQS.

The maximum absorption wavelength of the product was at 485 nm, which shifted185 nm to long wave compared to the maximum absorption wavelength of dapsone (300 nm) [12].

What is more, because dapsone can be determined in the range of visible light, much potential interference may be avoided in the determination of dapsone of biological materials and hem analysis. The principal advantage of our method is that the maximum absorption wavelength of dapsone shifted to the range of visible light from the range of ultraviolet light so that dapsone may be determined in the range of visible light. In addition, the method is simple and can be used for determining dapsone in the tablet.

Experimental

Instrumentation

The schematic diagram of FIA system is illustrated in Fig.2. It consisted from right to left- of peristaltic pump (ismatic , Germany), the homemade 4-port valve ,many new designs of valves were developed by the reaserchers[13-17]. UV-Visible spectrophotometer (Apple), flow cell (450 µL, Helmma), Kompensograph (C1032 Siemens, Germany) , and Teflon tubing throughout of i.d. 1mm is used.

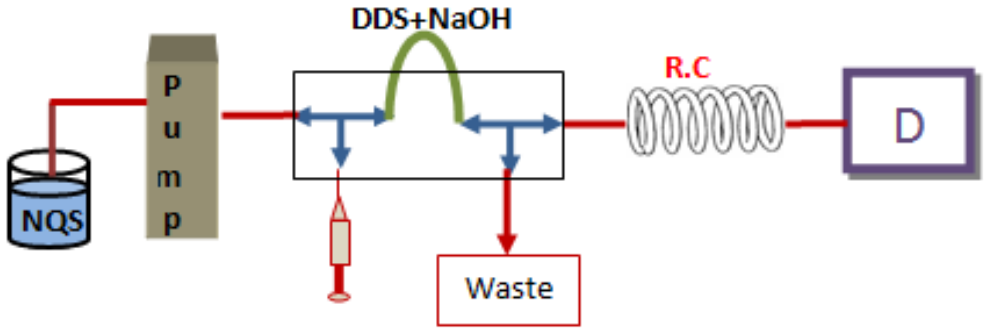

Fig.2: The schematic diagram of new FIA system .

Material and reagents

A standard solution of 500 µg.mL^{-1}Dapsonewas prepared by dissolving 0.05 g of Dapsone in 100 ml of (0.01 M) sodium hydroxide (NaOH) in calibrated flask, sodium-1, 2-naphthoquinone-4-sulfonate (NQS) solution of 0.03% (w/v) was prepared by dissolving 0.3 g in distilled water, transferred into a 1000 mL volumetric flask and diluted to the mark with distilled water and mixed well.

Results and discussion

Absorption spectra

As can be seen (Fig. 3), the maximum absorption wavelength of the colored product was at 485 nm. An excellent linear relationship existed between the absorbance and the concentration of dapsone(R = 0.999). In addition, the dapsone solution is colorless), the maximum absorption wavelength of Dapsone is at 300 nm, it has no absorption in the range of 340–485 nm , and its maximum absorption wavelength ofNQS was(360 nm) , therefore, dapsone can be determined conveniently at 485 nm against a reagent blank.

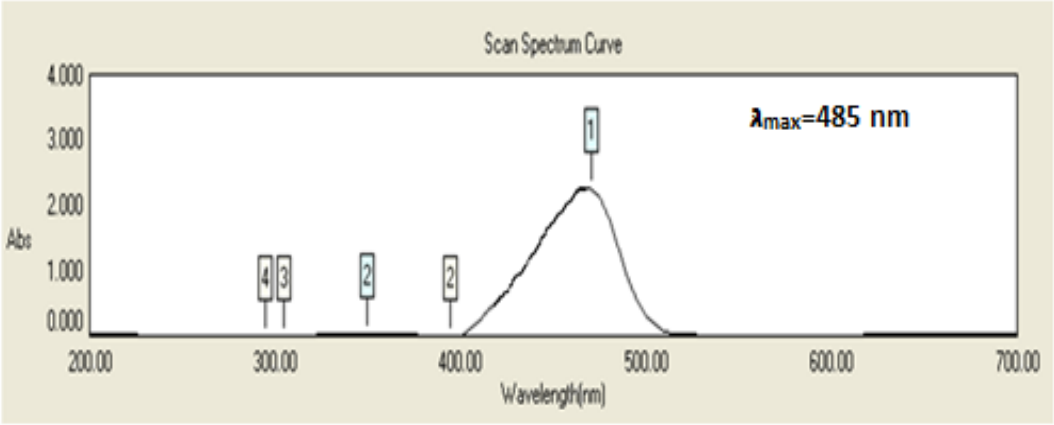

Fig.3: The UV-Visible spectrum of the product (Dapson- NQS).

Study of optimum conditions

Chemical conditions

After choosing the best design of FIA manifold (Fig.2). It was found that the best design with higher response by using (NQS) as a carrier in the flow injection designed unit. The effect of (NQS) concentration was studied. The range of (NQS) concentrations were from (0.01- 0.04) % , the flow rate was 5.25 ml.min^{-1}, the reaction coil length 60 cm , and at the concentration 100 µg.mL^{-1} of Dapsone . The preferred response was at the concentration 0.03% according to the results in table 1 and Fig. 4.

Table 1: Effect of the reagent concentration [NQS] on the peak height.

[NQS] %	Peak Height(cm)			Mean $\bar{Y}$	S.D	R.S.D%
0.01	2.80	2.90	2.90	2.87	0.0577	2.0140
0.02	3.60	3.60	3.60	3.60	0.0000	0.0000
0.03	5.10	5.10	5.10	5.10	0.0000	0.0000
0.04	3.50	3.55	3.55	3.53	0.0289	0.8170

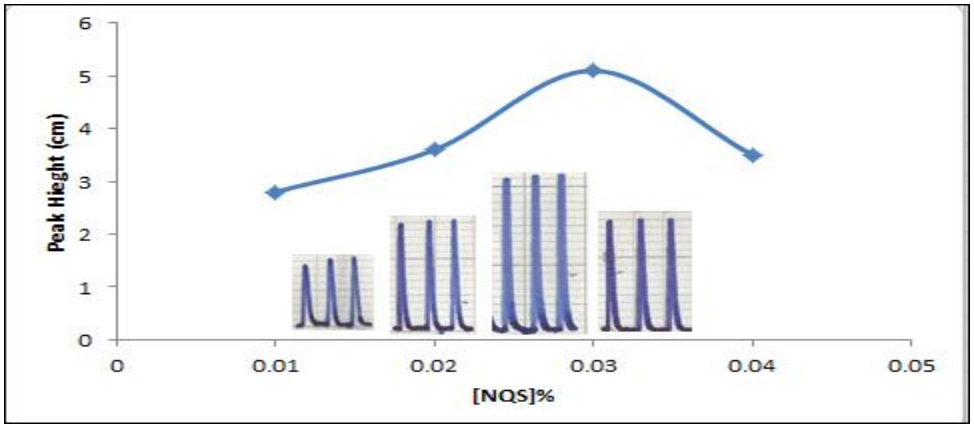

Fig. 4: Effect of NQS concentration on the response.

The effect of NaOH concentration (used for dissolving of Dapsone after standardization) was studied also and the range of concentration which gave the best response was 0.01 mol.L^{-1} , as shown in table:2 and Fig. 5.

Table 2: Effect of NaOH concentration on the peak height.

Conc. NaOH (mol / L)	Peak Height (cm)			Mean $\bar{Y}$	S.D	R.S.D%
0.001	1.800	1.800	1.800	1.800	0.0000	0.0000
0.005	2.400	2.420	2.420	2.413	0.0115	0.4785
0.010	5.300	5.300	5.300	5.300	0.0000	0.0000
0.020	4.900	4.900	4.880	4.893	0.0115	0.2359

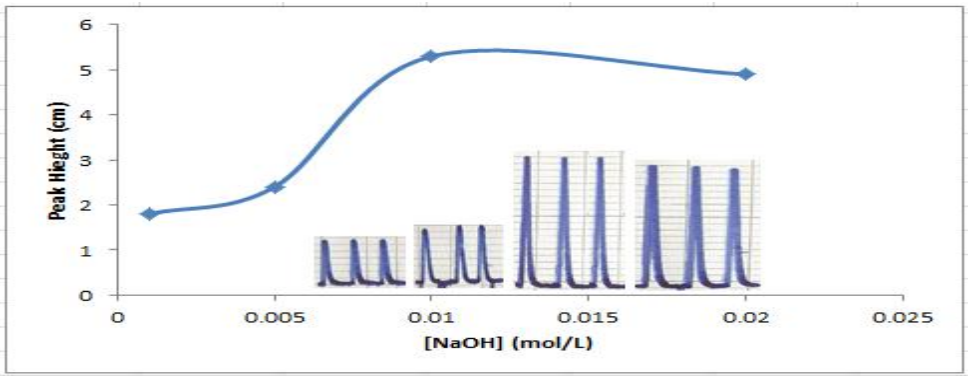

Fig. 5: Effect of NaOH concentration on the response

Physical parameters

Effect of flow rate

The effect of the flow rate on the peak height was studied in the range of (1.25-4.75) mL.min^{-1} (Table 3 and Fig. 6). Lower flow rate cause doublet peaks, possibly due to the fact that the carrier solution did not sufficiently disperse into the middle of the sample zone[18]. On other hand, the peak height decreased with the increasing flow rate[19]. Taking into consideration of the stability of the pump, peak shape and sampling time, the flow rate of the carrier solution was adjusted to 3.27 mL.min^{-1} for subsequent measurement due to highest sensitivity.

Table 3: Effect of the flow rate on the peak height.

Speed of pump round.min^{-1}	Flow rate mL.min^{-1}	Peak height (cm)			Mean $\bar{Y}$	S.D	R.S.D%
20	1.50	3.20	3.15	3.20	3.18	0.0288	0.9068
30	1.75	4.10	4.10	4.10	4.10	0.0000	0.0000
40	2.50	5.00	5.00	5.00	5.00	0.0000	0.0000
50	3.27	5.50	5.50	5.48	5.49	0.0115	0.2102
60	3.50	4.90	4.90	4.88	4.89	0.0115	0.2359
70	4.25	4.20	4.20	4.20	4.20	0.0000	0.0000
80	4.75	4.00	4.00	4.00	4.00	0.0000	0.0000

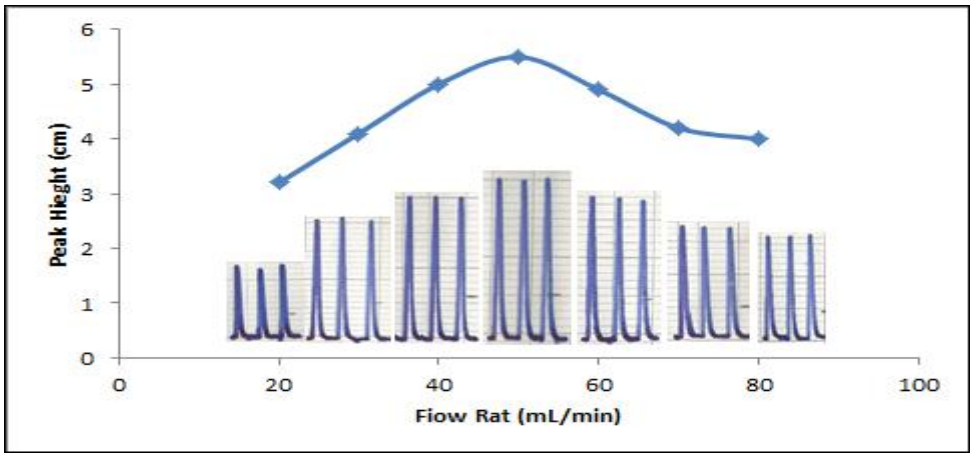

Fig. 6: Effect of flow rate (mL.min^{-1}) on the response (cm)

Effect of reaction coil length

This study was using different lengths of reaction coils (60 – 175) cm , at the flow rate was 5.25 ml.min^{-1}, the concentrations 100 µg.mL^{-1} of Dapsone , It was noticed that there is an increase in the sensitivity of response at 125 cm of reaction coil length. According to the results in table 4 and Fig. 7.

Table 4 : The relationship between reaction coil length (cm) and the response (cm)

Reaction coil length (cm)	Peak Height (cm)			Mean Ȳ	S.D	R.S.D %
without	2.4	2.4	2.4	2.4	0.0	0.0
60	5.7	5.7	5.7	5.7	0.0	0.0
100	6.5	6.5	6.5	6.5	0.0	0.0
125	7.4	7.4	7.4	7.4	0.0	0.0
175	7.2	7.2	7.2	7.2	0.0	0.0

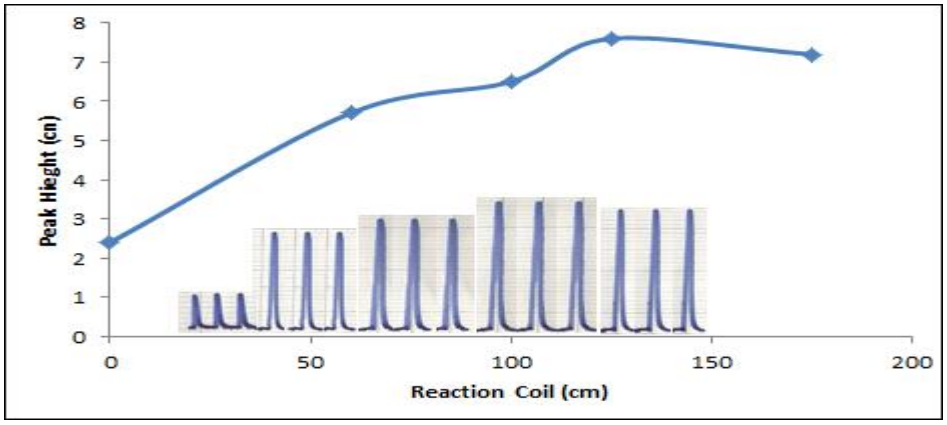

Fig. 7: The effect of reaction coil length on the response sensitivity

Effect of Dapsone volume

The influence of the sample volume on the peak height was investigated by injecting different volumes(117.86– 314.28) µL. The peak height increased to the maximum at 314 µL and after that volume, the peak height decreased. 196.25 µL was chosen for further work (Table 5 and Fig.8).

Table 5: The relationship between Dapsone volume (µL) and the response (cm)

L of PA (cm)	The volume of Dapsone (µL)	Peak Height (cm)			Mean $\bar{Y}$	S.D	R.S.D%
15	117.75	4.50	4.50	4.50	4.50	0.0000	0.0000
20	157.00	6.60	6.62	6.60	6.61	0.0115	0.2059
25	196.25	7.50	7.48	7.48	7.49	0.0115	0.1807
30	235.50	6.40	6.40	6.40	6.40	0.0000	0.0000
40	314.28	5.60	5.60	5.58	5.59	0.0115	0.2513

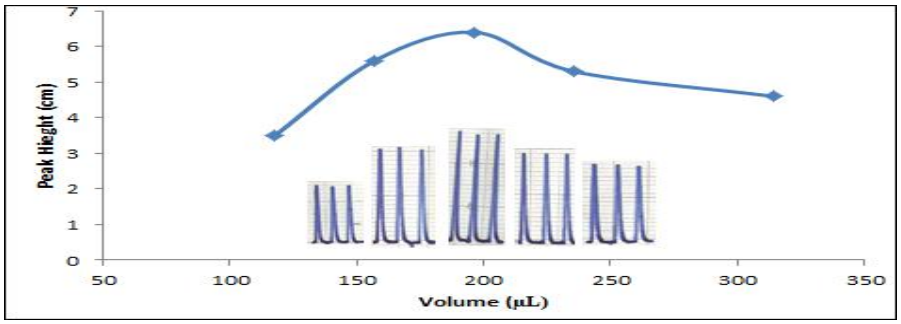

Fig. 8: Effect of Dapsone volume on the response

Study of the dead volume:

To ensure accurate results obtained from this unit, we must be studied. Wherever, the dead volume is small it means a best results. Two experiments were done, in the first the water (H_2O) was injected in the loop instead of Dapsone and there was no response ,in the second experiments the water (H_2O) was passed as the carrier instead of reagent [NQS] and there was no response. This shows the efficiency of the system, as illustrated in Fig. 9.

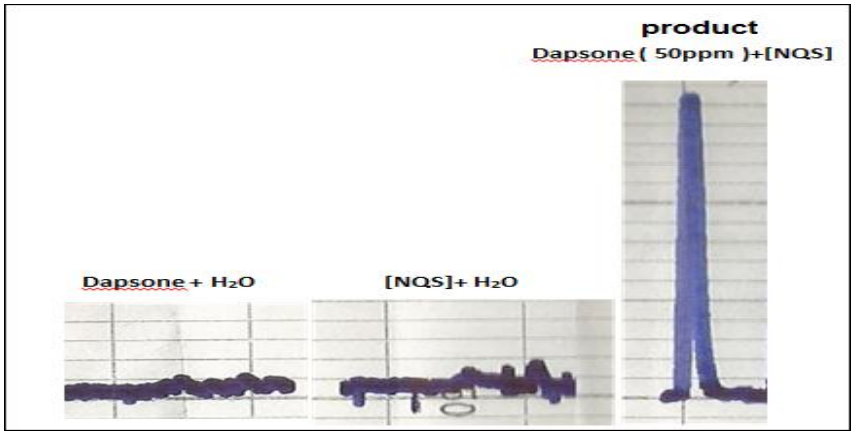

Fig. 9: Dead volume.

Calibration curve in FIA method:

Calibration curve was prepared at the optimum conditions of complexity and change through Dapsone concentration the result show in Table 7 and Fig.13. The calibration curve is linear in the range of 5 -110 mg. L^{-1}. The detection limit is (5) mg.L^{-1}.

Table 6 : Effect of Dapsone concentration on the response (Calibration graph).

Conc. of Dapsone. µg. mL^{-1}	Peak Height (cm)			Mean $\bar{Y}$	S.D	R.S.D %
5	0.20	0.20	0.20	0.20	0.0000	0.0000
10	0.90	0.90	0.90	0.90	0.0000	0.0000
20	1.60	1.60	1.58	1.59	0.0141	0.8876
30	2.40	2.40	2.40	2.40	0.0000	0.0000
40	3.20	3.20	3.15	3.18	0.0353	1.1106
50	4.10	4.00	4.10	4.07	0.0000	0.0000
60	4.90	4.90	4.80	4.87	0.0707	1.4530
70	5.60	5.60	5.50	5.57	0.0707	1.2703
80	6.40	6.40	6.30	6.37	0.0707	1.1106
90	7.10	7.10	7.10	7.10	0.0000	0.0000
100	7.90	7.90	7.90	7.90	0.0000	0.0000
110	8.80	8.80	8.80	8.80	0.0000	0.0000

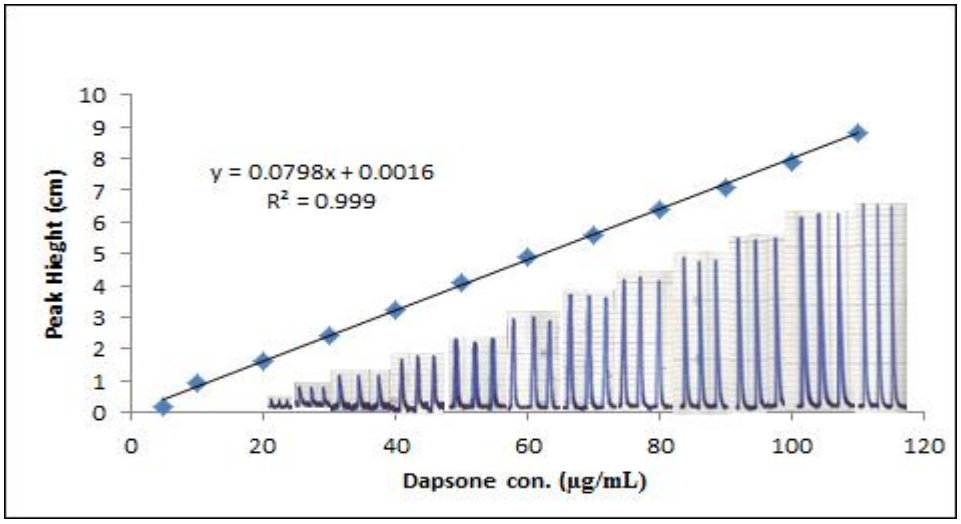

Fig. 10: The calibration graph for variable Dapsone concentrations.

Reproducibility

For study Prevision range and effective method in determination of Dapsone was studied through reproducibility injection and measure for multitudes, using 40 ppm and 80 ppm concentration of Dapsone, so that amount of standard deviation for (40 mg/L) and (80 mg/L) was n = 6 and amount of relative standard deviation was 0.8111% for accuracy and effective system for determination of Dapsone. The results are shown in Table 7 and Fig. 11.

Table 7 : The repeatability of responses

Conc. of Dapsone µg.mL^{-1}	Peak Height (cm) n=6						Mean $\bar{Y}$	S.D	R.S.D %
40	3.30	3.30	3.30	3.30	3.30	3.30	3.30	0.0000	0.0000
80	6.30	6.40	6.40	6.30	6.40	6.40	6.47	0.0516	0.8111

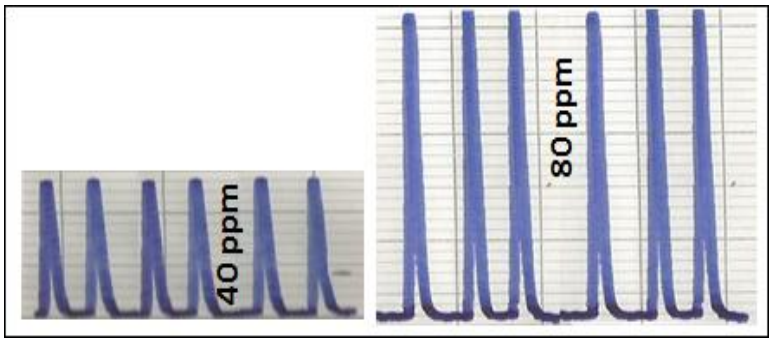

Fig. 11: The repeatability of responses.

Determination of dispersion

The dispersion is one of the important physical phenomenons. It is defined as the ratio of the concentration before and after the dispersion process has taken place in those elements of fluid, the coefficient of dispersion is the most popular experimental parameter able to measure the degree of dilution of the sample from injection point until its passage before the detector20-25.

expressed by : $D = H^o / H_{max}$

Where:

H^o : peak height without dilution outside the FIA system

H_{max} : peak height with dilution inside the FIA system

Dispersion was 1.38 , 1.43 for the two concentration 50 and 80 µg.mL^{-1} of Dapsone respectively . This values represent limit dispersion in the manifold. According to the result in table 8 and fig.12 .

Table 8: Determination of dispersion.

Dapsone Concentration (ppm)	**Response (cm)**		**Dispersion (D)**
	H_{max}	**H^o**	
50	4.50	6.20	1.38
80	6.50	9.30	1.43

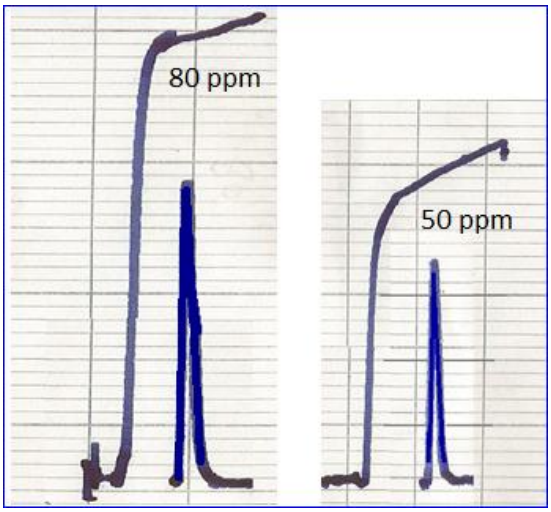

Fig.12: The dispertion for the two concentrations 50 ppm and 80 ppm.

Determination of Dapsone in pharmaceutical product.

The proposed method was successfully applied for the analysis of Dapsone in tablet and prepared solution. The results obtained show good agreement with the labeled information given by the manufacturer, and good agreement between the taken concentration and the recovered amounts of Dapsone, as shown above in table 9.

Table 9: Dapsone content found in the prepared solution and analyzed capsule.

Sample	Taken concentration $\mu g.mL^{-1}$	Found concentration $\mu g.mL^{-1}$	S.D	R.S.D %
Prepared solution	20	20	0.00	0.00
	70	70	0.00	0.00
Tablet	20	20	0.00	0.00
	70	69	0.71	1.02

Conclusion

The results presented in this paper demonstrated clearly that dapsone could be determined by the new FIA system. The results obtained by this method are selective, lowcost, rapidity and simplicity. The principal advantage of the proposed method can be used for the determination of dapsone in the tablet of dapsone.

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