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Determination of Lisinopril by Flow Injection Analysis Technique

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Abstract: The aim of this research is to design a new flow injection analysis unit for the determination of lisinopril through its reaction with NQS at $\bullet_{max}$ 550 nm. The method involves manufacturing of new valve from a cheap material which can be used in the chemical reactions. The optimum conditions such as sample volume, reagent volume, reagent concentration, flow rate and reaction coil length were studied. Beer's law is obeyed over the concentration range (5-60 ppm) with linearity coefficient (R^2) of 0.9968. The relative standard deviation was 1.094% for 20 ppm lisinopril solution (n = 3). The method was successfully applied for the determination of lisinopril in pharmaceutical formulations and aqueous solution.

Key words: Stop flow technique, lisinopril, merging zone, NQS, sample volume, reagent volume

INTRODUCTION

FIA is defined as "information gathering from a concentration gradient formed from an injected, well defined zone of a fluid, dispersed into a continuous unsegmented stream of a carrier (Meyers *et al*., 1970). This technique is used to determine different samples such as trace acids (Taha, 2002), iron (II) (Farhood *et al*., 2017 a, b), aniline blue and malachite green dye (Majeed *et al*., 2017). Lisinopril (LNP, Fig. 1) (S)-1-(N2-(1-carboxy-3-phenylpropyl)-L-lysyl)-L-proline dihydrate is an angiotensin converting enzyme inhibitor used in the treatment of hyper tension and heart failure. Lisinopril is white crystalline powder, many melt in water (American Society of Health-system, US Pharmacopeia Staff, 2008).

It determined through various spectrophotometric methods based on reaction between lisinopril and different reagents (Jamakhandi *et al*., 2011a, b; Cakar and Popovic, 2012; Ali and Elbashi, 2013; Raghubabu and Sandhyarani, 2015; Shraitah and Okdeh, 2016; Zaheer *et al*., 2016). Other techniques such as potentiometric methods (Razak *et al*., 2003) and chromatographic methods (Wagh *et al*., 2012; Sultana *et al*., 2013). The proposed method is based on the reaction of lisinopril with NQS in the presence of amonium hydroxide to form reaction which shows an absorption maximum at 550 nm Fig. 2.

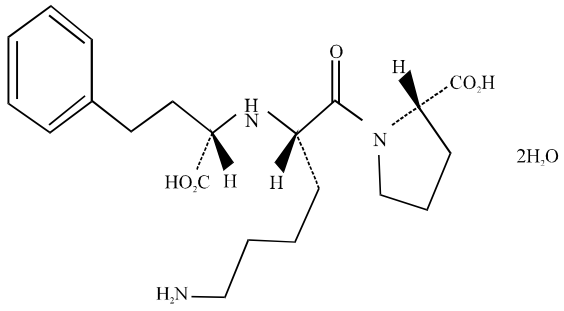

Fig. 1: Structure of lisinopril

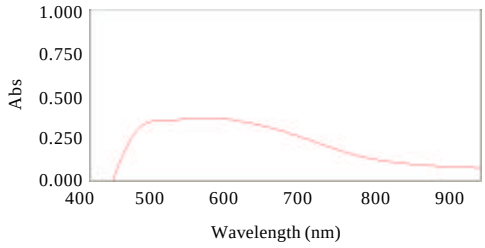

Fig. 2: The spectra of the mixture; Scan spectrum curve

MATERIALS AND METHODS

Apparatus: All spectral and absorbance measurements were achieved on a UV-visible single beam Labomed.inG (Japan) and double beam (T80). In FIA, a flow cell with 450 μL internal volume and 1 cm path length was utilized

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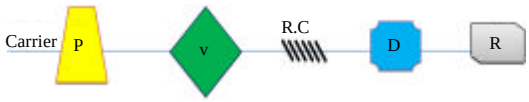

Fig. 3: Manifold employed for FIA-spectrophotometric determination of lisinopril where, V. Injection valve; RC. Reaction Coil; P. Peristaltic pump; R. Recorder and D. Detector

for the absorbance measurements. A one-channel man fold Fig. 2 was employed for the FIA spectrophotometric determination of lisinopril. A peristaltic pump (Ismatec Germany) was used to transport the carries solutions. injection valve was to provide appropriate injection volumes of solutions. Flexible teflon tubing of (1 mm) internal diameter was used for the peristaltic pump. Reaction Coil (RC) was of teflon and glass with internal diameter of (1 mm). Balance was utilized to weight the material and x-t chart graph recorder (Siemens Germany) was used for recording the peaks.

Preparation of standard solution

Materials: Freshly stock solutions (50 ppm) of lisinopril were prepared by weight (0.0025 g) from lisinopril and diluting with a distilled water to the mark in a weighing (50 mL) volumetric flask. Working solutions were prepared by diluting the above solution by distilled water.

Freshly (0.01 w/v%) of (NQS) was prepared by dissolving (0.005 g) in (50 mL) distilled water with continuous stir and concussion. The other solutions were prepared by diluting of the above stock solution. The 20% v/v of (NH_4OH) was prepared by diluting (20 mL) from ammonium hydroxide with distilled water in a (100 mL) volumetric flask. The other solutions were prepared by dilution of the above stock solution.

Pharmaceutical preparations

Tablets: Ten tablets of lisinopril were weighed and finally powdered. A weighed amount of the powder equivalent to 0.02 g of the pure lisinopril was dissolved in hot distilled water and made up to 100 mL in volumetric flask. The resulting solution was filtered off and was treated as described under recommended procedure.

Procedure for the FIA method: Samples containing different concentrations of lisinopril were prepared by simple dilution with distilled water of the freshly stock solution (100 μg/mL). The FIA spectrophotometric measurements were carried out using the manifold shown in Fig. 3 employing 196.25 μL of lisinopril, (235.5 μL) of NQS and (157 μL) of base with a flow rate of (12.3 mL/min) and reaction coil 100 cm. This reaction occurs at $\bullet_{max}$.

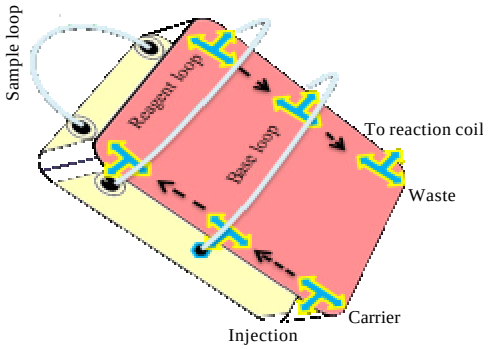

Fig. 4: The valve

Table 1: Effect of order of addition

Order of addition	Response (cm)
(NQS+Lis)+B	1.1
(NQS+B)+Lis	0.9
(Lis+NQS)+B	1.0

Table 2: Effect of mixing time of reaction

Mixing time	-------Peak height (cm)------			Means	SD	RSD (%)
0	1.100	1.250	1.000	1.116	0.125	11.200
1	1.650	1.650	1.500	1.600	0.086	5.375
3	2.000	2.000	2.000	2.000	0.000	0.000
4	2.500	2.450	2.500	2.483	0.026	1.047
5	2.300	2.200	2.200	2.233	0.056	2.507

RESULTS AND DISCUSSION

Unit design: A new valve was manufactured from low-cost materials and it can be used in chemical reactions. Figure 4 shows the valve.

Order of addition: The effect of order of addition was studies for the system which is completing and selecting the best response at: flow rate (8.1 mL/min), reaction coil (50 cm), sample volume (157 μL), reagent volume (157 μL), base volume (157 μL), mixing time (0), sample concentration (50 ppm) reagent concentration (NQS) (0.01 w/v%), base concentration (10 v/v%). The results Table 1 and Fig. 5 show that the response which increase at the order of addition ((NQS+Lis)+B) but decrease at the other addition.

Mixing time of reaction: To know the suitable mixing time of reaction this adverb was studied at, flow rate (8.1 mL/min), reaction coil (50 cm), sample volume (157 μL), reagent volume (157 μL), base volume (157 μL), order of addition ((NQS+Lis)+B), sample concentration (50 ppm), reagent concentration (0.01 w/v%), base concentration (10 v/v%). Via. stop time ofreaction the best response can be determined for Table 2 and Fig. 6 reaction between lisinopril and NQS. About 4 min gives the best shows that the time response.

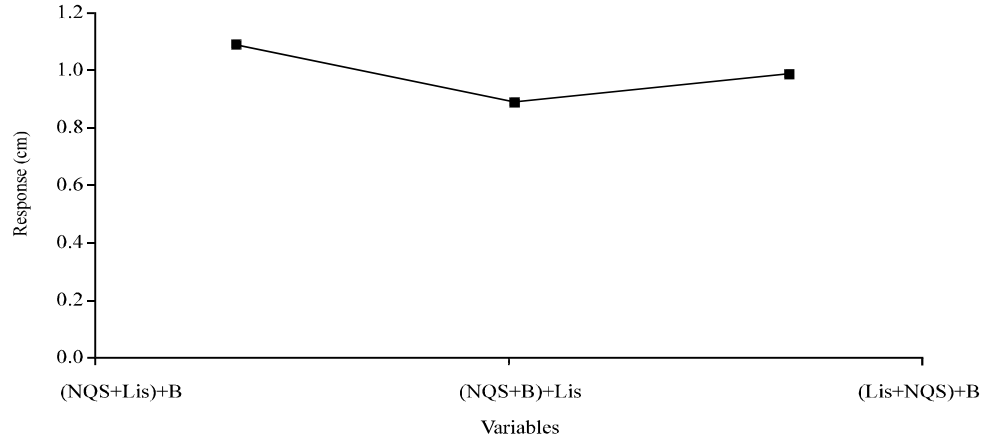

Fig. 5: Effect of order of addition

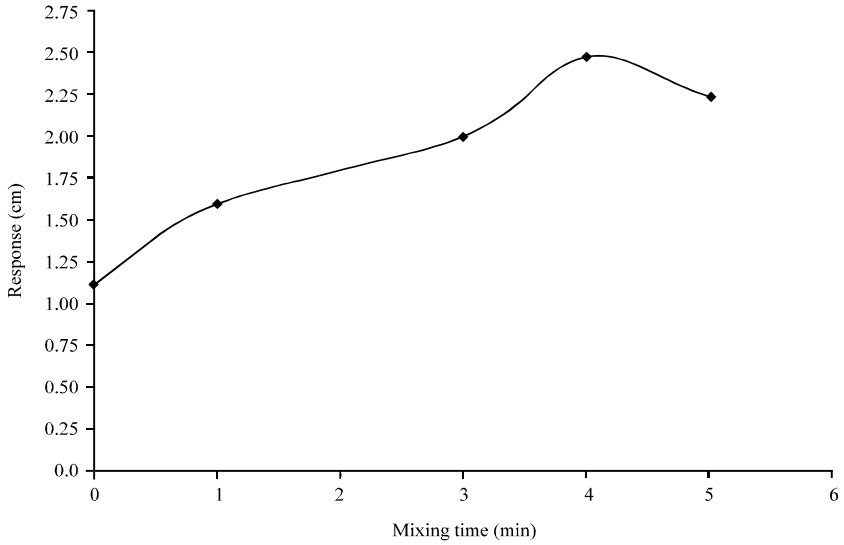

Fig. 6: Effect of reaction mixing time

Table 3: Effect of flow rate

Flow rate (mL/min)	------Peak length (cm)--------			Means	SD	RSD (%)
3.300	0.950	1.100	1.050	1.033	0.075	7.260
4.900	1.350	1.350	1.350	1.350	0.000	0.000
6.600	1.950	2.000	1.950	1.966	0.027	1.373
8.100	2.500	2.500	2.500	2.500	0.000	0.000
10.000	3.200	3.000	3.000	3.066	0.114	3.718
12.300	3.450	3.650	3.650	3.583	0.086	2.400
13.700	2.450	2.650	2.500	2.533	0.103	4.066

Flow rate: The effect of flow rate was investigated in the range (3.3-3.17 mL/min) at: mixing time (4 min), reaction coil (50 cm), sample volume (157 μL), reagent volume (157 μL), base volume (157 μL), order of addition ((NQS+Lis)+B) sample concentration (50 ppm), reagent concentration (0.01 w/v%), base concentration (10 v/v%). The results in Table 3 and Fig. 7 show that the flow rate of (12.3 mL/min) gives the best response.

Table 4: Effect of reagent volume

Reagent volume (μL)	---------Peak length--------- (cm)			Means	SD	RSD (%)
157.000	3.700	3.650	3.700	3.683	0.026	0.705
196.250	2.800	2.700	3.000	2.833	0.152	5.365
235.500	4.050	4.250	4.050	4.116	0.115	2.793
314.000	2.500	2.700	2.600	2.600	0.100	3.846

Reagent volume: The influence of the reagent volume on the peak height was investigated by using various length of reagent loop with different volume. The results obtained showed that an injection reagent volume of (235.5 μL) gave the best response for as shown in Fig. 8 and Table 4. This adverb was studied at: mixing time (4 min), reaction coil (50 cm), sample volume (157 μL), flow rate (8.1 mL/min) base volume (157 μL), order of addition ((NQS+Lis)+B), sample concentration (50 ppm) reagent concentration (0.01 w/v%), base concentration (10 v/v%).

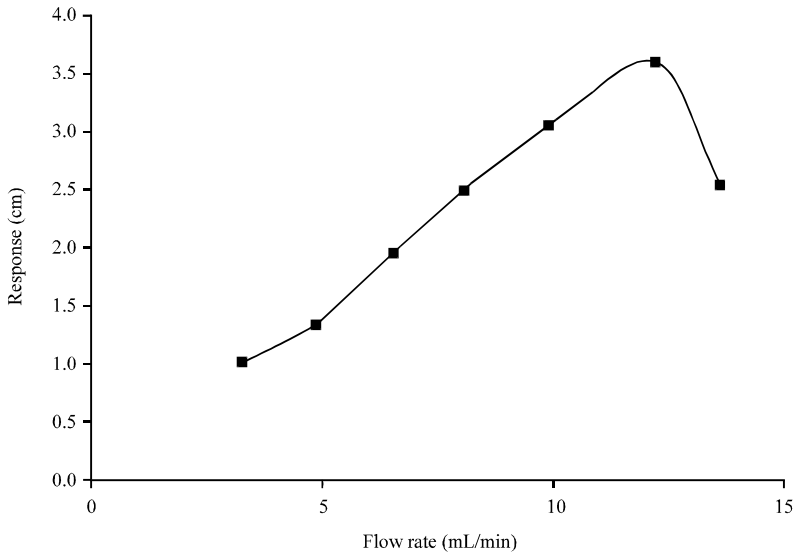

Fig. 7: Effect of flow rate

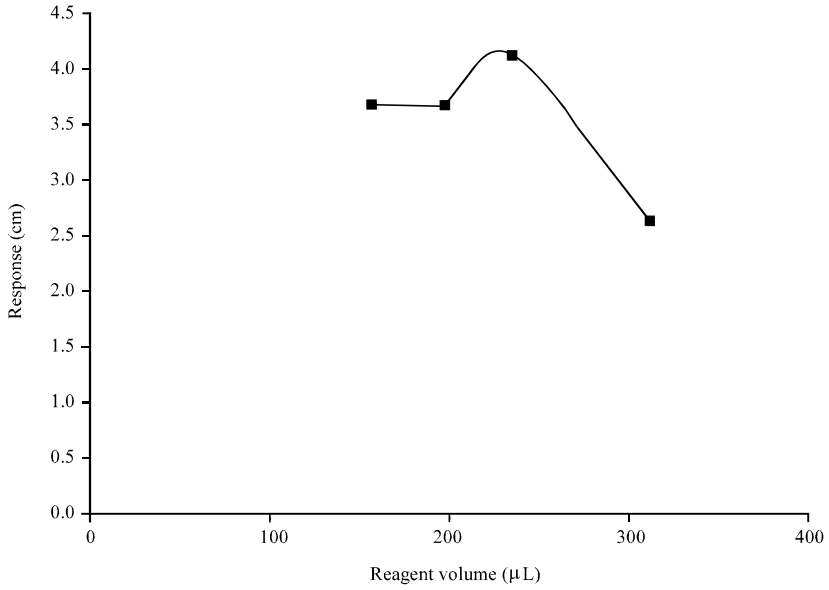

Fig. 8: Effect of reagent volume

Table 5: Effect of sample volume

Sample volume (µL)	Peak length (cm)			Means	SD	RSD (%)
157.000	4.100	4.000	4.100	4.066	0.057	1.401
196.250	4.750	4.650	4.500	4.633	0.125	2.698
235.500	3.800	3.750	3.800	3.783	0.026	0.687
314.000	2.100	2.100	2.100	2.100	0.000	0.000

Effect of sample volume: The effect of sample volume was investigated by injection of different volume through using different sample loop length of. The results obtained showed that an injection sample of (196.25 µL) gave the best response for lisinopril as shown in Fig. 9 and Table 5 the above adverb was deliberated at: mixing time (4 min), reaction coil (50 cm), reagent volume (235.5 µL) flow rate (8.1 mL/min), base volume (157 µL), order of addition ((NQS+Lis)+B), sample concentration (50 ppm) reagent concentration (0.01 w/v%), base concentration (10 v/v%).

Effect of base volume: Optimum volume of the base that gives the best response for the reaction between lisinopril and NQS is (157 µL) as shown in Table 6 and Fig. 10. The effect of base volume was investigated in the range

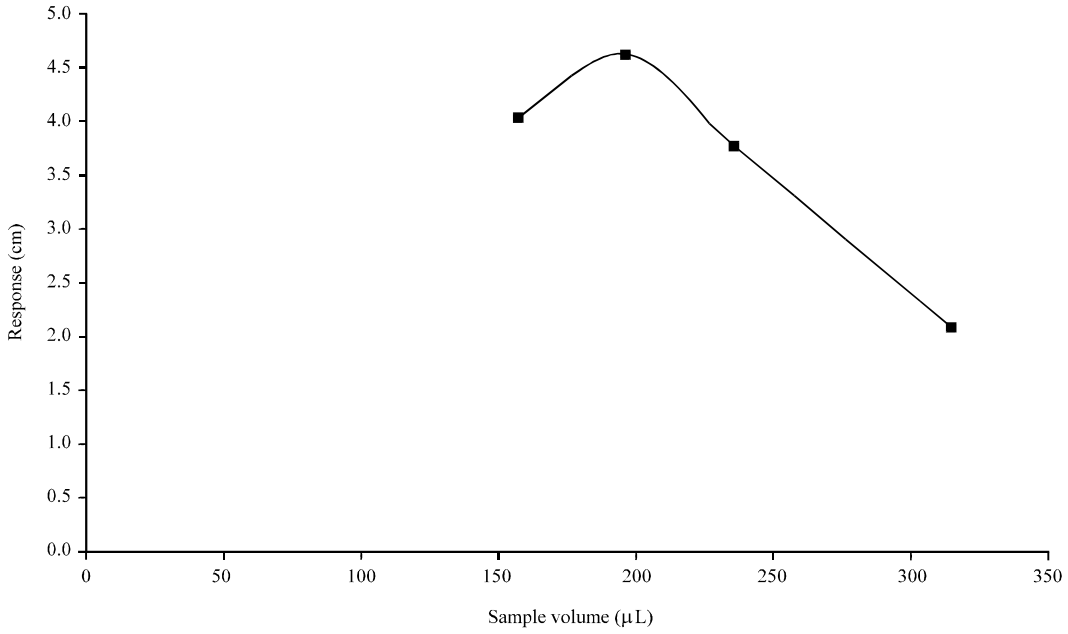

Fig. 9: Effect of sample volume

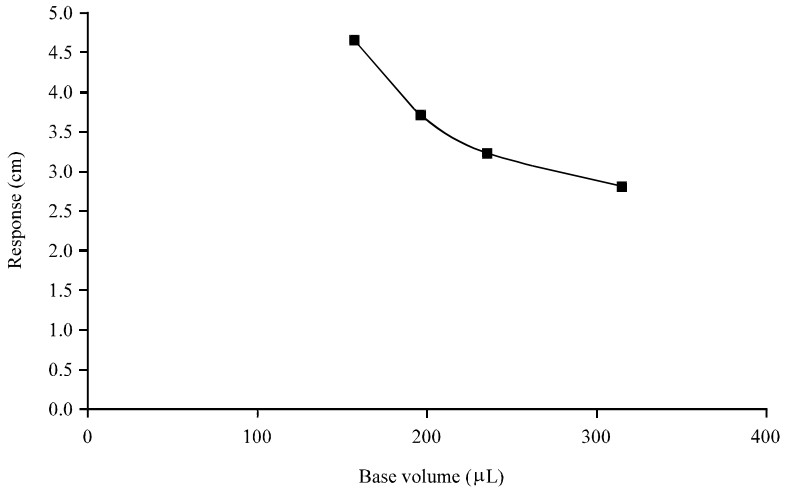

Fig. 10: Effect of base volume

Table 6: Effect of base volume

Base volume (µL)	-----Peak length (cm)-----			Means	SD	RSD (%)
157.000	4.650	4.650	4.650	4.650	0.000	0.000
196.250	3.800	3.600	3.700	3.700	0.100	2.702
235.500	3.250	3.150	3.250	3.216	0.057	1.772
314.000	2.800	2.800	2.800	2.800	0.000	0.000

Table 7: Effect of reaction coil

Reaction coil length (cm)	----Peak length (cm)-----			Means	SD	RSD (%)
30.000	4.250	4.300	4.200	4.250	0.050	1.176
50.000	4.600	4.600	4.600	4.600	0.000	0.000
100.000	4.850	4.850	4.850	4.850	0.000	0.000
115.000	3.400	3.250	3.300	3.316	0.075	2.261

(157-314 µL) at: mixing time (4 min), reaction coil (50 cm), reagent volume (235.5 µL), flow rate (8.1 mL/min) sample volume (196.25 µL), order of addition ((NQS+Lis)+B), sample concentration (50 ppm) reagent concentration (0.01 w/v%), base concentration (10 v/v%).

Effect of reaction coil: The coil length was investigated in the range of (30-115 cm). The results obtained showed that a coil length of (100 cm) gave a suitable response for as shown in Fig. 11 and Table 7. This parameter was studied at: mixing time (4 min), base volume (157 µL), reagent volume (235.5 µL), flow rate (8.1 mL/min)

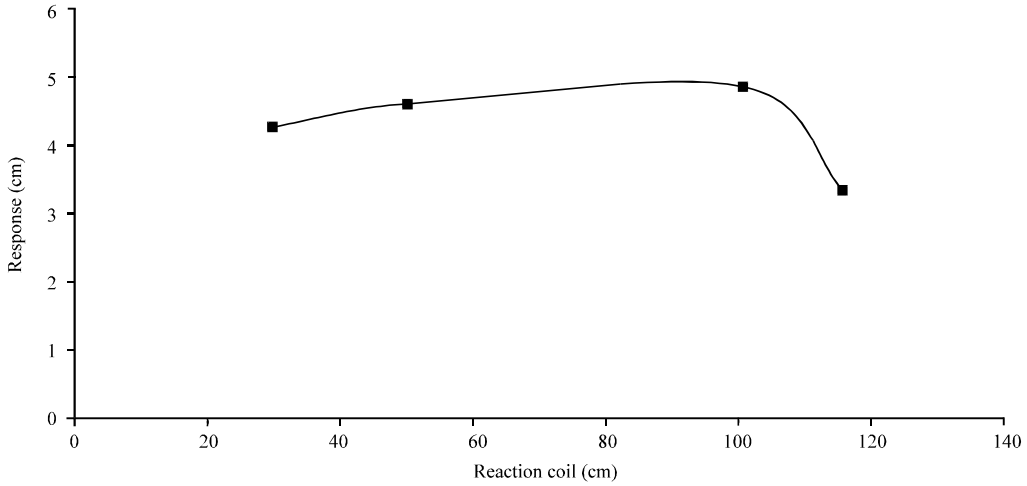

Fig. 11: Effect of reaction coil length

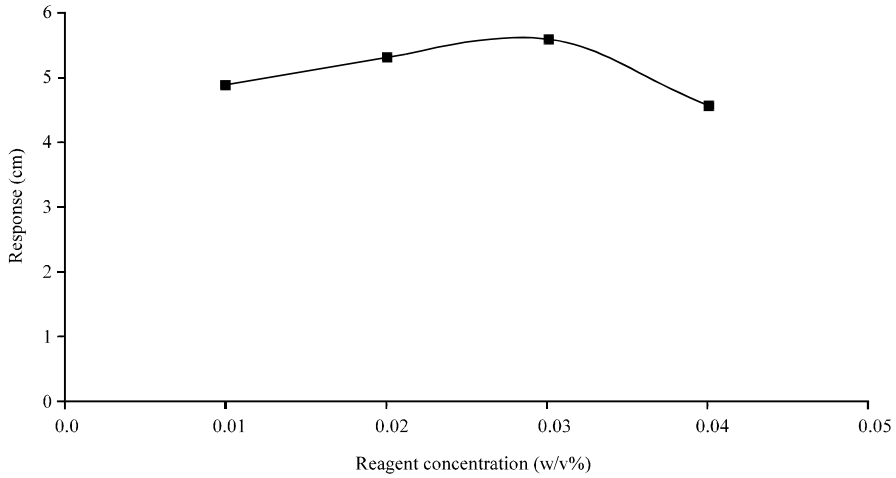

Fig. 12: Effect of reagent concentration

sample volume (196.25 µL), order of addition ((NQS+Lis)+B), sample concentration (50 ppm) reagent concentration (0.01 w/v%), base concentration (10 v/v%).

Effect of reagent concentration: The effect of reagent concentration was studied in the range (0.01-0.04 w/v%) The results obtained showed that the concentration of (0.03 w/v%) gave the best response as shown in Table 8 and Fig. 12. This parameter was studied at: mixing time (4 min), base volume (157 µL), reagent volume (235.5 µL), flow rate (8.1 mL/min) sample volume (196.25 µL) order of addition ((NQS+Lis)+B) sample concentration (50 ppm) reaction coil (100 cm), base concentration (0.03 w/v%).

Effect of base concentration: At the following parameter, the effect of base concentration was studied in the concentration of (8 v/v%) gave the greatest response as shown in Table 9 and Fig. 13. The constant parameter is: rang (6-14 v/v%). The results obtained showed that the

Table 8: Effect of reagent concentration

Reagent concentration (w/v%)	----Peak length (cm)-----			Means	SD	RSD (%)
0.01	4.850	4.900	4.900	4.883	0.026	0.532
0.02	5.400	5.200	5.400	5.333	0.114	2.137
0.03	5.600	5.600	5.600	5.600	0.000	0.000
0.04	4.600	4.600	4.500	4.566	0.057	1.248

Table 9: Effect of base concentration

Base concentration (v/v%)	-------Peak length (cm)------			Means	SD	RSD (%)
6	2.100	2.250	2.200	2.183	0.075	3.435
8	6.350	6.400	6.400	6.383	0.026	0.407
10	5.600	5.500	5.600	5.566	0.057	1.024
12	4.850	4.900	5.000	4.916	0.075	1.525
14	4.200	4.000	3.900	4.033	0.152	3.768

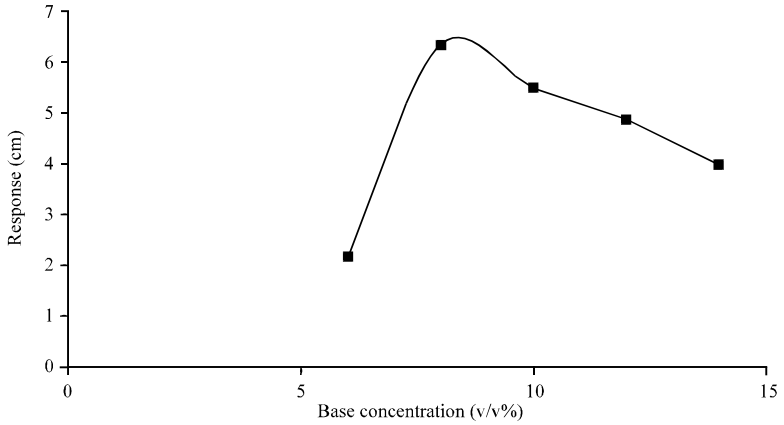

Fig. 13: Effect of base concentration

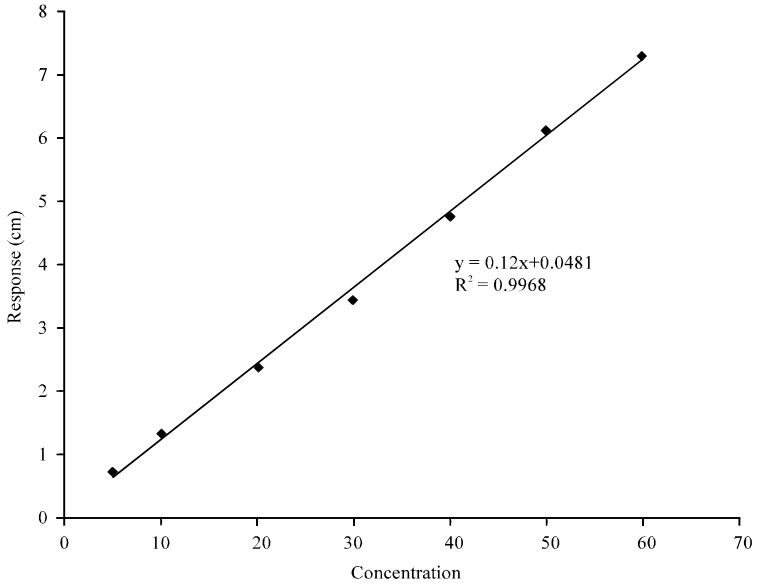

Fig. 14: Calibration graph

mixing time (4 min), base volume (157 µL), reagent volume (235.5 µL), flow rate (8.1 mL/min) sample volume (196.25 µL), order of addition ((NQS+Lis)+B), sample concentration (50 ppm) reaction coil (100 cm), reagent concentration (0.03 w/v%).

Calibration graph for the determination of lisinopril: Applying optimum condition mentioned above a linear calibration graph Fig. 14 and Table 10 was obtained over the concentration range of (5-60 ppm) with correlation coefficient of (0.9968) (Table 11).

Repeatability: To know the accuracy and the precision of the system, the repeatability was studied at the same perpetual parameters that it used for the constructed

Table 10: Calibration graph

Concentration (ppm)	------Peak length (cm)-----			Means	SD	RSD (%)
5	0.800	0.700	0.700	0.733	0.056	7.639
10	1.300	1.500	1.350	1.383	0.103	7.447
20	2.450	2.450	2.500	2.466	0.027	1.094
30	3.400	3.550	3.650	3.533	0.125	3.538
40	4.800	4.800	4.850	4.816	0.027	0.560
50	6.000	6.200	6.200	6.133	0.114	1.858
60	7.200	7.400	7.500	7.366	0.152	2.063

Table 11: Factors values obtained for calibration graph

Parameters	Values
Linearity range (ppm)	5-60
Linear regression equation	Y = 0.12 x+0.0481
R^2	0.9968
Correlation coefficient (r)	0.9983
Relative standard deviation of 20 ppm (n = 3)	1.094
Slope (m)	0.12
Intercept (i)	0.0481

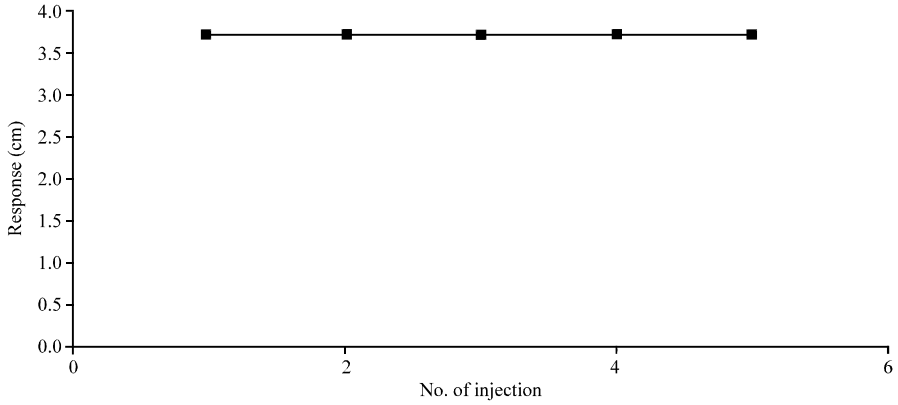

Fig. 15: Repeatability

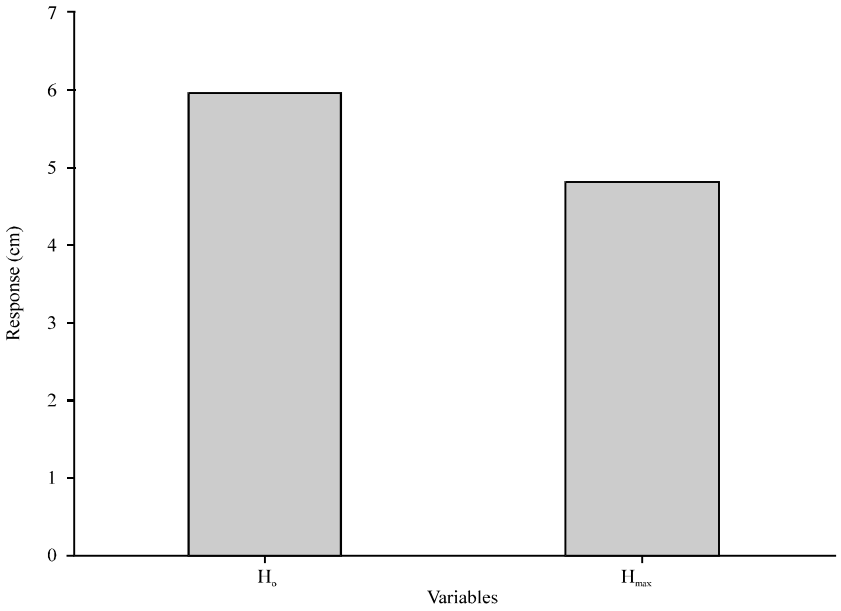

Fig. 16: The dispersion

Table 12: The repeatability

No. of injection	Response	Means	SD	RSD (%)
1	3.73	3.736	0.005	0.133
2	3.74			
3	3.74			
4	3.73			

Table 13: The dead volume

Addition	Response (cm)
NQS+Lis+B	1.25
Lis+NQS	0
NQS+B	0
Lis+B	0

calibration curve. The results Fig. 15 and Table 12 obtained exhibited that the system has a good repeatability.

The dispersion: To identify the degree of dilution of sample, the dispersion was studied at the same variable that is used of calibration curve for (40 ppm) concentration. The results attained Fig. 16 showed that the dispersion is within the desired limit.

Dead volume: To know the proficiency of the unit, the dead volume was studied Fig. 17 and Table 13 for (10 ppm) lisinopril at the optimum parameters.

Analytical application: The analytical application of the suggested methods was investigated for pharmaceutical drugs andaqueous solution. The analytical application is shown in Table 14 and Fig. 18.

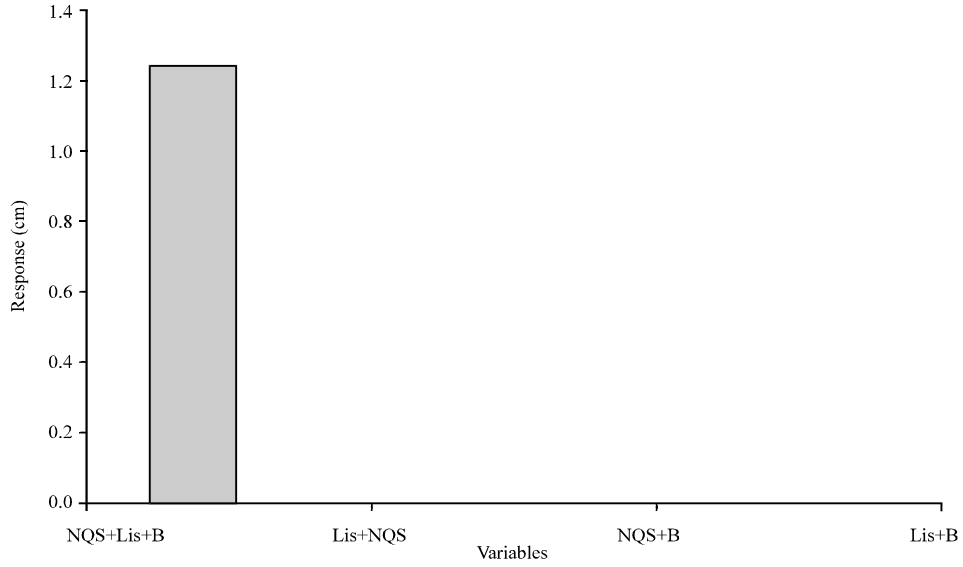

Fig. 17: The dead volume

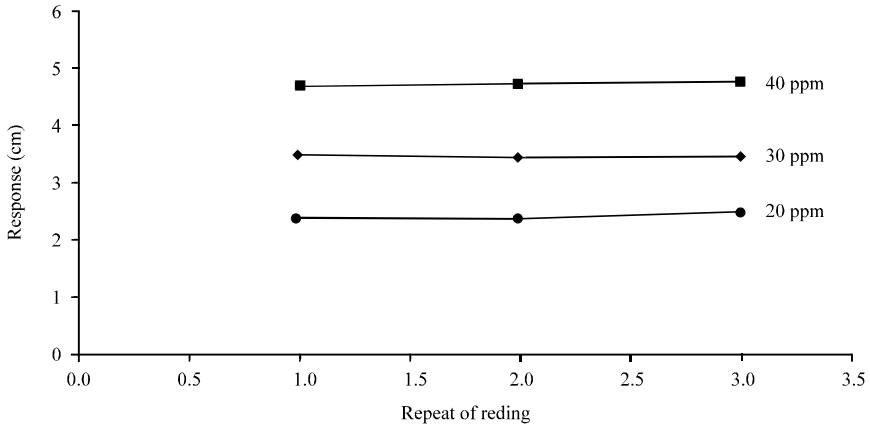

Fig. 18: Analytical application

Table 14: Analytical application

	Amount of sample (ppm)		Proposed method							
Sample/reagent	Taken	Found	Response (cm)			Means	SD	RSD (%)	Error (%)	Rec (%)
Drugs lisinopril										
NQS	20	19.874	2.400	2. 400	2.500	2.433	0.057	2.342	-0.630	99.370
	30	28.899	3.550	3.500	3.500	3.516	0.028	0.796	-3.670	96.330
Aqueous solution										
NQS	40	39.599	4.750	4.800	4.850	4.800	0.050	1.041	-1.002	98.997

CONCLUSION

Sensitive and simple FI method for the determination of lisinoprilhas been established. The developed processes based on the exchange reaction between lisinopril and NQS. This method were successfully applied inaqueous solution and pharmacy preparation.

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