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**Original Article**

# Utilizing the NAG-4SX3-3D analyzer at 0-180 degree coupling with continuous flow injection analysis to determine of loratadine in drugs by the precipitation method using sodium nitroprusside

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## ABSTRACT

In order to improve the sensitivity of the newly established methodology, a thorough examination was carried out on the essential parameter. A rapid and highly responsive technique has been developed for the detection of loratadine. This method involves the generation of pale white species through the reaction between sodium nitroprusside and loratadine. The transducer's energy response was evaluated using the NAG-4SX3-3D analyzer. The linear range for measuring loratadine is 0.01-10 mM (millimolary). For concentrations of 4 and 10 mM. The RSD (relative standard deviation) for six trials was significantly lower than 0.14 percent. The measurement of loratadine has a limit of detection (LOD) of 261.890 ng/sample for (n=13). The calibration graph shows a progressive dilution across the lowest concentration linear dynamic range, with a correlation coefficient (r) of 0.9984. The percentage linearity ($R^2$ %) is 99.68. The proposed approach was evaluated in comparison to the previous technique, which involved UV-spectrophotometric analysis at a wavelength of 275 nm. Based on the findings, it can be inferred that the technique exhibits enhanced sensitivity and surpasses the classic reference method's 10 mm irradiation, owing to its utilization of specific chemicals. Based on the aforementioned information, it is determined that the developed methodology is the most appropriate for analyzing loratadine in pharmaceutical samples when compared to the reference techniques.

## 1. Introduction

Loratadine, specifically known as ethyl 4-(8 – chloro - 5,6 – dihydro - 11H - benzo-cyclohepta [1, 2 - b] pyridine - 11 - ylidine) – 1 -piperidinecarboxylate (Fig.1), exhibits fast and sustained tricyclic antihistamine properties by selectively antagonizing peripheral histamine H1-receptors[1]. To reduce the symptoms of allergic rhinitis, urticaria, and other allergic dermatological diseases, loratadine is now prescribed. For adults and children who weigh more than 30 kg, loratadine dose recommendations are 10 mg given once day. Administering a daily dose of 5mg is advised for individuals aged 2 to 12 who weigh less than 30 kg [2].

A number of chemical techniques have been described that use light-emitting diodes (LEDs) as sources of incident light, many of which rely on continuous flow injection analysis [3]. There are some techniques that have been used to estimate allergen inhibitors such us: AFM [4]and NAG Dual & Solo (0-180º) analyzer [5]. The amount of loratadine

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in pure and pharmaceutical forms has been determined using a number of techniques, such as: HPLC [6], LC/MS/MS[7, 8], Cathodic stripping voltammetry (CSV)[9],Uv-Spectrophotometric[10] and x-ray photoelectron spectroscopy[11]. This study gives the first results on how to use the newly created NAG_4SX3_3D Analyzer, which has four sources of white snow LEDs set up in three rows, each corresponding to three detectors, to measure the amount of loratadine in turbidimetric samples using flow analysis. So, a small and inexpensive optoelectronic detector was made to provide accurate turbidimetric measurements in the context of continuous flow injection analysis, a noticeable bale white precipitate was created. The amount of loratadine was measured by observing how they mixed with sodium nitroprusside. Using a uniquely developed NAG_4SX3_3D(NAG4SX3) Analyzer, the precipitate result was examined at 0-180°.

## 2. Materials and Methods

### 2.1. Chemicals

All of the materials and substances used in this investigation were of analytical grade, unless explicitly stated differently. The key chemicals used as standard stock solutions in the present investigation are shown in Table 1. The original stock solution was diluted to provide supplementary standard solutions.

**Table 1.** A list of the essential chemicals and reagents utilized in this study

| Name<br>Concentration | Formula<br>details of stock solution | Company<br>supplier | Molecular weight<br>(g/mol) | Weight / volume or<br>Volume / volume | Remarks |
|---|---|---|---|---|---|
| *Acetic acid*<br>**[0.5M ]*<br>***[0.425M]* | $CH_3COOH$<br>99.8% Weight/ weight Specific gravity.1.05g/ml | BDH | 60.05 | 7.2 ml/250ml | Standardized with $Na_2CO_3$ solution |
| *Hydrochloric acid*<br>**[0.5M]*<br>***[0.463M]* | HCl<br>35%wt/wt<br>Specific gravity.1.16g/ml | BDH | 36.46 | 11.23 ml/250ml | Standardized with $Na_2CO_3$ solution |
| *Nitric acid*<br>**[0.5M]*<br>***[0.431M]* | $HNO_3$<br>70%wt/wt<br>Specific gravity.1.42g/ml | BDH | 63.01 | 7.92 ml/250ml | Standardized with $Na_2CO_3$ solution |
| *Sulfuric acid*<br>**[0.5M]*<br>***[0.43M]* | $H_2SO_4$<br>96%wt/wt<br>Specific gravity.1.84g/ml | BDH | 98.08 | 7ml/250ml | Standardized with $Na_2CO_3$ solution |
| *Phosphoric acid*<br>**[0.5M]*<br>***[0.433M]* | $H_3PO_4$<br>85%wt/wt<br>Specific gravity.1.84g/ml | BDH | 97.994 | 12.76ml/250ml | Standardized with $Na_2CO_3$ solution |
| *Ammonium acetate*<br>*[0.25M]* | $CH_3COONH_4$ | Fluka | 77.08 | 1.927 g/100ml | D.W |
| *Ammonium chloride*<br>*[0.25M]* | $NH_4Cl$ | Fluka | 53.49 | 1.3373g/100ml | D.W |
| *Sodium carbonate*<br>*[0.25M]* | $Na_2CO_3$ | BDH | 105.99 | 2.6498g/100ml | D.W |
| *Sodium chloride*<br>*[0.25M]* | NaCl | BDH | 58.44 | 1.461g/100ml | D.W |
| *Sodium sulfate*<br>*[0.25M]* | $Na_2SO_4$ | BDH | 142.04 | 3.551g/100ml | D.W |
| *Sodium sulfite*<br>*[0.25M]* | $Na_2SO3$ | BDH | 126..043 | 3.15g/100ml | D.W |
| *Potassium chloride*<br>*[0.25M]* | KCl | BDH | 74.55 | 1.8638g/100ml | D.W |
| *Potassium Iodide*<br>*[0.25M]* | KI | BDH | 166.00 | 4.15g/100ml | D.W |
| *Sodium nitroprusside*<br>*[0.02M]* | $C_5H_4FeN_6Na_2O_3$ | Fluka | 297.95 | 1.1406g/100ml | D.W |
| *Loratadine*<br>*[0.02M]* | $C_{22}H_{23}ClN_2O_2$ | Sigma | 382.88 | 3.8288g/500ml | Dissolved in methanol (Fluka) |

*The chemical compound's initial concentration before being standardized using sodium carbonate solution. ** The chemical compound's final concentration after being standardized using sodium carbonate solution.

### 2.2. Apparatus

Figure 1.A depicts the signal resulting from the decrease of light (0–180 degree). This signal is acquired using a flow chamber that has been constructed using an internally assembled NAG_4SX3_3D (NAG4SX3) analyzer. The potentiometric recorders utilized for recording output signals are produced by Siemens, a renowned German company. A Teflon sample loop, equipped with six ports, is interconnected with a peristaltic pump that possesses adjustable length. The UV spectrophotometric device produced by Shimadzu, a renowned manufacturer based in Japan, was employed to carry out the standard procedures.

### 2.3. Procedure

According to the information presented in Figure S1 (Supplementary file), the procedure for quantifying loratadine (LOT) involves the utilization of sodium nitroprusside (SNP) to produce a bale white precipitate [12, 13].

The (NAG4SX3) analyzer's manifold is composed of two lines that are interconnected. The system is equipped with a sample segment introduction device that comprises an injection valve featuring load and injection locations. This device facilitates the uniform and dependable delivery of a predetermined quantity by means of repetitive injections. The flow rate of the (NAG4SX3) analyzer is determined to be 1.8 ml/min. The device is connected to a Y-junction point, where the sample zones of the LOT are transporting by a carry line. The transported line, which is designed to transfer the LOT sample zones at a concentration of 8 mM, is distilled water. The volume of the inserted sample is 60 (µL).

The energy response of a transducer to various types of silt was the main focus of the experiment. The study the transported line aimed to evaluate the impact of light attenuation on the bale white precipitate surfaces. An analysis employing an x-y potentiometric record output was used to achieve this. The examination of each solution was conducted in three replications. Figure S2 (Supplementary file) proposes the precipitation of LOT 8 mM using 2 mM of DNSA.

It was illustrated that the progressive measurements of the NAG_4SX3_3D analyzer transducer output (Yzi mV) in relation to t.min (cm) for LOT concentrations of 8 mM. The LOT-SNP system demonstrates clear and coherent outputs that are synchronized and legibly displayed. The NAG4SX3 analyzer incorporates a novel synchronization strategy (Figure 1).

## 3. Results

### 3.1. Impact of chemicals

#### 3.1.1. Sodium nitroprusside (SNP)

Distilled water was used to dilute the original stock solution, creating a range of solutions with SNP concentrations between 0.2 and 5.0 mM.

The procedure for the experiment included the use of a 60 µL sample volume. The reagent and the carry line, which held distilled water, both had a constant flow rate of 1.8 milliliters per minute since the valve was in the open position. The experiment involved the replication of each measurement three times. In this study, a NAG4SX3 analyzer is utilized to examine the alterations in energy transducer response resulting from changes in the concentrations of SNP.

Figure 2 provides an illustration of this concept. The results of the experiments showed that incident light attenuation increased in proportion to an increase in SNP concentration. This increase continued until it reached its peak at a concentration of 0.8 mM. The sensitivity of the (S:N) energy transducer is reduced with an increase in the concentration of SNP above 0.8 mM. The observed decline in reaction could potentially be ascribed to the dispersion of precipitation particles. Therefore, it was determined that the ideal concentration of SNP for the LOT (8 mM-SNP) system is 0.8 mM.

Table 2(A) presents the results obtained, whereas Tables 2(B) and Figure 3 depict the segmentation technique employed to identify the most suitable segment. The optimal range for the (LOT 8mM-SNP) system is $S_2$ (0.5-2.0 mM).

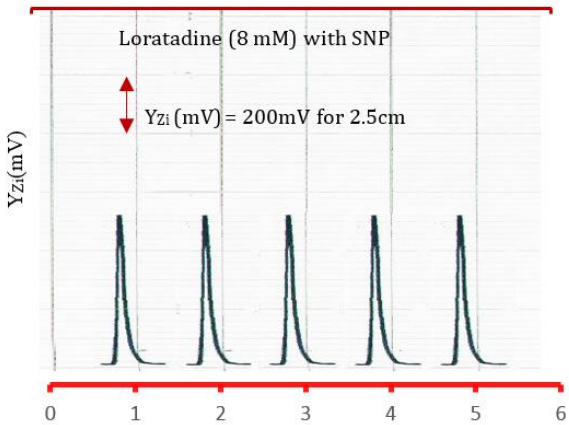


**Fig. 1.** Replicated responses using NAG4SX3 instrument for the reaction

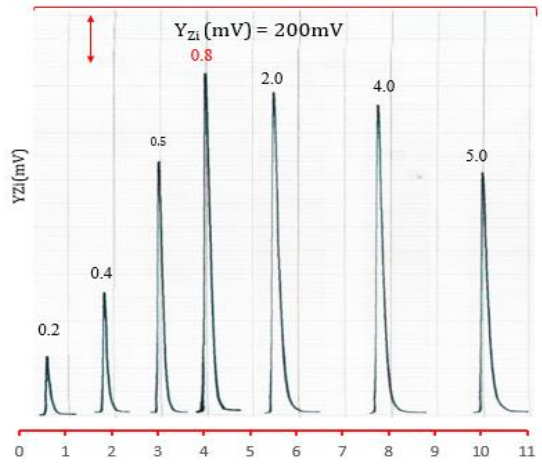


**Fig. 2.** Impact of [SNP] on the responses.

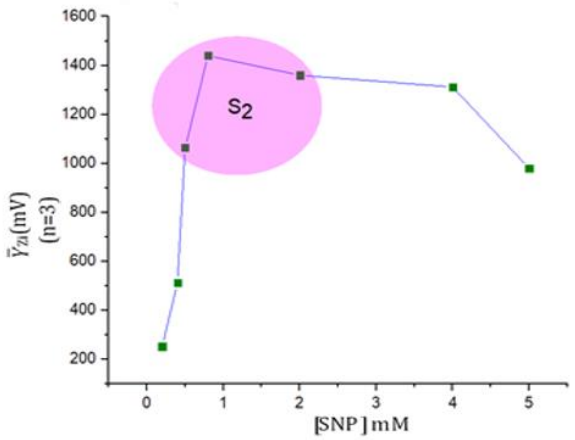


**Fig. 3.** The output (as $\bar{Y}_{Z\,i}$ (mV))( $\bar{Y}$-$_{Z\,i=3}$ ) transducer response

### 3.1.2. Impact of using various kinds of salts and acids

The reactions between loratadine (8 mM) and SNP utilized distilled water (aqueous medium) as a carrier stream. Therefore, other aqueous solutions ($CH_3COONH_4$, $NH_4Cl$, NaCl, $Na_2SO_4$, $Na_2SO_3$, KCl, KI, $CH_3COOH_3$, HCl, $HNO_3$, $H_2SO_4$, and $H_3PO_4$) have been created at 100 mM. Instead of using distilled water, these aqueous solutions were used to look into possible improvements in the (S:N) energy transducer response. Throughout the experiment, the reagent line and carrier stream line were kept in an open valve state, with a sample volume of 60µL and a flow rate of 1.8 ml/min.. When using different salts and acids as a carrier stream, it can be seen that the response's sensitivity increases due to a decrease in S/N energy transducer response. This might be explained by precipitate particles dispersing in an acidic and salty environment. Therefore, it was determined that the optimal medium (carrier stream) to get the largest reaction was $H_2O$ (Figure 4, Table 3) which summarizes the results gathered.

**Table 2.** A) Effect of SNP concentrations on precipitation of loratadine in two systems, B) Segmentation pattern: a (intercept mV), b (slope mV/ mM), r (correlation coefficient) and Θ (angle) with selection of optimum segment

**A**

| Reagent[mM] | *ȲZi. →3* | *(R.S.D.%)* | *C.I at 95 % ȲZi(mV)± t.SEM* |
|---|---|---|---|
| **0.2** | 252 | 0.43 | 252±2.683 |
| **0.4** | 512 | 0.24 | 512±3.056 |
| **0.5** | 1064 | 0.12 | 1064±3.205 |
| **0.8** | 1440 | 0.08 | 1440±3.807 |
| **2** | 1360 | 0.10 | 1360±3.329 |
| **4** | 1312 | 0.12 | 1312±3.826 |
| **5** | 980 | 0.12 | 980±3.031 |

**B**

| Segment | Reagent range mM | *(a)* | *(b)* | *(r)* | *(θ)* |
|---|---|---|---|---|---|
| **$S_1$** | 0.2-0.5 | -309.43 | 2505.71 | 0.9230 | 98.977 |
| **$S_2$** | 0.5-2.0 | 1153.91 | 121.905 | 0.4885 | 89.530 |
| **$S_3$** | 2.0-5.0 | 1628.00 | -112 | 0.8267 | -89.488 |

Ȳ.Zi.(mV):(S/N) responses of (NAG4X3) Analyzer in mV((S/N)-R.N.A), $t_{0.025,2}$=4.303, SEM= Standard error of mean, C.I: Confidence interval

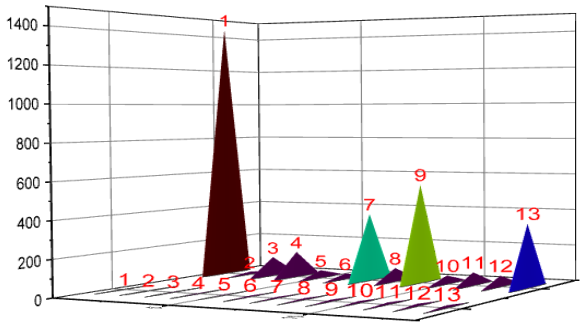


**Fig. 4.** The energy transducer response of the NAG4SX3 Analyzer is evaluated by observing the formation of bale white precipitate.

**Table 3.** Impact of various media

| | (salt & acid) [100mM] | *ȲZi. →3* | *(R.S.D. %)* | *C.I* |
|---|---|---|---|---|
| 1 | $H_2O$ | 1440 | 0.08 | 1440±2.807 |
| 2 | $CH_3COONH_4$ | 16 | 5.06 | 16±2.012 |
| 3 | $NH_4Cl$ | 108 | 0.86 | 108±2.310 |
| 4 | NaCl | 144 | 0.64 | 144±2.286 |
| 5 | $NaSO_4$ | 44 | 0.73 | 44±0.795 |
| 6 | $NaSO_3$ | 32 | 1.66 | 32±1.317 |
| 7 | KCl | 376 | 0.22 | 376±2.087 |
| 8 | KI | 76 | 1.20 | 76±2.261 |
| 9 | $CH_3COOH$ | 548 | 0.19 | 548±2.534 |
| 10 | HCl | 48 | 2.29 | 48±2.733 |
| 11 | $HNO_3$ | 72 | 1.28 | 72±2.286 |
| 12 | $H_2SO_4$ | 60 | 0.27 | 60±0.845 |
| 13 | $H_3PO_4$ | 348 | 0.09 | 348±0.820 |

### 3.2. Physical variables

#### 3.2.1. Flow rate (F.R)

The LOT (8 mM)-SNP (0.8 mM) system was employed in our study, with a sample volume of 60 µL . The experimental setup employed a variable flow rate ranging from 0.9 to 2.5 ml/min, as depicted in Figure 4. The results of the investigation are shown in Table 4 Lower frequency observations showed an increase in the peak response's maximum height deformation and base width (ΔtB). Dispersion factors rise as a result of the diffusion process. Peak height was found to decrease at flow rates greater than 1.5 ml/min. Dilution and dispersion are two elements that lower the vertical response profile. According to the experimental findings, a 1.5 mL/min (F.r) is ideal. There is an unpredictable response that happens when the filtration rate goes over 1.5 ml/min. Due to their high velocity, precipitated particles exhibit rapid movement, thereby traversing ahead of the measurement cells. The slope-intercept method was employed to determine the optimal carrier stream flow rate (F.r) within the designated section. The data presented in Figure 5 and Table 5 illustrate the values of $S_2$, which range from 1.3 to 1.8 ml/min.

#### 3.2.2. Sample volume (S.V)

The study utilized sample volumes ranging from 25 µL to 326 µL. The volumes of the Teflon tubes used in this study varied in length from 3.18 cm to 41.5 cm, with a consistent diameter of 1 mm. Figure .6 illustrates a gradual increase in the attenuation of incident light (S/N profiles) up to 228 µL. Increasing the sample size leads to greater formation of precipitate particles, which in turn leads to an increased height of the profile. A decline in the output response profile was noted when the volume surpassed 228µL. The presence of dense precipitate particles can impede the dispersion of all precipitated particles, leading to a decrease in the attenuation of incoming light. The 228 µL (S.V) has been determined to be the most satisfactory based on analysis and slope-intercept calculation. The conclusion is based on the findings from Table 6, Table 7 which indicate that the ideal segment for the sample plug falls within the range of 228-326 µL for both systems. The optimal parameters can be determined by selecting a sample volume from the chosen segment $S_3$ (228 -326 µL).

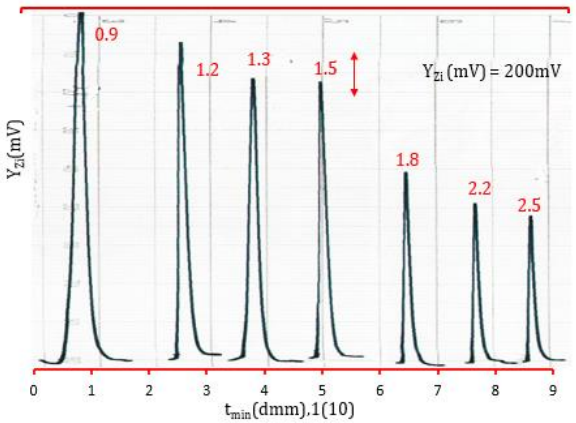


**Fig. 4.** Flow rate's impact

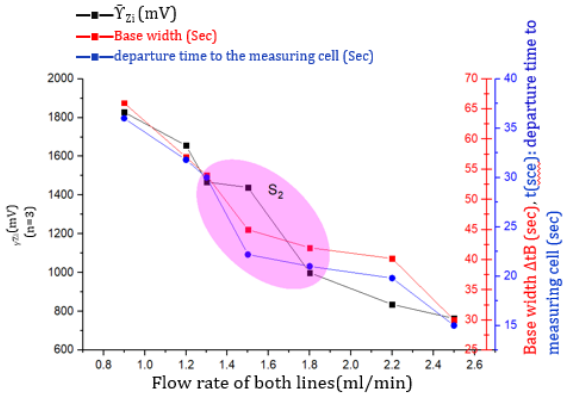


**Fig. 5.** F.r effect on energy transducer response

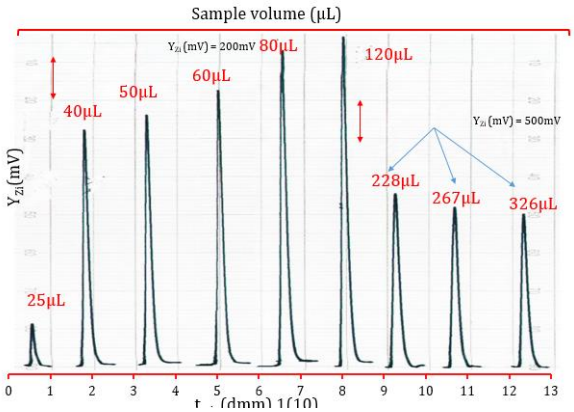


**Fig. 6.** Sample volume's impact on energy transducer response

#### 3.2.3. Effect of reaction loop lengths

In order to enhance the sensitivity of the reaction between loratadine and the SNP reagent efforts were made to increase the formation of precipitated particulate in the two-line manifold system. The study examined the the LOT-SNP system (8 mM, 0.8

mmol/L) using a (F.r) of 1.5 ml/min. The S.V used was 228µL. Each delay reaction coil was attached beyond the Y-junction point. To investigate the impact of mixing coil length onion pair formation, it is necessary to determine the reaction completion time between LOT and the reagent using a Teflon tube. The study investigated the optimization of a mixing coil varying lengths (10, 20, 25, and 30 cm), corresponding to volumes of (314 µL, 628 µL, 785 µL, and 942 µL). The results of the LOT (8 mmol/L)-SNP (0.8 mmol/L) system indicate that the sensitivity of the peak height does not improve when a mixing coil is used. This suggests that the reaction between LOT and SNP is already complete and that the manifold system does not require a mixing coil. The use of delayed reaction coils was avoided in this system due to the formation of larger particles and an increase in particulate weight. Consequently, the presence of these factors would pose challenges to the mobility of the particles inside the flow cell. The slope-intercept approach is used to ascertain the appropriate segmentation, namely segment S1, which ranges from 0 to 628 microliters (µL). The results have been compiled and organized in Table 8.

**Table 4.** Effect of flow rate (F.r) variation.

| Pump speed | F.r ml/min | $\bar{Y}_{Zi.} \rightarrow 3$ | *(R.S.D.%)* | *C.I* | $\Delta t_B$ *sec* | *V. (ml) at flow cell* | *C (mM)* | *D* | $t_{sec}$ |
|---|---|---|---|---|---|---|---|---|---|
| 5 | 0.9 | 1828 | 0.08 | 1828±3.826 | 66 | 2.04 | 0.235 | 25.50 | 36.0 |
| 10 | 1.2 | 1656 | 0.11 | 1656±4.670 | 57 | 2.34 | 0.205 | 29.25 | 31.8 |
| 15 | 1.3 | 1468 | 0.10 | 1468±3.702 | 54 | 2.4 | 0.200 | 30.00 | 30 |
| 20 | 1.5 | 1440 | 0.08 | 1440±2.956 | 45 | 2.31 | 0.208 | 28.88 | 22.2 |
| 25 | 1.8 | 1000 | 0.12 | 1000±3.006 | 42 | 2.58 | 0.186 | 32.25 | 21 |
| 30 | 2.2 | 836 | 0.18 | 836±3.677 | 40.2 | 3.01 | 0.160 | 37.60 | 19.8 |
| 35 | 2.5 | 764 | 0.17 | 764±3.279 | 30 | 2.56 | 0.188 | 32.00 | 15 |

$\bar{Y}_{Zi}$ (mV):(S/N) response of (NAG4X3) Analyzer in mV((S/N)-R.N.A), $t_{0.025,2}$=4.303, SEM= Standard error of mean ,CI: Confidence Interval ,$\Delta t_B$ (sec) :Base width of peak (sec), $t_{sec}$: Departure time of sample segment out of injection valve reaching the flow tube, C: Concentration, CI: confidence interval ,D: Dilution factor at flow cell

**Table 5.** Segmentation pattern with ideal choice.

| Segment | F.r ml/min | *(a)* | *(b)* | *(r)* | *(θ)* |
|---|---|---|---|---|---|
| $S_1$ | 0.9-1.3 | 2585.231 | -824.615 | -0.9533 | -89.931 |
| $S_2$ | 1.3-1.8 | 2802.105 | -977.895 | -0.9376 | -89.941 |
| $S_3$ | 1.8-2.5 | 1605.676 | -341.081 | -0.9903 | -89.832 |

**Table 6.** Results of S.V impact

| Length of S.Vcm r= 0.5m | (S.V) µL | *ȲZi. →3* | *(R.S.D.%)* | *CI* | $\Delta t_B$ *.sec* | *V. (ml)* | *C (mM)* | *D* | $t_{sec}$ |
|---|---|---|---|---|---|---|---|---|---|
| 3.18 | 25 | 168 | 0.50 | 168±2.087 | 27.0 | 1.76 | 0.145 | 55.00 | 6.0 |
| 5.10 | 40 | 1248 | 0.10 | 1248±3.056 | 33.0 | 1.69 | 0.189 | 42.25 | 9.0 |
| 6.37 | 50 | 1312 | 0.11 | 1312±3.677 | 36.0 | 1.85 | 0.216 | 37.00 | 12.0 |
| 7.64 | 60 | 1440 | 0.09 | 1440±3.205 | 45.0 | 2.31 | 0.208 | 38.50 | 22.2 |
| 10.20 | 80 | 1656 | 0.08 | 1656±3.180 | 46.20 | 2.39 | 0.268 | 29.88 | 24.0 |
| 15.30 | 120 | 1728 | 0.11 | 1728±4.894 | 48.00 | 2.52 | 0.381 | 21.00 | 25.2 |
| 29.00 | 228 | 2290 | 0.08 | 2290±4.794 | 51.0 | 2.78 | 0.657 | 12.18 | 27.0 |
| 34.0 | 267 | 2210 | 0.09 | 2210±4.993 | 54.0 | 2.97 | 0.720 | 11.11 | 28.2 |
| 41.5 | 326 | 2010 | 0.11 | 2010±5.267 | 57.0 | 3.18 | 0.821 | 9.74 | 29.4 |

**Table 7.** The ideal segment for the sample plug

| Segment | S.V (µL) | *(a)* | *(b)* | *(r)* | *(θ)* |
|---|---|---|---|---|---|
| $S_1$ | 25-50 | -924.211 | 47.832 | 0.9363 | 88.802 |
| $S_2$ | 60-120 | 1229.143 | 4.374 | 0.8910 | 77.115 |
| $S_3$ | 228-326 | 2963.682 | -2.900 | -0.9922 | -70.975 |

**Table 8.** Effect of the reaction coil with segmentation pattern

| Coil length cm r=0.5 mm | Coil volume µL | ŸZi. →3 | (R.S.D.%) | CI | $\Delta t_B$ .sec | V. (ml) | C (mM) | D | $t_{sec}$ |
|---|---|---|---|---|---|---|---|---|---|
| Without | 0 | 2290 | 0.085 | 2290±4.819 | 51.0 | 2.778 | 0.657 | 12.18 | 27.2 |
| 10 | 314 | 2170 | 0.087 | 2170±4.695 | 54.0 | 2.928 | 0.623 | 12.84 | 28.5 |
| 20 | 628 | 2160 | 0.099 | 2160±5.316 | 55.2 | 2.988 | 0.610 | 13.11 | 29.4 |
| 25 | 785 | 2150 | 0.104 | 2150±5.540 | 57.0 | 3.078 | 0.593 | 13.50 | 30.6 |
| 30 | 942 | 2140 | 0.103 | 2140±5.490 | 58.8 | 3.168 | 0.576 | 13.89 | 32.4 |
| Segment | Coil volume (µL) | | (a) | (b) | | (r) | | (Θ) | |
| $S_1$ | 0-628 | | 2271.667 | -0.207 | | -0.8985 | | -11.695 | |
| $S_2$ | 628-942 | | 2200.000 | -0.064 | | -1.0000 | | -3.644 | |

### 3.2.4. Impact of points of intersection

A process of mixing for the generation of precipitated particles has been conducted using several mixing chamber designs of different capacities. Prior to being introduced into the flow cell, several diameters were assessed in terms of their propensity for agglomeration, ability to regulate particles, and uniformity of distribution. This investigation was conducted subsequent to the optimization of the system. Table 9 provides a comprehensive summary of all the results. The present study observed reduced peak amplitude and a wide base. The responses have a distorted nature. The occurrence of incomplete reaction and non-uniform mixing of the complementary reactant inside the large mixing chamber might result in diverse sizes and shapes of the reactants, leading to turbulent flow within the measuring cell. The distribution of precipitated particles on the moving segment of the measuring cell is influenced by physical processes such as dilution and dispersion, resulting in its dispersibility. The study revealed that optimal outcomes for precipitated particles are attained by combining reactants inside a cylindrical vessel with an inner diameter of 2 mm and an outer diameter of 4 mm, therefore resulting in a volume of 12.56 µL.

**Table 9.** Results obtained for the effect of volume of Y-junction & premix chamber

| | Y-junction type | Volume лГ²h | Ȳ-zi(n→3) | $t_{sec}$ | V.mL | C (mM) D |
|---|---|---|---|---|---|---|
| | | | | | At junction point | |
| Intersection junction point | 2 mm (ID)(two inlet) 4mm (length)(outlet) | 12.56 µl* | 2290 | 27.0 | 1.578 | 1.156 8.65 |
| | 4 mm (ID)(two inlet) 6 mm (length) (outlet) | 75.36 µl | 690 | 28.2 | 1.638 | 1.114 8.98 |
| Premix chamber | 14 mm (ID) (outlet) 12 mm(length) | 1.85 mL | 640 | 29.4 | 1.698 | 1.074 9.309 |
| | 14mm (ID) (outlet) 13 mm (length) | 2.00 mL | 460 | 30.6 | 1.758 | 1.038 9.638 |
| | 14 mm (ID) (outlet) 14 mm (length) | 2.15 mL | 370 | 32.4 | 1.848 | 0.987 10.13 |

t: Time (Sec) from injection valve till the flow cell, C: Concentration before junction point or premix chamber & DF: Dilution factor, * optimum Y-junction for two systems

### 3.3. Using NAG4S3XAnalyzer and comparison with the classical methods to determination of LOT

### 3.3.1. UV-Spectrophotometry method (reference method)

UV-Vis spectrophotometric measurements were conducted using a Shimadzu model 1800 double-beam spectrophotometer and a 4.00 cm quartz cell. The maximum absorbance of the LOT was observed at 275 nm, which was selected as the peak wavelength [14]. To estimate the scatter plot, dynamic range, working range, and linear range. LOT concentrations ranging from 0.05 to 9.0 mM were prepared using distilled water. LOT conducted statistical calculations and found a linear range of 0.05-9.0 mM, with a correlation coefficient (r) of 0.9983 and a coefficient of determination ($r^2$) of 0.9965. Table 1s (Supplementary file) presents a summary of the statistical analysis conducted on the regression line derived from the UV-spectrophotometry method.

According to the optimal values for physical and chemical variables those have been determined for LOT figure 3s (Supplementary file). We prepared a series of solutions containing LOT in the LOT-SNP system, with concentrations ranging from 0.01 to 25 mM. Each measurement was conducted in triplicate. The transducer energy response was measured and plotted against the concentration of Loratadine. The results of LOT-SNP system were obtained above 25 mM a correlation coefficients is going to decrease and diverge from linearity. The likely cause of this phenomenon is an increase in the number of particles in front of a detector, which could be attributed to the attenuation of the radiation. Furthermore, the results obtained indicated that there is a direct relationship between the variables up to concentrations of 25 mM. This might be due to increased precipitated particulate and its competence forming a relatively hard missing inter particulate spacing preventing remained light to reach the detector. Evaluation and assessment of the newly developed methodology to determine of LOT was compared with available reference method (UV-Spectrophotometry) which results have been explained previously. The results those obtained by using NAG4S3XAnalyzer have been tabulated in table 2s (Supplementary file).

### 3.3.3. Detection of limit (LOD)

Table 3s (Supplementary file) presents the use of three separate methodologies to ascertain the limit of detection of Loratadine[15].

### 3.3.4. Repeatability

The assessment of precision attained by the complete assay procedure, as depicted in Table 4s (Supplementary file), encompasses the amalgamation of measures obtained for two different concentrations of LOT-SNP system. Each measurement was repeated six times consecutively. The data indicates that the percentage relative standard deviation [16] was below 0.14% concentration.

The standard addition method was utilized to determine the level of Loratadine (LOT) in four different samples from four different companies. This was done using the NAG4S3X analyzer, and the results were compared with the classical spectrophotometric method, specifically measuring λmax at 275nm. To perform the analysis, a series of solutions were prepared for each pharmaceutical drug, with a concentration of 5 mM and 0.1914 gm of active ingredient in 100 ml. From each solution, 1.0ml was transferred to five volumetric flasks with a capacity of 10 ml. Gradual volumes of a 0.02 mM standard solution of Loratadine were then added to each flask, as shown in Table 5s (Supplementary file) and Table 6s (Supplementary file). A presents a summary of the findings obtained using the standard additions technique for three samples containing the amount of LOT in pharmaceutical products. Table 12.B presents a concise overview of the outcomes derived from two distinct methodologies. The present findings include the empirical data pertaining to the active ingredient's practical content, ascertained with a confidence level of 95%. Furthermore, the table presents data on the efficacy of determination and the t-test for comparison at two distinct pathways.

Individual t-test [17]: A comparison is made between a newly devised approach and the officially reported value (μ0=10 mg) for four different substances: Lartin from Iraq, Lorasam from Iraq, Lohist from Oman, and Pressing from Serbia, as shown in Table 12.B .

There is a lack of statistically significant difference seen in the averages of practical content across four distinct firms ($\bar{W}i$) when compared to the stated amount (μ0 = 10 mg).

Based on the data obtained, it may be inferred that the observed tTab for medicines exceeds the calculated tcal with a confidence level of 95%. This finding suggests that there is no statistically significant disparity between the stated value and the computed t-value.

Paired t-test [18]: A comparative study was performed to assess the efficacy of a devised way of analysis, specifically using the NAG4SX3analyzer, in contrast to conventional methods such as spectrophotometry. This investigation included the examination of four samples obtained from distinct firms. When considering the comparison between different

manufacturers, it is important to acknowledge the potential ignoring of individual differences.

A hypothesis can be estimated as a follow: Null hypothesis $H_o$: µNAG-4SX3-3D analyzer = µUV-Spectrophotometric

µNAG-4SX3-3D analyzer = official method
Since calculation $t_{cal}$ of /-2.185/< 3.182 at 95 % confidence level. Therefore; $H_0$ is accepted against $H_1$

i.e., that there is no significant difference between three methods.

### 3.3.6. Statistically data treatment using analysis of variance one way- ANOVA

The one-way analysis of variance (ANOVA) method [19] was used to compare the means of three or more groups when only a single variable was considered. This study aims to evaluate the performance of the NAG4SX3 analyzer in the measurement of LOT in various pharmaceutical samples. The results from the NAG4SX3 analyzer are compared to those from the official method and the UV-spectrophotometric technique, which are two common ways to do this kind of testing Table 7s (Supplementary file).

In the absence of mean differences, the estimation of between-group variance will be nearly equivalent to the estimation of within-group variance, leading to an F-value of 1. When the F-test score exceeds 1, it indicates that the null hypothesis should be rejected in favor of the alternative hypothesis. The statistical approach widely known as analysis of variance (ANOVA) is often used .

The ANOVA test was performed with a significance level (α) set at 0.05, which corresponds to a confidence level of 95%. The presented table, designated as Table 8s (Supplementary file) displays the results of a hypothesis test (ANOVA) and a comparative analysis involving four distinct samples of Loratadine .

## 4. Discussion

The results indicate that there is not a statistically significant difference between the means of the samples, as shown by the calculated F-value (3.712) being lower than the critical F-value [20-22].

A decently touchy spectrophotometric strategy for the assurance of four antipsychotic phenothiazine drugs has been created and fittingly approved. The strategy is less difficult, speedier and touchier than numerous spectrophotometric strategies proposed prior. The solidness of the color framework is an advantage over the prior strategies [23-26].

The comes about of examination of bona fide tests and bulk drugs uncover that the strategy is both precise and exact. Commonly experienced excipients and added substances don't meddled. Be that as it may, other drugs with fundamental centres are anticipated to allow comparative response with chloranilic corrosive, so the strategy is restricted to the test of single medicate definitions [23-26].

Consequently, the null hypothesis will be rejected in favor of the alternative hypothesis. These findings indicate that there is no statistically significant difference seen across the four distinct firms across all samples utilized in the study.

## 5. Conclusion

The approach presented in this study utilizes equipment and reagents that are more cost-effective compared to the conventional methods. The NAG-4SX3-3D analyzer was used in this research to enhance the precision and efficiency of determination.

The relative standard deviation (RSD) for the repetition with a (n= 6) was found to be much lower than 0.2%. This suggests that the proposed approach is both accurate and adequate for the intended purpose. This technique may also be used for the quantification of loratadine, with the advantage of attaining elevated responsiveness with no the need of thermal treatment or extraction. The statistical analysis produced findings that were comparable to those derived from the conventional approach.

## Conflict of Interests

All authors declare no conflict of interest.

## Ethics approval and consent to participate

No human or animals were used in the present research.

## Consent for publications

All authors read and approved the final manuscript for publication.

## Informed Consent

The authors declare not used any patients in this research.

## Availability of data and material

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Authors' contributions

All authors had equal role in study design, work, statistical analysis and manuscript writing.

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