Baghdad Science Journal

Volume 23 | Issue 2 Article 10

2-23-2026

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Mezaal, Elham N. N. and Turkey, Nagam S. S. (2026) "Determination of Mebeverine – HCl Using 3, 5–Dinitrosalicylic Acid and Multiple Continuous Flow Cell That Works as a Solo Flow Cell with 4S×3 – 3D Analyzer," *Baghdad Science Journal*: Vol. 23: Iss. 2, Article 10.
DOI: https://doi.org/10.21123/2411-7986.5202

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BAGHDAD SCIENCE JOURNAL 2026;23(2):525–535

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RESEARCH ARTICLE

Determination of Mebeverine – HCl Using 3, 5–Dinitrosalicylic Acid and Multiple Continuous Flow Cell That Works as a Solo Flow Cell with 4S×3 – 3D Analyzer

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ABSTRACT

A new method, simple and sensitive was utilized in determining mebeverine – HCl (MB-HCl) (3, 4-Dimethoxy benzoic acid ethyl 2, 4 methoxy4-phenyl-1-methyl ethyl amino-butyl ester) in pure and pharmaceutical formulations via utilization this multiple continuous flow cell. The method is dependent on genesis for complex of ion pair(4-((3, 4-dimethoxybenzoyl) oxy)-N-ethyl-N-(1-(4-methoxyphenyl) propan-2-yl) butan-1-aminium-2-hydroxy-3,5-dinitrobenzoate) among mebeverine–HCl (MB-HCl) and 3,5-Dinitrosalicylic acid (3,5-DNSA) in ammonium acetate middle to configure a whiteish yellow precipitate compound via utilizing multiple continuous flow cell that works as a solo flow cell with 4S×3 – 3D analyzer. Optimum parameters were studied to raise the sensitivity for improving the method. The linear dynamic range of calibration graph 0.5 – 60 mmol / L and LOD 582.5 ng /125 μL with correlation coefficient (r) 0.9783, RSD% was less than 0.5 %, (n = 6) for estimate of (MB-HCl) in concentration (13, 30) mmol / L. The results were compared together, traditional way method UV-Sp, via using the method of measuring additions by t-test and F-test, in 95% confidence plane. Comparing results explained that multiple continuous flow cell that works as a solo flow cell with 4S×3 – 3D analyzer is the good choice and widely utilized in applications.

Keywords: 3,5-Dinitrosalicylic acid, Flow injection analysis, Flow cell, Improved, Optimum parameters

Introduction

Mebeverine–HCl (MB-HCl) is white crystalline, powder, molecular with weight = 466 g / mol, Molecular Formula = $C_{25}H_{35}NO_5$.HCl, Fig. 1. (MB-HCl) is soluble in water and ethanol, but not soluble in diethylether.[1] Mebeverine–HCl has name in IUPAC 3, 4-Dimethoxy benzoic acid ethyl 2, 4 methoxy4-phenyl-1-methyl ethyl amino-butyl ester. MB-HCl is widely utilized as a relaxant and antispasmodic medication of gastrointestinal tract especially colonic spasm and irritable bowel syndrome.[2]

Several analytical methods were revealed when scanning the literature to determine of mebeverine–HCl including simultaneous spectrophotometric method,[3] ion association reaction,[4] development method,[5] pillarization technique[6] HPLC,[7] RP-HPLC,[8,9] HPLC using degradation products,[10] ion selective Electrodes,[11,12] Voltammetry,[13,14] potentiometric,[15] and CFIA[16] to estimate the pharmaceutical potion of MB-HCl. There are several other techniques that have been used to estimate some drugs, for example using HLPC,[17] gas chromatography,[18] RP-HPLC,[19] CFIA,[20] and a new method was introduced within the continuous

Received 14 March 2024; revised 16 July 2024; accepted 18 July 2024.
Available online 23 February 2026

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https://doi.org/10.21123/2411-7986.5202
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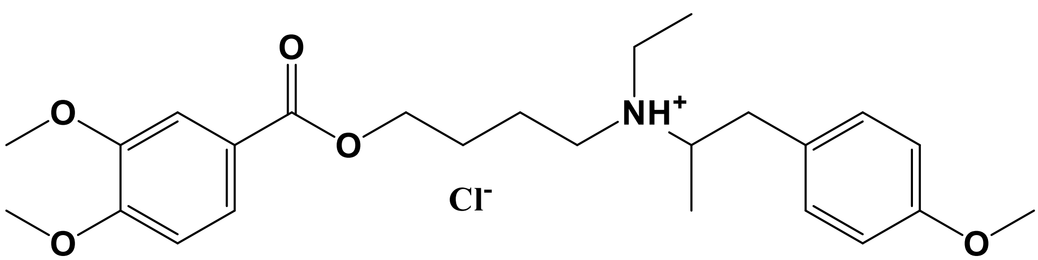


Fig. 1. Gestalt of Mebeverine–HCl (MB-HCl) (3, 4-Dimethoxy benzoic acid ethyl 2, 4 methoxy4-phenyl-1-methyl ethyl amino-butyl ester).

flow injection analysis technique using homemade cells which depend on fluorescence or turbidity as it is an easy, simple safe and inexpensive method to control the quality of DPH- cottoning drug tablets using homemade Ayah 6S ×1-ST-2D.[21] Therefore, we designed our experiment to improved FIA method, which is distinguished as easier, fast and very precise to measure the potion of MB-HCL within pharmaceutical formulations. Each drug has a different effect on the human body, so many researchers have resorted to study its effects, and we are one of those researchers.[22–24] Other methods have been used by researchers to estimate using the uv-vis technique.[25]

This research used multiple continuous flow injection analysis with turbidimetric measurement for MB-HCl determination using multiple continuous flow cell that works as a solo flow cell with 4S×3 – 3D analyzer. Measurements rely on (color whiteish yellow) the composition of the precipitated particles for MB-HCl - 3, 5-DNSA- CH_3COONH_4 system. Chemical factors were studied: concentration effect from reagent, effect of salt and acid medium of reaction and effect of ammonium acetate concentration as for the studied physical factors which include flow rate, volume sample and mixing coil. The best conditions studied were used to evaluate the drug and its application.

Materials and methods

All materials used are analytical reagents and dissolved by distilled water. The solution of standard 100 mmol/L of mebeverine-HCl was made via dissolving 4.6600 g in 100 ml of distilled water. A series of 3, 5-dinitrosalicylic acid solutions were made of the dilution for solution of standard 100 mmol / L together with water and be distilled.

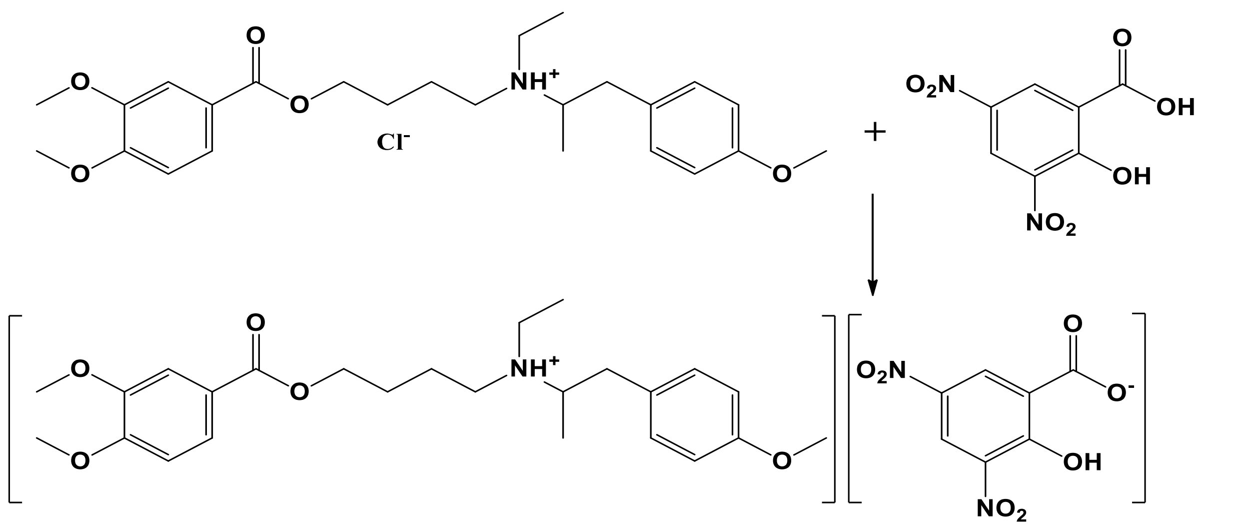
Information about the apparatus

The request involved using triplet flow cell composed of three flow cells made of clear borax glass in the form of tube, each of 60 mm length with inlet diameter of 2 mm, connected to these tubes a 600 mm Teflon tube into stages. Each of 300 mm length of 1mm was inside diameter. Intension in using two different diameter was used for different distances to insure good mixing and lengthen the flow cell in a total length of $3\times60 = 180$ mm with 2mm inside diameter added to this length 600 mm of 1mm Teflon tube (hydrophobic). This 600 mm length was in the two stages, each of which is 300 mm. Two different materials were used : glass and Teflon, glass has a hydrophilic property via H- bonding with 2mm inside diameter i.e.; slow down fluid movement. On the contrary Teflon with 1mm inside diameter with its hydrophobic properties causes to enhance fluid movement i.e.; different fluid speed and delay or enhance movement causes much homogenization of fluid stream containing precipitated particulate and allowing enough time to give smooth noise – free responses as main homogeneity occur in the Teflon part which has no detection. Two stages recognized detection region and non-detecting location for completion of signal obtained in the glass tube and collect all these were in one single response of clean noise free response with excellent repeatability.[21]

Methodology

Using a manifold of two lines connected with 4S×3 – 3D analyzer to determine mebeverine-HCl via its reaction with 3, 5-dinitrosalicylic acid in ammonium acetate medium. It consists of 2 lines. One line as a vector current (CH_3COONH_4 20 mmol / L) at 1.75 ml / min, the flow rate to for crossing during the valve of the injection to tote the segment from sample of mebeverine-HCl (20 mmol / L) run into one another 3, 5-dinitrosalicylic acid (5 mmol/L) in line two 1.75 ml/min of flux an average for reagent in Y-junction dot prior it is come into 4S×3 – 3D analyzer.[21]

Scheme 1 prospect mechanism for reaction of mebeverine-HCl together with 3, 5-dinitrosalicylic acid in ammonium acetate medium.



Scheme 1. Displays in prospect mechanism interaction path of mebeverine-HCl together with 3, 5-dinitrosalicylic acid in ammonium acetate medium.

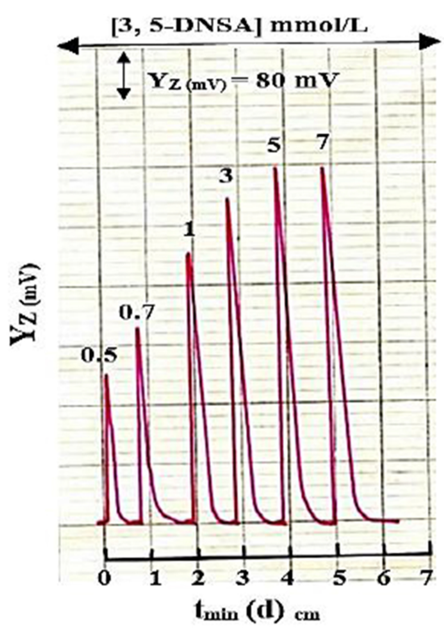


Fig. 2. Effect of variable concentration of 3, 5-Dinitrosalicylic acid (3, 5-DNSA) on: profile (S/N response to the power adapter).

Table 1. Effect variable concentration from 3, 5-DNSA on the response of the transducer S/N for MB-HCl 20 mmol/L - 3, 5-DNSA system, utilization flow rate for each line 1.5 ml / min and 125 μL of sample volume.

[3,5-DNSA] mmol/L	Average for peak heights (n = 3) $\bar{Y}_{Zi(m\ V)}$	$\bar{Y}_{Zi(mV)} \pm$ t SEM
0.5	253	253 ± 1.23
0.7	334	334 ± 1.56
1	455	455 ± 1.98
3	542	542 ± 2.24
5	595	595 ± 2.98
7	590	590 ± 2.31

Note. $\bar{Y}_{Zi\ (m\ V):}$ (S/N) response to the power adapter (i.e.; the average height of the peaks for n = 3 in mV. $t_{0.05/2,n\text{-}1} = t_{0.025,2}$ = 4.303, SEM = standard error of mean, t SEM = confidence interval.

Results and discussion

Optimization of variable

- Chemical variables

Concentration effect from reagent

A range of concentrations of 0.5–7 mmol/L of 3, 5-DNSA reagent was studied using a 125 μL volume of sample injected through a conveyor stream. 20 mmol/L of MB-HCL was injected at a flow rate of 1.5 mL/min per line. Fig. 2 shows an increase in peak height with increasing concentration of 3, 5-DNSA. This is likely due to increasing the color of the deposited particles, which work to absorb part of the light. While at a concentration higher than > 5 mmol/L this may lead to increased agglomeration of particles and an increase in the spaces between those particles, which helps to penetrate a greater amount of light and reduce the height of the response. Therefore 5 mmol/L was chosen as the optimal concentration of 3, 5-DNSA reagent. The results obtained are shown in the Table 1.

Effect of salt and acid

The reaction between MB-HCl (20 mmol/L) with 3,5-DNSA (5 mmol/L) to form a whiteish yellow color precipitate was studied in various saline

Table 2. The effect of the difference in the middle on response measurement to the power adapter for determination MB-HCl.

Type for medium Salt (30 mmol/L) Acid (50 mmol/L)	Average for peak heights (n = 3) $\bar{Y}_{Z\,i\,(m\,V)}$	$\bar{Y}_{Zi(mV)} \pm t$ SEM at 95%
Water	595	595 ± 2.98
Sodium chloride	382	382 ± 3.13
Ammonium chloride	486	486 ± 2.97
Sodium acetate	302	302 ± 2.94
Ammonium acetate	644	644 ± 2.31
Potassium chloride	438	438 ± 3.42
Potassium nitrate	503	503 ± 2.49
Ascorbic acid	238	238 ± 1.92
Tartaric acid	331	331 ± 1.78
Salicylic acid	519	519 ± 3.22
Acetic acid	428	428 ± 2.32
Hydrochloric acid	489	489 ± 3.21

Note. $t_{0.05/2,n-1} = t_{0.025,2} = 4.303$, SEM = standard error of mean, t SEM = confidence interval.

environments (sodium chloride, ammonium chloride, sodium acetate, ammonium acetate, potassium chloride, potassium nitrate) at 30 mmol / L and various acidic media (ascorbic acid, tartaric acid, salicylic acid, acetic acid, hydrochloric acid) at a concentration of 50 mmol / L in addition to the aqueous medium as a carrier current. The study showed that different media reduce the S/N response. This may be attributed to increasing the conglomeration and the intensity of fusion together and then raising the intensity of the light through it as there will be more empty spaces amidst the conglomerations of the particles except for the ammonium acetate which leads to an increase in the S/N response due to the effect of small solid particles which may lead to a reduction of the spatial areas and an increase in the limit from the incident light. Therefore ammonium acetate medium was used as vector current in the following studied. A results obtained are shown in Table 2.

Effect of ammonium acetate concentration

The reaction between MB-HCl (20 mmol/L) with 3,5-DNSA (5 mmol/L) to form a whiteish yellow color precipitate was studied at variable concentrations of ammonium acetate ranging (5–35 mmol/L) as a carrier stream in order to decide the most favorable concentration that will fit the methodology that was adopted in this conducted research work. It was noticed that a raise for ammonium acetate concentration up to 20 mmol/L leads to increased solubility or dissociation of some of the precipitate particles. Mostly the shape will be particles of small size can be mainly nucleus shaped which in turn will aid in clumping, leading to increased attenuation of incident light. More than 20 mmol/L leads to an increase of solubility of small size particulate. Therefore 20 mmol/L of ammonium acetate concentration was chosen as optimum carrier stream. The set of results obtained are summarized in Table 3.

Table 3. The effect for ammonium acetate concentration in the measurement of response to the power adapter for determination of MB-HCl using MB-HCl (20 mmol/L) - 3, 5-DNSA (5 mmol / L) system, 125 μL the volume of sample in 1.5 ml/min flow rate of each line.

[Ammonium acetate] [CH_3COONH_4] mmol/L	Average for peak heights (n = 3) $\bar{Y}_{Z\,i\,(m\,V)}$	$\bar{Y}_{Zi(mV)} \pm t$ SEM at 95%
5	452	452 ± 2.13
7	489	489 ± 2.91
10	502	502 ± 2.98
13	578	578 ± 3.12
15	620	620 ± 2.37
20	698	698 ± 3.21
25	666	666 ± 3.98
30	644	644 ± 2.31
35	560	560 ± 3.21

- Physical parameter

Flow rate

Using all previous experimental factors related to chemicals difference concentrations for complementary materials of this reaction of MB-HCl (20 mmol/L) - 3, 5-DNSA (5 mmol/L) - CH_3COONH_4 (20 mmol / L) system. Changing of flow rate was carried out utilizing 0.55–3.0 ml / min for each line. It was noticed that a raise in S/N- response profile up to 1.75 ml/min, the carrier current that might be attributed to the conglomerate has added a hardness to the particulate and it's weight on the other will cause compression and act as a wall because of its bigger size and bigger than the wavelength, so it will allow it to reflect all wavelengths and raise the attenuating of incident light. At rise speed more than 1.75 ml / min carrier stream might be to form a tiny or semi-transparent particulates and therefore, the light falling on it will suffer whatever its source is a reflection or refraction inside and outside the precipitating particulates causing a reduce to an insignificance level as shown by the obtained responses. Therefore; 1.75 ml/min of flow rate for each line. The results are summarized as in the Table 4.

The volume of sample

The effect for the volume of sample was studied utilizing using variable volume of teflon tube ranging (50–200) μL of diameter (D) 1 mm.

High sample volume is not a recommended in the CFIA as a methodology as this type of scale will form

Table 4. Different effect for flow rate on the attenuation of incident light using 125 μL and 20 mmol/L concentration for MB-HCl and concentration 5 mmol/L for 3,5-DNSA.

Pump speed	flow rate (ml/min) for each Line1, Line2	Average for peak heights (n = 3) $\bar{Y}_{Zi(m\ V)}$	$\bar{Y}_{Zi(mV)}$±t SEM at 95%	Base width Δt (sec)	V_{add} (m l) in flow cell	Concentration (mmol / L) in flow cell	Df in flow cell
5	0.55	588	588 ± 3.15	70	1.4083	1.7752	11.27
10	0.75	593	593 ± 3.12	45	1.2500	2.0000	10.00
15	1.25	620	620 ± 2.97	35	1.5833	1.5790	12.67
20	1.5	698	698 ± 3.21	28	1.5250	1.6393	12.20
25	1.75	753	753 ± 2.42	25	1.5833	1.5790	12.67
30	2.00	750	750 ± 2.23	22	1.5917	1.5706	12.73
35	2.25	701	701 ± 2.13	21	1.7000	1.4706	13.60
40	2.50	688	688 ± 1.98	20	1.7912	1.3957	14.33
45	3.00	610	610 ± 1.38	19	2.0250	1.2346	16.20

Note. Δt: (sec) base breadth of peak, Df: dilution factor for a measured cell.

Table 5. The impact for difference volume for segment on reduction for incident light via concentration 20 mmol / L for MB-HCl together concentration 5 mmol/L for 3, 5-DNSA and a flow rate of the each line 1.75 ml/min.

Sample volume (μL)	Average for peak heights (n = 3) $\bar{Y}_{Zi(m\ V)}$	$\bar{Y}_{Zi(mV)}$±t SEM at 95%	Base width Δt (sec)	V_{add} (ml) in flow cell	Concentration (mmol / L) in flow cell	Df in flow cell
50	400	400 ± 1.35	18	1.1000	0.9091	22.00
75	510	510 ± 1.67	20	1.2417	1.2080	16.56
100	633	633 ± 2.34	22	1.3833	1.4458	13.83
125	753	753 ± 2.42	25	1.5833	1.5790	12.67
150	745	745 ± 2.97	27	1.7250	1.7391	11.50
175	740	740 ± 2.48	29	1.8667	1.8750	10.67
180	710	710 ± 3.12	30	1.9300	1.8653	10.72
200	700	700 ± 3.97	31	2.0083	1.9917	10.04

locally in the concentration of a precipitate that can decompose, i.e.; at least part of it due to the continuous flow of carrier current which will result in Ksp of the precipitate > from doubling the concentration of the reactant species raising to the strength of their participation in the contributing force.

Low sample size will represent a rapid passage of the reaction product in front of the detector, which is solar cells that are not characterized by a fast response compared to PMT that can be detected at the nanosecond level. Therefore, a very small sample size may not be an appropriate choice, so the solution in this study was to choose an appropriate size 125 μl, and the results shown in the Table 5 were obtained.

Mixing coil

The effect of the reaction coil size on the peak height was studied, as it is attached before the measuring cell. Coil sizes from 0 to 350 μL were used. Whilst preservation all other changeable steady (MB-HCl (20 mmol / L), 3, 5-DNSA (5 mmol / L), the flow rate for each line (ammonium acetate and 3,5-DNSA) equal 1.75 ml / min, volume of sample 125 μl. The raise of volume coil leads to reduce and distort profile within raise of the base amplitude and departure time of the injected sample section via the valve reaching into the cell. This may be attributed to the diffusion and dispersal that occur of precipitated particles for sample which in turn causes a raise of dispersed regions and especially lead to piling up for the precipitate particles, leading to an increase the inter-spaces between large precipitate particles that causes reduction in the attenuation of incident light. So its ability can be seen clearly at 100 μL the mixing coil necessary of completion the reaction among MB-HCl with 3, 5-DNSA in ammonium acetate (CH_3COONH_4) medium. Table 6. tabulates all the results.

Assessment of linear range for the scatter plot of difference for mebeverine- HCl against response S/N to the power adapter

A range of mebeverine – HCl concentrations (0.5–100 mmol/L) was used, and the peak height was measured with the best chemical and physical variables. The height of the transducer response increases when the sample concentration is increased. Fig. 3 explains the contrast ranges (the scatter of plot in the run (0.5–100) mmol / L, the dynamic range at (0.5–80) mmol / L, working range at (0.5–70) mmol / L and linear dynamic range at (0.5–60) mmol / L. The results summed up in the Table 7.

Table 6. Effect volume of reaction coil on energy transducer response expressed as an average peak heights (mV) for determination of MB-HCl (20 mmol / L) by 3,5-DNSA (5 mmol / L), 1.75 ml / min flow rate for vector current and 125 μL volume of sample.

Volume of reaction coil (μL)	Average for peak heights (n = 3) $\bar{Y}_{Z\,i\,(m\,V)}$	$\bar{Y}_{Zi(mV)}\pm$t SEM at 95%	Base width Δt (sec)	V_{add} (ml) in flow cell	Con. (mmol / L) in flow cell	Df in flow cell
0*	753	753 ± 2.42	25	1.5833	1.5790	12.67
100	788	788 ± 2.42	28	1.7583	1.4218	14.07
200	760	760 ± 3.21	35	2.1667	1.1538	17.33
250	632	632 ± 3.49	40	2.4583	1.0170	19.67
300	600	600 ± 4.21	46	2.8083	0.8902	22.47
350	588	588 ± 4.32	52	3.1583	0.7916	25.27

Note. 0* without coil, Δt: sec breath of peak.

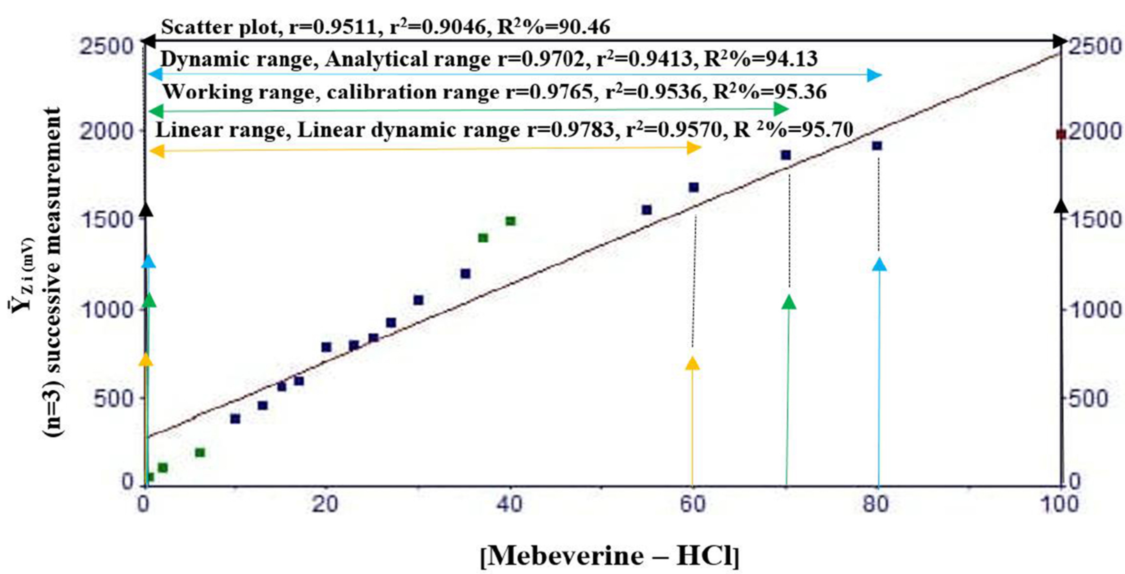


Fig. 3. Effect for Variable range of concentration of mebeverine – HCl on reduction of incident light, scatter plot in range (0.5–100) mmol / L for n = 20, dynamic range at (0.5–80) mmol / L for n = 19, working range at (0.5–70) mmol / L for n = 18 and linear range at (0.5–60) mmol / L for n = 17.

Table 7. The result of linear regression for difference of response S/N to the power adapter together with concentration of mebeverine – HCl using the equation for the first degree as in the model $\hat{Y}$ = a + bx in the best conditions.

Mode species	[MB-HCl] extent mmol / L(n)	$\hat{Y}_{Zi\,(m\,V)} = a_{mV} \pm S_a\,t + b\,(\Delta y_{mV}/\Delta x_{mmol\,/\,L}) \pm S_b t$ [MB-HCl] mmol / L in confidence level 95%, n-2	r, r^2, R^2 %	t_{tab} at 95%, n-2	Calculated t -value t_{cal}= /r/ $\sqrt{n-2}$ / $\sqrt{1-r^2}$
Scatter plot	0.5–100 (20)	273.8208 ± 147.6076 + 21.5922 ± 3.4732 [MB-HCl] mmol/L	0.9511, 0.9046, 90.46	2.101	<< 13.0644
Dynamic range or analytical range	0.5–80 (19)	195.7670 ± 118.5436 + 25.0160 ± 3.1969 [MB-HCl] mmol/L	0.9702, 0.9413, 94.13	2.110	<< 16.5107
Working range or calibration range	0.5–70 (18)	149.7945 ± 105.7325 + 27.3114 ± 3.1940 [MB-HCl] mmol/L	0.9765, 0.9536, 95.36	2.120	<< 18.1331
Linear range or linear dynamic range	0.5–60 (17)	113.5844 ± 100.7933 + 29.2781 ± 3.4132 [MB-HCl] mmol/L	0.9783, 0.9570, 95.70	2.131	<< 18.2719

Note. n: number of measurement, $\hat{Y}_{Zi\,(mV)}$: evaluated value in mV for improved method, r: correlation coefficient for each range, r^2: coefficient for estimation, R^2% = percentage capital R-squared: explained difference as a percentage / total difference and t_{tab}= $t_{0.05\,/\,2,\,n-2}$.

Table 8. Limit of detection of mebeverine – HCl at best parameters using 125 μL as an injection from sample volume, 1.75 ml / min flow rate for both line, 3, 5-DNSA (5 mmol / L).

Practically based on the progressive mitigation of lower concentration in scatter plot (0.5 mmol / L)	Theoretical based on the amount of slope $x = 3\ S_B$ / slope	Theoretical based on of the linear equation $\hat{Y} = Y_b + 3S_b$
0.01 mmol/L 582.5000 ng / 125 μL	1.7883 μg / 125 μL	653.2839 μg / 125 μL

Note. X = LOD based on slope from linear dynamic range and S_B= standard deviation of blank refined for 13 times Y_b= rate response of blank= an intercept, S_b= standard deviation amounting into S y / x = residual from linear dynamic range, $\hat{Y}$: estimated response (mV).

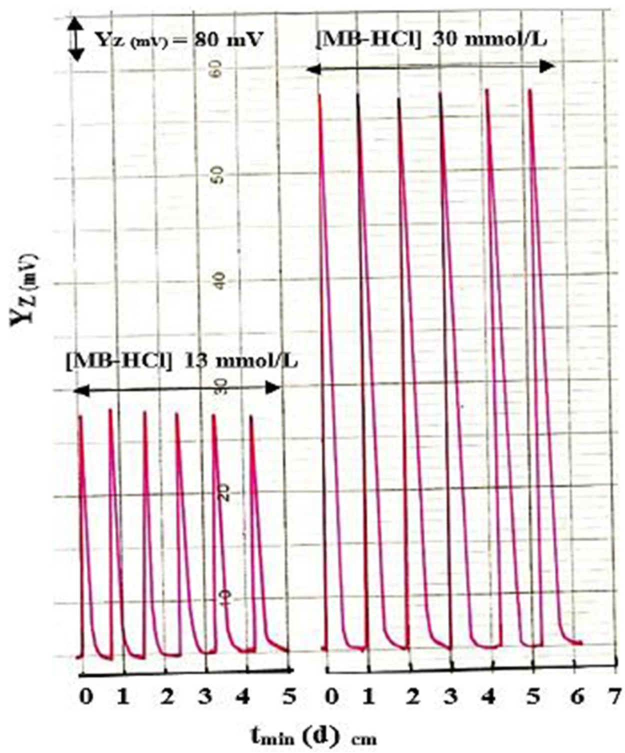


Fig. 4. Response to six successive repeatable measurement concentration of mebeverine – HCl (13 and 30 mmol / L) using 3, 5-DNSA (5 mmol / L), 1.75 ml / min flow rate for each line and 125 μ L volume of sample.

Table 9. Repeatability of mebeverine – HCl in best parameters with 125 μ L volume of sample.

[MB – HCl] (mmol / L)	Average for peak heights (n = 6) $\bar{Y}_{Zi\ (m\ V)}$	RSD %	Confidence interval in (95%) $\bar{Y}_{Zi(mV)} \pm t_{0.05\ /\ 2,\ n\text{-}1}\ \sigma_{n\text{-}1} / \sqrt{n}$
13	460	0.1304	460 ± 0.6298
30	1050	0.1247	1050 ± 1.3750

Note. (n= 6) the number of injections, t_{tab}= $t_{0.05/2,7}$ = 2.365.

LOD

Limit of detection (LOD) was studied for mebeverine – HCl during three different approach as shown in the Table 8. as an injected 125 μ L from sample volume.

Repeatability

The relative standard deviation = RSD % of mebeverine – HCl for 13 and 30 mmol / L as shown in Table 9. The relative standard deviation minimal than 0.5 % was obtained indicating that via using this method, a reliable measurement can be achieved using this way. Fig. 4 shows the response profile.

Assessment of multiple continuous flow cell that works as a solo flow cell with 4S×3 – 3D analyzer for determination of mebeverine- HCl in drugs

The newly developed methodology mebeverine – HCl was estimated in three drugs from three

Table 10. Standard addition method for determination of MB – HCl in three types of drugs utilization multiple continuous flow cell that works as a solo flow cell with 4S×3 – 3D analyzer and classical method UV- Spectrophotometric (UV-Sp.).

No. for sample	Commercial name, Company, Country, Content	Type of method — Newly developed methodology — UV- Spectrophotometric (UV-Sp.) traditional method absorbance measure in λ_{max} = 219 nm: Confidence interval for the rate Weight of tablet $\bar{w}$ i ± 1.96 σ_{n-1} / $\sqrt{n}$ in 95 % g	Theoretical content of the active ingredient in 95 % (mg) $\bar{w}i \pm 1.96\ \sigma_{n-1}/\sqrt{n}$	Practical of concentration (mmol / L) in 10 ml in 100 ml	Efficiency of determination Rec.% Newly method (UV-Sp.)	t –test the comparison among methods: $t_{cal} = \bar{X}d\ \sqrt{n}\ /\ \sigma_{n-1}$; t_{tab} in 95% confidence level	F-test the comparison among methods: $F_{cal} = S^2_1\ /\ S^2_{2\,(UV\text{-}Sp.)}$; F_{tab}	**r** r^2 R^2%
1	Duspatalin, Abbott, France, 135 mg	0.4183 ± 0.0028	135 ± 0.9036	2.0850 5.2134	104.25 104.35	$\bar{X}d$ =–3.8461 σ_{n-1} = 5.4662 /–1.2187/ < 4.303	σ^*_{n-1}= 3.9048, S^2_1 = 15.2475 σ^*_{n-1}= 1.7073, S^2_2= 2.9149 5.2309 << 39.0	0.9866 0.9734 97.34
2	Meva, Jamjoom Pharma, Saudi Arabia, 135 mg	0.4035 ± 0.0021	135 ± 0.7026	2.0560 5.1400	102.79 103.74			0.9981 0.9962 99.62
3	Colospasmin, Eipico, Egypt, 135 mg	0.3621 ± 0.0034	135 ± 1.2676	1.9730 4.9325	98.67 106.17			0.99974 0.99949 99.949

Note. $\bar{X}d$: the average of variation between two method (improved & traditional), n(number for sample) = 3,σ_{n-1}: standard of deviation for variation, $\bar{W}_i$: mg practically weight, $t_{tab} = t_{0.05/2,2}$ = 4.303 of t-test, $F_{tab} = F_{0.95,V1,V2} = F_{0.95,2,2}$ = 39, σ^*_{n-1} : standard deviation (F-test), UV–Sp. : UV- Spectrophotometric, S^2_1 = variation for developed method, S^2_2 = variation of classical method (UV- Spectrophotometric), $t_{tab} = t_{0.05/2,\infty}$ = 1.96 at 95%.

Table 11. Result obtained by other researchers.

Method	Reagent	Linear rang	RSD%	R	Ref.
Potentiometric	Poly vinyl chloride	1×10^{-1}–1×10^{-6} M	< 2%	1.0000	12
Turbidmetric	Sodium persulfate	2–10 μmol.L^{-1}	<1%	0.9981	16
Multiple continuous flow cell	3,5-dinitrosalycylic acid	0.5–60 mmol.L^{-1}	<0.5%	0.9783	-

different companies Duspatalin, Abbott, France, 135 mg, Meva Jamjoom, Pharma, Saudi Arabia, 135 mg and Colospasmin, Eipico, Egypt, 135 mg.

A multiple continuous flow cell that works as a solo flow cell with 4S×3 – 3D analyzer for the determination of mebeverine – HCl in drugs and was compared with method which includes UV-Spectrophotometric. A several of sol were intended for each drug (5 mmol / L) by transferring 4 ml to each of five volumetric flask (10 m L) he follows by the addendum of 0, 0.2, 0.4, 0.6 and 0.8 ml from 50 mmol / L for standard solution of drug to get 0, 1, 2, 3 and 4 mmol / L for suggested method. The results were processed mathematically using the method of measurement additions. Table 10 shows practical content of active ingredient in 95% confidence plane and efficiency for the appreciation in addendum to the t-test and F-test. The obtained results no significant variation amidst improved and traditional method in 95% the plane of confidence for estimation of mebeverine – HCl in pharmaceutical drugs.

Table 11 showing a comparison of the results obtained by other researchers in estimating the same drug and using different methods.

Conclusion

The assessment of multiple continuous flow cell that works as a solo flow cell with 4S×3 – 3D analyzer among this research action was applied using comparison among 4S×3 – 3D analyzer with classical UV-spectrophotometric method using mebeverine–HCl (MB-HCl) with 3,5-Dinitrosalicylic acid in medium ammonium acetate. In this research work the physical and chemical factors were studied. It was known that a narrower extent is obtained together UV-spectrophotometric kind, whilst widely extent was property for 4S×3 – 3D analyzer. A multiple continuous flow cell that works as a solo flow cell with 4S×3 – 3D analyzer is the option together with excellent detection range and a wide application. Future use a multiple continuous flow cell that works as a solo flow cell with 4S×3 – 3D analyzer for estimation and study most of the drugs that are chosen.

Acknowledgment

Author express their sincere thanks and appreciation to Prof. Dr. Issam Mohamed Ali Shakir for offering valuable devices for completing the research.

Authors' declaration

- Conflicts of Interest: None.
- We hereby confirm all the Figures and Tables in the manuscript are ours. Any Figures and images, that are not ours, have been included with the necessary permission for re-publication, which is attached to the manuscript.
- No animal studies are present in the manuscript.
- Author(s) signed on ethical consideration's approval.
- Ethical Clearance: The project was approved by the local ethical committee at University of Baghdad.

Authors' contribution statement

N.S.T. conceived of the presented idea, E.N.M. performed the computations and wrote the manuscript.

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تقدير الموبيفرين – حامض الهيدروكلوريك باستخدام حامض 5,3 – ثنائي نايتروسالسيلك وخلية التدفق المستمر المتعددة التي تعمل كخلية تدفق منفردة مع محلل 4S× 3-3D

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الخلاصة

تم استخدام طريقة جديدة وبسيطة وحساسة لتقدير عقار الموبيفرين في صورته النقية وفي المستحضرات الصيدلانية عن طريق استخدام خلية التدفق المستمرالمتعددة . تعتمد الطريقة على تكوين معقد ايوني بين الموبيفرين والكاشف حامض 5,3- ثنائي نايتروسالسيلك في وسط من خلات الامونيوم لتكوين مركب راسب اصفر مبيض باستخدام محلل خلية التدفق المستمر المتعددة تعمل كخلية تدفق منفردة مع محلل 4S×3-3D . تمت دراسة الظروف المثلى لرفع الحساسية للطريقة المطورة . النطاق الديناميكي الخطي للمعايرة 0.5-60 مليمول / لتر وحدود كشف 582.5 نانوغرام لكل 125 ميكرولتر مع معامل ارتباط 0.9783 وكان الانحراف القياسي النسبي المئوي اقل من 5 % لعدد قراءات يساوي 6 لتقدير عقار الموبيفرين بتراكيز 30,13 مليمول / لتر. النتائج تمت مقارنتها مع الطريقة التقليدية UV-Sp. وذلك باستخدام طريق اضافات القياس باستخدام اختبار t-test و اختبار F-test عند مستوى الثقة 95%. توضح نتائج المقارنة ان خلية التدفق المستمر المتعددة التي تعمل كخلية تدفق منفرد مع محلل 4S×3-3D هي الخيار الجيد وتستخدم على نطاق واسع في التطبيق.

الكلمات المفتاحية: حامض 5,3 -ثنائي نايتروسالسيلك، التحليل بالحقن الجرياني، خلية الجريان، تحسين، الظروف المثلى.