ISSN: 0067-2904
GIF: 0.851

New mode for the on –line determination of metoclopramide hydrochloride in pure and pharmaceutical preparations via the use of homemade Ayah 6SX1-T-2D Solar cell CFI Analyser

Nagam S. Turkey Al-Awadie* and Kefah H. Ismael Al-saadi
Department of chemistry, College of science, University of Baghdad, Baghdad, Iraq.

Abstract:

A newly developed analytical method characterized by its speed and sensitivity for the determination of metoclopramide hydrochloride (MCP-HCl) in pure and pharmaceutical preparations via absorbance measurement by Ayah 6SX1-T-2D Solar cell-CFI Analyser. The method is based on the oxidation of the drug with Ce(IV)sulfate in acidic medium to form a red color species which determined using homemade Ayah 6SX1-T-2D Solar cell . Chemical and physical parameters were studied and optimized. The calibration graph was linear in the range of 0.05- 16 mMol.L^{-1}with correlation coefficient r = 0.9855. The limit of detection(S/N = 3) 0.332 µg/sample from the step wise dilution for the minimum concentration in the linear dynamic ranged of the calibration graph. The RSD% at 2 and 6mMol.L^{-1} metoclopramide hydrochloride is less than 0.6% (six replicate). The method was successfully applied for the determination of metoclopramide hydrochloride in three pharmaceutical drugs. A comparison was made between the newly developed method analysis with the classical method (UV-Vis spectrophotometry at λ max 474 nm) using the standard addition method via the use of t-test. It was noticed that there was a significant difference between two methods at 95 % confidence level.

Keywords: Metoclopramide hydrochloride, flow injection analysis, spectrophotometry

نمط جديد للتقدير الاني للميتاكلوبراميد هايدروكلورايد في المستحضرات الصيدلانية والنقية من خلال استخدام محلل مصنع محليا للحقن الجرياني المستمرAyah 6SX1-T-2D Solar cell

نغم شاكر تركي العوادي * ، كفاح حسن اسماعيل الساعدي
قسم الكيمياء، كلية العلوم، جامعة بغداد ، بغداد ، العراق.

الخلاصة :

طورت طريقة جديدة تميزت بالسرعة والحساسية لتقدير الميتاكلوبراميد هايدروكلورايد في المستحضرات الصيدلانية والنقية .استندت الطريقة على اكسدة الدواء بوساطة كبريتات السيريوم (IV) في الوسط الحامضي لتكوين اصناف ملونة حمراء والتي قدرت باستخدام محلل الحقن الجرياني المستمر Ayah 6SXI-T-2D Solar cell . تم دراسة كافة المتغيرات الكيميائية والفيزيائية . مدى الخطية لمنحني المعايرة للميتاكلوبراميد هايدروكلورايد 0.05 – 16 مللي مول لتر$^{-1}$ بمعامل ارتباط (r) 0.9855 . حد الكشف=0.332 مكغم / انموذج من التخفيف التدريجي لأقل تركيز في منحني المعايرة . الانحراف القياسي النسبي المئوي لتركيز 2و6 مللي مول .لتر$^{-1}$ اقل من 0.6 % (بتكرارية لست مرات). طبقت الطريقة بنجاح لتقدير الميتاكلوبراميد هايدروكلورايد في ثلاث عقاقير دوائية .

---

* Email: nagamturkey2013@Gmail.com

اجريت المقارنة بين الطريقة المستحدثة والطريقة التقليدية (مطيافية UV- Vis) باستخدام الاضافات القياسية
بوساطة اختبار t المزدوج ولوحظ انه هنالك فرق جوهري بين الطريقتين عند مستوى قناعة 95%.

Introduction

Metoclopramide(MCP-HCl),4-amino-5-chloro-2-methoxy-N-(2-diethylamino-ethyl)benzamide Figure -1, MCP-HCl is available as white or almost white, crystalline powder or crystals, which is very soluble in water, freely soluble in alcohol, sparingly soluble in methylene chloride,it melts at about 183C^{o}with decomposition ,store protected from light [1] .

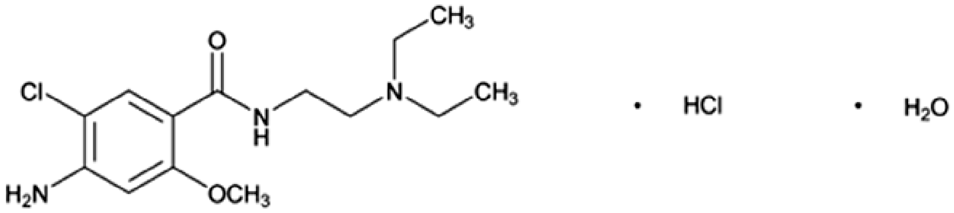


Figure 1- Chemical structure of metoclopramide hydrochloride

MCP-HCl used in disorders of decreased gastrointestinal motility such as gastroparesis or ileus; in gastro-oesophageal reflux disease and dyspepsia and in nausea and vomiting associated with various gastro-intestinal disorders, with migraine, following surgery and with cancer therapy [2]. Metoclopramide is a dopamine antagonist and may cause extrapyramidal symptoms. Other adverse effects include restlessness, drowsiness, dizziness, headache and bowel upsets such as diarrhoea. Hypotension, hypertension and depression may occur [3].

Literature survey revealed that MCP-HCl has been estimated by spectrophotometric and HP-TLC [4], spectrophotometric [5-9], solid phase extraction–molecularly imprinted polymer [10], chemiluminescence [11,12], hydrophilic interaction chromatography with electrospray ionization tandem mass spectrometric (HILIC/MS)[13], potentiometric [14] , voltammetric [15] and reversed phase high performance liquid chromatography (RP-HPLC)[16,17].

The purpose of this work is to describe a simple, precise and sensitive flow injection method with the use of Ayah 6SX1-T-2D Solar cell –CFI Analyser [18] for determination of metoclopramide hydrochloride in pharmaceutical formulations. The method based on the oxidation of metoclopramide hydrochloride by Ce(IV) sulfate in acidic medium to form a red species . The negative signal from absorbance of incident light can be recorded by Ayah 6SX1-T-2D Solar cell supplier with linear array of six super snow white light emitting diode as a source and two solar cell as a detector.

Experimental

Reagents and chemicals

All chemicals were used of analytical-reagent grade while distilled water was used to prepare the solution .A standard solution of metoclopramide hydrochloride ($C_{14}H_{22}Cl\ N_3O_2.HCl.H_2O$, M.Wt 354.3 g.mol^{-1}, SDI, 0.1Mol.L^{-1}) was prepared by dissolving 8.8575g in 250 ml distilled water. A stock solution (0.1 Mol.L^{-1}) of Ceric sulfate ($Ce(SO_4)_2$ M.Wt 332.298 g.moL^{-1} , Hopkin & Williams) was prepared by dissolving 16.6149 g in 500 ml of 1Mol.L^{-1} sulfuric acid . A 1Mol.L^{-1} of sulfuric acid solution (96% w/w, 1.84 g.ml^{-1},BDH) was prepared by pipetting 14 ml of concentrated sulfuric acid and dilute to 250 ml volumetric flask . A 1 Mol.L^{-1} of hydrochloric acid solution (35% w/w , 1.19 g.ml^{-1},BDH) were prepared by pipetting 22 ml of concentrated hydrochloric acid and completed the volume with distilled water in 250 ml . A 1Mol.L^{-1} of nitric acid solution (70% w/w, 1.42 g.ml^{-1},BDH)was prepared by pipetting 16 ml of concentrated nitric acid and completed the volume with distilled water to 250 ml . 1Mol.L^{-1} acetic acid solution (99.5% w/w , 1.05g.ml^{-1},BDH) was prepared by pipetting 15 ml of concentrated acetic acid and completed the volume with distilled water to 250 ml. Each acid was standardized against standard solution of 1Mol.L^{-1} from Na_2CO_3 (BDH,105.99 g.mol^{-1}); which prepared by dissolving 26.50 g in 250 ml distilled water .

Sample preparation

Thirteen tablets weight,crushed and grinded .Tablets containing 10 mg of metoclopramide hydrochloride for (Julphar- premsan , Actavis-metoclopramide) and 5 mg for (NDI-meclodin) were weight (1.089 , 1.158 , 2.009 g) equivalent to 88.575 mg of active ingredient 5 mMol.L^{-1} respectively . The powder was dissolved in distilled water followed by filtration to remove any undissolved residue affecting on the response and complete the volume to 50 ml with distilled water.

Apparatus

Peristaltic pump -2 channels variables speed (Ismatec , Switzerland)and rotary 6-port medium pressure injection valve, (IDEX corporation ,USA) with sample loop(0.7mm i.d.Teflon , different length) The response was measured by a homemade Ayah 6 SX1-T-2D Solar cell-CFI Analyser, which uses a six snow white LEDs for irradiation of the flow cell at 2 mm path length. Two solar cell used as a detector for collecting signals via sample travel for 60 mm length. The readout of the system composed of x-t potentiometric recorder(Kompenso Graph C-1032) Siemens (Germany) (1-500 Volt , 1-500 mV)or digital AVO-meter (auto range) (0-2volt) (China).UV-Vis spectrophotometer digital double beam type (UV-Vis spectrophotometer, UV-1800 , shimadzu, Japan) was also used to scan the spectrum of colored species using 1cm quartz cell. The flow diagram for the determination of metoclopramide hydrochloride is shown in Figure -2

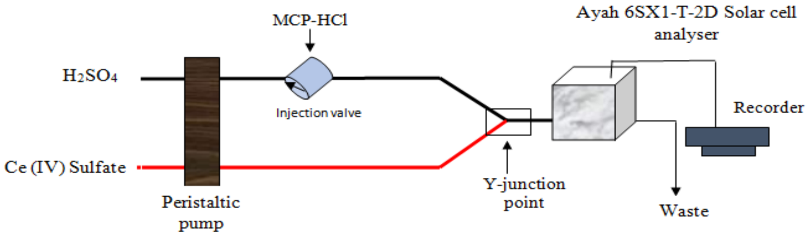
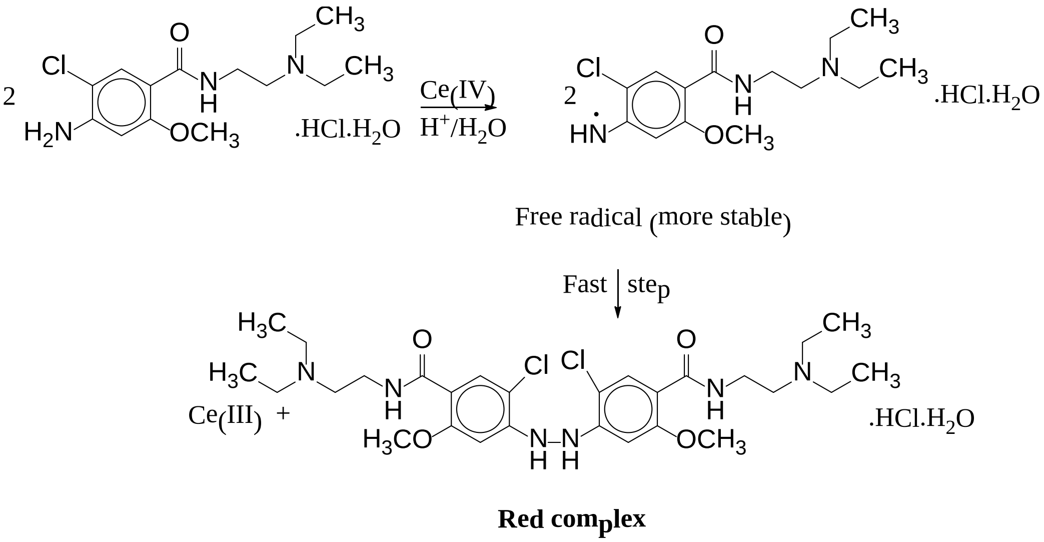


Figure 2- Flow diagram manifold system used for the determination of Metroclopramide hydrochloride

Methodology

The manifold system is composed from two lines was used for the determination of MCP-HCl by direct oxidation with Ce (IV) sulfate in acidic medium to form a red color species as shown in Figure -2. The first line supplied sulfuric acid 1Mol.L^{-1} as a carrier stream at 1.6 ml .min $^{-1}$ which leads to the injection valve for carring MCP-HCl (104 µl , sample volume) , the second line supplied Ce(IV) sulfate(50 mMol.L$^{-1)}$ at 2.3 ml .min $^{-1}$. Both of lines meet at junction (Y-junction) with an outlet for reactants product which passes through Ayah 6SX1-T-2D Solar cell CFI Analyser that work with six snow white light emitting diodes will be used as a source . Each solution injected was assayed in triplicate. The response profile of which was record on x-t potentiometric recorder to measure energy transducer response expressed as peak height in mV by absorbance of incident light. A proposed mechanism of oxidation of MCP-HCl by Ce(IV) sulfate in acidic medium is present in scheme -1 [9] .



Scheme 1- Proposed mechanism of reaction between MCP-HCl &Ce(IV) sulfate in acidic medium.

Results and discussion

Scanning of spectrum for MCP-HCl-Ce(IV)- H_3O^+ system

A scanning between 200-1100 nm was carried out to obtained λmax for colored complex (red) via the use of preliminary concentration of MCP-HCl (8 mMol.L^{-1}) oxidized by Ce(IV) sulfate (10 mMol.L^{-1}) in acidic medium (H_2SO_4, 100 mMol.L^{-1})system . It can be seen that a maximum absorbance of MCP-HCl at 213 nm (Figure-3-A) while the maximum absorbance of Ce (IV) sulfate (yellow color) in H_2SO_4 at 319 nm (Figure -3-B) . MCP-HCl mixed with Ce(VI) sulfate as oxidation agent , an intense (red) color product shows a maximum absorbance at 474 nm against reagent blank (Ce(IV) sulfate in the presence H_2SO_4) as shown in (Figure -3- C) .

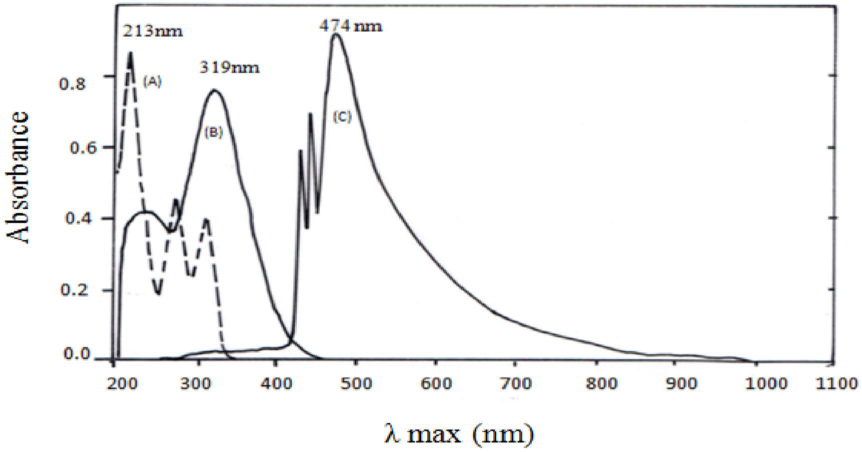


Figure 3- Absorbance spectra for:

A- MCP-HC
B- Ce(IV) sulfate in acidic medium (H_2SO_4, 100 mMol.L^{-1})
C- MCP-HCl – Ce(IV) sulfate –H_2SO_4 system

Variable optimization

Chemical parameters (mainly concentration of Ce(IV) sulfate and acidic medium for the reaction between MCP-HCl & Ce(IV) sulfate) as well as physical parameters (flow rate , sample volume , volume of coil & applied voltage) were studied , using two line manifold system (Figure-2). These variables were optimized by making all variables constant and varying one each at time.

Chemical variables

Ceric (IV) sulfate concentration

Using different concentrations of Ce(IV) sulfate (5-100) mMol.L^{-1} .A 8mMol.L^{-1} of MCP-HCl and 100µl sample volume was injected through the carrier stream (distilled water) at a flow rate 1.8 and 2.6 ml.min^{-1} for carrier stream and reagent respectively . The applied voltage to the LEDs was 2 volt DC. Each measurement was repeated for three time. The response profile for this study as shown in Figure - 3 -A. The results were summarized in Table -1. It was noticed ;the ideal concentration of Ce(IV) sulfate 50 mMol.L^{-1} .Figure - 4 -B shows the plot of results using Ayah 6SX1-T-2D- solar cell -CFI Analyser ,that an increase of response height of colored species with increase of concentration of Ce(IV) sulfate up to 50 mMol.L^{-1} , while at higher concentration (> 50mMol.L^{-1}) lead to decrease of response height followed by a constant response at 100 mMol.L^{-1}concentration of Ce(IV) sulfate .It really might be due to increase of the density of the colored product which work as an internal filter that really prevent the remaining light intensity after absorption process by the colored species from passes to the solar cell detector .Therefore 50 mMol.L^{-1} Ce(IV) sulfate concentration was regarded as the optimum concentration that used for the further work .

Table 1- Effect of Ce(IV) sulfate concentration on the measurement of energy transducer response for determination of MCP-HCl.

[Ce (IV)] mMol.L^{-1}	Energy transducer response expressed as an average peak heights(n=3) ȳi (mV)	RSD%	Confidence interval at (95%), n-1 ȳi ±$t_{0.05/2,n-1}$, σn-1/$\sqrt{n}$	*Δt_B (sec)
5	98	2.89	98±7.03	96
10	344	0	344 ± 0	90
50	458	0.62	458± 7.03	84
70	448	0	448±0	81
100	448	0	448±0	81

*Δt_B: Response base width

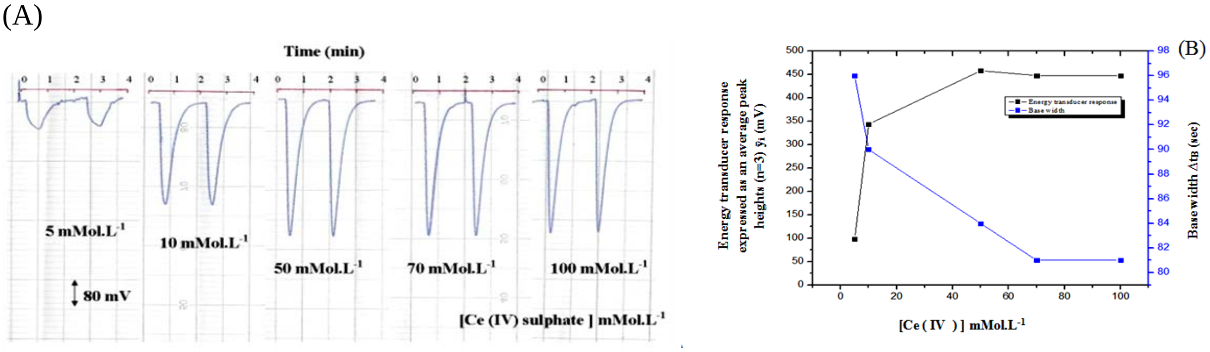


Figure 4- Effect of the Ce(IV) sulfate concentration on :
A- Response profile versus time
B- Energy transducer response expressed as an average peak heights in mV

Effect of H_2SO_4 concentration on MCP-HCl-Ce(IV)-H_3O^+system

Using MCP-HCl (8 mMol.L^{-1})-Ce(IV)sulfate (50mMol.L^{-1}) system .A series of sulfuric acid solution were prepared (0.005-1.96) Mol.L^{-1} ,in addition to use distilled water as a carrier stream , 100µl of sample volume at 1.8,2.6 ml.min^{-1} flow rate of carrier stream and reagent respectively .Figure -5-A shows the effect of H_2SO_4 concentration on height of response profile .The results obtained were summarized in Table.-2, in which that a starting with H_2O solution mean that zero acid concentration was added and thus original acid (500 mMol.L^{-1}) was the first solution to be measured . The rest of the prepared solutions is the added acid completed to 25 ml volumetric flask mark. Figure -5-B was obtained, in which that the increase of absorbance expressed as an energy transducer response of colored species with increasing concentration of sulfuric acid up to 1 Mol.L^{-1} , which shows that the used acid was necessary due to its catalyst action of the reaction , complete dissolution of Ce(IV) sulfate salt & for the ensurance of a complete homogenization of the solution . Therefore 1 Mol.L^{-1} of H_2SO_4 was regarded as the optimum medium for the next studies.

Table 2- Effect of H_2SO_4 concentration as a carrier stream on the transducer energy response for determination of MCP-HCl.

Added [H_2SO_4] Mol.L^{-1}	Energy transducer response expressed as an average peak heights (n=3) $\bar{y}i$ (mV)	RSD%	Confidence interval at (95%) $\bar{y}i \pm t_{0.05/2,n-1}\ \sigma n\text{-}1/\sqrt{n}$
0	464	0.24	464± 2.78
0.005	472	0.28	472± 3.28
0.01	472	0.23	472 ± 2.71
0.05	478	0.26	478± 3.06
0.1	484	0.35	484± 4.20
0.5	496	0.34	496±4.17
1	528	0.36	528± 4.77
1.96	544	0.35	544± 4.79

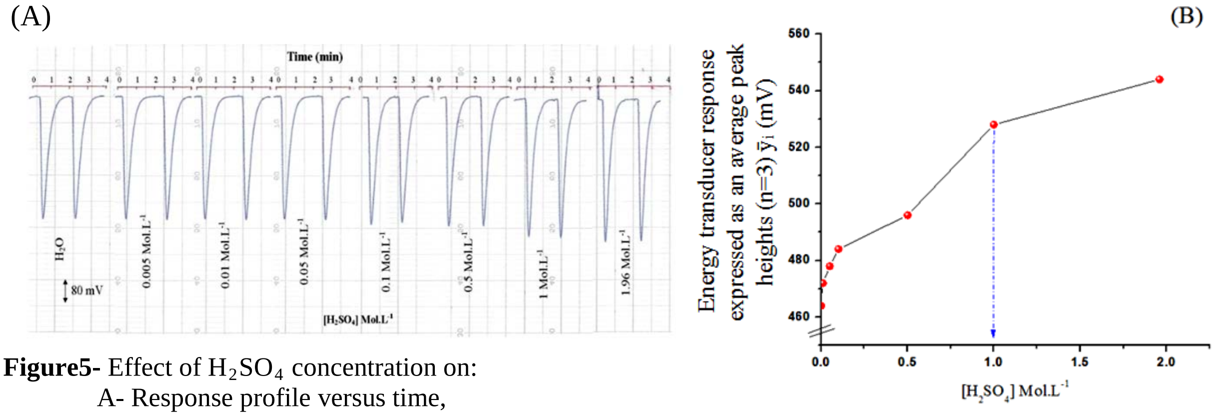


Figure5- Effect of H_2SO_4 concentration on:
A- Response profile versus time,
B- Energy transducer response expressed as an average peak heights.

Physical variables

Flow rate

Variation of flow rates(0.6- 2.8),(0.85-4)ml.min^{-1} for carrier stream and reagent respectively controlled by the peristaltic pump for determination of MCP-HCl at 8 mMol.L^{-1} was studied .While keeping other changeable constant (i.e. Concentration of Ce(IV)sulfate 50mMol.L^{-1} ,H_2SO_4 1 Mol.L^{-1} as a good carrier stream,100µl sample volume , open valve (10 sec), and applied voltage to the LEDs was 2 volt DC . Figure – 6 A shows that at low flow rate there is an increase in peak height & wider base width (increase analysis time), this might be attributed to the increase dispersion & area of colored segment in flow cell that causes a longer time duration of colored species in front of detector . While at higher pump speed (> 25) i.e.>1.6 & 2.3ml .min $^{-1}$ for carrier stream and reagent respectively (Table-3) although the effect of physical parameter was not very crucial on the response obtaining a regular responses and sharp maxima , but it is not very high (Figure -6 -B) due to departure of reactants from measuring cell prier to completion of oxidation MCP-HCl with Ce(IV) sulfate or unavailability of enough time for the response measurement before it is departure of the measuring cell at a short time . In addition to Figure -6 -C,-D shows the outcome of the study for the relation of the contribution of both lines without neglecting Δtb into consideration (i.e: relation between ratio versus Δtb (Figure-6-C) or energy transducer response with average of flow rate (Figure -6- D) , it was noticed that the an increase in contribution of the second line (i.e: reagent line compared with contribution of the first line (i.e: carrier stream) with an increase of flow rate , and on this basis with the compromise between sensitivity with an equal share of both lines ; a flow rate of 1.6 & 2.3 ml .min $^{-1}$ for carrier stream and Ce(IV) sulfate line respectively was chosen as optimum flow rate throughout this work .

Table 3- Effect of the variation of flow rate on the energy transducer response and relative contribution of both lines.

Pump speed (approximate)	Flow rate ml .min^{-1}		$\bar{X}$ ml.min^{-1}	*Ratio	Δt_b (cm)	Energy transducer response expressed as an average peak height (n=3) $\bar{y}i$ (mV)	RSD %	Confidence interval at (95%) $\bar{y}i \pm t_{0.05/2,n-1}\ \sigma n\text{-}1/\sqrt{n}$	Base width Δt_B (sec)	*t sec.
	Relative contribution (cm)									
	Carrier stream	Reagent								
10	0.6	0.85	0.725	1.31	6.6	544	0.18	544± 2.43	300	54.0
	2.9	3.8								
15	0.95	1.2	1.075	1.28	6.7	566	0.50	566±7.03	180	36.0
	2.9	3.70								
20	1.25	1.80	1.525	1.76	7.9	560	0.09	560± 2.61	120	30.0
	2.9	5.1								
25	1.6	2.3	1.95	2.03	8.6	540	0.18	540± 2.36	100	25.0
	2.9	5.90								
30	1.8	2.6	2.2	2.17	9.0	520	0.22	520± 2.78	90	21.0
	2.9	6.30								
35	2.2	3.1	2.65	2.34	9.4	520	0.23	520± 2.98	72	18.0
	2.9	6.80								
40	2.4	3.5	2.95	2.66	10.4	496	2.28	496±28.11	60	15.0
	2.9	7.70								
45	2.8	4.0	3.4	2.86	10.8	492	0.22	492± 2.68	54	13.8
	2.9	8.30								

$\bar{X}$- Average of flow rate for both line
*Ratio- Contribution of reagent line / contribution of carrier line
Δt_b - Relative output of both line (cm)
* t- Departure time for sample segment from injection valve to the measuring cell.

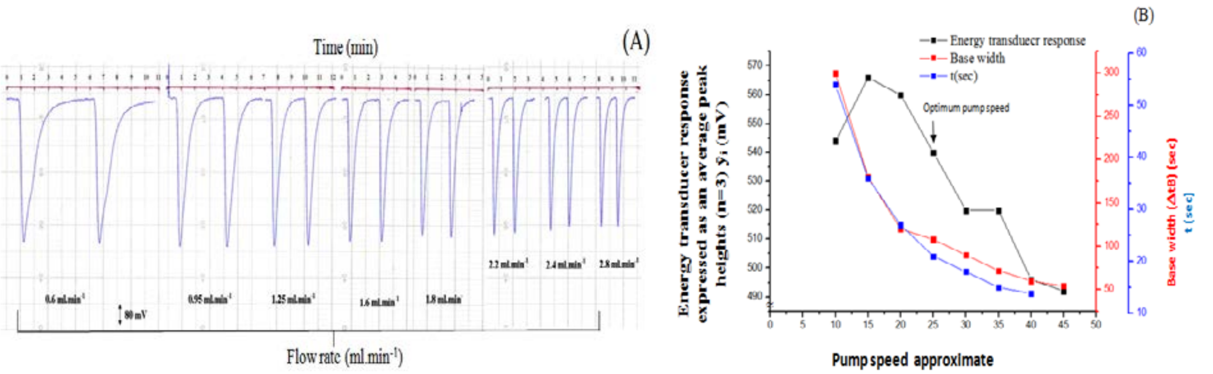


Figure 6- Effect of the variation of flow rate on:

A- Response profile versus time

B-Energy transducer response expressed as an average peak heights in mV, Base width and departure time for sample segment from injection valve to the measuring cell.

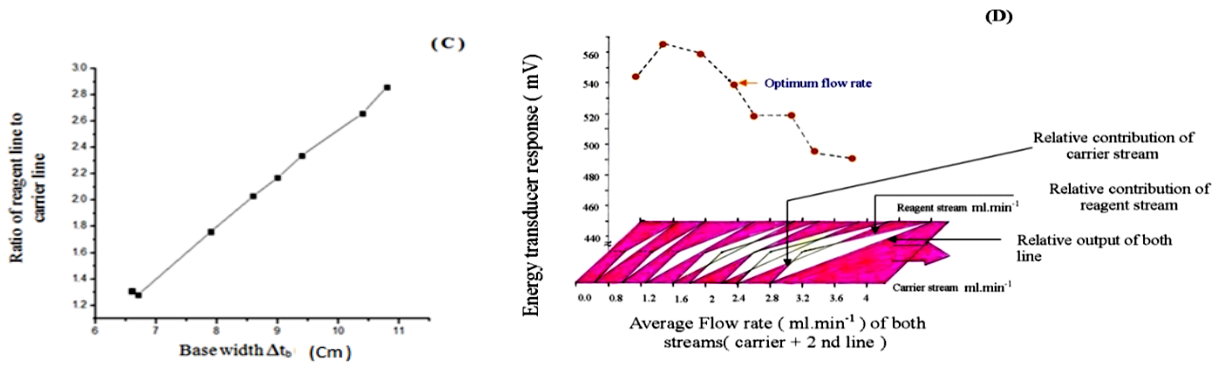


Figure 6- C- Variation of contribution ratio of line(2) (reagent) to line(1) (carrier stream) versus base width (Δtb) in cm . D- Plot of energy transducer response vs. average flow rate of both line (carrier + reagent). Indicating at the x-axis the contribution effect of each line also it shows the resultant output.

Sample volume

Using the optimum flow rate (1.6 and 2.3) ml .min $^{-1}$ for carrier stream and Ce(IV) sulfate line respectively , MCP-HCl (8mMol.L^{-1}) – Ce(IV) (50mMol.L^{-1})-H_2SO_4 (1Mol.L^{-1}) system .The injected volume of sample was varied in the range 70-112 µl by changing the length of the sample loop in the injection valve , open valve (10 sec) and applied voltage the to LEDs was 2 volt DC. It was found that an increase in the volume led to a significant increase in sensitivity, more perceptible than low volumes as shown in Figure -7- A which shows that the optimum sample volume of 104µl gave regular responses for the absorption of incident light. At the same time, when using sample volume > 104 µl it gave a constant height of response and base width (ΔtB) this is illustrated in Figure.-7-B . Therefore , as a compromise between sensitivity , peak shape , complete the reaction and consumption of the chemicals , 104 µl will be used as optimum sample volume in next studies .The obtained results were tabulated in Table - 4.

Table 4 - Effect of the variation of sample volume on the energy transducer response for determination of MCP-HCl using MCP-HCl –Ce(IV) –H_3O^+ system .

Loop length Cm r=0.35mm	Sample volume µl $V=r^2h\pi$	Energy transducer response expressed as an average peak heights(n=3)ȳi(mV)	RSD %	Confidence interval at 95% $\bar{y}_i \pm t_{0.05/2,n-1}\, \sigma_{n-1}/\sqrt{n}$	Base width Δt_B sec.	*tsec.
18	70	400	0	400± 0	78	18.0
19	73	412	1.37	412± 14.05	84	19.2
21	81	446	0.63	446±7.03	90	21.0
22	85	492	1.15	492±14.05	96	22.2
26	100	528	0	528± 0	99	23.4
27	104	568	0	568±0	102	24.0
29	112	568	0	568± 0	114	24.0

*t = Departure time for sample segment from injection valve to the measuring cell

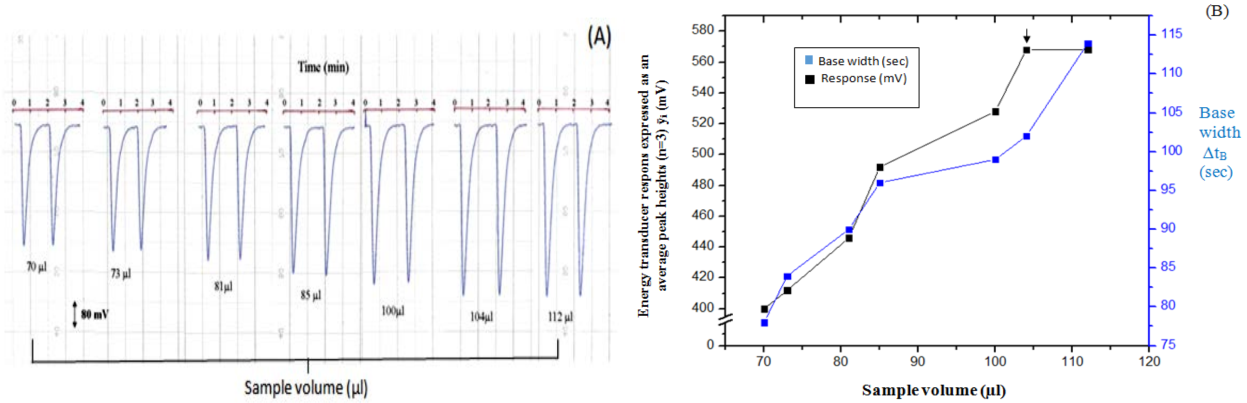


Figure 7- Effect of the variation of sample volume on:

A- Response profile by absorbance of colored species using Ayah 6SX1-T 2D -Solar cell CFI Analyser versus time

B- Energy transducer response expressed as an average peak heights in mV

Purge time

A study was carried out to determine the optimum duration of the injection time i.e: Allowed permissible time for purging of the sample segment from the injection valve. 2-13 second were used in this study. The optimum parameters achieved in previous section were kept a constant .Figure-8-A,-B shows the continuation of the height response with increase of injection time up to 8 second after that there was no larger significant differences in peak height or stay constant . The decrease in response when using less than 8 sec was attributed to the incomplete purge time of sample from sample loop in the injection valve. Therefore; 8 second chosen as optimum purge time for the departure of the sample segment completely from the injection valve. All results were tabulated in Table.-5.

Table 5- Effect of the variation of purge time on the energy transducer response for determination of MCP-HCl using 104 µl , MCP-HCl (8mMol.L^{-1})- Ce(IV) (50mMol.L^{-1})-H_2SO_4 (1 Mol.L^{-1})system &2 volt DC.

Purge time count	Purge time (sec)	Energy transducer response expressed an average peak heights (n=3) ȳi (mV)	RSD%	Confidence interval at 95% $\bar{y}_i \pm t_{0.05/2,n-1}\ \sigma_{n-1}/\sqrt{n}$
5	2	254	1.11	254±7.03
10	3	326	0.87	326±7.05
15	5	442	0.64	442±7.03
20	6	536	0	536±0
25	8	556	1.02	556±14.05
30 (Open valve)	10	556	1.02	556±14.05
40	13	562.4	0	562.4±0

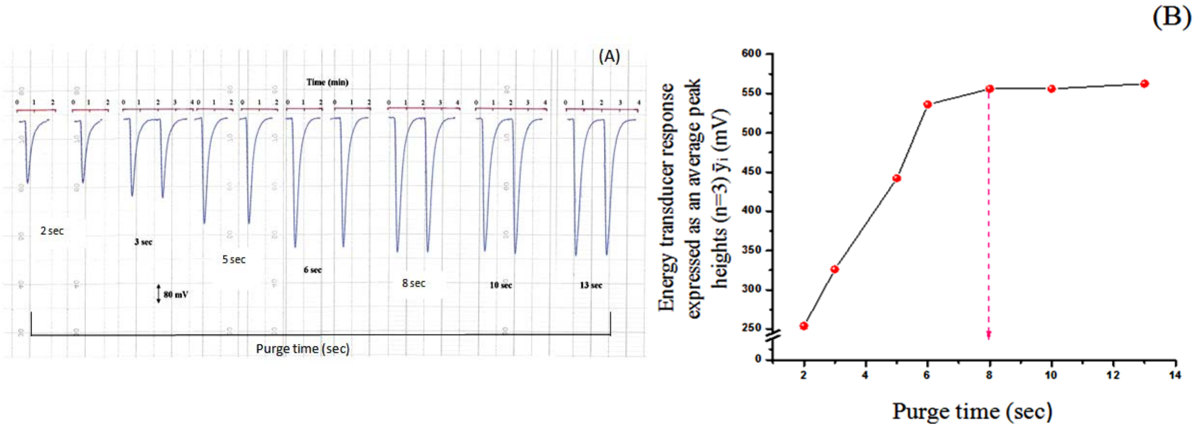


Figure 8- Effect of the variation of purge time on:

A- Response profile (i.e: via absorbance of incident light by colored species) versus time.

B- Energy transducer response expressed as an average peak heights in (mV).

Effect of reaction coil length

Using MCP-HCl(8 mMol.L^{-1})-Ce(IV) sulfate (50 mMol.L^{-1}) –H_2SO_4 (1 Mol.L^{-1})system . The effect of reaction coil was studied .The reaction coil length has a large role in the homogenization and completion of chemical reaction. Different coil lengths (0 – 100) cm were used, this rang of lengths comprises a volume of 0-0.785 ml which connected after Y-junction directly in flow system (Figure -2). Figure-9-A,-B shows that a decrease in peak height with increase coil length ,at the same time increase of the base width(ΔtB) ,V addition , broadening at the peak maxima and departure time for sample segment from injection valve to the measuring cell ,which might probably attributed to the increase effect of the dilution and dispersion on colored segment and continuous longer time duration of colored species in front of the detector. Therefore; two lines manifold system without reaction coil necessary for completion of oxidation MCP-HCl by Ce(IV) sulfate in acidic medium. Table.-6 shows all results of coil effect on energy transducer response.

Table 6- Effect of variation of coil length on energy transducer response for determination of MCP-HCl using 104µl , 2 volt DC.

Coil length cm	volume of coil ml $r^2\pi$ h, r =0.5 mm	Energy transducer response expressed as an average peak heights(n=3) ȳi (mV)	RSD %	Confidence interval at 95% $\bar{y}_i \pm t_{0.05/2,n-1}\sigma_{n-1}/\sqrt{n}$	*t (sec)	Base width Δt_B sec.	V_{add} ml	Concentration after dilution mMol.L^{-1}
0	0	568	0	568± 0	24.0	102	6.734	0.124
30	0.235	492	1.15	492± 14.05	25.8	105	6.929	0.120
60	0.471	440	0	440±0	30.0	114	7.514	0.110
100	0.785	408	0	408±0	36.0	120	7.904	0.105

*t= Departure time for sample segment from injection valve to the measuring cell

Vadd= addition volume (ml) at flow cell

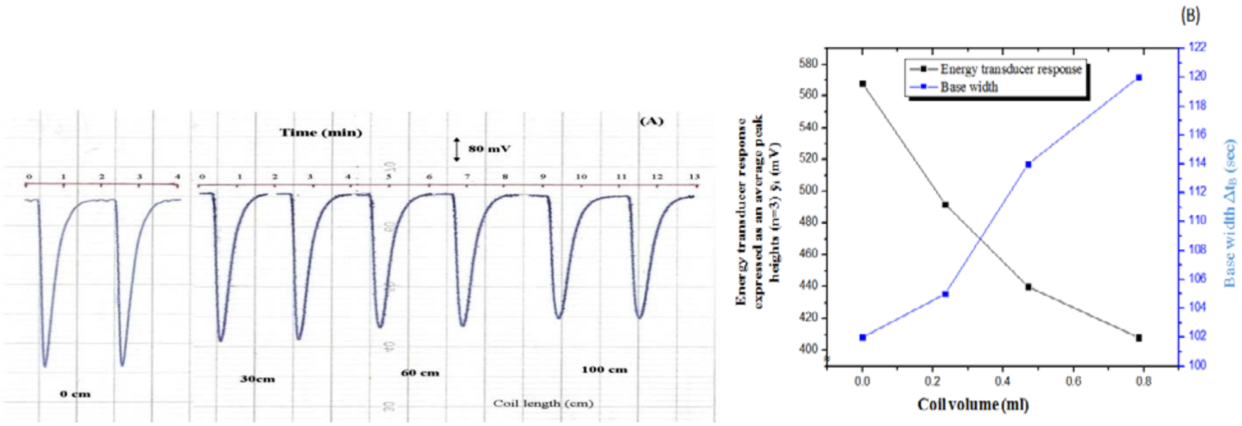


Figure 9- Effect of the coil length on the:

A- Response profile (via absorbance of incident light by colored species) versus time

B- Energy transducer response and base width

Intensity of light

Variation of light source intensity on the efficiency for determination of MCP-HCl at 8 mMol.L^{-1} was studied while keeping all other changeable fixed (i.e: Ce (IV) sulfate (50 mMol.L^{-1}) , H_2SO_4 (1 Mol.L^{-1}) as a carrier stream ,104 µl sample volume , flow rate (1.6,2.3) ml.min-1 for carrier stream and reagent respectively & purge time (8sec), the applied voltages to the LEDs were used (0.03-2) volt DC., by variation of light intensity knob operation where read by AVO- meter. Figure -10 -A shows the response height while the results were tabulated in Table -7. Figure-10 -B shows that an increase in the peak height with increase intensity of light source and Figure.-10-C showing the relationship between energy transducer response output versus applied voltage with correlation coefficient r = 0.9891 , So 2 volt DC. was selected as the optimum voltage for the snow white light emitted diode(LED), that can be supplied to give a better reproducible outcome as shown in Figure -10- A .

Table 7- Effect of intensity of light on the energy transducer response using Ce (IV) sulphate – MCP-HCl –H_2SO_4 system.

Intensity of light (Volt)	Energy transducer response expressed as an average peak heights(n=3) ȳi (mV)	RSD%	Confidence interval at 95% ȳi $\pm t_{0.05/2,n-1}\ \sigma_{n-1}/\sqrt{n}$ (mV)	Ŷi (mV)	r r^2
0.03	16	1.88	16 ± 0.75	-9.12	0.9891
0.07	24	2.08	24± 1.24	1.69	
0.16	40	3.58	40± 3.55	26.01	
0.24	48	2.29	48±2.73	47.63	0.9783
0.56	112	0.97	112± 2.71	134.12	
0.92	184	0.59	184±2.68	231.42	
1.29	296	0.39	296± 2.88	331.42	
1.50	360	0.37	360±3.28	388.17	
1.79	456	0.34	456±3.85	466.56	
1.85	520	0.36	520±4.70	482.77	
2.00	568	0.35	568±4.94	523.32	

Ŷi: Estimated value using linear equation

r = Correlation coefficient, r^2 = coefficient of determination (C.O.D)

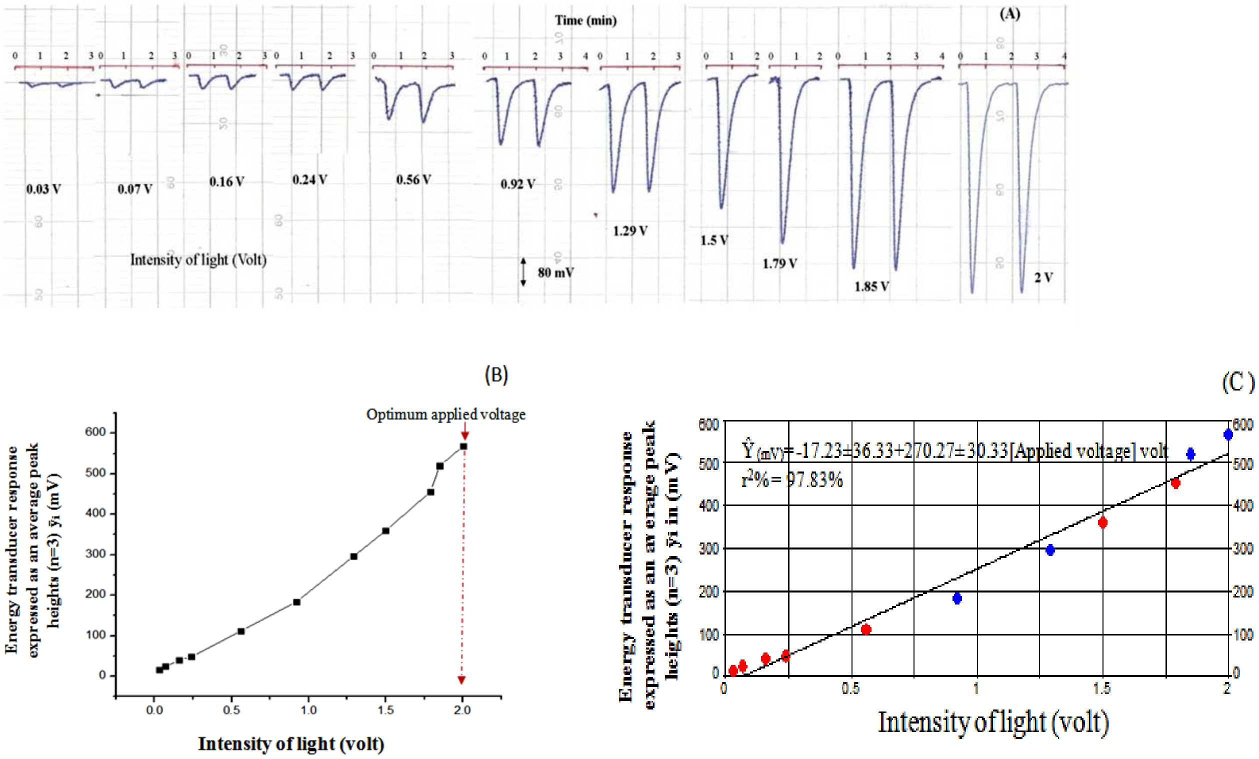


Figure 10- Effect of the variation of light intensity on the:

A- Response profile versus time,

B- Energy transducer response expressed as an average peak heights in (mV). Using MCP-HCl –Ce(IV) – H_2SO_4 system & Ayah 6SX1-T-2D Solar cell CFIA .

C- Calibration graph for the variation of applied voltages to the LEDs on the energy transducer response using linear equation

Scatter plot calibration curve for variation of MCP-HCl versus energy transducer response

Using the optimum chemical and Physical parameters; a series of MCP-HCl solution (0.05-25) mMol.L^{-1}were prepared, each measurement was repeated three times successive. Figure-11-A shows response profile & height for each MCP-HCl concentration A scatter plot diagram shows that a linear calibration graph range for the variation of the energy transducer response of Ayah 6SXI-T-2D solar cell CFI Analyser with MCP-HCl concentration was ranging from 0.05-16 mMol.L^{-1}with correlation coefficient (r): 0.9855 as shown in Figure -11-B . The results obtained were tabulated in Table.-8. It was noticed, above 16 mMol.L^{-1} a broad in the peak maxima was observed and increase of the base width (ΔtB) , this cause a deviation of correlation coefficient (i.e. deviate from linearity) ; most probably due to the high intensity of the colored species in front of detector and due to the effect of inner filter of colored species present in solution, which were results from the oxidation of MCP-HCl by Ce(IV)sulfate in acidic medium causing a decrease in transmitted light .Table.-8 summary of linear regression for the variation of energy transducer response with MCP-HCl concentration using first degree equation of the form ŷ=a+bx [19,20]at optimum conditions . In addition to calculate t-value at 95% confidence level which larger than tabulated t-value indicating clearing that the linearity against non linearity is accepted.

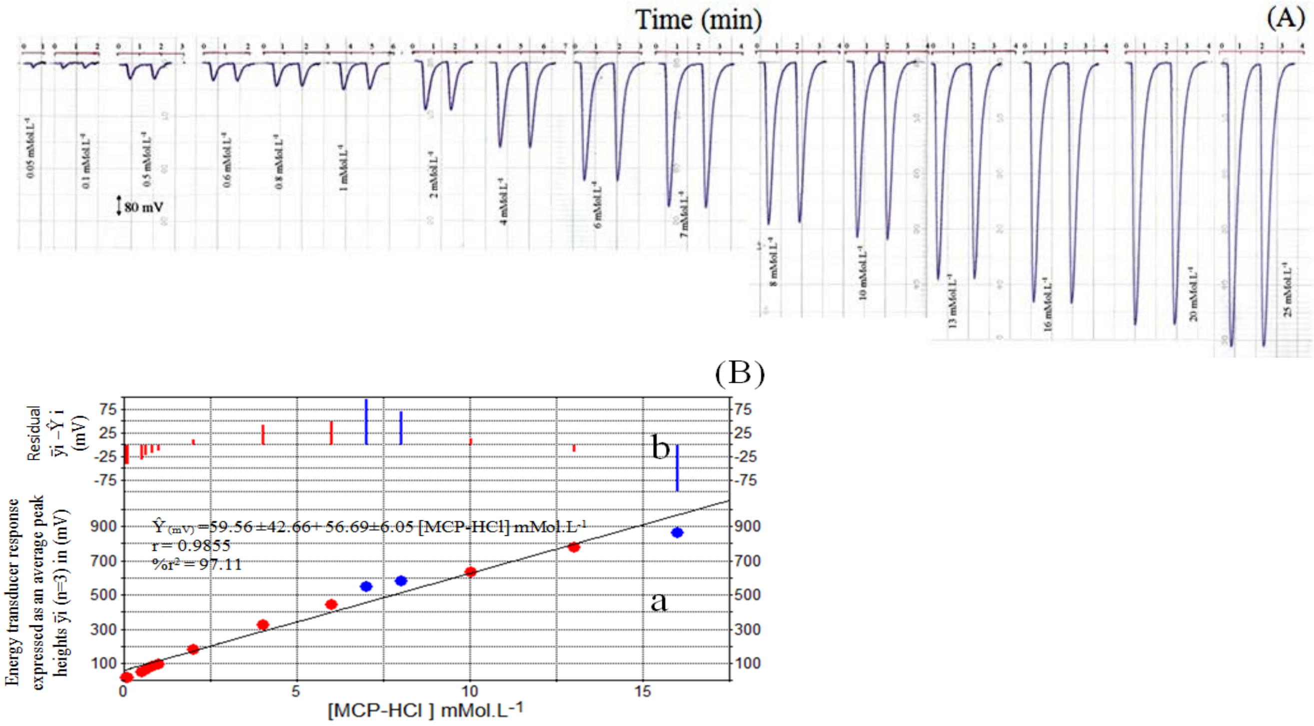


Figure 11- Calibration graph for the variation of MCP-HCl concentration on:

A- Response profile verses time

B-a - transducer energy response expressed by linear equation using Ayah 6SX1-T-2D Solar-CFI Analyser ,

b- residual (ȳi – Ŷi), ȳi :practical value, Ŷi: estimate value.

Table.8-Summary of results for the variation of energy transducer response metoclopramide hydrochloride concentration using first degree equation

Measured [MCP-HCl] mMol.L^{-1}	Range of [MCP-HCl] mMol.L^{-1} (n=14)	Ŷ(mV)=a±sat+b±sbt[MCP-HCl]m Mol.L-1 at confidence level 95%,n-2	r r^2%	ttab at 95%,n-2	$t_{cal} = \frac{\lvert r\rvert\sqrt{n-2}}{\sqrt{1-r^2}}$
0.05-25	0.05-16	59.56±42.67+56.69±6.05[X]	0.9855 97.11	2.179 << 20.097	

[X]=[MCP-HCl] mMol.L-1 , Ŷ=estimate value , r = correlation coefficient

r2% = Linearity percentage, r2= coefficient of determination (C.O.D)

Limit of detection (L.O.D)

A study was carried out to calculate the limit of detection of MCP-HCl through two methods: Practically based on the gradual dilution for the minimum concentration and theoretical based on the value of slope as tabulated in Table.-9 at injection sample volume of 104 µl.

Table.9- Limit of detection for MCP-HCl at optimum parameters using 104µl as an injection sample and optimum parameters.

Practically based on the gradual dilution for the minimum concentration (0.009 mMol.L^{-1})	Theoretical based on the value of slope x=3SB/slope for n=13
0.332 µg/ Sample	0.682 µg/Sample

X= value of L.O.D. based on slope, SB= standard deviation of blank repeated for 13 times.

Repeatability

The relative standard deviation expressed as percentage which is equally to the repeatability of the measurement. A repeated measurements for six successive injections were measured at fixed concentrations of MCP-HCl , while mainly two concentrations were used and the obtained results is tabulated in table 10 which shows that the percentage relative standard deviation was less than 0.6% . Figure-12 is shown response profile of repeatability at 2 and 6 mMol.L^{-1} respectively.

Table 10- Repeatability of MCP-HCl at optimum parameters with 104µl sample volume via absorbance of incident light by color species expressed as an energy transducer response.

[MCP-HCl] mMol.L^{-1}	Average response $\bar{y}i$ (mV) n*=6	RSD %	Confidence interval at 95% $\bar{y}i \pm t_{0.05/2}\ \sigma_{n-1}/\sqrt{n}$
2	184	0.53	184± 1.03
6	448	0.27	448± 1.29

n*=number of injection $t_{0.05/2,5=2.571}$

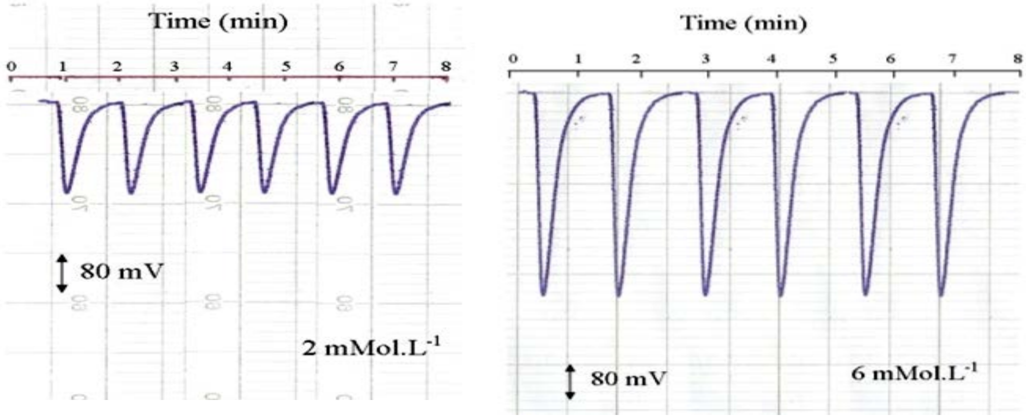


Figure 12- Response – time profile for six successive repeatable measurements of MCP-HCl concentration (2 mMol.L^{-1} & 6 mMol.L^{-1}) using Ayah 6SIX1-T-2D Solar cell CFIA .

A assessment of the use of Ayah 6SX1-T-2D solar cell CFI Analyser for the determination of MCP-HCl in the pharmaceutical preparation using MCP-HCl –Ce(IV)-H_2SO_4.

The CFIA via absorbance of incident light method using Ayah 6SX1-T-2D solar cell –CFI Analyser achieved in this work was used for the analysis of MCP-HCl in the three different drug manufactures (Julphar –UAE -10 mg , actavis-UK -10 mg , NDI –Iraq-5mg) and was compared with classical method spectrophtometric via the measurement at λmax (474 nm) by spectronic 20D +, Japan[9]. A linearity calibration curve was obtained for the concentration range of 0.07-3 mMol.L^{-1} of MCP-HCl as shown in Figure -13, correlation coefficient was 0.9983 and limit of detection was 60µMol.L^{-1} as tabulated in Table-11.

Table 11- Summary of linear regression for the determination of MCP-HCl –Ce (IV) – H_2SO_4 system, using classical method and limit of detection.

[MCP-HCl] mMol.L^{-1} measured	Rang at calibration curve n=9	Linear regression at confidence level 95%,n-2 $\hat{Y}$=a ±sat +b ± sbt [x]	r r^2 r^2%	ttab at 95%,n-2	$t_{cal} = \frac{\lvert r\rvert\sqrt{n-2}}{\sqrt{1-r^2}}$	D.L
0.05-4	0.07-3	0.00±0.03+0.50±0.03[x]	0.9983 0.9966 99.66%	2.365 << 45.037		60µMol.L-1

D. L: Detection limit based on the gradual dilution for the minimum concentration for calibration curve

[X]: [MCP-HCL] mMol.L^{-1},$\hat{Y}$: Estimate value(absorbance) from linearity equation

r= Correlation coefficient, %r^2= percentage linearity, r^2= coefficient of determination (C.O.D).

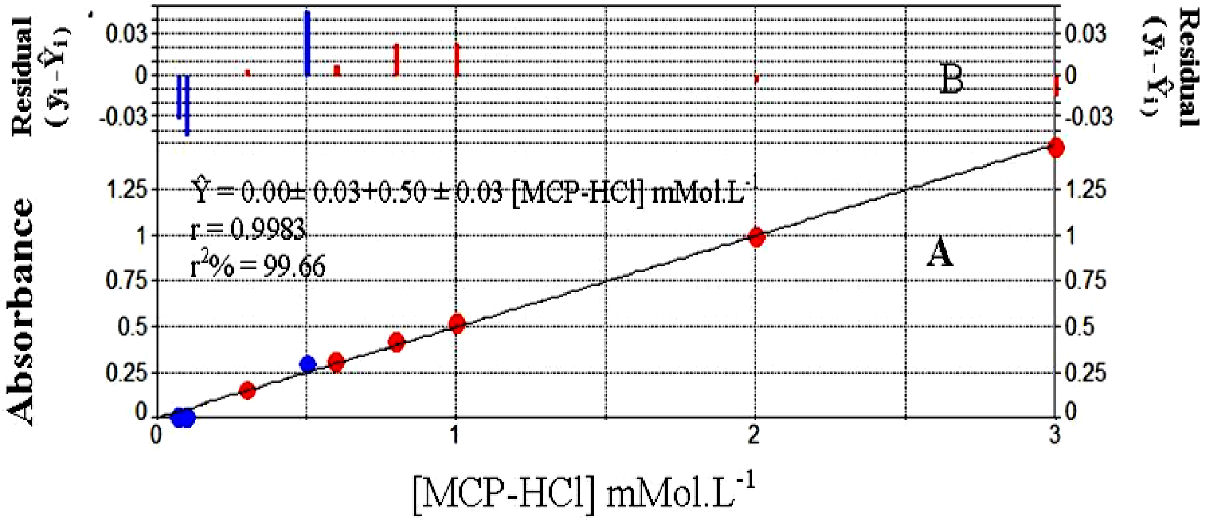


Figure 13- A- Calibration graph for the variation of MCP-HCl concentration versus absorbance using spectrophotometer (classical method), B- residual ($\bar{y}_i - \hat{Y}_i$), $\bar{y}_i$: practical value,$\hat{Y}_i$: estimate value .

A series of solution were prepared of each pharmaceutical drug (5mMol.L^{-1})(88.575 mg of active ingredient in 50 ml) by transferring 2 ml to each six volumetric flask (10 ml) , followed by the addition of gradual volumes of standard MCP-HCl (0, 0.3, 0.4, 0.5, 0.6) ml of 0.1Mol.L^{-1} to obtain (0, 3, 4, 5 , 6) mMol.L^{-1}when use Ayah 6SX1-T-2D Solar cell –CFI Analyser , while transferring 1ml to each six volumetric flask (10 ml) , followed by the addition of gradual volumes of standard MCP-HCl (0, 0.03, 0.05, 0.07, 0.1) ml of 0.1Mol.L^{-1} to obtain (0,0.3,0.5,0.7,1) mMol.L^{-1}for the use of spectrophtometric method . Flask no.1 is the sample .The measurements were conducted by both methods. Results were mathematically treated for the standard addition method .The results were tabulated in Table-12-A,at confidence level 95% ; showing practically concentration of MCP-HCl in each pharmaceutical drug using two method of analysis . Table-12-B was shown a practical content of active ingredient at 95% confidence level & efficiency of determination in addition to paired t-test which shows a comparison at two difference paths:

First test: Comparison of newly developed method with official quoted value (10 mg or 5 mg) [British pharmacopoeia] as shown in Table-12- B (column 8) by calculated t- values of each individual company and these comparison with tabulated t-value.

A hypothesis can be estimated as follow:

Null hypotheses: There is no significant difference between the means obtained from three source of three different companies ($\bar{X}$) and quoted value (μ0)

i.e. Ho : $\bar{X}$= μ0

for: Julphar , Actavis and NDI companies

against:

Alternative hypothesis : there is a significant difference between the means and quoted value

i.e. H1 : $\bar{X} \neq$ μ0

For three different companies.

Since all values obtained (t calculated) are < t tab (4.303) at confidence level 95 % and DF(degree of freedom) = n-1 ; Null hypothesis will be accepted will reject the alternative hypothesis ;these mean that there is no significant difference between the quoted active ingredient value and the measured value

Secondary test: paired t-test was used in order to compare between two methods of analysis, i.e. Ayah 6SX1-T-2D Solar cell CFIA with UV-Vis spectrophotometric as shown in Table- 12-B (column 11) .

Taking in to consideration that all sample from different companies are of the same population standard; i.e. neglecting individual differences between one manufacturer and another, as they all quoted value the same (10 mg for Julphar , actavis companies and 5 mg for NDI)

Assumption:

Null hypothesis H0: μ UV-Vis = μ Ayah 6SX1-T-2D

Against

Alternative hypothesis H1 : μ UV-Vis ≠ μ Ayah 6SX1-T-2D

The obtained results indicate clearly that there was a significant differences between newly Ayah 6SX1-T-2D Solar cell CFIA method and the spectrophotometric method at 95% (α = 0.05) confidence level as the calculated t-value (4.457) is more than critical tabulated t-value (4.303) and could be using the developed method as an alternative method for the analysis of MCP-HCl .

Table 12-A- Standard addition results for the determination of MCP-HCl in three pharmaceutical preparation

No. of sample	Commercial name, Company Content Country	Sample weight equivalent to 88.575 mg(5 mMol.L^{-1}) of the active ingredient (g)	Ayah 6SX1-T- 2D Solar cell CFIA							
			UV-Vis sp (classical method Absorbance measurement)							
			[MCP-HCl] mMol.L^{-1}					Equation of standard addition at 95% for n-2 $\hat{Y}_{i\,(mV)}$= a±sat+b±sbt[x] $\hat{Y}_i$ = a±sat+b±sbt[x]	r r^2 r^2%	Practical concentration mMol.l^{-1} in 10 ml 50ml
			0	3	4	5	6			
			0	0.3	0.5	0.7	1			
1	Premsan Julphar 10 mg Ras Al Khaimah U.A.E	1.0886	50	336	392	440	496	74.23±92.48+74.60±22.30[x]	0.9870 0.9742 97.42	0.995 4.975
			0.26	0.420	0.516	0.646	0.794	0.26±0.02+0.54±0.04[x]	0.9992 0.9985 99.85	0.479 4.793
2	Metoclopramide Actavis 10 mg UK	1.1577	50	328	392	440	480	75.13±97.82+73.02±23.59[x]	0.9849 0.9700 97.00	1.0289 5.145
			0.270	0.426	0.514	0.668	0.815	0.26±0.05+0.55±0.08[x]	0.9971 0.9943 99.43	0.474 4.735
3	Meclodin NDI 5mg Iraq	2.0088	60	336	392	448	504	80.38±27.58+74.34±18.72[x]	0.9907 0.9816 98.16	1.0812 5.406
			0.247	0.436	0.548	0.628	0.815	0.26±0.04+0.56±0.07[x]	0.9979 0.9958 99.58	0.462 4.621

$\hat{Y}$= Estimated response in mV for Ayah 6SX1-T-2D Solar cell CFIA and absorbance for UV-Vis method , [x] = [MCP-HCl] mMol.L-1 , r = Correlation coefficient ,% r^2= percentage linearity , r^2 = coefficient of determination (C.O.D) ,UV-Vis Sp = UV-Vis spectrophotometric method

Table 12-B-Summary of results for paired t-test, practical content and efficiency for determination of MCP-HCl in three samples of pharmaceutical preparation using MCP-HCl- Ce(IV)-H2SO4 system .

Sample no.	Confidence interval for the average weight $\overline{W}i\pm1.96\,\sigma_{n-1}/\sqrt{n}$ at 95% (g)	Sample weight equivalent to 88.575 mg (5mMol.L^{-1}) of the active ingredient (g)	Theoretical content of the active ingredient at 95% (mg) $\mu\pm1.96\,\sigma_{n-1}/\sqrt{n}$	Practical concentration (mMol.L^{-1}) and what is equivalent of active ingredient (mg)	Practical content $\overline{W}i\pm4.303\sigma_{n-1}/\sqrt{n}$ (mg) for (n=3) ,at 95%	Efficiency of determination (Rec. %)	Paired t-test			
							Individual comparison $(\bar{X}-\mu)\sqrt{n}/\sigma_{n-1}$ Ayah 6SX1-T-2D Solar cell-CFI Analyser with Quoted value $t_{0.05/2,2}=4.303$	Comparison between two method		
								Xd	$\bar{X}d$ (σ_{n-1})	$t_{cal}=\bar{X}d\sqrt{n}/\sigma_{n-1}$ at 95 %
				Ayah 6SX1-T- 2D Solar cell CFIA						
				spectronic 20D +, Japan instrument (classical method, Absorbance measurement)						
1	0.1229±0.0016	1.0886	10±0.127	4.975 88.127	9.949 ± 0.452	99.49	|-0.485|<<4.303	0.363	0.658 (0.256)	4.457 > 4.303
				4.793 84.906	9.586±1.267 9.949-9.586*	95.86				
2	0.1307±0.0003	1.1577	10±0.024	5.145 91.138	10.287±0.479	102.87	2.576<<4.303	0.817		
				4.735 83.885	9.470±0.581 10.287-9.470*	94.70				
3	0.1134±0.0017	2.0088	5±0.073	5.406 95.769	5.406 ± 0.472	108.13	3.701<<4.303	0.794		
				4.621 81.863	4.612±0.479 5.406-4.612*	92.426				

Xd: Difference between two method $\bar{X}d$: difference mean , σ_{n-1}:Difference standard deviation , n= no. of sample =3
$t_{0.025,\infty}$ = 1.96 at 95 % , µ : quoted value , * : range of practical content by classical method while 2 ml & 1 ml drawing volume for the proposed method and classical method respectively

Conclusion

The proposed methods for the determination of MCP-HCl in pure and pharmaceutical preparations is simple ,sensitivite and rapid based on oxidation of MCP-HCl by Ce(IV) sulfate in acidic medium forming red product .It was shown that newly developed method can be used as an alternative method for the analysis of MCP-HCl .

Acknowledgement

I would like to express my deepest gratitude to Prof. Dr. Issam M.A.Shakir Al-Hashimi for his appreciable advice, important comments, support and encouragement.

References

1. British pharmacopoeia . 2012. 7 th edition., The Stationery office ,Londone.
2. Manuchair , E. 2007 . *Desk Reference of clinical pharmacology* . *second edition* . CRC press , united states of America.
3. Ravi, G.A. , Fakhar, Z.K.,Kasara,S. and Eamonn ,K.1999. Instant *pharmacology* .John willy & Sons Ltd , England.
4. Amira , M., Nagiba ,Y., Fadia , H. and Mohammad ,A. 2013. Application and validation of two smart spectrophotometric and HP-TLC Densitometric methods for determination of metoclopramide hydrochloride /paracetamol in raw material and in pharmaceuticals. *International Journal of pharmacy* , 3(3) , pp: 470-481.
5. Raghad,S.2010.Spectrophotometric determination of metoclopramide hydrochloride in pharmaceutical tablets, by diazotization-coupling method with 1-naphthol as the coupling agent. *Baghdad Science Journal*,7(1),pp:1-8.
6. Aymen , A.J.and Kasim , H.K.2013.Spectrophotometric determination of metoclopramide hydrochloride in bulk and pharmaceutical preparation by diazotization-coupling reaction . *International Journal of Pharmaceutical Sciences* , 5(3) , pp: 294-298 .
7. Lamya ,A.S.,Salim,A.M. and Kasim , M.A.2011.Spectrophotometric determination of metoclopramide hydrochloride in pharmaceutical preparations using diazotization reaction . *Raf.J.Sci.*,22(3),pp:76-88.
8. Theia'a ,N.A. and Intesar , A.A.2006.Spectrophtometric determination of metoclopramide hydrochloride in bulk and pharmaceutical preparations . *National Journal of Chemistry* , 24, pp:561-570.
9. Najih , H.S. and Thura ,Z.A.2013.Spectophotometric assay of metoclopramide hydrochloride in pharmaceutical preparation via arsenazo III-Cerium(III) reaction .*Raf.J.Sci.*,*24*(1), pp:70-83.
10. Narges ,S., Mehran , J. and Leila ,H. 2010 . Solid – phase extraction and determination of metoclopramide in biological fluids and human urine by molecularly imprinted polymers . *J.Sci. I.A.U* , 20 (76) , pp: 69-78.
11. Shunli , F. ,Zhihao , W., Lei , Z. and Chao , L. 2002. Chemiluminescence determination of metoclopramide . *Analytical Letters* , 35(9),pp :1479-1489.
12. Nawal ,A. 2004. Flow-injection chemiluminescent determination of metoclopramide hydrochloride in pharmaceutical formulations and biological fluids using the [Ru(dipy) 3 2+] – permanganate system . Talanta ,62, pp:255-263.
13. Hye , W.L. ,Hye , Y. J.,Hoe , Y.K., Eun-Seok , P., Kang , C.L. and Hye , S.L. 2009 . Determination of metoclopramide in human plasma using hydrophilic interaction chromatography with tandem mass spectrometry . *Journal of Chromatography B* , 877(18-19) , pp: 1716-1720.
14. Omar , A.A.G. 2014 . PVC membrane sensors for potentiometric determination of metoclopramide in pharmaceutical preparations and in presence of its degradate . Analytical &Bioanalytical Electrochemistry , 6(3), pp:296-307.
15. Wei , G., Mingjiang ,G. and Lingyun ,Z. 2012. Electrochemistry of metoclopramide at multi – walled carbon nanotube modified electrode and its voltammetric detection . Analytical sciences , 28, pp: 693-698 .
16. Gaikwad , S.,Kondawar , M.,Nazarkar , S., Phase, S. and Narkhede , H. 2010. RP-HPLC method for the simultaneous determination of metoclopramide hydrochloride and paracetamol in tablet dosage form . *International Journal of Pharmacy &Life Sciences* , 1(3), pp:127-132.
17. Aaditya , S. and Shiv , B.2012. Simultaneous estimation succinate ,metoclopramide hydrochloride and paracetamol by RP-HPLC method . *Journal of pharmaceutical sciences and research* , 4(6) , pp: 1848-1851.

18. Nagam , S.T., Omar,A.Y.2014.New mode of CFI Analysis using multiple channel irradiation system in a linear array arrangement with twin solar cells for turbidimetric determination of analytically interesting species (study &application). MSc .Thesis . Department of chemistry , college of science , university of Baghdad . Bagdad , Iraq .

19. Miler ,J.C. and Miler,J.N. 1988. Statistics for *analytical chemistry* .2nd edition. John Wiley and N.Y.Sons .

20. Bluman,A.G. 1997.*Elementary statistics* .3rd edition .WCB/MC Graw –Hill , New York.