

Magnesium concentration in medicinal products using the fully controlled inkjet approach

Ihsan A. Mkashaf

Department of Chemistry, College of Education for pure sciences, University of Basrah, Basrah, Iraq.

ARTICLE INFO

Received 26 January 2024
Accepted 09 June 2024
Published 30 June 2024

Keywords :

Microfluidic, EDTA, magnesium.

Citation: I. A. Mkashaf, J. Basrah Res. (Sci.) **50**(1), 190 (2024).
[DOI:https://doi.org/10.56714/bjrs.50.1.16](https://doi.org/10.56714/bjrs.50.1.16)

ABSTRACT

The measurement of magnesium ion in homemade ph samples has been designed using a fully automated microfluidic device. This study involved the design of two channel microchips (45×3 cm). Arduino mega microcontrollers were used to operate the suggested system. The DIY micro-peristaltic pumping was operated by the first type that was used for remove specimens and chemical agents extracted from the microchip and transfer them to the UV. Visible spect. We are use the apparatus a 7-microliter flow cell in our lab, also the second type called mega, was employed as logger's data to alter, it was received and record the outcomes since highest point corresponding to concentrations using an Office Excel 2016 application. A correlation coefficient (R^2) 0.9997 and the linearity varied from 0.5 to 10 $\mu\text{g/mL}$. Ten measurements of Mg ion 8 $\mu\text{g/mL}$ had a relative standard deviation of (0.872%).

1. Introduction

User correction with a standardized solution called the ethylene di amine tetra - acetic acid was the standard method in determining **magnesium(II)** and other suitable cations ethylene di amine tetra (EDTA)[1]. The EDTA has the structure depicted below figure(1)[2]. Typically, the USP or NF procedures are used to assess pharmaceutical products containing **magnesium**, these methods are use validated titration with the disodium salt of ethylene di nitrile tetra acetic acid (EDTA) using hydroxy naphthol blue as the indicator[3]. The science and technology of systems that use microchips with tiny pores that are between tens and hundreds of micrometers in size to process small amounts of liquid (10^{-9} - 10^{-18} liters) is known as microfluidics[4-6]. Microfluidic systems are widely utilized as cost-effective analytical tools due to their ability to simplify and enhance various analytical processes. Their key advantages include the use of minimal sample and reagent volumes, precise control of fluid flow, and improved system performance. By integrating multiple analytical operations—such as mixing, separation, and detection—into a single compact device, microfluidics significantly reduce experimental complexity and analysis time. Moreover, these systems enable accurate estimation of different elements in solution form, making them highly suitable for applications in pharmaceutical, environmental, and biochemical analysis where efficiency, reproducibility, and resource optimization are essential [7]. These advantages include high sensitivity and accuracy in detection and separation operations, as well as short analysis times, low costs, and little production waste [8-10]. Total

*Corresponding author email : Ihsan.mkashaf@uobasrah.edu.iq



Microanalysis Systems, often known as chip-on-Lab technology, are systems that use very small quantities of liquid to carry out one or more chemical reactions for the purpose of analysis (LOC) [11-13]. Several metal ions react with electron pair donors to form coordination compounds in the molecular or complex ions chemical [14]. The formation of a particular class of coordination compounds chemical, called chelates, are especially well suited for quantitative methods [15]. A chelate is formed when a metal ion can be coordinated with two (or more) donor groups of a single ligand in the molecular [16]. Tertiary amine compounds chemical such as ethylene di amine tetra acetic acid (EDTA) are widely used for the formation of chelates in more compound like use in analytical chemistry [17-21]. Complexometric titrations with EDTA have been reported for the analysis of nearly all metal ions [22, 23]. Because of the chemical nature EDTA has four acidic protons, the formation of metal-ion/EDTA complexes is dependent upon the pH chemically. For the titration of Mg^{2+} [24], one must buffer the solution to a pH of 10 so that complex formation will be quantitative. The reaction of Mg^{2+} with EDTA may be expressed as [25-27 [ENREF 25](#)]:

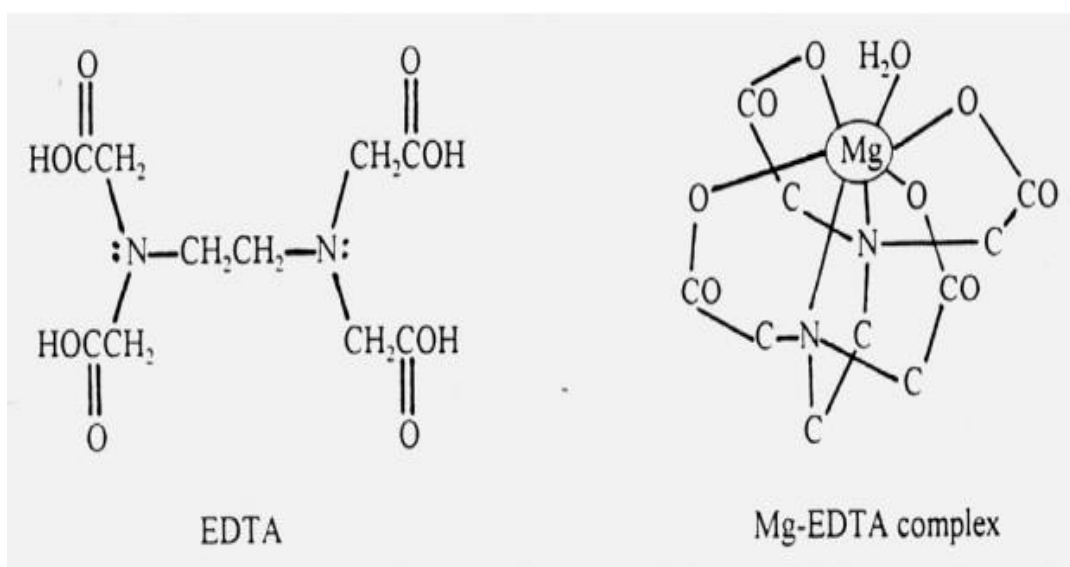


Figure.1. Structure of EDTA with Mg(II).

Research goal: Create a DIY, entirely computerized capillary system to measure magnesium sulfate in pharmaceutical preparations. Applying EDTA reagent.

2. Materials and Methods

Microfluidic system design for determination of Mg^{+2}

A homemade microfluidic system designed was created to measure magnesium (II) in medications. A $45\ \mu\text{L} \times 4\ \text{cm}$ three-channel micro disc was created, with a $15\ \mu\text{L}$ volume in each channel. This allowed for the use of extremely tiny chemical and sample volumes. A peristaltic pump, which gathers samples and reagents, is controlled by an Arduino type of microcontroller, the first of which is a UNO type. Upon receiving the analog signal from the detector, the second type of mega transforms it into a digital signal and forwards it to the computer processor to draw the peak. The computer processor publishes the digital signal locally and as data in Microsoft Excel 2016.2.2. Solutions and reagents for measuring magnesium (II) in pharmaceutical formulations are prepared. High-purity chemicals of every kind have been employed, along with ion-free distilled water.

1. **magnesium** sulfate (MgSO_4) was used to create the standard solution of **magnesium** (II) at a concentration of $100\ \mu\text{g/mL}$.
2. Added 2ml of ammonium buffer solution chemical and one pinch EBT indicator colour were added in it. The colour of the solution become wine- red on mixing solution.
3. The solution was then titrated with given known strength EDTA solution chemical (taken in the burette) until the wine red colour turns to blue colour.

3. Result and Discussion:

Under the ideal conditions examined, the locally constructed microfluidic system Figure (2) with a wavelength (620 nm) in Figure was utilized to determine the amount of magnesium (II) in pharmaceutical formulations(3). where the sample is represented by R1, the reagent by R2, and the current carrier liquid by R3.

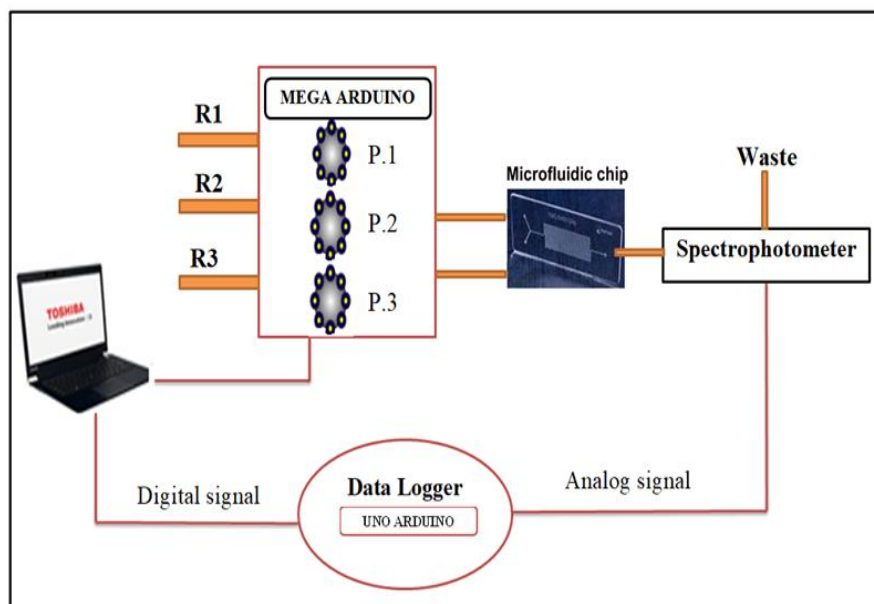


Figure. 2 Microfluidic Device for Magnesium (II) Measurement in Pharmaceutical Compounds

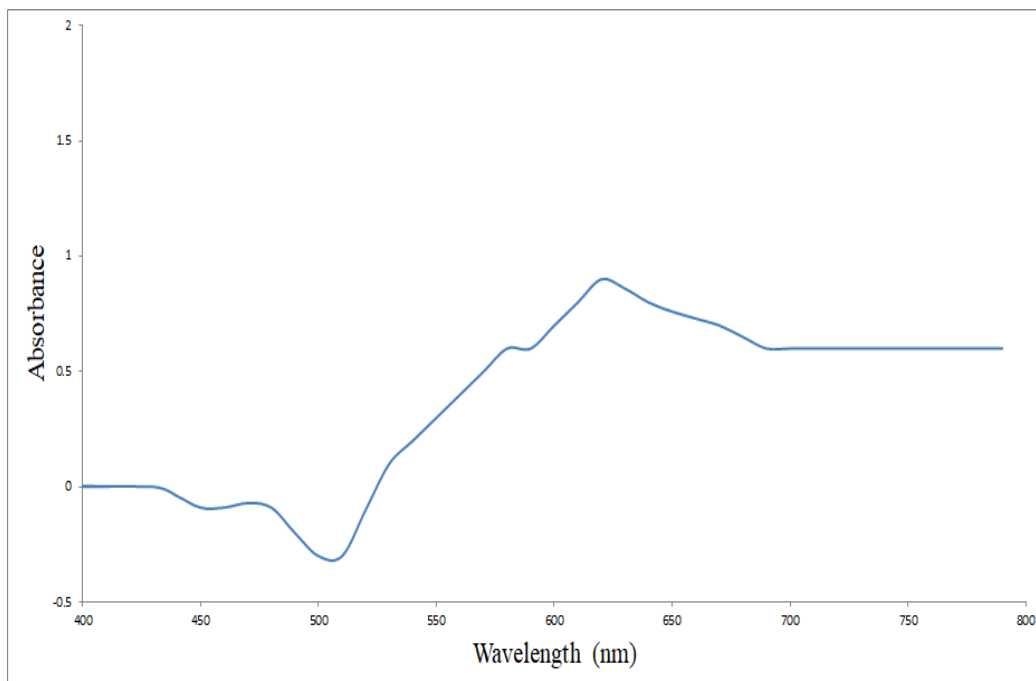


Figure. 3 The maxim wavelength of the MG -EDTA complex

3.1 Ideal Conditions for Magnesium (II) Measurement in Medicines

3.1.1 The effective of the flow rete:

A peak height resulting from Magnesium (II) reaction withdrawal (4 PPM) was tested in relation to flow rate between 0.5 and 3.5 ml/min, since the formation of the resulting complex causes the peak height to drop with higher flow rate table (1) and Figure (4). So, in order to get a quick analysis time and a quick modeling pace, the speed (1 ml/min) was used.

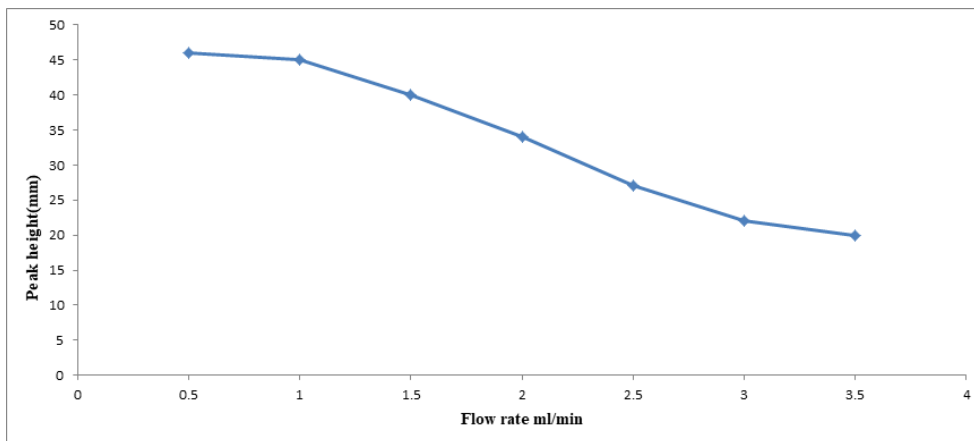


Figure. 4 Impact of flow rete on peak height following withdrawal of magnesium (II) (4 $\mu\text{g/mL}$)

Table 1 The flaw's effect injection at the highest point as a result of the removal (4 $\mu\text{g/mL}$) of Magnesium (II).

Flaw rate (ml/mint)	peak height rate (mmeter)
0.52	46
1.20	45
1.51	40
2.01	34
2.50	27
3.00	22
3.5	20

3.1.2 Slide slit length's impact.

When the length of the slice's incision is increased, a peak height created by pulling away (4 $\mu\text{g/mL}$) When the slice's incision is extended, magnesium (II) exhibits a discernible rise in height that soon starts to drop within the acceptable range. (1-7 cm) due to the increase in dillution. deciding that the ideal incision length for further research should be 3 cm (Figure 5) and table (2).

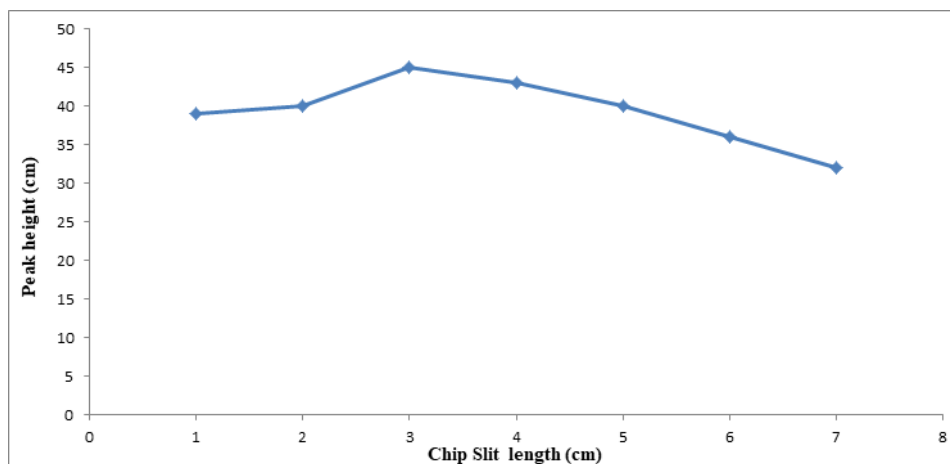


Figure. 5 Impact of the chip slit's length on the height of peak following the removal of 4 PPM of magnesium.

Table 2. The amount of magnesium (4 $\mu\text{g/mL}$) that is removed determines how long the slice is cut at the top.

Slit length (centimetre)	peak height rate (mm)
1	39
2	40
3	45
4	43
5	40
6	36
7	32

3.1.3 The effect of sample volume:

Upon increasing a sample value within the range of (10-70 μL), a rise Cloud formation at the top (4 %) was observed. This made it possible for the complex to form when the model's size was increased because we determined that the size of 50 μL was the ideal size to investigate other situations. After the reaction slit's length (3 cm) and velocity (1 ml/min) were stabilized, Figure (6) and Table (3) were created.

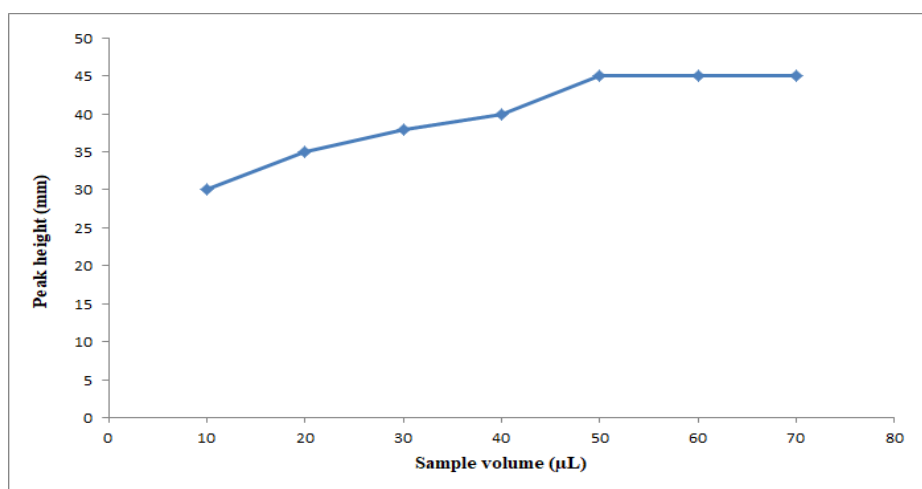


Figure. 6 Influence of quantity of sample on the peak's height following (4 PPM) removal of the Magnesium (II).

Table3: Impact for population of the sample on height of the peak following (4 µg/mL) magnesium withdrawal.

Sample volume (µL)	peak height rate (mm)
10	30
20	35
30	38
40	40
50	45
60	45
70	45

3.1.4 Effect of EDTA reagent concentration:

The fluid flow speed (1 ml/min), amount of sample (50 L), and sheet puncture area were all fixed. a rise in EDTA reagent concentration causes a rise in the highest point brought on by the removal of Magnesium (II) (4 µg/mL) (3cm). In order to use the sample used and the quantity of reagent that was available, the concentration (0.35 %) was selected for further research as soon as the peaks at high detector concentrations that measured began to decline and fell within the range used of (0.04 -0.4%). Figure (7) and table (4).

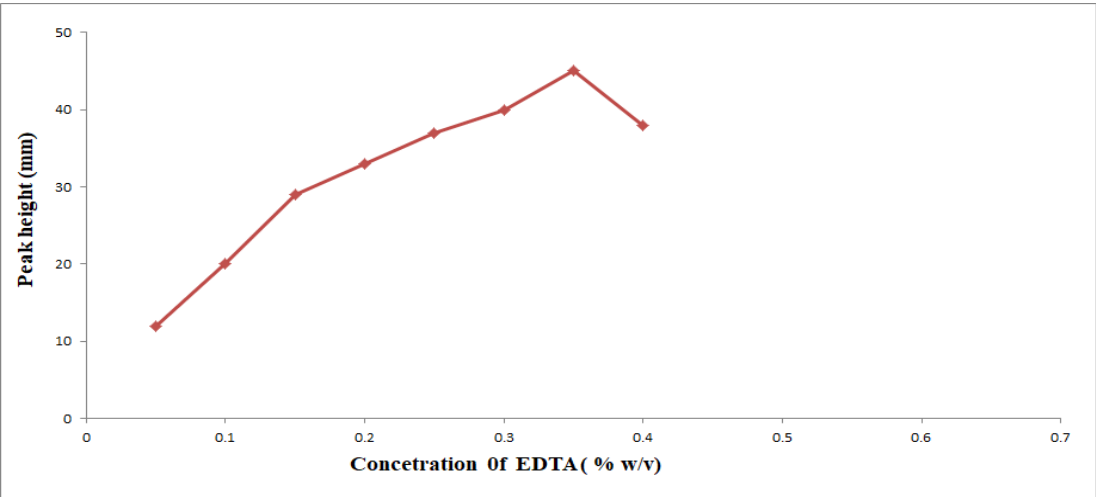


Figure. 7 Effect of EDTA focus on pinnacle ascent brought on by magnesium deficiency (4 µg/mL).

Table 4. Impact of EDTA dosage on withdrawal-induced peaks (4 µg/mL) of Magnesium

peak height rate (mm)	Conce. %
12	0.05
20	0.1
29	0.15
33	0.2
37	0.25
40	0.3
45	0.35
38	0.4

3.1.5 The volume of ammonium buffer solution effect:

Because of the lack of absorption at high acid volumes, when the volume of ammonium buffer solution increases within the range (1–2 ml), the rise in the peak caused by the removal of (4 µg/mL) of magnesium quickly experiences a decline. After adding the following parameters: a 50 µL sample volume, a 1 ml/min flow rate, and a 1.5 cm slit incision length were stabilized, the optimal volume for the study was determined to be 0.5 ml, as shown in Figure (8) and Table (5).

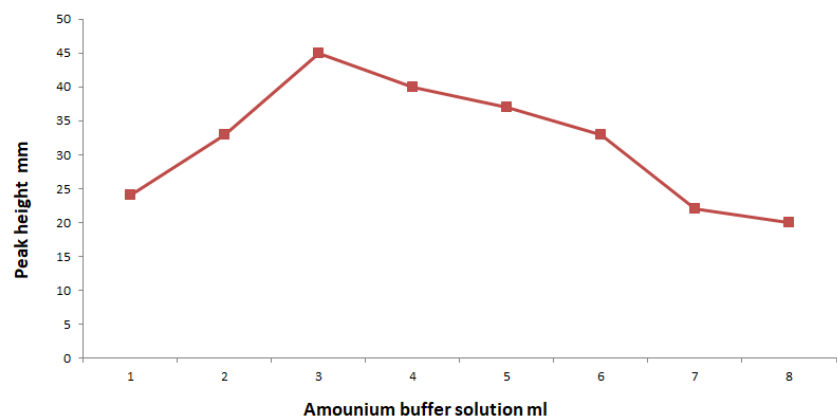


Figure.8. The impact of the Ammonium buffer solution on the highest possible following the removal of four parts per million of magnesium.

Table 5. The impact of NaOH volume on the highest point resulting from the removal (4 µg/mL) magnesium.

peak height rate (mm)	Volume of NaOH (ml)
1	24
5	33
10	45
15	40
20	37
25	33
35	22
40	20
1	24
5	33

Table 6. Ideal circumstances for measuring magnesium in pharmaceutical formulations.

The value	Factors
1	Flow rate ml/min
2	Ammonium buffer solution
50	Sample volume µL
3	Slit chip length cm
0.35	EDTA concentration w/v %

3.2 A Causal Conventional Circle.

After achieving optimal experimental conditions, the standard calibration curve for the magnesium solution was evaluated using the fully automated microfluidic method, as illustrated in Figure 9(a) and presented in Table 6. This method was employed for the quantitative determination of magnesium (II) ions in pharmaceutical formulations. A linear correlation was observed between peak height and magnesium concentration in the range of 2–10 ppm when complexed with EDTA, as shown in Table 7 and Figures 9(a)–9(b).

As illustrated in Figure 9(c), the calibration curve exhibited a strong linearity with a correlation coefficient (R^2) of 0.9997, confirming the reliability of the analytical method. The relative standard deviation (RSD%) for ten repeated measurements was 0.872%, indicating high precision, while the detection limit was determined to be 0.125 $\mu\text{g/mL}$. The relationship between peak height (y) and concentration (x) was expressed by the equation $y = 5.6727x$.

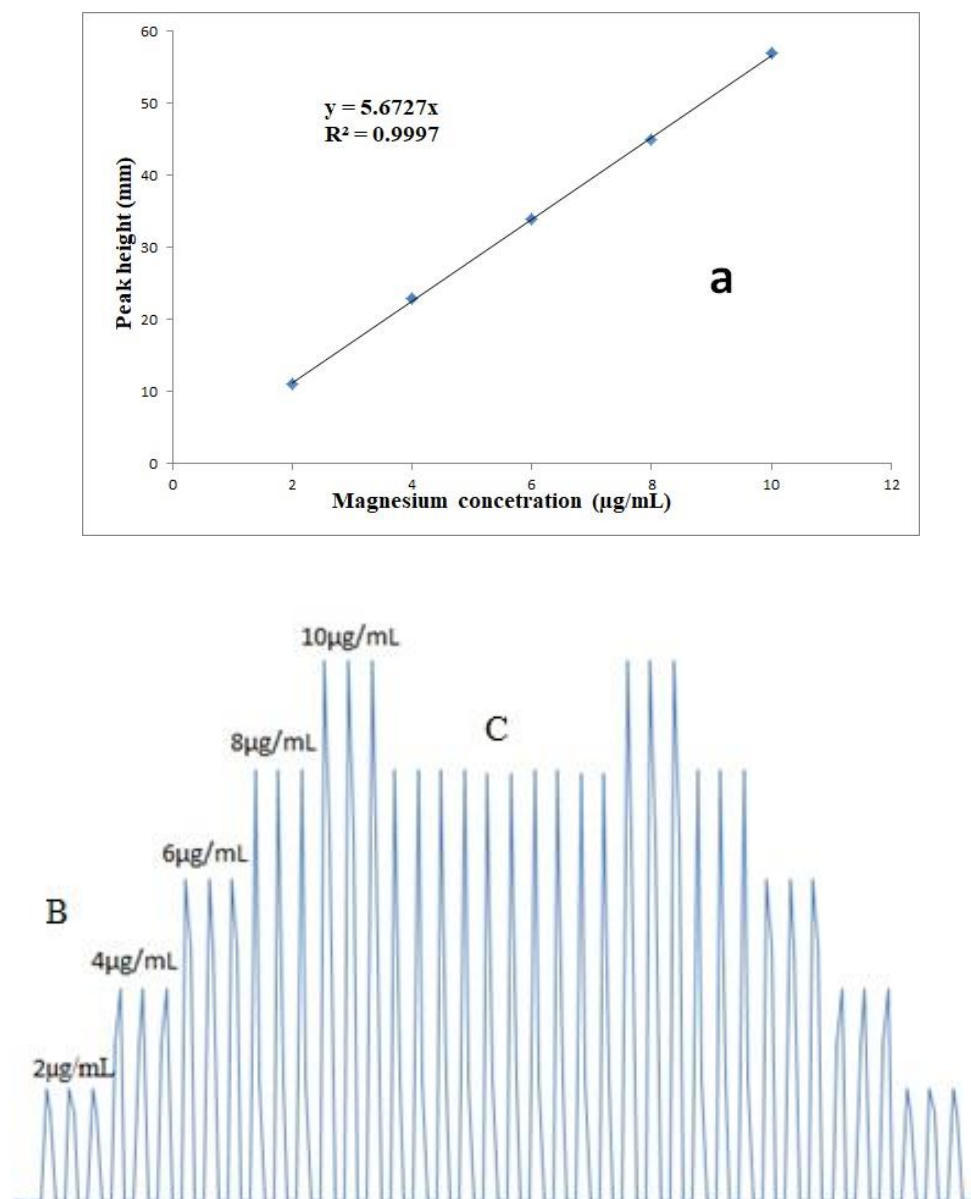


Figure. 9. (a) A curve calibration for the micro measurement of magnesium ions in drugs. (b) For every level, the corresponding magnesium peaks were extracted three times. (c) A peak levels brought about by the removal (8 $\mu\text{g/mL}$) magnesium

Table 7. The measurements of the calibration curve's peaks.

peak height rate (mm)	Concentration (µg/mL)
11	2
23	4
34	6
45	8
57	10
11	2
23	4

3.3 Distribution:

As shown in Figure (10), a manifold unit of the planned apparatus had a dilution factor of 1.05.

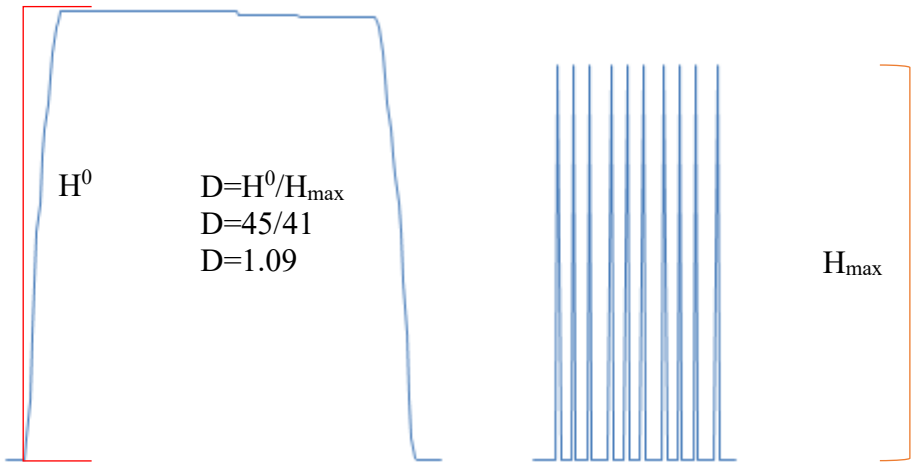


Figure. 10. The magnesium ion determination system's dispersion factor

3.4 Applications in analysis

Four on-site samples from pharmacies in the Basra region were tested using the microfluidic technology intended for measuring magnesium ions in the range 2–10 µg/mL Table (8).

Table 8. Magnesium concentrations in specific drugs.

Sample	Magnesium (ppm)	Total Magnesium (ppm)	Total Magnesium found (ppm)	Recovery %
Tablet 1	8	0.2567	0.2459	96.86
Tablet 2	8	1.0389	1.0400	95.11
Tablet 3	8	0.1366	0.1359	95.78

3.5 Interruptions.

Table 9 presents the peak heights observed when 8 ppm of magnesium was measured in the presence of varying concentrations (1, 10, 100, and 1000 µg/mL) of interfering cations including Zn, Fe, Cu, Co, Ca, and Mn. The results indicate that most of these ions did not significantly affect the

determination of magnesium in pharmaceutical formulations. This stability in peak height confirms that the proposed method maintains high selectivity and accuracy even in the presence of common metal ions.

Table 9. Impact of Interferences

Foreign captions (+2)	Peak height m meter			
	Ties up			
	1	10	100	1000
Zn	50	47	42	36
Fe	51	46	40	34
Cu	44	39	32	26
Co	47	41	34	29
Ca	52	44	38	31
Mn	56	53	50	41

4. Conclusions

- To determine the presence of **Magnesium** binary ions in pharmaceutical formulations, we developed For the first time, a fully self-contained microfluidic system using microfluidic chips was used in our university laboratory.
- Making micro-pumps using materials found at the neighborhood market, each of which had a variable speed that was managed by an Arduino microcontroller.
- Using the Mega controller to convert the data provided by the analog signal into simple-to-process digital signals and displaying them in Excel 2016.
- The designed system, which included the use of models and reagents, was environmentally benign in terms of waste disposal due to the ability to use extremely small volumes.

5. References

- [1] R. Nkuna, G. N. Ijoma, and T. S. Matambo, "Applying EDTA in chelating excess metal ions to improve downstream DNA recovery from mine tailings for long-read amplicon sequencing of acidophilic fungi communities," *Journal of Fungi*, vol. 8, no. 5, p. 419, 2022. Doi: <https://doi.org/10.3390/jof8050419>
- [2] Y. Shinta, B. Zaman, and S. Sumiyati, "Citric acid and EDTA as chelating agents in phytoremediation of heavy metal in polluted soil: a review," in *IOP Conference Series: Earth and Environmental Science*, 2021, vol. 896, no. 1: IOP Publishing, p. 012023. Doi: <https://doi.org/10.1088/1755-1315/896/1/012023>
- [3] A. Haller et al., "Measuring calcium content of human milk on a microfluidic chip," *Procedia Engineering*, vol. 168, pp. 105-108, 2016. Doi: <https://doi.org/10.1016/j.proeng.2016.11.158>
- [4] T. Luo, L. Fan, R. Zhu, and D. Sun, "Microfluidic single-cell manipulation and analysis: Methods and applications," *Micromachines*, vol. 10, no. 2, p. 104, 2019. Doi: <https://doi.org/10.3390/mi10020104>
- [5] H. Chen, J. Sun, E. Wolvetang, and J. Cooper-White, "High-throughput, deterministic single cell trapping and long-term clonal cell culture in microfluidic devices," *Lab on a Chip*, vol. 15, no. 4, pp. 1072-1083, 2015. Doi: <https://doi.org/10.1039/C4LC01176G>

- [6] C. T. Culbertson, T. G. Mickleburgh, S. A. Stewart-James, K. A. Sellens, and M. Pressnall, "Micro total analysis systems: fundamental advances and biological applications," *Analytical chemistry*, vol. 86, no. 1, pp. 95-118, 2014. Doi: <https://doi.org/10.1021/ac403688g>
- [7] H. Amini, W. Lee, and D. Di Carlo, "Inertial microfluidic physics," *Lab on a Chip*, vol. 14, no. 15, pp. 2739-2761, 2014. Doi: <https://doi.org/10.1039/C4LC00128A>
- [8] P. Prapti et al., "Microfluidic chips: recent advances, critical strategies in design, applications and future perspectives," *Microfluidics and Nanofluidics*, vol. 25, no. 12, 2021. Doi: <https://doi.org/10.1007/s10404-021-02502-2>
- [9] B. Wu et al., "Development of microfluidic chip-based loop-mediated isothermal amplification (LAMP) method for detection of carbapenemase producing bacteria," *Microbiology spectrum*, vol. 10, no. 5, pp. e00322-22, 2022. Doi: <https://doi.org/10.1128/spectrum.00322-22>
- [10] S. T. Gebreyesus et al., "Streamlined single-cell proteomics by an integrated microfluidic chip and data-independent acquisition mass spectrometry," *Nature communications*, vol. 13, no. 1, p. 37, 2022. Doi: <https://doi.org/10.1038/s41467-021-27778-4>
- [11] I. Salmon et al., "Engineering neurovascular organoids with 3D printed microfluidic chips," *Lab on a Chip*, vol. 22, no. 8, pp. 1615-1629, 2022. DOI: 10.1039/D1LC00535A
- [12] Y. Xiao, X. He, A. W. Stuedlein, J. Chu, T. Matthew Evans, and L. A. Van Paassen, "Crystal growth of MICP through microfluidic chip tests," *Journal of Geotechnical and Geoenvironmental Engineering*, vol. 148, no. 5, p. 06022002, 2022. Doi: [https://doi.org/10.1061/\(ASCE\)GT.1943-5606.0002756](https://doi.org/10.1061/(ASCE)GT.1943-5606.0002756)
- [13] X. Chen and H. Lv, "Intelligent control of nanoparticle synthesis on microfluidic chips with machine learning," *NPG Asia Materials*, vol. 14, no. 1, p. 69, 2022. Doi: <https://doi.org/10.1038/s41427-022-00416-1>.
- [14] H. Geng et al., "Metal ion-directed functional metal-phenolic materials," *Chemical Reviews*, vol. 122, no. 13, pp. 11432-11473, 2022. Doi: <https://doi.org/10.1021/acs.chemrev.1c01042>
- [15] J. Ghassemi Nejad, R. Vakili, E. Sobhani, M. Sangari, A. Mokhtarpour, and S. A. Hosseini Ghafari, "Worldwide Research Trends for Chelates in Animal Science: A Bibliometric Analysis," *Animals*, vol. 13, no. 14, p. 2374, 2023. Doi: <https://doi.org/10.3390/ani13142374>
- [16] M. Ismael, A.-M. M. Abdel-Mawgoud, M. K. Rabia, and A. Abdou, "Synthesis, characterization, molecular modeling and preliminary biochemical evaluation of new copper (II) mixed-ligand complexes," *Journal of Molecular Structure*, vol. 1227, p. 129695, 2021. Doi: <https://doi.org/10.1016/j.molstruc.2020.129695>
- [17] I. Borthakur, S. Srivastava, S. Kumari, and S. Kundu, "Tandem synthesis of N-methylated tertiary amines via three-component coupling of carbonyl compounds, amines, and methanol," *Chemical Communications*, vol. 58, no. 70, pp. 9822-9825, 2022. Doi: <https://doi.org/10.1039/D2CC03115A>
- [18] D. Ruijten et al., "Hydrogen borrowing: Towards aliphatic tertiary amines from lignin model compounds using a supported copper catalyst," *ChemSusChem*, vol. 15, no. 19, p. e202200868, 2022. Doi: <https://doi.org/10.1002/cssc.202200868>
- [19] S. Z. Ali, B. G. Budaitis, D. F. Fontaine, A. L. Pace, J. A. Garwin, and M. C. White, "Allylic C-H amination cross-coupling furnishes tertiary amines by electrophilic metal catalysis," *Science*, vol. 376, no. 6590, pp. 276-283, 2022. Doi: <https://doi.org/10.1126/science.abn8382>
- [20] X. Li et al., "Phase Splitting Rules of the Primary/Secondary Amine-Tertiary Amine Systems: Experimental Rapid Screening and Corrected Quasi-Activity Coefficient Model," *Industrial & Engineering Chemistry Research*, vol. 61, no. 23, pp. 7709-7717, 2022. Doi: <https://doi.org/10.1021/acs.iecr.2c00533>
- [21] Z.-Q. Zhang et al., "Difluoromethylation of Unactivated Alkenes Using Freon-22 through Tertiary Amine-Borane-Triggered Halogen Atom Transfer," *Journal of the American Chemical Society*, vol. 144, no. 31, pp. 14288-14296, 2022. Doi: <https://doi.org/10.1021/jacs.2c05356>
- [22] K. Jo and E. Hwang, "Candidate primary reference measurement procedure for the amount-of-substance content of a complexing agent expressed as EDTA based on the coulometric titration with electrogenerated Hg ions," *Metrologia*, vol. 59, no. 4, p. 045016, 2022. Doi: <https://doi.org/10.1088/1681-7575/ac7f0d>

- [23] C. Paredes, D. Ahumada, and J. Ágreá, "Gravimetric Complexometric Titration Method to Determine Mass Fraction of Ethylenediaminetetraacetic Acid Disodium Salt Dihydrate in Candidate-Certified Reference Materials," MAPAN, vol. 38, no. 1, pp. 179-191, 2023. Doi: <https://doi.org/10.1007/s12647-022-00602-0>
- [24] E. Hafer, U. Holzgrabe, K. Kraus, K. Adams, J. M. Hook, and B. Diehl, "Qualitative and quantitative ^1H NMR spectroscopy for determination of divalent metal cation concentration in model salt solutions, food supplements, and pharmaceutical products by using EDTA as chelating agent," Magnetic Resonance in Chemistry, vol. 58, no. 7, pp. 653-665, 2020. Doi: <https://doi.org/10.1002/mrc.5009>
- [25] X. Mei, W. Luo, H. Li, and S. Pu, "Synthesis and photophysical investigation of Schiff base as a Mg^{2+} and Zn^{2+} fluorescent chemosensor and its application," Luminescence, vol. 38, no. 3, pp. 250-259, 2023. Doi: <https://doi.org/10.1002/bio.4443>
- [26] W. Yang and L. Feng, " Mg^{2+} -promoted high-efficiency DNA conjugation on polydopamine surfaces for aptamer-based ochratoxin A detection," Analytica Chimica Acta, p. 342382, 2024. Doi: <https://doi.org/10.1016/j.aca.2024.342382>
- [27] H. Wu et al., "Positively-charged PEI/TMC nanofiltration membrane prepared by adding a diamino-silane coupling agent for $\text{Li}^+/\text{Mg}^{2+}$ separation," Journal of Membrane Science, vol. 672, p. 121468, 2023. Doi: <https://doi.org/10.1016/j.memsci.2023.121468>

تركيز المغنيسيوم في المنتجات الطبية باستخدام أسلوب نفت الحبر الذي يتم التحكم فيه بالكامل

احسان عاشور مكشاف

قسم الكيمياء، كلية التربية للعلوم الصرفة، جامعة البصرة، البصرة العراق.

معلومات البحث	الملخص
الاستلام القبول النشر	تم تصميم جهاز محلي الصنع لقياس أيون المغنيسيوم في عينات باستخدام نظام ميكروفلويديك مؤتمت بالكامل. تضمنت هذه الدراسة تصميم شرائح دقيقة ذات قناتين (3 × 45 سم). تم استخدام المتحكمات الدقيقة من نوع Arduino لتشغيل النظام المقترح. تم تشغيل المضخات التمعجية الدقيقة كان النوع الأول الذي تم استخدامه لحقن العينات والكواشف الكيميائية التي تخرج من الشريحة المايكروية ونقلها إلى جهاز قياس الأشعة المرئية و فوق البنفسجية. ان الجهاز المستخدم وهو عبارة عن خلية ذات سعة 7 ميكروليتر والموجود في مختبرات قسم الكيمياء، وكذلك النوع الثاني يسمى Mega، تم استخدامه كمسجل بيانات لتغييرها، وتسجيل النتائج من أعلى نقطة تتوافق مع التركيزات باستخدام تطبيق Office Excel 2016. وكان معامل الارتباط (R ²) 0.9997 وتراوحت الخطية من 0.5 إلى 10 ميكروغرام/مل. كان انحراف المعيار النسبي لعشرة قياسات مستخدمة لأيون المغنيسيوم بتركيز 8 ميكروغرام / مل قدره (0.872%).
الكلمات المفتاحية	نظام المايكروفلودك وكاشف EDTA وايون المغنيسيوم الثنائي
Citation: I. A. Mkashaf, J. Basrah Res. (Sci.) 50(1), 190 (2024). DOI:https://doi.org/10.56714/bjrs.50.1.16	

*Corresponding author email : Ihsan.mkashaf@uobasrah.edu.iq

