Rafidain Journal of Science
https://rsci.mosuljournals.com

Vol. 32, No. 3, pp.9-20, 2023

A new Spectrophotometric Approach for Determination of Meropenem in Pharmaceutical Formulation

Ann H. Mahmood **Hana Sh. Mahmood**
Department of Chemistry/ College of Science / University of Mosul

p-ISSN: 1608-9391
e -ISSN: 2664-2786

Article information

Received: 1/8/2022
Revised: 1/11/2022
Accepted: 11/11/2022

DOI: 10.33899/rjs.2023.180272

corresponding author:
Ann H. Mahmood
annhashimmahmmod@gmail.com
Hana Sh. Mahmood
hanashukermahmood@uomosul.edu.iq

ABSTRACT

A new, sensitive spectrophotometric determination of meropenem (MRP) the broad-spectrum carbapenem antibiotic has been suggested using p-aminobiphenyl amine reagent and periodate in 6M HCl media to form one to one blue color complex with maximum peak at 716nm.The reaction is carried out at room temperature, Beer's law is followed from 10 to 125 µg/mL, the molar absorptivity is 1265.22 L/mole.cm., LOD, LOQ are 0.0202, and 0.0673 ppm respectively, the method has been applied for estimation of MRP in vials with high accuracy (error % 0.0106) and good precision (RSD % ±0.0319).

Keywords: Spectrophotometric, meropenem, periodate, p-aminobiphenyl amine

This is an open access article under the CC BY 4.0 license (http://creativecommons.org/licenses/by/4.0/).

INTRODUCTION

Meropenem (MRP) is a broad-spectrum carbapenem antibiotic, which is effective against most Gram-positive and Gram-negative bacteria (WHO, 2019). MRP is given by intravenous to treat severe infections (Bhowmick and Weinstein, 2020), it has high bio abundance percentage may reach to 100% with one hour as a half-life (Weinre *et al*., 2014), it is used to treat some types of complicated bacterial infections such as: Intra-abdominal infection, bacterial meningitis in children of more than three months age and infections of the skin (Fish, 2006) (Ku *et al*., 2015). It has been used to treat the infection caused by COVID- 19 (Xu *et al*., 2020). As a chemical compound MRP contain functional groups as amine group and carboxylic group, the sulfur link between two pentacyclic groups may consider the weaker linkage in MRP (Xu *et al*., 2020). The IUPAK name of MRP is 3- [5-(dimethyl carbamoyl) pyrrolidin-2-yl] sulfanyl-6- (1-hydroxyethyl)-4-methyl-7-oxo-1-azabicyclo [3.2.0] hept-2-ene-2-carboxylic (Meronem, 2021), with the chemical formula $C_{17}H_{25}N_3O_5S$ 383 and molecular mass 464 g/mole (USP 30, 2007).

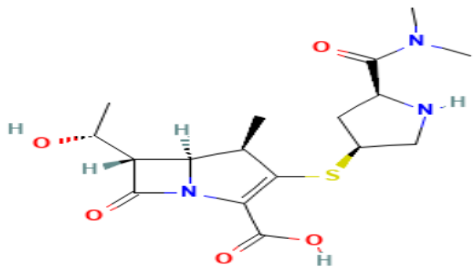


Fig. 1: The chemical structure of Meropenem

Many chromatographic methods for determination of MRP has been reported (Milla *et al*., 2020) (Sutherland *et al*., 2020) (Roth *et al*., 2017) (Negi *et al*., 2017), other more complicated techniques have been also published for determination of MRP such as photoluminescent (Samadi and Narimani, 2019) tandem-mass (Kammoun *et al*., 2020) and photocatalytic degradation (Altamirano *et al*., 2020). While little spectrophotometric methods have been noted in the literature review, one of these methods is based on charge -transfer reaction using 2,3 dichloro 5,6 dicyano 1,4 benzoquinone (DDQ) and measuring the produced complex at 345 nm (Khalil and Ibrahim, 2020), the other is based on the reduction of Fe (III) into Fe (II) by MRP and their subsequent Prussian formation with hexacyanoferrate measured at 720 nm, or with 1, 10-phenanthroline measured at 510 nm and at 520 nm with 2,2′-bipyridyl (Singh and Maheshwari, 2013). MRP reacts with brucine reagent (2,3-Dimethoxystrychnidin-10-one) and sodium periodate in acidic medium to form color measured at 520nm (Nakkella *et al*., 2020). It is also forming chelating complex with gold ion (III) measured at 477 nm. (Qassim, 2015). The stability monitoring of solid dosage form of MRP using UV has been published (Fayed *et al*., 2019), also UV with FT-IR and Raman spectra were recorded (Cielecka *et al*., 2013). Most of the above methods either use toxic reagent or use complicated technique. The oxidation by periodate and coupling with chromogenic reagent is an old procedure (Zakaria, 2011), (Lamya, 2013) to determine meropenem. The aim of the study is to move from toxic danger reagents to safer, and less hazard one, and from many analysis steps to eliminated one using simplest, and available technique.

Experimental

a. Instruments

A double-beam Jasco V- 630spectrophotometer with 1.0 cm matched glass cell.

b. Chemicals

- MRP solution (500 µg /ml): This solution was prepared by dissolving 0.05 g of MRP solution in the amount of distilled water then complete the volume to 100 ml in a volumetric flask.

-Potassium periodate 1%: This solution was prepared by dissolving 1g of solid pure potassium periodate in distilled water and the volume was completed to 100 ml in a volumetric flask.

- **p-aminobiphenyl amine (PADA)(1x10^{-3}M):** It was prepared by dissolving 0.0184g (184.242g/mole) of solid pure reagent in distilled water and the volume was completed to 100 ml in a volumetric flask.

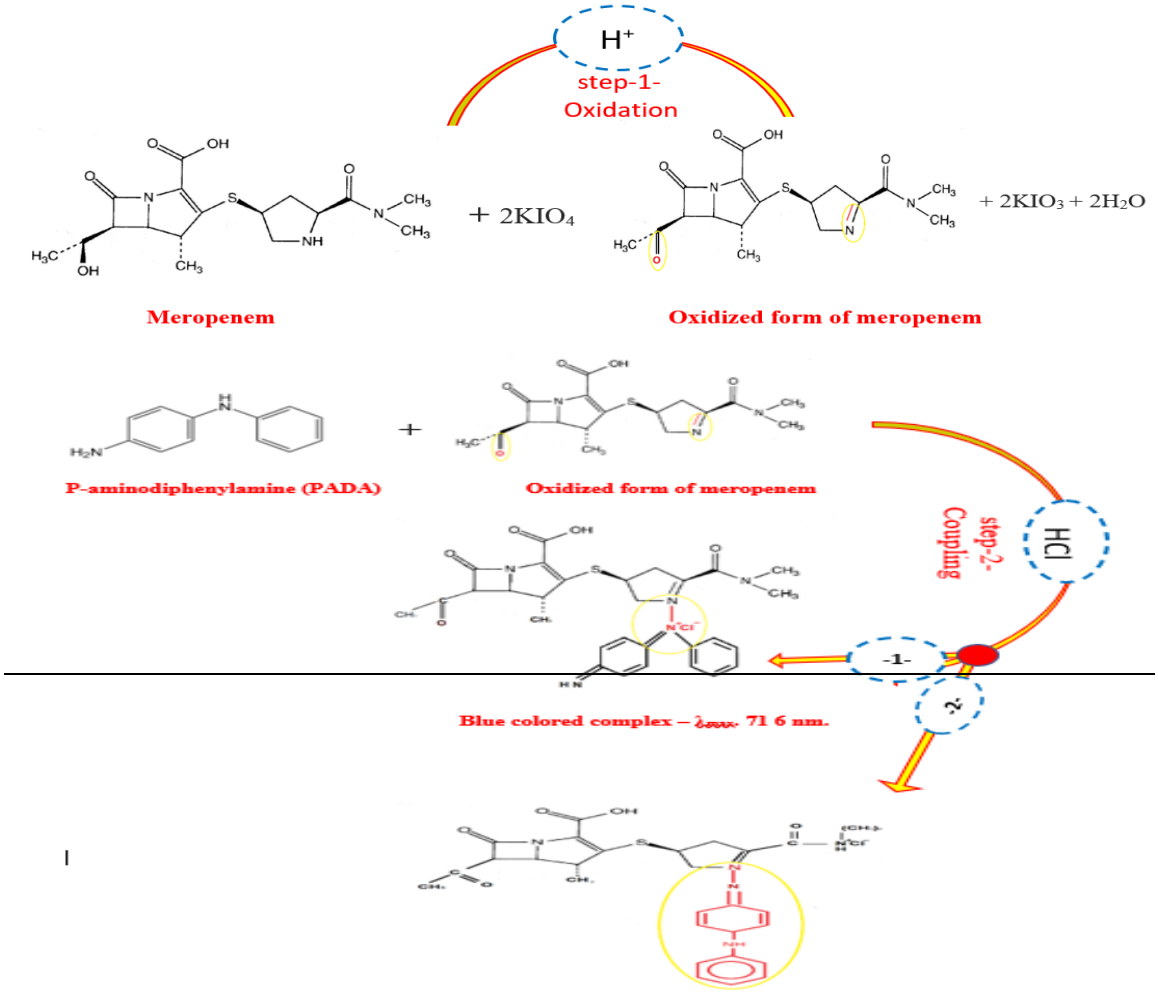
-Pharmaceutical preparation

Mer vials 500 mg / manufactured by (Fresenius Kabi / Germany): the content of one vail powder (0.5 g) has been dissolved in 100 ml distilled water, then 5ml of the solution has been diluted to 50ml with distilled water to prepare 500 µg /ml.

Mer vials 1g / manufactured (Labatec/ Switzerland): 0.05gm of the vial powder has been dissolved in distilled water to prepare 500 µg /ml.

Chemical reactions

MRP degradation in aqueous solution undergoes through opening of the beta-lactam ring (Jamieson *et al*., 2020), it may be decomposed when it exposes to level of alkalinity to produce the analog β-lactam ring-opened derivative (Mendez *et al*., 2008). The proposed experiment was occurred in acidic medium; Therefore, the suggested chemical reaction expects no cleavage of the ring of lactam. Meropenem is consider weak organic acid undergo hydrolysis and oxidation steps (Agudelo *et al*., 2020). Therefore, the chemical reaction undergoes oxidation of MRP by potassium periodate in acidic medium (step-1-) followed by (step-2-) reaction of MRP with PADA to form colored complex. Schem-1- shows the reaction steps.



Scheme 1: The suggested reaction pathway

RESULTS AND DISCUSSION

Preliminary reaction study

Under primary criteria, one ml of oxidant KIO_4 (1%) has been followed by another one ml of MRP, then half ml of HCl (6 M), and two ml of PADA reagent, finally the volume of solution mixture has been diluted to make 10 ml in calibrated volumetric flask, the prepared solution exhibits a blue color against yellow color of blank solution prepared in the same way but without the addition of MRP. The absorbance of the colored product was 0.2063 at maximum peak 712nm.

Study of the optimum reaction conditions

Effect of oxidizing agent

The reaction between MRP and PADA has been checked in acidic medium of 6 M HCl but in the presence of ferric (III)ammonium sulphate, ceric sulphate, N-bromosuccenamide (NBS)and in the absence of any oxidant, all cases show no reaction. while the reaction exhibits good response in the presence of KIO_4, therefore the effect of volumes (0.5-2.5) ml of (1%) KIO_4 has been studied against 50 µg of MRP. (Table 1) shows that 2 ml of oxidizing agent solution gives the best absorbance.

Table 1: Effect of oxidizing agent

ml of (1%) KIO_4 solution	Absorbance
0.5	0.0925
1	0.2061
1.5	0.2524
2	**0.2735**
2.5	0.2710

Effect of acid type and volume of acids

Effect of different amount of many acids on absorption intensity of the colored complex has been studied (Table 2). Table (2) shows negative effect on the absorption intensity of the colored compound of all acids except hydrochloric acid (6M) give the sensitivity of colored product exhibits a maximum at 1 ml of 6M HCl. The other acids decrease the absorbance which indicate the formation of chloride salt of the drug.

Table 2: Effect of acid type and volume of acids

Ml of Acid (6M)	0.1	0.5	1	1.5	2
H_3PO_4	0.0034	--------	--------	------	-------
HNO_3	0.0088	0.0038	-------	--------	------
H_2SO_4	0.0028	------	--------	------	-----
HCl	0.0932	0.2731	**0.3150**	0.250	o.1801
CH_3COOH	0.0034	0.0028	-----	------	------

Effect of time of oxidation

The oxidation time has been also followed, the results in (Table 3) shows that three minutes is sufficiently enough for oxidation.

Table 3: Effect of oxidation period

Time (min)	0	2	3	5	10
Absorbance	0.2443	0.3059	**0.3150**	0.2943	0.2432

Effect of surfactant

2ml of anionic [sodium dodecyl sulphate] (SDS), cationic [cetylpyridinium chloride] (CPC), and [cetyltrimethylammonium bromide] (CTAB) surfactants with different order of additions were followed (Table 4). The table show no enhancements on the absorption intensity.

Table 4: Effect of surfactants

Surfactant solution (1×10^{-3} M)	Absorbance / order of addition
SDS	0.1802
CTAB	0.1321
CPC	Turbid
With out	**0.3150**

Effect of coupling agent solution

2 ,3 and 4.0 ml of ($1x10^{-3}$M) PADA reagent has been followed against 10-75 µg of MRP under the reaction conditions, the absorbances of the colored product has been measured at 710 nm. Table (5) shows that 4 ml of reagent solution gives 0.9904 exhibits the higher determination coefficient and the sensitivity is best

Table 5: Effect of coupling agent

Ml of reagent (1×10^{-3}M)	Absorbance / µg of MRP in 10 ml						
	10	25	40	50	60	75	R^2
2	0.1321	0.2013	0.2601	0.3150	0.3992	0.4500	0.9868
3	0.2871	0.3890	0.4621	0.5210	0.6012	0.7921	0.9607
4	0.2991	0.4310	0.5901	**0.6310**	0.6992	0.8521	**0.9904**
5	0.3115	0.4632	0.5997	0.6631	0.7019	0.9673	0.9649

Effect of order of addition

The followed sequence was Ox= Oxidant, D= Drug, A= Acid, R=reagent, other three different sequences of addition have been checked, the results indicate that order one gives the best absorbance, the results are listed in (Table 6).

Table 6: Effect of order of addition

Number of orders	Order of addition	Absorbance
1	OX + D + A + R	**0.6301**
2	D + OX + A + R	0.4719
3	D + A + OX + R	0.5521
4	A + D + OX +R	0.5918

From (Table 6), the first sequence is the best, then the fourth, the third, then the second, this can be attributed to the successive addition of the drug and the acid without separating them with the oxidizing agent that may be consumed by side reaction before adding the acid that exhibits the oxidation action of periodate.

Effect of Solvents

Ethanol, methanol, propanol, and acetic acid have been used as diluent to reaction mixture instead of water. The absorption spectra in Fig. (2) shows no red shift were caused by these solvents, and (Table 7) shows that only ethanol exhibits increase in the absorbance of the formed complex.

Table 7: Effect of solvents

Solvent	Absorbance
Water	0.6310
Ethanol	0.6701
Methanol	Turbid
Acetic acid	0.2591
Propanol	0.6201

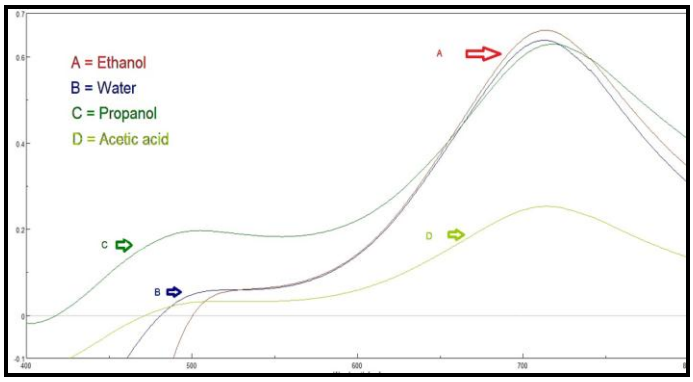


Fig. 2: Spectra using different solvents

Absorption Spectra and calibration curve OX + D + A + R

Under the observed reaction parameters, the sequence of addition is as follows: (2 ml of periodate 1%, 1ml of 500 µg\ml of MRP, 1ml HCl (6 M), standing for three minutes, then 4 ml of the PADA reagent ($1x10^{-3}$M), finally dilution to 10 ml, one minute then make measurements), the absorption spectrum of the colored product against blank was taken and shows that wavelength of maximum absorption intensity is 71 6 nm. Fig. (3).

To increasing volume (0.2-2.5) ml of 500µg.ml^{-1} standard of MRP solution, 4ml of ($1x10^{-3}$M) PADA and 2.0 ml of 1% KIO_4, 1 ml of 6M HCl, the solution was left for three minute as standing time, then the volumes were completed to 10 ml in volumetric flasks with distilled water, the absorbance has been measured at 716 nm against blank. Fig. (4) which is show that Beers law is obeyed over the range from 10 to 125 µg\ml, a negative deviation is occurred at increasing volumes.

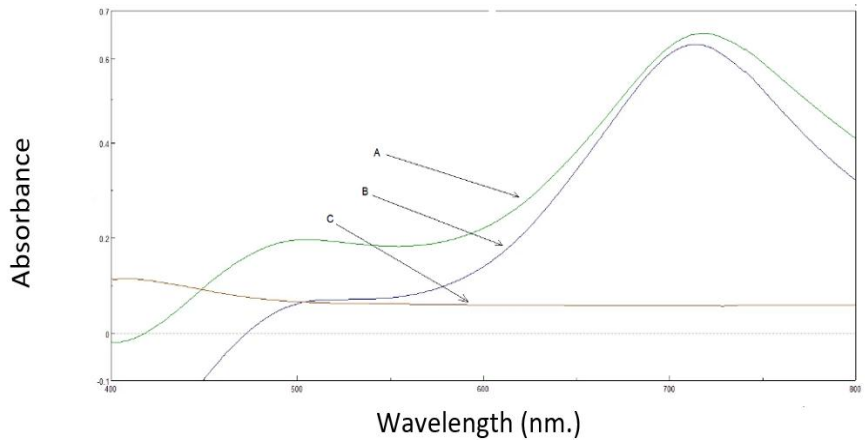


Fig. 3: The absorption spectrum of 50 ppm of A: Sample against distilled water, B: sample against blank, C = blank against distilled water

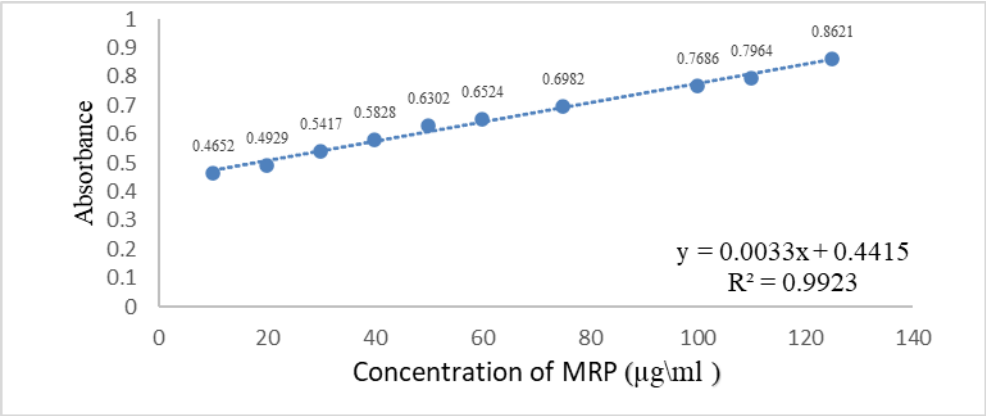


Fig. 4: The calibration graph of MRP determination

Statistical data of calibration curve

Calibration curve show acceptable determination coefficient 0.9923, high sensitivity in which the calculated molar absorptivity is $1.26522x10^4$ L/mole.cm. and Sandell's index is 0.30308 µg/cm^2, the figure shows high intercept in spite of the low detection limit (LOD = 0.0202 µg/ml) and low quantification limit (LOQ = 0.0673 µg/ml), this may refer to low level of reagent concentration ($1x10^{-3}$M). The application range is from 10 to 125 µg\ml.

Accuracy and precision

To check the accuracy of the calibration curve three deferent concentrations within the curve has been replicated five times to calculate the relative error percentage and relative standard deviation percentage. Table (8) shows the average relative error and average of relative standard deviation percentage.

Table 8: Accuracy and precision of the calibration curve

Amount of MRP (µg\ml)	Relative standard deviation %*	Relative error %*
30	0.03162	+0.018
50	0.03464	+0.079
100	0.02958	-0.065

*Average of five determinations

The reaction ratio and stability constant (Ks)of the colored product

Many sample solutions have been prepared by mixing of reaction components according to recommended criteria but using 0.5-3.5 ml of MRP (0.001 M) with 4.5-1.5 ml of PADA (0.001 M) to derive the ratio of the reaction between MRP and PADA by job method and 1.0 ml of MRP (0.001 M) with 0.5-2.5 ml of PADA (0.001M) by Mole-ratio method. Fig. (5) shows that the ratio one to one is the most likely ratio. While (Table 9) exhibits good calculated stability constant of the 1:1 formed complex; the average conditional stability constant is $2.63\ x10^7$ l/ mole.

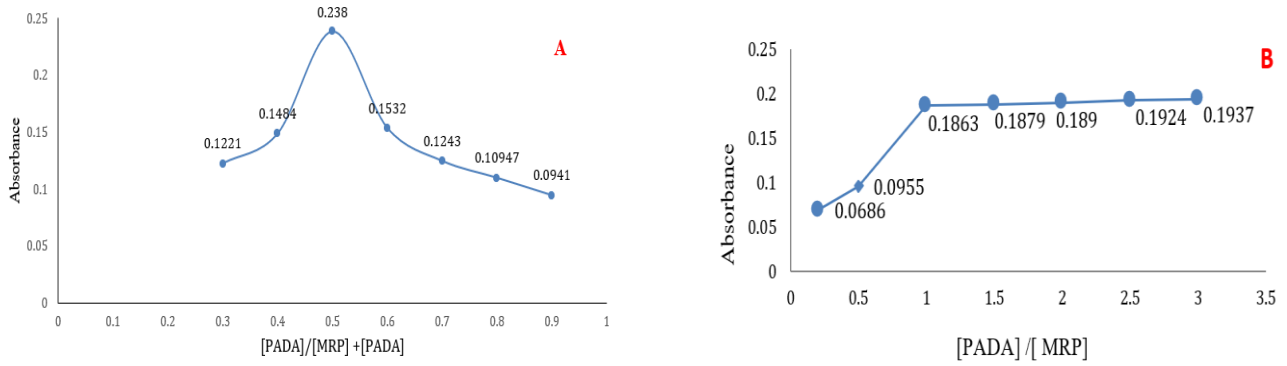


Fig. 5: The reaction ratio -A: Job's method B: Mole ratio method

Table 9: stability constant of the colored complex

Ml of (1x 10^{-3}) MRP	As*	Am**	α***	Ks x10^{-7} (1/ mol)	Mean of Ks (1/ mol)
0.5	0.0803	0.0854	0.05971	0.527	2.63 x10^{7}
1	0.1868	0.1896	0.0147	4.559	
1.5	0.1921	0.1951	0.0153	2.804	

*Absorbance of the same amount of sample and reagent (1 sample:1 reagent)
**Absorbance of a maximum amount of reagent (1 sample:10 reagent)
*** Ratio of dissociation (α= Am-As/As)

Application of the method

The method has been applied for determination of MRP in MRP vials 500mg /manufactured by Fresenius Kabi /Germany and in of MPR vials 1g /manufactured Switzerland by preparation of three different concentrations 20,50, and 100 µg\ml and follow the recommended procedure. Table (10) shows very good applicability of the method in which the mean recovery is 102.966%.

Table 10: Application of the method

MRP	Amount of MRP	Recovery * (%)	Found	Taken	Error
vials 500mg /manufactured by Fresenius Kabi/Germany	20	103.5	0.5102	0.4929	3.5+
	50	103.4	0.6521	0.6302	3.47+
	100	102	0.7841	0.7686	2.01+
vials 1g /manufactured Switzerland	20	99.6	0.4910	0.4929	-0.38
	50	99.9	0.6299	0.6302	-0.047
	100	99.6	0.7659	0.7686	-0.351

- Average of three determination

Standard addition Method

The content of MRP in dosage forms (vials 500mg /manufactured by Fresenius Kabi/Germany and in vials 1g /manufactured Switzerland) has been determined using the developed method by the addition of fixed amount of dosage form to two series of 10 ml calibrated flasks (the first contain 0.4 ml of 500 µg.ml^{-1} , and the second one contain 0.6 ml of 500 µg.ml^{-1}), 0 to 1.0 ml of MRP standard solution (500 µg.ml^{-1}) was added to optimum amount of oxidant ,followed by the selected amount of the acid and completed within the reaction conditions The absorbance was measured at 716 nm. The results in Fig. (6) (A, B, C, and D) and in (Table 11) indicated that the proposed

method gave satisfactory results, there is no any interferences effect caused by other excipients in the dosage form.

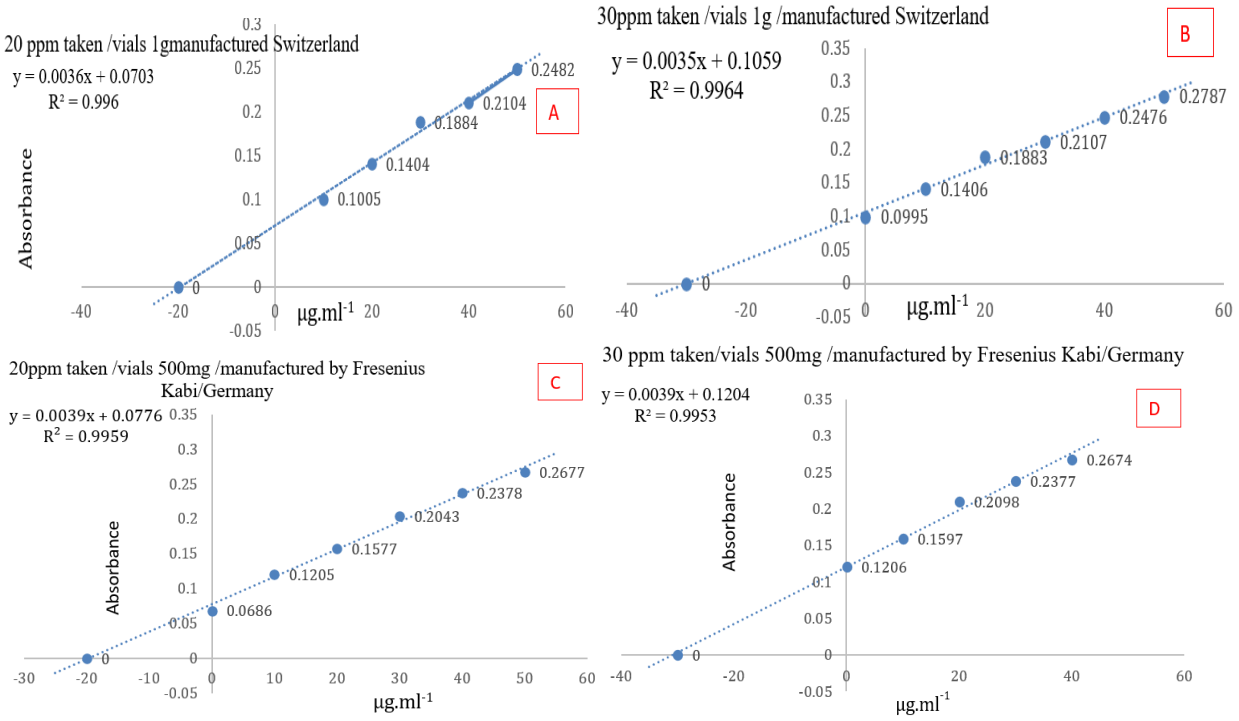


Fig. 6: Standard addition

Table 11: The results of standard addition method

Dosage forms	Amount Present µg.ml^{-1} Drug	Amount Fount µg.ml^{-1} Drug	Recovery%
vials 1g /manufactured Switzerland	20 30	19.52 30.257	97.638 100.857
vials 500mg /manufactured by Fresenius Kabi/Germany	20 30	19.897 30.87	99.487 102.905

Table (11) prove that there is no any interference caused by the presence of excipients in the dosage forms of meropenem, in which, the recovery percentage of the drug is between 97.639 to 102.905.

The comparison of the suggested method with the literature's method

The comparison of the suggested method with the literature's method show that the suggested method uses the safer reagent, easier procedure, with wide-range of linearity. Table (12) list the results.

Table 12: The comparison of the suggested method with the literature's method

Analytical parameters	Present method	Literature method (Singh and Maheshwari, 2013)	Literature method (Khalil and Ibrahim, 2020)	Literature method (Nakkella *et al.*, 2020)
Type of reaction	Oxidation coupling	Oxidation - Reduction	Charge- Transfer	Colored chromogen
Reagent used	p-amino di phenyl amine	Hexacyano ferrate (III)	2,3dichloro 5,6dicyano 1,4benzoquinone (DDQ)	Brucine
Maximum wavelength, nm	716	720	345	520
Molar absorptivity, l. mol.$^{-1}$. cm.$^{-1}$	0.126522 x10^4	3.355 x10^4	2.3889 x10^4	6.1 x10^5
Linearity, µg.ml^{-1}	10- 125	0.5- 6	0.6-12.5	0.02-0.12
RSD%	0.0319	2.15	3.32	0.0480
RE%	0.0106	…….	0.60 – 0.97	…….
LOD	0.0202	1.73	……..	0.00667
LOQ	0.0673	5.28	……..	0.0998
Application	Injection powder	Injection powder	Injection powder	Injection powder

CONCLUSION

A simple, and sensitive spectrophotometric determination of meropenem (MRP) has been carried out by oxidation with periodate in acidic medium, followed by coupling with p-aminobiphenyl amine reagent to form highly colored contrast blue-greenish complex against peal yellow blank. The suggested procedure cover expanded range of meropenem concentration from 10 to 125 with low limit of detection and determination 0.0202, and 0.0673 ppm respectively, the method has been applied for estimation of MRP in 500 mg and 1g dosage forms (vials) with high accuracy (error % 0.0106) and good precision (RSD % ±0.0319).

ACKNOWLEDGMENT

The authors are grateful to the University of Mosul and to the College of Science for providing facilities to carry out this work.

REFERENCES

Agudelo, E.; Santiago, A.; Cardona, G.; Alonso, S. (2020). Advanced oxidation technology (Ozone-catalyzed by powder activated carbon -portland cement) for the degradation of the meropenem antibiotic advanced oxidation technology (Ozone-catalyzed by powder activated carbon - portland cement) for the degradation of the meropenem antibiotic. *Ozone: Sci. and Engineer.*, **43.** 10. https://doi.org/10.1080/01919512.2020.1796582 .

Altamirano Briones, A.; Cóndor Guevara, I.; Mena, D.; Espinoza, I.; Sandoval-Pauker, C.; Ramos Guerrero, L.; Vargas Jentzsch, P.; Muñoz Bisesti, F. (2020). Degradation of meropenem by heterogeneous photocatalysis using TiO2/ fiberglass substrates. *Catalysts*, **10**(3), 344. https://doi.org/10.3390/catal10030344

Bhowmick, T.; Weinstein, M.P. (2020). Microbiology of meropenem-vaborbactam: a novel carbapenem beta-lactamase inhibitor combination for carbapenem-resistant Enterobacter ales infections. *Infectious Diseases and Therapy*, 1-11. https://doi.org/10.1007/s40121-020-00350-1

Cielecka-Piontek, J.; Paczkowska, M.; Lewandowska, K. (2013). Solid-state stability study of meropenem– solutions based on spectrophotometric analysis. *Chem. Centr. J.*, **7,** 98. https://doi.org/10.1186/1752-153X-7-98

Fayed, A.S.; Youssif, R.M.; Salama, N.N. (2019). Two-wavelength manipulation stability-indicating spectrophotometric methods for determination of meropenem and ertapenem: greenness consolidation and pharmaceutical product application. *Chem. Pap.*, **73,** 2723–2736. https://doi.org/10.1007/s11696-019-00824-8

Fish, D.N. (2006). Meropenem in the treatment of complicated skin and soft tissue infections. *Therap. and Clin. Risk Manag.*, **2**(4), 401-415. https://doi.org/10.2147%2Ftcrm.2006.2.4.401

Jamieson, C.; Allwood, M.C.; Stonkute, D. (2020). Investigation of Meropenem stability after reconstitution: the influence of buffering and challenges to meet the NHS Yellow Cover Document compliance for continuous infusions in an outpatient setting. *Europ. J. Hospital Pharm.*, **27,** e53-e57. doi:10.1136/ejhpharm-2018-001699

Kammoun, A.K.; Khedr, A.; Khayyat, A.N.; Hegazy, M.A. (2020). Ultra-performance liquid chromatography-tandem mass spectrometric method for quantitation of the recently Food and Drug Administration approved combination of vaborbactam and Meropenem in human plasma. *Royal Soc. Open Sci.*, **7**(7), 200635. doi: 10.1098/rsos.200635. eCollection 2020 Jul.

Khalil, N.; Ibrahim, W. (2020). Determination of meropenem by spectrophotometric-application to pharmaceutical preparations. *Tikrit J. Pure Sci.*, **25**(1), 68-74. doi:10.25130/j. v25i1.938.

Ku, L.C.; Boggess, K.A.; Cohen M. (2015). Bacterial meningitis in infants. *Clinics in Perinatol.*, **42**(1), 29–viii. https://doi.org/10.1016/j.clp.2014.10.004

Lamya, A.S. (2013). Spectrophotometric and high-performance liquid chromatographic methods for the determination of dapsone in a pharmaceutical preparation *Raf. J. Sci.*, **24**(1), 128-145. 495bd876df625b48

Mendez, A.; Chagastelles, P.; Palma, E.; Nardi, N.; Schapoval, E. (2008). Thermal and alkaline stability of meropenem: degradation products and cytotoxicity. *Internat. J. Pharmac.*, **350**(1-2), 95–102. https://doi.org/10.1016/j.ijpharm.2007.08.023.

Meronem, IV 1G [Internet]. Drugs.com. [cited 2021, Jan. 27]. Available from: https://www.drugs.com/uk/meronem-iv-1g-leaflet.html.

Milla, P.; Ferrari, F.; Muntoni, E.; Sartori, M.; Ronco, C.; Arpicco, S. (2020). Validation of a simple and economic HPLC-UV method for the simultaneous determination of vancomycin, meropenem, piperacillin and tazobactam in plasma samples. *J. Chromatogr.*, **B, 1148**, 122151. 2020; 1148, 122151. doi: 10.1016/j.jchromb.2020.122151

Nakkella, D.; Babu, K.; Raghu; Murthy, P. (2020). Spectrophotometric determination of meropenem in bulk and injection formulations by brucine. *Internat. J. for Innovat. Engineer. Manag. Research*, **9** (3), 89-95. https://ssrn.com/abstract=3561353

Negi, V.; Chander, V.; Singh, R.; Sharma, B.; Singh, P.; Upadhaya, K. (2017). Method development and validation of meropenem in pharmaceutical dosage form by RP-HPLC. *Indian J. Chem. Technol.*, **24**, 441-446.

Qassim, A. (2015). Spectrophotometric method for the estimation of meropenem in pure and in market formulation meronem. *Chem. and Mater. Research*, **7** (4), 59-66.

Roth, T.; Fiedler, S.; Mihai, S.; Parsch, H. (2017). Determination of meropenem levels in human serum by high-performance liquid chromatography with ultraviolet detection. *Biomed. Chromatogr.*, **31**(5), e3880.

Samadi, N.; Narimani, S. (2019). Simple and sensitive photoluminescent detection of meropenem using Cit-capped CdS quantum dots as a fluorescence probe. *Analyt. and Bioanalyt. Chem. Research*, **6**(1), 47-57. 10.22036/ABCR.2018.135958.1213

Singh, D.K.; Maheshwari, G. (2013). Development and validation of spectrophotometric methods for carbapenems in pharmaceutical dosage forms. *Med. Chem. Res.* **22**, 5680–5684.https://doi.org/10.1007/s00044-013-0522-7

Sutherland, C.A.; Nicolau, D.P. (2020). Development of an HPLC method for the determination of meropenem/vaborbactam in biological and aqueous matrixes. *J. Chromatogr. Sci.*, **58**(8), 726-730. doi: 10.1093/chromsci/bmaa041.

The United States Pharmacopeia (USP 30) (2007). United States Pharmacopeial Convection, Inc., Rockville, USA.

Weinre, R.N.; Aung, T.; Medeiros, F.A. (2014). The pathophysiology and treatment of glaucoma: a review. *JAMA*, **311**(18), 1901–1911. https://doi.org/10.1001/jama.2014.3192

WHO, (World Health Organization), (2019). World Health Organization model list of essential medicines: 21st list. **2019** (No. WHO/MVP/EMP/IAU/2019.06).

Xu, Z.; Shi, L.; Wang, Y.; Zhang, J.; Huang, L.; Zhang, W.F.S. (2020). Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *The Lancet Respirat. Med.*, **8**(4), 420-422. doi: 10.1016/S2213-2600(20)30076-X.

Zakaria, A.S. (2011). Spectrophotometric determination of oxymetazoline hydrochloride via oxidative coupling reaction with 4-aminoantipyrine in the presence of potassium periodate. *Raf. J. Sci.*, **22**(7), 97-108. aff66062e8ec4e04

طريقة طيفية جديدة لتقدير الميروبينيم فى المستحضرات الصيدلانية

آن هاشم محمود هناء شكر محمود

قسم الكيمياء/ كلية العلوم/ جامعة الموصل

الملخص

تم تحديد طريقة طيفية جديدة لتقدير الميروبنيم المضاد الحيوي ضمن عائلة الكاربابينيم واسعة الطيف في الصيغ الدوائية وذلك باستخدام كاشف بارا امينو ثنائي فينايل امين وبوجود عامل مؤكسد من بيرايودات البوتاسيوم وحامض الهيدروكلوريك بتركيز 6 مولاري لتكوين معقد ازرق مخضر عند درجة حرارة الغرفة يقاس عند الطول الموجي 716 نانوميتر ويظهر تبعية لقانون بيير ضمن مدى من الخطية تراوح من 10 الى 125مايكروغرام/ مل وكانت قيمة معامل الامتصاص المولاري 1265.22 لتر/ مول. سم وكانت قيم حد الكشف 0.02020 ميكروغرام / مل وحد التقدير الكمي 0.0673 مايكروغرام / مل وقد تم تطبيق الطريقة بنجاح لتقدير الميروبنيم في المستحضرات الصيدلانية بشكل حقن 500ملي غرام وكذلك 1 غرام بدقة عالية (نسبة الخطأ 0.0106% وبتوافقية جيدة (الانحراف القياسي النسبي)(RSD%0.0319) .

الكلمات الدالة: طريقة طيفية، ميروبنيم، بيرايودات، بارا–امينو ثنائي فنيل امين.