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Simple spectrophotometric method for determination of phenylephrine hydrochloride in pure and pharmaceutical forms

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Abstract

A simple, rapid, and accurate spectrophotometric method is suggested for the estimation of phenylephrine -HCl (PHE-H). The method included adding an excess amount (known) of N-bromosuccinamide (NBS) in an acidic medium to oxidize PHE-E, and then the residual NBS was estimated by the bleaching color of methyl orange dye(M.O), the intensity of bleaching dye at the 518 nm was measured. The NBS amount reacts to PHE-H concentration in the actual solution. Beer's law was obeyed in the 2-25 µg /20 ml range with good molar absorptivity of 1.0705×10^5 $l.mol^{-1}.cm^{-1}$ The proposed method was applied successfully to determine PHE-H in its pharmaceutical preparation.

Keywords: phenylephrine–HCl, methyl orange, bleaching color, spectrophotometric determination, N-bromosuccinamide.

Introduction

Phenylephrine hydrochloride (PHE-H),[(R)-1-(3-hydroxyphenyl)2 (methylamino) ethanol hydrochloride], is a white crystalline powder[1]. It is used to expand the pupil, to raise blood pressure, to relieve hemorrhoids, and as a decongestant [2]. Many analytical techniques have been achieved for the quantitative assay of PHE-H, including flow injection analysis [3,4], HPLC [5,6], RP-HPLC [7,8], HPTLC [9], U.V.spectroscopy[10,11], conductivity titration[12]. Various reagents have been reported in the spectrophotometric method for the determination of (PHE-H), such as ninhydrin in sulfuric acid [13], uranyl ion in the pH region 2.50-4.25[14], diazotized 2- amino benzothiazole [15], diazotized metoclopramide hydrochloride [16], Folin Ciocalteu in the presence of 10% sodium carbonate solution[17],2,2`-bipyridyl with Fe(II) [18], ion –pair complexes using alizarine, alizarine yellow G or quinolizidine, alizarine red S [19], coupling with 4-aminoantipyrine then reacts with copper (II)[20], reacting with hematoxylin in alkaline medium to form charge transfer complex [21]. The aim of the investigation reported in this paper is to suggest a suitable method for the estimation of PHE-H in an aqueous medium, either in pure form or in its pharmaceutical preparations.

The method is based on the oxidation of PHE-H in an acidic medium by NBS, then bleaching the color of M.O dye by the unreacted NBS, whose intensity is proportional to the amount of PHE-H.

Experimental

Instruments

The absorbance and spectrum were done using a Jasco UV Spectrophotometer (JascoV-630). Two silica cells were used.The pH was estimated using a HANA pH meter.

Reagents and solutions:

The chemicals used in this investigation are high-purity reagents.

The used solutions:

Standard phenylephrine-HCl, 100 µg.ml^{-1}. This solution was prepared by dissolving 0.01 g of phenylephrine-HCl (SDI-Iraq) in 10 ml ethanol, which was then diluted to 100 ml with D.W. in a volumetric flask.

Working phenylephrine-HCl solution,20µg.ml^{-1}. This solution was attended to with the appropriate dilution of the standard solution.

Methyl orange solution,1.5x10^{-5}M. This solution was attended by dissolving the accurately weighed amount of 0.0130 g of methyl orange(Fluka) in 100 ml D.W.

N-bromosuccinimide,4x10^{-4}M. This solution was prepared by dissolving 0.0071 g of N-bromosuccinimide (Fluka) in 100 ml D.W.

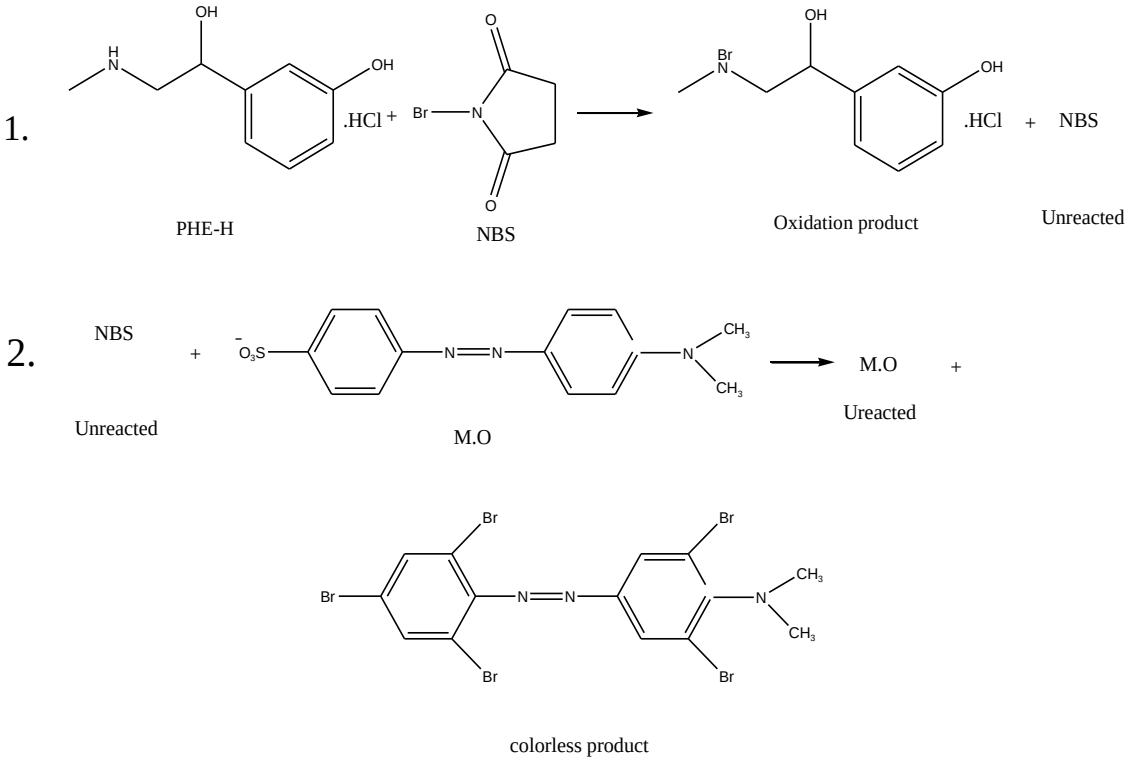
Hydrochloric acid solution,1M. This solution was attended by diluting 8.5 ml of concentrated acid (Fluka)to 100 ml with D.W.

Analytical procedure:

Into a series of 20 ml calibrated volumetric flasks, an increasing volume of PHE-H (20 µg.ml -1) solution was transferred to cover the range of the calibration graph (2 -25µg.20 ml^{-1}). Then 1.0 ml of HCl (1 M) and 2 ml of NBS (0.0004M) were added. The solutions were lifted for 15 min. at room temperature (25˚C), finally adding 1.25 ml of M.O, and after 5 min, the volumetric flasks diluted with distilled water to the mark. The wavelength 518 nm was used in measuring the absorbance.

Results and Discussion:

The method included oxidizing PHE-H by adding an excess of NBS, and then the unreacted NBS was used to bleach the color of M.O (Schem 1). Then, the absorbance of residual M.O was measured at 518 nm, which increased linearly with increasing concentration of PHE-H.



Scheme 1: Reactions of oxidation PHE-H and bleaching the color of M.O.

The effect of various parameters on the oxidation-reduction reaction was studied to select the optimum conditions for estimating PHE-H in pharmaceutical preparations.

Chosen the optimum concentration of the dye :

A preliminary experiment was performed to optimize M.O dye's useful and optimum concentration, which can be determined spectrophotometrically(Fig.1).

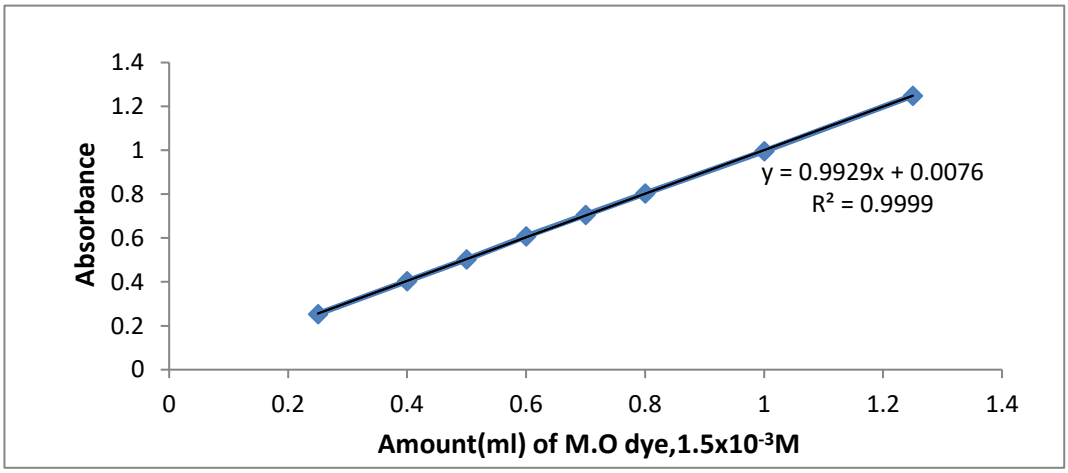


Fig.(1): The optimum amount of methyl orange on absorbance

Figure (1) shows that 1.25 ml of M.O dye was the best volume, it gave high.

intensity and excellent value of determination coefficient(R^2).

The effect of oxidant reagents:

NBS was a useful oxidizing agent; other oxidizing agents such as (NCS, $Ce^{+4}$and KIO_4) have also been tested, but none offered real advantages over NBS. Fig.(2).

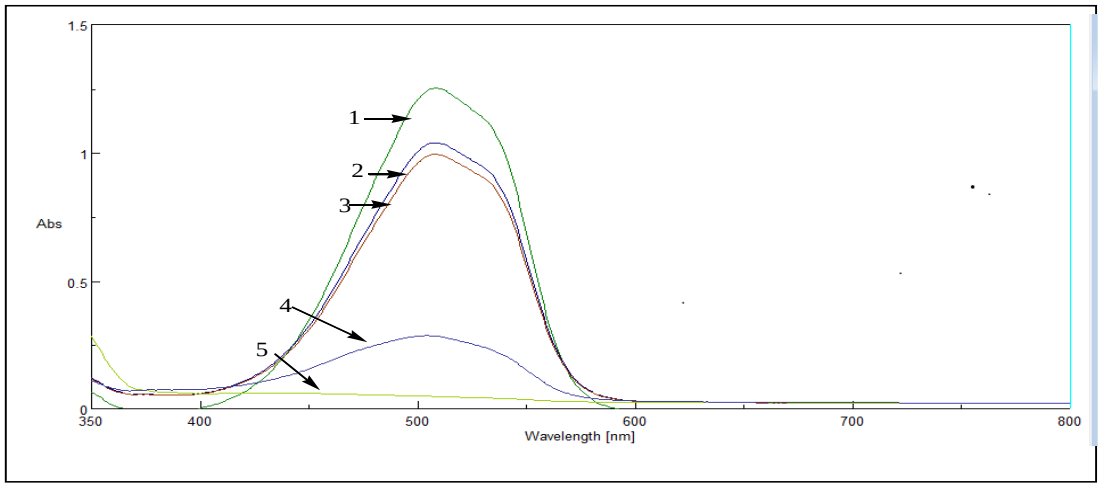


Fig. (2): The effect of oxidant agents on bleaching the dye, 1 is M.O dye,2 is M.O with potassium periodide, 3 is M.O with N-chlorosuccinimide , 4 is M.O with ceric ammonium sulphate ,5 is M.O with NBS.

Effect of oxidant amount:

After choosing NBS as an oxidant agent, the amount was studied by different volumes from 0.5 to 3 ml of 0.0004M of NBS and their effect on the absorbance of M.O color. In this experiment, all our studying without PHE-H.Fig. (3) shows that 2ml of NBS solution was enough to obtain a maximum bleaching of the color of M.O dye; therefore, it was recommended in the subsequent experiments.

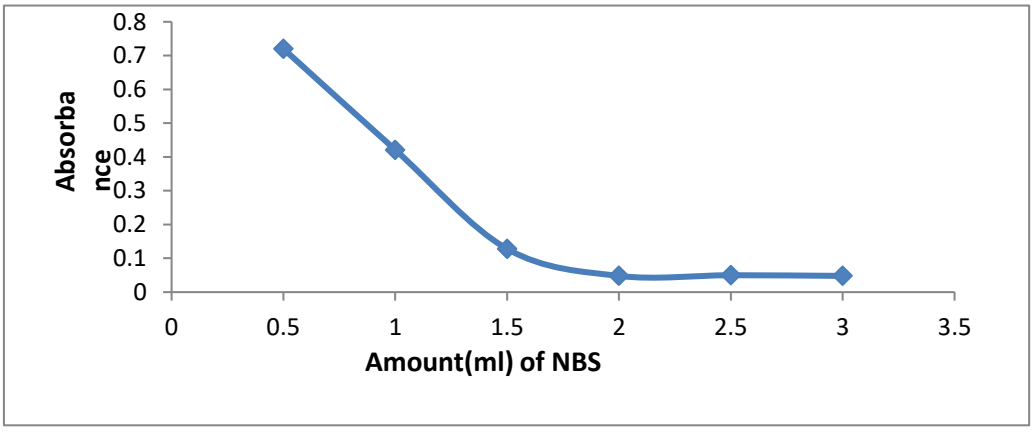


Fig3:The optimum amount of NBS on absorbance

Choice of acids and their amount

The oxidation of PHE-H was done in an acidic medium, so that different types of acids were examined (Table 1

Table 1: Selection of the acid

1M acid (1ml)	Absorbance	pH
H_2SO_4	0.721	3.42
HCl	0.945	3.34
HNO_3	0.697	3.26
CH_3COOH	0.422	3.60

The results shown in Table 1 indicate that HCl gives the highest absorbance with a final solution pH of 3.34. Also, the effect of different volumes of 1M HCl of solution has been investigated. A(1ml) of 1M HCl was selected for using in the next experiments because it gave the highest value of correlation coefficient (0.9994). Table (2).

Table2:Effect of acid amount on absorbance

1M HCl solution(ml)	Absorbance/µg of PHE-H				
	5	10	15	20	R
0.5	0.437	0.621	0.732	0.915	0.9830
1	0.467	0.637	0.780	0.948	0.9994
1.5	0.439	0.651	0.762	0.908	0.9913

The order addition of components

The components of reaction were added in various orders.The optimum order was mention in the general procedure according to high intensity .whether in other order lose in color occured. (Table 3).

Table3:Effect of the order of addition

Order number	Order of addition	Absorbance
I	PHE-H +HCl+NBS+MO	0.975
II	PHE-H+NBS+HCl+MO	0.228
III	PHE-H+NBS+MO+HCl	0.144
IV	PHE-H+HCl+MO+NBS	0.268

The effect of time on oxidation and bleaching the dye

The effect of time on oxidation of PHE-H by NBS and the time needed to optimum bleaching color of M.O were studied (Table4).

Table (4): The effect of time on oxidation and bleaching of the dye

Standing time after adding oxidant, min.	Standing time after adding the dye and before dilution, min							
	5	10	15	20	30	40	50	60
5	0.942	0.949	0.942	0.938	0.940	0.937	0.930	0.932
10	0.968	0.963	0.964	0.965	0.960	0.953	0.951	0.951
15	0.953	0.959	0.950	0.949	0.954	0.948	0.945	0.945

The results in Table (4) show that the standing time of 10 minutes was necessary for the complete oxidation of PHE-H and 5 minutes was necessary for bleaching of the color of M.O dye
. **Stability of dye**

The effect of time on the color of residual amount of M.O after oxidation of PHE-H and bleaching part of M.O dye by NBS was tested under the optimum conditions. The experimental results (Table 7) show that the change in absorbance is in the accepter value for at least 24 hours.

Table 7: stability of M.O

µg of PHE-H	**Absorbance/ min. standing time**								
	5	**10**	**15**	**20**	**30**	**40**	**50**	**60**	**24 hours**
5	0.472	0.472	0.472	0.475	0.473	0.473	0.472	0.472	0.473
10	0.648	0.654	0.653	0.655	0.658	0.654	0.654	0.654	0.653
20	0.970	0.967	0.967	0.966	0.963	0.964	0.965	0.965	0.973

Absorption spectrum

Fig. 4 shows that M.O dye has a maximum absorption at 518 nm, and adding an amount of PHE-H decreases the absorbance value due to the residual NBS bleaching of M.O color.

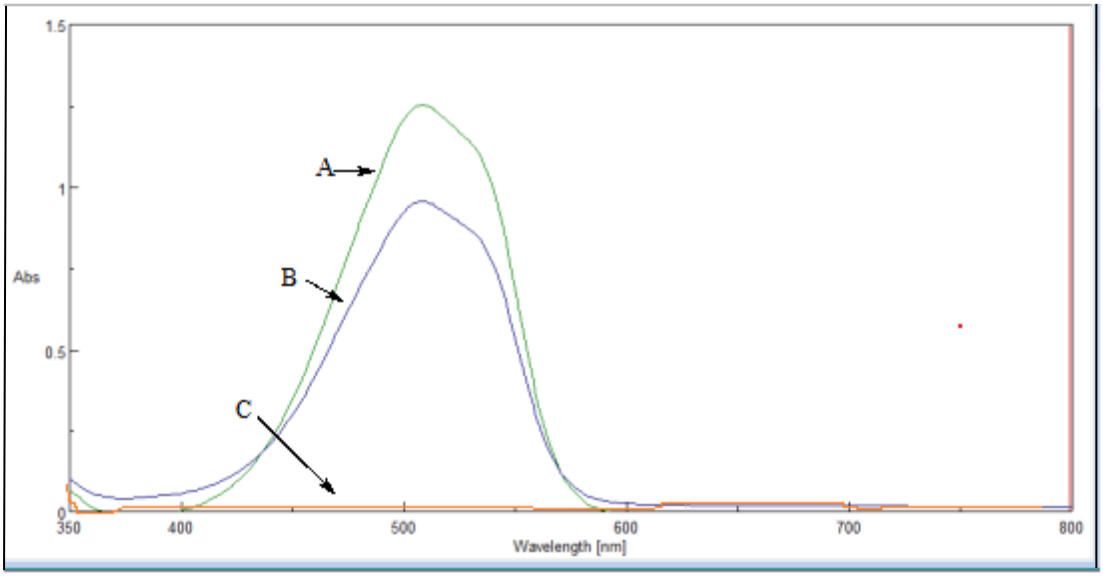


Fig.4: Absorption spectrum of (A) M.O dye,(B) residual M.O dye after oxidation 20µg PHE-H, and (C)blank against distilled water.

Calibration curve:

Following the general procedure, a linear relationship was obtained between the absorbance and PHE-H concentration within the range (2-25)µg.20ml^{-1} (0.1-1.25) µg.ml^{-1} ,with good value of determination coefficient (R2)Figure (5) .

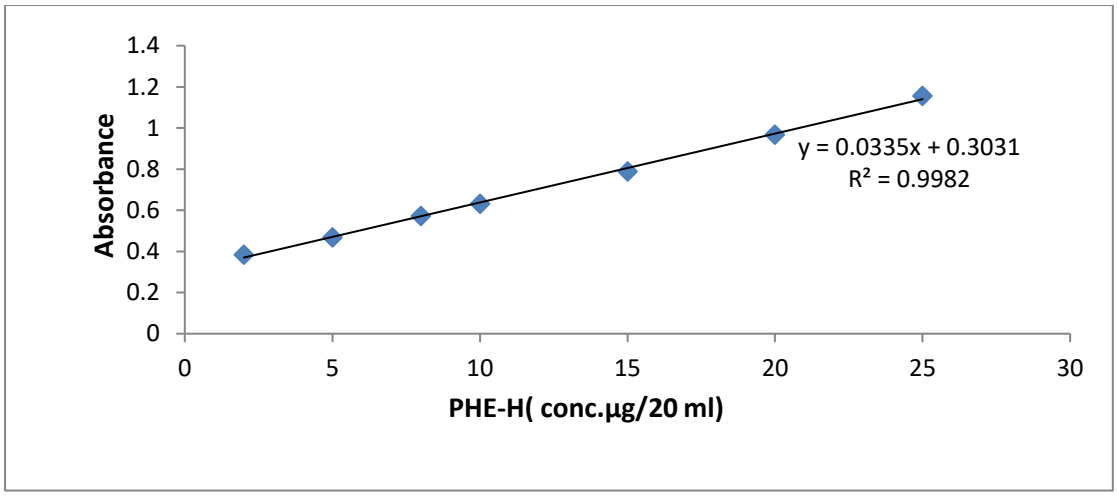


Fig. 5: The calibration graph of PHE-H is estimated according to the general procedure.

Application of the method

The suggested procedure has been applied to determine PHE-H in two types of nasal drops. The results in Table (9) indicate accuracy and good precision.

Table 9: Application of method

Drug	Amount taken µg/20ml	Recovery, %	RSD*,%
Nasophrine Nasal Drop (0.25%) SDI – Iraq	10	99.52	±0.89
	20	99.69	±0.41
Nasophrine Nasal Drop (1%w/v) Safa – Iraq	10	99.74	±0.39
	20	100.02	±0.41

***Average of four determinations.**

Comparison of method

Table (10) compares some of the analytical variables obtained from the suggested method with those of other literature spectrophotometric methods.

Table 10: Comparison of the method

Analytical parameters	Present method	Literature method [18]	Literature method [22]
λ_{max} (nm)	518	523	425
Beer's law range(ppm)	0.1-1.25	0.1-3.2	2-24
Molar absorptivity $l.mol^{-1}.cm^{-1}$	107050	71295	3442
Stability of the color	24 h	48 h	180 min
Medium of method	Acidic	Acidic	Alkaline
Reagent	Methyl orange	2,2-bipyridyl	Diazotized sulfacetamide sodium
Type of reaction	Oxidation –reduction	Oxidation-reduction	Diazotisation
Application of the method	Pharmaceutical preparation	Pharmaceutical preparation	Pharmaceutical preparation

The results indicate that the suggested method is sensitive and can be applied successfully to determine phenylephrine -HCl in pharmaceutical preparation.

Conclusion

The suggested method described a simple, sensitive, and accurate indirect spectrophotometric method for determining PHE-H using NBS as an oxidant agent. The unreacted NBS bleached the M.O dye.The method gave satisfactory values when applied to determining PHE-H in pharmaceutical formulations (nasal drops).

References

1.A. C. Moffat ,J.V. Jackson, M.S.Moss,Clarke's, Isolation and Identificattion of Drugs, The pharmaceutical press,London, (1986),893.

2.https://en.m.wikipedia.org/wiki/phenylephrine

3. JR. Rocha, CX. Galhardo, MA. Natividade, JC. Masini, Spectrophotometric determination of phenylephrine hydrochloride in pharmaceuticals by flow injection analysis exploiting the reaction with potassium ferricyanide and 4-aminoantipyrine. *National Institutes of Health*, (2002), 85(4):875-8.

4. M.Q. Al-Abachi and S.Subhi, Flow injection-spectrophotometric determination of phenylephrine hydrochloride and amoxicillin trihydrate in pharmaceutical preparations, *Journal of Al-Nahrain University*, (2013),16 (1):24-24.

5. H.çenyuva and T.Özden,Simultaneous high-performance liquid chromatographic determination of paracetamol, phenylephrine HCl and chlorpheniramine maleate in pharmaceutical dosage forms. *Journal of Chromatographic Science*,(2002), 40: 97-100.

6.N.H.AL-Shaalan,Simultaneous determination of chlorophineramine maleate,dextromethorphan HBR and phenylephrin HCl in codilar syrup using high performance liquid chromatography,*Journal. of Pharmaceutical and ScienceInnovation*,(2012),1(1):29-32.

7. R. Bandelwar, A. Nikam, S. Sawant ,Analytical method development and validation of phenylephrine hydrochloride,chlorpheniramine maleate, paracetamol and caffeine in bulk drug and tablet dosage form by RP-HPLC,*Indo American Journal of Pharmaceutical Research*,(2013),3(6):4330-4338.

8. K.Paidipala, SK.Kamarapu, Method development and validation of RP-HPLC method for simultaneous estimation of dextromethorphan hydrobromide, phenylephrine hydrochloride and triprolidine hydrochloride in bulk and combined tablets dosage forms, *Research Article Pharmceutical Science*, (2013), 3(3):172-179.

9.W.Janwitayanuchit, P.Lukkanatinaporn, Development of HPTLC method for determination of brompheniramine maleate and phenylephrine hydrochloride tablets, *International J. of Pharmacy and Pharmaceutical Sciences*, (2014), 6(6):106-109.

10. S. J. Wadher, T. M. Kalyankar, P. P. Panchal, Development and validation of simultaneous estimation of chlorpheniramine maleate and phenylephrine hydrochloride in bulk and capsule

dosage form by Ultra-Violet Spectrophotometry, *International Journal of ChemicalTechnical Research*, (2013), 5(5):2410-2419.

11. T. M Kalyankar, S. J Wadher and M. F Sayed,Force degrrded UV-spectrophotometer method for simultaneous determination of phenylephrine HCl and bromhexine HCl in combined tablet dosage form,*Research Pharmaceutica*, (2017),1(1):6-10.

12. S. H. Hasan ,N. S. Othman and K. M. Surchi, Determination of phenylephrine-HCl using conductometric titration method, *Current Analytical Chemistry*, (2016),12:1-5.

13.I.muszalska,M.zaiac,G.wrobelandM.nogowska,UV/VISspectrophotometric methods for determination of caffeine and phenylephrine hydrochloride in complex pharmaceutical prepations validation of the methods, *Acia Poloniae Pharmaceutica-Drug Research*, (2000),57(4):247-252.

14.L.Pavun,D.Malesev and D.Veselinovic, Sepectrophotometric investigation of the uranyl-phenylephrine system,*J.Serb.Chemical Society* , (2007),72(8-9):799-807.

15. N. S. Othman, N. Th. Abdul Fatah,Spectrophotometric determination of phenylephrine hydrochloride by coupling with diazotized 2-aminobenzothiazole,*Journal of Rafidin Science*, (2009), 20(4):69-81.

16. M. Q. Al-Abachi ,S.S. Abed, Spectrophotometric determination of phenylephrine hydrochloride and salbutamol sulphate drugs in pharmaceutical preparations using diazotized metoclopramide hydrochloride, *Baghdad Science Journal*, (2015),12(1):167-177.

17. U. P. Paresh, B.P. Harsh, Development and validation of visible spectrophotometric method for estimation of phenylephrine hydrochloride in pharmaceutical dosage form,*International Journal of Pharmaceutics and Drug Analysis*, (2014), 2(2):131-137.

18. N. S. Othman , N. Th. Abdul Fatah, Indirect spectrophotometric determination of phenylephrine hydrochloride in pharmaceutical preparations, *Tikrit Journal of Pure Science*, (2011) ,16 (2):74-81.

19. S.A Shama, Spectrophotometric determination of phenylephrine HCl and orphenadrine citrate in pure and in dosage forms, *J. of Pharmaceutical and Biomedical Analysis*, (2002),30(4):1385-1392.

20. Th. N. Al-Sabha, Spectrophotometric assay of phenylephrine hydrochloride using 4-aminoantipyrine and copper (II), *Pakistan Journal of Analytical Environment Chemistry*, (2010), 11(1):01–07.

21. I. S. Ahmed, A. S. Amin, Spectrophotometric microdetermination of phenylephrine hydrochloride in pure and in pharmaceutical formulations using haematoxylin, *Journal of Molecular Liquids* , (2007) ,130: 84–87.

22.W.A.Al-Uzri,Determination of phenylephrine hydrochloride in pharmaceutical preparations using spectrophotometric method,Asian Journal of Pharmaceutical and Clinical Research,(2019),12(5):1-5.

طريقة طيفية بسيطة لتقديرالفنيل افرين هيدروكلوريد بشكله النقي وفي مستحضراته الصيدلانية

صفاء عبدالعليم زكريا

قسم الكيمياء/ كلية العلوم/ جامعة الموصل

الخلاصة:

تم استحداث طريقة طيفية بسيطة وسريعة لتقدير كميات متناهية في الصغر من مركب الفنيل افرين هيدروكلوريد. تضمنت الطريقة اضافة زيادة معلومة من ن-برومو سكسيناميد في وسط حامضي لاكسدة الفنيل افرين هيدروكلوريد ثم تقدير المتبقي منه من خلال قصر لون صبغة المثيل البرتقالية . تم قياس الامتصاصية للصبغة المتبقية عند 518 نانوميتر وكانت حدود قانون بير في مدى التركيز 2-25 مايكروغرام /20 مل في حين كانت قيمة الامتصاصية المولارية1.0705× 10^5 لتر .مول$^{-1}$.سم$^{-1}$.طبقت الطريقة بنجاح في تقدير الفنيل افرين في مستحضره الصيدلاني.

الكلمات الدالة: فينل افرين هيدروكلوريد ,مثيل برتقالي , قصر اللون , طريقة طيفية , ن –برومو سكسيناميد