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Spectrophotometric determination of Domperidone and Phenobarbital in pure forms and in the pharmaceutical preparations by NQS reagent

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ABSTRACT

"A sensitive, rapid and economical" spectrophotometric methods for estimation of two drugs; Domperidone (Dom) and Phenobarbital (Phe), by "Sodium 1,2-naphthoquine- 4-sulfonate (NQS)" as reagent in an alkaline medium. These methods are summarized on the forming of "color products" among these drugs and the chromogenic reagent (NQS). Orange colored product formed at (pH 13) and $\lambda_{max.}$ 460 nm for (Dom), and orange colored product at (pH 13.5) and $\lambda_{max.}$ 460 nm for (Phe). Beer's Law is obeyed in a concentrations range of (20-80 µg/ml), (10-90 µg/ml), with molar absorptivity (6.644×10^3 L/mol.cm), (3.019×10^3 L/mol.cm), and correlation coefficient 0.9999, 0.9991, respectively, The detection limit were (0.463µg/ml, 2.022µg/ml), respectively. The suggested methods were prosperity implement to the estimation of "these drugs" in pure forms and in their pharmaceutical formulations as (Tablets).

Introduction

Domperidone (Fig.1(a)), "It is used to treat symptoms of stomach disorders. It may also be used to prevent nausea and vomiting caused by certain medications. Due to safety concerns, this medication is not to be used by breast-feeding women to increase production of breast milk" [1]. Molar mass is 425.911 gm/mol, M.P. = 242.5 °C, chemically known is 5-chloro-1-{1-[3-(2-oxo-2,3-dihydro-1H-1,3-benzodiazol-1-yl)propyl]piperidin-4-yl}-2,3-dihydro-1H-1,3-benzodiazol-2-one [2]. Several methods have been proposed for determination of this drug, such as HPLC [3,4], TLC [5], HPTLC [6], Voltammetry [7,8], UV spectrophotometry [9,10], UV-Vis. Spectrophotometry [11,12].

Phenobarbital (Fig.1(b)) is used to treat trouble sleeping, anxiety, and drug withdrawal and to help with surgery [13], It is used in the treatment of all types of seizures except absence seizures [14,15], It is no less effective at seizure control than phenytoin, however phenobarbital is not as well tolerated [16], Molar mass is 232.235 gm/mol, M.P. = 174 °C, chemically known is 5-ethyl-5-phenyl-1,3-diazinane-2,4,6-trione [2].

Several methods have been proposed for determination of this drug, such as HPLC [17-19], TLC [20], Voltammetry [21].

"Sodium 1, 2 – naphthoquinone – 4 - sulphonate (NQS) (Fig.1(c)), has been used as a chromogenic reagent for the spectrophotometric determination of many pharmaceutical amines. It is a popular spectrophotometric reagent due to its efficient reactivity with both primary and secondary amines, and high reaction rate" [22-24].

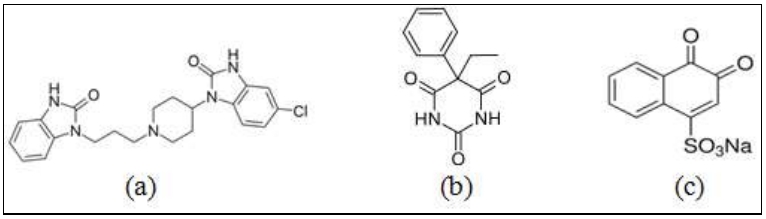


Fig. (1): Chemical Structures of (a) Domperidone (b) Phenobarbital (c) NQS reagent

Aim of the study

The research aims at finding a "simple, fast and economical" spectral methods for determination of Domperidone and Phenobarbital, by "chromogenic reagent NQS" in alkaline medium, As well as, the stoichiometry was studied by mole ratio and job method, and the success of the proposed methods for determination the two drugs in pharmaceutical preparations (as tablets).

Experimental

Apparatus

T90 UV-VIS spectrophotometer "double beam from PG Instruments Ltd, with

1 cm quartz cells", UV-VIS spectrophotometer "single beam from Genesys UV 10, pH meter InoLab pH/INO735 from Jenway 3310, Balance Kern 770GS/GJ from Sartorius BL210S, Oven from Memmert, Schutzart DIN 40050-IP20.

Materials

Domperidone %99, Phenobarbital %99 from (SDI Samarra-Iraq), "Sodium 1,2-naphthoquinone-4-sulphonate (NQS)" %97 from BDH, Sodium hydroxide (NaOH) %98 from (GCC), Ethanol %99.9 from (Scharlau).

Solutions

Domperidone Stock solution (1000 µg/ml): An exactly (0.1000 gm) of (Dom) "standard" were dissolved in (100 ml) ethanol.

Phenobarbital Stock solution (1000 µg/ml): An exactly (0.1000 gm) of (Phe) "standard" was dissolved in (100 ml) ethanol.

NQS (1×10^{-2}M): was prepared by dissolving (0.2602 gm) of NQS in (100 ml) distilled water.

NaOH (1M): was prepared by dissolving (4 gm) of NaOH in (100 ml) distilled water.

Procedures

Domperidone: A 3.0 ml from 500 µg/mL of (Dom) was carried into 25ml "volumetric flask", 5.0 ml from10^{-2} M "NQS" was added and followed by 1.0 ml from NaOH 1M. After (10 min.), the volume was supplemented to volume by distilled water, and was measured at 460 nm against "reagent blank".

Phenobarbital: A 3.0 ml from 500 µg/mL of (Phe) was carried into 25ml "volumetric flask", 5.0 ml from 10^{-2} M "NQS" was added and followed by 1.0 ml from NaOH 1M. After (10 min.), the volume was supplemented to volume with distilled water, and was measured at 460 nm against "reagent blank".

Procedures for "stoichiometric ratio"

The reactions of equivalence between these drugs and the reagent have been estimated by carrying out "molar ratio" and "continuous variation methods". In these methods, "equimolar" solutions of (Dom), (Phe) and "NQS" (5×10^{-3}M), were used. Varying aliquots of "NQS" were added to constant aliquots of drugs solutions, final volumes (25ml) and the absorbance were measured at 460 nm for two color products opposite the "reagent blank treated similarly". While in the latter method, a series of Dom-NQS, and Phe-NQS solutions were kept at (5ml) (0:5, 0.5:4.5, 1:4, 1.5:3.5, 2:3, …… 5:0).

Applications of the proposed methods

"Ten tablets" for each of drugs (Dom, Phe) were weighed (1.243gm, 0.679gm) and averages weights (0.1243gm, 0.0679gm) were computed. These tablets were grinded into exact powder. An precisely weighed amount of powders were transferred into a beaker and they were shaken with 50 ml of ethanol and filtered. The filtrates and the washings were collected in a 100ml "volumetric flask". This filtrate and the washing were diluted up to the mark with solvent to obtain final concentration as 100 µg/ml. The suggested methods were successfully implemented for the determination of (Dom), and (Phe) in various commercial tablets, the results are shown in Table (5).

Results and Discussion

Absorption spectra of "Dom-NQS", and "Phe-NQS" systems against reagent blank in an alkaline medium at room temperature (25°C) producing an "orange colored products" for Dom-NQS and Phe-NQS where absorbs maximally at 460 nm for two drugs, (Fig. 2, 3), and reagent blank against water (Fig. 4).

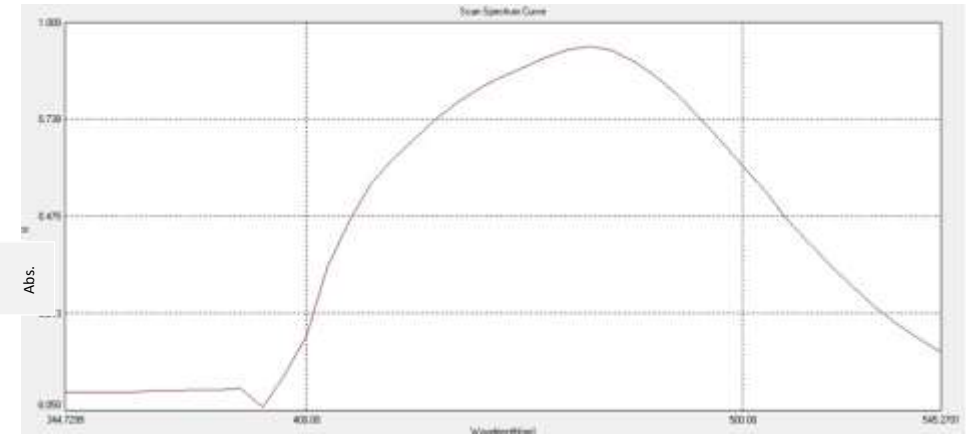


Fig. (2): Absorption spectrum of Dom-NQS system against blank

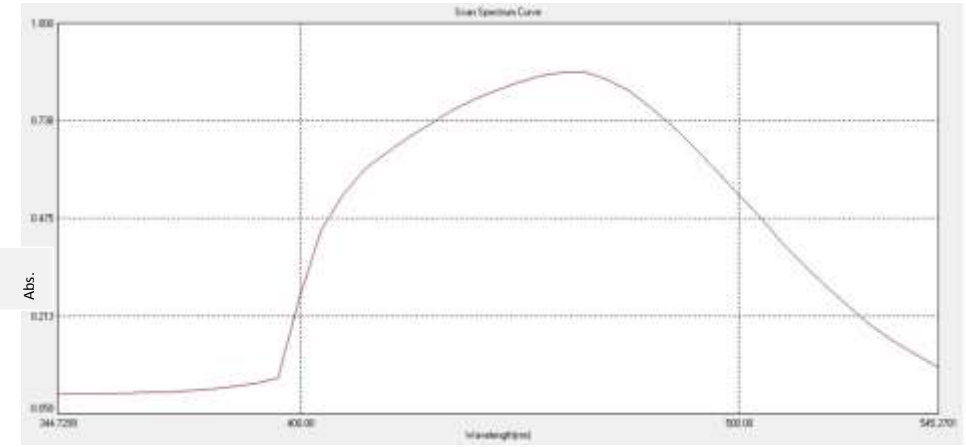


Fig. (3): Absorption spectrum of Phe-NQS system against blank

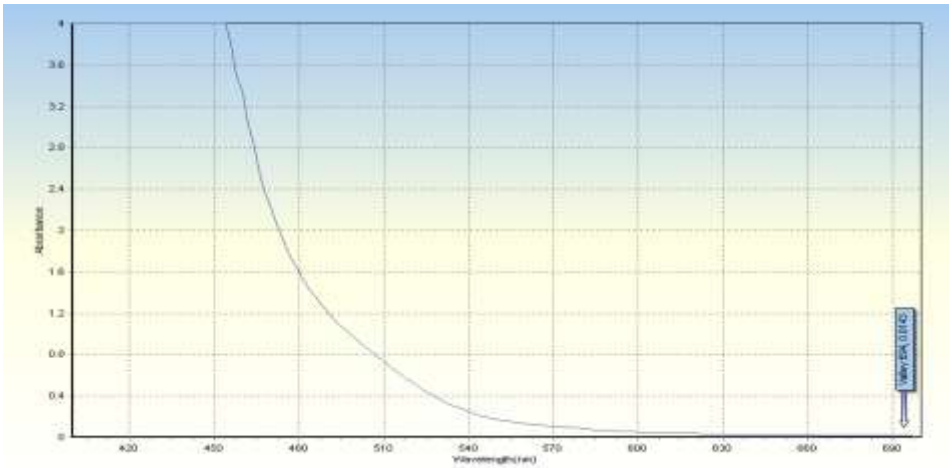


Fig. (4): Absorption spectrum of reagent blank against distilled water

Optimum conditions: For establish optimum conditions, required to creation of "colored product with maximum stability and sensitivity", the influence of volumes of "NQS", addition of "alkaline intermediate", "reaction time" and the "stability of colored products" were studied at "room temperature (25^0C)".

Effect of reagent concentration: The effect of reagent concentration on the reactions were studied at "room temperature". The reactions of (Dom), (Phe) with reagent were to rely on the concentrations of "NQS". So, it's concentrations were studied by different volumes from (1.0 to 10 ml) of (0.01 M) NQS, while the (Dom), and (Phe) concentrations were maintained constant at 60 µg/ml (As a final concentration from 500 µg/mL as a primary concentration) for each. The color intensity was found to increase with addition of NQS up to a particular concentration and then either decrease or remain steady, the highest absorption intensity were attained when the volumes of NQS were 5ml, of 0.01 M NQS, Therefore, these concentrations were used to prepare calibration curves, as shown in Fig. (5, 6).

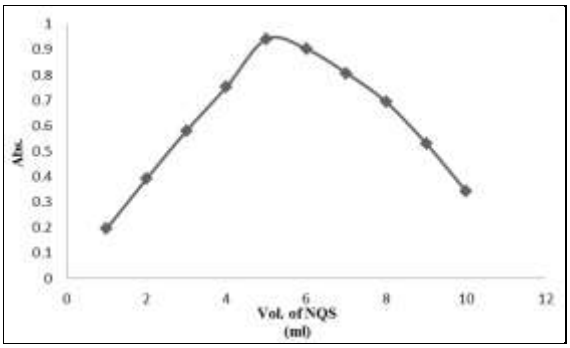


Fig.(5): Effect of conc. of NQS (0.01M) on Dom-NQS complex

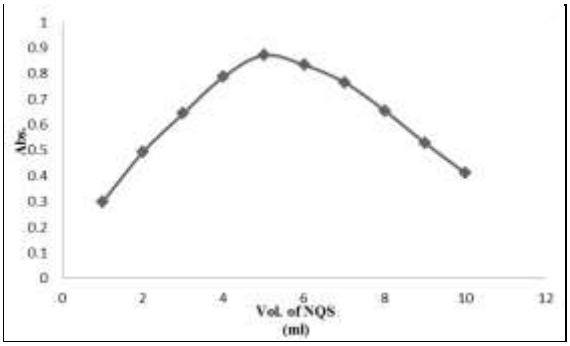


Fig.(6): Effect of conc. of NQS (0.01M) on Phe-NQS complex

Effect of pH: An alkaline medium was required, because these drugs does not reacts with "NQS" in acidic media, the results appeared that the absorbances at pH < 8 were close to 0, in the acidity intermediate, these drugs have difficulty to reacts with "NQS". Different concentrations from NaOH were tested, best results were at higher concentrations of NaOH (1M), with pH 13, 13.5 for (Dom), and (Phe) color products, respectively, As illustrated in Fig. (7, 8).

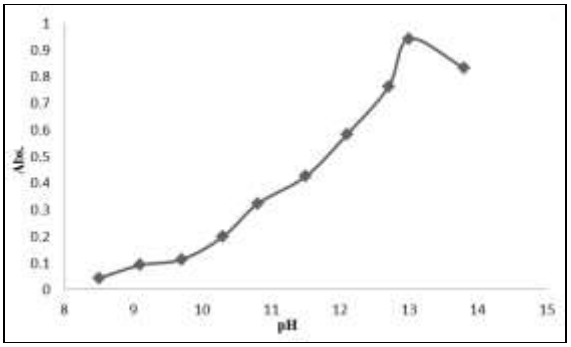


Fig. (7): Effect of pH on Dom-NQS color prouduct

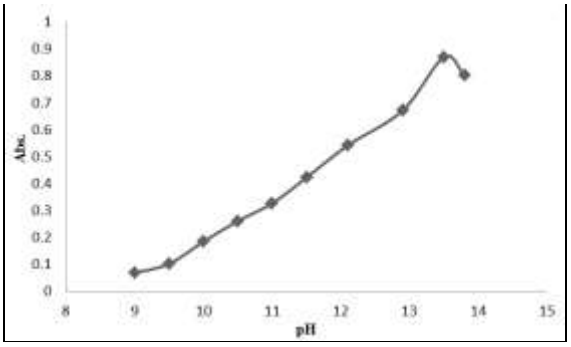


Fig. (8): Effect of pH on phe-NQS color prouduct

Effect of Time: Under the "optimum conditions", the effect of reaction time of (Dom), and (Phe) with reagent in "alkaline medium" were studied, and the products remained stable to 90 min. for (Dom), and to 120 min. for (Phe), As illustrated in Table (1).

Table (1): Effect of Time on color products constant

Time (min.)	Abs. of (Dom) color product	Abs. of (Phe) color product
5	0.939	0.869
10	0.932	0.869
20	0.941	0.870
30	0.941	0.869
40	0.940	0.869
50	0.939	0.868
60	0.939	0.870
70	0.940	0.871
80	0.941	0.871
90	0.938	0.869
100	0.927	0.868
120	0.901	0.868
130	0.892	0.856
140	0.889	0.849

Effect of Interferences

The effect of interferences on the composition of the product between DOM with reagent was studied, and not observed any effect, as shown in the Table (2, 3).

Table (2): Effect of interferences on (Dom) product

Interference	Added con. µg/ml	% RE	Added con. µg/ml	% RE
Lactose	80	1.913	120	- 1.72
Manitol	80	- 0.425	120	- 2.45
Sodium benzoate	80	- 2.125	120	-1.88

Table (3): Effect of interferences on (Phe) product

Interference	Added con. µg/ml	% RE	Added con. µg/ml	% RE
Lactose	20	- 1.494	40	- 2.12
Manitol	20	1.379	40	1.079
Sodium benzoate	20	- 0.805	40	0.982

Equivalent of the reactions

Under the "optimum conditions", (temperature, cons. of NQS, pH, time) "the stoichiometry" of the reactions between (Dom), and (Phe) with reagent were studied by mole–ratio and continuous variation methods. The equivalence between reagent and these drugs were 2:1 (Figs. 9, 10, 11, 12).

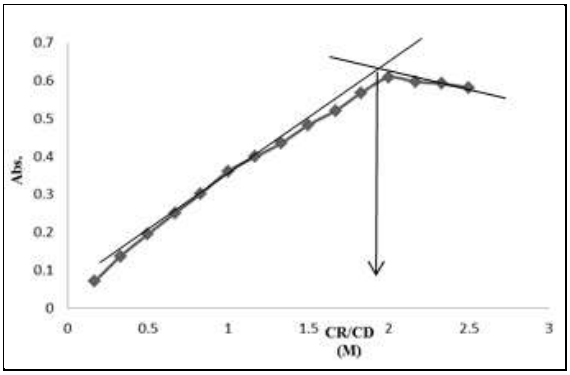


Fig.(9): Mole-ratio method of Dom-NQS product

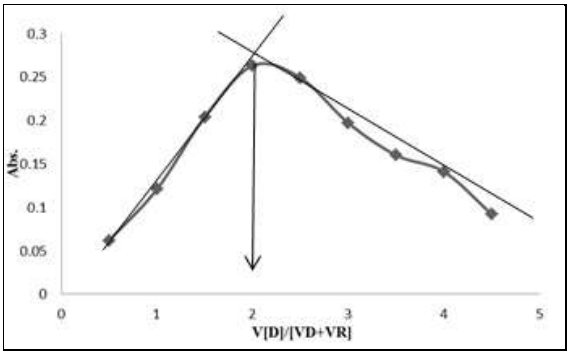


Fig.(10): Continuous variation method of Dom-NQS product

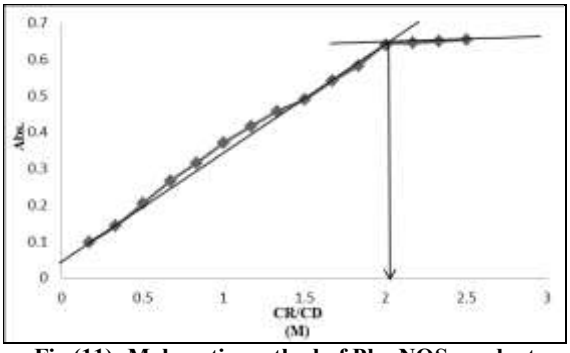


Fig.(11): Mole-ratio method of Phe-NQS product

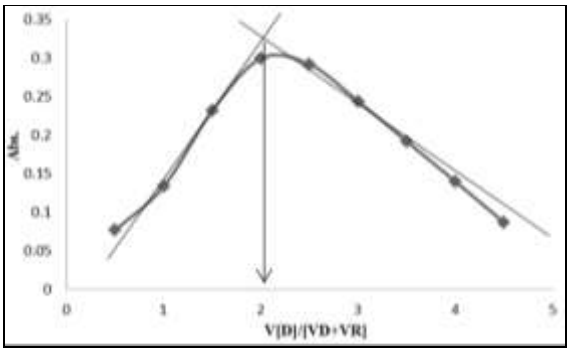


Fig.(12): Continuous variation method of Phe-NQS product

Calibration curves

The calibration curves for (Dom), and (Phe) standard forms through correlation with NQS showed the linearity at concentrations ranges of (20-80 µg/ml), and (10-90 µg/ml), respectively, as shown in Fig. (13, 14).

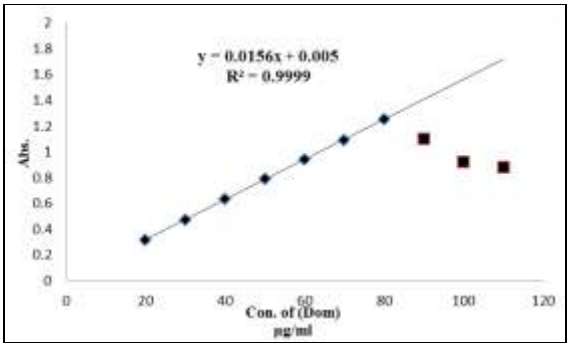


Fig. (13): Calibration curve of Dom-NQS product

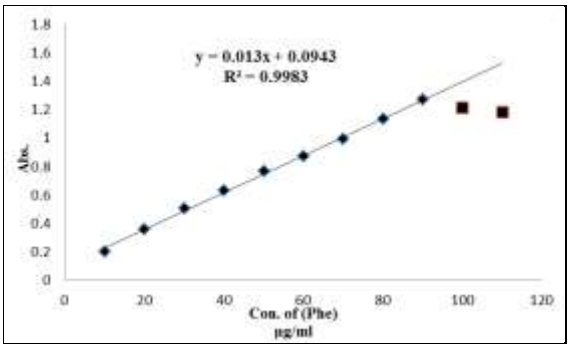


Fig. (14): Calibration curve of Phe-NQS product

Construction of calibration curves

Calibration curves were constructed according to the optimum conditions in Table (4).

Table (4): Optical characteristics of the calibration curves for spectrophotometric determination of (Dom), and (Phe) by NQS reagent

Parameter	(Dom)	(Phe)
$\lambda_{max.}$(nm)	460	460
Beer s law (µg/ml)	20-80	10-90
Molar absorptivity(L/mol.cm)	6.644×10^3	3.019×10^3
Correlation coefficient (r)	0.9999	0.9991
Limit of Detection (µg/ml)	0.463	2.022
Slope	0.0156	0.013
Intercept	0.005	0.0943
%RSD	0.372	0.314

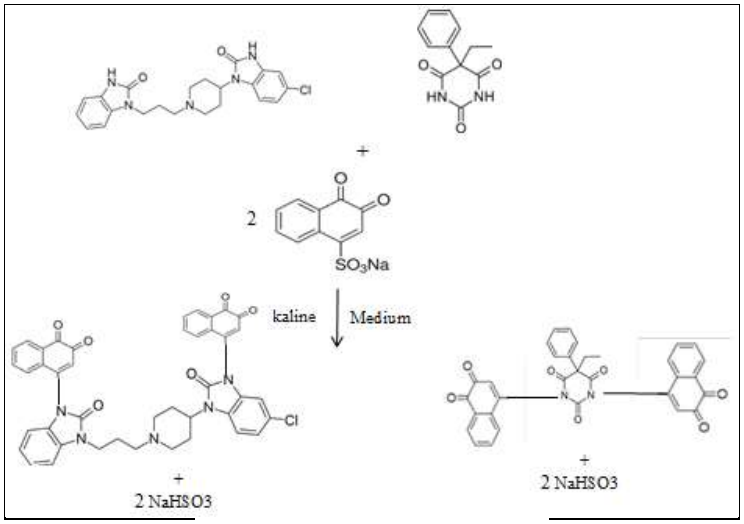
Application of the proposed methods

In Table (5), the result of determination of (Dom) and (Phe) in the pharmaceutical preparations (as tablets).

Table (5): Determination of (Dom), and (Phe) in commercial tablets by spectrophotometric method

Drug	Formulation	Content(mg) declared	Found(mg) by proposed method	% RE	% Recovery
(Dom)	Vomistop	10	9.92	- 0.8	99.2
	Domperidon	10	10.22	2.2	102.2
	Motilium	10	9.98	- 0.2	99.8
(Phe)	Luminal	15	14.97	- 0.2	99.8
	Phenobarbital	15	15.08	0.53	100.5

Suggested ractions: Suggested ractions can be as in the following equations (in scheme 1): (the drugs are associated with the reagent through the amine groups) [25,26]:



Scheme (1): Suggested ractions

Conclusion

These methods described in this study is "simple, rapid, convenient" and do not requires special working conditions unlike many other reported methods. The procedures showed shorter reactions time, stable colored species with inexpensive reagents. The determination can be performed at room temperature and do not require heating step. The proposed methods can be applied to determination of (Dom), and (Phe) in pharmaceutical preparations (Tablets).

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التقدير الطيفي للدومبيريدون والفينوباربيتال بأشكالها النقية وفي مستحضراتها الصيدلانية باستخدام كاشف NQS

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كلية التربية للعلوم الصرفة ، جامعة تكريت ، تكريت ، العراق

الخلاصة

استخدمت طرائق حساسة وسريعة واقتصادية لتقدير عقاقير مختلفة وهي: دومبيريدون وفينوباربيتال، باستخدام كاشف صوديوم 1،2- نفثوكينون-4-سلفونيت في الوسط القاعدي، هذه الطرائق تعتمد على تكوين نواتج ملونة بين تلك العقاقير والكاشف الكروموجيني (NQS). يتكون ناتج برتقالي اللون عند (pH 13) وله أعلى امتصاص عند 460 نانومتر للدومبيريدون، وكذلك يتكون ناتج برتقالـــي اللون وعند (pH 13.5) وله أعلى امتصاص عند 460 نانومتر للفينوباربيتـــال، طُبق قانون بيـــر في مـــدى من التراكيز (20-80 µg/ml)، (10-90 µg/ml)، وبامتصاصيـــة مولاريـــة مقدارهـــا (6.644×10^3 L/mol.cm)، (3.019×10^3 L/mol.cm)، ومعامـــل ارتبـــاط 0.9999، 0.9991، على التوالـــي، وكـــان حد الكشف (2.022 µg/ml, 0.463 µg/ml)، على التوالـي. طُبقت الطرائق المقترحة بنجاح في تقدير هذه العقاقير بشكلها النقي وفي مستحضراتها الصيدلانية على شكل (أقراص).