Spectrophotometric determination of drug compounds in pure forms and in the pharmaceutical preparations

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Keywords: spectrophotometric, Methyldopa, Fluvastatin Sodium, NQS reagent.

"Abstract"

A sensitive, rapid and economical spectrophotometric processes for estimation of two drugs; methyldopa (MTD) and Fluvastatin Sodium (FLV), by "Sodium 1,2-naphthoquine- 4-sulfonate (NQS)" as reagent in an alkaline interemediate. These methods are digested on the forming of "complexes" among these drugs and the chromogenic reagent (NQS). Orangish-brown colored complex formatted at (pH 12) and $\lambda_{max.}$ 462 nm for (MTD), and orange colored at (pH 11.7) and $\lambda_{max.}$ 466 nm for (FLV). Beer's Law is obeyed in a concentrations range of (4-40 µg/mL), (16-64 µg/mL), with molar absorptivity (14.101×10^4 L/mol.cm), (22.7×10^4 L/mol.cm), and correlation coefficient 0.9995, 0.9987, successively, The detection limit and quantification limit were (1.03×10^{-1} µg/mL, 3.12×10^{-1} µg/mL), and (1.36×10^{-1} µg/mL, 4.12×10^{-1} µg/mL), successively. The suggested methods were prosperity implement to the estimation of "these drugs" in pure forms and in their pharmaceutical formulations.

التقدير الطيفي لمركبات دوائية بأشكالها النقية وفي مستحضراتها الصيدلانية

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الكلمات المفتاحية: مطيافية، مثيل دوبا، فلوفاستاتين الصوديوم، كاشف NQS

الخلاصة

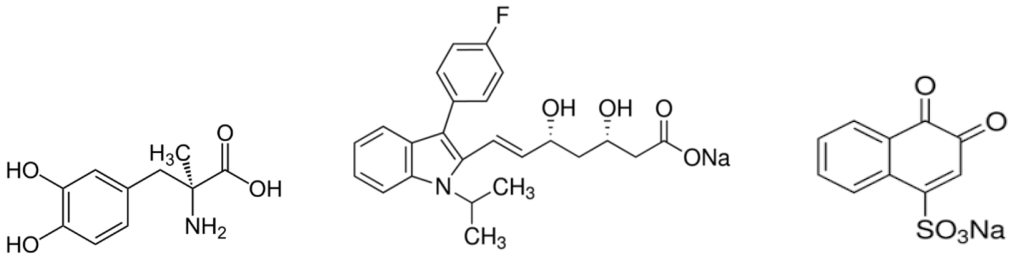
استخدمت طرائق حساسة وسريعة واقتصادية لتقدير عقاقير مختلفة وهي: مثيل دوبا، وفلوفاستاتين صوديوم، باستخدام كاشف صوديوم 1،2- نفثوكينون-4-سلفونيت في الوسط القاعدي، هذه الطرائق تعتمد على تكوين معقدات بين تلك العقاقير والكاشف الكروموجيني (NQS). يتكون معقد برتقالي-بني اللون عند (pH 12) وله أعلى امتصاص عند 462 نانومتر للمثيل دوبا، ومعقد برتقالي اللون وعند (pH 11.7) وله أعلى امتصاص عند 466 نانومتر للفلوفاستاتين صوديوم، طُبق قانون بير في مدى من التراكيز (4-40 µg/mL)، (16-64 µg/mL)، وبامتصاصية مولارية (14.101×10^4 L/mol.cm)، (22.7×10^4 L/mol.cm)، ومعامل ارتباط 0.9995، 0.9987، على التوالي، وكان حد الكشف وحد الكمية (1.03×10^{-1} µg/mL, 3.12×10^{-1} µg/mL)، (1.36×10^{-1} µg/mL, 4.12×10^{-1} µg/mL) على التوالي. طُبقت الطرائق المقترحة بنجاح في تقدير هذه العقاقير بشكلها النقي وفي مستحضراتها الصيدلانية على شكل (أقراص).

Introduction

Methyldopa (Fig.1), is treated “high blood pressure”, especially for pregnancy, one of types including very high blood pressure resulting in symptoms other medications are exemplary favored. It can be given by mouth or injection into a vein [1]. Molar mass is 211.215 gm/mol, M.P. = 290 °C, chemically known is α – methyl – 3 , 4 - dihydroxyphenylalanine, is a catechol derivative (catecholamine) [2]. Fluvastatin Sodium (Fig. 1), belongs to a group of medicines known as “statins”, it treated along with a “suitable diet to assist lower "bad" cholesterol and fats (such as LDL, triglycerides)” and “raise "good" cholesterol (HDL) in the blood”. It works by contracting the quantity of cholesterol made by the liver. Lowering "bad" cholesterol and triglycerides and raising "good" cholesterol decreases the risk of heart disease and helps prevent strokes and heart attacks [3]. Molar mass is 433.45 gm/mol, M.P. = 194-197°C, chemically known is “sodium, (E, 3R, 5S) – 7 - [3 - (4 - fluorophenyl) – 1 – propan – 2 – ylindol – 2 - yl] - 3, 5 - dihydroxyhept – 6 – enoate” [4].

Several methods have been proposed for determination of these drugs, such as HPLC [5,6], TLC [7], HPTLC [8], Flow injection analysis [9], voltammetry [10,11], UV spectrophotometry [12,13], UV-Vis. Spectrophotometry [14-16].

"Sodium 1, 2 – naphthoquinone – 4 - sulphonate (NQS) 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" [17-19].



(a) (b) (c)

Fig. (1): Chemical Structures of (a) Methyldopa, (b) Fluvastatin Na, (c) NQS reagent

Aim of the study

The research aims at finding a simple, fast and economical spectral methods for determination of Methyldopa and Fluvastatin Na, 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

UV-VIS spectrophotometer “single beam from A&E Lab (UK) -S60- Series with 1 cm quartz cells”, pH meter from (Senz pH tester, China), Balance from Mettler AB 104-S (Switzerland).

Materials

Methyldopa %99, Fluvastatin Na %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

Methyldopa Stock solution (1000 µg/mL): An exactly (0.1000 gm) of (MTD) “standard” were dissolved in (100 ml) distilled water.

Fluvastatin Sodium Stock solution (1000 µg/mL): An exactly (0.1 gm) of (FLV) “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

Methyldopa: A 1.0ml from 500µg/mL of (MTD) was carried into 25ml “volumetric flask”, 3.5ml from10^{-2}M “NQS” was added and followed by 1.0ml from NaOH 1M. After (15 min.), the volume was supplemented to volume by distilled water, and was measured at 462 nm against “reagent blank”.

Fluvastatin Na: A 2.0ml from 500µg/mL of (FLV) was carried into 25ml “volumetric flask”, 4.0ml from 10^{-2}M “NQS” was added and followed by 1.0ml from NaOH 1M. After (15 min.), the volume was supplemented to volume with distilled water, and was measured at 466 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 (MTD), (FLV) and “NQS” (8×10^{-3}M), and (6×10^{-3}M), were used respectively. Varying aliquots of “NQS” were added to constant aliquots of drugs solutions, final volumes (25ml) and the absorbance were measured at 462 nm, 466nm, respectively, opposite the “reagent blank treated

similarly". While in the latter method, a series of MTD-NQS, and FLV-NQS solutions were kept at (5ml) (0:5, 0.5:4.5, 1:4, 1.5:3.5, 2:3, …… 5:0).

Application of the proposed methods

"Twenty tablets" were weighed and averages weights 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 solvents 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 MTD, and FLV in various commercial tablets, the results are shown in Table (2).

RESULTS AND DISCUSSION

Absorption spectra of MTD-NQS, and FLV-NQS systems against reagent blank in an alkaline medium at room temperature (25ºC) producing an orangish brown colored product for MTD-NQS and FLV-NQS where absorbs maximally at 462nm, 466nm, respectively, (Fig. 2, 3), and reagent blank against water (Fig. 4).

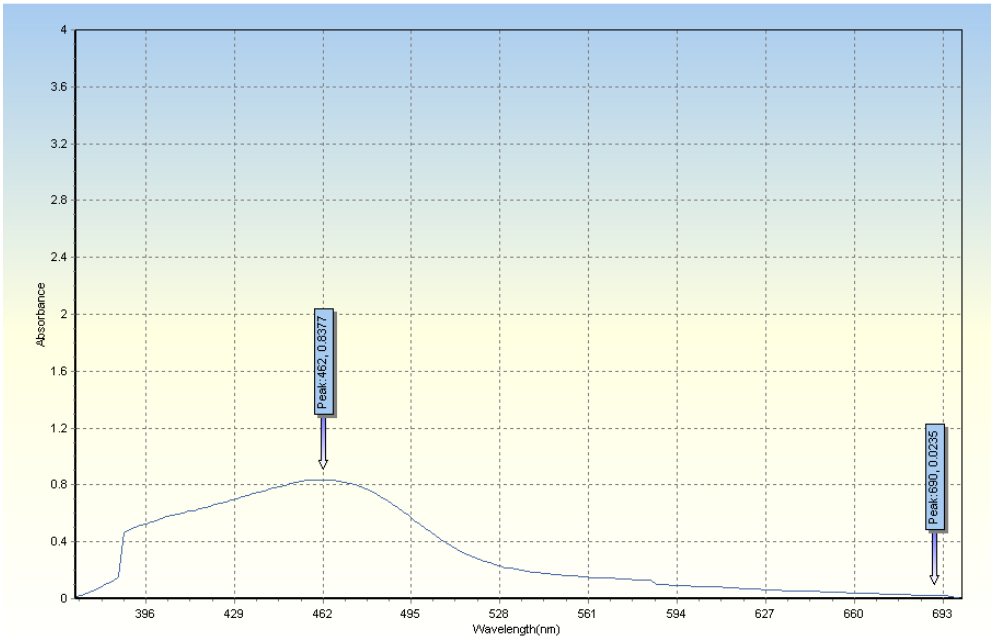


Fig. (2): Absorption spectrum of MTD-NQS system against blank

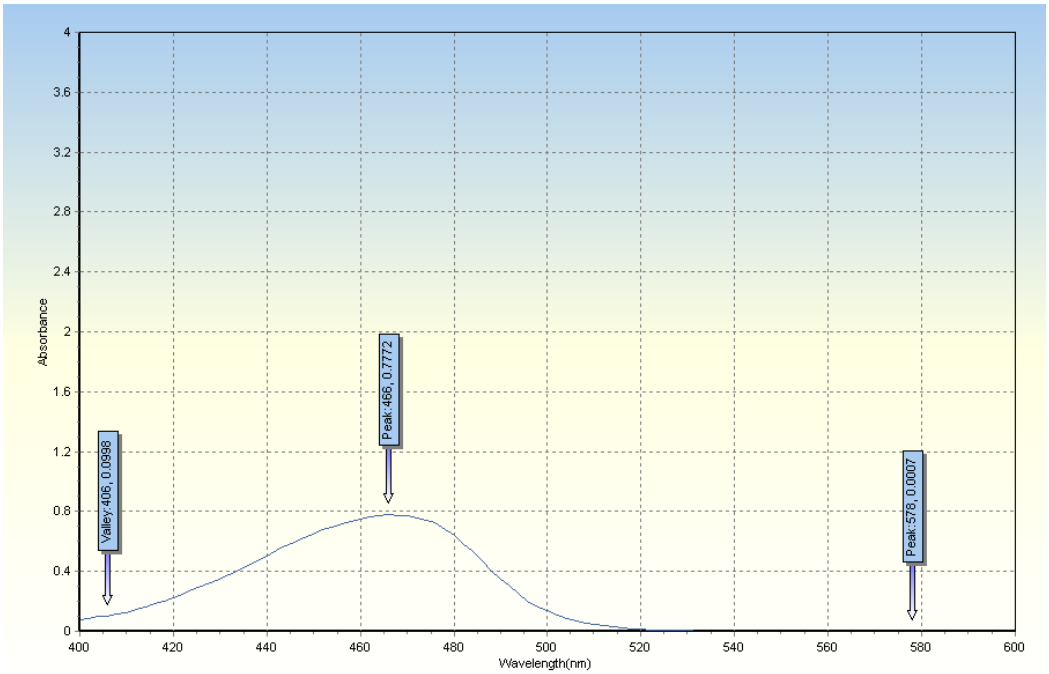


Fig. (3): Absorption spectrum of FLV-NQS system against blank

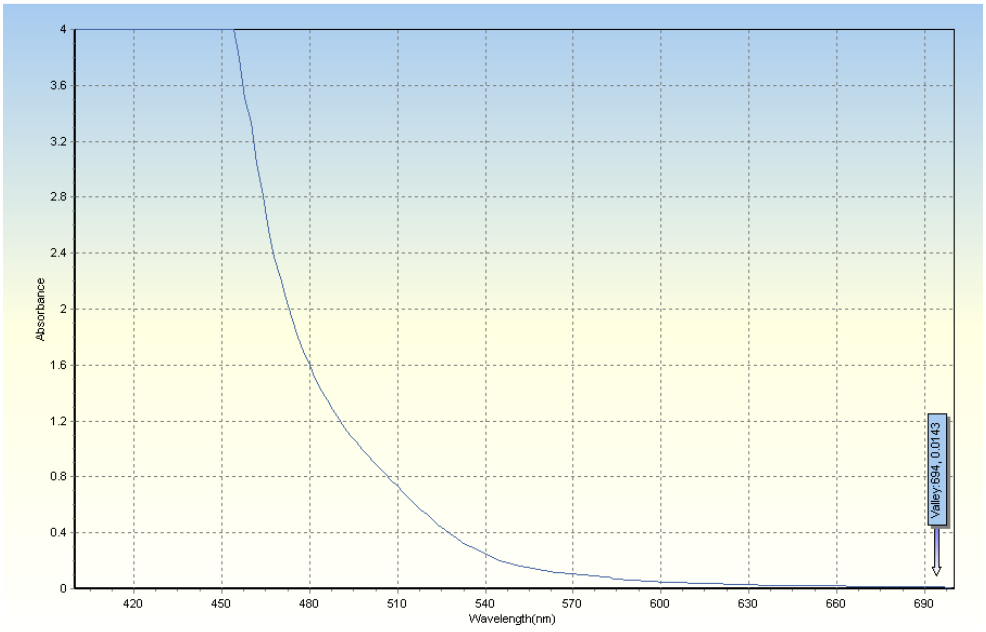


Fig. (4): Absorption spectrum of reagent blank against distilled water

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 product” 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 MTD, FLV with reagent were to rely on the concentrations of “NQS”. So, it’s concentrations were studied by different volumes of (0.01 M) NQS, while the MTD, and FLV concentrations were maintained constant at 20 μg/mL, and 40 μg/mL. 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 3.5ml, and 4 ml of (0.01 M) NQS, respectively, Therefore, these concentrations were used to prepare calibration curves, as shown in Fig. (5, 6).

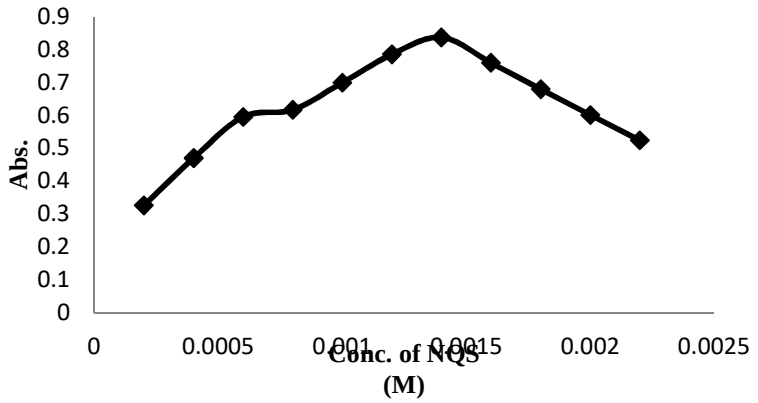


Fig.(5): Effect of conc. of NQS (0.01M) on MTD-NQS complex

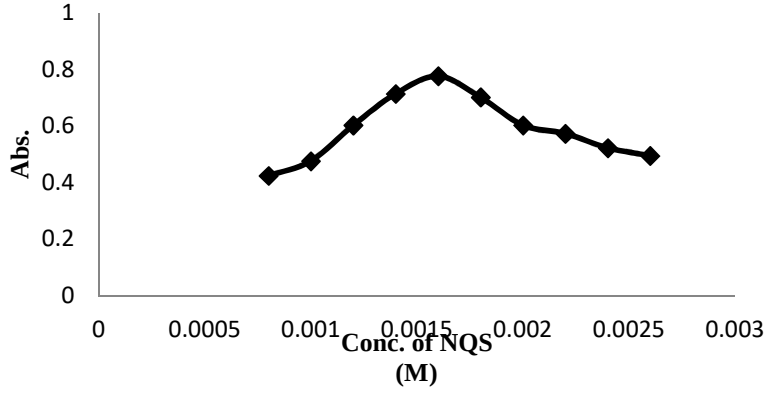


Fig.(6): Effect of conc. of NQS (0.01M) on FLV-NQS complex

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 hardness to reacts with “NQS”. Different concentrations from NaOH were tested, best results were at higher concentrations of NaOH (1M), with pH 12, 11.7 for MTD, and FLV complexes, respectively, As illustrated in Fig. (7, 8).

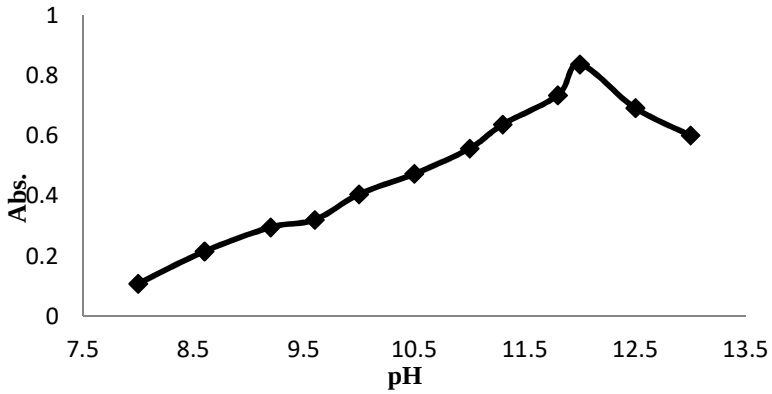


Fig. (7): Effect of pH on MTD-NQS complex

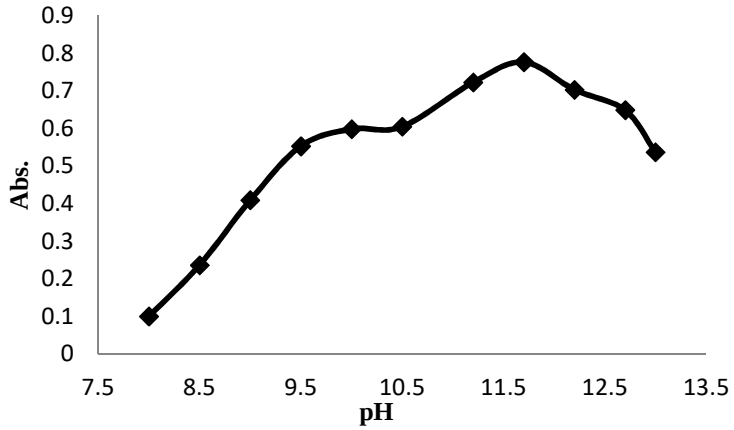


Fig. (8): Effect of pH on FLV-NQS complex

Effect of Time

Under the "optimum conditions", the effect of reaction time of MTD, and FLV with reagent in "alkaline medium" were constructed, and the products remained stable for 90 min., As illustrated in Fig. (9).

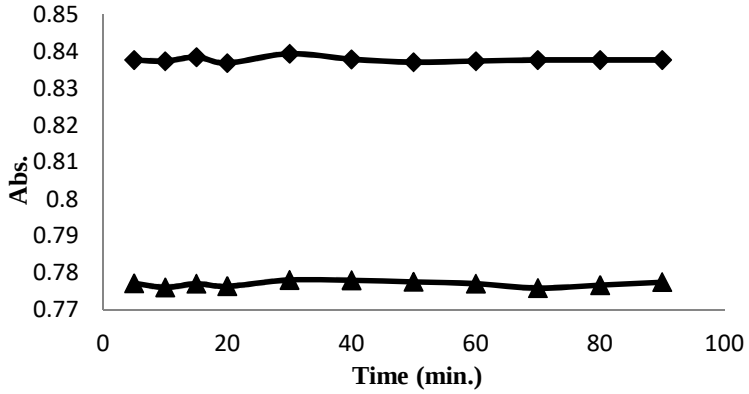


Fig. (9): Effect of time on complexes: —♦— MTD, —▲— FLV

Equivalent of the reactions

Under the "optimum conditions", (temperature, cons. of NQS, pH, time) "the stoichiometry" of the reactions between MTD, and FLV with reagent were studied by mole–ratio and continuous variation methods. The equivalence between reagent and these drugs were 1:1 (Figs. 10, 11, 12, 13).

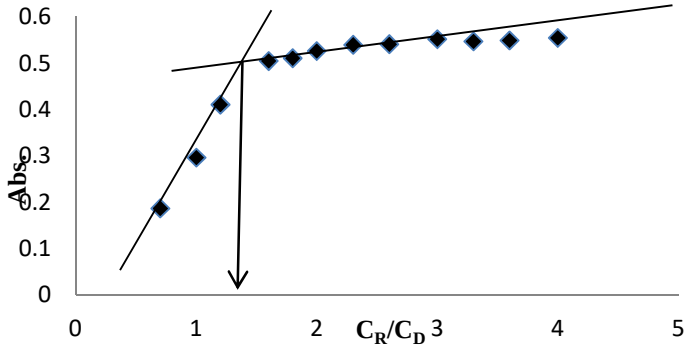


Fig.(10): Mole-ratio method of MTD-NQS complex

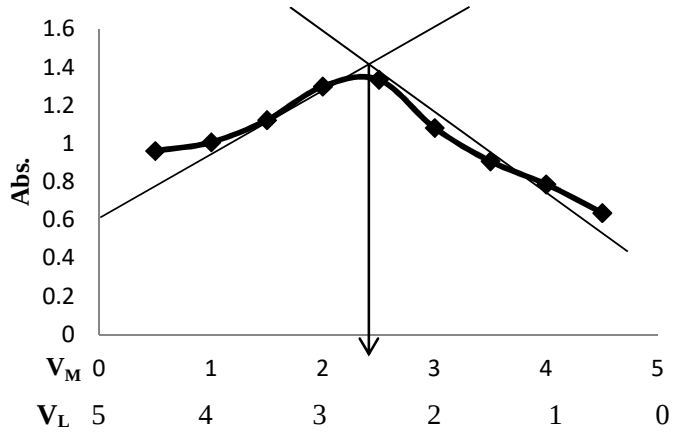


Fig.(11): Continuous variation method of MTD-NQS complex

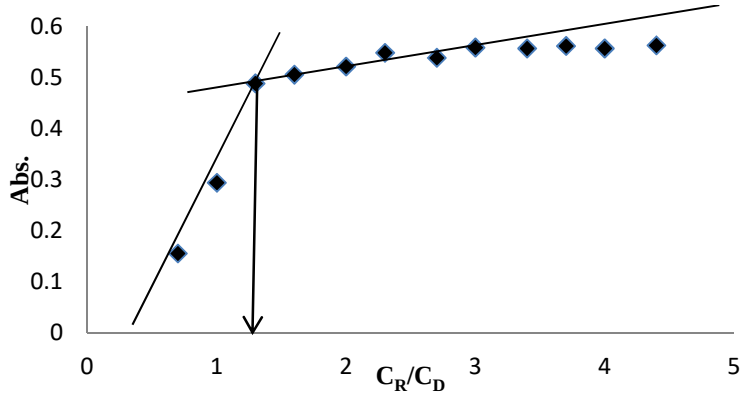


Fig.(12): Mole-ratio method of FLV-NQS complex

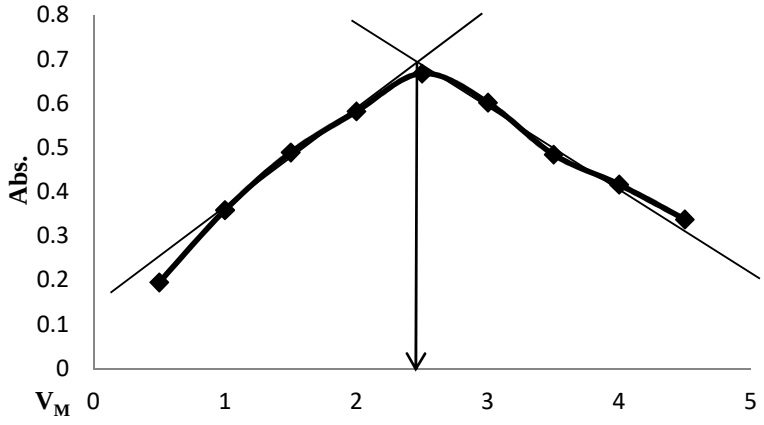


Fig.(13): Continuous variation method of FLV-NQS complex

Calibration curves

The calibration curves for MTD, and FLV pure forms through complexation with NQS showed the linearity at concentrations ranges of (4-40 µg/mL), and (16-64 µg/mL), respectively, as shown in Fig. (14, 15).

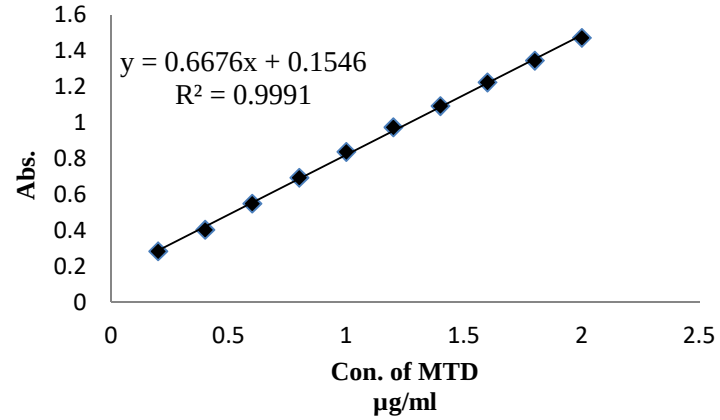


Fig. (14): Calibration curve of MTD-NQS complex

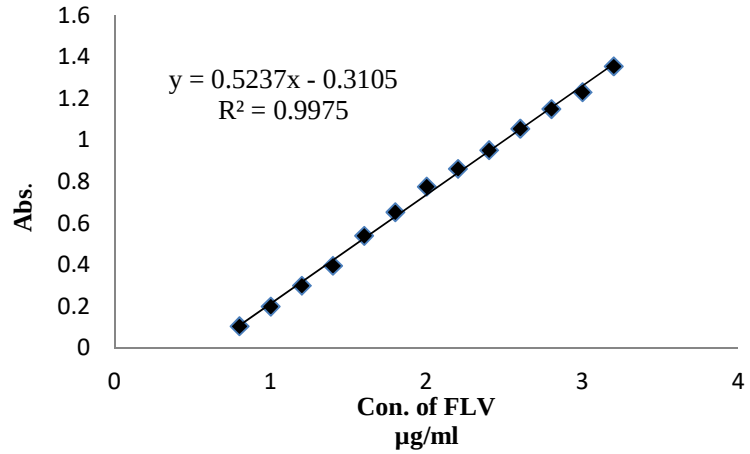


Fig. (15): Calibration curve of FLV-NQS complex

Construction of calibration curves

Calibration curves were constructed according to the optimum conditions in Table (1).

Table (1): Optical characteristics of the calibration curves for spectrophotometric determination of MTD, and FLV by NQS reagent

Parameter	MTD	FLV
λ_{max}.(nm)	462	466
Beer's law (µg/ml)	4-40	16-64
Molar absorptivity(l/mol.cm)	14.10×10^4	22.70×10^4

Correlation coefficient (r)	0.9995	0.9987
Limit of Detection (µg/ml)	0.103	0.136
Limit of Quantification (µg/ml)	0.321	0.412
Slope	0.6676	0.5237
Intercept	0.1546	-0.3105
%RSD	1.4	1.5

Application of the proposed methods

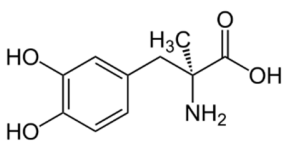
In table (2), the result of determination of MTD and FLV in the pharmaceutical preparations (as tablets).

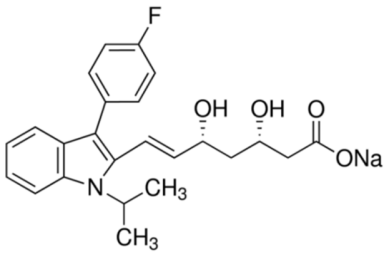
Table (2): Determination of MTD, and FLV in commercial tablets by spectrophotometric method

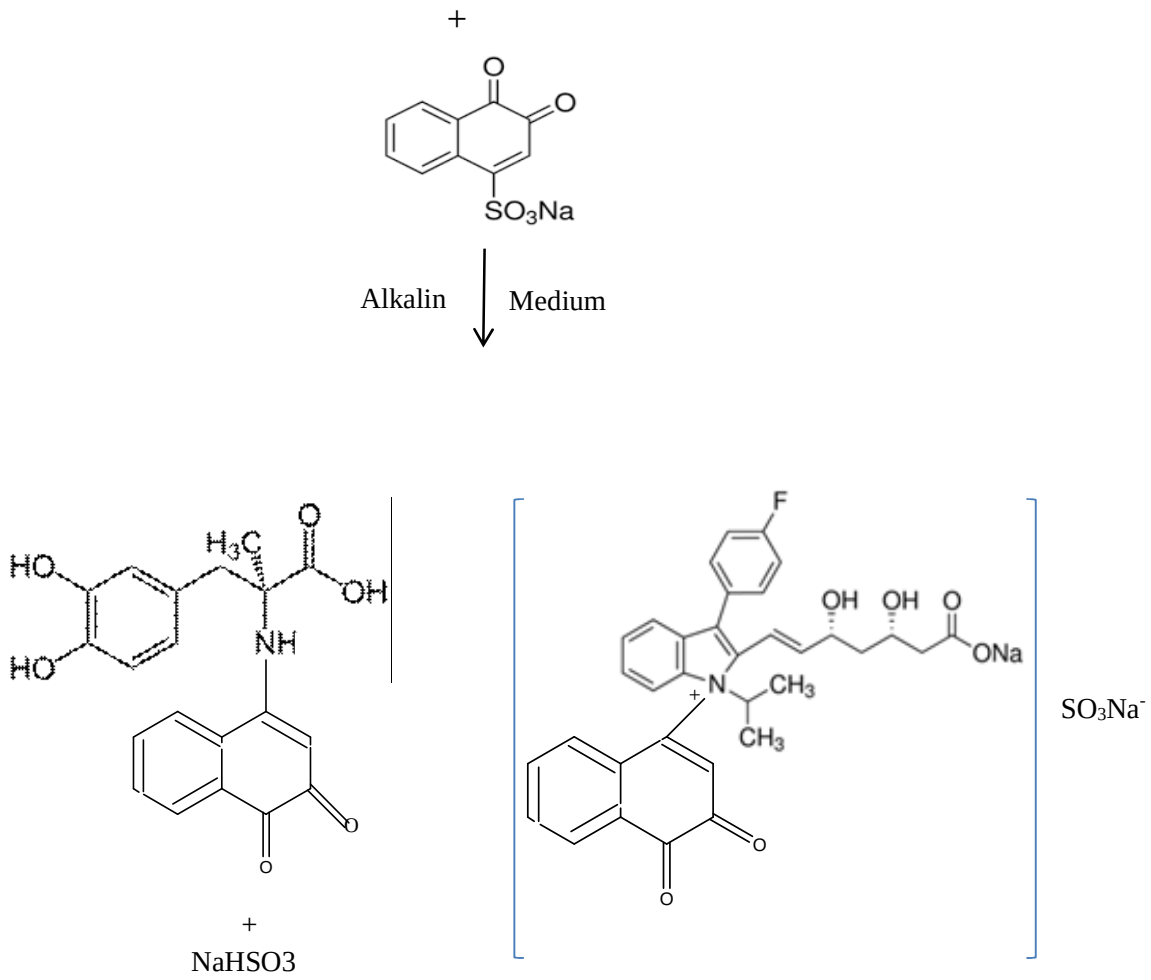
Drugs	formulations	Content(mg) declared	Found(mg) by proposed method	%E	%Recovery
MTD	Aldomet	250	251.38	0.552	100.552
	Methyldopa	250	250.96	0.384	100.384
	Apo-Methyldopa	250	250.08	0.032	100.032
FLV	LESCOL XL	80	80.55	0.688	100.688
	LESCOL	80	82.14	2.675	102.675
	Fluva	80	81.69	2.11	102.11

Suggested interactions

Suggested interactions can be as in the following equations (in scheme 1): (the drugs are associated with the reagent through the amine group) [16,20]:







Scheme (1): Suggested interactions

Conclusion

These methods described here 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 MTD, and FLV in pharmaceutical preparations (Tablet).

References

[1] "Methyldopa"- The American Society of Health-System Pharmacists- Retrieved 8 December 2016.

[2] Gotardo M. A., Lima L. S., Sequinel R., Rufino J. L., Pezza L. and Pezza H. R., (2008) A Simple spectrophotometric method for the determination of

methyldopa using pchloranil in the presence of hydrogen peroxide, **Ecletica Quimica**, 33: 7-12.
[3] WebMD - Drugs and Medications (Fluvastatin Sodium) 2017.
[4] PharmaCompass - Technical details about Fluvastatin Sodium, 2017.
[5] Sahithi M.V.L., Perumal V., Chandra Sekhar K., Vijay Babu P., (2013) Development and Validation of RP-HPLC method for simultaneous estimation of Methyldopa and Hydrochlorothiazide in Pharmaceutical Dosage Form, **Journal of Advanced Pharmacy Education & Research**, 3(4): 464-470.
[6] Abdallah M. Ola., (2011) RP-HPLC determination of three anti-hyperlipidemic drugs in spiked human plasma and in dosage forms, **E-Journal of Chemistry**, 8(2): 753-761.
[7] Skrdlant H. B., Wallace J. E. & Haegele K. D., (2006) Urinary Screen for α-Methyldopa by TLC, **Journal, Analytical Letters**, 10(10): 743-750.
[8] Ashok Akabari H., Umang Shah, Sagar Solanki, Mandev Patel B. N., Bhanubhai Suhagia, (2014) Development and validation of sensitive HPTLC method for quantitative analysis of Fluvastatin Sodium in bulk and pharmaceutical dosage form, **International Journal of Pharmaceutical Research,** 6(2): 73-78.
[9] Mohammed Hamzah J., Issam Shakir M. A., (2016) Flow injection photometric assay for determination of Methyldopa using Hydrogel Approch as a host for the Sodium Periodate solution, **Int. J. Pharm. Sci. Rev. Res.**, 41(1): 247-251.
[10] Vinod Kumar Gupta, Sahebe Khosravi, Hassan Karimi, Maleh, Mostafa Alizadeh, Shahryar Sharafi, (2015) A Voltammetric sensor for determination of Methyldopa in the presence of Hydrochlorothiazide using Fe:Co Nanoalloy modified Carbon paste electrode, **Int. J. Electrochem. Sci.**, 10: 3269-3281.
[11] Jin-Long Yan, (2006) Determination of Fluvastatin Sodium by differential pulse voltammetry, **Pakistan Journal of Biological Sciences**, 9: 2156-2158.
[12] Sawant R.L., Mhaske S.M., (2014) Analytical method development for simultaneous estimation of Saxagliptin and Methyldopa, **Asian J. Pharm. Res.**, 4(3: 134-140.
[13] Saminathan J., Sankar A. S. K., Anandakumar K. and Vetrichelvan T., (2009) Simple UV spectrophotometric method for the determination of Fluvastatin Sodium in bulk and pharmaceutical formulations, **E-Journal of Chemistry**, 6(4): 1233-1239.
[14] Muneer AL-Da'amy A. A., Rashwan AL-Moswi F., (2014) Spectrophotometric determination of Methyldopa in pharmaceutical preparation via oxidative coupling organic reaction with Para-Phenylenediamine in the presence of Potassium Periodate, **PAK Publishing Group, Growing Knowledge for Future**, : 130-137.

[15] Tehmina Fiaz, Nasreen Fatima, Zafar Abbas Zaidi S., Tanveer Abbas, Mohib Kazimi R., (2015) Investigation of Iron complex formation of anti-hypertensive drug: Methyldopa, **American Journal of Analytical Chemistry**, 6: 551-558.
[16] Safwan Ashour, Mahmoud Bahbouh, Mouhammed Khateeb, (2010) Kinetic spectrophotometric determination of Fluvastatin in pharmaceutical preparations, **Int. J. Biomed Sci.,** 6(1): 19-26.
[17] IA. Darwish, et al., (2009) Spectrophotometric study for the reaction between Fluvoxamine and 1,2-Naphthoquinone-4-sulphonate: Kinetic, mechanism and use for determination of Fluvoxamine in its dosage forms, **Spectrochim Acta Part A**, 72: 897-902.
[18] Li Q., and Zhang H., (2008) A novel spectrophotometric method for the determination of Aminophylline in pharmaceutical samples in the presence of methanol, **Spectrochim Acta Part A**, 70: 284-289.
[19] Li QM., and Yang ZJ. (2007) Spectrophotometric determination of Aminomethylbenzoic acid using sodium 1,2-Naphthoquinone-4- sulfonate as the chemical derivative chromogenic reagent", **Spectrochim Acta**, 66: 656-661.
[20] Aida M., and Abdalla A., (2014) Spectrophotometric method for determination of Primaquine in pharmaceutical formulations via derivatization with 1,2-Naphthoquinone-4-sulfonate, **Austin Journal of Analytical and Pharmaceutical Chemistry**, 1(4).