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New Spectrophotometric Method for the Determination of Tamsulosin Hydrochloride in Bulk and Pharmaceutical Dosage Forms

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Abstract:

A new, simple, sensitive, accurate, selective method has been developed for the determination of Tamsulosin hydrochloride in bulk and in pharmaceutical dosage forms. The developed method is a chemical derivatization method involving proton transfer from the 2,4,6-trinitrophenol (picric acid) to the secondary amino group of Tamsulosin in acetonitrile as a solvent to form a yellow charge transfer complex exhibiting maximum absorption (λ_{max}) at 400 nm. The method was linear in the concentration range [1-12 µg/ml] with correlation coefficient (R^2= 0.9979), intra-day, inter-day precision (as RSD)and accuracy were determined. The obtained results were statistically validated .The method was successfully applied to the determination of Tamsulosin hydrochloride in tablets. The percentage recovery was 102.3 % ± 0.591 (n=5).The developed method is considered to be simple, accurate and specific for Tamsulosin HCl determination as raw material or in tablets.

Key words: Tamsulosin Hydrochloride, Picric Acid, Chemical Derivatization, Charge Transfer Reaction, Spectrophotometer.

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طريقة طيفية جديدة لتحديد تامسولوسين هيدروكلورايد كمادة أولية وفي الأشكال الصيدلانية

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الملخص:

تم تطوير طريقة تحليلية جديدة بسيطة، دقيقة ونوعية لتحديد تامسولوسين هيدروكلورايد كمادة أولية وفي الأشكال الصيدلانية .

الطريقة المطورة هي طريقة اشتقاق كيميائي يتطلب انتقال بروتون من حمض البيكريك (2,4,6 ثلاثي نترو فينول) إلى مجموعة الأمين الثانوي لمركب التامسولوسين في محل الأسيتونتريل، ليتشكل معقد انتقال شحنة أصفر اللون يمتص الضوء المرئي أعظمياً عند طول موجة 400 نم.

كانت الطريقة خطية بين 1–12 مكغ/ مل، مع معامل ارتباط وقدره 0.9979 .

تم تحديد كل من الدقة الوسطى والتكرارية عن طريق حساب قيمة الانحراف المعياري النسبيRSD، كما قيمت النتائج احصائياً، تم تطبيق الطريقة لتحديد تامسولوسين هيدروكلورايد في المضغوطات بنجاح، وبلغت النسبة المئوية للاستعادة (عدد المكررات =5 0.591, ± 102.3 %) وأخيراً تعد الطريقة المطورة بسيطة، دقيقة، نوعية لتحديد التامسولوسين هيدروكلورايد كمادة أولية أو في المضغوطات.

الكلمات المفتاحيّة: تامسولوسين هيدروكلورايد، حمض البيكريك، الاشتقاق الكيميائي، تفاعل انتقال الشحنة، مقياس الطيف الضوئي.

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BPH	Benign prostatic hyperplasia
RSD	Relative standard deviation
HPLC	High-performance liquid chromatography
LOD	Limit of detection
LOQ	Limit of quantification
SD	Standard deviation

Introduction:

Tamsulosin is chemically (R)-5-(2-{[2-(2-ethoxyphenoxy) ethyl] amino} propel)-2-methoxy benzene-1-sulfonamide (figure 1) [1]. This medication is used by men to treat the symptoms of an enlarged prostate. It is known as an alpha 1 adrenoceptor blocker, used in the symptomatic treatment of benign prostatic hyperplasia (BPH) [2,3,4] . Tamsulosin is used to treat men who are having problems of urinating because of BPH. It is not approved for the treatment of high blood pressure, which can provide relief in some cases within 48 h. Tamsulosin also assists the passage of kidney stones by the same mechanism of muscle relaxation via alpha antagonism [5] .As literature showed it was commonly analyzed by HPLC in dosage forms or plasma[6-14] and fewer methods by spectrophotometer [15,16,17].

Among the various methods available for the quantitation of drugs, spectrophotometry continues to be the most convenient analytical technique, because of it's simplicity, accuracy, low cost and wide availability in most quality control laboratories [18].

Picric acid has been used as a derivatizing reagent in the development of spectrophotometric methods for the determination of many pharmaceuticals. Tamsulosin is bearing a secondary amino group, and is a potential candidate for the reaction with picric acid based on charge transfer complex formation [19,20,21] .In the present investigation, a new simple, rapid, accurate , and cost effective visible spectrophotometric method has been developed for the estimation of Tamsulosin HCl as raw material and in tablet dosage form.

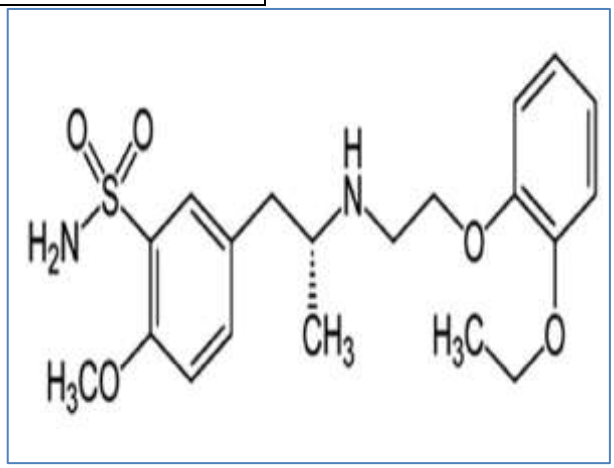


Figure (1): Chemical structure of Tamsulosin

Materials And Methods:

Materials:

Picric acid (2,4,6-trinitrophenol)
(Pure 99.8%,Merck,Germany).
Acetonitrile (analytical grade,pure 99%,Needham Market.Suffolk
England).
Pharmaceutical grade of tamsulosin hydrochloride , certified to contain 99.90% (origin from Nifty pharma PVTLTD –India) was kindly supplied from Unipharma for pharmaceutical industries (Syria) as a gift .
Tamsulosin tablets nominally containing 0.4 mg Tamsulosin hydrochloride per tablet, which were purchased from local market .

Apparatus:

-Optizen pop UV-Visible recording spectrophotometer.
Ultrasonic,Branson 200.-
- A SHIMADZU analytical balance with 0.01 mg.

Standard solutions and reagents:

Tamsulosin HCl stock solution (20 µg/mL) was prepared by dissolving 0.8 mg of standard material in 40 ml acetonitrile. Stock solutions were protected from light and kept refrigerated at 4C°. The stock solution was further diluted with the same solvent to obtain the other dilutions.

A Solution of 0.3% w/v reagent (picric acid) was freshly prepared by dissolving 150 mg picric acid in 50 ml acetonitrile.

Procedures:

Procedure of preparing standard series of standard drug:

Aliquots of the working standard solution of Tamsulosin HCl were transferred in a series of 10 ml volumetric flask to give final concentrations of 1-12 µg/ml . 1.5 ml of picric acid (0.3%w/v) was added to each flask and diluted to the volume with acetonitrile. Flasks then were shacked well and allowed to stand for 30 minutes to complete the reaction. The absorbance was measured for each flask at 400 nm against blank reagent prepared similarly. The drug concentration was calculated from the corresponding regression equation of the calibration graph.

Procedure of determination Tamsulosin HCl in commercial tablets:

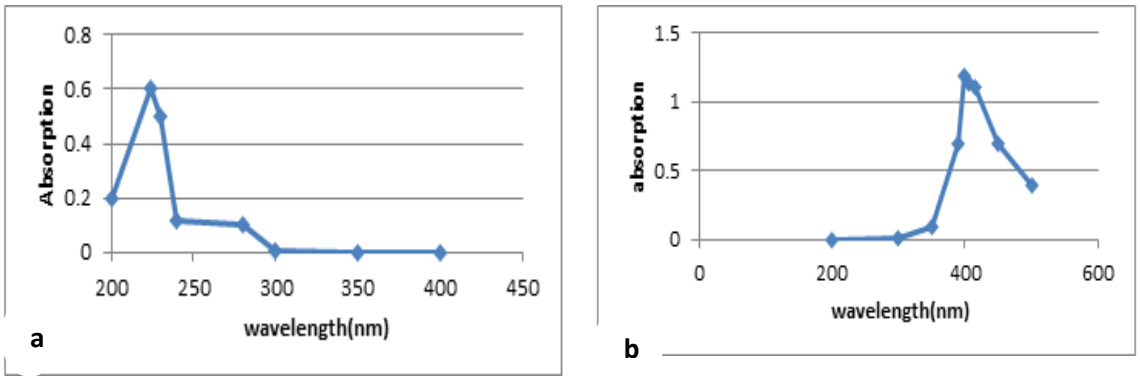
Twenty tablets of labeled claim 0.4 mg of Tamsulosin were weighed accurately . An average weight of each tablet was determined. An accurately weighed quantity of powder equivalent to 2 mg of Tamsulosin was transferred into 100ml volumetric flask and sonicated for 10 min with 40 ml of acetonitrile and dilute with water to the volume. The contents were mixed well then filtered rejecting the first portion of filtrate. The prepared solution concentration is 20 µg/ml. A 30 ml of 20 µg /ml solution was further diluted to 100 ml with acetonitrile to give final concentration of 6 µg/ml. Aliquots of the tablets solution were treated as under the general recommended procedures for the reaction with picric acid. Then the concentration of the drug was calculated using calibration curve.

Results And Discussion:

Absorption spectra:

Tamsulosin HCl shows maximum absorption at 224 nm using acetonitrile as a solvent (Fig.2.a) as well as in methanol [22]. The formation of complex based on the reaction between picric acid as Lewis acid[23,24](electron acceptor) and Tamsulosin as electron donor, at the same time the proton of the hydroxyl group of picric acid will transfer to the secondary amine of Tamsulosin. Molecular interactions between electron donors and acceptors are generally associated with the formation of intensely colored charge-transfer complexes which absorb radiation in the visible region[25].

The absorption spectra of the yellow colored products were recorded at 300–600 nm against the corresponding blank solution. The resulted product showed maximum absorbance at 400 nm as shown in (Fig.2.b)



Figure(2): Tamsulosin HCl spectra using acetonitrile as a solvent (a) Absorption Spectra of the product after derivatization (b)

Effect of reagent concentration on complex formation

It was found, that absorbance increases with increasing picric acid concentration and gave its maximum value by using the concentration of 0.3% w/v of picric acid as shown in figure (3).

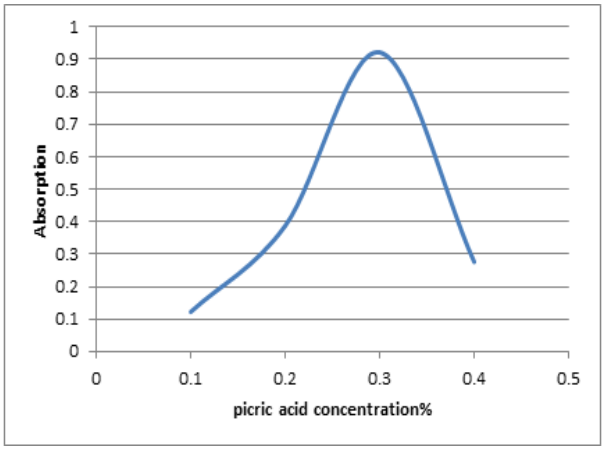


Figure (3): effect of the concentration of reagent on the absorption of the resulted product.

Effect of reagent volume:

It was found, that absorbance increases with increasing picric acid volume and gave its maximum value by using 1.5 ml of 0.3% w/v of picric acid then it decreases as shown in figure (4).

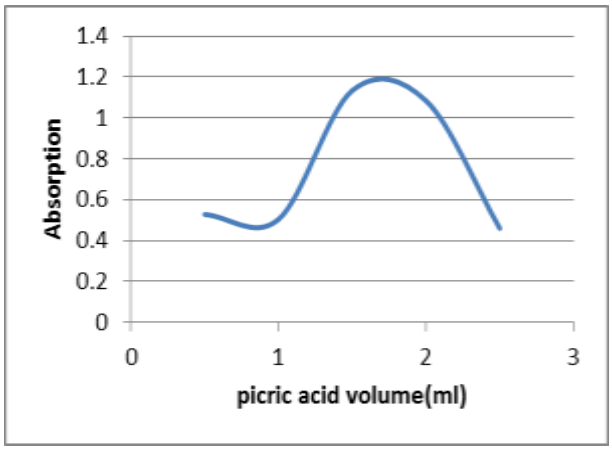


Figure (4): effect of the volume of the reagent on absorption of the resulted product

Effect of the solvent on reaction

Acetonitrile was an appropriate solvent, since it dissolved both of picric acid and Tamsulosin HCl as well, while dichloromethane was not suitable , because it did not dissolve the drug, and chloroform showed unstable results. Tamsulosin HCl is sparingly soluble in water, so it was avoided as a solvent.

Time Effect on reaction

It was found, that absorbance increases with increasing waiting time and reached its maximum value after 30 minutes then it decreases as shown in figure (5).

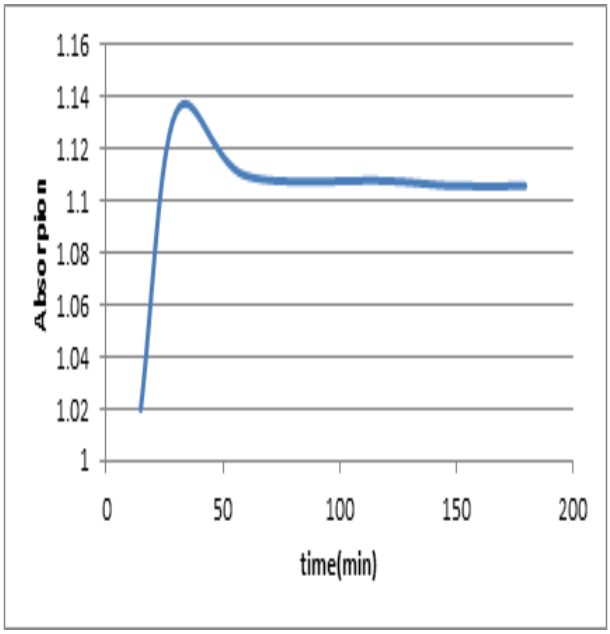


Figure (5): effect of time on absorption of the resulted product

Validation of the proposed method [26]

Linearity

The correlation coefficient (R^2) of the formed product was 0.9979 indicating good linearity

(Figure .6)The limit of detection (LOD) and limit of quantification (LOQ) for the proposed method were calculated using the following equations:

$LOD = 3.3\ \sigma / S$, $LOQ = 10\ \sigma / S$

Where σ is the standard deviation of intercept. S is the slope of calibration curve. The results are summarized in table 1.

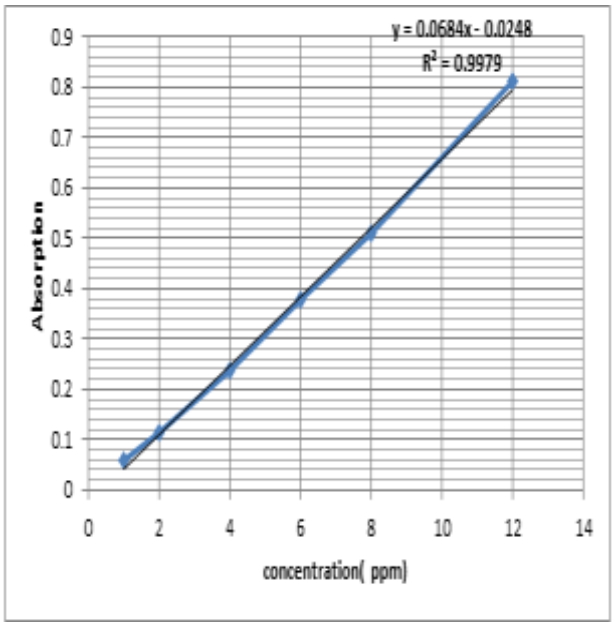


Figure (6): Calibration graph for Tamsulosin after derivatization with picric acid

Table (1): Quantitative parameters of the proposed method.

Value	parameter
Time of reaction	30 min
Stability of color	5 hours
Beer's law limits	1-12 (µg/ml)
Molar absorptivity ($l.mol^{-1}\ cm^{-1}$)	24891
Regression equation	Y=0.0684 X-0.0248
Correlation coefficient (R^2)	0.9979
slope	0.0684
intercept	0.0248
LOD	0.16 µg ml^{-1}
LOQ	0.48 µg ml^{-1}

X is the concentration of Tamsulosin HCl µg ml^{-1}, Y is absorption

Accuracy and precision:

They were checked at three concentration levels, five replicate measurements were recorded at each concentration level. Accuracy was calculated as percent Recovery.

Precision was estimated as relative standard deviation. The calculated relative standard deviations were less than 2% indicating a good precision of the proposed procedure at both levels of inter-day and intra-day precision, the results are summarized in table 2.

Table (2): Accuracy and precision of the proposed method for the determination of Tamsulosin HCl

Precision				Accuracy* %		Concentration (µg/ml)
Inter –day		Intra- day				
RSD*	Recovery ±SD*%	RSD*	Recovery ±SD*%			
0.735	99.27±0.73	1.537	99.51±1.53	99.5%		2
0.857	96.82±0.83	0.998	97.183±0.97	97.18%		8
0.625	100.85±0.63	0.157	101.67± 0.16	101.7%		12
*n=5, SD=standard deviation, RSD=relative standard deviation				99.45±0.886	Mean± SD*	
				0.897	RSD*	

Determination of Tamsulosin HCl in tablets

The proposed method was applied on the dosage forms and the content of tablets was found to be 102.3%± 0.591 of the label claim (table.3)

Table (3) Application of the proposed method for the analysis of dosage form containing Tamsulosin HCl

Dosage form (tablets)	Label claim (mg/tablet)	Amount found	Recovery*% ±SD	RSD*
Tamsulosin (local market)	0.4	0.4092	102.3± 0.591	0.609

*n=5.

Conclusion:

A new method which is selective , sensitive, and rapid has been developed and appropriately validated for the assay of Tamsulosin in bulk and pharmaceutical formulations .The analytical reagent is inexpensive and readily available in the most of analytical laboratories. The method does not require complex procedures or sophisticated equipment and is highly suitable for routine use in quality control laboratories.

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Statements And Declarations:

Competing Interests :

- On behalf of all authors, the corresponding author states that there is no conflict of interest .