DETERMINATION OF ACTIVE INGREDIENT IN TAMSULOSIN DRUG BY USING HPLC

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ABSTRACT

This study was aimed to development and modification the method of analysis for active ingredient in Tamsulosin drug by using high performance liquid chromatography (HPLC) also determined shelf life and storage conditions for Tamsulosin. Chromatographic conditions utilized stationary phase C18 (250*4.6) mobile phase 0.05Nmixture of di hydrogen ortho phosphate and Acetonitrile 55:45 , preserve the flow rate near (1ml/min) and length of wave has been 275nm, The retention time found to be 10 minute for the HPLC process . The Tamsulosin assay result was found to be 99.93% . The calibration curve linearity analysis results showed a strong linear relationship in the concentration range (10-200ppm) and the correlation coefficient, slope and intercept value were 0.9933,11796,190017, respectively The percentage recovery was found 99%. LOD value was found to 0.00053 µg/ml and LOQ value was found to 0.0016 µg/ml , Precision was found to be 99.49% Robustness was found to 99.69%. Our proposed procedure confirmed a group of merits such as Linear ,accurate ,precise ,and robust , could be recommended for determination of Tamsulosin.

Key words: validation methods, stability-indicating, method development, acetonitrile.

مجلة العلوم الزراعية العراقية -2022 :53(3):561-569 الشمري والعكيدي

تقدير المادة الفعالة في عقار التامسولوسين باستعمال تقنية كروموتوكرافيا سائلة عالية الاداء

وفاء طالب حسون الشمري احمد جاسم مخلف العكيدي
باحث أستاذ مساعد
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المستخلص

تهدف هذه الدراسة الى تطوير وتحوير طريقة تحليل المادة الفعالة الموجودة في عقار التامسولوسين باستعمال كروماتوغرافيا سائلة عالية الاداء وايضا تم تحديد تاريخ الصلاحية وظروف التخزين للتامسولوسين.الظروف الكروماتوغرافيا المستخدمة هي الطور الثابت عمود 18 (250*46) والطور المتحرك بتركيز 0.05 نورمالي مزيج داي هيدروجين اورثو فوسفات واسيتو نتريل بنسبة 45:55 ,معدل التدفق حوالي (1مل /دقيقة) والطول الموجي كان 275 نانوميتر, وجد زمن الاحتجاز هو 10 دقائق لعملية الكروماتوغرافيا السائلة عالية الاداء . وتم العثور على نتيجة فحص التامسولوسين 99.93 %.اظهرت نتائج التحليل الخطي لمنحني المعايرة وجود علاقة قوية في نطاق التركيز (10–200) وكانت قيم معامل الارتباط والميل والتقاطع بالتعاقب وتم العثور على نسبة الضبط99 % ووجد اقل تركيز يم اكتشافه واقل تركيز يمكن تقديره كميا وقيمة الاسترداد 99.94 والقوة تصل الى 99.96 %. اكد الاجراء المقترح مجموعة من المزايا منها الخطية والدقيقة والقوة ويمكن التوصية بها لتحديد التامسولوسين.

الكلمات المفتاحية: طرق تحقيقية، مؤشر الاستقرارية، طريقة تطوير،acetonitrile .

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INTRODUCTION

Tamsulosin is known as 5-[(2R)-2-{[2-(2-ethoxyphenoxy)ethyl]amino}propyl]-2-methoxybenzene-1-sulfonamide. The formula is chemical $C_{20}H_{28}N_2O_5S$ and molar mass 408.512 g/mol (18,30) In the prostate, prostatic capsule, prostatic urethra and bladder neck Tamsulosin is a selective antagonist of alpha1-A and alpha1-B adrenoceptors (10). At least three different subtypes of alpha adrenoceptor was identified as alpha-1A alpha-1B and alpha-1D heir distribution varies between tissue and organs of humans (16,17) . It is sold under the trade name Urimax, Veltam and Flomax is a medication used to treat symptomatic benign prostatic hyperplasia (BPH) (19) because, it is stimulate the muscle of bladder so lead to the urine pass out easily (13) also help with the passage of kidney stones, and for urinary retention along with other measures(7). About 70% of the alpha1-receptors is alpha-1A type. Blocking these receptors allows smooth muscles in the neck of the bladder to relax(23,5) . A common problem that affects about one third of men over 50 years of age is benign prostatic hyperplasia (BPH). In the United States, Over 14 million men have BPH symptoms(8). (BPH) is a non-malignant prostate enlargement, a wedge-shaped gland that, when it arises from the bladder, covers the male urethra. this enlargement is a natural consequence of aging, but it can be related to symptoms that may be distressing, but rarely life-threatening. firstly affects the inner parts of prostate. Enlargement of prostate gland causes a gradual squeezing of urethra, sometimes it causes difficulty in micturition and may create other urinary problems(9). drugs contains two main contents active ingredient and inactive ingredient. tamsulosin contain active ingredient is 0.4 mg that responsible for its effect and give curative benefit (29) . it is enables urine to pass easily , help the passage of kidney stones and decrease smooth muscle tension (8) while inactive ingredient it is substance that include in the composition and manufacture but not responsible for its effect and not curative benefit .the role give specific shape and texture such as titanium dioxide, ferric oxide and microcrystalline cellulose(4,11). In Pharmaceutical product stability testing is a complex series of procedures requiring significant costs, time consumption and scientific knowledge in order to build consistency, effectiveness and protection in the formulation of drugs(5) **.**Stability of a pharmaceutical produce may be characterized as the a capacity of a particular Ingredients Formulation stay within its microbiological ,physical, chemical, toxicological, protective and information requirements in a particular System of Container/Closure (24,27) .That is in other words, within the limits of the extent to which a substance retains defined, during its stocking and usage time, The same one characteristics and properties existed at the moment that it was packaged . The stability test thus tests the influence of ecological factors on the consistency of medicinal substance or a Producer used to predict the shelf life of the Determine proper conditions for storage and suggest labeling Instructions. Furthermore, The data produced during the stability test is an important prerequisite for any medication to be regulatory approved (12,14) One from the very significant parameters of pharmaceutical products is stability studies. The production of small molecule drug products is also important., mostly in the determination of stability properties, considering the value of the physical condition of the substance. Stability checking It is used to estimate shelf life for formulated items, to assess proper storage conditions (1) Stability Prior to chromatography investigations, many analyses quickly decompose for instance, Extraction, When preparation the sample solutions, While storing the prepared vials, Clean-up washing, phase transition (15). Stability is taken care of by the consistency test (26) Various analytical techniques they've been documented in the Survey of Literature for the study of Tamsulosin in drugs such as UV-Spectroscopy (6) Reversed-Phase High Performance Liquid Chromatography (RP-HPLC) (20 (21,25) , spectrophotometry (20) , Thin layer chromatography (TLC) (22) liquid chromatography mass spectrometry(LC –MS) (2) and UPLC method (28) . those methods have some disadvantages, such as the need for more time, an expert person, and a

high cost (3). Therefore, it is of great significance to develop rapid and straightforward methods for tamsulosin determination ,in this approach our job was to establish a suiTable procedure for the determination of tamsulosin .the present work deal with HPLC stability for tamsulosin because it was sensitivity, accuracy and reproducibility both in bulk and in other dosage types.

MATERIALS AND METHODS

Samples of medicines and reagents

Tamsulosin reference standard ,Tamsulosin pellets dosage , Acetonitrile ,Water distillated, Methanol, Potassium di hydrogen phosphate, phosphoric acid. All the other chemicals compounds used were from the pharmacopoeia grade.

Equipment& Instrument

HPLC system with auto sampler model SHIMADZU,PH meter ,balance ,Ultra Sonic Magnetic stirrer ,Single use filter unit 0.45 µm Filter paper factory, Buhner Disposable Syringe Filter.

standard solution preparation

To prepare standard solution by dissolving 50% of tamsulosin correctly measured, Conversion to 100 ml volumetric flask with the addition of 25 ml of diluent and son icated for 15 min and complete the volumetric flask with the diluent solution to the mark . Flasks were composed of diluents and labeled as a normal solution for stock.

Diluent

Acetonitrile and buffer phosphoric acid taken in the 45:55 ratio Based on the solubility of the medication, they were chosen.

Preparation of buffer phosphoric acid

The buffer solution was prepared with a pH of 3.2, prepared 0.01N solution of Potassium di hydrogen ortho phosphate Correctly. 1.36gm of Potassium di hydrogen phosphate was measured in a 1000ml volumetric flask adding water of 900ml and sonicated for 10min , Ultimately complete the volume with water after adjusted the PH to 3.2 with dil. phosphoric acid solution . 0.1 %phosphoric acid buffer: 1ml of ortho phosphoric acid with water was diluted to 1000ml.

Sample stock solution preparation

weighed five Tablets and measured the mean weight of each Tablet , the equal weight of one Tablet was then transfer to volumetric flask of 10 ml, was added diluent of 8ml and using ultra sonicator for 15min, used 0.45µm filter paper to filter this solution.

Mobile phase

A solution of 0.05N di hydrogen ortho phosphate and Acetonitrile (55:45) were prepared and filtered by using Single use filter unit 0.45 µm and degase.

Chromatographic conditions

Table 1. Optimized chromatographic conditions

Parameters	Method
Stationary phase (column)	C18(250*4.6)
Mobile phase	Acetonitrile : KH2PO4(45:55)
Flow rate	1ml/min
Run time	10min
Injection volume	20
Detection	UV
Wavelength	275nm

Validation of HPLC Method

Linearity : The solution was then found in six replicates on the HPLC plate to obtain a tamsulosin concentration of 10,25,50,100,150,200,500ppm per place of tamsulosin meanwhile. The Table (4) shown concentration vs. peak area .

Limit of detection(LOD) and Limit of quantitation (LOQ)

LOD : The limit of detection of an analytical person technique in a sample is the smallest quantity of analyte it is possible to detect this as an exact value, but not necessarily quantitated.

LOQ: The limit of quantitation of an individual analytical method is the smallest In a sample, the quantity of analyte that could be quantitatively measured With enough precision and accuracy. The sensitivity of the analytical methodology was measured by means of the lowest detection limit and the lowest quantitation limit. The LOD and LOQ were calculated using the mathematical equation given in the Table 2.

Table 2. Rules of LOD and LOQ

LOD	LOQ
LOD= 3.3(SD/S)	LOQ=10(SD/S)
Where :	
S= Slop of the curve for calibration	
SD=standard Response deviation	

Precision

Standard deviation or relative standard deviation is a measure of precision. The

sample solution containing 50% was analyzed at for three times.

Accuracy

Accuracy analysis at three stages of normal addition from the advertised formulation confirmed the accuracy of the process.. % recovery has been reported for Tamsulosin. The rang of the procedure justifies a recovery of between 98% and 102%.

Robustness

By measuring the impact of small but intentional variations in the chromatographic conditions, the robustness was examined. The implementation of minor improvements, such as changes in the flow rate. The impact of these modifications on the findings have been investigated.

RESULTS AND DISCATION

Method of Assay : Tamsulosin was the target of an assay. The protocol was followed in preparing the standard and sample solutions. chromatographic conditions used clarify in Table 1. the standard solution was injected in 2 replicates and the sample was injected in 2 replicates into the HPLC port. The assay results are listed in Table 3. and representative chromatograms are shown in Figures 1. and 2.

Table 3. Method of assay for tamsulosin

Parameters	Standard Area	Sample Area
Injection-1	5711047	5706820
Injection-2	5701258	5715740
Average Area	5706152	5711280
Assay (%)	99.93%	
Acceptance criteria	97-103%	

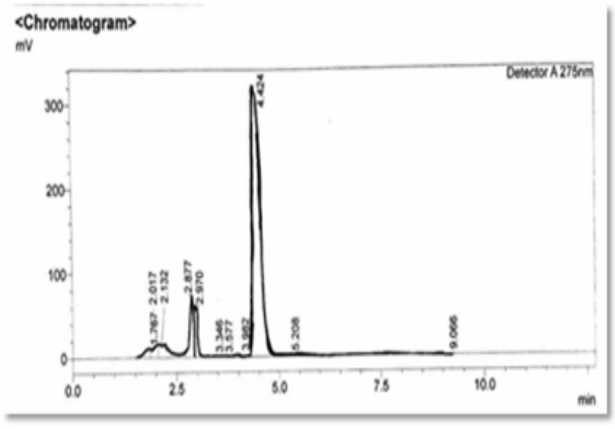
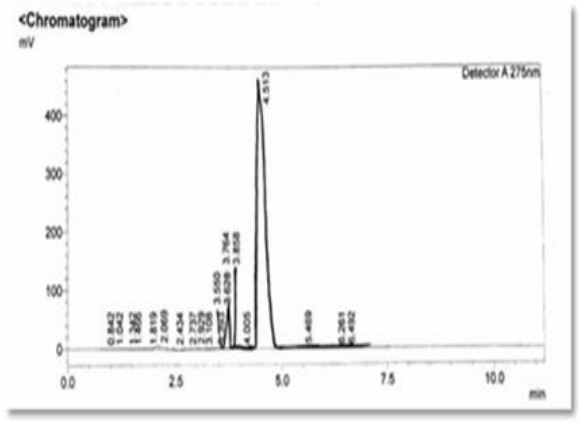


Figure 1. Chromatogram of standard



solution Figure 2. Chromatogram of sample solution

Linearity: The ability of an analytical procedure to yield results that are directly proportional to the concentration of analyte in samples is referred to as linearity .It was determined in different level of concentration 10 ,25 ,50 ,100 ,150 , 200 µg/ml . Figure 3. show calibration curve between concentration and peak area, Table 4. Show result the linearity of Tamsulosin from calibration curve in Figure 3. the results was found to be correlation coefficients (R^2) 0.9933 , slop =11796 and intercept =19007.

Table 4. Linearity of tamsulosin dru

S. No.	Concentration(ppm)	Area
1	10	110435
2	25.	241687
3	50	444203
4	100	857981
5	150	1400881
6	200	1971843
7	500	5852107

Method validation

In accordance with the International Conference on, the established method was validated for checking of assay procedures for its precision, accuracy, linearity, and robustness

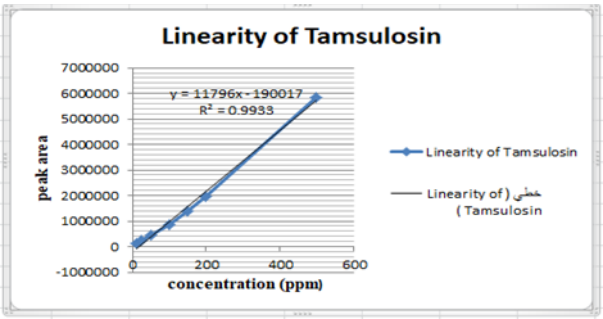


Figure 3. HPLC calibration curve of tamsulosin

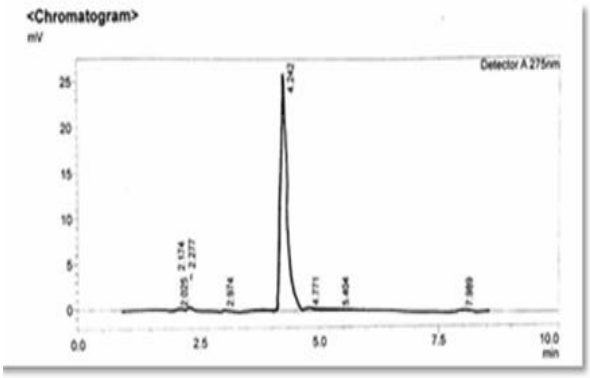


Figure 4. Chromatogram of linearity for tamsulosin (25ppm)

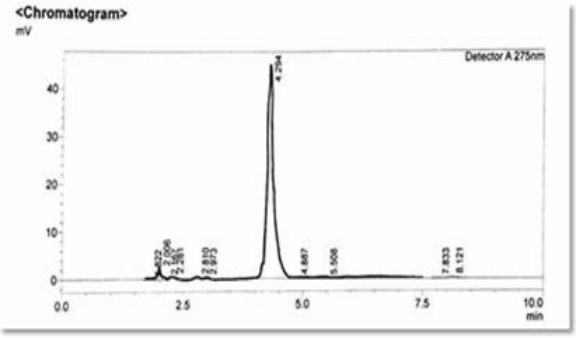


Figure 5. Chromatogram of linearity for tamsulosin (50ppm)

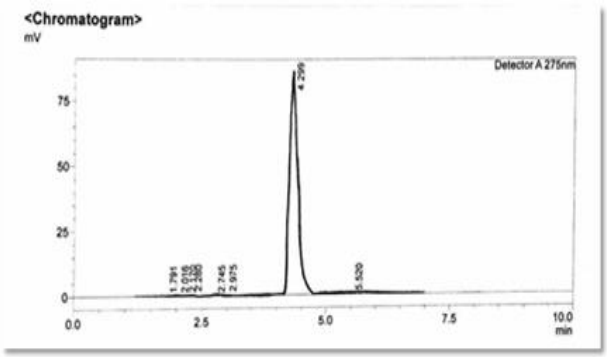


Figure 6. Chromatogram of linearity for tamsulosin (100ppm)

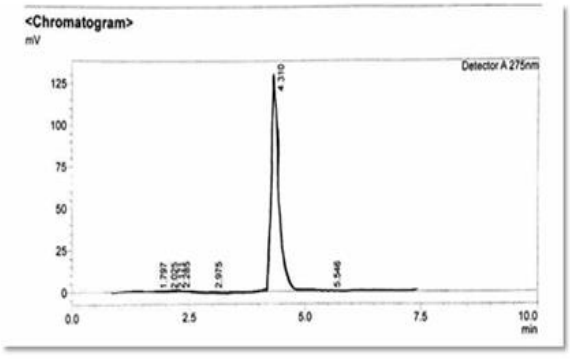


Figure 7. Chromotogram of linearity for tamsulosin (150ppm)

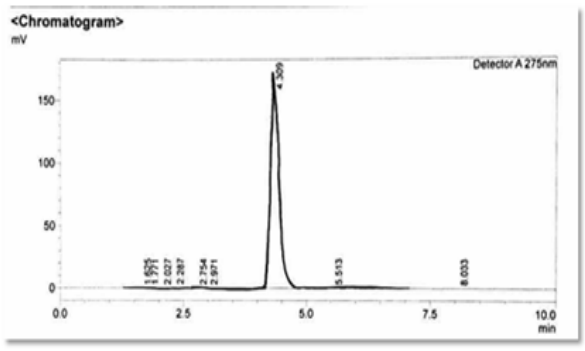


Figure 8. Chromotogram of linearity for tamsulosin (200ppm)

Accuracy : Is a measure of converge the experimental value to true value . the accuracy was determined in three level of concentration 25 , 50 , 75 % . The results of accuracy was found in rang (98-101) % within requirements USP ,that means this is method is accurate .The results of accuracy is presented in Table 5 .

Table 5. Accuracy results for tamsulosin drug.

S.NO	Accuracy Level	Area	Accuracy Area	%Accuracy	Average %Accuracy
1	25%	766437 765320	765878	98	
2	50%	774162 776140	775151	100	99%
3	75%	781982 782900	782441	101	

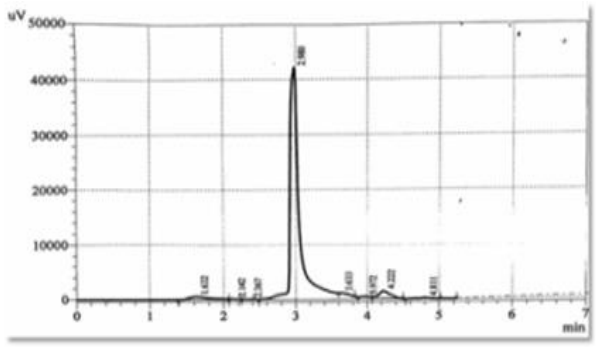


Figure 9 . Chromotogram of accuracy for tamsulosin (25%)

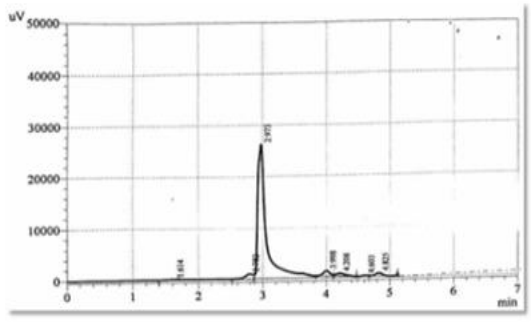


Figure 10 . Chromotogram of accuracy for tamsulosin (50%)

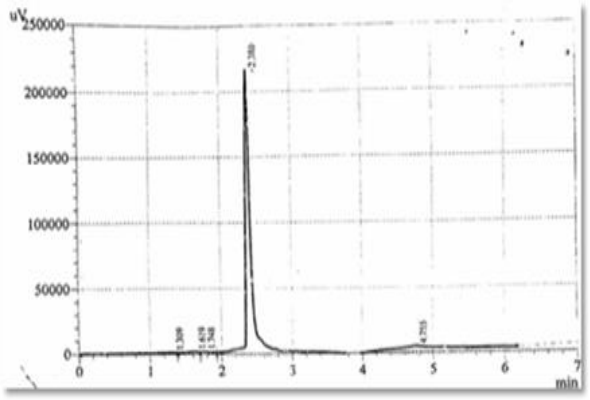


Figure 11 . Chromotogram of accuracy for tamsulosin (75%)

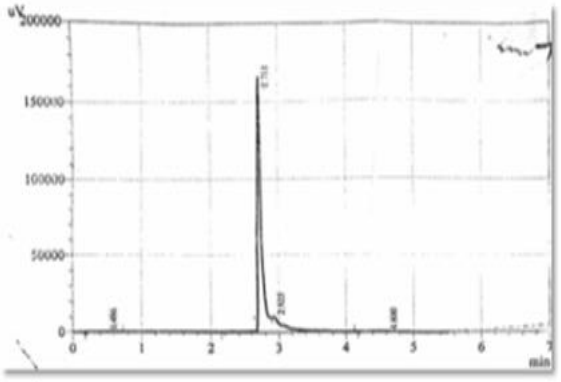


Figure 12. Chromotogram of standard solution for tamsulosin

Precision

Precision is the degree to which data values for a set of measurements under the same analytical conditions are identical to each other. The standard solution containing 0.05 µg/mL was injected three times ,The precision was determined by %RSD (Relative standard deviation) was found to be 1 less than 2 % .The results of system precision is presented in Table 6.

Table 6. Method precision results for tamsulosin

Peak Area	**776250**	**797621**	**789801**
	774520	**796200**	**78592`**
Average area	**775385**	**796910**	**787861**
Results(in %)	**100 %**	**102 %**	**101%**
RSD %		**1**	
Acceptance criteria		**≤ 2**	

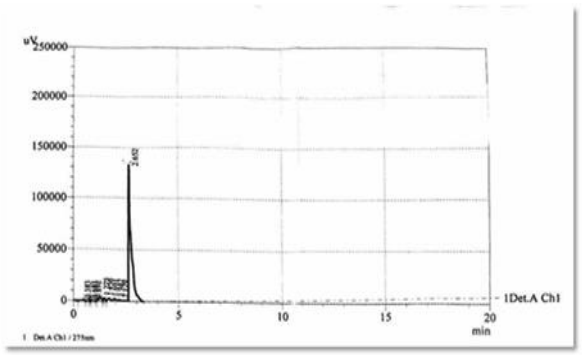


Figure 13. Precision of tamsulosin

LOD and LOQ

LOD denotes the lowest analyte concentration that can be detected, while LOQ denotes the lowest analyte concentration that can be quantified.. LOD and LOQ can be calculated by slope and standard deviation from calibration curve after applying equation in Table (2) the value was found LOD 0.00053 µg/ml and LOQ 0.0016µg/ml usually LOD high concentration LOQ .

Robustness: Robustness is a measure of method ability to remain unaffected by small changes such as change in flow rate from 1min/ml to 1.2 min/ml .No significant different data by change in flow right ,The robustness determined by RSD %was found 1.6 less than 2 % so, this is method was robust The results of robustness of the method for flow rate is presented in Table 7.

Table 7. Result of robustness for tamsulosin

Robustness Parameters	Condition	Retention time	Peak area	Average area
Normal Condition	**Flow rate 1min/ml**	**4.513**	**5706820 5715740**	**5711280**
Flow Rate in mL/min	**Flow rate 1.2 min/ml**	**4.406**	**781982 782100**	**782041**
%RSD		**1**		
Acceptance Criteria		**≤ 2**		

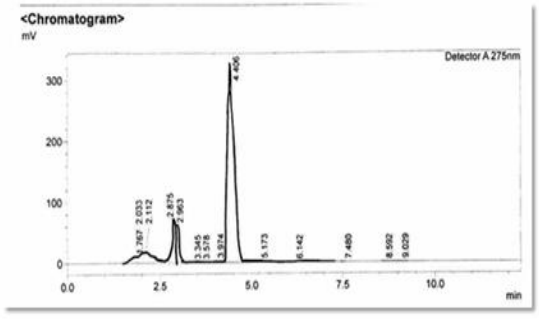


Figure 14. Robustness of tamsulosin

Stability study

Can be defined is a complex set of procedures due to great coast and continue long time may be 3 or 6 months to get quality , effective and safety for drugs . It is very important because determined shelf life after opening for Tamsulosin. In pharmaceutical Industries the research and development dept. work on the develop of the products and after finishing the products they put trail batch samples for each new product in the stability devise for period 3 months to make sure the new formula or new products is stable or not stable .The must do analysis for the same sample weekly ,monthly and check the result .if the sample no change in physical or chemical properties that mean is the sample formula is stable .The stability study result for 3 months continuously give you indication about the formula .by observing the result in Table 8. we find assay is 99% this means that is within limits and no change in description that mean is the formula is good and accepted and can transfer the Tamsulosin to the planning department or production department to product and sale in the market. From the results the shelf life after opening of Tamsulosin is 3 months .

Table 8. Results of stability study for tamsulosin

Test	Limits	Openings									
		1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th
Assay % of Tamsuloin	(97-103)% of the labeled amount of Tamsulosin	99.8	99.2	99.3	99.5	99.4	99.6	99.1	99.3	99.4	99.7
Description	White crystalline powder	comply	comply	comply	comply	comply	comply	comply	comply	comply	comply
Total pathogenic count	No thing	No thing	No thing	No thing	No thing	No thing	No thing	No thing	No thing	No thing	No thing
Total non-pathogenic count	Less than 10 CFU/ML	No thing	No thing	No thing	No thing	No thing	No thing	No thing	No thing	No thing	No thing
Total fungal count	Less than 10 CFU/ML	No thing	No thing	No thing	No thing	No thing	No thing	No thing	No thing	No thing	No thing

CONCLUSION

Finally , it concludes that all results within acceptable limit and this process is modification and development a procedure for determination of active ingredient in Tamsulosin HCl . The features of the proposed system was sensitivity , accurate , precise , robust ,high resolution and short retention time **.** Hence this method could be applied in

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