Spectrophotometric determination of Atorvastatin calcium by Multi wavelength method

التقدير الطيفي لعقار الاتورفاستاتين كالسيوم بطريقة الاطوال الموجية المتعددة

Khalaf F Alsamarrai
أ.م خلف فارس السامرائي
Alfarisalsamarrai2013@gmail.com
Bedour K. Hamad
بدور خضير حمد
Department of Chemistry, College of Education University of Samarra

Abstract
     An accuracy, precious and sensitive spectrophotometric method for determination of ATC in pure and pharmaceutical form was developed . This method based on the using of the linear regression equations of five different wavelengths (244.1, 246.1, 248.1, 250.1, 242.1 nm) to determination of ATC. Beer's law is obeyed in over concentration ranges 15-60 $\mu g.ml^{-1}$, the Rec% was between 96.008-103.292%, and RSD% was 0.924-363% .The proposed method was successfully applied to determination of ATC in pure and pharmaceutical forms.
Key word: Atorvastatin calcium, multi wavelength, spectrophotometric method.

الخلاصة

تم تطوير طريقة طيفية دقيقة ومضبوطة وحساسة لتقدير عقار ATC بشكله النقي وفي المستحضر الصيدلاني وتعتمد هذه الطريقة على استعمال معادلة الخط المستقيم الناتجة من العلاقة بين التركيز والامتصاصية وذلك عند خمسة اطوال موجية هي 242.1, 250.1, 248.1, 244.1,246.1 nm لتقدير عقار ATC الذي اظهر مطاوعة لقانون بير- لا مبرت عند مدى من التراكيز قدره $\mu g.ml^{-1}$ ٦٠-١٥ و تراوحت نسبة الاسترجاعية المئوية Rec% بين 103.292-96.008% بينما تراوح معامل الانحراف المعياري النسبي RSD% بين 0.924-0.363%. طبقت الطريقة بنجاح على تقدير العقار في شكله النقي وفي المستحضرات الصيدلانية

الكلمات المفتاحية: الاتورفاستاتين كالسيوم ، الاطوال الموجية المتعددة ، التقدير الطيفي

Introduction

Atorvastatin calcium is a group of statins classified as lipid-lowering drugs that reduce Cholesterol levels in people with Cardiovascular disease by inhibiting the MHG-CoA enzyme[1] .It is commonly used to treat hypertention[2,3] and prevents atherosclerosis[4].It is called chemically [R-(R*, R*)]-2-(4-fluorophenyl)-β, δ-di hydroxyl - 5-(1-methylethyl)-3-phenyl-4-[(phenyl amino) carbonyl]-1H¬pyrrole- 1-heptanoic acid, calcium salt (2:1) tri hydrate , it is molecular formula has ($C_{33}H_{34}FN_2O_{5،}Ca.H_2O$) either formula that can be expressed in figure 1[5]
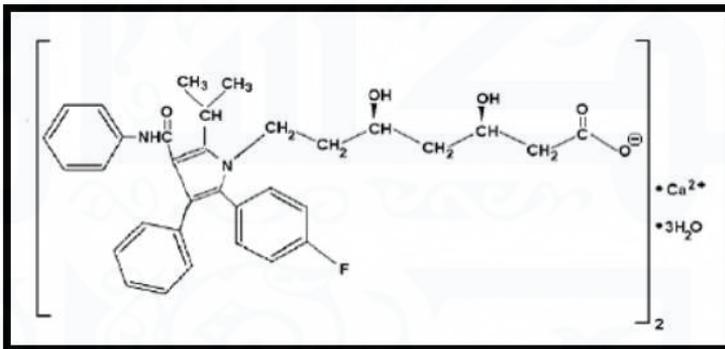

Figure 1 molecular structure of ATC

Multi wavelength method: the method is based on the use of the straight line equation resulting from the relationship between the concentration of the material to be analyzed and the absorbance at wavelengths chosen from the absorption spectrum of this material. the method of multiple wavelengths can be used when the spectrum is wide and results are better than in the case of wavelength ,the material to be analyzed (X) was measured at five wavelengths λ_1, λ_2, λ_3, λ_4, λ_5 , the equation of the straight line is as follows:

$A_{\lambda_1} = aC_X + K_1$ 1
$A_{\lambda_2} = bC_X + K_2$ 2
$A_{\lambda_3} = cC_X + K_3$ 3
$A_{\lambda_4} = dC_X + K_4$ 4

$$A_{\lambda_5} = eC_X + K_5 \text{...................... 5}$$

Here A represent the absorbance of the analyze under test, a, b, c, d, e are the slopes and k_1, k_2, k_3, k_4 and k_5 are the intercepts of linear regression equation for the analyze corresponding to five wavelengths and C_X represents the concentration of analyze. All these equations (1) can be combined as follows

$$A_T = aC_X + bC_X + cC_X + dC_X + eC_X + K_T \text{...................... 6}$$

The simplified form of this equation is

$$A_T = C_X(a + b + c + d + e) + K_T \text{.........................7}$$

Where A_T and K_T correspond to the sum of absorbance and sum of intercepts obtained of equations. So from the above equation concentration of analyze X, in an unknown solution can be found as fallows [6]:

$$C_X = \frac{A_{T\_}K_T}{(a + b + c + d + e)} \text{... ... ... 8}$$

ATC has been estimated in a number of analytical methods, such as chromatographic methods [7] and a number of spectral methods, either for a substance [8, 9] or in mixtures with other drugs [10, 11].

The current research aims to develop a spectral method for estimating ATC in its pure form and in its pharmaceutical formulation by multi wavelength method.

Experimental part

Instrumentals and chemicals

- All spectral and absorbance measurement were carried out in a Double beam UV-Vis spectrophotometer-1800 . Equipped with a 1 cm quarts cell .
- Water bath (Lab. Companion , BS - 11) .
- Electronic balance (Sartorius AG GÖTTINGEN B2 2105 Gerrmany) .

Stock solutions:

All chemicals used were of analytical-reagent grade .
-stock solutions from drug (100 μg.ml-1) of ATC (SDI) were prepared by dissolving (0.01)gm of LATC in methanol and diluting to the mark in 100 ml volumetric flask . Working solutions were prepared by diluting the solution in methanol.

Selection of wavelength

The absorbance spectrum of the ATC as shown in figure 2, which shows that the method of multi wavelength can be used to obtain better results than in the case of one wavelength .thus, the five wavelengths the five are 244.1, 246.1, 248.1, 250.1, 252.1 nm.
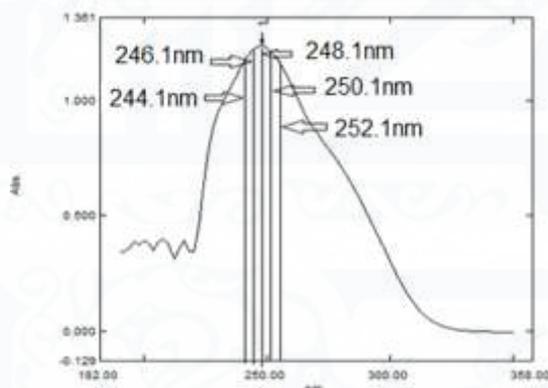

Fig 2 : absorption spectrum of ATC at concentration $30 \mu g.ml^{-1}$

Procedure and Construction of Calibration Curve

The calibration curve was prepared by transferring increasing volumes 1-7ml of the concentration 100µg.ml^{-1} of ATC to a volume 10 ml of volumetric flask, the volume was completed with methanol to the marker to obtain concentration of 10-70µg.ml^{-1} and the absorbance values were measured at 244.1, 246.1, 248.1, 250.1, 252.1nm wavelengths versus the blank solution as in fig 3.

Precision and Accuracy of the Proposed Method

The method precision and accuracy were tested in terms of the relative standard deviation and the percentage recovery respectively for the calibration curve and for the five time for each of which we were in table 2.

Studying of Excipients Effective

The effect of the presence of some excipients, namely acetyl ph. 302, sodium citrate, magnesium stearate, starch, and aerosol, was studied on the absorption value of ATC, with concentration of up to100µg.ml^{-1} on concentration 10µg.ml^{-1} ATC with addition of 1-10ml excipient to 1ml ATC, in 10ml volumetric flask, then complete the volume to the mark with methanol and measure absorbance at wavelength 244.1, 246.1, 248.1, 250.1, 252.1 versus the blank solution.

Analysis of ATC Dosage Form

1- Direct Method

Concentration 17µg.ml^{-1} and 42µg.ml^{-1} were prepared from the pharmaceutical preparation solution of the Indian ATC drug (Atorvastatin calcium) with the concentration 100µg.ml^{-1} in 10ml volumetric to demonstrate the success of the proposed method using the straight line equation of the calibration curve in the estimation of the drug ATC in its pharmaceutical form.

2- Multi Standard Additions Method

In seven volumetric flask 10ml put in each one of 1ml of the solution of the pharmaceutical form (same in direct

method) and then add increasing volume 0-3ml of the standard ATC solution with concentration 100µg.ml^{-1} , then complete the volume to mark with methanol and measured the absorbance at 244.1, 246.1, 248.1, 250.1, 252.1nm and polted the absorbance values for each solution versus the volume taken from the drug solution.

Results and Discussion

The absorbance spectrum were drawn by a spectral scan of the ATC at a concentration 30µg.ml^{-1} of in arrange between 200-400nm and five wavelength 244.1, 246.1, 248.1, 250.1, 252.1 nm were selected. The ATC was quantified in its pure and in its pharmaceutical forms.

Calibration Curve

The calibration curve was constructed at each wavelength 244.1, 246,1 248.1, 250.1, 252.1nm to estimate ATC in final volume 10ml as shown in fig 3(a, b, c, d, e, f) , which shows the compliance of the beer law in a range of concentration 15-60µg.ml^{-1} , table 1 shows the results obtained from the calibration curve at each wavelength of selected wavelengths to estimate   ATC , the molar absorption coefficient 5.008x10^4 L.mol^{-1}.cm^{-1}, the sandell's index 0.0234µg.cm^{-2}, the L.O.D 0.0404 µg.ml^{-1}, and the L.O.Q 0.1358 µg.ml^{-1} . By the combining the straight line equation for each calibration curve, we obtained the general equation for the proposed method.

$$y = 0.2054 \ X + 0.0990 \quad \ldots\ldots\ldots 1$$

From equation 1, the concentration of the material to be analyzed is determined from the equation below:

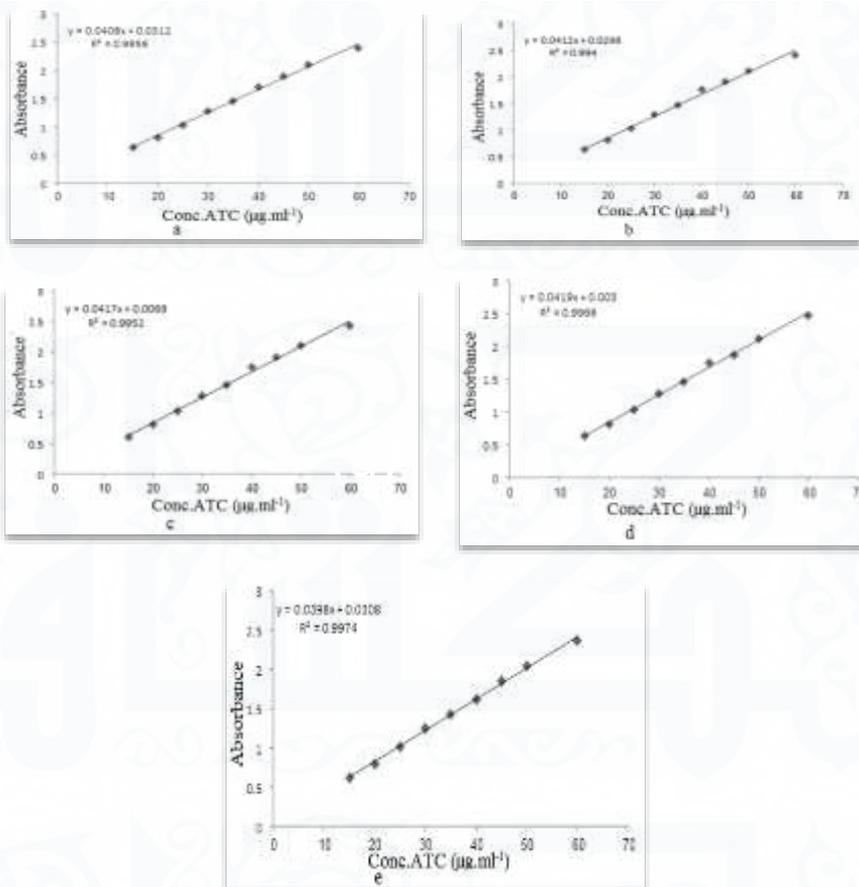$$x = \frac{y_T - 0.0990}{0.2054} \ \ldots\ldots.2$$

Fig 3 The calibration curves to estimate the drug for the ATC at wavelength   a) 244.1nm   b) 246.1nm   c) 248.1nm   d) 250.1nm   e) 252.1nm

Precision and Accuracy of the Proposed Method

The proposed method has high accuracy and precision, with the percentage of recovery Rec% ranged between 96.008-103.292% and the relative standard deviation RSD% was between 0.363-0.924% ,the range of concentration between 15-60µg.ml^{-1} after data collection at the wavelength selected as in table 2.

Studying of Excipients Effective

The effect of the excipient were studied on the determination of ATC. It is noted that all of them do not

affect the uptake of the drug even when it's present in concentration up to ten times the concentration of drug. As the percentage of recovery Rec% ranged between 97.470-101.600%.

Table 1 shows the results obtained from calibration curve at each wavelength

Parameter	At 244.1	At 246.1	At 248.1	At 250.1	At 252.1	Multi[*]
Conc. range $\mu g.mL^{-1}$	15-60	15-60	15-60	15-60	15-60	15-60
Molar absorptivity $L.mol^{-1}.cm^{-1}$	4.934×10^4	4.98×10^4	5.043×10^4	5.674×10^4	4.407×10^4	5.008×10^4
Shandell's index $\mu g.cm^{-2}$	0.024	0.024	0.023	0.021	0.025	٠.٠٢٣٤
LOD $\mu g.mL^{-1}$	0.071	0.028	0.034	0.034	0.035	٠.٠٤٠٤
LOQ $\mu g.mL^{-1}$	0.236	0.094	0.116	0.116	0.117	٠.١٣٥٨
R	0.9977	0.9969	0.9975	0.9982	0.9986	٠.٩٩٧٧٨
					Regression equation	
Intercept	٠.٠٤٠٨	٠.٠٤١٢	٠.٠٤١٧	٠.٠٤١٩	٠.٠٣٩٨	٠.٠٤١٠٨
Slope	0.0312	0.0298	0.0069	0.003	0.0308	٠.٠١٩٨

*multivariate data

Table 2 shows the accuracy and precision of the proposed method for estimation of ATC

Parameter	Multi	
Taken conc. $\mu g.ml^{-1}$	Rec%	%RSD
15	98.393	0.61
20	96.008	0.368
25	98.129	0.563
30	102.094	0.74
35	99.693	0.5
40	103.292	0.397
45	101.133	0.363
50	101.366	٠.718
60	97.309	0.924

Analysis of ATC Dosage Form
1- Direct Method

Concentration 17µg.ml^{-1} and 42µg.ml^{-1} were selected from the concentrated solution of the pharmaceutical form with a concentration 100µg.ml^{-1} of and its absorbance was determined at the selected wavelength to test the success of the proposed method in estimating ATC in its pharmaceutical form.

Table 3 show the application of the proposed method to the pharmaceutical product is ATC

Wave length Nm	Taken conc. µg.ml^{-1}	Found conc. µg.ml^{-1}	Rec%	RSD %
Multi	17	16.260	95.574	1.022
Multi	42	41.431	99.003	0.54

2- Multi Standard Additions Method

The method of multi standard additions was used to estimate the concentration of 10µg.ml^{-1} of the ATC property and the percentage recovery was 100.757%. The relative standard deviation was0.168% and table 4 shows the results obtained.

Table 4 The result of standard addition method of ATC

Concentration µg.ml^{-1}		Rec%	RSD%
Taken	Found		
10	10.0757	100.757	0.168

Conclusion

The multi wavelength method was used to estimate the drug ATC in its pure form and in its pharmaceutical product. The proposed method was simple, sensitive, accurate, and well controlled and could be used in quality control laboratories and in the daily work of estimating the drug.

References

1. Bozhanov S and Maslarska V. spectroscopic and high-performance liquid Chromatography methods for determination of statins. pharmacia. 2016;63,(2):35-48.

2. Sharma Y, Kumar K, Padhy SK. Formulation and evalsartanuation of atorvastatin calcium niosomes. Int J Life Sci Scienti Res. 2016;2(4):462-465.

3. Tariq MH, Khan IU, Ahmad B, Abdul Raheem A, Yasmeen M. Evalsartanuation of in-vitro bioequivalsartanence of commonly prescribed generics of poorly water soluble drug-atorvastatin calcium. Int J Pharm Sci Rev Res. 2013;23(1):290-294.

4. Singh S and Dahiya R. Staiblty –indicating RP-HPLC method for estimation of atorvastatin calcium in solid dosage form. Bulletin Pharm Res. 2014;4(1):9-13.

5. Erturk S, Onal A, Cetin SM. Analytical methods for the quantitative determination of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors in biological samples. J Chromatogr B. 2003;793(2):193-205.

6. Siddiqui FA, Sher N, Hasan N, Shafi N,Shamshad H, Beg MA, Sial AA and Sial AW. spectrophotometric multivariate calibration approach: application inquantitative determination of mebeverine inbulk drug andpharmaciuticalformulation. world app Sci J. 2014;32(7):1418-1422.

7. Kurakula M, Tariq R Sobahi TR, El-Helw AM and Abdelaal MY. Development and validation of a RP-HPLC method for assay of atorvastatin and its application in dissolution studies on thermosensitive hydrogel-based nanocrystals. Trop J Pharm Res. 2014;13(10):1681-1687

8. Shyni B, and Molly M. Spectrophotometric method of estimation of atorvastatin calcium using sulfo-phospho-vanillin Reaction. J Appl Pharm Sci. 2012;2(6):150-154.

9. Manasa G, prakash KV and Vandana P. Validated UV-Visible spectrophotometric method for the estimation of atorvastatin in pure and pharmaceutical dosage form using methyl orange reagent. British Biomed Bull. 2014;2(3):521-527.

10. Patel NN, Patel PR, Tandel FA, Kothari CS, Shah SA. Ratio derivative spectrophotometric method for simultaneuo estimation of olemsartan medoxomile and atorvastatin calcium in their combined tablet dosage form. Int J Pharma Pharm Sci. 2012;4:222-226.

11. Bernard S, Mathew M, Senthilkumar KL, Girija KN. simultaneous estimation of atorvastatin calcium and amlodipine besylate by UV Spectrophotometric method using hydrotropic solubilization. Hygeia J D Med. 2015;5(1):105-112