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Determination of atorvastatin calcium and pioglitazone HCl in pharmaceutical formulations form by using atomic absorption spectrometry

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The simple, accurate, precise and sensitive methods for Atorvastatin calcium and Pioglitazone HCl have been developed using atomic absorption spectrometer. We are new developed method with Disodium Edetate Calcium solution and Sodium chloride solution in the pharmaceutical preparation.These methods are based on reaction of both the drugs with Disodium Edetate Calcium solution and Sodium chloride to give purssion pink colour and violet colour metal complexes respectively. These complexes are readily extracted with chloroform and estimated via determination of copper and cobalt content in the formed complexes after digestion with 1.0 M sulphuric acid by atomic absorption spectrometer. Atorvastatin calcium and Pioglitazone HCl can be determined in the concentration ranges 1.5-15.0 and 2.0-34.0 μgml^{-1} with mean percentage recovery 99.98 ± 1.12 and 100.0 ± 0.24% respectively. In sodium chloride; Atorvastatin calcium and Pioglitazone HCl can be measured in the concentration ranges 4.0-19.5 and 3.5-21.0 μg ml^{-1} with mean percentage recovery 101.01 ± 0.09 and 100.05 ± 0.08 % respectively.

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Keyword: Atomic absorption spectrometry (AAS), Atorvastatin calcium and Pioglitazone HCl, Disodium Edetate Calcium solution and Sodium chloride

1. Introduction

Atorvastatin (ATV), [(ßR, δS)-2-(4-fluorophenyl)-ß, δ-dihydroxy-5-(1-methylethyl)-3-phenyl 4[phenylamine] carbonyl]-1H-pyrrole-1heptanoic acid calcium salt [1-5] is a lipid lowering agent acting through the inhibition of HMG-Co-A reductase. It is used in hypercholesterolemia; several methods for its estimation using HPLC [6-7] and HPTLC [9] are reported. Pioglitazone hydrochloride, Chemically [(±) -5-[[4-[2-(5-ethyl-2-Pyridinyl) ethoxy]phenyl]methyl]-2,4] thiazolidine-dione monohydrochloride, is thaizolidine-dione derivative that highly selective agonist for peroxisome proliferator – activated receptor gamma (PPAR) and is used as an adjunct to diet to improve glycemic control in patient with type 2 diabetes (non-insulin dependent diabetes mellitus). The literature survey reveals the chromatographic methods are reported for simultaneous estimation of pioglitazone and its metabolites in human plasma, human serum, and urine [8-12]. The proposed atomic absorption spectrometric methods are simple, sensitive, less expensive and hence more suitable for application in quality control laboratories for analysis of both the drugs.

2. Experimental

2.1. Material and methods

ATV and PIO pure powder were procured as gifts sample from Sun Pharmaceutical Industries Silvassa Dadra and Nagar Hawali India. The tablet dosage form, PIAT (Label claim ATV 10 mg, PIO 10mg) by Cadila Ltd Ahmedabad were procured from local market. Other chemicals were purchased from SD fine chemical Ltd (Ahmedabad, India) their standard stock solutions containing 0.5 mg ml^{-1} were prepared in methanol. Each was further diluted to five dilutions ranging from10 to 250 μgml-1 with distilled water.

2.2. Disodium Edetate Calcium method

One ml of each dilution was transferred to 50 ml volumetric flasks. Added 25 ml (0.1%) Disodium Edetate Calcium solution and shaken vigorously for 25 minutes. All volumes were made up to mark with distilled water. These were transferred quantitatively to separating funnels and extracted with (3×10 ml) chloroform. Chloroform extracts were evaporated to dryness and digested with 5ml (0.5 M) nitric acid. Aspirated the acid extracts directly in the atomic absorption spectrometer and measured their absorbance at 288.2 nm for Disodium Edetate Calcium. Regression analysis was applied for generating standard curves for both the drugs (Table 1).

Table 1. Quantitative parameters for determination of Atorvastatin Calcium and Pioglitazone HCl with Disodium Edetate Calcium solution.

Bulk drug	Linearity range	slope	Intercept	Coefficient Corr.
Atorvastatin calcium	1.5-15.0	0.014	0.24	0.973
Pioglitazone HCl	2.0-34.0	0.079	0.61	0.987

2.3. Sodium chloride method

One ml of each dilution was transferred to 10 ml volumetric flasks. Added 15 ml (5%) sodium chloride reagent and heated at 60^{o}C for 10 minutes. Added 5 ml (0.5%) triethylamine reagent and made volume up to mark with distilled water. Transferred quantitatively to separating funnels and extracted with (3×10 ml) chloroform. These chloroform extracts were evaporated and digested with 35 ml (0.5 M) sulphuric acid. Aspirated the acid extracts directly in the atomic absorption spectrometer and measured their absorbance at 227.7 nm for sodium chloride. Regression analysis was applied for generating standard curves for both the drugs (Table 2).

Table 2. Quantitative parameters for determination of Atorvastatin Calcium and Pioglitazone HCl with sodium chloride.

Bulk drug	Linearity range	slope	Intercept	Coefficient Corr.
Atorvastatin calcium	4.0-19.5	0.67	0.070	0.994
Pioglitazone HCl	3.5-21.0	0.33	0.081	0.999

2.4. Analysis of pharmaceutical formulations

Twenty tablets of each market sample were weighed and crushed to fine powder separately for ATV and PIO. An amount of powdered tablets equivalent to 10 mg were weighed accurately for each drug, shaken with (3×10 ml) ether filtered and washed. Alcoholic extracts were combined and evaporate to dryness and made volume up to 50 ml with distilled water. Suitable dilutions were made to carry out analysis on AAS as shown in both the methods for pharmaceutical drug (Table 3-4).

Table. 3 Determination of the investigated drugs in tablets by Atorvastatin Calcium and Pioglitazone HCl method (Disodium Edetate Calcium).

Sample	Label Claimed	Amount Found	%age of Label Clamed Found	Percentage Recovery	Coefficient Corr.
Atorvastatin calcium	10	10.08	99.986	99.98	0.41
Pioglitazone HCl	10	10.17	100.105	100.10	0.67

*Mean of six estimations.

Table 4. Determination of the investigated drugs in tablets by Atorvastatin Calcium and Pioglitazone HCl method (sodium chloride).

Sample	Label Claimed	Amount Found	%age of Label Clamed Found	Percentage Recovery	Coefficient Corr.
Atorvastatin calcium	10	10.11	100.11	100.18	0.22
Pioglitazone HCl	10	10.09	100.09	100.13	0.58

*Mean of six estimations.

2.5. Reagents

A 10^{-3} M ATV and PIO solution was prepared by dissolving the accurate weight of the drug into dilute methanolic ammoniumhydroxide or ethanol. Similarly, 10^{-3} M solutions of [Cu (NH3)4] SO_4 were prepared by dissolving the required amounts of $CuSO_4$ into distilled water and adding ammonium hydroxide until a permanent pink

Color was achived [13]. A 0.1 M NaCl solution, adjusted to the required pH. Working solutions of lower concentrations were prepared by dilution from the stock standard solutions.

Standard solution for AAS

A standard solution (1000 g/mL) of Disodium Edetate Calcium solution and sodium chloride was prepared by transferring 14.361 g of anhydrous pure copper sulfate into a 1000 mL measuring flask; 50 mL of concentrated nitric acid was added. The solution was well shaken and made up to the mark with distilled water.

2.6. Atomic absorption

Measurement parameters

Disodium Edetate Calcium solution was measured by AAS in the absorption mode at 288.2 nm using air/acetylene. A slit width of 6.18 A ^{0}was used. Sodium chloride solution was measured by AAS in the absorption mode at 227.7 nm using air/acetylene. A slit width of 4.21 A^0 was used.

Calibration graph for AAS

A calibration graph was Solutions having concentrations of 2.0, 4.0, 6.0, 8.0, 10.0 _g/mL Disodium Edetate Calcium and Sodium chloride were measured. Each measurement was performed at least four times to check the reproducibility.

3. Result and discussion

Atomic Absorption spectrometry provided a new and alternate route for analysis of like Atorvastatin calcium and Pioglitazone HCl. In the present work investigated drugs are found to react with Disodium Edetate Calcium solution and Sodium chloride to form suitable molecular complexes. These complexes are insoluble in aqueous phase, but are readily extractable with chloroform. Therefore they were extracted with dilute Sulphuric acid and measured their atomic absorptions at 288.2 nm and 227.7 nm for Disodium Edetate Calcium solution and Sodium chloride respectively. In Disodium Edetate Calcium solution method; Atorvastatin calcium and Pioglitazone HCl can be determined in the concentration ranges 1.5-15.0 and 2.0-34.0 μg· ml^{-1} with mean percentage recovery 99.98 ± 1.12 and 100.0 ± 0.24% respectively. (Table 1) In sodium chloride; Atorvastatin calcium and Pioglitazone HCl can be measured in the concentration ranges 4.0-19.5 and 3.5-21.0 μg ml^{-1} with mean percentage recovery 101.01 ± 0.09 and 100.05 ± 0.08 % respectively. (Table 2) These methods were also applied for the analysis of pharmaceutical formulations of both the drugs as shown in Table (3&4) along with recovery studies. These methods can be employed for routine analysis of Atorvastatin calcium and Pioglitazone HCl in quality control laboratories.

4. Conclusion

The proposed methods proved to be sensitive, accurate and precise, as well as simple to handle with higher tolerance limits relative to previously published methods. We are new developed method with Disodium Edetate Calcium solution and Sodium chloride solution in the pharmaceutical preparation .This paper reports a new example of associate complex application in drug analysis. AAS has the advantages of being fast and simple compared to other analytical techniques. The AAS method showed wide dynamic range, high sensitivity, low quantification limit and no interference. Atomic Absorption spectrometry provided a new route for analysis of cholesterol related drug like Atorvastatin calcium and Pioglitazone HCl in pharmaceutical formulations.

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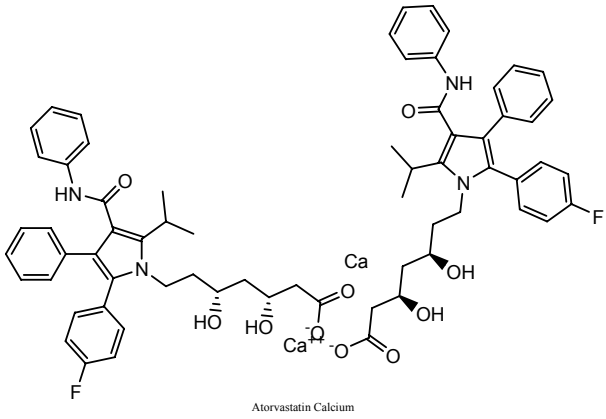

Fig. 1. Atorvastatin calcium molecule.

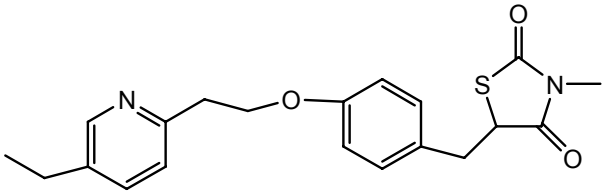

Fig. 2. Pioglitazone molecule.

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