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SIMULTANEOUS SPECTROPHOTOMETRIC ESTIMATION OF OLMESARTAN MEDOXOMIL, AMLODIPINE BESYLATE AND HYDROCHLOROTHIAZIDE IN PHARMACEUTICAL DOSAGE FORM

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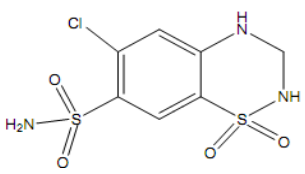
ABSTRACT

Two simple, accurate and rapid methods were developed for the simultaneous estimation of Amlodipine besylate, Olmesartan medoxomil and hydrochlorothiazide in bulk and in combined tablet dosage form.The method A is based on the simultaneous equation method. Olmesartan medoxomil, Amlodipine besylate and Hdrochlorthiazide has absorbance maxima at 266.2 nm, 238.5 nm and 271.2 nm respectively.The method B is based on the absorption correction method is based upon determination of Olmesartan medoxomil, Amlodipine besylate and Hydrochlorthiazide has absorbance maxima at 266.2 nm, 359 nm and 316.4nm respectively

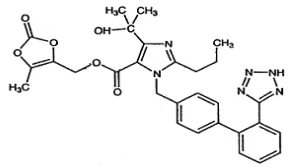
KEY WORDS: Simultaneous equation, Absorption correction method,Methanol.

1.INTRODUCTION

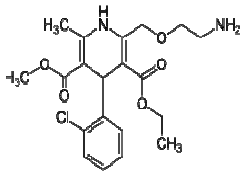
Olmesartan Medoxomil is chemically (5-methyl-2-oxo-2H-1,3-dioxol-4-yl)methyl 4-(2-hydroxypropan-2-yl)-2-propyl-1-({4-[2-(2H-1,2,3,4-tetrazol-5-)phenyl]phenyl}methyl)-1H-imidazole-5-carboxylate.Amlodipine besylate is chemically 3-Ethyl 5-methyl (4RS)-2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate benzene sulphonate. Hydrochlorothiazide is chemically 6-chloro-1,1-dioxo-3, 4-dihydro-2H-enzo[e][1,2,4] thiadiazine sulfonamide. Amlodipine besylate and Hydro chlorothiazide are official in IP (2007). Literature survey revealed that various methods such as UV (Lakshmi,2010; Bebawy,2005; Medhul,2009; Wankhede,2009; Dhabale,2009; Harinath and Prafulla,2009; Kakde,2008; Hemke,2010), HPLC (Demiralay,2010), HPTLC (Chabukswar,2010), LC-MS/MS are available in single and combination with other drugs. However, no spectrophotometric method has yet been reported for simultaneous estimation of Olmesartan Medoxomil, Amlodipine besylate and Hydrochlorothiazide in tablet dosage forms.



Hydrochlorothiazide



Olmesartan Medoxomil



Amlodipine besylate

Fig.1: Structures of the Drugs

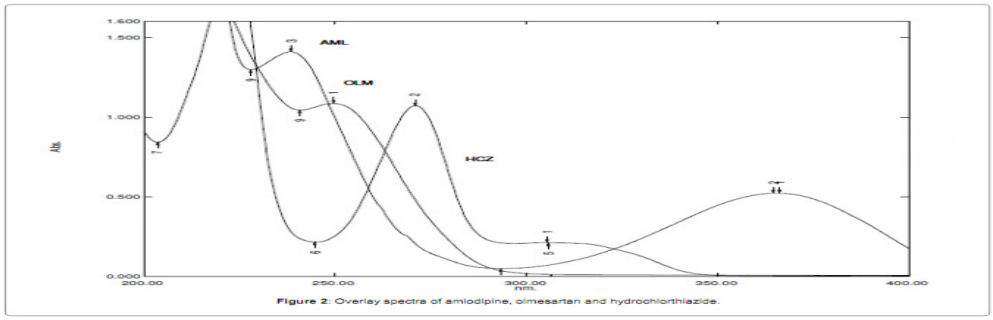


Fig.2: Spectra of Amlodipine, Olmesartan and Hydrochlorothiazide

2.MATERIALS AND METHODS

Instrumentation: An Elico UV/Visible spectrophotometer SL 164 model with a Spectral band width of 10nm and wavelength accuracy of ±5nm with 1 cm matched quartz cells.

Preparation of Standard Drug Solution: The standard stock solution of Olmesartan medoxomil, Amlodipine besylate and Hydrochlorthiazide were prepared by dissolving 25mg of each drug in 25ml of volumetric flask separately using methanol.The standard stock solutions were further diluted to get the concentration of 10 µg/ml of each and the solutions were scanned between the range 200 -400 nm in 1 cm cell against blank and the overlain spectra was recorded

(figure 2). The λmax of Olmesartan medoxomil (OLM), Amlodipine (AMB) and Hydrochlorothiazide (HCT) were 266.2 nm, 238.5 nm and 271.2 nm respectively.From the overlain spectrum of AMB, OLM and HCT in methanol , it was also observed that OLM and HCT have zero absorbance at 359 nm, where as AMB has substantial absorbance.Thus AMB was estimated directly at 359 nm without interference of OLM and HCT. At 316.4 nm, OLM has zero absorbance.For estimation of HCT, the absorbance of AMB was measured at 316.4 using standard solution. The contribution of AMB was deducted from the total absorbance of sample mixture at 316.4 nm. The calculated absorbance was called as corrected absorbance for HCT. At 266.2 nm, these three drugs were showed the absorbance. To estimate the amount of OLM, the absorbance of AMB and HCT were corrected for interference at 266.2 nm by using absorptivity values.

Simultaneous Equation Method: Standard solutions having the concentrations ranges as OLM (4-24 µg/ml), AMB (6-36µg/ml) and HCT (4-24µg/ml) respectively for both were prepared in methanol.The absorbance of resulting solution was measured at 266.2 nm, 238.5 nm and 271.2 nm calibrations were plotted at these wavelengths. The absorptivity co-efficients of these drugs were determined using calibration curve equations are

$A_1 = ax_1\ bcx + ay_1\ bcy + az1bcz$, $A_2 = ax_2\ bcx + ay_2\ bcy + az2bcz$, $A_3 = ax_3\ bcx + ay_2\ bcy + az_3\ bcz$

Method 2: Absorbance correction method: A set of three equations were framed using absorptivity coefficients at selected wavelengths.

$Cx = A_1 / ax_1$, $Cy = A_2 - ax_2cx/ay_2$, $Cz = A_2 - (ax_2cx + ay_3cy)/ax_3$

A_1, A_2, A_3 = Absorbance of sample at 359,316.4,266.2nm respectively.

ax_1, ax_2, ax_3= Absorptivities of Amlodipine at 359,316.4,266.2nm respectively

ay_2, ay_3 = Absorptivities of Hydrochlorthiazide at 316.4,266.2nm respectively

az_3= Absorptivities of Olmesartan at 266.2nm respectively

Analysis of Tablet Formulation: Twenty tablets were weighed and average weight was found. The tablets were triturated to a fine powder. An accurately weighed quantity of powder equivalent to 20 mg of OLM was transferred in to 50 mL volumetric flask and added a minimum quantity of methanol to dissolve the substance and made up to the volume with the same. The solution was sonicated for 15 minutes, centrifuged for another 15 minutes at 100 rpm and filtered through Whatmann filter paper No. 41. From the clear solution, further dilutions were made and the absorbance of sample solutions were measured at all selected wavelengths. The content of AMB, OLM and HCT in sample solutions of tablet was calculated. This procedure was repeated for six times.

VALIDATION OF METHODS

Linearity: For the linearity study, aliquots of the drug solutions were further diluted with methanol to get the final working standards of concentration ranges as OLM (4-24 µg/ml), AMB (4-24µg/ml) and HCT (4-24µg/ml) respectively. Calibration curves (n = 6) were plotted between concentration and absorbance of drugs. Optical parameters were calculated.

Precision: The precision of the method was confirmed by repeatability and intermediate precision. The repeatability was performed by the analysis of formulation was repeated for six times with the same concentration. The amount of each drug present in the tablet formulation was calculated. The % RSD was calculated.

Accuracy: To check the accuracy of the developed method and to study the interference of formulation excipients, analytical recovery experiments were carried out by using standard addition method in three different concentrations. From the total amount of drug found, the percentage recovery was calculated. This procedure was repeated for three times for each concentration. The % RSD was calculated.

3.RESULTS AND DISCUSSION

An attempt has been made to develop a fast, precise, reproducible and economical analytical method for simultaneous estimation of OLM, AMB and HCT in their combined dosage form. The drugs obeys Beer's law in the concentration range of 4-24 µg/ ml, 4-24 µg/ ml and 4-24 µg/ ml for OLM, AMB and HCT respectively for both the methods. Sampling wavelengths based upon the direct UV spectroscopic data. There was no interference from tablet excipients was observed in these methods. The optical parameter values of % RSD and correlation of coefficient for simultaneous determination are reported in Table 1. The result of recovery studies for tablet is reported in Table 2. It indicates that there is no interference due to excipients present in the formulation. It can be easily and conveniently adopted for routine quality control analysis. Statistical analysis proves that, these methods are repeatable and selective for the analysis of OLM, AMB and HCT.

4.CONCLUSION

A method was developed for the determination of tablets which is simple, quick, reliable, inexpensive and simple. The results indicate that the described method can be used for quantitative analysis of the compound.

5.ACKNOWLEDGEMENT

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Table 1: OPTICAL PARAMETERS

Parameter	OLM	AMB	HCT
λ_{max} (nm)	266.2	238.5	271.2
Beer's law limits (µg / ml)	4-24	4-24	4-24
Molar absorptivity (L. mole^{-1} cm^{-1})	5.23 x 10^2	1.04 x 10^3	1.46 x 10^4
Regression equation (Y = a+ bc): Slope (b)	0.001105	0.002418	0.031167
Standard deviation of slope (Sb)	7.37 x 10^{-6}	4.35 x 10^{-5}	3.19 x 10^{-4}
Intercept (a)	0.0187	-0.0047	0.0135
Standard deviation of intercept (Sa)	2.44 x 10^{-3}	7.21 x 10^{-3}	3.17 x 10^{-3}
Standard error of estimation (S_e)	2.33 x 10^{-3}	6.87 x 10^{-3}	3 x 10^{-3}
Correlation coefficient (r)	0.9992	0.9994	0.9996
% Relative standard deviation*	0.4834	0.5011	0.5985

Table 2: ANALYSIS OF PHARMACEUTICAL FORMULATION

Pharmaceutical Formulation	Labelled Amount (mg)	Amount Found By Proposed Method (mg)	Recovery By Proposed Method (%)
Olmat-AMH	20	19.8±0.4	99.85±0.41
	5	5.08±0.2	99.95±0.54
	12.5	12.47±0.4	99.47±0.29

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