REVISTA CIENTÍFICA | FACULTAD DE FARMACIA. UNIVERSIDAD DE GRANADA. ESPAÑA
Ars Pharmaceutica
2013;54(3):7-11
http://farmacia.ugr.es/ars
ISSN: 0004-2927

Originales

Revisiones

Originales Breves

Ars Pharmaceutica

Novel Spectrophotometric Method for Estimation of Olmesartan Medoxomil from its Tablet Dosage Form Using Hydrotropic Solubilization

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Original Paper
Artículo Original

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Competing interest / Conflicto de interes:
Authors declared that there was no conflict of interest associated with this research work.

Fundings / Financiación:
The authors declare that they haven't received funding.

Received: 6/03/2013
Accepted: 24.06.2013

RESUMEN

Objetivo: La estimación cuantitativa de fármacos poco solubles en agua implica el uso de disolventes orgánicos. En la presente investigación, se emplea la solubilización hidrotrópica para mejorar las solubilidades acuosas fármacos poco solubles en agua como el olmesartán medoxomilo dosificado en comprimido.

Material y Métodos: Este método emplea acetato sódico 0,05 M como agente solubilizante hidrotrópico, mostrando el olmesartán medoxomilo una absorbancia máxima a 256 nm. La solución de acetato 0.05 M no muestra ninguna interferencia con la longitud de onda de muestreo. El agente hidrotrópico y los aditivos utilizados en la elaboración de los comprimidos no interfieren en el análisis.

Resultados y conclusiones: El fármaco obedece a la Ley de Beer en el intervalo de concentraciones 2-14 mg / ml con un de coeficiente de correlación de 0,9987. El método desarrollado fue validado estadísticamente siguiendo las directrices ICH Q2B (R1) . El análisis estadístico demostró que el método era sencillo y rápido para la estimación de olmesartán medoxomilo y se puede utilizar para análisis de rutina de olmesartán medoxomilo en laboratorios de control de calidad.

PALABRAS CLAVES: Olmesartán medoxomilo, Hidrotropía, Estimación espectrofotométrica de acetato de sodio.

ABSTRACT

Aim: Quantitative estimation of poorly water-soluble drugs involves use of organic solvents. In the present investigation, hydrotropic solubilization is employed to enhance the aqueous solubilities of poorly water-soluble drugs like Olmesartan Medoxomil in tablet dosage forms.

Material and methods: This method utilizes 0.05 M Sodium acetate solution as hydrotropic solubilizing agent Where Olmesartan Medoxomil shows maximum absorbance at 256 nm. The 0.05 M Sodium acetate solution does not show any interference with the sampling wavelength. The hydrotropic agent and additives used in the manufacture of tablets did not interfere in the analysis.

Results and Conclusion: The drug obeys the Beer's Law in the concentration range 2-14 µg/ml with correlation coefficient value of 0.9987. The developed reliable method was validated statistically following ICH Q2B (R1) guidelines. Statistical analysis proved that the method was simple and rapid for the estimation of Olmesartan Medoxomil and can be used for routine analysis of Olmesartan Medoxomil in quality control laboratories. The *ex vivo* mucoadhesion time of patches ranged between 109 min (FA10) to 126 min (FB14). The *ex vivo* mucoadhesive force was in the range of 0.278 to 0.479 $Kg.m.s^{-2}$. The *in vitro* drug release studies revealed that formulation FA8 released 84% and FB16 released 99.01% of drug in 140 min.

KEY WORDS: Olmesartan Medoxomil, Hydrotropy, Sodium acetate spectrophotometric Estimation.

INTRODUCTION:

Olmesartan Medoxomil is chemically (5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl-4-(1-hydroxy-1methylethyl)-2-propyl-1-[4-[2-(tetrazole-5-yl)phenyl]methylimidazole-5-carboxylate (figure 1) is a potent and selective angiotensin AT1 receptor blocker, which has been approved for the treatment of hypertension in the united states, Japan and European countries. The drug contains a Medoxomil ester moiety and is cleaved rapidly by an endogenous esterase to release the active metabolite Olmesartan[1-4]. Many analytical methods like UV spectroscopy, HPLC were reported for determination of Olmesartan Medoxomil alone and combination with other antihypertensive drugs[5-10]. In the analysis of Olmesartan major problem is solubilization of Olmesartan in most of solvents during analysis[11-12]. Quantitative estimation of poorly water-soluble drugs involves use of organic solvents. Major drawbacks of organic solvents include high cost, volatility and toxicity. In the present investigation, hydrotropic solubilization is employed to enhance the aqueous solubilities of poorly water soluble drugs like Olmesartan Medoxomil in tablet dosage forms. In a proposed method, this problem has been solved by using 0.05 M sodium acetate solution[13-15]. Hence in this communication we have reported new UV spectrophotometric method for determination Olmesartan Medoxomil using hydrotropic solubilization.

MATERIALS AND METHOD:

Instrumentation:

Spectrophotometric analysis was carried out on a JASCO V-630 UV-Visible spectrophotometer using a 1 cm quartz cell. The instrument settings were zero order and band width of 1.0 nm in the range of 200–400 nm.

Reagents and Chemicals:

Pharmaceutical grade Olmesartan Medoxomil was obtained from Macleods Pharmaceuticals Ltd, Mumbai, India. Commercial formulation of brand name Olsertain™-40 (Dr REEDY'S Lab. Ltd, Hyderabad, India) was purchased from local commercial sources. All reagents and chemicals used were of analytical reagent grade obtained from Loba Chemie Pvt. Ltd, Mumbai, India. Water purified by glass distillation apparatus.

Selections of solvent:

In the present study, different hydrotropic agents were investigated to develop a suitable UV spectrophotometric method for the analysis of Olmesartan in bulk and formulation. For selection of diluent, the criteria employed were the solubility of the drug, the easiness of the sample preparation, specificity of the method. Sodium acetate 0.05 M solution was used as the diluent because of the total solubilization of the drug in this diluent. The diluent was not interfering with absorption of analyte in UV region.

Figure 1. Figure 1: Structure of Olmesartan Medoxomil.

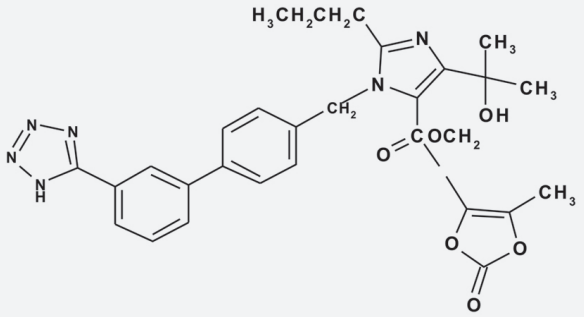
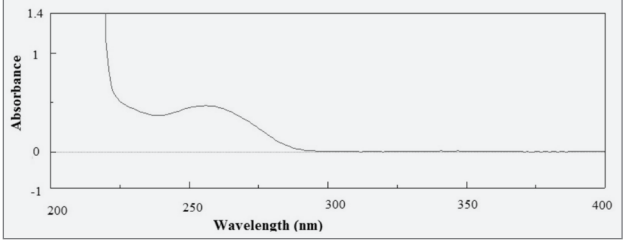


Figure 2. Structure of Olmesartan Medoxomil.



Preparation of standard drug solution:

For hydrotropic solubilization 20 mg of pure Olmesartan Medoxomil was weighed and transferred to 100 ml clean, dry volumetric flask containing 70 ml 0.05 M sodium acetate solution. It was then sonicated to dissolve the drug and made up the volume with 0.05 M sodium acetate solution. The solution was filtered through Whatmann filter paper no. 41. This solution was further diluted with 0.05 M sodium acetate solution to prepare working concentrations of 100 µg/ml of Olmesartan Medoxomil.

Procedure for plotting Calibration curve:

For plotting calibration curve, standard drug solutions containing 100 µg/ml Olmesartan Medoxomil were prepared by using 0.05 M sodium acetate solution. Further diluted this solution with same solvent to get linearity concentration 2-14 µg/ml of Olmesartan Medoxomil. These solutions were scanned in the spectrum mode from 400 nm to 200 nm. The maximum absorbance of Olmesartan medoxomil was found to be at 256 nm shown in Figure 2. Calibration curve for Olmesartan Medoxomil was plotted by recording absorbance at the selected wavelength (256 nm) against the concentration of drug standard. The drug obeyed Beer's law in the concentration range employed for analysis. By using quantitative modes of instrument slope, intercept and correlation coefficient values for calibration curve was obtained.

Procedure for analysis of tablet formulation:

Twenty tablets were weighed and triturated to a fine powder. Tablet powder equivalent to 10 mg Olmesartan Medoxomil was weighed and transferred to 100 ml clean, dry volumetric flask containing 70 ml 0.05 M sodium acetate solution. It was then sonicated to dissolve the drug and made up the volume with 0.05 M sodium acetate solution. The solution was filtered through Whatmann fitter paper no. 41 and the first few ml were rejected. The filtrate was diluted suitably with 0.05 M sodium acetate to get 10 µg/ml of. Olmesartan Medoxomil. The absorbance at 256 nm was measured and the amount of drug present in the sample solution was obtained from the slope and intercept values obtained from the calibration curve (Table 1). From these concentrations, the composition of the tablet was obtained. The results of analysis of tablet formulations are recorded in Table 2. After 48 hours, the solutions were reanalyzed to determine chemical stability and precipitation, if any.

Effect of placebo interference:

To assess the usefulness of the method for estimation of Olmesartan Medoxomil in pharmaceutical dosage forms, the effects of diluents, excipients and additives which often accompany Olmesartan Medoxomil in its dosage forms (talc, starch, HPMC, methyl cellulose, lactose, magnesium stearate and sodium alginate) were studied. The results indicated that there is no placebo interference, indicating a high selectivity for determining the Olmesartan in its dosage forms.

Table 1. Optical Characteristics of Olmesartan Medoxomil.

Parameters	Results
Wavelength (nm)	256 nm.
Beer-Lambart's Law limit (µg/ml).	2-14 µg/ml.
Regression Equation	Abs = mx+c
Slope (m)	0.0464
Intercept (c)	0.0118

Method Validation:

The method was validated according to ICH Q2B R1 guidelines for validation of analytical procedures in order to determine the linearity, sensitivity, precision, robustness and accuracy for the analyte [16-17]. Accuracy and precision of analysis was determined by performing recovery studies by spiking different concentrations of pure drug in the preanalyzed tablet sample. Results of validation parameters are shown in Table 3 and 4.

RESULTS AND DISCUSSION:

There is less solubility of Olmesartan Medoxomil in water hence it becomes necessary to use organic solvents. Major drawbacks of organic solvents include high cost, volatility and toxicity. In the present investigation, hydrotropic solubilization is employed to enhance the aqueous solubilities of poorly water-soluble drugs like Olmesartan Medoxomil in tablet dosage forms. The results of solubility studies indicated that enhancement in aqueous solubility of Olmesartan Medoxomil in 0.05 M sodium acetate solution

Table 2. Results of Analysis of Marketed Tablet Formulation (OlsertainTM-40) and Precision Studies.

Conc. Olmesartan Medoxomil (µg/ml)	Intra-day assay precision(n=9)		Inter-day assay precision(n=9)	
	Percent estimated (Mean± S.D.)	% R.S.D.	Percent estimated (Mean± S.D.)	% R.S.D.
10	99.70±1.4164	1.4206	100.11±1.4048	1.4032

S.D.: Standard Deviation; R.S.D.: Relative Standard Deviation; n.: No of Readings.

Table 3. Results of Recovery Studies.

Analyte	Amount of drug taken (mg)	Drug added (spiked) (mg)	%Recovery (Mean±S.D.) (n=3)	% R.S.D.
Olmesartan Medoxomil	10	8	100.98±0.7002	0.6934
	10	10	100.79±1.7707	1.7568
	10	12	100.96±0.6252	0.6193

S.D.: Standard Deviation; R.S.D.: Relative Standard Deviation; n.: No of Readings.

Table 4. Results of Robustness Studies.

Robustness parameter	Label Claim (mg/tablet)	% Label Claim estimated (Mean± S.D.) (n=6)	% R.S.D.
Analysis using 0.1 M sodium acetate solution	40	100.24±1.6567	1.6526
Analysis using 0.05 M sodium acetate solution	40	99.34±1.3985	1.4076

S.D.: Standard Deviation; R.S.D.: Relative Standard Deviation; n.: No of Readings.

was more than 6-7 folds as compared to their solubilities in distilled water. Therefore, this solution was employed to extract Olmesartan from the fine powder of tablet formulation and thus analysis will become easier one.

An attempt has been made to develop a fast, sensitive, precise, reproducible and economical analytical method for estimation of Olmesartan from dosage form. The wavelength selected was 256nm. The Olmesartan Medoxomil obeys Beer's law in the concentration range of 2-14 µg/ml. The results of estimation of Olmesartan Medoxomil in tablets Olsertain™-40 tablet shown in Table no. 1 Quantitative estimation of poorly water soluble drugs involves use of organic solvents. The result of analysis of tablet formulation showed % relative standard deviation values in the range of 0.619 to 1.652 for Olmesartan, which indicates preciseness of the method. The results indicated excellent recoveries ranging from 98.76 to 101.72% for Olmesartan. Recoveries obtained for the drug do not differ significantly from 100%, which showed that there was no interference from common excipients used in the formulation.

CONCLUSION

It is evident from results of validation studies that methods are accurate, sensitive, selective, precise and robust for spectroscopic estimation of Olmesartan. Moreover the method is economic, simple and rapid, hence can be employed for routine analysis in quality control laboratories for estimation of Olmesartan form marketed formulations. Further optimization of method will make it useful for analysis of Olmesartan Medxomil from biological fluids.

ACKNOWLEDGEMENT:

The authors wish to acknowledge, Macleods Pharmaceuticals Ltd, Mumbai, India, for providing the gift sample of Olmesartan Medoxomil, and also thank the authorities of the Bharati Vidyapeeth College of Pharmacy, Kolhapur, for permission and facilities.

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