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Stability Testing of Olmesartan and Cilnidipine in Bulk and Formulations by RP-HPLC

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ABSTRACT

The stability of drug product or a drug substance is a critical parameter which may affect purity, potency and safety. The stability indicating method is that employed for the analysis of stability samples in pharmaceutical industry. Forced degradation studies show the chemical behavior of the molecule which in turn helps in the development of formulation and package. Forced degradation is a degradation of new drug substance and drug product at conditions more severe than accelerated condition. Thus, this review discuss the current trends in performance of stability indicating method to force degradation by providing strategy for conducting studies on degradation mechanism Stability testing by reversed-phase high-performance liquid chromatographic (RP-HPLC) method has been performed of cilinidipine and olmesartan. All the drugs were separated. The retention time of cilinidipine and olmesartan was founded respectively. Ranges of 50 - 300µg/ml for cilinidipine and 25 – 150 µg/ml for Olmesartan.

Keyword: Olmesartan, Cilnidipine, RP-HPLC.

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INTRODUCTION

Cilnidipine serve as a calcium channel blocker which lower the blood pressure in patients its IUPAC name is 1,4-dihydro-2,6-dimethyl-4-(3-nitro phenyl)-3,5-pyridine carboxylic acid 2-methoxyethyl(2E)-3-phenyl-propenyl. Olmesartan medoxomil is an angiotensin-II antagonist which is used to treat high blood pressure and it's IUPAC name is 2,3-Dihydroxy-2-butenyl4(1-hydroxy-1-methylethyl)-2-propyl-1-[p-(o-1H-tetrazol-5phenyl) benzyl] imidazole carboxylate. According to literature survey it is reviled that UV and HPLC method for stability study of Cilnidipine and stability study of Olmesartan medoxomil are reported alone. The report state that the HPLC method for cilnidipine and Olmesartan is combination with other drugs so as per our knowledge and literature review there is no stability indicating RP-HPLC assay method for Olmesartan and cilnidipine is combine dosage form is reported the validated stability indicating RP-HPLC method for combination of cilnidipine and Olmesartan medoxomil was main aim of these work. Chemicals structures of CIL and OLM are shown in Figure 1and Figure 2, respectively.

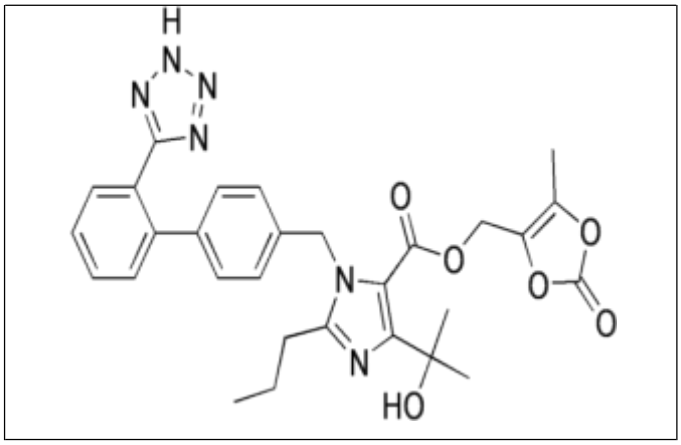

Figure 1: Molecular structure of Olmesartan

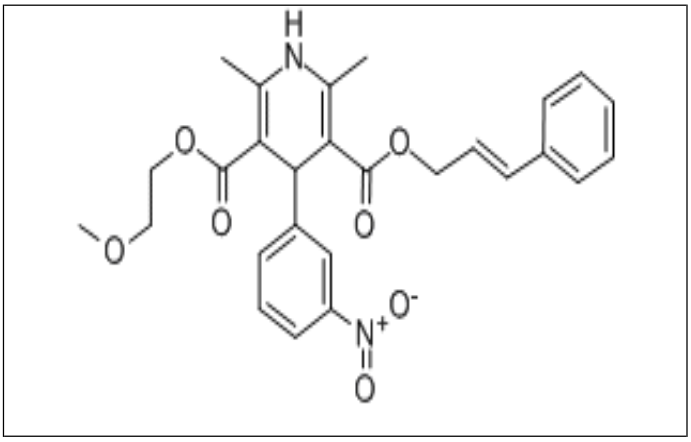

Figure 2: Molecular structure of Cilnidipine.

MATERIALS AND METHOD

Materials

Reagents and chemicals:

Analytically pure samples of Olmesartan and Cilnidipine were procured from RAP Lab. The marketed combined pharmaceutical dosage form of Olmesartan (10 mg) and Cilnidipine (20mg)i.e. CILNY O (INTAS) was purchased from local market. Distilled water, acetonitrile, phosphate buffer, methanol, potassium di-hydrogen phosphate buffer, ortho-phosphoric acid from Qualigens.

Instrument:

HPLC instrument used was of WATERS HPLC 2965 SYSTEM with auto injector and PDA detector. Software used is Empower 2. UV-VIS spectrophotometer PG Instruments T60 with special bandwidth of 2mm and 10mm and matched quartz was be used for measuring absorbance for Olmesartan and cilnidipine solutions.

Methods:

Preparation of buffer (0.1% OPA):

1ml of ortho phosphoric acid was diluted to 1000ml with water

Preparation of mobile phase:

The mobile phase was prepared by mixing of buffer and acetonitrile (42:58v/v) and the Ph adjusted to 4.8 by using ortho-phosphoric acid. The mobile phase was sonicated for 15min and then it was filtered through 0.45µ Whatman filter paper.

Standard preparation:

(100µg/ml cilnidipine & 200µg/ml Olmesartan)accurately weighed and transferred1 0mg & 20mg of cilnidipine and Olmesartan working standards into a 10ml clean dry volumetric flask, add 7ml of diluent, sonicated for 30 minutes and make upto the final volume with diluents. From the above stock solution, 1 ml was pipetted out in to a10ml volumetric flask and then make up to the final volume with diluent.

Sample Preparation Method

Oxidation:

Pipette out 1 ml of stock solution of cilnidipine and Olmesartan into volumetric flask and 1 mlof20% hydrogen peroxide (H2O2) was added. Then, the solutions were kept for 30 min at 60c. For HPLC study, the resultant solution was diluted to obtain 100µ g/ml & 200µ g/ml solution and10µl were injected into the system and the chromatograms were recorded to assess the stability of sample.

Acid Degradation studies:

Pipette 1 ml of stock solution of cilnidipine and Olmesartan into volumetric flask and 1 ml of 2N Hydrochloric acid was added. Then, the solutions kept for 30 mins at 60^0C. The resultant solution was diluted to obtain 100µ g/ml & 200µ g/ml solution and 10 µ l solutions were injected into the system and the chromatograms were recorded to assess the stability of sample.

Alkali degradation studies:

Pipette 1 ml of stock solution of cilnidipine and Olmesartan into volumetric flask and 1 ml of2Nsodium hydroxide was added and refluxed for 30 mins at 60^0C. The resultant solution was diluted to obtain 100µ g/ml & 200µ g/ml solution and 10 µ l were injected into the system and the chromatograms were recorded to assess the stability of sample. Dry heat degradation study The standard drug solution was placed in oven at 105°C for 6 h to study dry heat degradation. For HPLC study, the resultant solution was diluted to 100µ g/ml & 200µ g/ml solution and 10µlwere Injected into the system and the chromatograms were recorded to assess the stability of the sample.

Photo stability Studies:

The photochemical stability of the drug was also studied by exposing the 300g/ml & 10µ g/ml&25µg/mlsolutiontoUVLightbykeepingthebeakerinUVChamberfor7daysor200Watthours/m2 in photo stability chamber. For HPLC study, the resultant solution was diluted to obtain 100µ g/ml &200µ g/ml solutions and 10 µ l were injected into the system and the chromatograms were recorded to assess the stability of sample.

Neutral degradation studies:

Stress testing under neutral conditions was studied by refluxing the drug in water for 6hr. temperature of 60ºc. For HPLC study, the resultant solution was diluted to 100µg/ml & 200µg/ml solution and 10µl were injected into the system and the chromatograms were recorded to assess the stability of the sample

Assay:

Standard preparations are made from the API and sample preparations are from formulation. Both sample and standards are injected six homogeneous samples. Drug in the formulation was estimated by taking the standard as the reference. The average % assay was calculated and found to be 100.14% and 100.01% for Olmesartan and cilnidipine respectively.

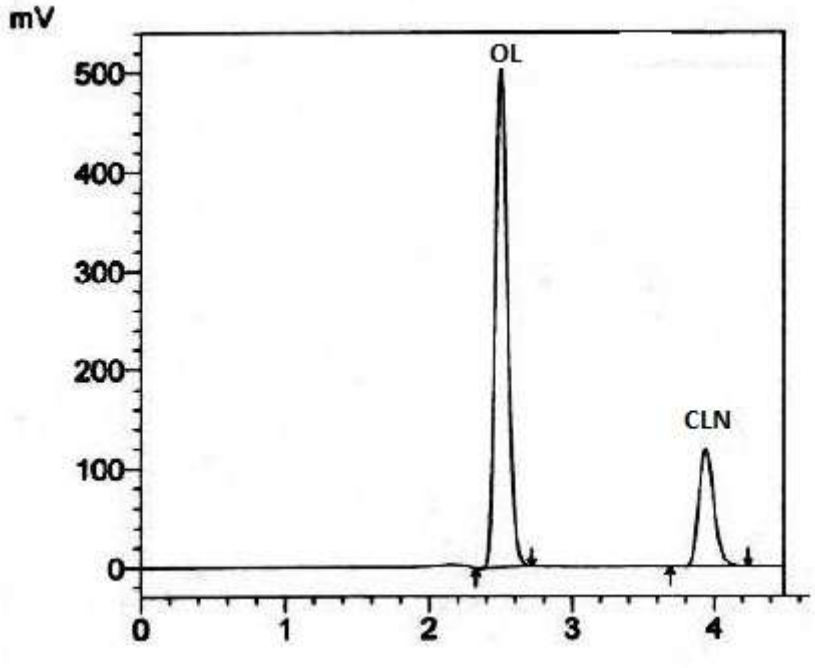

Figure 3: Optimized chromatogram of Olmesartan and Cilnidipine

Property	Olmesartan	Cilnidipine
Retention time (Rt)	2.317± 0.3 min	3.763±0.3min
Theoretical plates (N)	7548 ± 163.48	7382± 163.48
Tailing factor (T)	1.18 ±0.117	1.13± 0.117

RESULTS AND DISCUSSION

Optimized Method:

Drugs were eluted with good retention time, resolution, all the system suitable parameters like plate count and tailing factor were within the limits.

Column used	O DS, 250 x 4.6 mm, 5m.
Buffer used	0 .1% OPA
Mobile phase	Buffer: Acetonitrile(42:58A)
Flow rate	1 m l/min
Diluents	Firstly dissolved in methanol then made up With water and acetonitrile in the ratio of (30:70).
Wavelength	240 nm
Temperature	30o C
Injection volume	10µl

Table.1. Assay of tablet

Dosage form	Active ingredients	Labeled amount (mg/tab)	Mean%±SD	Assay	%RSD
CILNY O	Cilnidipine	10 mg	10.014 ±0.36	100.14	0.36
TAB	Olmesartan	20 mg	20.002 ±0.60	100.01	0.60

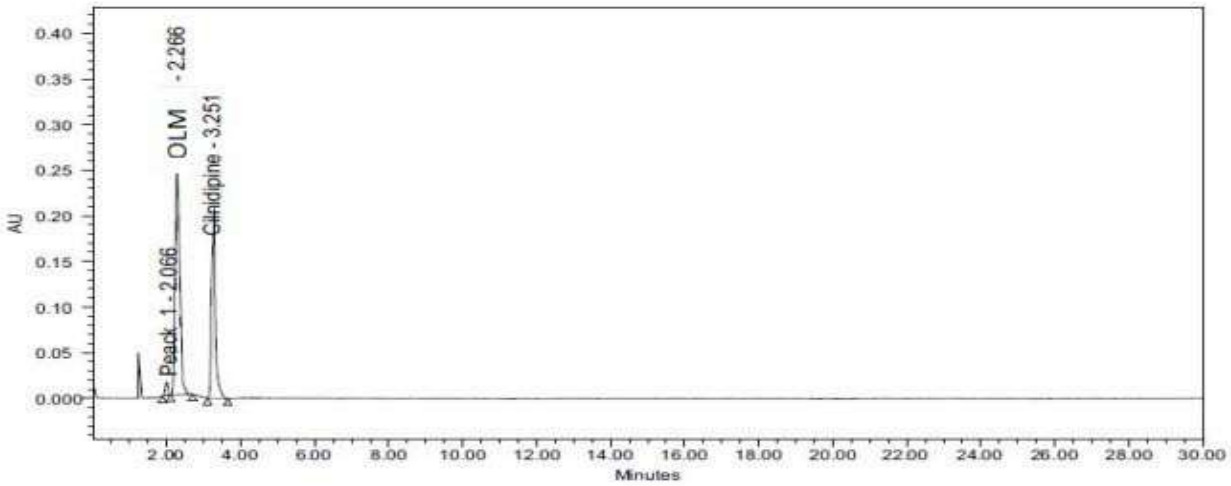

Figure 4-Acid degradation chromatogram

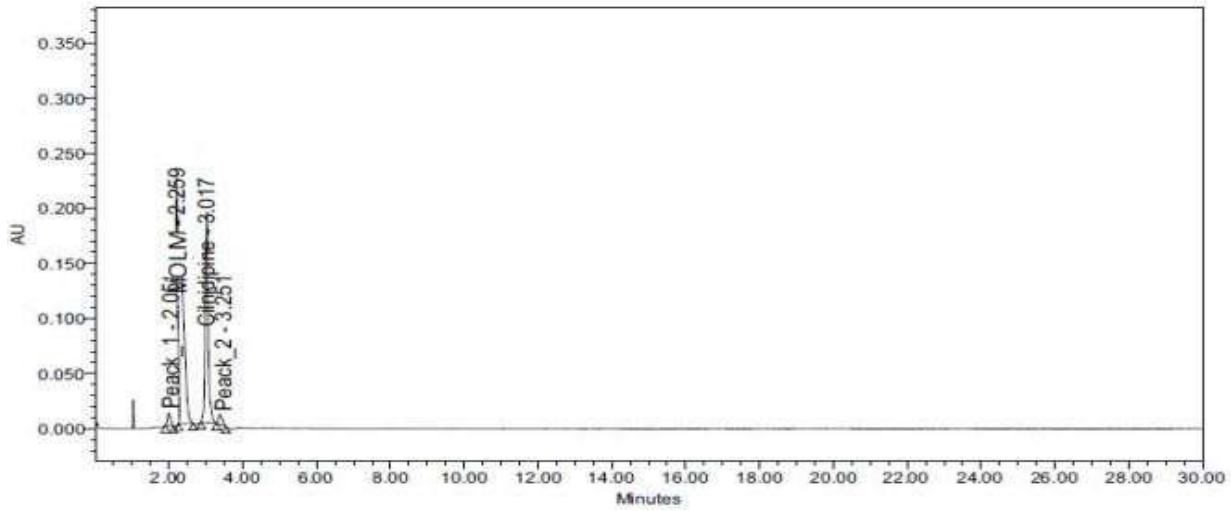

Figure 5-Base degradation chromatogram

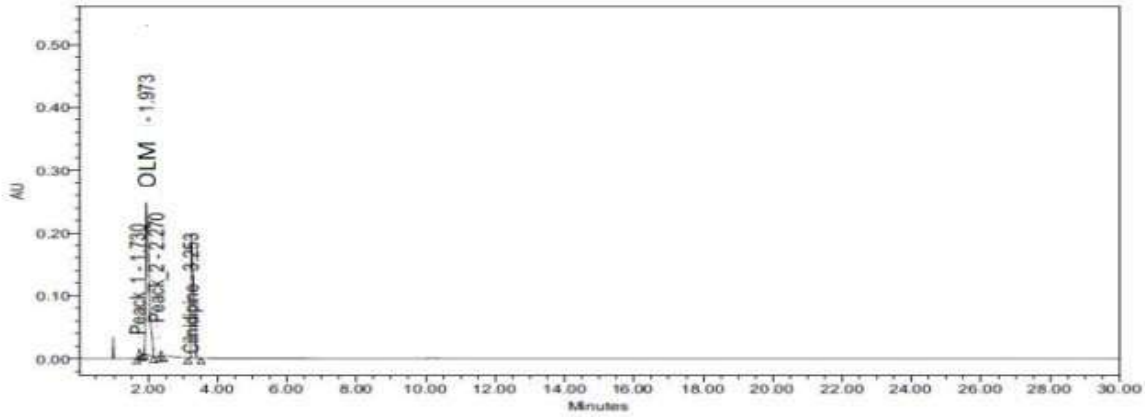

Figure 6-Oxidative degradation chromatogram

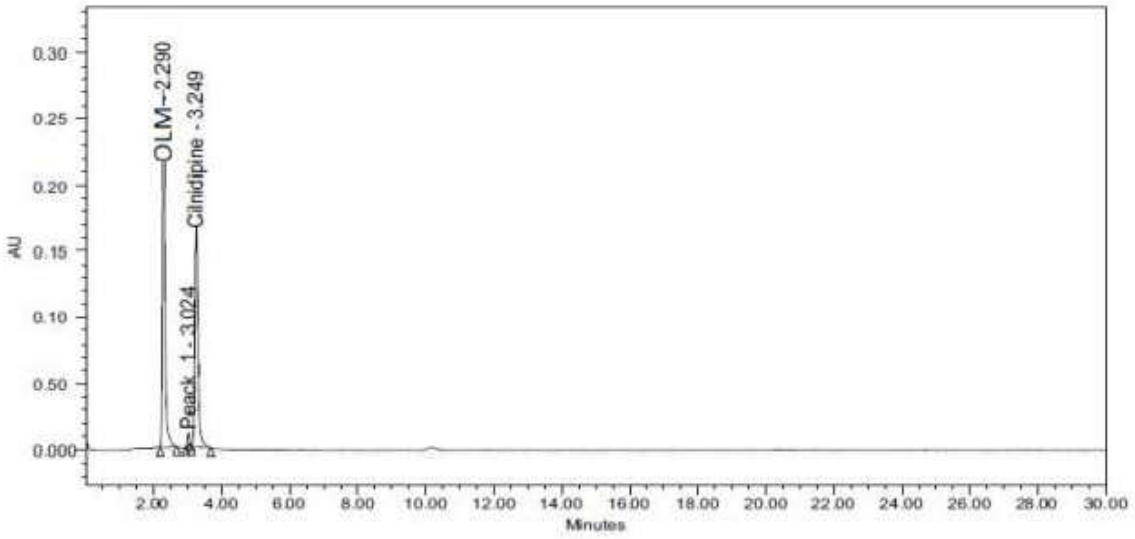

Figure 7-Thermal degradation chromatogram

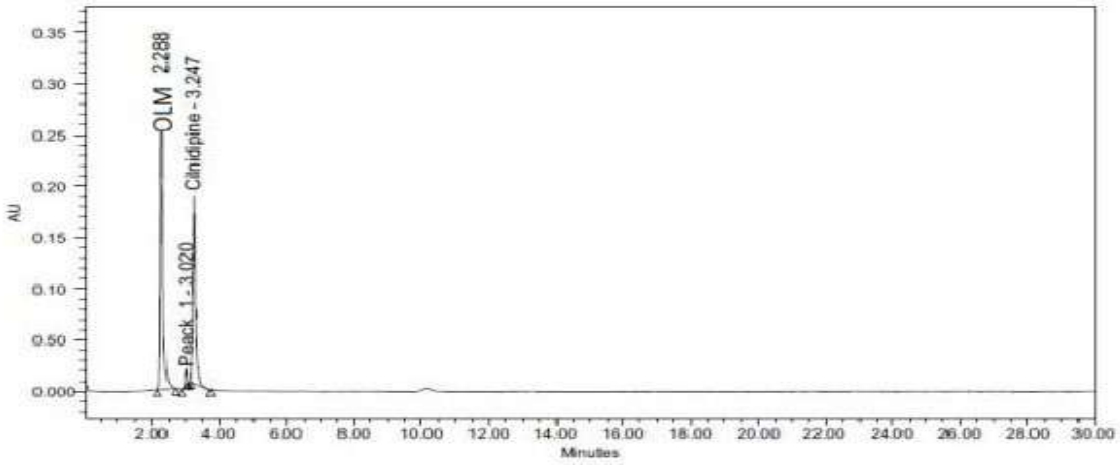

Figure 8-UVdegradationchromatogram

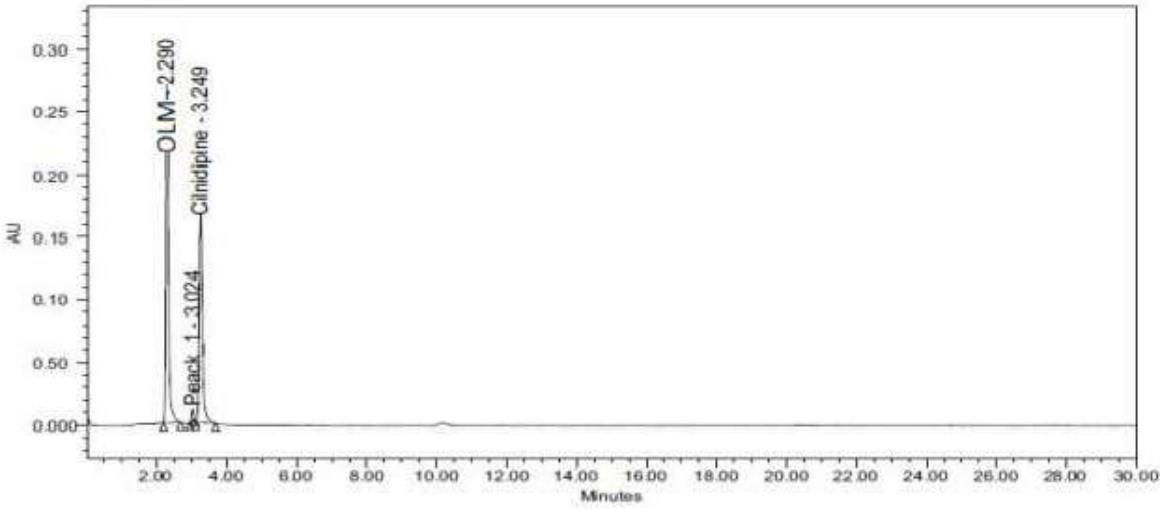

Figure 9- Water degradation chromatogram

Table 2- Degradation Result

Sr. NO	Degradation condition	% Drug degraded	Purity angle	Purity threshold	% Drug degraded	Purity angle	Purity threshold
1	Acid	7.81	0.313	0.411	7.42	0.190	0.406
2	Alkali	6.57	0.413	0.411	6.73	0.311	0.590
3	Oxidation	5.80	3.054	0.304	5.76	0.248	0.428
4	Thermal	4.82	0.494	0.691	4.92	0.282	0.392
5	UV	1.25	0.484	0.597	1.72	0.190	0.402
6	Water	0.85	0.442	0.564	0.84	0.249	0.402

CONCLUSION

In this research, work was accurate and stability indicating RP-HPLC method for resolution f CLN and OLM in the presence of degradation products was developed .Under force degradation study the stability of CLN and OLM using various stress condition were investigated. The stability indicating power of the method of all the degraded products were well determined from the target analytes. For the quality control studies of pharmaceutical dosage form of this combination, the presented information can be used. For routine analysis of CLN and OLM in combine tablet form this method can be used.

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